Effect of Repetitive Loading on Tibiotalar Cartilage and Lower Limb Biomechanics: Application to Long-Distance Unshod Running

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A thesis submitted in fulfilment of the requirements for the degree of

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The University of Auckland, 2019

Abstract

The effect of repetitive loading on ankle (tibiotalar) cartilage and its relationship to running biomechanics in response to long-distance unshod running are poorly understood. This thesis integrates gait analysis, magnetic resonance (MR)-derived T2 maps and finite element (FE) modelling of joint cartilage stress to investigate the effects of 5km unshod running on the tibiotalar cartilage and the lower limb biomechanics. Twenty healthy, young participants underwent a 3.0-Tesla MR scan and unshod running gait assessment before and after 5km unshod running. An 8-camera Vicon motion analysis system and three force platforms were used to collect 3D kinematic and ground reaction force during unshod running. Plantar pressure distribution was also measured by the Novel emed® pressure platform during unshod running. For further statistical tests, participants were stratified by their running experiences (novice and marathon-experienced groups) and gender (male and female groups). After 5km running, significant ankle kinematic alterations were observed in female runners, which were strongly associated with lowering plantarflexion moment. Plantar loading was also shifted from the medial to the lateral forefoot after running, with greater change seen in the novice group and the female group. This suggests that modified ankle kinematics and elevated loading of the lateral forefoot after unshod running may create a foot loading environment that changes the ankle's range of motions, especially in female runners. Novice runners also revealed a significant T2 elevation in the anterior, posterior, and lateral tibiotalar cartilage after running, while other groups showed no significant T2 changes. These results suggest that increases in plantar loading with activity amongst novice runners corresponds to the location of increased T2 signal, whereas ankle kinematics did not appear to directly influence T2 changes. Finally, a 3D anatomically-based FE foot model was adopted to investigate *in vivo* internal stresses in tibiotalar cartilage following 5km unshod running as well as the connection between FE predicted cartilage stress and T2 maps. It was found that FE-predicted tibiotalar cartilage stress patterns correspond to T2 map patterns, reporting large stresses in the anterior, posterior, and lateral tibiotalar cartilage corresponding to high T2 uptake. This suggests that tibiotalar cartilage stress may likely play a mechanical role in fluid build-up and possible inflammation. This notion is further supported by high T2 uptake in those regions. Furthermore, unshod marathon-experienced runners appear to reduce tibiotalar cartilage stress and prevent elevated fluid levels in cartilage (measured by T2 maps) whereas novice runners are less experienced and appear to maintain similar stress levels after running which lead to elevated T2 levels. This suggests that it may be the repetitive loading in novice runners at consistently high cartilage stress levels that leads to increased T2. In contrast, marathon-experienced runners reduce their cartilage loading so this effect is not observed or possibly delayed. In conclusion, tibiotalar cartilage stress and plantar loading may likely play a mechanical role in hydration build-up and possible inflammation, supported by high T2 uptake. Ankle kinematics on the other hand did not appear to directly affect the T2 levels. Information derived from the FE model and plantar pressure may provide in-depth knowledge regarding ankle responses which can be used in practical and clinical applications.

Preface

This PhD project, which is a collaborative research between medical sciences and bioengineering, began January 2016 and provides the significance of magnetic resonance findings in ankle cartilage and its relationship to running biomechanics in response to long-distance unshod running.

This thesis is submitted as a thesis with publications, and includes a total of three original research articles (under revision) and two review articles (published). Minor aspects such as references styles and methodology of these publications have been modified to avoid repetition and to ensure a cohesive structures.

- **Kim, H. K.,** Mirjalili, S. A., & Fernandez, J. (2018). Gait kinetics, kinematics, spatiotemporal and foot plantar pressure alteration in response to long-distance running: Systematic review. Human Movement Science, 57, 342-356.
- **Kim, H. K.,** Fernandez, J., & Mirjalili, S. A. (2017). Evaluation of MR Images of the Ankle and Foot in Response to Long-Distance Running: A Systematic Review. Advanced Techniques in Biology & Medicine, 05 (02).10.4172/2379-1764.1000222.

In addition, I have presented the findings of my research at six international conferences.

- **Kim, H. K.,** Fernandez, J., Doyle, A., Mirjalili, S. A. (November 2018). Effect of Running Barefoot on T2 Relaxation Time in Tibiotalar Cartilage and Ankle Biomechanics. *Oral presentation at the Radiological Society of North America.*

- **Kim, H. K.,** Fernandez, J., Doyle, A., Mirjalili, S. A. (October 2018). Effect of Excessive Loading on Ankle Cartilage and Plantar Pressure: Application to Barefoot Running. *Oral presentation at the 7th Asian Society of Sport Biomechanics.*
- **Kim, H. K.,** Fernandez, J., Doyle, A., Mirjalili, S. A. (September 2018). Effect of long-distance unshod running on the ankle cartilage and its relationship to the lower limb biomechanics. *Poster at the U21 Health Sciences Group Doctoral Student Forum.*
- **Kim, H. K.,** Mirjalili, S. A., Fernandez, J. (July 2018). Effect of Running Barefoot on T2 Relaxation Time in Tibiotalar Cartilage and its Relationship to Running Biomechanics. *Oral presentation at the 8th World Congress of Biomechanics.*
- **Kim, H. K.,** Mirjalili, S. A., Fernandez, J. (December 2017). Barefoot running modifies lower limbs kinetics and kinematics. *Oral presentation at the Australian and New Zealand Association of Clinical Anatomists.*
- **Kim, H. K.,** Pontre, B., Mirjalili, S. A., Fernandez, J. (July 2017). Barefoot Running Modified Foot Pressure and T2* Relaxation Time: Evaluation of a Dancers Foot using Pressure Maps and T2 MRI. *Poster at the XXVI Congress of the International Society of Biomechanics*.

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Many people have also contributed to this thesis and none of these works would have been completed without you all. Anthony Doyle, Greg Tarr, Christabel Logan, Yanxin Zhang, Beau Pontre and Seb Barfoot thanks for your dedication and making this work possible. I must also thank all the staff at the Centre for Advanced MRI and the gait lab for all of your encouragement, support and assistance in completing these studies.

To my family and Jay, thank you for your love, patience and support during my many years of university, but more importantly thanks for believing in me and standing by me at all times. It would not be possible to have made it here without you.

The last three years of my PhD has been a great journey.

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List of Abbreviations

3D	3-dimensional
AH	Abductor hallucis muscle
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
AZ	Anterior zone
BME	Bone marrow edema
BMI	Body mass index
CT	Computed tomography
CZ	Central zone
EDL	Extensor digitorum longus muscle
EHL	Extensor hallucis longus muscle
EMG	Electromyography
F	Female
FA	Flip angle
FDL	Flexor digitorum longus muscle
FE	Finite element
FHL	Flexor hallucis longus muscle
FLASH	Fast low angle shot
FOV	Field of view
GRE	Gradient echo
GRF	Ground reaction force

h	hour
HR	Heart rate
ICC	Intra-class correlation coefficient
IFC	Initial foot contact
KINM	Kinematics
KIN	Kinetics
LED	Light-emitting diode
LH	Lateral heel
LM	Lateral midfoot
LS	Lateral section
M	Male
M1, M2, M3, M4, M5	First – fifth metatarsals
ME	Marathon-experienced runners
MeS	Medial section
min	minutes
MH	Medial heel
MiS	Middle section
MM	Medial midfoot
MRI	Magnetic resonance imaging
MR	Magnetic resonance
ms	milliseconds
NMV	Net magnetization vector
N s	Newton-second
n.s	Non specified
p	rho

PA	Plantar aponeurosis
PB	Peroneus brevis
PD	Proton density
PL	Peroneus longus muscle
PP	Plantar pressure
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
PZ	Posterior zone
QI	Quality index
RANK, LANK	Right and left lateral malleoli of the ankle
RANM, LANM	Right and left medial malleoli of the ankle
RASI, LASI	Right and left anterior superior iliac spines
RELB, LELB	Right and left elbows (the lateral epicondyles of the humeri)
RHEE, LHEE	Right and left heels (the posterior aspect of the calcanei)
RKNE, LKNE	Right and left lateral femoral epicondyles of the knee
RKNM, LKNM	Right and left medial femoral epicondyles of the knee
ROI	Region of interest
RPE	Rated perceived exertion
RSHO, LSHO	Right and left shoulders (the tip of the acromia)
RS1, RS2, RS3, LS1, LS2, LS3	Right and left triads consisting of three markers on the lateral side of shanks
RT1, RT2, RT3, LT1, LT2, LT3	Right and left triads consisting of three markers on the lateral side of thighs

RTOE, LTOE	Right and left second metatarsal heads
RTRI, LTRI	Right and left triceps (the muscle belly of the triceps brachii)
RWRI, LWRI	Right and left wrists (midpoint of the styloid process of radii and ulnae)
SACR	The superior aspect of the sacrum
SPACCE	Sampling perfection with application optimized contrasts using different flip angle evolution
ST	Slice thickness
STIR	Short Tau inversion recovery
T	Tesla
T1	First toe (hallux)
T2-T5	Second - fifth toes
TA	Time of acquisition
TAE	Turbo spin echo
TE	Echo time
TiA	Tibialis anterior muscle
TIRM	Turbo inversion recovery magnitude
TP	Tibialis posterior muscle
TR	Repetition time
TS	Temporal spatial
TSE	Turbo spin-echo
TrS	Triceps surae muscle
yr	Years old

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Extent of contribution by PhD candidate (%)	85

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Justin Fernandez	Conception, data interpretation, critical review of manuscript

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Justin Fernandez	Conception, data interpretation, critical review of manuscript
Yaodong Gu	Data analysis
Liangliang Xiang	Data analysis

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Name	Nature of Contribution
Gregory P. Tarr	Data analysis, critical review of manuscript

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Chapter 8

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Anthony Doyle	Analysis of data

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Anthony Doyle	Interpretation of data, critical review of manuscript

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Justin Fernandez	Conception, analysis and interpretation of data, critical review of manuscript

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Appendix A

Kim, H. K., Fernandez, J., Mirjalili, A. Non-Symptomatic Diagnosed Inflammation on the Cuneiforms on T2* maps and its Relationship to Plantar Pressure: A Case Report.

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Chapter 1. Introduction

The popularity of unshod and/or minimalist shod running has surged in recent years since a number of biomechanical studies reported the possibility of reducing running-related injuries by lowering collision force, impact force, impact rate, and stride length (De Wit, De Clercq, & Aerts, 2000; Lieberman et al., 2010). In a study by Lieberman et al. (2010), unshod running was shown to naturally encourage runners to adopt forefoot or midfoot strike techniques, which was characterized by a softened strike with lower impact rates and shorter and quicker strides, hence lowering the risk factors of running-related injuries. Since then, many laboratory studies have examined the effect of unshod running on the lower limbs biomechanics (Divert et al., 2008; Fleming et al., 2015; Franz, Wierzbinski, & Kram, 2012; Hanson et al., 2011; Squadrone et al., 2015). However, the running time was very short (4 - 7 minutes) which naturally would affect the fatigue state of participants and this is important to be considered. More recently, two studies (Kasmer, Ketchum, & Liu, 2014; Lussiana et al., 2016) performed relatively longer distance running (50 km and 50 minutes, respectively), but there were several limitations such as analysis of kinematics at only in a singular plane (Lussiana et al., 2016), running distances uncommon to the general public (Kasmer et al., 2014), small study sample size (Kasmer et al., 2014), and wearing barefoot-simulated shoes (Kasmer et al., 2014; Lussiana et al., 2016). Although the barefoot-simulated shoes are designed to mimic the unshod running style, the foot strike techniques are still different between unshod and barefoot-simulated shoes (Bonacci et al., 2013). Thus, further research is required to examine the influence of unshod running with a common running distance on running biomechanics **(First main study).**

Moreover, despite its biomechanical advantages, it remains unclear whether those supposed advantages of unshod running have a clinical relevance. It also remains controversial whether the repetitive and high-rate loading imposed on the lower limbs during long-distance unshod running have a deleterious effect on the ankle cartilage. Numerous studies employed magnetic resonance imaging (MRI) to examine pathological and/or morphological changes in the lower limb articular cartilage following long-distance shod running (Hinterwimmer et al., 2014; Hohmann, Wortler, & Imhoff, 2004; Kersting et al., 2005; M. A. Kessler et al., 2008; Luke et al., 2010; Mosher et al., 2005; Mosher, Liu, & Torok, 2010; Schueller-Weidekamm et al., 2006; Stahl et al., 2008; Stehling et al., 2011; Subburaj et al., 2012). Generally, subtle structural changes of the knee and ankle were observed including joint effusion, bone marrow edema, and marginally increased meniscal signal intensity. The knee cartilage thickness and volumes at the tibia, femur, patella, and meniscus were also reduced after long-distance shod running, suggesting that these regions may provide important mechanical contribution during running. Unlike the knee cartilage, very limited information is available on the ankle cartilage in the literature. To the best of our knowledge, only one study quantitatively examined the ankle cartilage using T2* maps in response to long-distance shod running (Schutz et al., 2014)(Schütz et al., 2014)(Schütz et al., 2014)(Schütz et al., 2014). This study reported a significant T2* elevation during an ultra-marathon, but the T2* was recovered as the running distance increased. As very limited information is available on the ankle cartilage, it was difficult to draw conclusions about the effect of long-distance running on the ankle cartilage. Besides, none of the previous studies examined the influence of unshod running on the ankle cartilage.

Therefore, further research is required to provide an MRI analysis on the ankle cartilage after unshod running so that the benefits and/or limitations of unshod running can be fully realized **(Second main study).**

In addition, while the ankle and foot complex is one of the most commonly injured parts of the human body during running (Macintyre et al., 1991; Nicholson, Berlet, & Lee, 2007), the mechanical behaviour and possible aetiology of injury following long-distance running are not well understood. This is possibly because of inherent limitations in many experimental studies such as the difficulties of quantifying internal stress. This investigation can be accomplished using a three-dimensional (3D) anatomically-based finite element (FE) foot model. While MRI can specifically reveal the pathological changes such as edema/inflammation in soft tissues, it may provide limited information about the internal stress of the foot and ankle. More importantly, it remains unclear whether *in vivo* internal stresses in articular cartilage correspond to T2 maps. Thus, a study investigating the internal mechanical properties of the ankle cartilage using a FE foot model is required **(Third main study).**

1.1 Aims and Hypothesis of this Thesis

The main research question of my Ph.D. study was ***"What is the effect of repetitive loading during long-distance unshod running on the ankle cartilage and its relationship to running biomechanics"***. The central hypothesis of the thesis was that long-distance unshod running increases T2 relaxation time in the ankle cartilage, increases plantar pressure under the lateral aspect of the foot and decreases predicted stress in the ankle cartilage. To find answers to the main question, three different but inter-related studies were conducted.

The first study aimed to evaluate kinetics and kinematics of the lower limb joints after 5km unshod running and to determine if the 5km running results in different adaptations depending on the runners' running experience and/or gender. It was hypothesized that long-distance unshod running alters running biomechanics and plantar pressure distribution and that the variation of the gait kinetics and kinematics of the lower limbs and plantar pressure are different depending on the runners' running experience and gender **(Chapter 4)**.

The second study aimed to determine whether long-distance unshod running induces T2 relaxation time within ankle (tibiotalar) cartilage depending on runners' experience level and gender. It was hypothesized that T2 relaxation time is increased in the tibiotalar cartilage after running and the variation of T2 is different depending on runners' running experience and gender **(Chapter 6).**

The purpose of the third study was to evaluate the internal stress of the ankle cartilage in response to 5km unshod running using FE analysis and its relationship to T2 maps. It is hypothesized that 5km unshod running will induce von Mises stress of the ankle cartilage and that this predicted stress will correspond to T2 values **(Chapter 8).**

1.2 Background

Serving as background, *1)* the tolerable level of joints for mechanical loading, *2)* anatomical sites of common running-related injuries, *3)* gait differences between overground and treadmill running, and *4)* gait difference between shod and unshod running were summarized below.

1.2.1 Tolerable Level on Lower Limb Joints for Mechanical Loading

According to the previous *in vitro* laboratory studies (Adams & Swanson, 1985; Repo & Finlay, 1977), the joint forces in the normal physiologic range seemed unlikely to cause degenerative alterations. A cadaveric study (Adams & Swanson, 1985) investigated the effect of physical activities on the pressure of the cadaveric human hip joint during simulated walking. They directly measured surface pressure by inserting piezoelectric pressure transducers through the acetabulum in nine cadaveric hips. Even under the highest force subjected (resultant force during the heel off), the articular surface pressures ranged from 4.93 to 9.57 MN/m^2 (mega newton per square meter), which was not enough to cause fibrillations in joint cartilage. Another study (Repo & Finlay, 1977) also reported that no chondrocyte death or structural damage was observed after controlled impact on articular cartilage until the applied intrinsic cartilage stress level reached 25 MN/m^2. However, the reported maximum hip articular surface contact stresses during daily activities such as walking was ranged from 4 to 9 MN/m^2 (Adams & Swanson, 1985; Brown & Shaw, 1983; Iglic et al., 1993) and approximately 10 MN/m^2 during running. Combined findings of these studies may suggest that physiological stresses during running or jumping seem unlikely to cause injury to healthy joints.

Contrary of these findings, despite the toughness of articular cartilage, the acute and cumulative impact and torsional joint loading during sports activities may be associated with articular rupture or tear, pain and dysfunction (J. Buckwalter, 2002; J. A. Buckwalter & Lane, 1997). While the tolerate level of human joints for chronic or cumulative stresses has not been well documented, several studies informed that articular degeneration or damage may possibly occur at stress levels lower than 25 MN/m^2 (Brown & Shaw, 1983;

Brown et al., 1988; Hadley, Brown, & Weinstein, 1990; Maxian, Brown, & Weinstein, 1995).

Several studies reported that there is a strong relationship between the rate of loading and joint diseases. The viscoelastic properties allow articular cartilage to adapt to slow and rapid mechanical loading (Mow & Rosenwasser, 1988). When a load is applied to the surface of articular cartilage, the fluid movement occurs within the articular cartilage matrix to distribute loads effectively to the subchondral bone. During slow load application, this water movement in the cartilage matrix has sufficient time to redistribute force, thereby allowing deformation and decreasing the force applied to the matrix macromolecular framework. On the other hand, when a loading is applied too rapidly for water movement within the cartilage matrix to adequately re-distribute itself, a greater stress occurs to the macromolecular framework of the matrix. A quantitative analysis study reported that articular cartilage ruptures were more likely to occur during rapid impact loading, with the converse being true of slow loading (Kafka, 2002); with very quick impact load, superficial fissures were observed, whereas slowly applied loading (even with heavy loading) did not cause any lesions. These findings suggest that the rate of loading is an important factor in determining articular surface damage.

Multiple *in vitro* studies indicated that applying certain types of mechanical loads might provoke cartilage breakdown (Dekel & Weissman, 1978; Weightman, Chappell, & Jenkins, 1978; Zimmerman et al., 1988). Dekel and Weissman (1978) investigated the effect of shear stress combined with axial overload on the knee joint of living rabbits. They found degenerative articular alteration in the knee joints under simultaneous shear stress and axial overloading, but the shear stress alone did not show any pathological changes. This may suggest that the added axial overloading is more responsible for degenerative changes in joints. Repetitive loads may also lead to progressive cartilage degeneration. Zimmerman et al. (1988) investigated the effect of mechanical repetitive loading on patellar osteochondral specimens. This study found progressively worse cartilage damage as the load and number of cycles increased. At 250 cycles of compression of 1000 psi (7×10^6 N/m^2) cyclic load, surface abrasion of the cartilage was developed, 500 cycles initiated fissures penetrating to the calcified cartilage, and 1000 cycles provoked secondary fissures extending from the primary fissures. At 8000 cycles, coalescence of fissures and cartilage fragments were detected. When higher loads were applied, similar changes were found after fewer cycles. In another *in vitro* study (Weightman et al., 1978), the effect of applied mechanical loads and cyclic load on samples of human femoral head cartilage was examined. A high frequency cyclically loading resulted in fibrillation of the cartilage surface. Their data suggested that articular cartilage failure might also occur at physiologic stress levels if the loading frequency is high enough.

In summary, these *in vitro* studies identified multiple factors for development of pathogenesis on the joints. The high rate loads, repetitive loads and certain types of loads (i.e. shear stress) seemed to be associated with cartilage degeneration. However, these results from *in vitro* laboratory studies might provide insufficient information to explain the human conditions *in vivo.*

1.2.2 Common Injuries on Running

There are several weight bearing anatomical sites in the lower limb such as the tibia and calcaneus (body weight is shifted from the tibia to the talus to the calcaneus) or the arches of the foot, and hence the likelihood of injuries on these anatomical sites can be increased. Numerous studies have reported on lower limb injuries to runners of all activity levels, from novice to professional, but most studies focussed on non-professional runners. The most common site of running injury by far was the knee (Marti et al., 1988; Taunton et al., 2003). A prospective study surveyed a total of 844 recreational runners who were registered in training clinics administered by The Sports Medicine Council of British Columbia (Taunton et al., 2003). They reported the most commonly injured anatomical site was the knee for both male (36%) and female (32%) and that tibial stress syndrome was the most commonly diagnosed injury. In order of declining frequency, the shin, foot and ankle were also noted as frequently injured. In a retrospective study of 4,173 running injuries seen at the sports medicine clinic over a 4-year period, the knee was found to be the most common site of injury, accounting for 48% of the total injuries (Macintyre et al., 1991). The lower leg and foot were also frequently injured, accounting for 20.4% and 17.2% respectively. In this study, they grouped runners as recreational, marathon (participated in at least one marathon per year), or elite runners (competing at a distance of 800-5000 m) based on their training distance. Recreational runners reported more injuries on the knee than the elite and marathon runners. However, elite runners for both genders had a higher frequency leg and foot injuries and had a much lower rate of injuries to the knee than recreational or marathon runners. This may be because elite runners were more exposed to high-intensity interval training than other groups, or less shock absorption characteristics due to the use of spikes or racing flats shoes with lower heel lifts. Patellofemoral pain syndrome was the most common overall diagnosis, with recreational runners having a higher frequency than the marathon or elite runners (Macintyre et al., 1991). Tibial stress syndrome, Achilles tendinitis, patellar tendinitis, or plantar fasciitis were also commonly reported (Macintyre et al., 1991).

1.2.3 Gait Differences between Treadmill Gait and Overground Gait

Understating of the gait difference between overground and treadmill running is essential when designing a methodology for the gait test. As this thesis includes running unshod on a treadmill, the potential influences of this running surface on the gait need to be properly understood when interpreting the results.

Using a treadmill has numerous advantages such as requiring minimal space, better control of environmental aspects, speed, and slope, and the ability to allow sequential, multiple gait cycles and repeatability. However, the results from previous studies investigating the effect of difference running surface on human locomotion are often conflicting. During treadmill running, the ankle excursion to peak angle and the hip flexion at foot-strike were significantly decreased when compared to those of overground running, with a greater peak ankle eversion also observed during treadmill running (Sinclair et al., 2013). The lower angle between ground and shoe sole at foot impact and more forward leaning of the upper body were also observed (Wank, Frick, & Schmidtbleicher, 1998). In overground running, peak pressure in the total foot area and forefoot peak pressures were greater than treadmill running (Baur et al., 2007). When the fatigue state was taken into account, the plantar pressure under the hallux, medial metatarsals, and the heel were still greater and the contact time was lower in overground than treadmill running (García-Pérez et al., 2013).

In contrast, several studies suggested that running on a treadmill could produce similar features of the kinetic and kinematic parameters to those of overground gait, if sufficient treadmill accommodation period was allowed for runners (Fellin, Manal, & Davis, 2010; Riley et al., 2008; Schache et al., 2001). The hip, knee and rearfoot kinematics were generally similar between treadmills and overground running (Fellin et al., 2010; Riley et al., 2008). However, large individual differences were also observed, indicating treadmill running may not simulate the same overground running pattern for some subjects (Fellin et al., 2010). Another study also indicated that the kinematics of the lumbar spine and pelvis were similar between treadmills and overground running (Schache et al., 2001). They found that the use of high-powered treadmills, which have minimal belt speed fluctuations, minimised the differences between treadmill and overground conditions and thus resulted in more typical patterns of kinematics in the lumbar spine, pelvis and hip.

Several possible explanations can be suggested for the discrepancy of the aforementioned results:

- First, a warm-up period on a treadmill for familiarization allowed participants to adapt to the treadmill running and consequently produce consistent gait mechanics. Matsas et al. (2000) reported that after 6 minutes of treadmill walking for familiarization, the knee kinematics and temporal-spatial gait parameters were similar between treadmill and overground walking. In addition, if subjects already have running experience on a treadmill, the variability of running patterns may be minimal (Schieb, 1986). Another study also indicated that familiarization was achieved when unshod running on a treadmill between 11 and 20 minutes (Moore & Dixon, 2014).
- Second, the large variation of intra-stride belt-speed may produce the conflicting results. Schache et al. (2001), as noted earlier, suggested that using a high-powered treadmills resulted in smaller mechanical differences between overground and treadmill running.
- Third, the use different treadmill brands between studies may also affect the results. A previous study investigated the effect of running with two different treadmills on

the kinetic parameters and they found different power rates for shank acceleration between two treadmills (Lafortune, Hennig, & Milani, 1994). This may be the reason for the conflicting results between earlier studies as they did not adopt the same treadmill.

- Lastly, different methodology for measuring the kinematics (e.g. video cameras vs. motion capture system) may also potentially or partially explain the contradictory results.

In summary, the results from the previous studies investigating the effects of different ground surface properties on gait analysis were often inconsistent. A few studies suggested that a treadmill could be used as a validated instrument for gait analysis, but only if high-powered, with a stiff surface and with minimal fluctuation of belt-speed. On the contrary, when the ground surface properties are changed, runners may adjust their leg stiffness (to increase safety mechanics in treadmill running) and this resulted in subtle changes in lower limb kinematics and kinetics during the gait cycle. The current study is more focused on the effect of repetitive loading on the foot/ankle complex, meaning we may concern ourselves less with mimicking an overground running style on the treadmill environment. That is, those subtle differences of gait between treadmills and overground running would minimally affect the current study. However, in order to minimize possible external factors, it would be ideal to provide a familiarization period, use the same treadmill for all the participants and have participants wear the same shoes during the intervention run and the gait test.

1.2.4 Gait Difference between Shod and Unshod (or minimal shod)

A number of studies have reported the biomechanical differences of gait between shod and unshod (or minimal shod) running. Contrary to the intuitive idea that more cushioned shoes may decrease the rate of running-related injuries, extra support by advanced footwear actually may lead to high injury rate during running; excessive cushioning may result in unnecessary high foot pronation, which is associated with lengthening of the fascia and deltoid ligaments in the medial foot and eventually this may cause injuries such as plantar fasciitis (Lieberman et al., 2010). In this regard, the popularity of minimal shoes (or unshod running styles) has been recently increasing. These shoes have minimal cushioning and are highly flexible. They are also lightweight, position the heel at the same height level with respect to the toes (approx. 4-8mm height), offer no stability function, and prevent foot exposure. Despite the debate about whether these minimal shoes truly mimic unshod running, this review did not go further on this matter as it would be beyond the scope of the current topic.

The greatest difference between shod running and unshod running is the foot strike techniques. In most cases, habitual unshod runners tend to use either the forefoot or midfoot strike (Hatala et al., 2013; Lieberman et al., 2010), whereas shod runners clearly used the rearfoot-strike (Larson et al., 2011). Unshod with heel strike landing results in excessively high vertical impacts much higher than those of shod heel landing (Lieberman et al., 2010), potentially causing excessive soreness. In addition, using a bare rearfoot technique resulted in the greater deformation of the fat-pad (for shock attenuation) under the calcaneus compared with rearfoot-strike in shoes (De Clercq, Aerts, & Kunnen, 1994). Therefore, unshod running naturally encourages forefoot-strike pattern, as the heel landing is not suitable for attenuating the high cumulative impacts during unshod running.

Landing with the forefoot distributes impact forces more efficiently (Lieberman et al., 2010). On hard surfaces, even smaller collision forces were generated from unshod runners than conventional shod runners (Lieberman et al., 2010) and therefore significantly lower ground reaction force (GRF) were produced in unshod runners. This may relate to the body's sensory mechanisms (I. S. Davis, Rice, & Wearing, 2017); the plantar surface provides the sensory input to protect rest of the body from unexpected surfaces, resulting in an avoidance response. This eventually leads to a quick unloading response. Unshod forefoot strikers also tend to decrease a stride length with higher cadence and less contact time than shod rearfoot-strikers do; this results in lower loads experienced by the body to protect from impact-related injuries (Hamill et al., 2011). As shown in Figure 1.1, the typical GRF curve shows the difference between shod rearfoot-strike and unshod forefoot-strike runners. The impact transient of GRF, which is the initial peak during the GRF at approximately 13% of the stance phase, is also smaller in unshod, forefoot-strike runners than in conventional shod rearfoot-strike runners. The loading rate, which is the slope of the GRF line from the first contact to the impact peak, is three time less in unshod running compared with shod running (Lieberman et al., 2010). Leg stiffness was also found to be significantly greater during the stance phase of unshod running (De Wit et al., 2000) or unshod hopping (Bishop et al., 2006) compared to the shod condition.

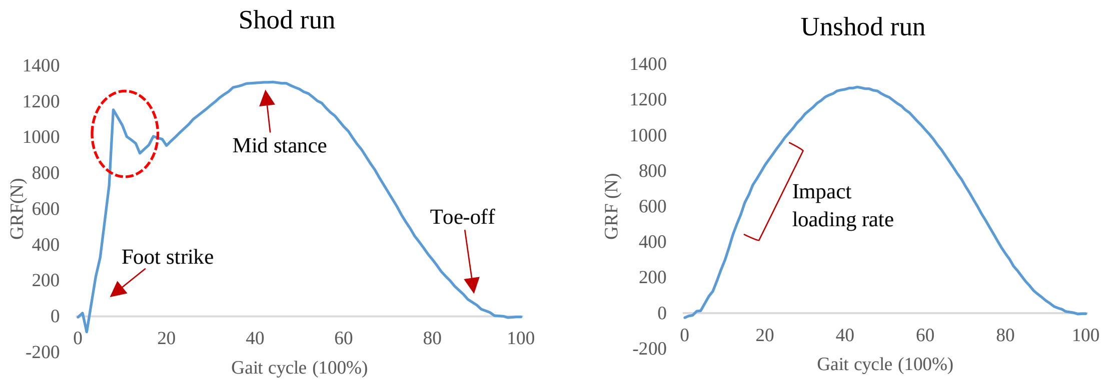

Figure 1.1. The typical pattern of the vertical GRF during shod and unshod running.

The red circle indicates impact loading - it is the force related with the foot striking just before the centre of gravity travelling downward and it results in the initial impact peak. The impact loading rate is the slope of the impact peak, representing how fast the impact force is applied (i.e. a steeper slope indicates a quicker collision). (Data extracted from experiments detailed in Chapter 4: Running Biomechanics Responses after Acute Transition to 5km Unshod Running)

However, it should be also noted that there are potential injury risks with unshod running. Forefoot techniques may cause high loading to the posterior aspect of calf musculature and this results in high risk of Achilles tendinitis and calf strains (Hamill et al., 2011). Increasing load in the metatarsal heads with forefoot-strike has also been reported, resulting in development of metatarsal stress fractures (Giuliani et al., 2011). However, without providing external or internal factors such as training patterns, history of injuries, it is unclear whether the forefoot-strike is the sole reason for developing stress fractures. Additionally, unshod running could the runner to more risk of bruises, wounds or cuts as the whole foot is exposed.

1.3 Thesis Outline

This thesis consists of 9 chapters as follows:

- Chapter 1 – provides a general introduction to the thesis including aims and hypothesis.
- Chapter 2 – provides an overview of laboratory tools and procedures used in this thesis.

Chapter 3 – 8 (except chapter 7) present the manuscripts.

- Chapter 3– systematically evaluates the effect of long-distance running on gait kinetics, kinematics, spatiotemporal and foot plantar pressure.
- Chapter 4 - investigates the acute effects on lower limb biomechanics in response to 5km unshod running.
- Chapter 5 - systematically presents an overview of the literature describing the evaluation of MR of ankle and foot following long-distance running.
- Chapter 6 - evaluates T2 relaxation time of tibiotalar cartilage and ankle biomechanics following 5km unshod running.
- Chapter 7 –systematically determines how previous studies developed their FE models and analysed foot biomechanics in response to excessive loading.
- Chapter 8 - investigates the effect of unshod running on *in vivo* internal stresses in tibiotalar cartilage and the association between FE predicted cartilage stress and MRI derived T2 maps.
- Chapter 9 – provides summary of key findings of this thesis and discusses the implication of these findings, and describes strengths and limitations of this study.

- References – provides reference lists.
- Appendices – presents a case study (reporting the effects of subtle inflammation on the cuneiforms on the plantar pressure distribution during gait), Tegner scale, and consent form.

Chapter 2. General Methodologies

This chapter provides an overview of the general methodologies and procedures used in the studies comprising this thesis. Specific processes and techniques used to collect and analyse data are described in each individual study. This section gives general methods that are simplified to avoid repetition of procedures in the final published form. All procedures were approved by the University of Auckland Human Participants Ethics Committee (ref: 016488).

2.1 Three-Dimensional (3D) Gait Analysis

Gait analysis provides useful information regarding human locomotion and is able to calculate kinetics, kinematics, and spatiotemporal parameters in real time. The motion capture system has often been used in analysing patients' movements during clinical testing (e.g. cerebral palsy, stroke, and Parkinson's disease), for improving sports performance, and for making animations. The Vicon motion capture system (Oxford Metric, Oxford, UK) combined with three force plates (Bertec Corporation, Ohio, USA) were used in this thesis to capture the human motion in real time to create 3D motions during unshod running. As shown in Figure 2.1, 3D motion capture in human movement requires high-resolution cameras that contain a ring of light-emitting diode (LED) strobes which permits detection of infrared radiation reflected off markers. Eight high-resolution cameras were used for this study and were positioned surrounding the capture area (Figure 2.2) to measure kinematics such as joint angle, stride length and stride rate during running. Three force plates were also used simultaneously for measuring ground reaction forces based on Newton's third law of motion. It allows us to calculate 3D torque and 3D power at the lower limb joints during running.

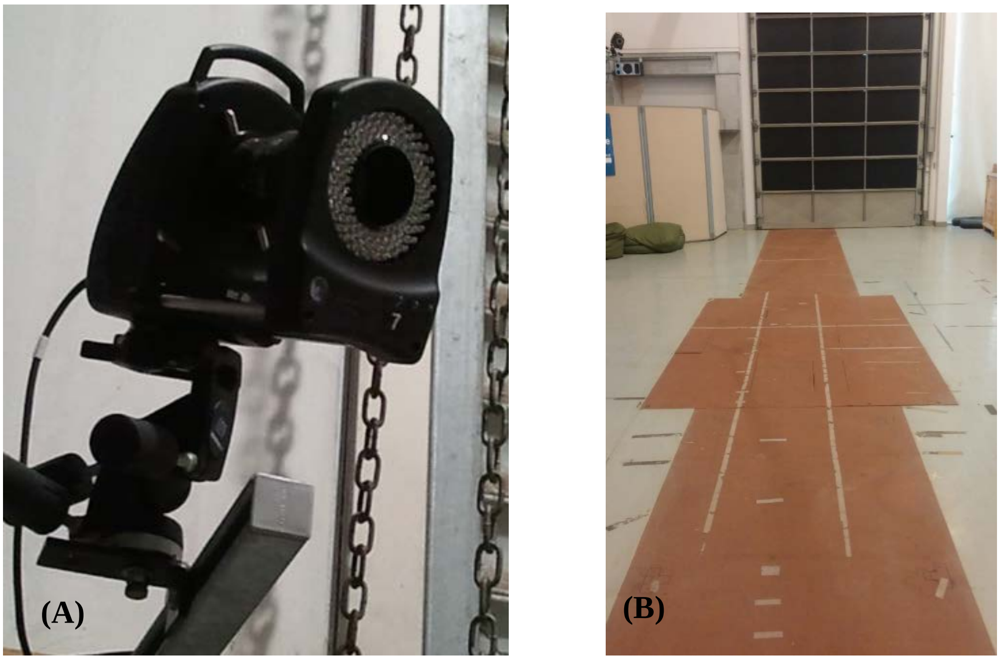

Figure 2. 1. 3D Vicon motion analysis system.

(A) Vicon infrared motion capture camera. (B) Embedded three force plates under the walkway

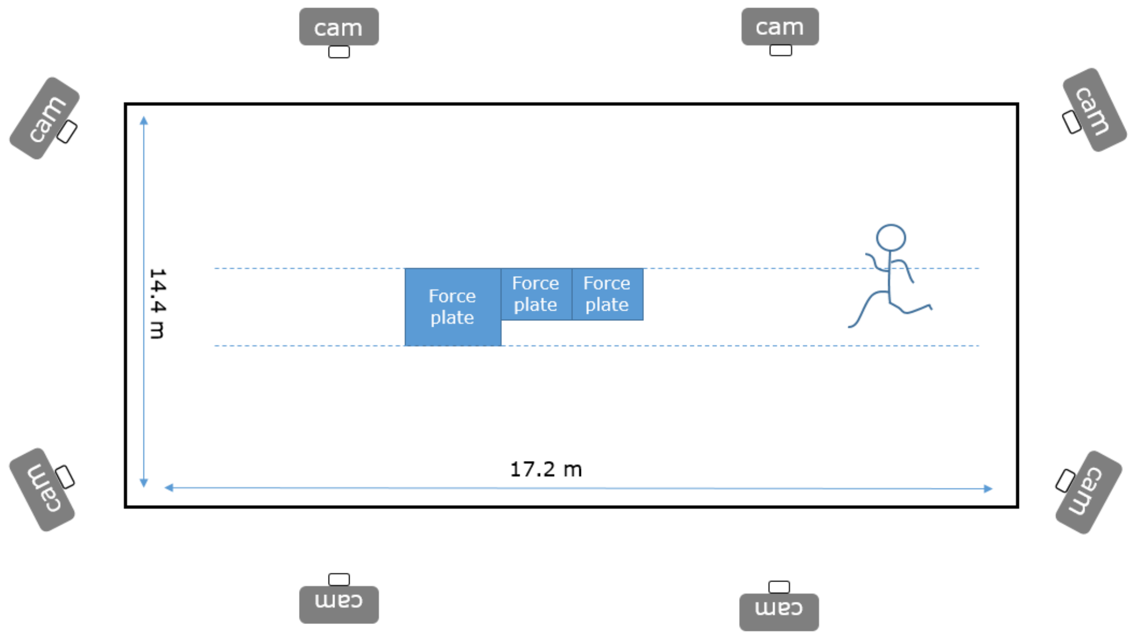

Figure 2. 2. Capture volume.

2.1.1 Calibration of Motion Capture System

Calibration of Vicon cameras and force plates plays a crucial role in improving the reliability and accuracy of our measurements. The calibration was performed in two parts – static calibration and dynamic calibration.

The purpose of the static calibration was to determine the origin of capture volume. A four-marker triangular L-frame (Figure 2.3, A) was used and placed at the edge of the force plate to establish absolute spatial reference points - x, y, z coordinate system. By using the two axes of the L-frame, the third axis (usually z-axis) was determined. Generally, y represents vertical, x is perpendicular to y-axis, and z is perpendicular to both y- and x-axis. A 2D view of the entire area from each camera was automatically recorded using Vicon workstation software (Oxford Metrics, Oxford, UK).

Once static calibration was completed, the L-frame was then removed from the capture area and the dynamic calibration was performed.

The aim of the dynamic calibration was to calculate the relative points and orientation of the cameras as well as to determine its mean residuals (the quality of calibration). An operator used a calibrating wand with three markers (Figure 2.3, B) and waved it throughout the entire capture area for about 1 minute to make sure all positions in the capture area were covered by the wand. Then the cameras' mean residual and the wand visibility were automatically calculated using Vicon workstation. If the residuals or visibility values were not acceptable, the dynamic calibration was conducted again until a mean residual was lower than 1 mm and wand visibility was greater than 60%.

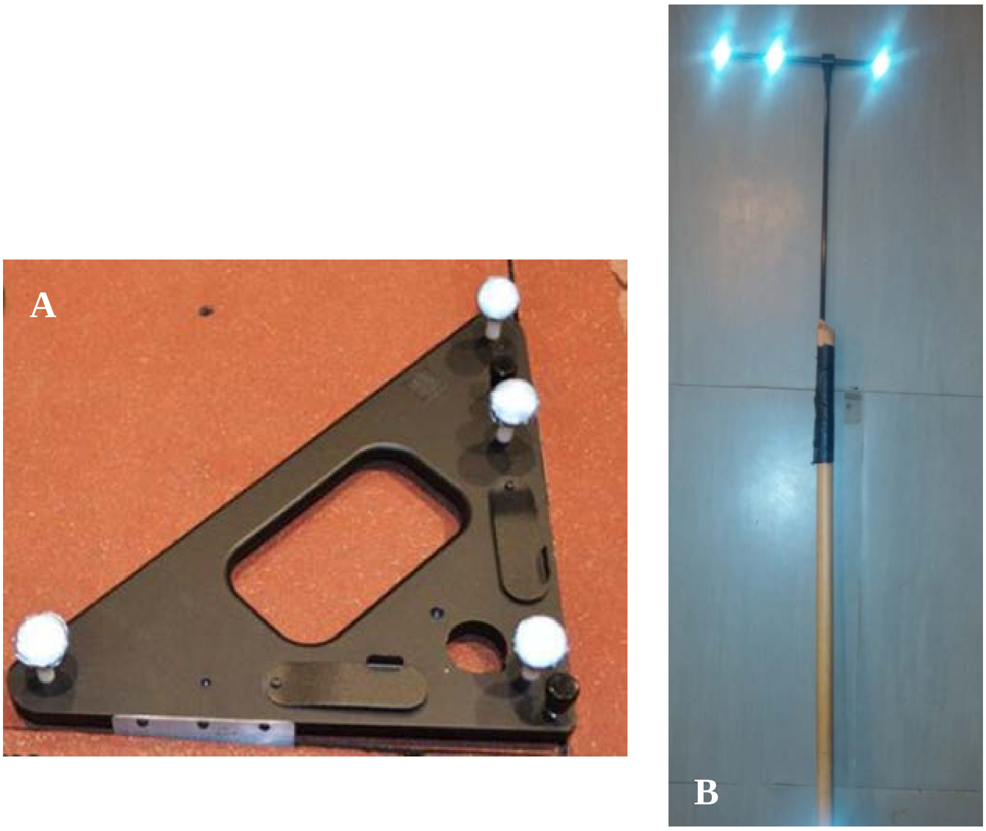

Figure 2. 3. Calibration tools.

(A) A four-marker triangular L-frame was used for the static calibration. (B) A three-marker wand was used for the dynamic calibration.

2.1.2 Clinical Gait Marker Set

In this thesis, the whole-body Cleveland marker set was adopted for gait analysis during unshod running. Thirty-five spherical reflective markers were placed on the upper and lower body (Figure 2.4), although we only calculated kinetics and kinematics at the lower limb joints. At least three markers were required per segment to determine its rotation. The pelvis was determined by three bony landmarks – the anterior superior iliac spines and the second sacral vertebra (midpoint), which were relatively easy to find and reliable bony landmarks. If any of these markers were misplaced, the pelvis kinematics would be incorrect. For instance, if the marker on the sacrum was placed on the first sacral vertebra instead of the second sacral vertebra, it may erroneously indicate an anterior pelvic tilt. Finding bony landmarks for the thigh was a bit more challenging as the hip joint is relatively deep and hidden under layers of muscles and tendons. Hence, a triad of markers placed mid-thigh was used to create a triangular-shaped region and used to estimate the position of the hip joint.

Details of marker placement are as follow (Figure 2.4): the tips of the acromia (RSHO, LSHO); the mid-point of the muscle belly of the triceps brachii (RTRI, LTRI); the lateral epicondyles of the humeri (RELB, LELB); the midpoint between the styloid processes of the radius and ulna on the dorsal aspect of the forearms (RWRI, LWRI); the anterior superior iliac spines (RASI, LASI); the superior aspect of the sacrum at sacral vertebra 2 in the midline (SACR); lateral femoral epicondyles of the knee (RKNE, LKNE); medial femoral epicondyles of the knee (RKNM, LKNM); medial malleoli of the ankles (RANM, LANM); lateral malleoli of the ankles (RANK, LANK); triads consisting of three markers and positioned on the lateral sides of the thighs (RT1, RT2, RT3, LT1, LT2, LT3); triads consisting of three markers and positioned on the lateral sides of the shanks (RS1, RS2, RS3, LS1, LS2, LS3); the second metatarsal heads (RTOE, LTOE); and at the posterior aspect of the calcanei (RHEE, LHEE).

Marker placement was always done by the same experienced investigator for consistency. All markers were directly attached onto the skin using double-sided tape. For consistency of the maker placements between pre- and post-run gait tests, a photo of the maker placement was taken for each participant.

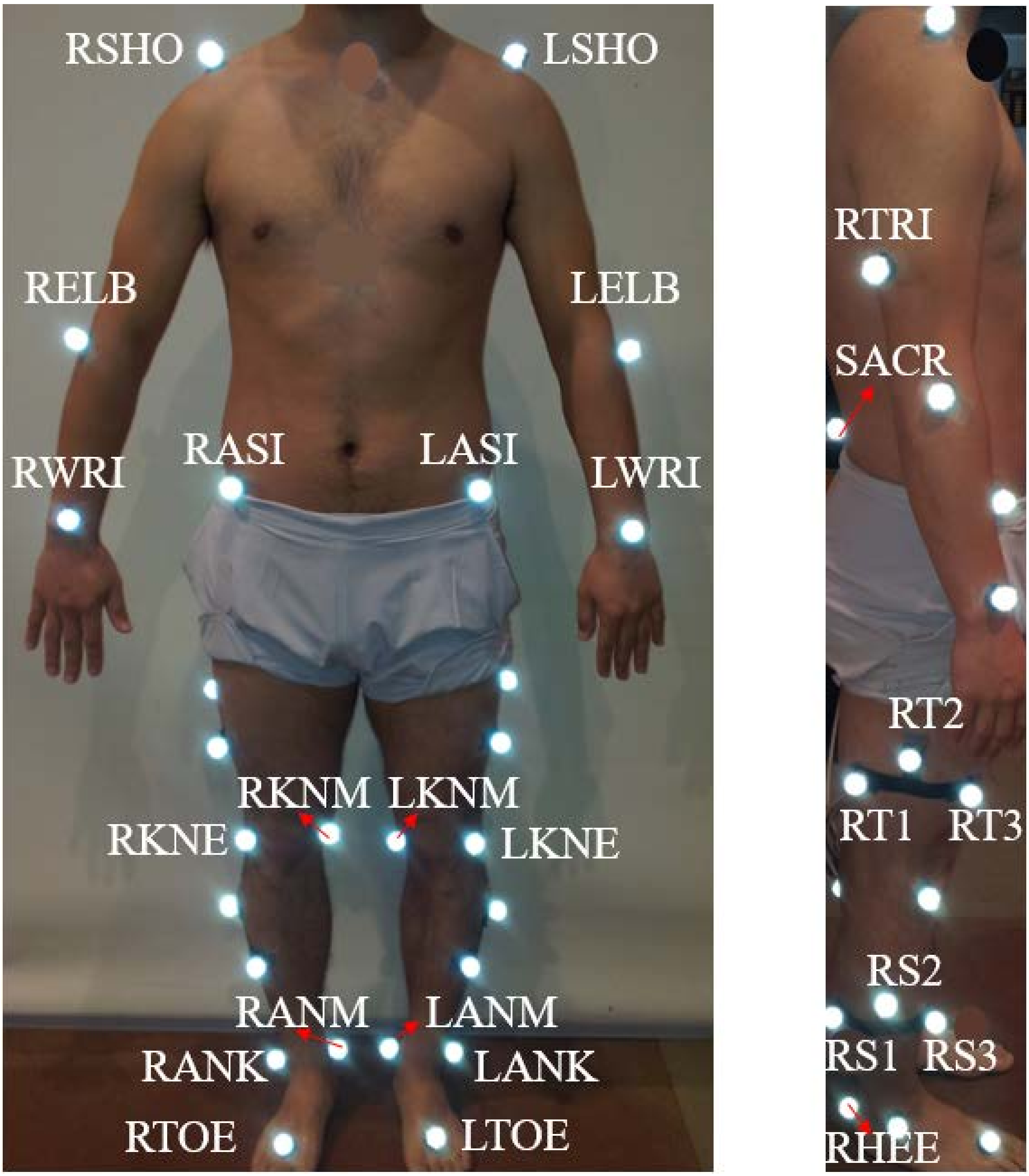

Figure 2. 4. Cleveland marker set.

35 reflective markers were placed on participant's body.

2.1.3 Gait Analysis Parameters

In this thesis, we calculated 3D kinetics and 3D kinematics at the lower limb joints during unshod running using Vicon workstation and Nexus (Oxford Metrics, Oxford, UK). Kinetics generally refers to ground reaction force, impact loading rate, joint torque, and joint power during walking or running. Kinematics indicate spatiotemporal parameters (e.g. stride length, stride rate, cadence) and joint angles. Prior to calculating gait parameters, a gait cycle should be defined - from the initial foot contact (IFC) with the ground to the next initial foot contact with the ground in the same limb (Figure 2.5).

As shown in Figure 2.6, a running gait cycle generally consists of 40% of stance phase, 30% of float and 30% of swing phase for healthy runners. Stance phase during running is subdivided into IFC, midstance and toe-off. Float phase represents the period in which two limbs are in the air. Swing phase refers when one foot is off the ground.

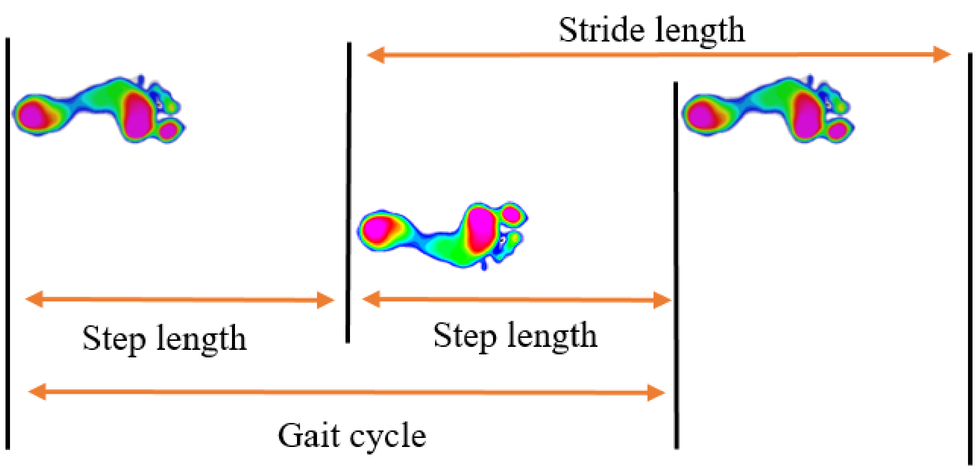

Figure 2. 5. Illustration of gait cycle, step length, and stride length.

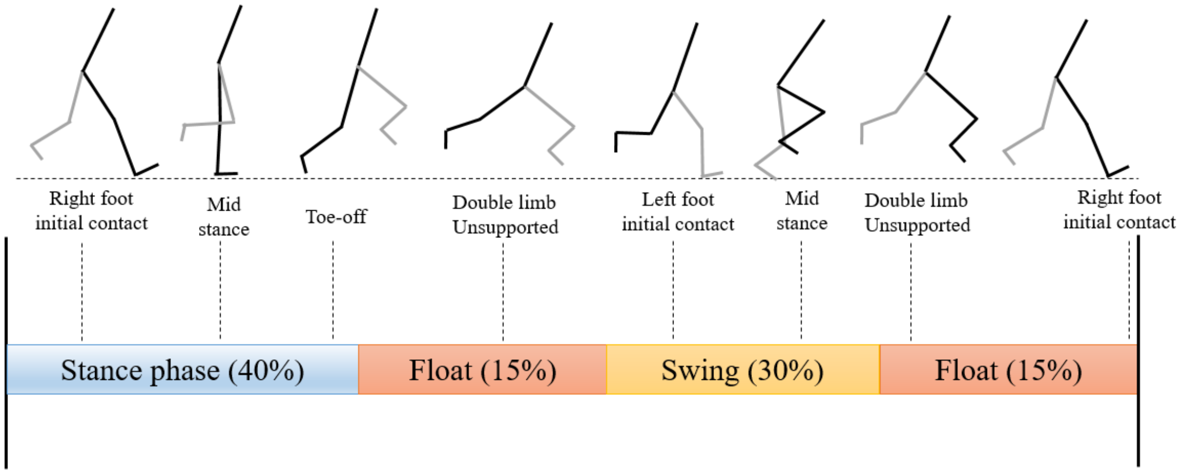

Figure 2. 6. Illustration of running gait.

2.1.4 Potential Confounding Factors

There are several confounding factors in gait assessments including gait speeds, environmental conditions, running styles, and level of exertion. All these known confounding factors have been controlled during gait assessment in this thesis. It has been reported that variation in gait speed may contribute to data variation (Lelas et al., 2003). In this thesis, we found that the running speed of each participant during each assessments was the same as that of his/her 5km unshod run. Different environmental conditions such as environmental temperature, wind, running surfaces during 5km unshod running and gait assessments would also affect the running biomechanics (Morgan, Martin, & Krahenbuhl, 1989). To control these confounding factors, all the experiments were conducted under the laboratory condition which means that all participants ran in the same place with the same conditions. Different running style (e.g. heel strike vs. forefoot strike techniques) is another confounding factor (Becker et al., 2012). Thus, we have only recruited runners who are normally run with shod with heel strike technique. The level of exertion during 5km unshod running may affect running biomechanics (Morgan, Martin, & Krahenbuhl, 1989). In this thesis, however, we have normalised the level of exertion by distance, rather than speed.

2.2 Plantar Pressure

Plantar pressure measurements have been widely used in biomechanics and sport-related research. Plantar pressure distribution may provide important information for identifying lower limb abnormalities, designing shoes and insoles, improving sports performance, preventing injury and more. In this thesis, the Novel emed® pressure platform (Figure 2.7) was employed to reveal plantar pressure distribution, force distribution, impulse and contact area in response to long-distance unshod running. This platform is a flat, stationary, and arranges a rigid array of sensing elements in a matrix configuration. This can be used for both static (standing) and dynamic (walking and running) situations under the laboratory conditions but we were only interested in dynamic pressure during unshod running in this thesis.

Strengths and limitations of using a pressure platform should be addressed. This relatively small and flat platform makes real-time measurements easy to assess. Using a platform of this type is also fairly easy and user-friendly. It doesn't require much space and it can be moved easily. Using a platform of this type outdoors, however, would be not ideal as it requires a power source and computer which may be adversely affected by the environment. As such it is generally only used under indoor laboratory conditions. Also, the plantar pressure measurements we are investigating are distorted through the use of shoes and hence measurements may only be reliably taken whilst unshod. Furthermore, participants require a familiarisation period be included to ensure natural gait; as a single valid step is required (step into the centre of platform) for accurate data reading, generally a participant takes some time to get familiar with this platform. Additionally, when participants are not able to walk properly due to a neurological disorder (e.g. stroke, cerebral parsley, Parkinson) or injuries of their lower limbs, this will increase the limitations of using this platform. In such cases, in-shoe sensors are sometimes used for patients involved in clinical research as an alternative to the platform used in this study.

2.2.1 Potential Confounding Factors

Different foot arch types may cause different results in plantar pressure distribution. O'Brien and Tyndyk (2014) reported that the pressure distributions were difference between normal feet, flat feet, and high arch feet. In this thesis, therefore, we have only recruited participants who have normal arch feet. It has been also reported that the foot shape is different between Asian, Indian and Caucasian, which influence plantar pressure distribution (Hawes et al., 1994; Putti, Arnold, & Abboud, 2010). Thus, this thesis recruited Caucasian participants only to minimise the foot shape influence.

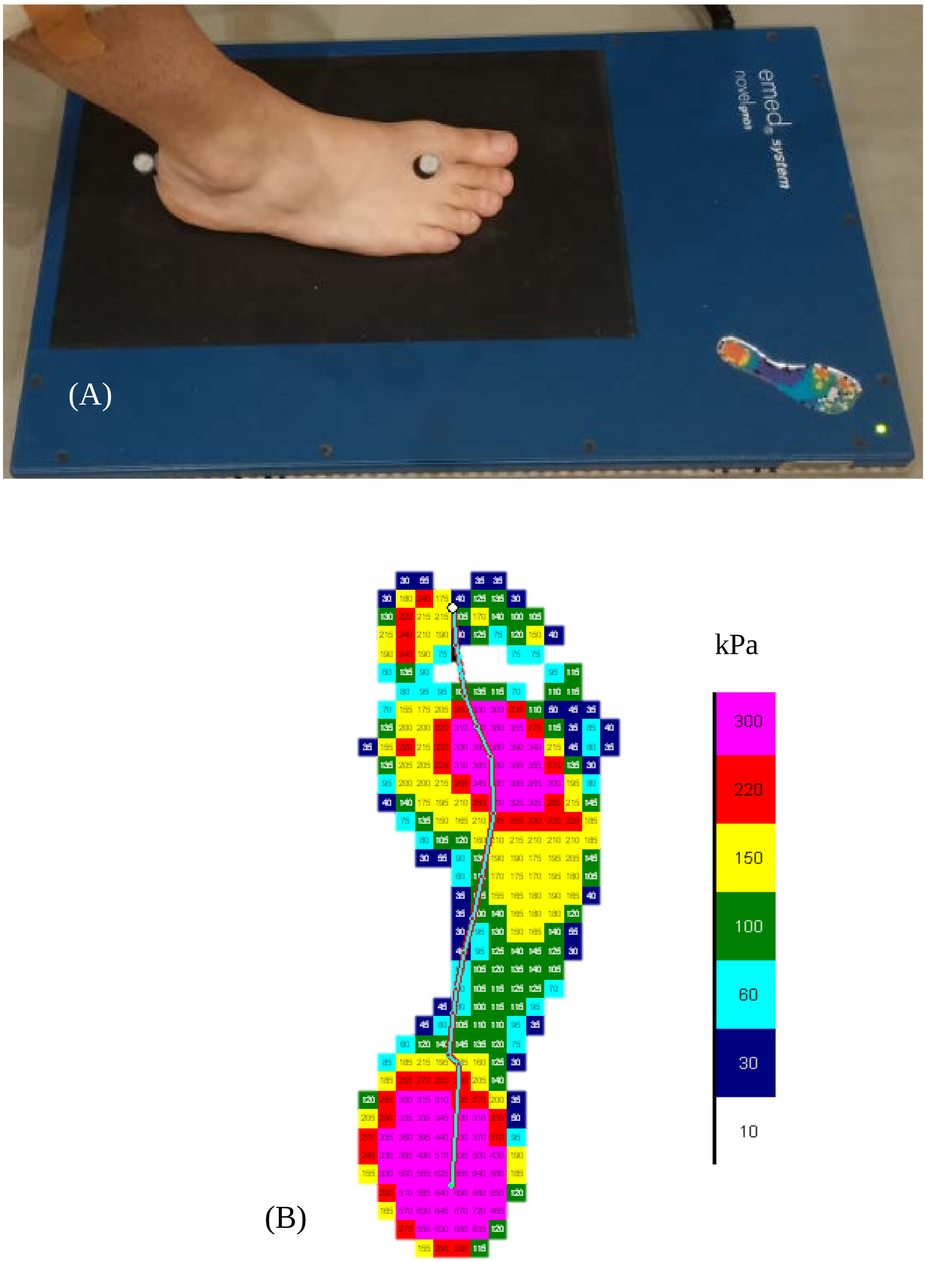

Figure 2. 7. Plantar pressure.

(A) The Novel emed® pressure platform. (B) Plantar pressure map showing the pressure distribution in unshod running.

2.3 Magnetic Resonance Imaging (MRI)

MRI is a non-invasive, useful technology, which can specifically reveal pathological changes such as edema or inflammation in soft tissues. In this thesis, a 3.0-Tesla MR scanner (Siemens Skyra, Erlangen, Germany) was used to evaluate ankle cartilage. Using an MRI has several benefits as follows:

- Unlike a computed tomography (CT) scanner, there is no risk of exposure from ionising radiation.
- Without repositioning patients, images can be obtained in multiple planes.
- MRI scanning has the ability to provide superior soft tissue contrast when compared to CT scans.
- MRI investigates more physiological parameters when compared to CT scans.
- Using the functional MRI, active parts of the brain can be seen during activities.

On the other hands, using an MRI scanner also has several disadvantages:

- MRI is expensive when compared to CT scans.
- MRI scans are usually more time-consuming issues when compared to CT scans.
- If patients have metal implants, MRI scans may not be safe.
- It may be uncomfortable or distressing if the patient has claustrophobia.

2.3.1 How does MRI work? - The Basic Principle of MRI

To understand generating MRI images, knowledge regarding the nuclear spin is essential. Atoms are composed of a nucleus and its orbiting electron(s) (Figure 2.8). The human body is comprised of approximately 60% water, which is hydrogen atoms that contains a single proton and a single electron. As the most abundant spins within the body are water protons, these nuclei can be detected by an MRI scan. As the proton is a spinning charged particle, it generates a magnetic moment with its own direction (generally random direction) that is along the axis of rotation of the spin and are all of equal energy. However, in the presence of a magnetic field, the nuclear spins of all protons are forced to either align along the direction of the applied magnetic field or against the field direction. The direction of the magnetic moment does not point exactly in the same direction as the magnetic field due to the angular momentum of the nuclear spin. When the magnetic field is applied, the magnetic moments still rotate around the same direction of the field, and this is called precession and the rate of precession is called the "Larmor frequency". Although the magnetic moment tends to align with the same direction of the applied field, some may align opposing the magnetic field. Generally, these opposing orientations have a greater energy state than those where the spins align with the field. The Larmor frequency can be determined by the field strength B_0 because the energy difference between low energy state and high-energy state is directly proportional to the applied magnetic strength B_0. This principle may play a critical role in MRI and it is called the Larmor equation: $\omega_0 = \gamma B_0$ (ω_0 refers to Larmor frequency in radians/second and γ indicates gyromagnetic ratio). The number of spins in the two energy level can be determined by the energy difference (magnetic moments aligned with the field have lesser energy than those aligned against) and the temperature of the system. This can be used to calculate the relative spin population and the Larmor frequency. Under the magnetic field, the total average of all of the magnetic moments can be obtained by simply adding all of the spin vectors, and it refers to this as the net magnetization vector (NMV). That is, the NMV is the sum of the all the magnetic moments of hydrogen nuclei. By the fading of this NMV during the MRI scans, we can obtain the signal in the MRI image.

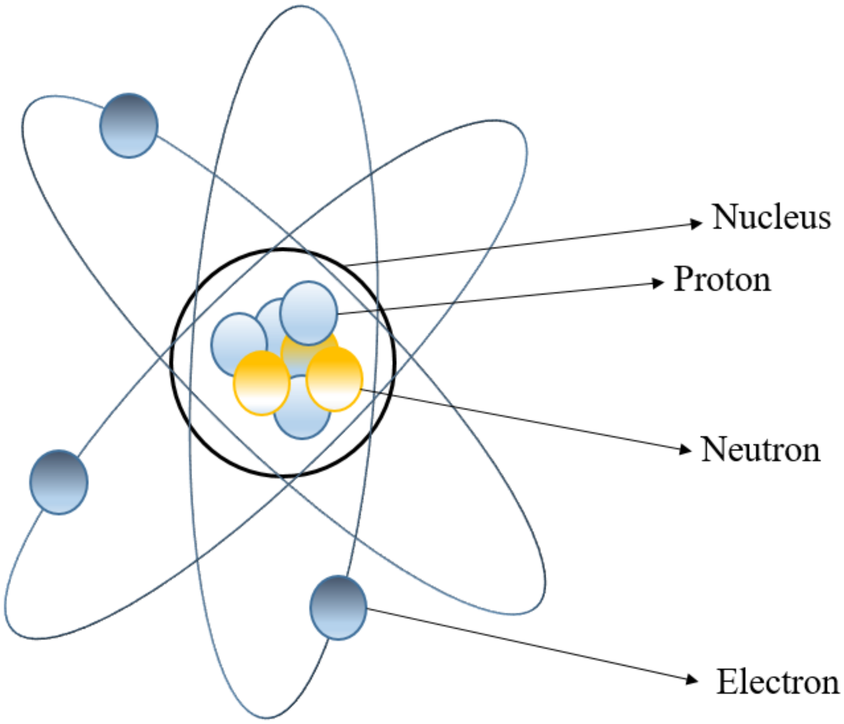

Figure 2. 8. Illustration of an atom that consists of a nucleus and its orbiting electrons.

2.3.2 T2 Mapping

In this thesis, a T2 mapping technique was employed for quantitatively evaluating the tibiotalar cartilage in response to unshod running. The sequences that we were used in this thesis were consulted with Dr Beau Pontre (Senior lecturer, Anatomy and Medical Imaging department) and Associate Professor Anthony Doyle (30 years of experience in musculoskeletal radiology).

T2 mapping is a biochemically sensitive modality, which allows evaluation of the cartilage composition, as the transverse relaxation time reflects the exchange of proton properties inside the cartilaginous matrix, which can be used in detecting the earlier changes of the articular damage (Liess et al., 2002). When cartilage is compressed due to an external force, water content and collagen fibre orientation of the extracellular matrix can be altered, and this influences the T2 values (ms). Quantitative data in T2 maps is shown as a colour map representing the variation in relaxation time within cartilage. As shown in Figure 2.9, red indicates greater T2 values in the posterior tibiotalar cartilage, while blue/black indicates lower values.

It has been reported that T2 changes are correlated with cartilage damage (Dunn et al., 2004; Koff, Amrami, & Kaufman, 2007). Greater T2 values were observed in osteoarthritic cartilage when compared with normal cartilage (Dunn et al., 2004). Moreover, it has been reported that high physical activity may also affect the T2 values; after long-distance running, T2 values within the knee cartilage was changed (Luke et al., 2010).

2.3.3 Potential Confounding Factors

It has been reported that there is potential diurnal effect in the cartilage T2 relaxation time (Coleman et al., 2013). In this thesis, therefore, the pre-run MR scan was always conducted in the morning to minimise potential diurnal effect. The post-run scans were performed following 5km unshod running on the same day and always in the afternoon. Although there was always a difference in MR scans time (e.g. pre- and post-run scans), it was consistent and hence this would not affect this thesis conclusions.

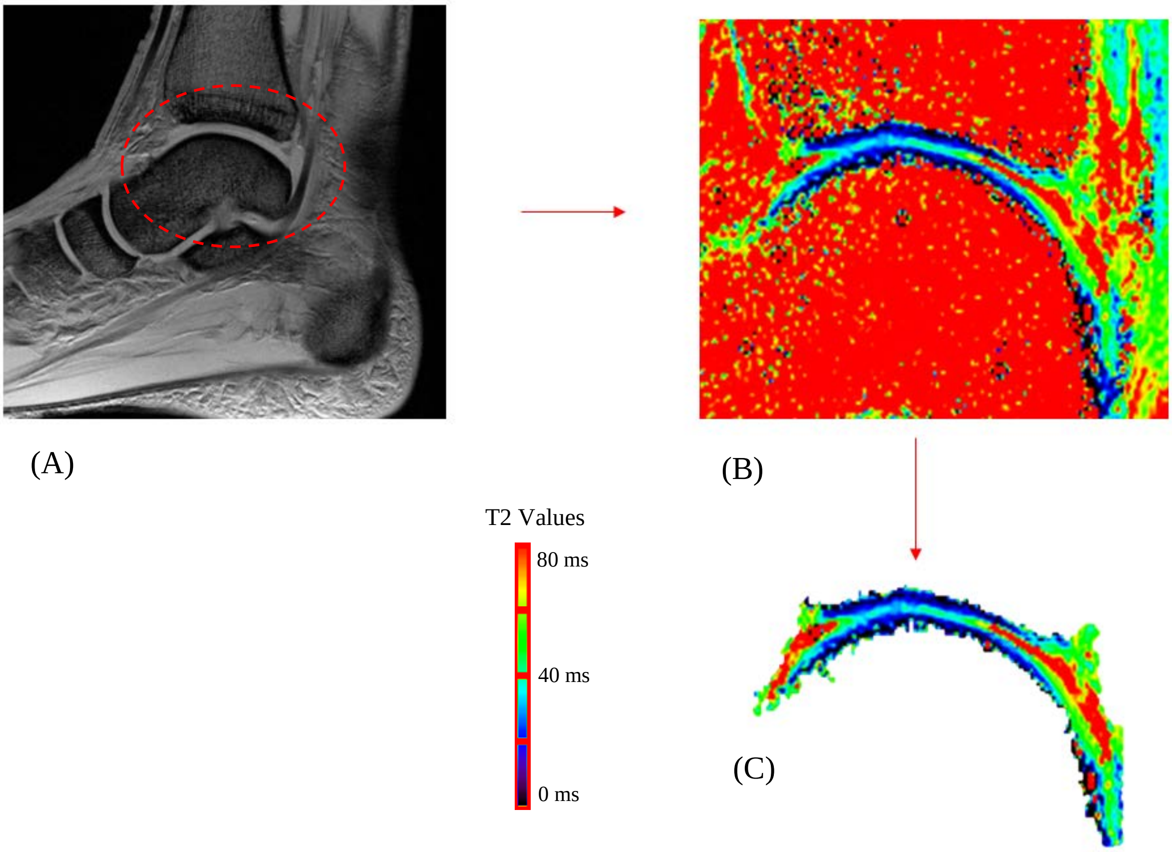

Figure 2. 9. Sagittal view of MR images.

(A) Conventional MR imaging of the ankle. (B, C) T2 mapping of the ankle cartilage.

Chapter 3. Gait Kinetics, Kinematics, Spatiotemporal and Foot Plantar Pressure Alteration in Response to Long-Distance Running: Systematic Review

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3.1 Preface

There is little information on how repetitive and high rate loading during long-distance running affects lower limb biomechanics. This chapter is the first study to systematically evaluate the effect of long-distance running on gait kinetics, kinematics, spatiotemporal and foot plantar pressure data to obtain an improved insight of the present state of knowledge.

3.2 Introduction

Long-distance running (e.g. 5km-42km) has become a popular sport, even at the amateur level. While running has obvious health benefits, the lower limbs are often exposed to higher than normal joint stress levels, which may lead to gait modifications. The literature presents many studies that associate running related injuries to shifts away from normal gait, but does not necessarily explain the cause of injury. For example, a prospective study (Willems et al., 2006) indicated that subjects present with lower leg pain with altered biomechanical running patterns compared with controls, including more central heel-strike, increased pronation along with high plantar pressure under the medial side of the foot and more lateral roll-off. A systematic review also reported that kinematic foot variables, including high pronation velocity, and great peak plantar pressure can be associated with increased risk of Achilles tendinopathy, patellofemoral pain, and other non-specific overuse injuries (Dowling et al., 2014). Increased peak knee internal rotation during stance phase was also observed in runners who were diagnosed with iliotibial band syndrome (Aderem & Louw, 2015).

A review of parameters for healthy shod runners may provide a better understanding for future injury studies that deviate from healthy baseline controls. Plantar pressure, temporal-spatial, kinematic, and kinetic measurement have been widely used as indicators of overall gait performance. For instance, several studies reported the greater biomechanical alterations in healthy participants, on different gait speed (Rosendaum et al., 1994), on different surfaces (Baur et al., 2007), and on different shod conditions (Wiegerinck et al., 2009). These parameters also have shown the greater association with long-distance running in healthy shod runners (Degache et al., 2013; Dierks et al., 2010; Willems et al., 2012). However, there is no study synthesised the gait alternations after long-distance running in a single review paper.

Therefore, the objective of this systematic review was to obtain an improved insight of the present state of knowledge regarding the effect of long-distance running on gait patterns and plantar pressure distribution in healthy runners. An appreciation of biomechanics for ‘high and repetitive loading’ imposed on the lower limb joints would be of great value for informing running injury prevention. While different surface types (road and trail) and running duration will produce different grades of loading, we do not differentiate these factors in this study. We have been motivated by numerous MRI studies that have reported ankle (Kim, Fernandez, & Mirjalili, 2017) and knee cartilage degenerative changes in marathon running (W. Krampla et al., 2001), and short running such as 30-minutes on a treadmill (Boocock et al., 2009), or asphalt running (Mosher et al., 2005), and 5-20km track running (M. Kessler et al., 2006), that are all associated with initiating degenerative changes. Further, most long-distance runners are shod and there is a trend emerging towards unshod and minimalist long-distance running. We must fully understand the shod case before the benefits of unshod running can be fully realised.

3.3 Methods

3.3.1 Search strategies and selection process

This systematic review followed the guidelines of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol (Moher et al., 2009). Electronic databases of Scopus, Web of Science, SportDiscus, and Ovid Medline were searched for assessing gait parameters before and after long-distance running, with restriction for English language and published between 1990 and 2016. The final search was completed on 7th March 2016. The search terms used a combination of 1) biomechanic* OR kinematic* OR kinetic*; AND 2) running OR run OR jog OR jogging OR marathon OR long distance; AND 3) plantar pressure OR foot pressure. The reference lists of included articles were also looked through for additional relevant articles.

The study selection process was performed by a single reviewer (H.K.K) and this whole process was evaluated by another reviewer (S.A.M). After removed duplication, abstracts and titles were initially predetermined based on eligibility criteria as shown below. Full-text articles were retrieved from this initial screening and the full text was read for inclusion. If there were any disagreement for the study selection between two reviewers, a third reviewer (J.F) adjudicated.

3.3.2 Eligibility criteria

Studies were identified based on the following inclusion criteria: 1) healthy or asymptomatic adult populations were included; 2) the intervention running must be a continuous long-distance run or be a multi-days run but single case; 3) long-distance run should be at least 30-minutes; 4) the studies must report at least one of the following outcomes; kinetics (impact loading rate, GRF, impact acceleration), kinematics (hip kinematic, knee kinematic, ankle kinematic, foot strike), plantar pressure, and/or spatiotemporal parameters (contact time, contact area, stride length, stride frequency, step length, step frequency, aerial time, running velocity) during gait tests following long-distance running; 5) gait tests and/or plantar pressure measurement should be conducted before and after long-distance running; 6) OR the measurements were conducted simultaneously with long-distance running.

Studies were excluded based on the following exclusion criteria: 1) a short last run such as sprint or interval runs was excluded; 2) review, conference abstract, and press papers were excluded; 3) non-English articles were excluded.

3.3.3 Data extraction

Characteristics of studies (i.e. authors, year), characteristics of participants (i.e. sample size, demographics data, biometric data, training history, fitness level, injury history, if available), long-distance running types (i.e. speed, distance, environment, shoes, surfaces, if available) and study method (aim, study design, measurements, outcomes) were extracted. Inclusion and exclusion criteria were also noted. More details are presented in Table 1.

3.3.4 Methodological Quality Assessment

Selected articles were evaluated for methodological quality by using a modified version of a quality index (QI), originally developed by Downs and Black (Downs & Black, 1998). This QI tool allows assessing the quality of reporting, external validity, internal validity (bias and confounding) and power. In this review study, the power scale (question 27) was excluded due to its uncertainty (Deeks et al., 2003). Each question can be answered ‘yes’, 'no' or 'unable to determine'. If the answer was 'yes', it awarded one point, while scored zero. Question five was an exception where 'yes' was scored two, 'partially' was one and 'no' was zero. Thus, 27 was the maximum scores from the QI tool. The following cut-off was used for the current review which was adopted from previous studies (Carroll et al., 2015; Meyer et al., 2014; Weierink, Vermeulen, & Boyd, 2013): A high-quality study, ≥ 80%; a moderate quality study, ≥47% and <80%; a poor-quality study, <40%.

3.4 Results

3.4.1 Search strategies

A search of the electronic databases produced 1243 articles. After removed duplication, 1031 articles remained. Based on the eligibility criteria, title and/or abstract were initially screened and 1008 articles were excluded. Twenty-six articles met the initial search criteria as potentially relevant to the current study. After reading the full-text articles, six of the 26 articles were included. Another six articles were included after searching through the references lists of the 26 articles. Therefore, the final selection of studies included 13 articles. The search history and selection process are presented in Figure 3.1.

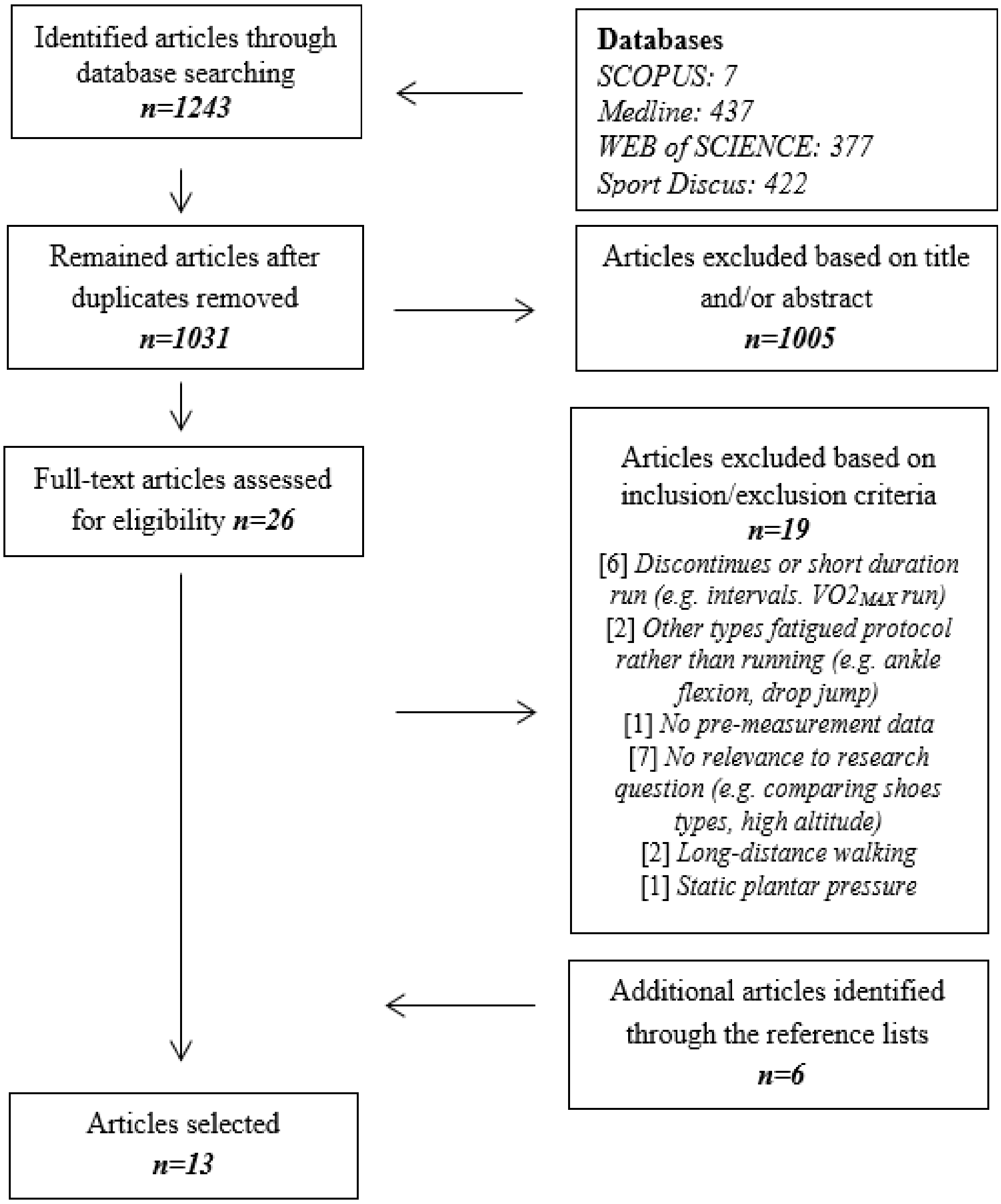

Figure 3. 1. Flow diagram of the search history and selection process.

3.4.2 Description of the studies

Thirteen selected studies (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008; Degache et al., 2013; Dierks, Davis, & Hamill, 2010; Karagounis et al., 2009; Kyröläinen et al., 2000; Millet et al., 2009; Mizrahi et al., 2000; Morin et al., 2011b; Morin, Samozino, & Millet, 2011a; Nagel et al., 2008; Peltonen et al., 2012; Willems, De Ridder, & Roosen, 2012) investigating the effect of long-distance running on kinetic, kinematic, plantar pressure and/or spatiotemporal parameters were included in this systematic review. All the variables were collected during gait tests before and after long-distance running or obtained simultaneously during long-distance running. The types of distance running were varying from a 30-minute intensive run to ultra-marathon for 8,500km in 161 days. The runners' training experience were also diverse; generally ran at least 16km to 40km per week and have been running for 13 years to 24 years. None of these studies recruited professional or national level runners. The details of included studies are described in Table 3.1.

Table 3. 1. Characteristics of 13 selected studies

Authors	*Measurement Time-Points*	*Running Types (Distance or Speed or Time)*	*Population (Gender, age)*	*Gait Analysis Tool*	*Extra Measurements*	*Gait Protocol (average speed)*	*Gait Parameters*			
							TS	*KINM*	*KIN*	*PP*
Degache et al. (2013)	• Baseline • Follow-up (immediate)	5 h uphill/downhill run (37.5±5.5km)	8 long-distance runners (♂8, 42.5±5.9yr)	Instrumented treadmill dynamometer	Spring-mass behaviour	Run on a treadmill (10, 12, and 14km/h for all participants), no shoe information.	●		●	
Willems et al. (2012)	• Baseline • Follow-up	20km race (10.9(8.2-15.38)km/h)	52 healthy individuals (♂36, ♀16, 44(23-62)yr)	Platform system (1 meter in length)	Infrared gate during gait tests and chip timing system during a race for measuring speed	Run on pressure mats with own shoes (self-selected pace, but asked to maintain the same speed as during the race. Pre-race:10.27±1.07km/h; post-race:10.30±1.07km/h)	●			●
Peltonen et al. (2012)	• Baseline (2 days) • 1 hour follow-up	42km or 21km race (11.2±0.3km/h)	12 marathon runners (♂8,♀4, 37±12.6yr)	A high speed digital camera	Respiratory data for running economy, Achilles tendon stiffness	Run on a treadmill with own shoes (sub-maximal speed according to each subject's target time)		●		
Alfuth and Rosenbaum (2011)	• Baseline • Follow-up (immediate)	10km outdoor run (50.42±5.16min)	15 recreational runners (♂10, ♀5, 32.1±11.4yr)	Insole plantar system	HR, RPE, Sensory test	Run on a treadmill with own shoes (20% slower than the best time of previous 10km race, 11.2±1.1km/h)	●			●

Morin et al. (2011a)	• Baseline • Every 2 hours • At the end of the run	24h treadmill run (153±15km, freely chosen pace)	10 ultra-long-distance runners (♂10, 40.4±6.5yr)	Instrumented treadmill dynamometer	Spring-mass behaviour, Muscle biopsy (Vastus lateralis)	Run on a treadmill (10km/h for all participants), no shoe information.	●		●	
Morin et al. (2011b)	• Baseline (1-2days) • 3h follow-up	Mountain ultra-marathon race (166km, 37.9±6.2h)	18 ultra-marathon experienced runners (39.1±7.6yr)	Platform system (7-meter long walkway)	Spring-mass behaviour	Run on a PP platform walkway (12km/h for all participants; controlled by two photocells), no shoe information.	●		●	
Dierks et al.(2010)	• Baseline (at the beginning of the run) • At the end of the run	Intensive 45±12min treadmill run until reached exertion state (2.6m/s±0.3, self-selected pace that best-represented individual's typical running pace)	20 recreational runners (22.7±5.6yr)	6-camera VICON 3D motion analysis	RPE, HR	Run on a treadmill with provided running shoes (2.6m/s±0.3=9.36km/h)	●	●		
Karagounis et al.(2009)	• Baseline • Follow-up (immediate) • 1 day follow-up	Ultramarathon race (246km)	46 experienced runners (♂46, 44±8.2yr)	Platform system	N/A	Walked barefoot across a PP platform embedded in a soft walkway (normal walking speed)	●			●
Millet et al. (2009)	• Baseline (3 weeks) • 3 weeks follow-up • 5 months follow-up	Running from Paris to Beijing (8,500km)	1 experience ultra-endurance runner (♂, 58yr)	Instrumented treadmill dynamometer	Knee isokinetic strength, Respiratory data for running economy, HR, Blood lactate	Run on a treadmill (8, 10, 12, 14, & 16km/h increases speed every 2 minutes), no shoe information.	●		●	
Nagel et al. (2008)	• Baseline (2 days) • 1 h follow-up	Full marathon race	200 recreational runners (♂167, ♀33, 39.5±8.8yr)	Platform system	N/A	Walked barefoot across a PP platform embedded in a soft walkway (normal walking speed)	●			●

Bisiaux and Moretto (2008)	• Baseline • Follow-up (immediate) • 30 min follow-up	Intensive 30-min track run (80% of the maximal aerobic speed, speed was controlled by pre-recorded soundtrack)	11 healthy (♂23, 9±5.32yr)	Insole plantar system	Maximal aerobic test, HR, Blood lactate	Walked with the same type of neoprene shoes on a treadmill (comfortable pace that was determined during pre-test)	●			●
Mizrahi et al. (2000)	• 10th, 15th, 20th, 25th and 30th min during run	Intensive 30-min treadmill run (exceeding the anaerobic threshold by 5%, 3.5±0.2 m/s)	14 healthy (all ♂, 24.2±3.7yr)	Accelerometer Digital video camera	Maximal aerobic test	Run on a treadmill with the same type running shoes (3.5±0.2 m/s = 12.6km/h)		●		
Kyröläinen et al.(2000)	• Baseline • Follow-up	Full marathon outdoor run (speed was pre-selected from a submaximal run test, 3.82±0.33 m/s=13.8km/h, a cyclist paced together)	7 experienced triathletes (♂6, ♀1, 29±5yr)	Optical encoder Digital video camera	Submaximal run test, Metabolic measurements, Respiratory data, HR, Blood samples, Optical encoder	Run on a treadmill (submaximal 3.82±0.33 m/s=13.8km/h), no shoe information.	●	●		

Abbreviations: TS-temporal spatial; KINM-kinematics; KIN-kinetics; PP-plantar pressure; ♂-male; ♀-female; yr-years old; h-hour; min-minute; RPE-Rated Perceived Exertion; HR- heart rate.

Note: "Race" refers to competition. "Run" refers to running under the laboratory condition.

3.4.3 Plantar pressure distribution

Five (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008; Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012) of the 13 studies (38.5%) measured the plantar pressure of the foot, subdividing into seven to eleven areas including hallux, 2nd-5th toes, 1st-5th metatarsals, lateral/medial midfoot, and lateral/medial heel for the analysis of pressure distribution. The platform or insole plantar system were used.

Metatarsal regions

All five studies (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008; Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012) indicated that the pressure under the metatarsals 2nd and 3rd were increased at the first follow-up after long-distance running. Of these, two studies conducted (Bisiaux & Moretto, 2008; Karagounis et al., 2009) second follow-up; after a 30-minutes rest period, the loading under the 2nd and 3rd metatarsal head remained significantly increased compared to the pre-run measurement (Bisiaux & Moretto, 2008). However, after a 24-hours rest period, no significant differences were observed for the peak pressures in the all metatarsal regions (Karagounis et al., 2009).

In regard with the 1st, 4th and 5th metatarsals, inconsistent results were observed. A significant increasing load under the 1st metatarsal was shown with two studies (Karagounis et al., 2009; Willems et al., 2012), while other two studies (Bisiaux & Moretto, 2008; Nagel et al., 2008) reported insignificant decreasing after long-distance running. The loading under the 4th and 5th metatarsals were also significantly increased with three studies (Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012), whereas one study showed decreased (Bisiaux & Moretto, 2008).

Toe regions

The load under the toe regions were decreased after long-distance running. Four (Bisiaux & Moretto, 2008; Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012) of the five studies showed a significant decrease and one remaining study (Alfuth & Rosenbaum, 2011) also revealed a similar trend of decreasing but without reaching a significant level. After a 30-minute and a 24-hours rest following long-distance running, the loading under the hallux and toe regions all returned to the initial values (Bisiaux & Moretto, 2008; Karagounis et al., 2009).

Midfoot regions

Conflicting findings were observed for the midfoot region. Four (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008; Karagounis et al., 2009; Nagel et al., 2008) of the five studies showed decreased peak pressure under the medial and lateral midfoot. However, one remaining study (Willems et al., 2012) showed completely contrasting results, increasing the load under the midfoot region. After 30-minute rest, peak pressure under the medial midfoot was still significantly decreased (Bisiaux & Moretto, 2008). However, all returned to pre-measurement values after a 24-hours rest.

Heel regions

Inconsistencies were found from the heel region. Three (Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012) of the five studies showed increased load under the medial and lateral heel but only one study reached a significant level under the medial heel (Willems et al., 2012). In contrast, the two remaining studies (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008) reported insignificant decreases at the first follow-up. At the second follow-up with a 30-minute rest, however, the load under the medial heel region was significantly decreased (Bisiaux & Moretto, 2008).

3.4.4 Spatiotemporal gait parameters

Eleven (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008; Dierks et al., 2010; Karagounis et al., 2009; Kyröläinen et al., 2000; Millet et al., 2009; Morin et al., 2011b; Morin et al., 2011a; Nagel et al., 2008; Willems et al., 2012) of 13 studies (77%) reported spatiotemporal gait parameters including contact time, step length and frequency, stride length and frequency, contact area, aerial time, and running velocity.

Contact time

Nine studies (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008; Degache et al., 2013; Karagounis et al., 2009; Kyröläinen et al., 2000; Millet et al., 2009; Morin et al., 2011a; Nagel et al., 2008; Willems et al., 2012) measured contact time, yet conflicting results were observed. Of these, three studies (Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012) reported significant increases in contact time. Regarding the total foot contact time, one study (Willems et al., 2012) showed a significant increase after long-distance running. In terms of specific regions of interest, contact time in metatarsals (Nagel et al., 2008; Willems et al., 2012), heel (Karagounis et al., 2009; Nagel et al., 2008), midfoot and 3rd-5th toes (Nagel et al., 2008) was significantly increased after long-distance running. On the contrary, a significant decrease in contact time was observed by two studies (Degache et al., 2013; Morin et al., 2011a). The remaining four studies (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008; Kyröläinen et al., 2000; Millet et al., 2009) found contact time was maintained at a constant level between baseline and follow-up.

Contact area

Contact area (cm^2) was examined from two studies (Alfuth & Rosenbaum, 2011; Karagounis et al., 2009) and none of these studies provide the evidence that the contact area was influenced by long-distance running.

Stride length

One study (Kyröläinen et al., 2000) measured stride length and it was significantly decreased.

Stride frequency

One study (Kyröläinen et al., 2000) measured stride frequency and it was significantly increased.

Step length

One study (Bisiaux & Moretto, 2008) measured step length, but there was no evidence to support step length is influenced by long-distance running.

Step frequency

Five studies (Bisiaux & Moretto, 2008; Degache et al., 2013; Millet et al., 2009; Morin et al., 2011b; Morin et al., 2011a) measured step frequency and it was increased after long-distance running. Of these, four studies reached a significant (Degache et al., 2013; Millet et al., 2009; Morin et al., 2011b; Morin et al., 2011a), while remaining one study (Bisiaux & Moretto, 2008) showed an insignificant increase.

Aerial time

Four studies (Degache et al., 2013; Millet et al., 2009; Morin et al., 2011b; Morin et al., 2011a) measured aerial time. Three studies (Millet et al., 2009; Morin et al., 2011b; Morin et al., 2011a) reported a reduction of aerial time but only one study (Morin et al., 2011b) reached a significant level. However, one study (Degache et al., 2013) reported no changes.

Running velocity

One study (Willems et al., 2012) measured running velocity and there was no evidence to support it was influenced by long-distance running. However, it should be noticed that participants were instructed to maintain the same running speed during gait tests with the speed during long-distance running. Thus, it cannot specify whether the running velocity was affected by long-distance running.

3.4.5 Kinetics gait parameters

Five studies (Degache et al., 2013; Millet et al., 2009; Mizrahi et al., 2000; Morin et al., 2011b; Morin et al., 2011a) measured kinetic gait parameters including impact loading rate, vertical GRF, and impact acceleration on the shank. Gait kinetics were measured using the accelerometer, pressure plates, and instrumented treadmill dynamometer.

Impact loading rate

Three studies (Degache et al., 2013; Millet et al., 2009; Morin et al., 2011a) measured loading rate at impact, reporting that it was similar between baseline and follow-up.

GRF

Four studies (Degache et al., 2013; Millet et al., 2009; Morin et al., 2011b; Morin et al., 2011a) measured maximal GRF, reporting that it was generally decreased after long-distance running. Three studies (Degache et al., 2013; Morin et al., 2011b; Morin et al., 2011a) showed that peak vertical GRF was significantly reduced. The one remaining case-study (Millet et al., 2009) also showed a decrease of GRF, but it was insignificant.

Impact accelerations

One study (Mizrahi et al., 2000) measured impact acceleration on the shank at foot strike using an accelerometer attaching to the tibial tuberosity of the right leg. Impact acceleration (g) was gradually and significantly increased over long-distance running.

3.4.5 Kinematics gait parameters

Four (Dierks et al., 2010; Kyröläinen et al., 2000; Mizrahi et al., 2000; Peltonen et al., 2012) of 13 studies (31%) reported kinematics gait parameters including joint angles and foot strike techniques. High-speed digital cameras combined with accelerometers or optical encoders and a motion capture system was adopted.

Hip kinematics

Two (Dierks et al., 2010; Mizrahi et al., 2000) studies measured hip kinematics by using 2D video camera (Mizrahi et al., 2000) or 3D motion capture systems (Dierks et al., 2010). Hip vertical excursion (obtained as peak position subtracted from minimum position preceding the peak) between maximum position and peak acceleration position was significantly increased over long-distance running (Mizrahi et al., 2000). Another study (Dierks et al., 2010) also measured excursion, peak angles and peak velocity at the hip adduction in the frontal place and hip internal rotation in the transverse plane by using the Vicon 3D motion analysis system. Significant increases were found in peak hip adduction angular velocity only, while no significant differences were observed for the hip internal rotation.

Knee kinematics

Two studies (Dierks et al., 2010; Mizrahi et al., 2000) reported that knee kinematics was influenced by long-distance running. The knee flexion angle resulting from foot strike was significantly decreased, while the knee angle at the maximum extension position was significantly increased (Mizrahi et al., 2000). The knee internal rotation of excursion (obtained as peak angle subtracted from minimum angle preceding the peak), peak angle, and peak angular velocity were all significantly increased, while the knee flexion of peak velocity was significantly decreased (Dierks et al., 2010).

Ankle kinematics

Two studies (Dierks et al., 2010; Kyröläinen et al., 2000; Peltonen et al., 2012) measured ankle kinematics. One study (Kyröläinen et al., 2000) measured angular displacement of the ankle during contact phase, but the value was stable between baselines and follow-up. Another study (Dierks et al., 2010) reported that rearfoot eversion excursion, peak angle, and peak angular velocity were all significantly increased over long-distance running.

Foot strike

Changing foot strike techniques was observed using a high-speed digital camera in one study (Peltonen et al., 2012). 75% of participants changed their strike techniques from forefoot contact to either midfoot contact or heel contact or from heel contact to midfoot.

3.4.6 Methodological quality assessment

Moderate quality ranging from 41% to 63% of maximum scores were found from all the selected studies (Table 3.2). Reporting and internal validity on bias were generally addressed well. In contrast, question 8 (reporting), 11, 12 (external validity), 14, 15 (internal validity on bias) and 21-24 (internal validity on confounding) were scored all zero.

Table 3. 2. *Quality assessment.*

	Items	*Authors*												
		Degache et al. (2013)	Willems et al. (2012)	Peltonen et al. (2012)	Alfuth and Rosenbaum (2011)	Morin et al. (2011a)	Morin et al. (2011b)	Dierks et al. (2010)	Karagounis et al. (2000)	Millet et al. (2000)	Nagel et al. (2008)	Bisiaux and Moretto (2008)	Mizrahi et al. (2000)	Kyröläinen et al. (2000)
Reporting	1. Are hypothesis/aims described clearly?	1	1	1	1	1	1	1	1	1	1	1	1	1
	2. Are the main outcomes described clearly?	1	1	1	1	1	1	1	1	1	1	1	1	1
	3. Are the characteristics of participants described clearly?	1	1	1	1	1	1	1	1	1	1	1	1	1
	4. Are the intervention described clearly?	1	1	1	1	1	1	1	1	1	1	1	1	1
	5. Are distribution of principal confounders described clearly?	1	1	1	1	1	1	1	1	1	1	1	1	1
	6. Are the main findings described clearly?	1	1	1	1	1	1	1	1	1	1	1	1	1
	7. Are estimates of the random variability provided?	1	1	1	1	1	1	1	1	1	1	1	1	1
	8. Are any possible adverse events reported?	0	0	0	0	0	0	0	0	0	0	0	0	0
	9. Are the characteristics of participants lost to follow-up described?	0	0	1	1	0	0	1	1	1	1	1	1	1
	10. Are actual probability values reported?	0	1	1	1	0	1	0	0	0	1	0	0	0

External validity	11. Were the participants asked to join the study representative of the entire population?	0	0	0	0	0	0	0	0	0	0	0	0	0
	12. Were the participants preparing to participate representative of the entire population?	0	0	0	0	0	0	0	0	0	0	0	0	0
	13. Were the intervention representative of that in use in the source population?	1	1	1	1	1	1	1	1	0	1	1	1	1
Internal validity bias	14. Was the intervention blind for participants?	0	0	0	0	0	0	0	0	0	0	0	0	0
	15. Was the main outcomes of intervention blind?	0	0	0	0	0	0	0	0	0	0	0	0	0
	16. Was it clear if results were based on “data dredging”?	1	1	1	1	1	1	1	1	1	1	1	1	1
	17. Was the length of the follow-up same?	1	1	1	1	1	1	1	1	-	1	1	1	1
	18. Were the statistical tests for assessing main outcomes appropriate?	1	1	1	1	1	1	1	1	1	1	1	1	1
	19. Was compliance with intervention reliable?	1	1	1	1	1	0	1	0	0	1	1	1	1
	20. Were the measurements used for main outcomes accurate?	1	1	1	1	1	1	1	1	1	1	1	1	1
Internal validity confounding	21. Were the study group and controls recruited from the same population?	0	0	0	0	0	0	0	0	0	0	0	0	0
	22. Were the study group and controls recruited from the same period of time?	0	0	0	0	0	0	0	0	0	0	0	0	0
	23. Were participants randomised to intervention groups?	0	0	0	0	0	0	0	0	0	0	0	0	0
	24. Concealed the randomised intervention?	0	0	0	0	0	0	0	0	0	0	0	0	0
	25. Was confounding adequately adjusted?	0	1	1	1	1	1	1	0	0	0	1	1	1
	26. Were losses of participant to follow-up taken into account?	0	0	1	1	0	0	1	1	-	1	1	1	1
QI scores total (% of maximum score)		13 (50)	15 (56)	17 (63)	17 (63)	14 (52)	14 (52)	16 (59)	14 (52)	11 (41)	16 (59)	16 (59)	16 (59)	16 (59)

3.5 Discussion

The purpose of this review was to provide an overview of literature describing the effect of long-distance running on gait parameters and plantar pressure distribution. The findings from this systematic review indicate that biomechanical gait parameters and plantar pressure distribution are possibly altered by long-distance running.

3.5.1 Effect of long-distance running on plantar pressure distribution

In the current review, variations of plantar pressure after distance running have been examined in five studies (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008; Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012), showing similar trends increasing the load under the metatarsals and decreasing under the toe regions. Despite the variety of protocols, the pressure under the 2nd and 3rd metatarsal were commonly increased after long-distance running. This increased loading has previously been confirmed by an *in vivo* study (Arndt et al., 2002); they found deformation of the 2nd metatarsal with a high strain rate by inserting titanium staple mounted gauges in the 2nd metatarsal over the dorsal aspect during fatiguing unshod walking. Another study with a high-intensity treadmill run for 13.6±6.5 minutes near the anaerobic threshold also reported similar results (Weist, Eils, & Rosenbaum, 2004); they found a significant increase in loading under the 2nd and 3rd metatarsal heads and a significant decrease in electromyography activity in the medial and lateral gastrocnemius and soleus muscles after the high-intensity running. The authors (Weist et al., 2004) suggested that transferring the load from the toes to the metatarsal heads is probably because of local muscles fatigue, which is reflected in the toe flexor muscles. Inactivity of the toe flexor muscles may result in decreased contact area of the toe regions and a transfer of loading to the forefoot. A greater pressure under the 2nd metatarsal may also result in an increased bending moment in the 2nd metatarsal (Bisiaux & Moretto, 2008). These greater bending moments occurred with decreases in the muscle activity of tibialis posterior and toe flexors, and thus it predisposes to a stress reaction (Jacob & Zollinger, 1992).

Decreasing the involvement of the toes during the push-off phase following long-distance running leads to reduced loading under the toes. It causes increased dorsiflexion in the metatarsophalangeal joints and eventually resulting in high load under the forefoot regions (Nagel et al., 2008). The loss of cushioning function of the foot due to the loss of active control mechanisms for the toes during the push-off phase could be also associated with metatarsal stress fractures (Williams Iii, McClay, & Hamill, 2001). However, it seems that the plantar pressure under the whole foot region returns to the initial state after 24-hours rest possibly due to the local muscle recovery with a restoration of their function (Karagounis et al., 2009).

Regarding the loading under the 1st, 4th, and 5th metatarsals, midfoot, and heel, inconsistent findings were observed. The differences in methodology of measuring plantar pressure (i.e. hardware) and/or equipment (i.e. insole plantar shoes vs. embedded walkway) could be the possible explanation for the discrepancy in results. Using sensor insoles may be beneficial to measure the pressure simultaneously with exercise, but it can be influenced by the type of shoes and it may cause discomfort to the runners so that running postures may be changed, thereby affecting plantar pressure (Nagel et al., 2008). The types of surface during running also significantly modifies the plantar pressures (García-Pérez et al., 2013). For instance, running on a treadmill may cause lower peak pressures than over-ground running.

The difference of foot arch types (Chuckpaiwong et al., 2008; Obrien & Tyndyk, 2014), shoe types (Queen et al., 2010), and foot strike techniques (Becker et al., 2012) may also cause inconsistent findings. The different types of long-distance running could be also another factor. Three studies (Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012), showed increased load under the heel, performed under real competition with relatively long-distance (e.g. 20km, 42km, and 246km), while two studies (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008) ran relatively short distances for 10km and 30-minutes under laboratory conditions. In real competitions, runners may ambulate with high speed and it may cause increased load under the heel region: an evidence study (Ho et al., 2010) reported that the plantar pressure at the heel region was significantly increased with increase in speed from 1.5m/s to 2.5m/s, but no changes were observed in the medial forefoot and hallux regions. Thus, the heel region may be more sensitive to increases in speed. Three running studies first conducted long-distance running of more than 30-minutes but then measured plantar pressure post as a walking activity (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008; Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012). We feel that the pressure patterns captured still reflect the result of the long-distance run.

3.5.2 Effect of long-distance running on spatiotemporal gait parameters

The current review shows that runners are generally experienced increasing stride frequency and step frequency and decreasing stride length and aerial time in response to long-distance running. The spatiotemporal gait parameters innately interact during gait. For example, a reduction in contact time has been linked to an increased step frequency and a decreased step length. Runners decrease the amount of time in stance phase in order to increase their step frequency, while maintaining or increasing their swing time (Napier et al., 2015). The reasons for these changes can be related to a tendency to limit the overall loading. As the muscular function may be impaired by excessive loading during long-distance running, the human body is likely to limit the overall loading (Millet et al., 2009) and thereby run with more a soften strike with lower impact rates and shorter and quicker step frequency.

Ground contact time is the duration of the runner's foot in contact with the ground. Generally, when running speed increases, ground contact time is decreased. The altered contact time may cause running injuries: longer contact time in metatarsals combining with high lateral plantar pressure may increase a risk of ankle sprains and/or stress fractures (Willems et al., 2012). In the current review, contact time seems to be affected by long-distance running, yet with conflicting results. As with the plantar pressure, one of the possible explanations for this discrepancy results is the different types of running surface (i.e. overground and treadmill). Running on a treadmill generally resulted in a significantly longer contact time compared to over-ground running (García-Pérez et al., 2013; Schache et al., 2001). The air resistance (Pugh, Lewis Griffith Cresswell Evans, 1970), the variations of intra-stride treadmill speed (Savelberg et al., 1998), and different methods for measuring contact time could also affect the results. Three studies (Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012) employed the pressure plate (embedded in the walkway), reporting a significantly increased contact time, while other studies used an insole (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008) or instrumented treadmill pressure plate (Degache et al., 2013; Morin et al., 2011a), reporting a reduction in contact time.

3.5.3 Effect of long-distance running on kinetics gait parameters

Lower vertical GRF and higher impact acceleration are exhibited after long-distance running. These alterations of kinematics can be interpreted as a reaction to the decreased capacities of the musculoskeletal system by enhancing running safety.

Impact loading is the rapid force applied to the ground by the foot at initial heel contact, and vertical loading rate is how quickly the impact loading is applied. The magnitude of impact loading (Hreljac, Marshall, & Hume, 2000; J. Mercer et al., 2003) and the rate of impact loading (Hreljac et al., 2000; Napier et al., 2015) have been speculated to be a cause of lower limb overuse injuries.

By using an accelerometer externally attached on the tibial tuberosity, a significant increase in impact acceleration has been reported over a 30-minutes run (Mizrahi et al., 2000). When the foot initially contacts the ground, the rapid deceleration gives rise to a shock wave that is transmitted throughout the body (Derrick, Hamill, & Caldwell, 1998; Derrick, 2004). This wave energy is then absorbed by several elements, including the muscles, ligaments, bones, running shoes and running surface. This shock attenuation along with the impact acceleration are one of the essential variables in gait analysis because these are hypothetically related to potential injuries (Mizrahi, Verbitsky, & Isakov, 2001) and fatigue (J. Mercer et al., 2003). Previous studies have been shown that runners who had overuse injuries such as tibial stress fractures had significantly greater peak axial tibial accelerations, vertical mean loading rate, vertical impact peak, and vertical instantaneous loading rates compared with controls (I. Davis, Milner, & Hamill, 2004; I. Davis, Bowser, & Mullineaux, 2010). Similar findings have been also shown in recreational runners during fatigued running (Abt et al., 2011; Derrick, Dereu, & McLean, 2002; J. Mercer et al., 2003; Mizrahi et al., 2000; Verbitsky et al., 1998). This increase in impact acceleration are likely the result of a number of factors including a reduced protection capacity of the fatigued muscles (Mizrahi et al., 2000; Verbitsky et al., 1998).

Leg acceleration has been correlated with GRF during running (Derrick, 2004). Derrick (2004) reported that increasing the knee flexion angle at initial ground contact resulted in decreasing the peak vertical GRF, while it also resulted in increasing the peak impact acceleration. The similar findings were observed from the current review; peak vertical GRF tended to be reduced after running (Millet et al., 2009; Morin et al., 2011b; Morin et al., 2011a), while impact acceleration on the shank was increased (Mizrahi et al., 2000). According to Millet et al. (2009), a runner may adopt a “smoother” running pattern as shown by a lower vertical GRF, an increased stride frequency, and a decreased aerial time without a change in contact time. When mechanical stresses are increased, running style tends towards a safer pattern in order to decrease the load imposed on their lower limb joints during foot strike (Gerlach et al., 2005; Morin et al., 2011a) by limiting the muscle activity at landing (resulting in a lower loading rate) and decreased peak vertical force. While this may suggest that plantar pressure may also be decreased it is likely that the net plantar pressure goes down, but this may not apply to all spatial locations on the foot. For example, the 2nd and 3rd metarsal may still increase while other plantar regions decrease.

3.5.4 Effect of long-distance running on kinematics gait parameters

The lower limb joints appear to be influenced by long-distance running. Altering knee and ankle kinematics may not be surprising given that running-related injuries are most likely to occur on the knee and ankle joints (Jacobs & Berson, 1986; Macintyre et al., 1991). Increased hip excursion can be also associated with fatigued muscles. Previous research reported on developing quadriceps fatigue in parallel with increased vertical hip excursion (Mizrahi et al., 2001). It has also been reported that weakness of hip-stabilizing muscles is one of the major risk factors for running injuries because it causes abnormal lower limb mechanics during running (Ferber, Hreljac, & Kendall, 2009). However, it should be noted that increased hip excursion identified in the current review might be related to restrict running speed on a treadmill. Reduced stride frequency at a constant running velocity due to treadmill gait may imply an increase in the hip vertical displacement of the centre of mass (Anderson, 1996).

Changing landing technique was also observed after long-distance running (Peltonen et al., 2012) from the current review. An early research (Nigg, 1985) reported that in fatigued conditions, runners might change their landing technique from a heel-toe to midfoot landing strategy. Changing landing techniques may be due to compensating for neuromuscular fatigue because a reduced maximum voluntary contraction during plantar flexion of the ankle was observed after the race. This indicates that changing running technique was in part due to muscle fatigue (Peltonen et al., 2012). However, change in landing techniques does not mean more efficiency in running. One study (Peltonen et al., 2012) reported that the running economy was diminished along with changing the landing techniques, as evidenced by their increased cost of transport ($mlO_2kg^{-1}km^{-1}$).

3.5.5 Limitations

This review should be considered with the knowledge that relevant studies may have been overlooked due to not considering non-English journals. Different study design, running types, and gait types might also affect the findings of the reviewed studies. Using a wide range of methodologies to obtain and define gait parameters is complicated for summarising data across all different studies and it may produce inconsistent results. Different unit values due to the use of different techniques and/or software presented further challenges when synthesising findings. Conducting a gait analysis on either overground or treadmill may also affect gait patterns (García-Pérez et al., 2014; Garcia-Perez et al., 2013; Hong et al., 2012) and introduce discrepancies. Further, if shoe conditions are not equivalent between long-distance running and gait tests, the biomechanical results might also present differences due to the different strike techniques between shod and unshod runners. As the plantar pressure is shoe-dependent, different shoe types may also introduce inconsistent outcomes.

3.6 Conclusions

This is the first systematic review that has determined the effect of long-distance running on the gait patterns and plantar pressure distribution in healthy runners. Despite limited evidence, long-distance running appears to alter the plantar pressure, kinetics, kinematics, and spatiotemporal parameters. However, whether those modified parameters eventually lead to the development of running injuries is unclear. For future studies, we recommend a comparison study between magnetic resonance image findings and biomechanical changes to determine whether the biomechanical alteration has a clinical relevance.

Chapter 4. Running Biomechanics Responses after Acute Transition to 5km Unshod Running

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4.1 Preface

This chapter investigates the acute effects on lower limb biomechanics in response to long-distance unshod running, which has yet to be investigated. This study is a novel study evaluating running biomechanics and plantar pressure distribution in response to 5km unshod running in both novice and marathon-experienced runners, including males and females in equal numbers.

4.2 Introduction

Understanding of lower limb biomechanics in response to unshod running provides valuable information for improving existing knowledge regarding the unshod performance and identifying features of running-related injuries. Unlike an intuitive idea that cushioning shoes decreases the rate of running-related injuries, extra support by advanced footwear may result in over-pronation, which is associated with lengthening of the fascia and deltoid ligaments in the medial foot, and possibly predispose to running-related injuries such as plantar fasciitis (Lieberman et al., 2010). In this regard, the popularity of unshod running has been increasing. The greatest biomechanical difference between shod and unshod running is the foot strike techniques. In most of the cases, unshod runners likely adopt either forefoot strike or midfoot strike and it leads to lowering GRF, loading rate, and stride length (Lieberman et al., 2010), whereas shod runners generally adopt rearfoot strike (Larson et al., 2011). However, most of the previous studies (Bonacci et al., 2013; Paulson & Braun, 2014; Squadrone & Gallozzi, 2009) investigated relatively short running bouts (i.e. 5-7 minutes) despite the importance of the fatigue state and particularly focused on the biomechanical difference between shod running and bare-simulated shod running.

More recently, biomechanical changes with relatively longer distance were examined over 50km (Kasmer et al., 2014) and 50-minutes (Lussiana et al., 2016) in bare-simulated shoes and compared with those observed in conventional shoes. After 50km running, four experienced bare-simulated forefoot runners showed a tendency of midfoot strike patterns with increased muscle activity of the tibialis anterior in the pre-contact phase and increased peak pressure under the medial forefoot (Kasmer et al., 2014). Another bare-simulated shod running study (Lussiana et al., 2016) reported decreased leg stiffness and plantarflexion angle at the initial foot contact after 50-minutes running. However, there were limitations including recruiting only four runners (Kasmer et al., 2014), uncommon distances (Kasmer et al., 2014), analysed kinematics in the single plane (Lussiana et al., 2016), and wearing bare-simulated shoes (Kasmer et al., 2014; Lussiana et al., 2016), which has been reported that running in bare-simulated shoes is actually different compared with unshod running (Bonacci et al., 2013). Although the effect of long-distance shod running on the running biomechanics is well documented (H. K. Kim et al., 2017; Morin et al., 2011), it remains unclear how biomechanical lower limb functions are altered after long-distance unshod running. Further, the adaptation of unshod running may differ depending on either fitness levels or gender. According to a review study (Macintyre et al., 1991), recreational runners reported more injuries on the knee, while elite runners exhibited a higher frequency of leg and foot injuries. Female runners are also more likely to experience running-related injuries compared to male runners (Taunton et al., 2002). Considering these limitations, further research is required to provide a complete analysis in response to long-distance unshod running, and hence the benefits and/or limitation of unshod running can be fully realised. Therefore, the purpose of this study was to examine the kinetics and kinematics at the lower limb joints and assess foot plantar pressure in response to 5km unshod running depending on the runners' fitness level and gender.

4.3 Methods

4.3.1 Participants

Anthropometric information on the participants are presented in Table 4.1. Ten marathon-experienced runners (ME) and 10 novice runners (NOVICE) (50% female) voluntarily participated in this study. The ME regularly participated in a half- or full-marathon within three years, while the NOVICE has never taken part in any form of long-distance running. To discriminate runners' fitness level more accurately, Tegner activity scale (Stahl et al., 2008; Tegner & Lysholm, 1985) was employed and scored them between level 1 (work-sedentary) and level 10 (competitive sports, national elite) on their daily basis. All runners recreationally participated in cycling, soccer, or dance. As previous studies reported the foot shape differences between Caucasian and Asian participants, which affects the foot plantar pressure (Hawes et al., 1994; Putti, Arnold, & Abboud, 2010), this study only recruited Caucasian volunteers. The inclusion criteria were *a)* healthy adults (18–50 years old), *b)* no history of significant lower limb injuries in the past, *c)* run habitually in shoes, and *d)* having a heel strike running technique. Those who have a body mass index (BMI) outside of a range of 18-30 and professionally participate in other types of exercise were excluded. Prior to participation, participants signed an informed consent form approved by the University of Auckland Human Participants Ethics Committee (reference number: 016488).

Table 4. 1. *Demographic information and training status in 20 participants.*

Groups	N	Gender (M:F)	Age (yrs)	Height (m)	Weight (kg)	BMI (kg/m^2)	Training status		
							Tegner scale	Km/week	Years training
NOVICE	10	5:5	29±6.8	1.7±0.1	65.6±9.8	22.7±2.0	2.9±1.8	5.4±6.9	2.4±2.9
ME	10	5:5	31.2±9.8	1.73±0.1	65.4±9.8	21.7±1.5	6.5±0.7	31.4±26.1	9.4±5.6
Male	10	-	33.1±9.2	1.75±0.1	72.1±9.2	23.5±1.7	4.4±2.7	23.2±29.1	6.9±6.2
Female	10	-	27.1±6.5	1.68±0.1	59.5±4.8	21.1±1.3	5±1.8	13.6±14.34	4.9±5.24

4.3.2 Protocol

The data collection was conducted on two separate days. On the first day, a pre-run gait assessment during unshod running was performed. On the second day, participants were instructed to run unshod for 5km on a treadmill at a self-selected speed. Before starting the 5km unshod run, all runners walked for seven-minutes with unshod on a treadmill for familiarisation (Matsas et al., 2000). Immediately after the 5km unshod run, the post-run gait assessment was conducted with the same methodology as the pre-run assessment.

4.3.3. Gait Assessment

3D motion capture

An 8-camera Vicon motion analysis system (Vicon Oxford Metrics, Oxford, UK) and three force platforms (Bertec Corporation, Ohio, USA) were used to collect kinematic (sampling rate of 100 Hz) and GRF (sampling rate of 1000 Hz), respectively. Twenty-seven spherical reflective markers were placed on participants based on the Cleveland Marker set. Details of marker placement included: both the anterior superior iliac spines; the superior aspect of the 5th lumbar vertebra–sacral; lateral and medial femoral epicondyles of the knees; lateral and medial malleoli of the ankles; triad consisting of three markers and positioned on the lateral side of the thighs; triad consisting of three markers and positioned on the lateral side of the shanks; between the 1st and 3rd metatarsal heads; at the posterior aspect of the calcaneus at the same height as the metatarsal heads marker. After some participant practice, the gait test was started. All participants ran unshod across the force platforms in the motion capture space and were instructed to run with the similar speed as the 5km unshod run.

Plantar pressure

Foot plantar pressure distribution of the right foot was measured by the Novel emed® pressure platform during unshod running. For the analysis of the foot pressure, the footprint was subdivided into eleven anatomical zones (Figure 4.1): hallux (T1), second-fifth toes (T2-5), metatarsal 1-5 (M1, M2, M3, M4, M5), medial midfoot (MM), lateral midfoot (LM), medial heel (MH), and lateral heel (LH). After practice, participants were asked to run unshod across the plantar pressure mat.

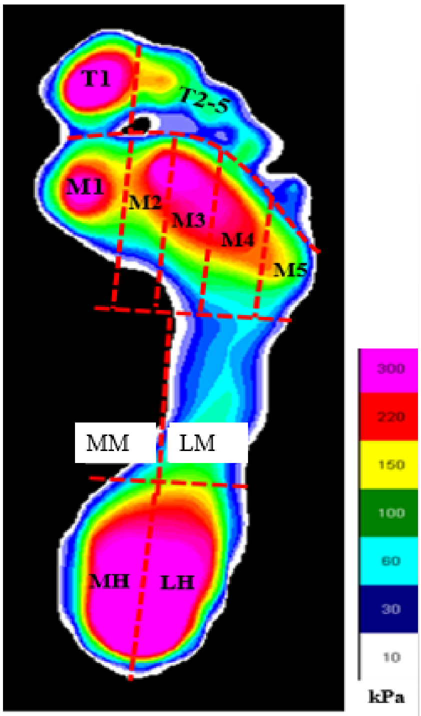

Figure 4. 1. *The location of eleven anatomical regions of interest in the plantar pressure.*

4.3.4 Data Processing and Analysis

Three valid right gait cycle phases were obtained (i.e. foot strike and toe-off should occur within a single force plate). The marker trajectories and GRF data were filtered using an 8 Hz low-pass, fourth-order, zero-lag Butterworth filter. After modelling of each trial, one gait cycle of the right leg was determined by Nexus (Oxford Metrics, Oxford, UK). Three-dimensional joint angles (˚), powers (W) and moments (Nm) of the hip, knee, and ankle were produced by Polygon (Oxford Metrics, Oxford, UK). Powers and moments were normalised by body weight. The angle at the initial foot contact (IFC), maxima, and minima of each plane was extracted for statistical tests from the entire phase (Tables 4.2, 4.3, and 4.4). Spatial-temporal parameters including stride length (m), stride time (s), and cadence were obtained. For kinetic parameters, the maxima and minima were obtained from stance phase for the statistical tests. For plantar pressure, peak pressure (kPa), peak force (N), impulse (N s), and contact area (cm^2) were obtained from each region of interest (ROIs). All these parameters were taken from the means of three valid trials.

4.3.5 Statistical Analysis

SPSS^{TM} (IBM Statistics, SPSS Inc.) was used for statistical analysis. The data were initially assessed for normality by using a Kolmogorov-Smirnov test. The significance of mean differences between pre- and post-gait tests was evaluated using a paired t-test (two-tailed) with a significance set at $P \leq 0.05$. To assess the effect size, Cohen's *d* coefficient was employed. The score was evaluated as small difference ($0.15 \leq d < 0.4$), moderate difference ($0.4 \leq d < 0.75$), large difference ($0.75 \leq d < 1.1$), and very large difference ($d > 1.1$). Additionally, simple linear regressions (Pearson product-moment) were performed to test for correlation between plantarflexion moment and the ankle kinematics and plantar pressures.

4.4 Results

4.4.1 Time-distance Parameters

The mean time for the 5km unshod run was 31.66±6.84 minutes. There was no significant difference between the mean speed of pre-run gait tests and the post-run gait tests (Table 4.2). The stride length was significantly decreased in the NOVICE ($P = 0.004$, *effect size* = 0.52) and female ($P = 0.01$, *effect size* = 0.75) groups, while stride time was significantly increased in NOVICE ($P = 0.03$, *effect size* = 0.5) and male ($P = 0.02$, *effect size* = 0.54) groups.

4.4.2 Kinematics

Overall, the ankle kinematics showed the most prominent modification after 5km unshod running, especially in the female group (Table 4.2). When the participants were stratified by fitness level, there were not many differences at the ankle joints, except for a significant reduction of the peak plantarflexion in the ME. However, when the participants were stratified by gender, all the 3D angles showed significant modifications in the female group - peak plantarflexion (P = 0.005, *effect size* = 0.96) and peak internal rotation (P = 0.006, *effect size* = 1.56) were decreased, and peak inversion (P < 0.001, *effect size* = 1.5) and peak external rotation (P = 0.004, *effect size* = 1.32) were increased after running. Looking at the ankle angle at the IFC in the coronal plane, insignificant decreases in the NOVICE, ME, and male groups were observed, while the female group exhibited significant increases (P = 0.05, *effect size* = 0.89). At the IFC in the transverse plane, the ankle showed a significant external rotation in the female group (P = 0.01, *effect size* = 1.07), while the ME and male groups showed an insignificant reduction.

At the knee joint (Table 4.3), adduction-abduction angle at the IFC showed a significant alteration in the NOVICE group (P = 0.04, *effect size* = 0.78). Other groups showed no significant changes at the knee joint.

At the hip joint (Table 4.3), the angle at the IFC in the sagittal plane showed increases across all the groups, but only the NOVICE (P = 0.006, *effect size* = 1.08) and male (P < 0.001, *effect size* = 1.1) groups reached a significant level. Looking at the IFC in the transverse plane, the male group presented a significant increase (P = 0.02, *effect size* = 1.2), while the NOVICE group showed a significant decrease (P = 0.04, *effect size* = 0.53).

4.4.3 Kinetics

Only peak plantarflexion moment at the ankle was significantly decreased in the female group (P = 0.02, *effect size* = 0.95) after the 5km run. The power generation and absorption showed no significant changes.

4.4.4. Plantar Pressure

In general, the load underneath the toe regions (T1, T2-5) and medial forefoot (M1, M2, M3) were decreased, while the lateral forefoot (M4, M5) and lateral midfoot (LM) were increased after the 5km unshod run (Table 4.4). More specifically, in the female group, peak pressure and peak force underneath T1 was decreased significantly (P = 0.005, *effect size* = 1.21, P = 0.02, *effect size* = 0.85, respectively) and underneath M1 (P = 0.003, *effect size* = 2.07, P = 0.004, *effect size* = 1.7, respectively). In contrast, peak pressure and peak force, and impulse underneath M4 was significantly increased (P = 0.04, *effect size* = 0.71, P = 0.03, *effect size* = 0.89, P = 0.1, *effect size* = 1.05, respectively), underneath M5 (P = 0.007, *effect size* = 0.84, P = 0.01, *effect size* = 0.74) and underneath LM (P = 0.004, *effect size* = 1.44, P = 0.003, *effect size* = 1.19, P = 0.002, *effect size* = 1.31, respectively) in the female group.

The NOVICE group also showed the similar trend. Peak pressure underneath T1 was significantly reduced (P = 0.04, *effect size* = 1.04) and underneath T2-5 (P = 0.04, *effect size* = 0.63). Peak pressure and peak force underneath M1 was also decreased significantly (P = 0.008, *effect size* = 1.24, P = 0.03, *effect size* = 1.12, respectively). Meanwhile, peak pressure and peak force under M5 was significantly increased (P = 0.04, *effect size* = 0.5, *P* = 0.01, *effect size* = 0.4, respectively). Peak pressure and impulse underneath LM significantly elevated (*P* = 0.01, *effect size* = 0.67, *P* = 0.04, *effect size* = 0.66, respectively).

In the ME group, peak pressure and peak force also showed significant decrease underneath M1 (*P* = 0.008, *effect size* = 1.01, *P* = 0.008, *effect size* = 1.3, respectively), underneath M2 (*P* = 0.04, *effect size* = 0.92, *P* = 0.003, *effect size* = 1.04, respectively), and underneath M3 (*P* = 0.02, *effect size* = 1.19, *P* = 0.02, *effect size* = 0.61, respectively). In contrast, underneath LM only the peak pressure significantly increased (*P* = 0.05, *effect size* = 1.01).

In the male group, a significant peak pressure reduction was observed underneath M1 (*P* = 0.02, *effect size* = 0.73), underneath M3 (*P* = 0.04, *effect size* = 0.92), and M4 (*P* = 0.01, *effect size* = 0.6), while no elevation in peak pressure was observed. Impulse underneath MM was significantly increased (*P* = 0.01, *effect size* = 0.04), underneath MH (*P* = 0.04, *effect size* = 0.89), and underneath LH (*P* = 0.04, *effect size* = 0.87).

Table 4. 2. *Mean (SD) for 3D kinematic and kinetic data at the ankle and spatiotemporal parameters.*

T-test showed difference (P ≤ 0.05. ** P ≤ 0.001) between pre and post. Positive values indicate plantarflexion, inversion, and internal rotation.*

Ankle	NOVICE (N=10)		ME (N=10)		Male (N=10)		Female (N=10)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Plantar-dorsiflexion (Sagittal plane)								
Angle at IFC (°)	6.9 (3.8)	5.7 (3.5)	6.2 (2.4)	8.5 (4.7)	7.5 (3.1)	9.3 (5.1)	5.7 (3.2)	5.9 (3.2)
Peak dorsiflexion (°)	23.8 (3.2)	22.8 (5.4)	25.2 (3.2)	25.8 (2.7)	25.3 (3.8)	23.6 (5.7)	23.7 (2.4)	25.1 (2.7)
Peak plantarflexion (°)	-18.9 (6.3)	-14.7 (8.3)	**-22.6 (5.3)**	**-17.2 (6.4)***	-19.5 (5)	-17.1 (6.9)	**-22 (6.9)**	**-14.8 (8) ***
Peak plantarflexion moment ($Nm.kg^{-1}$)	2.7 (.5)	2.5 (.6)	2.8 (.8)	2.3 (.9)	2.4 (.5)	2.1 (1.1)	**3.1 (.5)**	**2.5 (.7) ***
Peak generation ($W.kg^{-1}$)	8.3 (4.1)	6.9 (1.1)	9.3 (4.4)	7.5 (3.5)	7.8 (4.2)	7.5 (3.1)	9.6 (4.2)	7 (2.1)
Peak absorption ($W.kg^{-1}$)	-1.9 (1.6)	-1.9 (1.3)	-1.4 (1.2)	-1.4 (1.7)	-1.2 (1.1)	-1.2 (1.5)	-2 (1.3)	-2 (1.5)
Inversion-eversion (Coronal plane)								
Angle at IFC (°)	.7 (1.4)	.3 (.3)	.6 (.5)	.5 (.7)	1 (1.1)	.3 (0.8)	**.1 (.6)**	**.54 (.3)***
Peak inversion (°)	1.7 (1.7)	1.7 (1.3)	1.3 (.6)	1.8 (1.2)	1.9 (1.6)	1.1 (0.9)	**1.1 (.7)**	**2.5 (1.1)****
Peak eversion (°)	-4.7 (2.8)	-4.2 (3)	-5.2 (2.3)	-3.9 (1.7)	-4.9 (2.7)	-3.9 (2.6)	-5 (2.4)	-4.2 (2.2)
Peak eversion moment ($Nm.kg^{-1}$)	1.4 (.9)	1.9 (.4)	1.3 (1)	1.6 (1)	.6 (.7)	.9 (.9)	1.4 (1.1)	1.2 (1.1)
Internal-external rotation (Transverse plane)								
Angle at IFC (°)	-4.8 (7.9)	-5 (5.7)	-4.5 (5.1)	-4.5 (3.8)	-6.9 (5.5)	-3.5 (5.3)	**-1.8 (5)**	**-6.3 (3.4)***

Peak internal rotation (°)	7.6 (5)	5.16 (3.1)	6.9 (3.7)	2.9 (2.8)	4.7 (3.5)	3.1 (3)	**9.9 (3.2)**	**5 (3)***
Peak external rotation (°)	-12.8 (7.4)	-14.1 (6.6)	-11.4 (5.9)	-14.4 (3.3)	-13.6 (6.8)	-11.6 (5.8)	**-10.6 (6.3)**	**-16.9 (2.4)***
Peak external rotation moment ($Nm.kg^{-1}$)	-.4 (.14)	-.4 (.12)	-.3 (.2)	-.4 (.2)	-.3 (.2)	-.3 (.2)	-.4 (.2)	-.5 (.2)
Spatiotemporal parameters								
Gait speed (km/h)	11.08 (1.39)	10.77 (1.43)	11.07 (1.59)	10.21 (1.35)	11.53 (1.51)	11.12 (1.44)	10.74 (1.51)	9.96 (1.32)
Stride length (m)	**2.27 (.33)**	**2.09 (.36) ***	2.31 (.37)	2.12 (.27)	2.39 (.34)	2.26 (.27)	**2.19 (.32)**	**1.96 (.29) ***
Stride time (s)	**.71 (.04)**	**.73 (.05) ***	.73 (.04)	.74 (.03)	**.71 (.06)**	**.74 (.05) ***	.73 (.03)	.74 (.04)
Cadence	168.73 (10.66)	161.23 (15.77)	163.93 (9.19)	161.47 (5.75)	168.97 (12.65)	159.7 (14.68)	163.7 (5.89)	163 (7.77)

IFC, initial foot contact. ME, Marathon-experienced runners

Table 4. 3. *Mean (SD) for 3D kinematic and kinetic data at the knee and hip in four groups.*

T-test showed difference ($P \leq 0.05$. ** $P \leq 0.001$) between pre and post. Positive values indicate flexion, adduction, and internal rotation.*

Knee	NOVICE (N=10)		ME (N=10)		Male (N=10)		Female (N=10)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Flexion-extension (Sagittal plane)								
Angle at IFC (°)	21.4 (5)	24.2 (3.7)	18.5 (2.5)	20.8 (7.3)	19.1 (4)	24.7 (6.7)	20.7 (4.4)	20.3 (4.8)
Peak flexion (°)	89.1 (10.7)	89.5 (10.9)	84.8 (11.3)	83.5 (8.7)	88.8 (13.1)	88.1 (10.6)	85.1 (8.5)	84.9 (9.9)
Peak extension moment ($Nm.kg^{-1}$)	3.6 (1.3)	4.1 (1.8)	3.8 (1.3)	3.9 (1.5)	3.2 (1.5)	3.3 (2)	4.2 (0.7)	4.6 (1)
Peak power generation ($W.kg^{-1}$)	3.2 (2.2)	5 (1.4)	3.2 (2.6)	4.1 (2.5)	2.7 (2.4)	4.5 (1.9)	3.6 (2.3)	4.6 (2.2)
Peak power absorption ($W.kg^{-1}$)	-3.3 (3)	-5.9 (3.6)	-4.2 (3.8)	-5.5 (4.7)	-3.2 (3.5)	-5.6 (4.5)	-4.2 (3.3)	-5.8 (3.9)
Adduction-abduction (Coronal plane)								
Angle at IFC (°)	**0.2 (4.4)**	**1.7 (3.2)***	3.4 (2.2)	2.9 (3.7)	2.3 (3.8)	2.6 (4.4)	0.9 (3.6)	2.5 (2.7)
Peak adduction (°)	16.4 (7.7)	17.4 (6.4)	21.8 (5)	21.8 (4.4)	19.3 (5.7)	19 (6.5)	19 (8.2)	20.2 (5.3)
Peak abduction moment ($Nm.kg^{-1}$)	1.2 (.8)	1.1 (.9)	.6 (.5)	.6 (.5)	1.6 (2.2)	1.5 (2.7)	1 (1)	.9 (.9)
Internal-external rotation (Transverse plane)								
Angle IFC (°)	-13.5 (8.5)	-12.6 (10.9)	-16.5 (7.4)	-17.3 (9.3)	-13.1 (9.3)	-9.9 (10.6)	-15.7 (7.1)	-19.6 (7.7)
Peak external rotation (-)	-25.9 (7)	-25.7 (9.9)	-25.9 (11.2)	-25.7 (7.4)	-23.5 (6.3)	-22.8 (8.2)	-28.3 (11.1)	-28.5 (8.2)
Peak external rotation moment ($Nm.kg^{-1}$)	.4 (.3)	.3 (.3)	.1 (.1)	.1 (.1)	.3 (.3)	.2 (.2)	.2 (.3)	.3 (.3)

Hip								
Flexion-extension (Sagittal plane)								
Angle at IFC (°)	**35.7 (4.3)**	**39 (2.9) ***	31 (4.6)	32.5 (5.5)	**33.1 (4.1)**	**38 (4.9) ****	32.8 (5)	33.9 (5.9)
Peak flexion (°)	45 (6.4)	47.6 (4.3)	40.2 (6.8)	41.2 (6)	42.2 (7.8)	44.4 (4.6)	43 (6.2)	44.4 (7.5)
Peak extension moment ($Nm.kg^{-1}$)	1.5 (.3)	1.5 (.3)	1.6 (.3)	1.7 (.4)	1.4 (.3)	1.3 (.3)	1.7 (.3)	1.7 (.3)
Peak generation ($W.kg^{-1}$)	1.5 (1.4)	1.7 (1.9)	1.3 (1.8)	.7 (1.1)	1.4 (1.5)	1.6 (2.1)	1.4 (1.7)	.9 (1)
Peak absorption ($W.kg^{-1}$)	-3.8 (2.4)	-3.5 (2.1)	-3.4 (1.6)	-3.2 (1.7)	-3.5 (2.2)	-2.7 (1.5)	-3.6 (1.9)	-3.8 (2.1)
Adduction-abduction (Coronal plane)								
Angle at IFC (°)	5.7 (4.4)	5.2 (3.9)	8 (4)	5.4 (3.8)	5.3 (3.2)	4.5 (3)	8.5 (4.4)	6 (4.3)
Peak adduction (°)	10.4 (3.5)	10.9 (4.6)	13.9 (4.7)	13 (3)	10.5 (3.7)	9.8 (3.7)	13.8 (4.6)	14.1 (3.2)
Peak abduction (°)	-8 (3.9)	-7.2 (4.3)	-8.7 (3.7)	-9.7 (4.5)	-8.6 (4.5)	-10.2 (4.8)	-8.1 (3)	-6.6 (3.4)
Peak abduction moment ($Nm.kg^{-1}$)	2.6 (1.3)	2.5 (1.4)	2.7 (1.2)	2.4 (1.1)	2.1 (1.3)	1.9 (1.2)	3.2 (1)	3 (1.2)
Internal-external rotation (Transverse plane)								
Angle at IFC (°)	**1.9 (8.4)**	**-.72 (9) ***	1.9 (3.1)	-.5 (8.4)	**-3.3 (3.8)**	**-8 (4.1) ***	7.5 (7.2)	5.3 (5.7)
Peak internal rotation(°)	8.2 (7.2)	8.7 (6.4)	8.5 (8.9)	7.5 (7)	3.3 (5.3)	3.8 (4)	13.4 (6.9)	12.3 (5.8)
Peak external rotation (°)	-5.1 (8.5)	-6.4 (7.3)	-5.2 (9.2)	-7.9 (7.1)	-10.8 (5.7)	-12.1 (4.6)	0.5 (7.4)	-2.2 (5.4)
Peak external rotation moment ($Nm.kg^{-1}$)	.5 (.3)	.6 (.3)	.8 (.7)	.6 (.3)	.4 (.3)	.5 (.3)	.8 (.6)	.7 (.2)

IFC, initial foot contact. ME, Marathon-experienced runners

Table 4. 4. *Mean (SD) for peak pressure, peak force, impulse, and contact area.*

T-test showed difference (P ≤ 0.05) between pre and post.*

	NOVICE (N=10)		ME (N=10)		Male (N=10)		Female (N=10)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Peak pressure (kPa)								
T1	**480.7 (217.9)**	**296.4 (127.3)***	426.9 (162.2)	309.5 (196)	438.9 (204.5)	340.6 (166.7)	**468.7 (181.9)**	**265.3 (154.3)***
T2-5	**230.2 (89.1)**	**174.9 (87.2)***	239.9 (81.9)	219.7 (77.6)	246.7 (95.7)	207.5 (90.6)	223.4 (72.5)	187.1 (79.3)
M1	**510.6 (175.8)**	**313.7 (139.1)***	**571.2 (249.8)**	**316.5 (250.4)***	**576.7 (267.1)**	**389.8 (241.3)***	**505.1 (145.4)**	**240.4 (106.7)***
M2	413.2 (165.6)	351.4 (79.5)	**472.9 (173.6)**	**354(58.7)***	458.5 (155.9)	356.1 (76.3)	427.5 (186.2)	349.3 (62.6)
M3	406.2 (114.6)	369.9 (68.1)	**434.7 (76.7)**	**364.9 (32.3)***	**446.6 (105.3)**	**365 (68.1)***	394.3 (82.9)	369.8 (32.3)
M4	353.8 (124.7)	351.6 (117.6)	343.9 (85.9)	360.7 (103.8)	**396.3 (106.2)**	**336 (93.8)***	**301.4 (81.9)**	**376.3 (122.3)***
M5	**302.8 (145.9)**	**394.1 (219.2)***	263.1 (141.8)	332 (193.4)	307.2 (130.4)	310.9 (188.1)	**258.6 (154.8)**	**415.2 (214.9)***
MM	92.6 (58.6)	86.5 (61.8)	107.6 (51.9)	113.2 (58.8)	115.8 (46.6)	129.6(46.6)	84.4 (59.5)	70.2 (59.4)
LM	**200.4 (72.3)**	**257.4 (96.5)***	**149.1 (32.7)**	**219.7 (93.7)***	197 (69.1)	218.7 (95.2)	**152.5 (43.4)**	**258.4 (94.5)***
MH	315.6 (120.5)	296.6 (137.9)	367.5 (104.8)	376.7 (120.4)	339.9 (121.2)	382.4 (103.8)	343.1 (111.1)	290.8 (147.1)
LH	313.2 (124.3)	301.4 (148.6)	353.3 (93.9)	362.6 (105.9)	336.6 (123.9)	386.6 (108.4)	329.9 (98.9)	277.4 (130.4)
Peak force (N)								
T1	167.5 (63.9)	123.3 (58.3)	149.6 (56)	130.1 (91.9)	164.3 (69.7)	151.9 (75.7)	**152.8 (49.7)**	**101.5 (68.9)***
T2-5	83.8 (42.5)	70 (42.4)	75.1 (27.3)	75 (31.4)	81.9 (31.6)	71.7 (35.8)	77 (39.8)	73.3 (38.9)

M1	**317.4 (126)**	**216.3 (88.3)***	**309.1 (50.2)**	**199.8 (107.5)***	**339.7 (123)**	**247.3 (90.4)***	**286.9 (42)**	**168.9 (88.9)***
M2	264.4 (89)	216.1 (65.9)	**262.8 (52.5)**	**201.1 (65.1)***	289 (76.8)	228.8 (61.8)	**238.2 (57.8)**	**188.4 (63.1)***
M3	260.4 (76)	251.1 (68.5)	**262.2 (50.4)**	**233.2 (44.9)***	294.7 (67)	259.1 (69.1)	227.8 (36.7)	225.2 (38.4)
M4	193 (58.8)	207.2 (70.1)	169.7 (47.2)	188.3 (50.6)	207.6 (53.4)	200.9 (73.2)	**155.1 (40.1)**	**194.6 (48)***
M5	**100.5 (44.9)**	**123 (57.1)***	77.5 (34.5)	91 (41.8)	96.5 (41.5)	99.8 (56.4)	**81.5 (40.6)**	**114.3 (47.7)***
MM	16.8 (19.1)	17.2 (19.9)	25.2 (19.3)	19.6 (14.9)	22.9 (18.7)	25.1 (17.8)	19.2 (20.4)	11.6 (14.3)
LM	224.9 (113.4)	262.6 (124.7)	157.8 (81.5)	202.3 (99.2)	248.8 (113.1)	241.2 (133.2)	**133.9 (43.4)**	**223.6 (97.4)***
MH	274.7 (110.6)	262.7 (127.2)	299.8 (85.9)	330.7 (110.1)	316.6 (106.4)	381.7 (88.9)	257.9 (82)	211.7 (83.2)
LH	259.4 (96.9)	271.5 (143.2)	284.5 (62.5)	294.2 (84.9)	303.4 (90.2)	353.4 (102.8)	240.5 (57.4)	212.3 (79.8)
Impulse (N s)								
T1	23.4 (8.6)	18.6 (8.8)	22.9 (9.5)	21.2 (15.1)	22.8 (10)	23.1 (13.7)	23.5 (8)	16.7 (10)
T2-5	13.3 (9.1)	11.5 (7.3)	11.6 (4.1)	13 (5.7)	11.5 (5)	11.1 (5.6)	13.4 (8.6)	13.3 (7.3)
M1	44 (16.7)	33 (13.9)	44.6 (8.4)	32 (18.3)	45.9 (16.6)	37.7 (14.9)	**42.7 (8.4)**	**27.3 (15.7)***
M2	38.3 (12.2)	34.5 (9.6)	**41.6 (11.6)**	**34.1 (12.2)***	42.6 (12.4)	35.9 (11.2)	37.3 (10.9)	32.7 (10.5)
M3	36.5 (9.4)	39.2 (8.9)	40.8 (10.8)	39.4 (8 .6)	42.5 (10.9)	39.3 (10.5)	**34.8 (8)**	**39.3 (6.6)***
M4	**26.1 (9.2)**	**30.7 (10.6)***	24.2 (6.2)	29.9 (9.8)	27.6 (7.1)	28.4 (10)	**22.7 (7.8)**	**32.2 (10.1)***
M5	**12 (6.3)**	**16.6 (8.9)***	9.8 (4.3)	12.7 (7)	11.4 (5.2)	12.5 (7.7)	**10.5 (5.8)**	**16.8 (8.2)***
MM	1.2 (1.5)	1.5 (1.9)	1.8 (1.5)	1.8 (1.4)	**1.6 (1.4)**	**2.1 (1.6)***	1.4 (1.6)	1.2 (1.6)
LM	**19.9 (9.6)**	**28 (14.5)***	15.5 (8.4)	22.5 (13)	22.2 (10.4)	24.1 (14.7)	**13.3 (4.8)**	**26.4 (13.3)***
MH	22.4 (15.1)	26.3 (20.8)	**23.8 (6.7)**	**33.3 (12.6)***	**25.8 (14.1)**	**39.4 (16.5)***	20.5 (7.9)	20.2 (11.7)
LH	18.1 (11.1)	23.5 (17.4)	**18.4 (5)**	**27.1 (9.3)***	**20.3 (10.7)**	**31.2 (14.1)***	16.2 (5)	19.4 (11)
Contact area (cm^2)								

T1	11 (1.1)	10.4 (1.6)	10.1 (1.5)	9.9 (2.4)	10.7 (1.6)	10.6 (2)	10.3 (1.2)	9.6 (2.1)
T2-5	12.1 (2)	11.4 (3.6)	11.4 (2.4)	11.8 (2.7)	12.2 (1.8)	11.6 (3.5)	11.4 (2.6)	11.6 (2.9)
M1	13.7 (1.8)	13.1 (2.1)	13.1 (1.8)	12.2 (2.8)	14.1 (2)	13.5 (2.3)	12.8 (1.2)	11.8 (2.4)
M2	10.7 (1.5)	10.4 (1.9)	10.3 (1.7)	9.7 (1.9)	11 (1.8)	10.8 (2)	10 (1.3)	9.4 (1.6)
M3	**11.4 (1.3)**	**11.6 (1.3)***	15 (12.3)	10.6 (1.6)	11.8 (1.5)	11.6 (1.5)	14.6 (12.4)	10.7 (1.4)
M4	9.6 (1)	9.7 (1.3)	9.5 (1.6)	9.6 (1.5)	9.8 (1.3)	10.1 (1.6)	9.3 (1.3)	9.2 (1)
M5	6.2 (0.7)	6.7 (1.3)	6 (1.3)	5.9 (0.9)	6.2 (1.2)	6.7 (1.4)	6 (0.9)	5.9 (0.7)
MM	2.7 (2.7)	2.7 (2.7)	3.7 (2.9)	2.7 (2)	3.5 (2.8)	3.7 (2.4)	3 (2.9)	1.7 (1.8)
LM	24.2 (5.1)	23.3 (4.3)	21.4 (5.8)	20.4 (7.5)	26.2 (4.4)	23.2 (7.6)	**19.4 (4.2)**	**20.6 (4.1)***
MH	15.8 (2.3)	15.9 (3.6)	16.4 (2.7)	16.3 (3.5)	17.3 (2.6)	18.3 (3.3)	**14.9 (1.8)**	**13.9 (2)***
LH	15.9 (2.3)	16.3 (3.3)	16 (2.5)	16.3 (2.9)	**17.2 (2.3)**	**18.2 (2.8) ***	14.7 (1.6)	14.4 (1.8)

4.4.5 Effect of Moment Changes

After analysing all the gait kinetics and kinematics, a further question was raised about why the female group only showed the significant changes compared to other groups, especially in the ankle. It is possible that the reduced plantarflexion moments after the 5km unshod run lead to modifying the ankle kinematics as well as plantar pressure in the female group. To test this assumption, a differentiation between pre and post was obtained from each gait parameter and we performed the correlation test against a differential plantarflexion moment. The differential plantarflexion moment showed a significant negative correlation with the differential plantar pressure under the M5 (r = -0.89, n = 10, P = 0.001), M4 (r = -0.91, n = 10, P = 0.0002), and LM (r = -0.85, n = 10, P = 0.002) in the female group (Figure 4.2). Among the kinematics, internal rotation angle at the ankle revealed a significant negative correlation with the plantarflexion moment (r = -0.73, n = 10, P = 0.02).

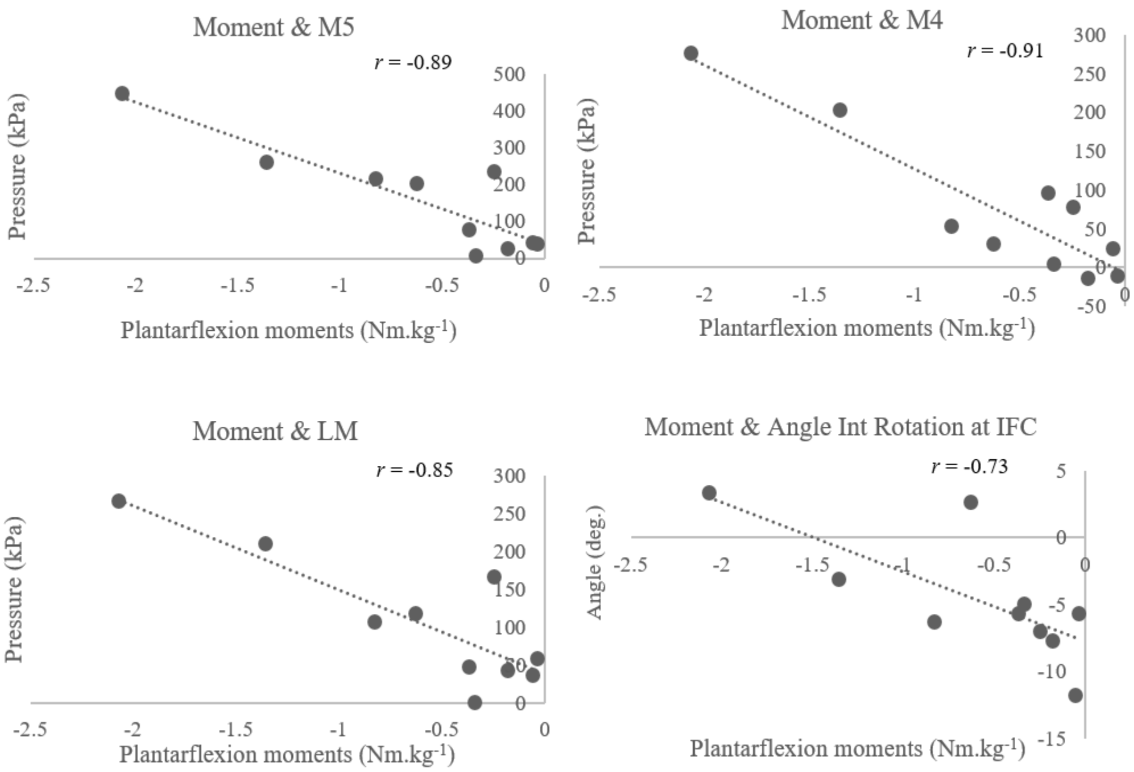

Figure 4. 2. Scatter plot of pre and post changes in plantar pressure, internal rotation angle at IFC, and plantarflexion moments in the female group.

4.5 Discussion

Results from the current study support the following conclusions. *First*, ankle kinematics and kinetics following 5km running showed significant changes. *Second*, females were significantly affected by 5km unshod running, highlighted by modification of ankle kinematics and plantar pressure. *Third*, 5km unshod running resulted in an increased loading under the lateral forefoot (M4, M5) and lateral midfoot (LM), while the load underneath the toe regions (T1, T2-T5) and medial forefoot (M1, M2, M3) decreased, especially for females and NOVICE runners. *Fourth*, modification of ankle kinematics in females may be associated with lowering of the plantarflexion moment, suggesting that the fatigued plantar-flexor muscles after 5km running may play a role (and further EMG evaluation is required). *Fifth*, kinetic and kinematic results do not demonstrate differences following 5km running when participants were stratified by fitness level. This may suggest that in healthy runners, fitness level is less likely a predictor of running-related changes in 5km unshod running.

In the current study, there was a trend of decreasing plantarflexion angle, especially in the female group. The previous study confirmed that plantarflexion angle decreased over a 50-minutes treadmill run in a bare-simulated shoe (Lussiana et al., 2016). Such kinematic changes may indicate that there was a transition of the strike patterns from forefoot to rearfoot as exercise duration increases, and this might be related to the muscle fatigue. The peak plantarflexion moment was decreased after the 5km unshod running across all the groups (Table 4.2), but only the female group reached a significant level, which might suggest their plantar flexors were fatigued.

Further, female runners showed a trend of increasing inversion and external rotation and lowering plantarflexion in the current study. This combination of the ankle movement in the closed kinematic chain might be related to the supinated foot. Excessive supination might be one of the risk factors of running-related injuries (Burns, Keenan, & Redmond, 2005) as landing with a smaller area of the foot (4^{th} and 5^{th} metatarsals and lateral midfoot) would be less ideal for shock absorption, and hence reducing efficient force distribution. Interestingly, this inward roll of the foot kinematic change was only observed in the female group, and this might be associated with the muscle strength, flexibility, and anatomical difference between genders. As shown in the knee and hip kinematics (Table 4.3), different trends of changing joint angles were often observed between the male and female groups. For instance, the hip angle for the female was internally rotated, while the male was externally rotated at the IFC over running. The knee peak adduction and external rotation angle were increased in the female group, while the male was shown to be decreased after the 5km run. Further, it has been reported greater ligamentous laxity of the lateral ankle was observed in the female when compared with the male (Wilkerson & Mason, 2000), which might be related to the inward roll of the foot. The previous study also reported that the frequency of the females' injuries was 1.6 times greater than males, and the most frequently injured body site was the ankle (Zelisko, Noble, & Porter, 1982). Female athletes who had greater tibial varum and calcaneal eversion range of motion were also more likely to suffer ankle ligament trauma than males (Beynnon et al., 2001). Further, we found that there was a strong, negative correlation between plantarflexion moment and pressure that measured under the M4, M5, and LM, and internal rotation angle at IFC in the female group. This suggests that the lack of functional activity of plantar flexor muscles may cause lack of controlling forefoot motion during running, and hence altering the ankle kinematics.

With regards to the plantar pressure, the decreased involvement of the toes and medial forefoot was observed after the running in the current study. This decreased loading under M1, M2, and M3 post-run are contrary to the previous shod running studies of Bisiaux and Moretto (2008) and Nagel et al. (2008) that reported an increase in the loading under M1, M2, and M3. This contrasting result might be due to the difference of foot strike patterns. Shod runners generally adopt a heel strike technique, which results in the load increasing under the medial forefoot (i.e. M2, M3) and heel (Bisiaux & Moretto, 2008; Nagel et al., 2008). In contrast, unshod runners usually adopt a forefoot strike technique, which possibly causes the load increasing under the lateral forefoot. These findings are similar to the previous unshod running studies, reporting greater peak pressure under the lateral forefoot during unshod running when compared to shod running (Bergstra et al., 2015; Mei et al., 2015). Further, the plantar pressure under the lateral edge of the metatarsals was shown to be higher in habitual unshod walkers than shod walkers, suggesting greater load bearing under the lateral forefoot (D'AoÛt et al., 2009). In the current study, the contribution of the medial aspect was clearly decreased, while the lateral aspect was increased in all groups after the run, suggesting long-distance unshod running increases the risk for 4th and 5th metatarsal stress fractures.

A few limitations were identified that should be considered when interpreting the results of this study. Although we analysed the plantar pressure distribution along with the 3D joint angles, care should be taken to interpret the kinematic results, as there remains some possibility of including errors in the joint transverse plane during the motion capture. The low reliability and high errors reported in a previous systematic review (McGinley et al., 2009), but the current study showed that alteration of 3D angle corresponded with the modification of the plantar pressure. Less than 5 ˚ of SD is also generally acceptable for the ankle joint with the exception of the hip and knee rotation (McGinley et al., 2009). In addition, our relatively small study sample size may result in statistical power issues in this study, although we included the effect size. Further, the different running speeds between pre and post tests were difficult to control for each participant. However, there was no significant differences observed between pre- and post-running in the current study. In addition, due to the absent of control intervention with shod running, all of the effects observed in this study may not be entirely explained by 5km unshod running. Finally, although we suggest some roles that muscles play in our discussion we did not measure EMG and inferred our results from joint moments.

Chapter 5. Evaluation of MR Images of the Ankle and Foot in Response to Long-Distance Running: A Systematic Review

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5.1 Preface

Very little information is available in the literature on the effects of long-distance running on the ankle joint, and also there is no study systematically determining it. This chapter represents the first study to systematically present an overview of the literature describing the evaluation of ankle and foot MRIs following long-distance running.

5.2 Introduction

Over the past decades the number of amateur participants in long-distance running events (i.e. 5km–42km) has been increasing, becoming one of the most popular fitness activities (Jokl, Sethi, & Cooper, 2004). Despite obvious health benefits, it remains controversial whether the repetitive and excessive loading imposed on the lower limbs have a deleterious effect on the joints. According to in-vitro laboratory research, acute and cumulative impact and torsional joint loading may cause articular damage and joint dysfunction (J. Buckwalter, 2002; J. A. Buckwalter & Lane, 1997). An animal model study found degenerative articular alterations in the knee joint under simultaneous shear stress and axial overloading (Dekel & Weissman, 1978). Repetitive loads also provoked progressive cartilage degeneration on patellar osteochondral specimens (Zimmerman et al., 1988). In the humans, although this excessive loading is generally well absorbed and distributed by muscles, ligaments, and cartilages, the lower limbs are still exposed to a substantial burden during long-distance running, especially when the muscle becomes fatigued. Thus, excessive loading with long duration imposed on the lower limb joints may lead to running-related injuries such as tibial stress syndrome, metatarsal stress syndrome, patellar tendinitis, Achilles tendinitis, and plantar fasciitis.

Numerous studies have employed MRI to examine pathological, morphological and/or biochemical changes in response to long-distance running, but such studies have mainly focused on the knee joint (Hinterwimmer et al., 2014; Hohmann et al., 2004; Kersting et al., 2005; M. A. Kessler et al., 2008; W. Krampla et al., 2001; W. W. Krampla et al., 2008; Kursunoglu-Brahme et al., 1990; Lohman et al., 2001; Luke et al., 2010; Mosher et al., 2005; Mosher et al., 2010; Schueller-Weidekamm et al., 2006; Shellock & Mink, 1991;

Stahl et al., 2008; Stehling et al., 2011; Subburaj et al., 2012). Many of these studies found significant changes including bone marrow edema (BME), joint effusion and cartilage thickness and volume, but such changes seem to return to baseline after a rest period (one-hour to eight-weeks) (Hesper et al., 2015; M. A. Kessler et al, 2008; W. Krampla et al., 2001). While the ankle and foot complex is one of the most common injured sites in response to long-distance running (Macintyre et al., 1991; Taunton et al., 2003), very little information is available determining the effect of long-distance running on the ankle and foot. Therefore, the objective of this systematic review is to present an overview of the literature describing the evaluation of MRI of the ankle and foot in response to long-distance running.

5.3 Methods

5.3.1 Search Strategies and Selection Process

This systematic review was conducted and reported based on principles from the PRISMA guidelines (Moher et al., 2009). Studies were identified from searches of Scopus, Web of Science, Embase, and Ovid Medline, published in English between 1990 and present. The final search was conducted on 19 September 2016. The following search terms were used: 1) mri OR "magnetic resonance imaging, AND 2) running OR run OR runners OR jog OR jogging OR marathon OR long distance OR distance run, AND 3) foot OR feet OR ankle.

Titles and abstracts of all identified studies were initially screened by a single reviewer (HKK) using specific eligibility criteria as shown below, and another reviewer (SAM) checked this process. Full articles were retrieved from this initial screening, and full-text was read for further narrowing down. Reference lists from the full-text articles were also examined for additional relevant articles.

5.3.2 Eligibility Criteria

Studies were included if it meets all of the following inclusion criteria: 1) the duration of long-distance running should be at least 30-minutes; 2) long-distance running can be performed within a day or over several days; 3) MRI should be undertaken before (baseline) and after (or during, follow-up) long-distance running; 4) the outcome of interest was MRI findings of the ankle and/or foot; 5) only healthy and asymptomatic populations were included. Studies were excluded if: 1) they were cadaver or animal studies; 2) full-text articles were written in non-English language; 3) studies were review, conference abstract, and press papers.

5.3.3 Data Extraction

Data extracted included study design, number of participants, participant demographics (gender, age, body mass index (BMI), injury history of lower limb, and training history if available), inclusion and exclusion criteria, types of long-distance running (speed, distance, and environment if available). MRI findings, magnetic field, MRI sequences, body sites for MRI, the time points of MRI for baseline and follow-up were also noted. Data was extracted by a single reviewer (HKK) and was checked by a second reviewer (SAM). The included study characteristics were given in Table 5.1.

5.3.4 Methodological Quality Assessment

A modified version of the Quality Index (QI) (Downs & Black, 1998) was used to evaluate the methodological quality of the selected studies. This original tool includes 27 questions for evaluation of reporting, external validity, internal validity (bias and confounding) and power. Of these 27 questions, the power-related question (question 27) was excluded because it was not applicable to the current review (Deeks et al., 2003). Each question was rated as ‘yes’, ‘no’ or ‘unable to determine’; if the answer was positive, it scored one, and otherwise zero. Question five was the exception that had three ratings: 2=‘yes’; 1=‘partially’; and 0=‘no’. Thus, 27 was the maximum score from the QI. Studies were considered to be high-quality if the summed QI was ≥80%; studies were considered to be moderate-quality if the QI was ≥47% and <80%; studies were considered to be poor-quality if the QI was <40% (Carroll et al., 2015; Meyer et al., 2014; Weierink et al., 2013)

5.4 Results

5.4.1 Search Results

With initial search terms, 533 articles were produced after removing the duplication. All abstracts and titles were screened, and 523 articles were removed based on the eligibility criteria. Ten articles were identified as potentially relevant to the current study and six articles were removed after reading full-text. Four articles were finally selected in the current review. A flow diagram of selection process and search results was shown in Figure 5.1.

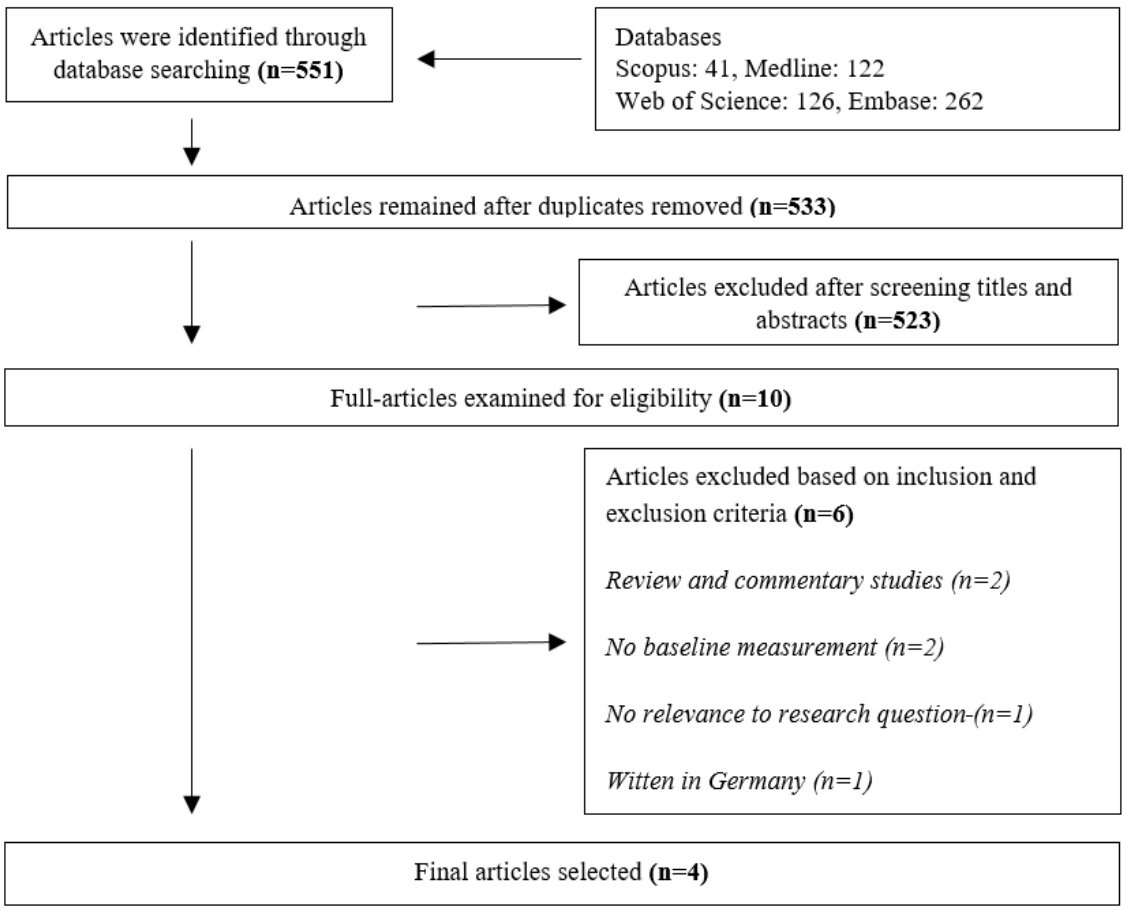

Figure 5. 1. Flow diagram of study selection process.

5.4.2 Description of Studies

Four studies (Freund et al., 2012; Kornaat & Van de Velde, 2014; Schutz et al., 2014; Trappeniers et al., 2003) investigating the effect of long-distance running on the ankle and foot complex using MRI were included in this systematic review. All the studies compared MRI results between baseline and follow-up within the same participants. None of these studies performed a single long-distance running. Two studies (Freund et al., 2012; Schutz et al., 2014) performed an ultra-marathon race (4486km-4487km) for about consecutive 64 days, and one study (Trappeniers et al., 2003) conducted 30-minutes outdoor run per day for consecutive seven days. The remaining study (Kornaat & Van de Velde, 2014) conducted seven-month intensive training, consisting of six training sessions per week and two major international races. All the studies recruited healthy adults without gender restriction. The participant's fitness levels varied from sedentary individuals to professional runners. The details of demographic information of participants and inclusion and exclusion criteria are provided in Table 5.1.

5.4.3 MRI Protocol

All the selected studies repeated MRI before and after or during long-distance running. The magnetic field of all studies was 1.5T (Tesla). Two studies (Kornaat & Van de Velde, 2014; Trappeniers et al., 2003) conducted MRI examination twice, once at baseline and one during follow-up. Baseline MRI was performed prior to initiation of running (Trappeniers et al., 2003) or one month prior to a training season (Kornaat & Van de Velde, 2014). Follow-up study was conducted 10-20 hours following exertion (Trappeniers et al., 2003) or one month after the completion of the training season (Kornaat & Van de Velde, 2014). Another two studies (Freund et al., 2012; Schutz et al., 2014) performed MRI examination repetitively (five times in total), before and during long-distance running, approximately every 900km-1000km. Two studies used a dedicated foot coil with 8-channals (Freund et al., 2012; Schutz et al., 2014), while one study adopted a head coil (Trappeniers et al., 2003) and the remaining study (Kornaat & Van de Velde, 2014) did not describe their technique. T2* mapping was performed in one study (Schutz et al., 2014) to assess biochemical changes in the tibiotalar cartilage along with measuring its thickness. One study determined

(Freund et al., 2012) the Achilles tendon diameter, signal intensities in the tendons, bones and soft tissue in the ankle and hind foot regions. Two remaining studies (Kornaat & Van de Velde, 2014; Trappeniers et al., 2003) assessed BME of the ankle and foot, and one (Kornaat & Van de Velde, 2014) of these included multiple joints including the hips, knees, ankles and feet. Details of MRI protocols can be found in Table 5.1.

5.4.4 MRI Grading System

Three (Kornaat & Van de Velde, 2014; Schutz et al., 2014; Trappeniers et al., 2003) of four studies adopted quantitative grading systems. One study (Schutz et al., 2014) used the Outerbridge MRI grading system which was modified by Mosher (2006). Another study (Kornaat & Van de Velde, 2014) used the Knee Osteoarthritis Scoring System which was modified and validated by Kornaat et al. (2005). One study (Trappeniers et al., 2003) used a four-point grading scale system, but further details were not provided.

5.4.5 MRI Findings

Ankle bones

Two (Kornaat & Van de Velde, 2014; Trappeniers et al., 2003) of four studies assessed edema in ankle bones including talus, tibia and/or fibula. These two studies reported that a number of participants (30%-88%) already had edema on the talus (Kornaat & Van de Velde, 2014; Trappeniers et al., 2003) and tibia (Kornaat & Van de Velde, 2014) at baseline. The fibula was observed by one study (Kornaat & Van de Velde, 2014), but no visible pathology was seen at baseline or follow-up. For sedentary individuals (Trappeniers et al., 2003), the edema scores in the talus were significantly increased at follow-up. For elite runners (Kornaat & Van de Velde, 2014), the amount of edema showed fluctuation, with new lesions appearing and old lesions disappearing, when comparing baseline with follow-up. However, this study (Kornaat & Van de Velde, 2014) did not describe which bones had these fluctuating appearances.

Foot bones

Three (Freund et al., 2012; Kornaat & Van de Velde, 2014; Trappeniers et al., 2003) of four studies assessed bone edema and/or signal intensity in the foot bones. Two studies (Freund et al., 2012; Kornaat & Van de Velde, 2014; Trappeniers et al., 2003) reported that bone lesions already existed at baseline. Of these, one study (Trappeniers et al., 2003) indicated that the changes in edema scores and the number of affected bones (i.e. the calcaneus, navicular, cuboid, 5th metatarsal) were significantly increased at follow-up. Another study (Kornaat & Van de Velde, 2014) reported that BME on os calcaneus, os naviculare, os cuboideum and os cuneiforme were observed. However, information of which bones had changed through baseline and follow-up was not provided. Another study (Freund et al., 2012) examined hind foot bones and soft tissues. This study reported that the number of bone lesions (not specific to which bones), signal intensity in the calcaneus at the Achilles tendon insertion, and signal intensity in an innocuous area of the calcaneus were significantly increased over long-distance running.

Tibiotalar cartilage - T2* mapping and thickness

One (Schutz et al., 2014) of four studies used T2* mapping of the tibiotalar cartilage. One baseline and four follow-up scans were conducted over long-distance running. T2* signal was significantly increased in the tibial plafond and talar dome cartilage at the first and second follow-up. However, a significant T2* decrease was observed as the running distance increased with the third and fourth follow-up scans. The thickness of this tibiotalar cartilage was also measured by the same study (Schutz et al., 2014), but it did not show any significant changes.

The Achilles tendon

One study (Freund et al., 2012) described the Achilles tendon with regards to diameter, signal intensity and lesions. Over long-distance running, the diameter of Achilles tendon was significantly increased from a mean of 6.8mm to 7.8mm. When comparing the Achilles tendon in race finishers with non-finishers (aborting the race), there was no significant difference.

Plantar aponeurosis

One study (Freund et al., 2012) assessed signal intensity and edema in the plantar aponeurosis. Over long-distance running, no significant changes were observed. However, when comparing race finishers with non-finishers, non-finishers showed significantly higher rates of edema in the plantar aponeurosis than race finishers.

Subcutaneous tissues

One study (Freund et al., 2012) determined significantly increased subcutaneous edema over long-distance running. A comparison between race finishers and non-finishers showed that non-finishers had significantly higher rates of edema in the subcutaneous space than race finishers.

Subchondral bone

Subchondral bone was assessed by one study (Schutz et al., 2014). No changes were observed over long-distance running.

Intraosseous signal

The intraosseous signal was assessed by one study (Freund et al., 2012) and this value was significantly increased over long-distance running. However, when it compared between the race finishers and non-finishers, there was no different.

5.4.6 Reliability of MRI Findings

MRI scans were interpreted by at least two radiologists (Freund et al., 2012; Schutz et al., 2014; Trappeniers et al., 2003), except one study (Kornaat & Van de Velde, 2014) assessed by a single radiologist. To calculate correlation coefficient on the intra- and inter-rater reliability, two studies (Freund et al., 2012; Schutz et al., 2014) used Lambda as proposed by Jepsen et al. (2006). The values for both studies were ranging from 0.88 to 0.998, indicating that the reliability was excellent. Another study (Kornaat & Van de Velde, 2014) reported the intra- and inter-rater reliabilities (intraclass correlation coefficient) and the values were 0.93 and 0.91, respectively. One remaining study (Trappeniers et al., 2003) did not provide any information on the reliability of MRI findings.

Table 5. 1. *Study characteristics.*

Authors	Participants Demographics					Inclusion-Exclusion Criteria	Running Types	MRI			
	Number	Gender (F:M)	Weight, Height (or BMI) (average ± SD or range)	Age (average ±SD or range)	Runners Level			MRI Time Points	Magnetic Field	MRI Sequences	Scan Sites
Trappeniers et al. (2003)	10	2:8	72.9kg (55-88) 1.79m (1.62-1.88)	25.7 (22-30)	Sedentary individuals	• No history of ankle trauma • No use of medication • No flat foot, varus and valgus deformity	30-minute outdoor run per day for 7 consecutive days	• Baseline • 10-20 hours follow-up	1.5T	• Sagittal and transverse STIR	Both feet
Freund et al. (2012)	22	2:20	70.9kg (±11.3) 1.74m (±0.09)	49.1 (±11.5)	n.s.	• Participation in the ultra-marathon race • No contraindications for MRI.	4487km ultra-marathon	• Baseline • Approx. every 1000km during the race	1.5T	• Sagittal fat saturated STIR	Both feet
Kornaat et al. (2014)	16	3:13	67.8kg (±6.8) 1.82m (±0.06)	23 (±2.7)	National level of mid- and long-distance runners	• Top 8 placement at the European Championships or top 12 placement at the World Championship • No significant lower limb injuries.	7-months intensive training season	• Baseline (1-month before starting the training season) • One month follow-up	1.5T	• Coronal T2-weighted fat-suppressed • Coronal 3D SPACE fat-suppressed	Both hips, knees, ankles
Schutz et al. (2014)	13	1:12	73kg (±11.3) 23.4kg/m^2 (±2.5)	45.4 (±10.7)	n.s.	• Participation in the ultra-marathon race • Race finishers • No contraindications for MRI.	4486km ultramarathon	• Baseline • Approx. every 900km during the race	1.5T	• FLASH T2*-weighted GRE • TIRM • Fat-saturated PD-weighted	Right ankle

Abbreviations: F-female; M-male; T- Tesla; n.s.-not specified; SPACE- sampling perfection with application optimized contrasts using different flip angle evolution; FLASH–fast low angle shot; STIR- short Tau inversion recovery; GRE- gradient echo; TIRM- a turbo-inversion-recovery-magnitude; FLASH-a fast low angle shot; PD-proton density

5.4.7 Methodological Quality Assessment

Moderate quality was found for the four identified studies (Freund et al., 2012; Kornaat & Van de Velde, 2014; Schutz et al., 2014; Trappeniers et al., 2003) (Table 5.2). Of the four sub-scales, the quality of reporting was generally addressed well. All studies scored zero on questions 8 (reporting), 12 (external validity), 14, 15 (internal validity on bias) and 24, 25 (internal validity on confounding). Question 19 (internal validity on bias) was also scored poorly. All studies well addressed on questions 1-7 (reporting), 13 (external validity), 16-18, 20 (internal validity on bias) and 26 (internal validity on confounding).

Table 5. 2. *Modified quality index (QI) to assess quality of methodology*.

Sub-areas	***Questions***	***Authors***			
		Trappeniers et al. (2003)	Freund et al. (2012)	Kornaat et al. (2014)	Schutz et al. (2014)
Reporting	1. Described hypothesis/aims clearly?	1	1	1	1
	2. Described main outcomes clearly?	1	1	1	1
	3. Described characteristics of participants?	1	1	1	1
	4. Described intervention?	1	1	1	1
	5. Described the distribution of principal confounders?	1	1	1	1
	6. Described main findings?	1	1	1	1
	7. Provided estimates of the random variability for main outcome?	1	1	1	1
	8. Reported all adverse events?	0	0	0	0
	9. Described characteristics of participants lost to follow-up?	1	0	1	1
	10. Reported actual probability values for the main outcome?	1	1	0	1
External validity	11. Were participants asked to join in the study representative of the entire population?	0	1	0	1
	12. Were participants preparing to participate representative of the entire population?	0	0	0	0
	13. Was the intervention representative of that in use in the majority of the population?	1	1	1	1
Internal validity bias	14. Did participants have no way to know which intervention they received?	0	0	0	0
	15. Were the main outcomes of intervention blind?	0	0	0	0
	16. Was it clear if results were based on “data dredging”?	1	1	1	1
	17. Was the time period of follow-up same?	1	1	1	1
	18. Used appropriate of statistical tests?	1	1	1	1

	19. Was compliance with intervention reliable?	1	0	0	0
	20. Described the main outcome measures clearly?	1	1	1	1
Internal validity confounding	21. Were participants in different groups recruited from the same population?	0	0	0	0
	22. Were participants in different groups recruited from the same time period?	0	0	0	0
	23. Were participants randomised to intervention group?	0	1	0	1
	24. Concealed the randomised intervention?	0	0	0	0
	25. Adjusted confounding adequately?	0	0	0	0
	26. Reported losses of the participant to follow-up?	1	1	1	1
QI scores total (% of maximum score)		**16 (59%)**	**16 (59%)**	**14 (52%)**	**17 (63%)**

5.5 Discussion

The findings of this review indicate that long-distance running may cause subtle changes with regards to BME, signal intensity, Achilles tendon size and within the soft tissue space in the ankle and foot. However, there is no described clinical correlation or relevance given to these findings.

Among the ankle bones, the talus and tibia seem to be affected by long-distance running. Studies included in this review (Kornaat & Van de Velde, 2014; Trappeniers et al., 2003) highlighted the high rate of BME in the talus and tibia for both sedentary individuals and elite runners. Following seven days of running for 30-minutes per day in sedentary individuals (Trappeniers et al., 2003), 50% of participants showed edema involving in the talus, calcaneus, navicular, cuboid and 5th metatarsal. However, as this study did not provide any information about running conditions such as speed, surface, shoes, and running techniques, it is unclear if the edema occurs due to other constitutional factors. Another study (Kornaat & Van de Velde, 2014) of 16 elite runners evaluated multiple lower limb joints before and after a seven month training season, reporting that the number of lesions fluctuated. However, information of which bones had changed through baseline and follow-up was not provided. Moreover, there were a few clinical complaints during the season, but these did not appear to relate to the presence of BME lesions. Thus, the incidental BME seen on MRI scan may have no clinical relevance. The possibility that the runners were exposed to other types of training (i.e. weight training and plyometric training) during the seven months should be also considered as a confounder.

Several foot bones including the calcaneus, navicular, cuboid, and cuneiform also seem to be influenced by long-distance running. The tarsals and metatarsals are typically involved in overuse injuries (Matheson et al., 1987). This finding is consistent with biomechanical studies assessing the foot plantar pressure before and after long-distance running. These studies found that the loading under the 4th and 5th metatarsals and the heel were significantly increased (Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012). Thijs et al.(2008) also reported that the greater plantar pressure under the metatarsals and lateral heel regions can be related to patellofemoral pain in runners.

With regards to the tibiotalar cartilage, one study (Schutz et al., 2014) employed T2* mapping to assess quantitative biochemical cartilage analysis along with thickness changes in response to ultra-marathon. The articular cartilage of the ankle is much thinner and stiffer than the knee; probably due to this reason, no morphological changes were observed in the current review. Another possible reason for no thickness change could be the absence of controlling for diurnal effects. Unlike the ankle joint, the knee cartilage generally loses thickness and/or volume even after shorter distance running (5km-20km) for both trained and recreational runners (M. Kessler et al., 2006; M. A. Kessler et al., 2008; Mosher et al., 2005; Mosher et al., 2010), and all these knee studies made efforts to minimize the diurnal effect.

In the current selected study (Schutz et al., 2014), T2* values were significantly increased in almost all regions of the tibial plafond and talar dome cartilage during the initial 2000km-2500km. However, a significant T2* decrease was observed as the running distance increased beyond 2500km. Hence, this study suggests that the human ankle has the capacity to be resilient to excessive loads during the extreme running distance. However, as only one study used T2* mapping on the tibiotalar cartilage over ultra-marathon, a further study may be required with more typical running distance (i.e. 5km-20km) including other joint cartilage such as subtalar joint, talocalcaneonavicular joint, and calcaneocuboid joint.

Over long-distance running, the Achilles tendon seems to be altered. Achilles tendinopathy is a very frequent problem amongst elite runners (Nicholson, Berlet, & Lee, 2007). It has been reported that runners who have trained more, covering longer distances tend to have more Achilles tendinopathy compared with less experienced and shorter distance runners (Haglund-Åkerlind & Eriksson, 1993). Thickening of the Achilles tendon in the anteroposterior dimension is considered when diagnosing tendinosis using MRI. For healthy people, a range of 5.2mm to 6mm is generally considered a normal tendon size (Nicholson et al., 2007; Soila et al., 1999), whereas more than 6mm is considered pathological (Soila et al., 1999). The current selected study (Freund et al., 2012) reported that the diameter of Achilles tendon was already at an average of 6.8mm at baseline, and it was significantly increased to an average of 7.8mm over ultra-marathon. There would already be overloading even prior to the race, thereby explaining a larger Achilles tendon. This finding is in accordance with previous research (Kongsgaard M. et al., 2005), reporting that elite endurance runners generally have a larger cross-sectional area in the Achilles tendon than controls. However, when comparing race finishers with non-finishers, the plantar aponeurosis and subcutaneous edema were the only significantly different factors (not Achilles tendon properties). The authors (Freund et al., 2012) suggested that soft tissue edema might be more associated with abortion of the race than Achilles tendon properties.

5.5.1 Limitation

Meta-analysis could not be performed as all studies adopted different study populations, study designs, running types, and MRI grading systems. As none of the studies had a control group and/or second follow-up test following a rest period, and had small population numbers, it is difficult to know if any changes are clinically relevant. All the selected studies adopted 1.5T MRI, while 3.0T MRI gives improved visualization of fine pathological features. In addition, there is a possibility that a relevant study has been omitted if a full-text was not written in English. One excluding German study (Freund et al., 2011) seems to be relevant our current review, reporting changes in retrocalcaneal bursa volume, the Achilles lesion volume, and signal intensity of the calcaneus after a marathon. Some possible confounding factors were not reported: gender, age, background of lower limb injuries, occupational risks, family history of osteoarthritis and pre-existing malalignment should be considered for future studies. Furthermore, as the ultra-marathon represents an outlier in extreme sport, the findings related to this would be hard to generalise to a general running population.

5.6 Conclusion

The findings from this systematic review suggest that long-distance running may cause subtle changes in tarsal bones, metatarsal bones, tibiotalar cartilage, the Achilles tendon, subcutaneous and intraosseous in healthy adults. However, as very limited information is available with small participant numbers, variable study designs, and various population groups, it may difficult to interpret the findings and draw conclusions about whether long-distance running has a deleterious effect on the ankle and foot. Investigating the acute effect of a single long-distance running with more typical running distance on the ankle and foot is needed. As advanced T2/T2* mapping or T1p (rho) may detect more subtle and early changes and able to provide high signal-to-ratio with high resolution, these techniques would be ideal to examine the thin ankle cartilage.

Chapter 6. Biochemical Tibiotalar Cartilage Alteration in T2 Mapping after Long-Distance Unshod Running and its Relationship to Ankle Biomechanics

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6.1 Preface

There are no studies investigating the acute effects of long-distance unshod running in the ankle cartilage using T2 maps. Most of the previous MR studies examined the knee following long-distance shod running. Very little information is available for the ankle/foot complex. This chapter is the first study to quantitatively evaluate T2 relaxation time of tibiotalar cartilage and ankle biomechanics following 5km unshod running.

6.2 Introduction

Unshod running has been reported to be biomechanically beneficial for runners as it reduces impact force, impact rate, and stride length (De Wit et al., 2000; Lieberman et al., 2010) compared with traditional shod running. However, it remains unclear whether these advantages of unshod running have a clinical relevance and/or whether the cumulative loading has a deleterious effect on the ankle joint (tibiotalar cartilage).

Magnetic resonance imaging (MRI) has been proposed as a desired diagnostic tool as it is a non-invasive imaging technique and it provides an *in vivo* assessment of articular cartilage. Pathological and/or morphological changes including a bone marrow edema (BME) lesion, joint effusion, and cartilage deformation have been reported after long-distance shod running (Hesper et al., 2015b; Mosher et al., 2005; Schutz et al., 2014; Stehling et al., 2011). However, most of the previous MR studies typically focused on the knee cartilage rather than ankle cartilage. A recent systematic review (H. K. Kim et al., 2017) also reported that very little information is available on investigating the ankle and foot structures in response to long-distance shod running, and reported subtle pathological and biochemical alteration in the ankle and foot after the running. Investigating the acute effects of unshod running on the ankle cartilage using the MRI has to date never been conducted yet.

T2 mapping is a biochemically sensitive modality and is able to quantify the biochemical composition of cartilage, characterizing the extracellular water content and collagen degradation (Mosher & Dardzinski, 2004). When cartilage is compressed by applying an external force, water content and collagen fiber orientation of the extracellular matrix are altered and it influences on the T2 values, hence it can identify early cartilage degeneration (Mosher & Dardzinski, 2004). It should be noted that T2 changes may also be non-specific and resolve spontaneously. Recent studies reported that long-distance shod running has acute effects on the knee (Subburaj et al., 2012) and ankle (Schutz et al., 2014) articular cartilage by observing the changes in T2, T2* and/or $T1_{rho}$ values. Biomechanical studies also reported that strike pattern, tibialis anterior muscle activity, and plantar pressure were changed after long-distance bare-simulated shod running (Kasmer et al., 2014) or long-distance shod running (H. K. Kim et al., 2017). However, MR findings in ankle cartilage and its relationship to running biomechanics in response to unshod running are poorly understood. Therefore, the aims of this research are: *1)* to quantitatively assess ankle (tibiotalar) joint T2 cartilage relaxation time in response to 5km unshod running; *2)* to investigate whether fitness level (novice and marathon-experience runners) or gender affects T2 values in the ankle cartilage in response to 5km unshod running; and *3)* to evaluate whether plantar pressure, ankle kinematics or both are associated with T2 changes post 5km unshod running.

6.3 Methods

The ethical approval was obtained from our institution of Human Ethics Committee (ref: 016488) and all participants signed a written informed consent form.

6.3.1 Study Population

10 marathon-experienced runners (ME) and ten age-matched novice runners (NOVICE) including males and females were recruited from the local community. To accurately determine their general activity levels, the Tegner scale (Stahl et al., 2008; Tegner & Lysholm, 1985) was employed and scored them between 1 (sedentary behaviors) and 10 (highly competitive sports level). Inclusion criteria for the ME runners were as follows: *1)* they have regularly participated in half- or full marathon races in the last three years, *2)* the Tegner scale should be greater than 6. Inclusion criteria for the NOVICE runners were as follows: *1)* they may run recreationally, but have never been involved in any high-level sports and marathon races, *2)* the Tegner scale should be lower than 4. Common inclusion criteria for all participants were: *1)* healthy Caucasian adults (18–50 years old), *2)* no history of lower limb injuries and/or major pathologies in the past, *3)* run normally with shoes, *4)* and having a heel strike running technique. The exclusion criteria were: *1)* professionally or heavily participating in other sports activities, *2)* outside of a range of 18-30 in a body mass index (BMI), and *3)* contraindication to MRI. For statistical analysis, the 20 participants were divided into four groups (Table 6.1) based on their fitness level and gender.

6.3.2 Experimental Protocol

The experiment was conducted on two separate days. On the first day, the pre-run scan of the right foot and pre-run gait data during unshod running were acquired. To minimize potential diurnal effect in the cartilage T2 values (Coleman et al., 2013), the pre-run scan was conducted in the morning. All participants were also instructed not to participate in any training before their pre-run scan day. On the second day, all participants ran for a 5km unshod run on a treadmill at a self-selected pace. All participants used the same treadmill under the laboratory condition and hence the temperature and humidity were always controlled. Immediately after the running, post-run gait data was acquired. 3.20±0.97 hours later (due to travel time), post-MR scans of the right foot were also obtained with the same methodology as the pre-scans.

6.3.3 MR Data Acquisition

MR scans of the right foot and ankle (dominant) were acquired with a 3.0-Tesla MR scanner (Siemens Skyra, Erlangen, Germany) and with a 16 channel foot coil while the participant was lying supine with a natural position of the ankle. To stabilize the ankle and foot within the coil, sponge cushions were used to minimize any inadvertent variation in the location of the ankle cartilage.

To assess quantitative biochemical (T2 maps) changes in the tibiotalar cartilage as well as conventional MR evaluation of the ankle/foot, the following sequences were used:

1. Sagittal T1 turbo spin echo (TAE). Flip angle (FA) = 140 degrees, echo time (TE) = 140 ms, repetition time (TR) = 600 ms, slice thickness (ST) = 2.5 mm, field of

view (FOV) = 250 mm, Bandwidth = 257 Hz/Pixel, time of acquisition (TA) = 2.57 minutes.

2. Sagittal T2 DESS gradient echo water excitation. FA = 28 degrees, TE = 5 ms, TR = 12.90 ms, ST = 0.6 mm, FOV = 250 mm, Bandwidth = 310 Hz/Pixel, TA = 4.51 minutes.
3. Sagittal and coronal short tau turbo inversion recovery (STIR) for showing pathological changes in soft tissues. FA = 150 degrees, TE = 50 ms, TR = 4,000 ms, ST = 2.5 mm, FOV = 250 mm, Bandwidth = 248 Hz/Pixel, TA = 4.18 minutes.
4. Sagittal and coronal T2 mapping. FA = 180 degrees, TE = 13.8 ms, TR = 1,600 ms, ST = 3 mm, FOV = 140 mm, Bandwidth = 230 Hz/Pixel, TA = 4.16 minutes.

6.3.4 MR Image Analysis

An experienced radiologist (30 years of experience in musculoskeletal radiology) together with a senior and junior radiology resident independently evaluated all the MR scans using Osirix Lite v.9.0.1 (Pixmeo, Geneva, Switzerland).

Qualitative Analysis.

Pre- and post-run scans were reviewed separated by a two-week interval. The T1 weighted STIR and DESS images were evaluated for the presence of cartilage lesions in the ankle, bone marrow edema (BME) in the ankle joint, Os trigonum, and other pathologies; joint lesion/arthritis elsewhere in the foot, Achilles tendinopathy, ankle ligament tears, plantar fasciitis, and Haglund lesion.

Quantification of T2.

The MR images were transferred to the Osirix Lite for quantification of T2 relaxation times. For quantitative T2 analysis, three images that represented the surface of the ankle cartilage were selected from sagittal image data sets. To minimize the effect of partial volume artifact, we have excluded the medial and lateral malleolar regions of the ankle (including tibial, fibular, and talar) in the analysis. Each image in a single sagittal plane was manually and equally divided into three zones - anterior zone (AZ), central zone (CZ), and posterior zone (PZ) (Figure 6.1, A). Then, these three zones were determined in each section (lateral, middle, and medial) (Figure 6.1, B). Hence, nine regions were identified in the three sections of each ankle. In total 180 regions were generated from 20 ankles.

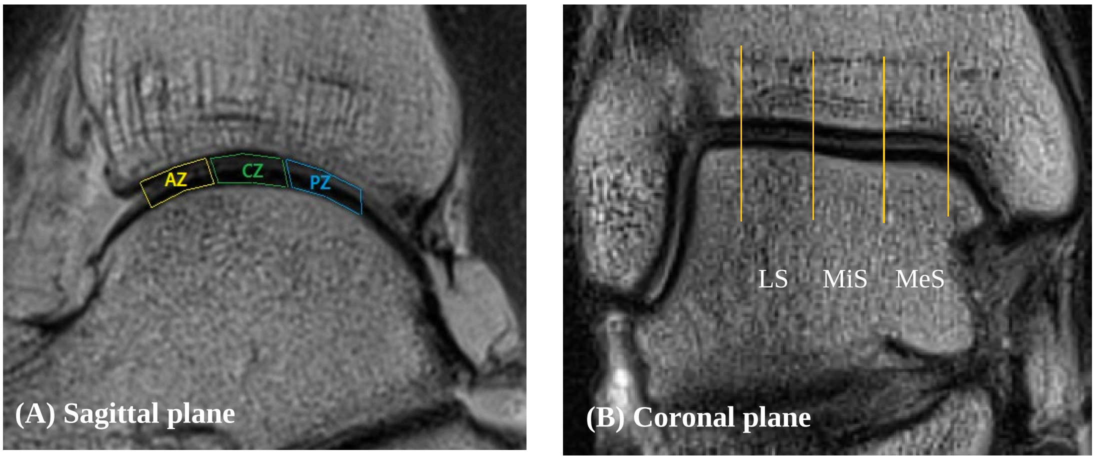

Figure 6. 1. Post-processing for T2 map.

T2 maps post-processing for quantification of T2 relaxation time in the ankle cartilage. (A): three zones of ankle cartilage in sagittal plane – anterior zone (AZ), central zone (CZ), and posterior zone (PZ). (B): three sections of ankle cartilage in coronal plane – lateral section (LS), middle section (MiS), and medial section (MeS).

6.3.5 Gait Test Protocol

To collect three-dimensional kinematic data during running unshod, an 8-camera Vicon motion analysis system (Vicon Oxford Metrics, Oxford, UK) was employed with a sampling rate of 100 Hz. The ground reaction force was also obtained simultaneously using three force plates (Bertec Corporation, Ohio, USA) with sampling rate 1000 Hz. Based on the Cleveland marker set, 27 reflective markers were placed on the anterior superior iliac spines; the sacrum (midpoint); the lateral and medial femoral epicondyles of the knees; the medial and lateral malleoli of the ankles; the lateral side of the thighs and shanks (using a triad consisting of three markers); 2nd metatarsal heads; and the posterior aspect of the calcanei. All participants were asked to run unshod across the force plates in the motion capture area with the similar speed of the 5km unshod run.

A plantar pressure of the right foot was also measured by the Novel emed® pressure platform during running unshod. The foot map was divided into 11 regions of interest (ROIs) for further analysis, including hallux (T1), toes 2-5 (T2-T5), all metatarsals (M1, M2, M3, M4, M5), medial and lateral midfoot (MM, LM), and medial and lateral heel (MH, LH).

6.3.6 Gait Data Processing and Analysis

All the motion capture data was exported to the Nexus (Oxford Metrics, Oxford, UK) and were filtered using an 8 Hz low-pass, fourth-order, zero-lag Butterworth filter. Three best trials of the right full gait cycle were determined. Three-dimensional angle, torque, and power at the lower limb joints were calculated using Polygon (Oxford Metrics, Oxford, UK). Power ($W.kg^{-1}$) and torque ($Nm.kg^{-1}$) were normalized by body weight, and the maxima and minima were obtained from stance phase for statistical analysis. The angle (degree) at the initial foot contact, maxima, and minima were also acquired from the full gait cycle for statistical analysis. Peak plantar pressure (kPa) was obtained from each ROI. All these gait parameters were taken from the means of three best trials.

6.3.7 Reproducibility Measurements

An intra-class correlation coefficient (ICC) was performed to determine the reproducibility of T2 measurements in the ankle cartilage regions. Inter and intra-reliability on the T2 measurements were estimated between investigators.

6.3.8 Statistical Analysis

SPSS Version 20 (IBM Corporation, Armonk, NY, USA) was used for statistical analysis. The normality test was initially performed by using the Kolmogorov–Smirnov and Shapiro–Wilk. The Wilcoxon signed rank test was used to compare qualitative MRI parameters between pre- and post-run scans. For testing on the difference of T2 relaxation time between pre- and post-run, a paired (two-tailed) t-test was conducted for each ankle cartilage regions. The effect size (Cohen's *d* coefficient) was also calculated and the scores were interpreted as follows: $0.15 \leq d < 0.4$ small difference; $0.4 \leq d < 0.75$ moderate difference; $0.75 \leq d < 1.1$ large difference; $d > 1.1$ very large difference. To investigate the differences in T2 relaxation time within ankle cartilage regions and within the groups, a one-way analysis of variance (ANOVA) was employed. When the main ANOVA was significant, the Tukey's honestly significant difference post hoc test was carried out to see which ankle cartilage regions or groups differed. Additionally, a two-way analysis of covariance (ANCOVA) was conducted to evaluate whether fitness level or gender affects the T2 values in response to 5km unshod running whilst controlling for the pre-run values as a covariate. The significance level was set at $p \leq 0.05$.

6.4 Results

All 20 participants completed the 5km unshod run over 31.66±6.84 minutes. The ICC for reproducibility of T2 measurements on the tibiotalar cartilage showed good agreement for both intra- (range, 0.76 – 0.94) and inter-reliability (range, 0.75 – 0.98).

6.4.1 Study Population

Demographic information on 20 healthy volunteers is presented in Table 6.1. Age and height revealed no statistical difference between the four groups. Weight ($p = 0.02$) and BMI ($p = 0.03$) were significantly higher in the MALE than FEMALE, while the ME and NOVICE showed no statistical difference. Regarding the training status, the Tegner scale ($p < 0.0001$), running distance per week ($p = 0.05$), running days per week ($p = 0.01$) and training years ($p = 0.03$) were significantly greater in the ME when compared with the NOVICE. The training status showed no statistical difference in the FEMALE and the MALE.

Table 6. 1. *Demographic information for each group.*

Parameters	NOVICE (n=10)	ME (n=10)	FEMALE (n=10)	MALE (n=10)
Gender (F:M)	5:5	5:5	-	-
Age (yr)	29±6.8	31.2±9.9	27.1±6.5	33.1±9.1
Height (m)	1.69±0.1	1.73±0.1	1.68±0.1	1.75±0.1
Weight (kg)	65.6±9.8	65.4±9.9	59.5±4.8	71.5±9.5
BMI (kg/m^2)	22.7±2	21.7±1.5	21.1±1.2	23.3±1.6
Training status				
Tegner scale	2.9±1.8	6.5±0.7	5±1.8	4.4±2.7
Distance/week (km)	5.4±6.9	31.4±26.1	13.6±14.3	23.2±29.1
Days/week	1.1±1.2	3.5±1.5	2.2±1.6	2.4±2
Years training	2.4±2.9	9.4±5.6	4.9±5.2	6.9±6.2

6.4.2 Qualitative Analysis of Ankle MR Before and After Exercise

The qualitative results are presented in Table 6.2. There was no major structural abnormality in any of the imaged ankles between pre- and post-run scans. The ankle BME seemed to be most common, which was observed across all groups, while none of the group had ankle cartilage lesions, plantar fasciitis, or Haglund lesions. Two out of 10 ME females showed minor ankle ligament tears, while this was not observed in other groups. Two out of 10 ME (one male and one female) also revealed asymptomatic Achilles tendinopathy, whereas the others showed no tendinopathy.

Table 6. 2. *Qualitative analysis.*

Wilcoxon signed-rank test was conducted to compare between pre- and post-run for each group. Presented data are number of patients.

	NOVICE (n=10)			ME (n=10)			FEMALE (n=10)			MALE (n=10)		
	PRE	POST	*P* value	PRE	POST	*P* value	PRE	POST	*P* value	PRE	POST	*P* value
Ankle cartilage lesions	0	0	-	0	0	-	0	0	-	0	0	-
Ankle BME	1	2	.32	2	2	-	2	3	.32	1	1	-
Os trigonum	1	1	-	1	1	-	2	2	-	1	1	-
Achilles tendinopathy	0	0	-	2	2	-	1	1	-	1	1	-
Ankle ligament tears	0	0	-	2	2	-	2	2	-	0	0	-
Plantar fasciitis	0	0	-	0	0	-	0	0	-	0	0	-
Haglund deformity	0	0	-	0	0	-	0	0	-	0	0	-

6.4.3 Quantification of T2 Cartilage Maps Before and After Exercise

The detailed T2 changes of tibiotalar cartilage before and after 5km unshod running is presented in Figure 6.2. Regarding the zonal differences in the sagittal plane, T2 values measured in the PZ demonstrated the greatest values, while the AZ showed the lowest values in the four groups for both pre- and post-run scans (Figure 6.3). When the PZ was compared with the CZ, however, only the NOVICE showed a significant difference for both pre- and post-run scans. After the running, the rest of groups also showed a significant difference between the PZ and CZ.

Comparing between pre- and post-run scans, the NOVICE was most significantly affected by unshod running (Figure 6.2 and 6.3). More specifically, the NOVICE demonstrated that T2 values measured in the AZ (p = 0.02, *effect size* = 0.9) and PZ (p = 0.003, *effect size* = 1.51) were significantly increased after the running. Moreover, when the T2 values were analyzed in the coronal plane, only the NOVICE showed a significant elevation in the lateral section (p = 0.03, *effect size* = 0.87) after unshod running. The MALE also showed T2 elevation in all three zones of the sagittal plane after the running, but only the PZ reached a significant level (p = 0.05, *effect size* = 0.5). However, the ME and FEMALE groups showed an insignificant reduction in the T2 values after the running. As shown in Table 6.3, the two-way ANCOVA showed that the effect of gender was not statistically significant on the T2 values. However, there was a significant effect of fitness level on T2 in the PZ (p = 0.02). There was no interaction effect on T2 values between fitness level and gender.

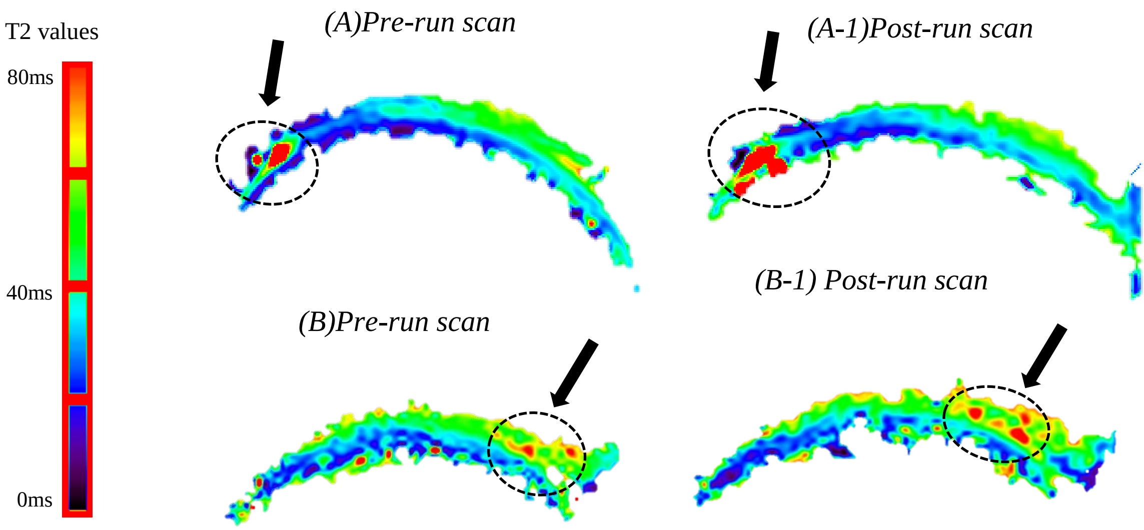

Figure 6. 2. Example of T2 changes in pre- and post-run scans of the tibiotalar cartilage in the lateral section sagittal plane.

34-year-old male novice runner showed high T2 values (ms), indicated by red pixels, in the AZ (A) and PZ (B) after running. High T2 values were also generally observed in the border of the cartilage.

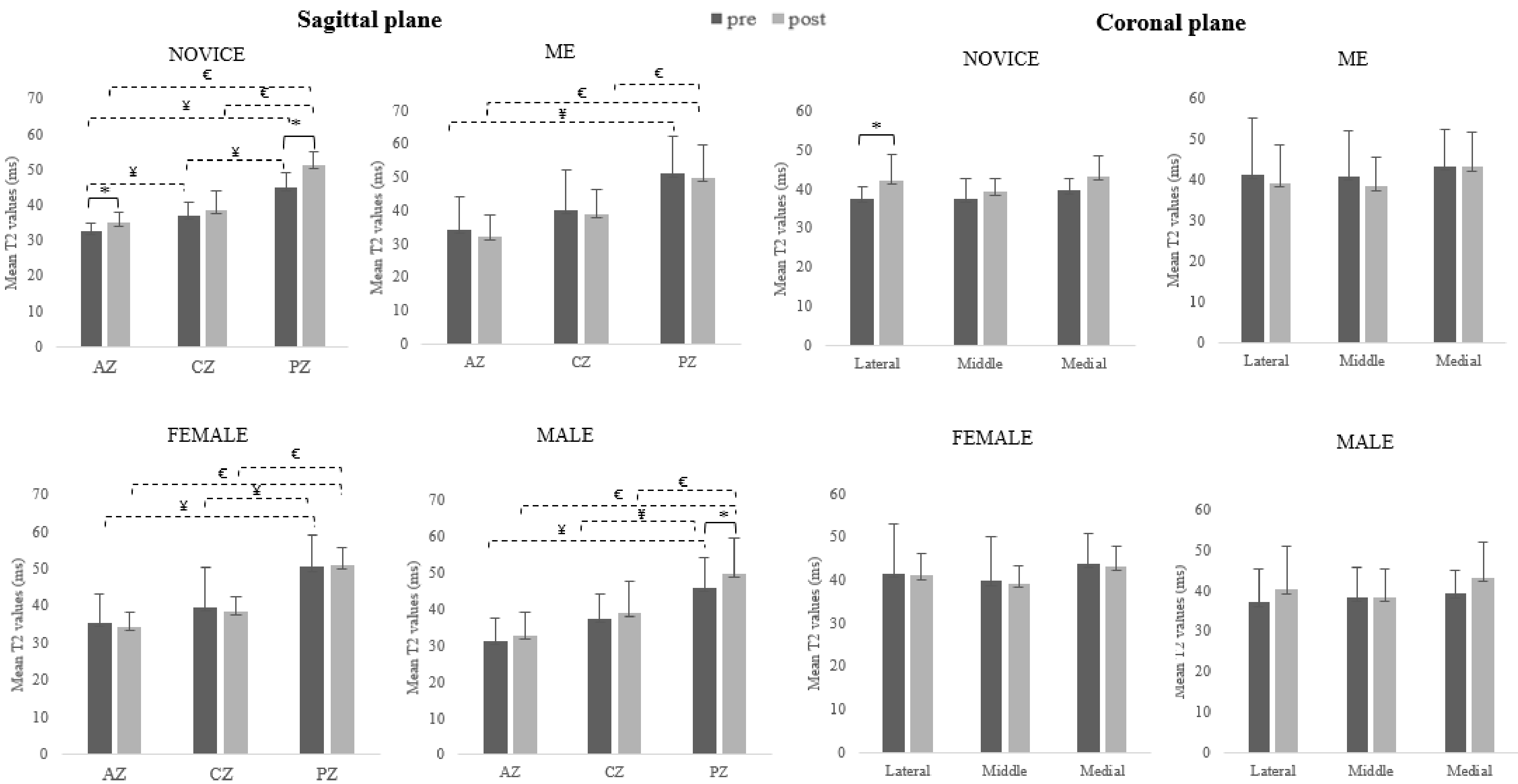

Figure 6. 3. T2 relaxation times in the pre- and post-unshod run for three zones/sections of tibiotalar cartilage for each group.

*: a paired t-test (solid line) showed a significant level ($p \leq 0.05$) between pre and post. ¥ (pre-run) and € (post-run): one-way ANOVA (dotted lines) demonstrated significant zonal differences ($p \leq 0.05$) between the three zones.

Table 6. 3. *Mean values of T2 (ms) for each group.*

Two-way ANCOVA showed main- and interaction-effects of the fitness level and gender on T2 values.

	Groups	AZ (ms)	CZ (ms)	PZ (ms)
Pre	NOVICE	32.55±2.36	37.16±3.48	45.1±4.18
	ME	34.09±10.15	40.23±11.83	51.14±11.18
	FEMALE	35.24±7.76	39.81±10.6	50.4±8.84
	MALE	31.4±6.45	37.58±6.51	45.84±8.56
Post	NOVICE	35.06±3.15	38.74±5.38	51.18±3.88
	ME	32.02±6.82	38.77±7.64	49.73±10.02
	FEMALE	34.34±3.98	38.39±3.85	50.88±4.75
	MALE	32.73±6.65	39.12±8.5	50.03±9.68
Two-way ANCOVA for the effect of participants' fitness level and gender				
	Fitness level (F)	0.97	0.76	**0.02***
	Gender (G)	0.11	0.63	0.26
	F × G	0.27	0.1	0.44

6.4.4 Ankle Biomechanics

After the 5km unshod running (Figure 6.4), the FEMALE exhibited a significant reduction of peak plantar flexion (pre: -22±6.9 degrees, post: -14.8±8 degrees, p = 0.004, *effect size* = 0.96) and internal rotation (pre: 9.9±3.2 degrees, post: 5±3 degrees, p = 0.005, *effect size* = 1.57) and a significant elevation of peak inversion (pre: 1.1±0.7 degrees, post: 2.5±1.1 degrees, p = 0.0004, *effect size* = 1.51) and external rotation (pre: -10.6±6.3 degrees, post:-

16.9±2.4 degrees, *p* = 0.003, *effect size* = 1.32). At the initial foot contact, inversion-eversion was increased (pre: 0.1±0.6 degrees, post: 0.54±0.3 degrees, *p* = 0.05, *effect size* = 0.93), while internal-external rotation was decreased (pre: -1.8±5 degrees, post: -6.3±3.4 degrees, *p* = 0.01, *effect size* = 1.05) in the FEMALE group after the running. The ME group only showed a significant increase in the peak plantarflexion after the running (pre: -22.6±5.3 degrees, post: -17.2±6.4 degrees, *p* = 0.01, *effect size* = 0.92). No overall ankle kinematic and kinetic change occurred in the NOVICE and MALE groups.

After the 5km unshod running, kinetic alteration was only observed in the FEMALE among the four groups, decreasing the ankle plantarflexion torque (pre: 3.1±0.5 $Nm.kg^{-1}$, post: 2.5±0.7 $Nm.kg^{-1}$, *p* = 0.01, *effect size* = 0.99).

Regarding the peak plantar pressure (Figure 6.5), the loading under the toes and medial forefoot was decreased after the running, while the loading under the lateral forefoot and lateral midfoot showed elevation. More specifically, significant reduction of the pressure under T1 in the FEMALE (pre: 468.7±181.9 kPa, post: 265.3±154.3 kPa, *p* = 0.005, *effect size* = 1.2) and the NOVICE (pre: 480.7±217.9 kPa, post: 296.4±127.3 kPa, *p* = 0.03, *effect size* = 1.03) and T2-T5 in the NOVICE (pre: 230.2±89.1 kPa, post: 175±87.2 kPa, *p* = 0.03, *effect size* = 0.6) were observed. All groups showed a significant decrease under M1, but only the MALE and ME showed a significant reduction under M2 and M3. In contrast, a significant elevation under the M4 (pre: 301.4±81.9 kPa, post: 376.3±122.3 kPa, *p* = 0.03, *effect size* = 0.7) and M5 (pre: 258.63±154.8 kPa, post: 415.2±214.9 kPa, *p* = 0.007, *effect size* = 0.8) in the FEMALE and M5 in the NOVICE (pre: 302.8±145.9 kPa, post: 394.1±219.2 kPa, *p* = 0.03, *effect size* = 0.5) were found. Peak pressure under LM also showed a significant increase in the ME (pre: 149.1±32.7 kPa, post: 219.7±93.7 kPa, *p* =

0.004, *effect size* = 1.4), FEMALE (pre: 152.5±43.4 kPa, post: 258.4±94.5 kPa, p = 0.01, *effect size* = 0.7), and NOVICE (pre: 200.4±72.3 kPa, post: 257.4±96.5 kPa, p = 0.01, *effect size* = 0.7).

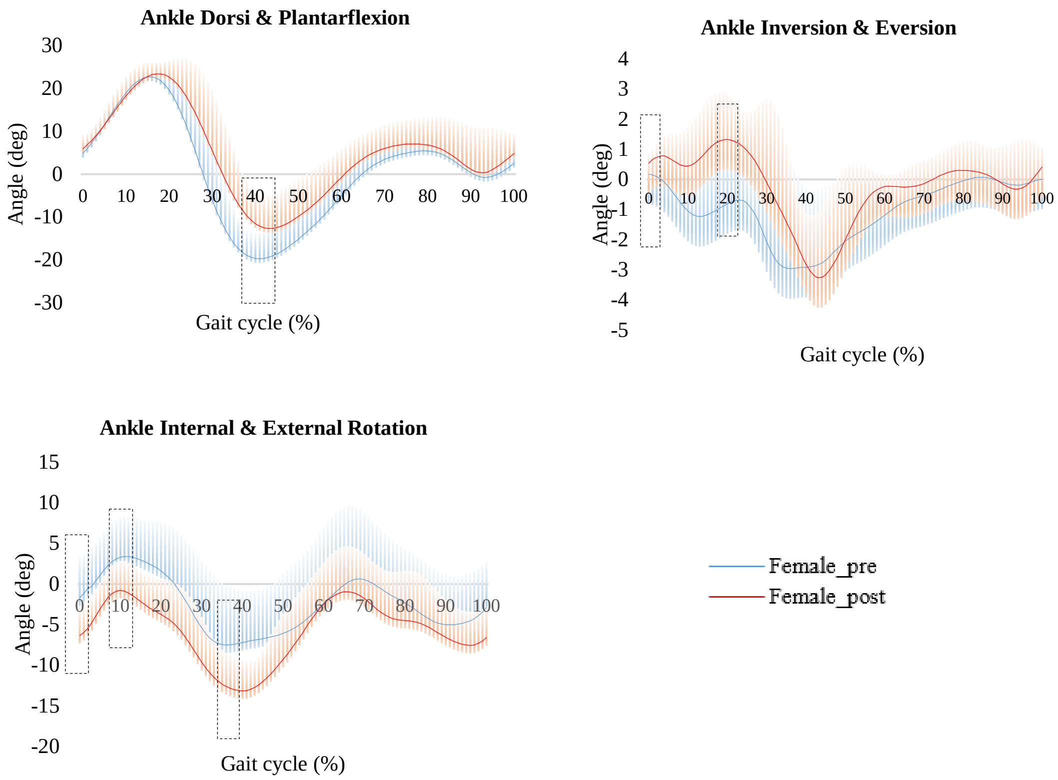

Figure 6. 4. 3D ankle kinematic changes in the FEMALE group before and after the 5km run.

Blue line indicates pre-run and red line indicates post-run. Dotted squares indicate significant different between pre- and post-run at the peak and/or initial foot contact. Positive values indicate dorsiflexion, inversion, and internal rotation. A significant reduction of peak plantar flexion and peak internal rotation as well as a significant elevation of peak inversion and peak external rotation were observed.

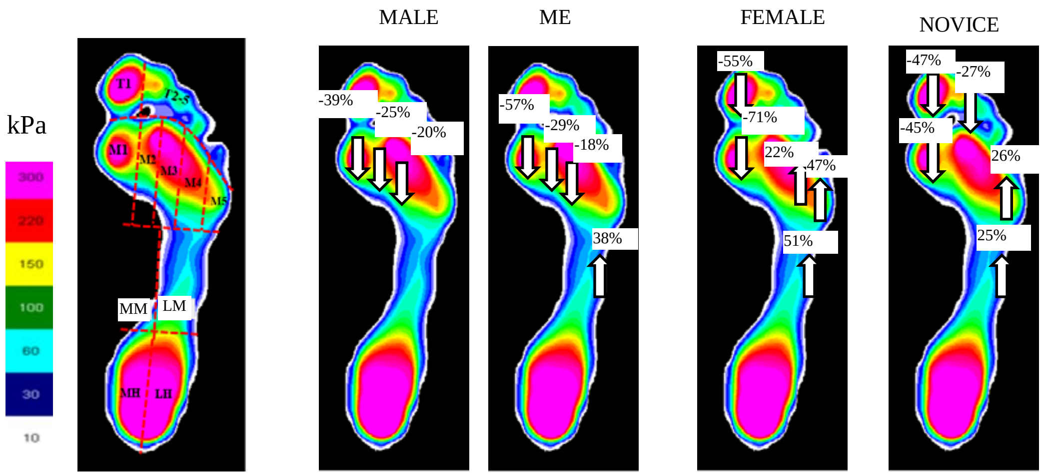

Figure 6. 5. Plantar pressure map - 11 regions of interests.

Arrows indicate significant changes of plantar pressure after the 5km run for each group.

6.5 Discussion

This study investigated the effects of 5km unshod running on T2 relaxation times of the tibiotalar cartilage and its relationship to the ankle biomechanics in young, healthy, first time unshod runners. The results of this study support the following conclusions. ***First***, 5km unshod running has an acute effect on the tibiotalar cartilage, which may indicate deformation of collagen fibers and increasing extracellular water content. ***Second***, depending on the fitness level, the variation of T2 values in response to 5km unshod running was different - the NOVICE runners demonstrated a significant increase in T2 values after the running, while the ME runners showed no change. Given this evidence, 5km unshod running may have a considerable biochemical effect on the ankle joints in NOVICE runners. ***Third***, the T2 increase was only pronounced in NOVICE on the lateral section of the tibiotalar cartilage. This change was associated with increased plantar pressure on the 5th metatarsal and lateral midfoot in NOVICE group. However, significant changes in ankle kinematics following 5km unshod running were only exhibited in FEMALE. This suggests plantar pressure may play a role in tibiotalar cartilage fluid development but not ankle kinematics.

Our results agree with the previous studies that running had an acute effect on the lower limb articular cartilages by observing a significant alteration in T2 values (Mosher et al., 2005; Stehling et al., 2011). It should be noted that their study design, MR acquisition sequences, shod condition and running distance were all different compared with the current study and that they were investigating the knee joint specifically. To the best of our knowledge, only one study (Schutz et al., 2014) quantitatively (using T2* maps) evaluated the ankle cartilage in response to long-distance shod running (4,486km, 64 days) in 13 race finishers. This study found that T2* values were significantly increased during the initial 2,000 – 2,500km, but a significant T2* decrease was also observed as the running distance increased beyond 2,500km. This study suggested that the human ankle may have a capacity to repair over time through the running. In a study by Stehling et al. (2011), a significant increase in $T1_{rho}$ and T2 values in both menisci of the knee after a marathon race was found, indicating modification of the biochemical composition of meniscal tissue by running. The result of alteration of the meniscal signal after running is consistent with other studies (W. Krampla et al., 2001; Schueller-Weidekamm et al., 2006), but the changes were insignificant. Regarding unshod running, there were only a few MRI studies investigating the effect of unshod running on the ankle and foot complex. In a study by Ridge et al. (2013), they evaluated BME in runners' feet after a 10-week transition from traditional running shoes to bare-simulated shoes and compared them with a control group. This study reported that more people in the bare-simulated shod group increased in BME in the 2nd and 3rd metatarsals, talus, calcaneus, and navicular after the 10-week period when compared with the control group, but both groups showed no soft-tissue changes. One case study (Giuliani et al., 2011) also found 2nd metatarsal stress fracture in two experienced runners after 3 to 6 weeks of training with bare-simulated shoes. Both studies concluded that caution is required when training with such shoes, but it was still unclear what the acute effect of a single unshod run on the ankle cartilage and biomechanics may be.

The current study showed the alteration of T2 value was significant in NOVICE group, while the ME group showed no change. Previous MR studies also showed similar results, reporting that marathon-experienced runners may have no significant effect on their knee or ankle joint after a long-distance run (Lohman et al., 2001; Stahl et al., 2008). Stahl et al. (2008) reported that marathon-experienced runners may have no significant effect on their knee or ankle joint after a long-distance run. They found that the marathon-experienced runners had higher cartilage abnormalities and BME patterns predominantly at the lateral patella than the active controls. However, both groups showed a high percentage of pathologic conditions on MRI scan after a marathon race, suggesting a single marathon race may not alter MR scans and also that there was no significant difference between groups. Lohman et al. (2001) also observed several abnormalities in the ankle and foot after a marathon race in 19 marathon-experienced runners, but the MR appearances were very similar to those seen in the physically active controls. In general, none of these studies, including our study, reveal a significant MR difference in experienced runners.

Unlike the significant T2 alteration in the NOVICE, their ankle kinematics showed no changes after the 5km unshod running, suggesting kinematic changes may have less contribution of T2 values. However, the plantar pressure seemed to anatomically correspond to location of the T2 changes. The plantar pressure was transferred from the medial to the lateral side and the T2 increase was only pronounced in novice runners on the lateral tibiotalar joint. To the best of our knowledge, there is no study investigating whether T2 values are associated with the altered plantar pressure, although it has been reported that neuropathic feet resulted in increasing plantar pressure (Bus et al., 2005). Further studies examining the relationship between T2 values of the joint cartilage and plantar pressure changes are required.

When participants were stratified by gender, only MALE showed a significant T2 increase in the PZ of the ankle cartilage. This can be due to the novice males, but the two-way ANCOVA showed there was neither gender effect nor interaction effect. This indicates that the effect of gender on T2 values did not change depending on their fitness level.

Although there was no control group in the current study, we believe that the observed finding were due to immanent to unshod running rather than due to general fatigue during 5km running. The current study revealed elevation of T2 values in the lateral tibiotalar cartilage and increased in plantar loading under the lateral aspect of the foot after 5km unshod running. However, completely opposite results were observed from the previous long-distance shod running studies. For instance, the plantar loading was decreased under the lateral aspect of the foot (Alfuth & Rosenbaum, 2011; Willems, De Ridder, & Roosen, 2012) and T2 values were increased in the medial tibiotalar cartilage after long-distance shod running (Schutz et al., 2014).

Limitations of the current study should be acknowledged while interpreting the results. The fitness level of the participants was self-reported, although the Tegner scale was employed for objectively assessing the activity level in this study. It should be also noted that the fitness level was varying between the marathon-experienced runners. Time for the post-run scan was also varied due to the traveling time. However, all participants completed the post-run scans within four hours. The small sample size may also cause statistical power issues, although we reported the effect size and also used intra-individual design to maximize power. Another limitation of this study is that all participants reported that they are right handed, but one person was ambidextrous although he showed no significant differences in gait. Moreover, as this study recruited Caucasian participants only, the current results can be different in other ethnicities.

6.5 Conclusion

This is a first-time study to evaluate the effect of 5km unshod running on T2 relaxation time in tibiotalar cartilage in healthy, young Caucasian, first time unshod runners. The findings suggest that 5km unshod running had an acute effect on T2 relaxation time in AZ, PZ, and lateral tibiotalar cartilage, but only in the novice runners group. Increases in plantar pressure with activity amongst novice runners corresponds to the location of increased T2 signal and plays a role in tibiotalar cartilage damage, whereas ankle kinematics did not appear to directly influence the T2 changes. These significantly higher T2 values in the novice runners may indicate potential cartilage damage, but longitudinal monitoring of T2 would be required for further study. The association between ankle biomechanics and T2 values in the tibiotalar cartilage needs further study.

Chapter 7. Evaluation of Internal Biomechanics of Ankle Cartilage: A Systematic Review

7.1 Preface

A literature review was conducted in a systematic review manner to provide an overview of the literature describing the internal foot biomechanics using a finite element (FE) foot model. This chapter systematically determines how previous studies developed their models (i.e. material property, boundary and loading condition) for analysis of FE models in response to repetitive loading on the foot and ankle complex.

7.2 Introduction

A finite element (FE) model is a common tool used in biomechanical experiments to obtain biomechanical information such as internal stress (von Mises) of the bones, soft-tissues, and articular cartilage. Biomechanical assessment using FE models of the foot and ankle have been applied for understanding certain injuries, designing orthoses, designing footwear, designing insoles, predicting surgical outcomes, and for general understanding of foot biomechanics. However, investigations into the effects of excessive loading induced by long-distance running on the ankle (tibiotalar) cartilage using FE modelling have never yet been conducted. In addition, investigating the differences in foot biomechanics between trained and novice runners is essential to allow improved understating of running-related injuries because runners of differing experience level may have different coping strategies during long-distance running.

Therefore, the aim of this systematic review was to provide the current state of knowledge with regards to developing and analysing FE models of the foot and ankle. For practical reasons, the current review only focused on FE model studies investigating foot regions that are affected during walking or running. Some other studies focusing on the design of insoles or footwear were all excluded. More details of the inclusion/exclusion criteria are explained in the eligibility criteria section.

7.3 Methods

7.3.1 Search strategies

All findings were based on a databased search of SCOPUS, Web of Science and Ovid MEDLINE published from 2000 to 2016. The search keywords used are as follows: 1) finite element OR FE; AND 2) foot OR feet; AND 3) stress* OR strain*; AND 4) gait OR walk OR walking OR run OR running OR long distance. The final search was completed on July 2016.

The database search resulted in a number of articles and the following criteria were used for eligibility for inclusion:

1. a healthy adult (over 18 years) with no trauma history and no foot pathology
2. the studies should include development of a comprehensive FE foot model with three-dimensional (3D) actual geometry of foot skeletons and soft tissues

3. the studies were designed to estimate strain and stress within the bones, soft tissues, and ligamentous structure of the foot with simulation of a static, quasi-static or dynamic loading condition
4. full-text was written in English

Articles were **excluded** if:

1. the aims of the studies were designed to develop insoles, footwear and/or orthoses
2. the studies were developed FE model based on the injured foot
3. the studies only included part of the foot (e.g. metatarsal or heel region only)
4. the studies included aged people or children
5. the studies were conference or review papers

7.4 Results and Discussion

A search of Web of Science, SCOPUS and Ovid MEDLINE produced 277 articles in total (Figure 7.1). After duplicates were removed, 255 articles remained. Based on the eligibility criteria, title and/or abstract were initially screened, and 238 articles were removed. The remaining 17 articles were initially included as potentially relevant to the current study. After reading the full text of these 17 articles, only four of them were included because the rest of the articles did not meet the eligibility criteria. One more article was included after searching through the reference lists. Therefore, **five** articles were finally selected for the current systematic review.

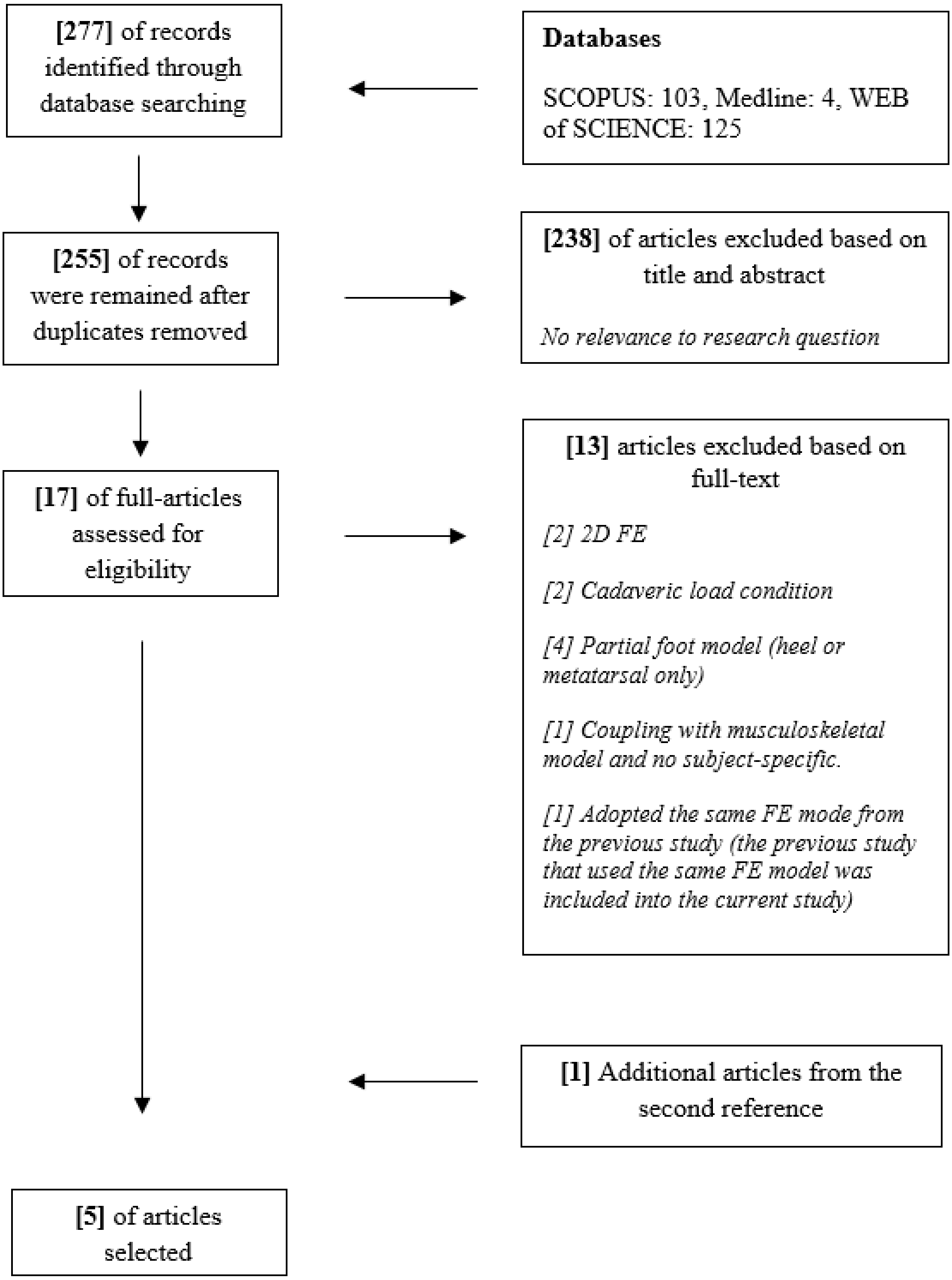

Figure 7. 1. Flow diagram of the systematic review process and search history.

7.4.1 Description of the studies

The five FE foot model studies included in this review all had different aims and specific questions in mind: elucidating the biomechanical behaviours of the plantar aponeurosis (PA) (Lin et al., 2014); developing an advanced-detailed 3D foot (Chen et al., 2010); evaluating the effect of PA stiffness on the foot (Cheung, Zhang, & An, 2004); quantifying plantar stress distribution (Chen, Tang, & Ju, 2001); investigating fatigued-related foot injury mechanisms (Gefen, 2002). The overview of selected studies is described in Table 7.1.

Table 7. 1. *Characteristics of developed FE models from the five selected studies.*

Author	Aim	Reconstruction of model					Material property	Boundary and loading conditions	
		Images	Number of Bones / elements	PA / elements	Ligaments / elements	Soft tissues / elements		Simulation / devices	Muscles
Lin et al. (2014)(Lin et al., 2014)(Lin et al., 2014)	Biomechanical response of the PA during stance phase of gait	MRI / healthy male	26 8-noded hexahedral linear solid elements.	Ultrasound was used to find the location & thickness. 8-noded hexahedral linear solid elements	Long plantar ligament, short plantar ligament, spring ligament, lateral spring ligament & collateral ligaments connecting the metatarsal head with the phalanx Cable discrete-beam elements	Plantar soft tissues only. 8-noded hexahedral linear solid elements	Isotropic, incompressible, & homogeneous Bones (MPa, *v*): 7300, 0.3 Cartilages: 10, 0.49 Ligaments: 260, n/a Soft tissues: n/a, 0.49 PA: n/a, n/a - transversely isotropic.	Entire gait phase. Motion capture & force plate	Muscle forces are assumed to already be incorporated in to the FE model as the gait results from the synergy of the musculoskeletal system
Chen et al. (2010)	Develop a detailed 3D FE foot model	CT / healthy male	30 incl. sesamoids. 4-node tetrahedral elements.	Defined based on the anatomical descriptions. 5 sub-bands of PA. 2-node tension-only truss elements	Major ligaments (no information) 2-node tension-only truss elements	Plantar soft tissues only. 4-node tetrahedral continuum elements	Bone, ligament, PA: linear isotropic manner Plantar soft tissue: isotropic, incompressible, hyperelastic 2nd-order polynomial formulation. Bones (MPa, *v*): 7300, 0.3 Cartilages: 1.01, 0.4 Ligaments: 260, 0.4	Static standing. Plantar pressure mat.	Incl. the gastrocnemius-soleus muscle force at the Achilles tendon. Estimated muscle load of 162.5N was applied on the foot during standing

							Soft tissues: hyperelastic PA: 350, 0.4		
Cheung et al. (2004)	Effect of PA stiffness on the PP.	MRI / healthy male	28 (incl. distal segments of the tibia & fibula). 3D tetrahedral elements.	Defined based on the anatomical descriptions Tension-only truss elements	Major ligaments (no information). Tension-only truss elements.	3D tetrahedral elements.	Homogeneous, isotropic and linearly elastic Bones (MPa, *v*): 7300, 0.3 Cartilages: 1, 0.4 Ligaments: 260, n/a Soft tissues: 0.15, 0.45 PA: 0-700, n/a	Static standing. Plantar pressure mat.	Only the Achilles tendon loading was considered. Other muscles forces were not simulated.
Gefen et al. (2002)	Investigating fatigue-related foot injury mechanisms	MRI / Open source from two males and one female)	17 Tetrahedral elements	Incl. PA, but no information	Dorsal ligaments, Plantar ligaments, Transverse ligaments, Long plantar ligaments, Plantar aponeurosis, Ligaments at the talocalcaneal joint. Tetrahedral elements	Tetrahedral elements	Homogeneous, isotropic, and linear elastic Bones (MPa, *v*): 7300, 0.3 Cartilages : 1, 0.1 Ligaments: nonlinear Soft tissues: nonlinear PA: nonlinear	Quasi-static. Optical contact pressure display Method & digital radiographic fluoroscopy system	Muscle forces of TiA, EHL, EDL, TrS, TP, FHL, FDL, PL, PB and AH were incorporated into the FE model

Chen et al. (2001)	Quantify stress distribution of the foot during unshod gait	CT / healthy male	26 4-node tetrahedral elements	Node cable elements	2-node cable elements	4-node tetrahedral elements	Homogeneous, linear, elastic solids Bones (GPa, *v*): 10, 0.34 Cartilages (MPa, *v*) : 10, 0.4 Ligaments: 11.5, n/a Soft tissues: 1.15, 0.49	Quasi-static. Motion capture	Muscles forces were not simulated.

PA- Plantar Aponeurosis; TiA-Tibialis Anterior; EHL-Extensor Hallucis Longus; EDL- Extensor Digitorum Longus; TrS-Triceps Surae; TP-Tibialis Posterior; FHL-Flexor Hallucis Longus; FDL- Flexor Digitorum Longus; PL-Peroneus Longus; PB- Peroneus Brevis; AH- Abductor Hallucis

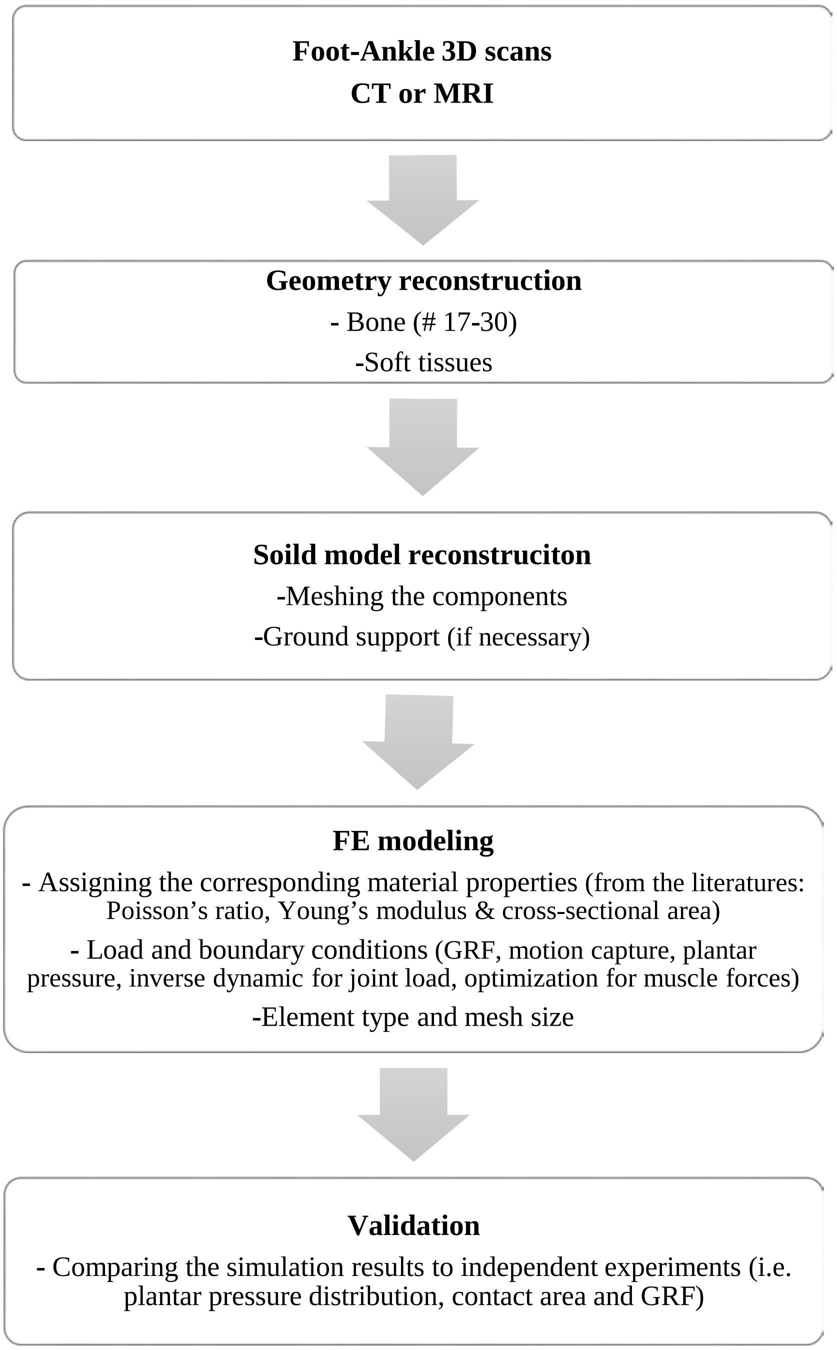

Figure 7. 2. Typical processes of developing FE model.

7.4.2 Methodology of developing FE model

Construction of geometrical and connective component

When building their FE models, all five studies obtained the geometry of the ankle/foot complex from either MRI or CT scans with a healthy male subject in a neutral foot position. The intervals of imaging were generally 1mm–2mm in the coronal plane. The intention of 2mm intervals was for reducing the redundant details of the surface texture of the bone.

The FE models from the five studies consisted of 17-30 bony segments. The foot bones of those containing 17 consisted of the talus, calcaneus, navicular, cuboid, three cuneiforms, five metatarsals, and five phalanges (Gefen, 2002a). For simplification of models, proximal, middle and distal phalanges were unified within each digit to form a single unit. It was assumed that this might not cause significant inaccuracies for estimation of stress distribution because the interphalangeal joints have minimal contribution during normal gait (Saltzman & Nawoczenski, 1995). Although these joints have less contribution to gait, this foot model (Gefen, 2002a) could be more suitable when the foot is in static simulation. Another two studies (Chen et al., 2001a; Lin et al., 2014) included 26 of the foot bones, including the talus, the calcaneus, the navicular, the cuboid, three cuneiforms, five metatarsals, and 14 phalanges. In the final two studies, the distal segments of the tibia and fibula (Cheung et al., 2004) and hallux sesamoids (Chen et al., 2010) were also included in addition to the 26 foot bones, making a total of 28 and 30 bony segments, respectively. The reason for including the sesamoids bones was because previous studies (Morag & Cavanagh, 1999; Mueller et al., 2003) indicated that sesamoid bones are the main “stress risers” in the foot. Chen et al. (2010) confirmed their findings by quantitatively reporting the largest stress concentration in the lateral sesamoid bone.

Articular joint movements among the tibia, fibula, talus, calcaneus, navicular, cuboid, cuneiforms, and metatarsals were created as surface-to-surface “contact” elements, meaning that the articulating movements were considered as frictionless and allowing relative articulating movement. Thus, only compression forces were accounted for when transmitting the force through adjacent bone contact. The geometry of articular cartilage was not considered in all studies, while their mechanical properties of contributing to normal joint loading transfer was taken into account. It was assumed that the overall joint stiffness against shear loading was governed by the encapsulated soft tissues, ligaments and contacting stiffness between the adjacent articulation surfaces (Cheung et al., 2004; Gefen, 2002a). On the other hand, the governing stiffness during contact was obtained from the literature with 1.01 MPa (Chen et al., 2010). The other two remaining studies (Chen et al., 2001a; Lin et al., 2014) did not mention anything about the governing stiffness.

The foot bones, encapsulating soft tissues and cartilage were meshed by 8-noded hexahedral linear solid elements (Lin et al., 2014) or tetrahedral elements (Chen et al., 2001a; Chen et al., 2010; Cheung et al., 2004; Gefen, 2002a). These two types of elements shapes are most generally used for mesh generation. Hexahedral mesh generation is generally more computationally expensive and requires user intervention, while tetrahedral meshing is more automated (Mitchell, 2002). As a result, most of the selective studies utilized tetrahedral elements. Nonetheless, hexahedral elements are also preferred due to their high performance of convergence rate and accuracy of the solution. Tadepalli et al. (2011) investigated the pros and cons of hexahedral and tetrahedral elements under several loading conditions, which are generally seen in foot biomechanics. They found that hexahedral elements consistently performed well, predicting reasonable contact pressure and shear stresses under a range of simulation loadings and footwear condition (unshod or with insole). However, tetrahedral elements performed poorly and it suggested that it could be only used under frictionless contact or material incompressibility conditions. Especially in barefoot condition, tetrahedral elements resulted in very poor shear stress estimation. Therefore, utilizing hexahedral mesh generation could be ideal for future FE foot analysis, although it causes increased computational cost.

PA (or plantar fascia) was represented by hexahedral with tension-only material behaviours (Lin et al., 2014), tension-only truss (Chen et al., 2010; Cheung et al., 2004) or 2-node cable element (Chen et al., 2001a). As Lin et al. (2014) were more focused on the stress distribution within PA, they adopted tension-only material behaviours combining with hexahedral element because this is a very effective technique for investigating plantar stress distribution (Tadepalli et al., 2011). The use of tension-only truss may limit the capability of predicting the force or elongation distribution and stress/strain distribution on the PA (Lin et al., 2014). Other major ligaments such as long and short plantar ligaments, spring and lateral ligaments and collateral ligaments connecting metatarsophalangeal joints were also incorporated into the model. In order to simulate the ligamentous structures, it was defined by cable-discrete beam (Lin et al., 2014), tension-only truss (Chen et al., 2010; Cheung et al., 2004) or 2-node cable (Chen et al., 2001a). In accordance to ligaments' physiological function, truss elements with a "no compression" option was utilized (Chen et al., 2010; Cheung et al., 2004). By using this option, these truss elements resisted tension-producing forces while stabilizing the foot.

The attachment points of ligaments and PA were determined based on anatomical descriptions because these could not be reconstructed from MRI or CT. One study (Lin et al., 2014) determined the location and thickness of the PA by using an ultrasound system.

Material property

The bone and cartilage component materials were generally assumed to behave in a homogeneous (i.e. having the same property or degree of value at every points), isotropic (i.e. uniformity in all directions), and linearly elastic manner (i.e. linear relationship between stress (internal forces) and strain (measure of deformation) as explained by Hooke's law). The material properties such as Poisson's ratio, Young's modulus, and cross-sectional area were adopted from the literature. Young's modulus is one of the elastic moduli and it defines the relationship between stress and strain in a material. Poisson's ratio is the negative ratio of transverse to axial strain. For the foot bones, Young's modulus was 7300 MPa and the Poisson ratio was 0.3. For the cartilage, Young's modulus was 1 - 10 MPa and the Poisson ratio was 0.1 – 0.49. The values for the ligaments, soft tissues and plantar fascia were varied and more details are given in Table 7.1. In addition, one study (Lin et al., 2014) determined the material property of the plantar heel soft tissue by using an in-house ultrasound-based loading-unloading device. The subject's right foot was embedded on the device and unloaded thickness and maximal loaded thickness were measured by ultrasonography images.

The boundary and loading conditions

For obtaining input conditions of the FE analysis, participants were generally instructed to perform either dynamic walking or static balanced-standing.

The centre of pressure, GRF, foot-shank position and/or kinematic parameters of the foot should be known to simulate the physiological loading condition on the foot. These parameters were obtained by using a motion capture system with a force plate or a plantar pressure mat. In the FE analysis, static standing (Chen et al., 2010; Cheung et al., 2004), quasi-static (Chen et al., 2001a; Gefen, 2002a) or entire stance phase during dynamic gait were simulated (Lin et al., 2014). Two studies (Chen et al., 2001a; Gefen, 2002a) performed simulation under a quasi-static state, which assumed that bones are linearly elastic. While the quasi-static approach may cause some overestimation of the resulting stresses, it may be suitable for investigating the relative effects of muscle fatigue on structural loading (Grimston & Zernicke, 1993). The loading and boundary conditions used by the Chen et al. (2001a) was achieved by constraining the upper surface of the foot model and moving the ground toward the foot with a constant linear speed and the angular speed according to the gait data. The acceleration of the foot in association with the ground was assumed zero, which is not a realistic condition. For taking into account the actual loading conditions of the foot, the variation of velocities, the varus-valgus, internal and external rotation of the foot during gait should be considered (Chen et al., 2001a). Two studies (Chen et al., 2010; Cheung et al., 2004) considered the Achilles tendon loading for the simulation of standing. The vertical force was estimated with a subjects' body mass and it was applied on each foot during standing. For example, if a subject's body mass was 70 kg, approximately 350 N was applied. Other intrinsic and extrinsic muscles forces were all ignored and only the Achilles tendon force was considered (Cheung et al., 2004). In addition to the Achilles tendon loading, Chen et al. (2010) considered the gastrocnemius-soleus muscle force acting through the Achilles tendon as well, estimating the muscle load as 162.5 N. It was assumed that the superior surface of the soft tissues, distal fibula and tibia were fixed and the ankle joint was in its neutral position during standing. However, the limitations of static or quasi-static FE analysis should be acknowledged; it only allows for biomechanical information to be provided during certain loading conditions or during a certain period. Thus, in order to obtain a more comprehensive geometric foot model, the boundary and loading condition should be obtained from human motion analysis (Wang, Wong, & Zhang, 2016).

Unlike other previous studies, Lin et al. (2014) adopted the motion capture system to collect the kinematic data of foot bone motion by placing 15 reflective markers on the foot. As the gait movement results from the synergy of the musculoskeletal system, it can be assumed that the intrinsic factors such as muscle activation is already incorporated into the FE model. Therefore, including the muscle force into the FE model was unnecessary in this study. While analysing these markers, the initial position of the FE model was defined and the boundary condition was incorporated. One person was asked to walk at a speed of 1.4 m/s for six trails and the averaged translational and rotational data obtained from these six trials were adopted as the input conditions for FE analysis. Another study (Chen et al., 2001a) also used the motion capture system but it was only for obtaining the kinematics of the foot with respect to the floor; that is, in order to define the axis of the foot, only two reflective markers were placed on the lateral malleolus and the 2nd metatarsal head. The angular displacements, velocities, and accelerations of the foot with respect to the ground were calculated from these two markers. However, as Lin et al. (2014)'s study had the assumptions that the metatarsus and the mid-foot behaved as a rigid element, the relative motions were ignored, although they adopted a motion capture system.

Validation of FE model

Validation is a crucial part of developing FE models. Except one study (Chen et al., 2001a), all the models were validated by comparison of subject-specific barefoot plantar pressure distribution, contact area and GRF between experimental measurement and FE analysis. For instance, the peak plantar pressure was compared between plantar pressure distribution estimated by the model and experimental data gathered during standing or midfoot stance. The pressure values were peaked around the centre of the heel, indicating that both the FE predicted stress and the experimental data showed similar patterns of plantar pressure distribution. It should be noted that the values predicted by the model and those of the experiments could be slightly different, although they showed a similar trend or the coefficient value was close to 1. Using the simplified segments (e.g. using only seven segments of the foot) in the FE models may cause the discrepancy of results. In addition, the skin movement artefacts of the reflective markers can be another factor that may lead to the differences (Lin et al., 2014). The differences in resolution of pressure measurement and prediction may also cause the deviation (Cheung et al., 2004).

In contrast, Chen et al. (2001a) compared the plantar pressure patterns with measurement results from previous literature and they found that the patterns were similar. However, obtaining the experimental data of the same participant used for developing the FE model would be more accurate for validation of the model due to the difference of measuring techniques or variation among participants.

7.4.3 Analysis of FE model

The parameters predicted by the FE models were as follows: Tensile force and von Mises stress in the PA (Lin et al., 2014) or in the regions of interests of the bony structures (Chen et al., 2010; Cheung et al., 2004; Gefen, 2002a); Internal and plantar soft-tissues deformation (Chen et al., 2010); strain of the ligaments (Cheung et al., 2004); arch height (Cheung et al., 2004); and plantar pressure distribution (Chen et al., 2001a).

Chen et al. (2001a) conducted an early study to estimate the stress distribution in the healthy foot during mid-stance to push-off phase in barefoot walking using a 3D FE analysis. This study reported that the plantar pressure was gradually increased in the forefoot regions from mid-stance to push-off. The peak von Mises stress was chosen for displaying the bone stress; the 3rd metatarsal bone always showed the highest values, ranged between 2.12 MPa and 6.91 MPa, followed by 4th, 1st, 5th and 2nd metatarsal bones in descending order during mid-stance to push- off. The plantar distribution patterns were similar with previous experimental studies, but small, inconsistent results were also observed because they used different techniques and participants. Although it would be ideal to obtain the experimental data from the same subject that was used for developing the FE model, this study compared the current result with previous experimental results due to a lack of experimental equipment.

To the best of our knowledge, only one study (Gefen et al., 2002a) examined the effects of muscular fatigue induced by 2 km treadmill walking on foot stability and its internal stress during the stance phase. The electromyography (EMG) data during the marching was incorporated into the 3D FE model (Gefen et al., 2002a) and consequently resulted in increasing stress concentration on the metatarsals and calcaneal regions. Incorporation of the fatigued muscles information into the FE model resulted in increasing stress concentrations at the calcaneal and metatarsal regions. This may contribute to development of stress fractures. However, this study did not adopt a subject-specific model. The 3D FE model was adopted from the previous study (Gefen et al., 2000a) and the 3D shape of each bone in the foot was reconstructed from the Open MR images obtained from three different subjects. The muscle force was also obtained from four volunteers during 2 km marching on a treadmill. Moreover, they used a computerized X-ray assessment which was not able to measure the 3D planes, and hence the images of the foot motion during gait was only taken in the sagittal plane.

Chen et al. (2010) predicted the internal stress and plantar soft-tissue deformation in the forefoot regions during standing. This study found that the greater internal stresses were likely to occur near the bony prominence of metatarsal heads (i.e. sesamoids). The lateral 1st sub-metatarsal showed the highest von Mises stress, followed by medial 1st sub-metatarsal, while the 2nd – 4th sub-metatarsals showed similar levels of von Mises stresses during simulation of balanced standing. The plantar soft-tissues thickness (mm) was also predicted by the FE model and the value was compared with a previous *in vivo* sonography study (Bygrave & Betts, 1993); although the geometry of the model and loading conditions were different in this study, the deformation values in the model were within acceptable range. The deformed tissues thickness under the 2nd sub-metatarsal showed the highest value, followed by the 3rd and 4th sub-metatarsals. The author suggested that the deformation under the metatarsal heads is affected by the compression against the bones; that is, greater von Mises stress occurs where soft-tissue interacts with geometrically irregular bony structures (Chen et al., 2010). This study (Chen et al., 2010) showed a possible way to examine the complexity of the mechanical behaviour in the plantar soft-tissue by using the FE model. However, as this study was performed in the static model during balanced standing, it is limited in its scope to understand the internal stress and bone motion during walking, which would be very different. In addition, the internal stress was derived from the innermost soft-tissue boundary and this is not realistic of the internal structures of the plantar soft-tissue, which consists of four layers of muscles and a plantar fat pad. Including the four layers of the muscles for the future study may provide more precise information.

The effect of the different level of plantar fascia stiffness (manipulating by elastic modulus ranged between 0-700 MPa) on the arch, ligaments, bones and encapsulated soft-tissue structures of the foot was investigated by Cheung et al. (2004). This study found that decreasing the Young's modulus of plantar fascia resulted in a significant increase in maximum strains of the long and short plantar and spring ligaments. As the plantar fascia is the major stabilizer of the arch during the gait cycle, with zeroing (i.e. laceration or resection of structures) of the plantar fascia, other major ligamentous structures have to contribute to this stabilizing role instead of the plantar fascia. With further decrease of fascia stiffness, increasing stress concentration was detected at the plantar ligaments' attachments point of the cuboid bone. When zeroing the Young's modulus of fascia, reduction of the arch height and midfoot pronation were also observed during load bearing, but it did not lead an entire collapse of the foot arch. This study concluded that the plantar fascia had an important stabilizing role during mid-stance of the gait cycle. Reduction of its stiffness to less than 50% may cause significant strains/stress in the bony and ligamentous structures. Similar to other modelling studies, however, homogeneous and linearly elastic material properties were employed in order to simplify the analysis, and this limited the simulation of the model to produce results that are more accurate. The ligaments within the toes and other intrinsic and extrinsic muscle forces were not considered, but only the Achilles tendon loading was taking accounted. In addition, simulation of balanced standing may not provide enough information (e.g. the plantar fascia's role in the foot during the gait cycle) as the gait phase is more complex. The point of centre of pressure was assumed unchanged as it was simulated under balanced standing state. Hence, the effect of fascia stiffness could be different in different phases of the gait cycle.

More recently, the biomechanical response of the PA during all phases of the gait cycle was investigated by Lin et al. (2014). A peak tensile force on the PA was observed during the terminal-stance phase. The peak stresses were all observed near the proximal calcaneal body site which was the insertion point of the PA. When the contralateral foot begins to swing, the heel in the supporting limb starts to rise with the hallux dorsiflexion; in this moment, the force of the PA increases and reaches its peak. With regards to von Mises stress distribution on the PA, the medial regions of the PA showed the highest peak values compared with the central and lateral regions. The great stress in medial region was not too surprising as the medial longitudinal arch has a higher arch height than the lateral longitudinal arch, and therefore a greater tensile force can be observed during weight-bearing (W. Kim & Voloshin, 1995). Caravaggi et al. (2010) also suggested large von Mises stress in the medial region may be because of the greater dorsiflexion angle of the 1st metatarsophalangeal joint during toe-off when compared to other metatarsophalangeal joints.

7.4.4 Limitations

It should be made aware that some simplifying assumptions were included when developing the FE models in order to overcome the technical difficulties associated with computational limitations. The material property of bones and cartilage were mostly assumed to behave in a homogeneous, isotropic, and linearly elastic manner; that is, it is assumed to be kept constant in time. Nakamura et al. (1981) indicated that this assumption could be suitable for bone analysis during simulated dynamic loading but a quasi-linear viscoelastic assumption might be more appropriate for the cartilage analysis in FE models.

Ligaments and plantar fascia were also usually simplified as trusses. This simplified element type for the connective tissues and joints is not able to accurately represent their anatomical features, thereby possibly resulting in inaccuracy of analysis. Moreover, as the material properties could not be obtained from the same subject who provided their medical images for construction of the FE models, all the parameters were adopted from previous studies, which might differ from the subject. This might result in another possible discrepancy of the FE analysis.

Lin et al. (2014) made assumptions that the metatarsus and the mid-foot behaved as a rigid body and thereby any relative motions were ignored. Gefen et al. (2002) unified phalanges within each toe because they assumed that the interphalangeal joints might not play an important role in a normal gait. Models with rigid bodies of the tarsal bones (Chen et al., 2001a), calcaneus, metatarsus and phalanges (Lin et al., 2014) are not capable of representing the real joint mobility. Although these assumptions may have minimal effect on the results, the possibility of discrepancy should be considered. However, this assumption may be suitable when simulating the static standing.

In addition, most of the studies performed static standing or quasi-static simulation during mid-stance phase. However, the bone motions and tissue stresses would be significantly different between gait phases. Simulation of entire phase with a comprehensive FE model should be required for the future study.

7.5 Conclusion and Future Studies

This systematic review identified five studies in the literature that developed foot/ankle FE models for analysing the plantar pressure distribution, strain/stress and von Mises stress on the PA, bones and ligamentous structures. All of these five models were developed from a healthy foot in order to investigate the biomechanical responses during a static standing and/or a gait phase. These five studies generally reported greater stress concentration on the metatarsal bones (e.g. 2^{nd} and 3^{rd}), the calcaneal region near the attachment site of the PA, the sesamoid bones of the hallux, and the medial region of the PA in response to external loadings. Obviously, these regions are also associated with running-related injuries such as plantar fasciitis, and metatarsal stress fractures. In one study (Gefen, 2002a) the researchers integrated the muscular fatigued conditions into the FE analysis; however, this study did not adopt a subject-specific model and walking was performed over a relatively short distance (2 km). Furthermore, the biomechanical behaviours of the ankle and foot complex in response to the walking and running very different.

The obtained information from FE analysis would be useful to understand the general behaviour of the foot structures. In addition, as some runners may be injured in response to long-distance running while others are not, investigating the internal stress and strain of the foot between trained and novice runners would be the essential part that allows improved understanding of running-related injuries because they may have different coping strategies for extensive running. Analysis of the FE model, developed from both trained and novice runners, would be ideal for future work to obtain the knowledge of running-related injuries and to provide mechanisms of pathological pathway.

Chapter 8. Tibiotalar Cartilage Stress Corresponds to T2 Mapping: Application to Unshod Running in Novice and Marathon-Experienced Runners

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8.1 Preface

There are no studies investigating the internal biomechanics of the ankle using FE modelling in response to unshod running. A previous study reported stress reduction in unshod running when compared with shod running, but this study focused on the patellofemoral joint (Bonacci et al. 2014). This chapter represents the first study to investigate the effects of unshod running on *in vivo* internal stresses in ankle (tibiotalar) cartilage and the association between FE predicted cartilage stress and MRI derived T2 maps.

8.2 Introduction

Repetitive and high rate loading on the ankle and foot complex during long-distance running can be a potential risk factor for running-related injuries (Kennedy J.G., Knowles B., Dolan M., & Bohne, 2005). Consequently, many biomechanical experiments have been conducted to quantify kinetics, kinematics, and plantar pressure distribution in response to 10km – 42km running (Kyröläinen et al., 2000; Nagel et al, 2008; Willems, De Ridder, & Roosen, 2012). However, quantifying *in vivo* internal stress associated with bones, cartilage, and soft-tissues is difficult and inaccurate because the loading condition during *in vitro* experiments is very different from the actual physiological loading condition. Alternatively, a finite element (FE) model may be employed in many biomechanical experiments due to its ability to model irregular multi-segment geometries, diverse loading, physiological boundary conditions, and various material properties (Wang et al., 2016). Furthermore, the FE model can evaluate internal soft tissue stresses that are hard to measure *in vivo*.

Many biomechanical studies have advocated unshod running as it may reduce the risk factors of running injuries by lowering collision force with better running performance (Jenkins & Cauthon, 2011; Lieberman et al., 2010). However, to the best of our knowledge, the effect of unshod running on the ankle cartilage using FE analysis has yet to be investigated. One study (Gefen, 2002) examined the effect of muscular fatigue induced by 2km marching on the foot stability and its internal stress. The electromyography data during marching was incorporated into a three-dimensional (3D) FE model and reported to increase stress concentrations on the metatarsals and calcaneal regions, which may contribute to the development of stress fractures. However, the biomechanical behaviour of the ankle and foot complex in response to walking and running would be very different.

Recently several clinical studies employed T2 or T2-star (T2*) map modality to quantify stress of the knee and ankle cartilage in response to a marathon race (W. Krampla et al., 2001; Schueller-Weidekamm et al., 2006; Stehling et al., 2011). However, it remains unclear whether *in vivo* internal stresses in articular cartilage is associated with T2 maps which allows may detect the early stages of cartilage damage. Therefore, the purpose of this study was to evaluate tibiotalar cartilage stresses and T2 relaxation times (ms) in response to long-distance unshod running. It was hypothesized that cartilage stress patterns may be associated with T2 maps and that T2 values may be influenced by cartilages stresses following running as predicted by FE modelling.

8.3 Methods

8.3.1 Experimental Data Collection

Participants

Ten novices (5 female, age: 29±6.8yrs, height: 1.7±0.1cm, weight: 65.6±9.8kg) and ten experienced runners (5 female, age: 31.2±9.8yrs, height: 1.73±0.1cm, weight: 65.4±9.8kg) were recruited for this study. All participants were free from lower-limb injury at the time of data collection and they were first-time unshod runners. They were habitually run with conventional running shoes with heel strike techniques. Novice runners have never participated in any type of long-distance running prior, while experienced runners have regularly participated in half- or full-marathon races. Before participation, a written informed consent form was signed by all participants. This study was approved by the human ethics committee in our institution (ref: 016488).

Running protocol

5km unshod running was performed on a treadmill with self-selected pace. Before start the running, participants walked for seven minutes for familiarisation. The treadmill was located in a laboratory so that humidity, wind, and temperature were controlled all the times.

Plantar Pressure

Plantar pressure was measured before and after 5km unshod running on a treadmill. The dynamic plantar pressure of the right foot was measured during unshod running with the

Novel Emed® pressure platform (www.//novel.de/novelcontent/emed). All runners were instructed to maintain a similar speed with their 5km unshod running. The pressure map was subdivided into 11 anatomical region of interests (ROIs) – hallux (T1), second, third, fourth, and fifth toes (T2-T5), five metatarsals (M1, M2, M3, M4, M5), medial midfoot (MM), lateral midfoot (LM), medial heel (MH), and lateral heel (LH). Immediately after the 5km running, the dynamic plantar pressure was measured. Three valid trials (a single step within the border of the pressure mat) were selected and averaged for further analysis. Peak plantar pressure and peak force were obtained from each ROI.

Magnetic Resonance Imaging

Before and after running, MRI data of the right foot and ankle were acquired with a 3.0-T scanner (Siemens Skyra, Erlangen, Germany) and with a 16-channel foot coil. Following sequences were used for MR data acquisition: *1)* sagittal T1 turbo spin echo (flip angle [FA], 140 deg; echo time [TE], 140 ms; repetition time [TR], 600 ms; slice thickness [ST], 2.5 mm; field of view [FOV], 250 mm; Bandwidth, 257 Hz/Pixel; time of acquisition [TA], 2.57 minutes), *2)* sagittal T2 DESS gradient echo water excitation (FA, 28 deg; TE, 5 ms; TR, 12.90 ms; ST, 0.6 mm; FOV, 250 mm; Bandwidth, 310 Hz/Pixel; TA, 4.51 minutes), *3)* sagittal T2 DESS gradient echo water excitation (FA, 28 deg; TE,5 ms; TR, 12.90 ms; ST, 0.6 mm; FOV, 250 mm; Bandwidth, 310 Hz/Pixel; TA, 4.51 minutes), *4)* sagittal and coronal short tau turbo inversion recovery (STIR) for showing pathological changes in soft tissues (FA, 150 deg; TE, 50 ms; TR, 4,000 ms; ST, 2.5 mm; FOV, 250 mm; Bandwidth, 248 Hz/Pixel; TA, 4.18 minutes), and *5)* sagittal and coronal T2 mapping (FA, 180 deg; TE, 13.8 ms; TR, 1,600 ms; ST, 3 mm; FOV, 140 mm; Bandwidth, 230 Hz/Pixel; TA, 4.16

minutes). 3.20±0.97 hour later post-run MR scans were performed with the same methodology of the pre-run measurements.

To quantify the T2 relaxation times of the tibiotalar cartilage, the MR scans were transferred to the Osirix Lite v.9.0.1 (Pixmeo, Geneva, Switzerland) and independently evaluated by two experienced musculoskeletal radiologists. Three sagittal images - lateral, middle, and medial sections - were selected through tibiotalar cartilage (Figure 8.1). Each sagittal image then divided into three zones – anterior, central, and posterior zones. Therefore, nine regions were identified from each ankle, and 180 regions were created from 20 ankles in total.

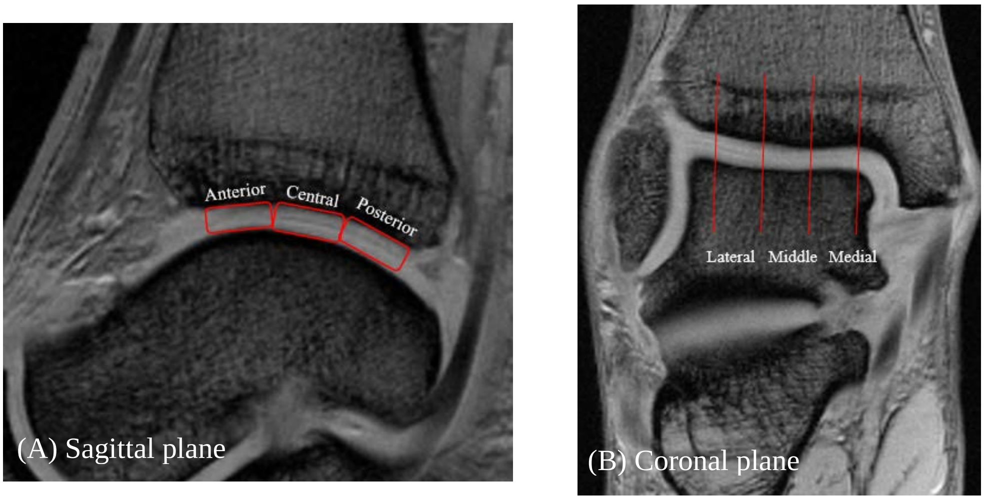

Figure 8. 1. Post-processing of MR image for T2 relaxation time of tibiotalar cartilage.

(A) Three zones were equally divided into anterior, central, and posterior zones in sagittal plane. (B) Three sagittal images (lateral, middle, and medial sections) were selected through tibiotalar cartilage.

8.3.2 Finite Element Foot Model

This study adopted a previously developed 3D anatomically-based FE foot model by Fernandez et al. (Fernandez, Haque, Hunter, & Mithraratne, 2012). That model was developed from magnetic resonance images (T1-weighted) of 2 mm intervals in a neutral unloaded position of a healthy adult male (age: 35 years, height: 1.74 m, weight: 78.7 kg) who was free of pathology or deformity. That model consisted of 21 musculotendon units (the interossei group, three brevis flexors, two brevis extensors, two abductors, adductor hallucis, four lumbrical muscles, and quadratus plantar). The model of Fernandez et al. (Fernandez et al., 2012) was previously validated by comparisons of predicted finite element plantar pressure against that measured from an EMED pressure platform of the same subject. The contact pressure and internal Von Mises stresses were also in the range previously reported (Gefen et al., 2000; Spears, Miller-Young, Waters, & Rome, 2005). In this study we adopted the Abaqus software for finite elastic simulations and mapped the bones, muscles and remaining soft tissue into a hexahedral mesh format with element resolution of 1.5 mm (Figure 8.2). This was chosen after a mesh convergence study that found the peak von Mises stress changed by less than 1% at this element size. The model was loaded in 11 plantar zones with the pressure maps from all twenty subjects. Thus, we have 40 FE models including pre- and post-run (Figure 8.3). The only component that remained fixed in the model was the top of the tibial bone, which is required for a quasi-static simulation. Each model solved in 5 minutes on a quad-core processor and predicted internal tissue von Mises stress. For this study we concentrated on the tibiotalar cartilage and divided the cartilage into anterior, central, posterior, medial, middle, and lateral to be consistent with the T2 map metrics (Figure 8.2, C, D). Average von Mises stress from each of the elements in these cartilage regions were extracted for statistical analysis.

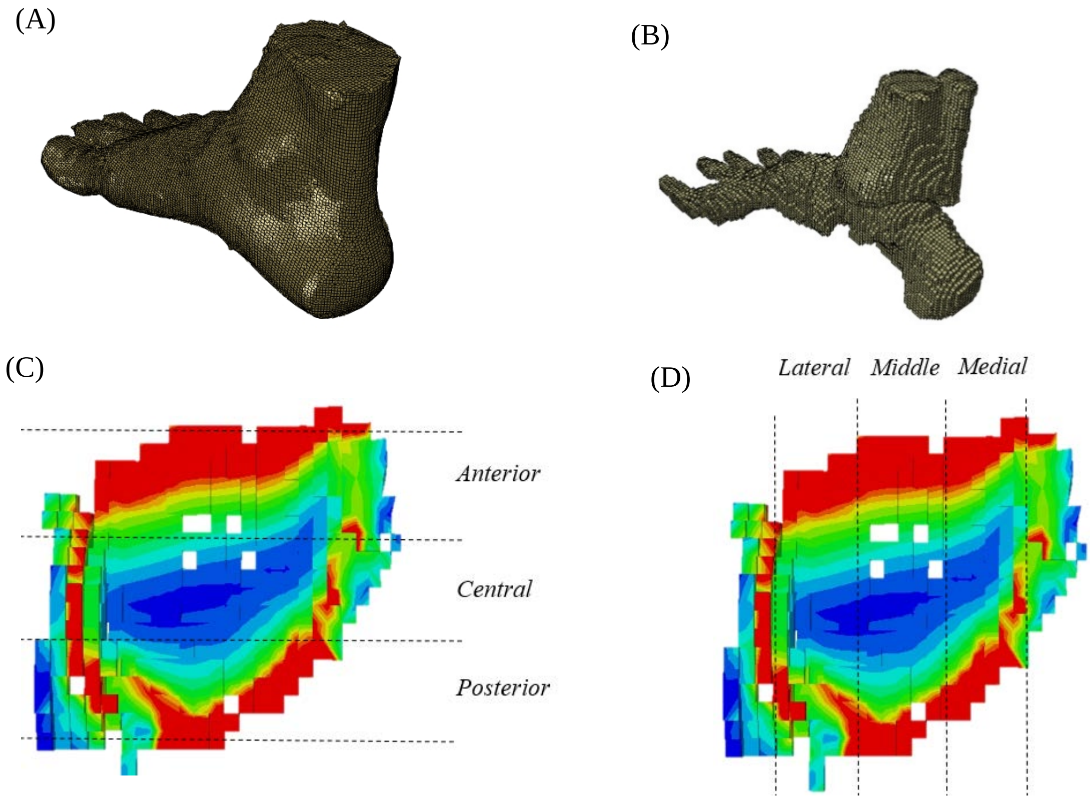

Figure 8. 2. Hexahedral mesh of entire foot (A) with bones extracted (B) and tibiotalar articular cartilage (C, D).

Representative of the tibiotalar cartilage showing the measured regions in transverse plane. Red pixel: ≥ 20 MPa, orange pixel: 19 ~ 16 MPa, yellow pixel: 15 ~ 11 MPa, green pixel: 10 ~ 4 MPa, dark blue pixel: ≤ 3 MPa

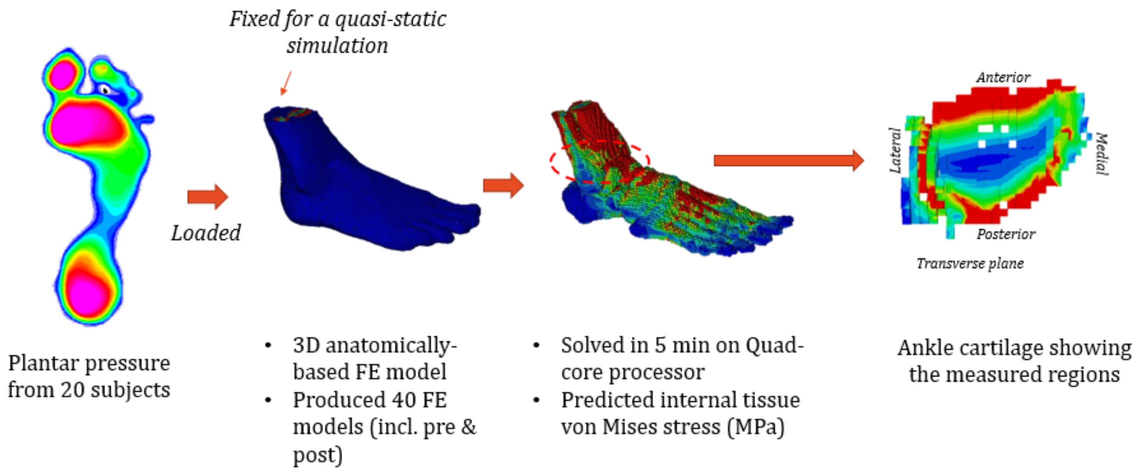

Figure 8. 3. Modelling process in this study.

A generic FE model was simply loaded with different foot pressure patterns that was measured from 20 participants during unshod running before and after 5km unshod running. Thus, 20 FE models from the pre 5km run and 20 FE models from the post 5km run were produced. Mean von Mises stress was obtained from each FE model and it was compared between pre- and post-run.

8.3.3 Statistical Analysis

Statistical analysis was conducted using SPSS software (version 20, IBM Statistics, SPSS Inc.). Von Mises stress, T2 values, and plantar pressure were presented as mean ± standard deviation. A paired student's *t* test was used to compare pre- and post-run values. Regional T2 and stress levels within ankle cartilage were compared using a one-way analysis of variance (ANOVA) with the Tukey's honestly significant difference post hoc test for multiple comparisons. Regional differences were compared either between anterior, central, and posterior or lateral, middle, and medial. To determine the reproducibility of T2 assessments between investigators, intra-class correlation coefficient (ICC) was conducted.

8.4 Results

8.4.1 Tibiotalar Cartilage Stress

The predicted von Mises stress of the tibiotalar cartilage during unshod running is presented in Figure 8.4. The novice and ME groups showed similar patterns in von Mises stress, showing a stress reduction after the running but only the ME group reached a significant level. In the ME group, von Mises stress was significantly decreased by 16.4%, 18.4%, 17.1%, and 16.8% in anterior (pre: 21.93±3.92 MPa, post: 18.33±3.44 MPa, $P = 0.05$), posterior (pre: 17.13±3.15 MPa, post: 13.98±2.97 MPa, $P = 0.05$), lateral (pre: 15.6±2.81 MPa, post: 12.93±2.55 MPa, $P = 0.05$), and middle (pre: 17.57±3.13 MPa, post: 14.62±2.78 MPa, $P = 0.05$) tibiotalar cartilage respectively. However, no significant stress differences were observed in the novice group between pre- and post-run measurements. Among the measured regions, the highest mean von Mises stress was observed in anterior tibiotalar cartilage in both groups and in both pre- and post-run measurement.

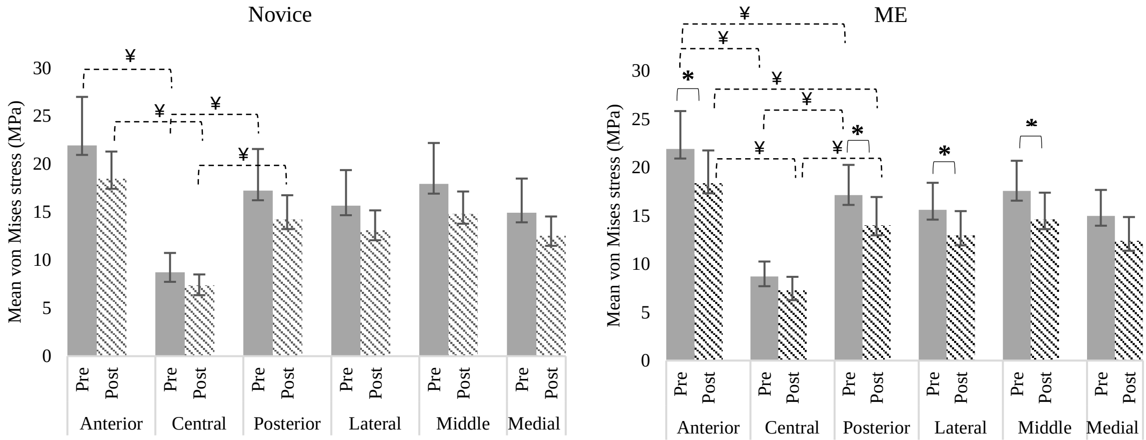

Figure 8. 4. Average von Mises stress of the tibiotalar cartilage pre- and post-running in each group.

* sign with a solid line indicates a significant difference ($P \leq 0.05$) between pre- and post-run measurement. ¥ sign with a dashed line indicates a significant ($P \leq 0.05$) regional difference either between anterior, central, and posterior, or lateral, middle, and medial.

8.4.2 MR Quantification - T2 Maps

Intra-reliability ranged from 0.76-0.94 and inter-reliability was 0.75-0.98, which indicated a good agreement. A detailed bar graph of mean relaxation time (ms) for each region of the tibiotalar cartilage of pre- and post-run MR scan is displayed in Figure 8.5.

In novice runners, the comparison of the T2 values before and after the running revealed a significant increase in anterior (pre: 32.55±2.36 ms, post: 37.16±3.48 ms, P = 0.02), posterior (pre: 45.1±4.18 ms, post: 51.18±3.88 ms, P = 0.003), and lateral (pre: 37.6±3.11 ms, post: 42.19±6.8 ms, P = 0.03) tibiotalar cartilage. In contrast to novice runners, ME runners showed no significant changes after running, although T2 values were all insignificantly decreased after the running. Among the measured regions, the T2 values in posterior tibiotalar cartilage were higher when compared with anterior and central cartilage, while anterior cartilage showed lower T2 values in both pre- and post-run scans.

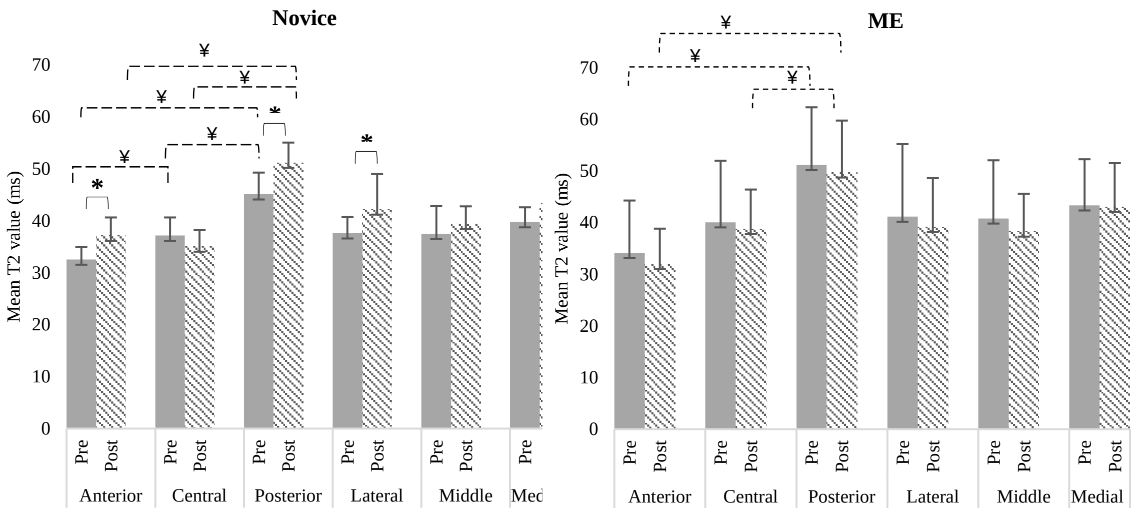

Figure 8. 5. T2 relaxation time (ms) pre- and post-running in each group.

* sign with a solid line indicates a significant (P ≤ 0.05) difference between pre- and post-run scans. ¥ sign with a dashed line indicates a significant (P ≤ 0.05) regional difference either between anterior, central, and posterior, or lateral, middle, and medial.

8.4.3 Plantar Pressure

A detailed illustration of the peak plantar pressure and peak force for each group of pre- and post-run is shown in Figure 8.6. The results revealed that 5km unshod running modified plantar pressure in both novice and ME runners. More specifically, in novice runners, the peak pressure under T1, T2-T5, and M1 were significantly reduced by 38.4%, 24%, and 38.6% respectively after the running (P = 0.04, P = 0.04, P = 0.01 respectively). In contrast, the peak pressure under M5 and LM were significantly increased by 23.2% and 22.1% respectively after the running (P = 0.04, P = 0.01 respectively). Peak force under M1 was decreased by 31.9% (P = 0.03), while increase under M5 by 18.3% (P = 0.01).

The ME group also showed similar patterns in peak plantar pressure to the novice group, but their pressure distributions were more focused on the middle of the foot. After the running, the pressure under M1, M2, and M3 were significantly decreased by 44.6%, 25.1%, and 16.1% respectively (P = 0.01, P = 0.04, P = 0.02 respectively), while the pressure under LM was increased by 32.3% (P = 0.05). Peak force under M1, M2, and M3 were significantly decreased by 35.3%, 23.5%, and 11.1% after the running (P = 0.01, P = 0.003, P = 0.01 respectively), but there was no force increase in other regions of the foot.

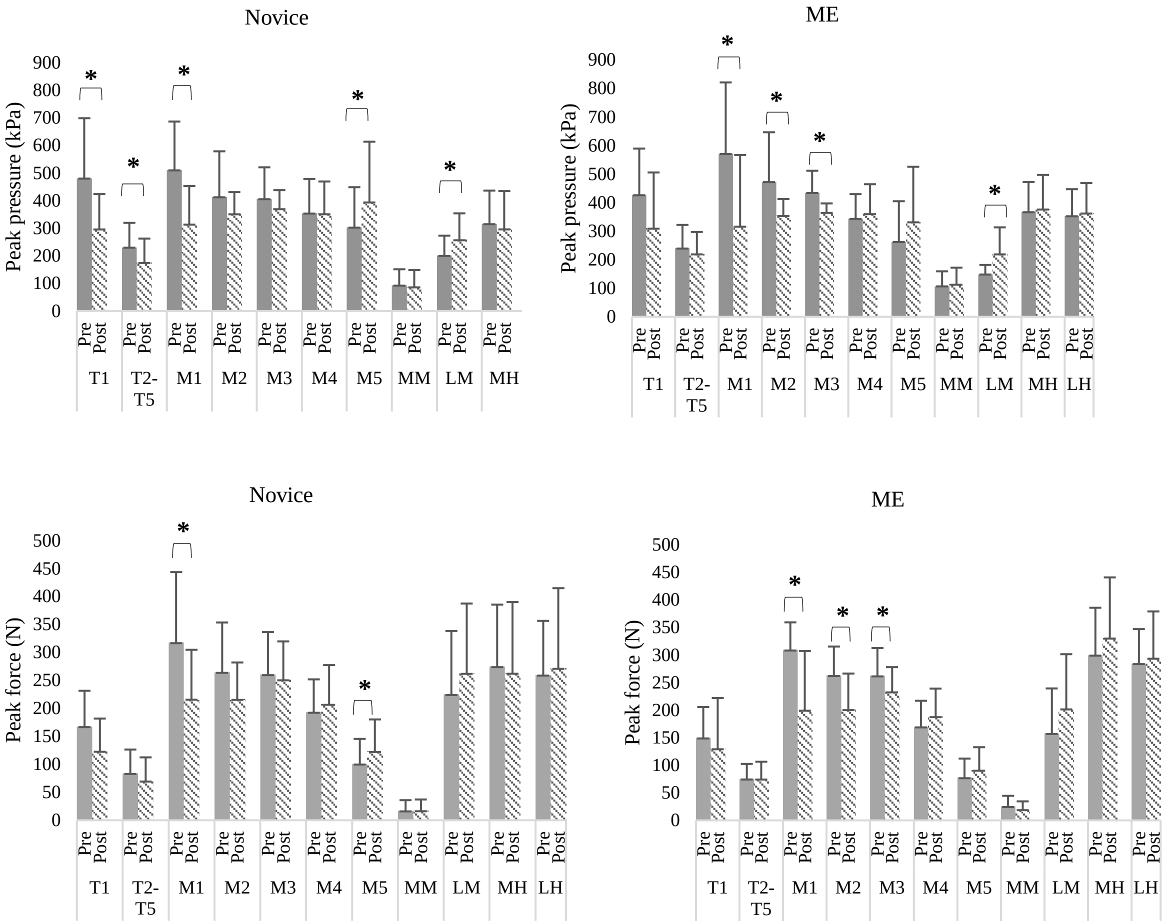

Figure 8. 6. Peak pressure (kPa) and peak force (N) pre- and post-running in each group.

* sign indicates a significant (P ≤ 0.05) difference between pre- and post-run measurements.

8.4.4 Association between T2 and Stress

The patterns of von Mises stress and T2 values in the tibiotalar cartilage are shown in Figure 8.7. In general, the stress patterns associated with high T2 uptake. High von Mises stresses were observed in the anterior, posterior and lateral tibiotalar cartilage in both pre- and post-running and similar T2 value patterns were also observed in the same regions of the tibiotalar cartilage. Central tibiotalar cartilage showed relatively low von Mises stress in both pre- and post-run, and low T2 values were also observed in the same regions of the tibiotalar cartilage.

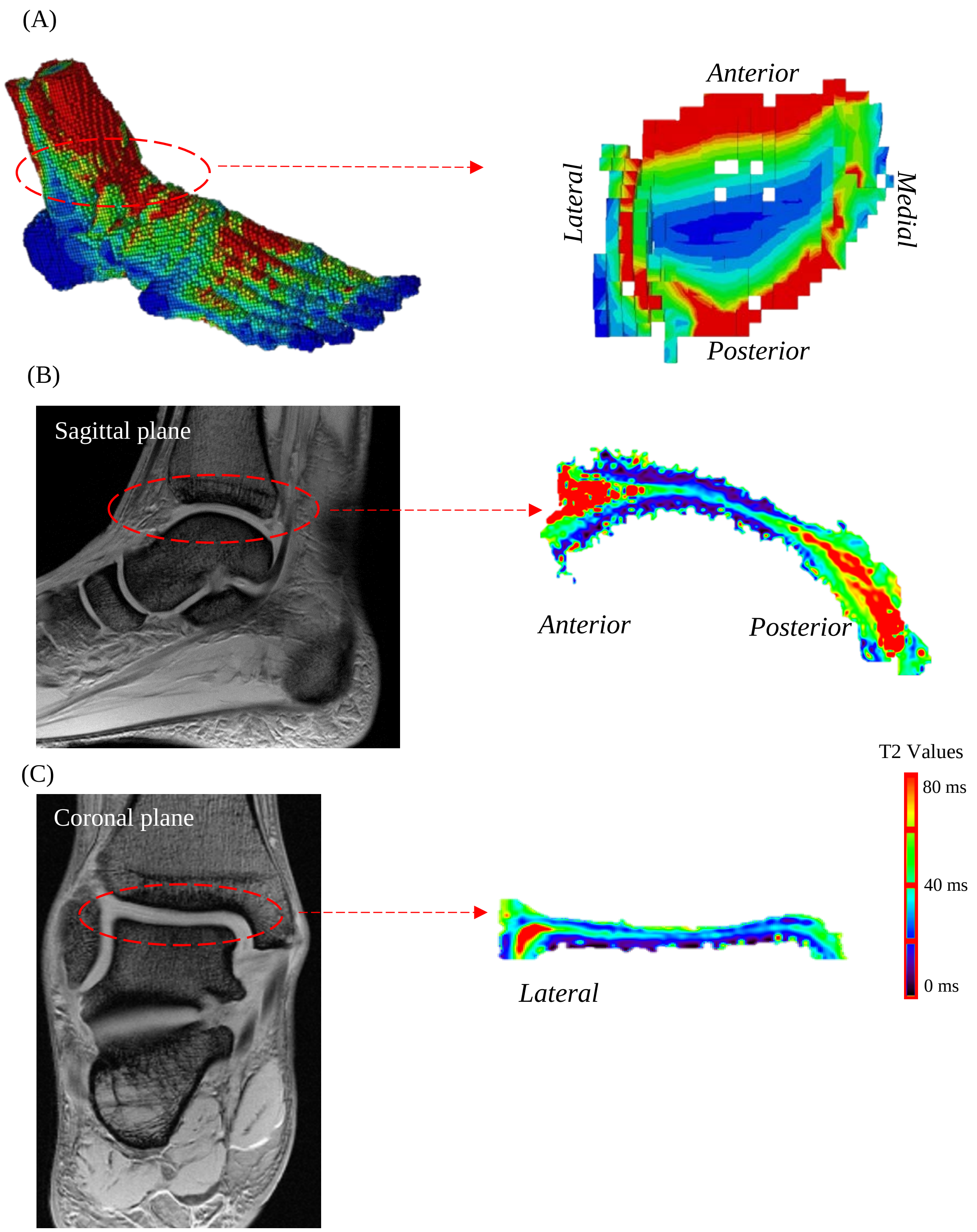

Figure 8. 7. Representative von Mises stress distribution of the tibiotalar cartilage from FE analysis (A). Representative T2 maps of tibiotalar cartilage in sagittal plane (B) and coronal plane (C).

8.5 Discussion

This study integrates gait analysis, FE modelling of joint cartilage stress and MRI-derived T2 maps to investigate association of predicted tibiotalar cartilage stress with T2 functional imaging in response to long-distance unshod running. The findings from this study support the following conclusions. First, FE predicted tibiotalar cartilage stress patterns correspond to T2 map patterns, reporting large stresses in the anterior, posterior, and lateral tibiotalar cartilage corresponding to high T2 uptake. This suggests that tibiotalar cartilage stress may play a likely mechanical role in fluid build-up and possible inflammation supported by high T2 uptake in those regions. Second, unshod ME runners exhibited reduced tibiotalar cartilage stresses post running corresponding with no increase in baseline T2 values. The experienced runners in this study support previous findings that show unshod running can be beneficial as it may reduce peak impact force and impact rate (Lieberman et al., 2010). However, in contrast, novice runners from this study showed T2 elevation and were unable to reduce stress reduction in their ankle cartilage. This is likely in part due to the different running strategies displayed by ME and novice runners. ME runners presented a coping strategy post-running where they reduce loading primarily in the medial metatarsals and shift this to the lateral metatarsals and midfoot. In contrast, novice runners showed a different strategy by reducing loading in the medial toes and shifting this to the lateral toes and midfoot. ME runners appear to reduce stress and prevent elevated fluid gathering in cartilage (measured by T2 maps) whereas novice runners appear to be less experienced and maintain similar stress levels after running leading to elevated T2 levels. This suggests that it may be the repetitive loading in novice runners at consistently high cartilage stress levels that leads to increased T2. In response, ME runners reduce their cartilage loading so this effect is not observed or possibly delayed.

The predicted von Mises stress was decreased within the tibiotalar cartilage following 5km unshod running in ME runners. Many biomechanical studies have reported that unshod running leads to lower peak impact force, impact rate and altering strike patterns (De Wit, De Clercq, & Aerts, 2000b; Lieberman et al., 2010). A reduction in the plantarflexion angle (Lussiana et al., 2016a), knee flexion excursion (Perl, Daoud, & Lieberman, 2012), and ankle dorsiflexion, eversion, and internal rotation torque (Kerrigan et al., 2009) were also observed in unshod running. This lower ankle torque in unshod running when compared with shod running may partly explain reduced cartilage stress. Although there is no computational modelling study investigating the ankle cartilage following unshod running, Bonacci et al. (2014) reported that running unshod reduced peak patellofemoral joint stress by 12% in 22 highly trained runners when compared with shod running. They concluded that unshod running may contribute to decreasing the cartilage reaction force and hence stress was decreased in unshod running. The current study also showed reduced stress in the tibiotalar articular cartilage but due to different running experience and strategy. Contrasting pre and post running loading on the foot, a trend was observed exhibiting shifting from medial forefoot to lateral forefoot and midfoot in both groups (ME and novice). However, only ME runners showed a reduction in peak force under the forefoot. These foot loading changes suggest a different coping mechanism where ME runners were able to limit the loading experienced in the tibiotalar joint after 5km running. It has been also reported that running biomechanics of strike patterns and spatiotemporal parameters are highly variable among elite and non-elite runners. Faster distance runners had more chance to adopt midfoot strike techniques than slower runners (Hasegawa, Yamauchi, &

Kraemer, 2007), while most of the recreational runners run with a rearfoot striking (Larson et al., 2011). Rearfoot striking leads to more knee extension and more ankle dorsiflexion at initial foot contact. Also, elite distance runners tended to use longer stride lengths when compared with non-elite distance runners at a given velocity (Dillman, 1975). Altering stride length and/or stride rate may directly affect overall running biomechanics including ground reaction force, impact attenuation, and energy absorption at the lower limb joints (Schubert, Kempf, & Heiderscheit, 2014). There are no single studies investigating plantar pressures between novice and ME runners following long-distance unshod running, and findings in this study suggest plantar pressure patterns after long-distance running may be different depending on running experience. A previous study found no significant changes in plantar pressure over a competitive marathon race in 10 experienced runners (Hohmann, Reaburn, Tetsworth, & Imhoff, 2016), while healthy recreational runners showed increased peak force under the forefoot and medial heel and deceased under the 2^{nd}–5^{th} toes (Willems et al., 2012). However, it should be noted that it is difficult to objectively discriminate runners' fitness level between various studies and also their running distance, equipment, and shoe types were all different.

Moreover, previous studies reported T2 alteration in the knee cartilage following long-distance shod running (Mosher et al., 2005; Stehling et al., 2011), but there was no single study investigating T2 values in the ankle cartilage. Only one study reported T2* modification in the ankle cartilage over an ultra-marathon race, although T2* is different to T2 (e.g. T2* is the physical T2 relaxation without cancellation of local magnetic inhomogeneities). None of these studies also investigated the effect of runners' fitness level on T2 values of the articular cartilage. Biochemically, it has been suggested that cartilage T2 is highly influenced by altering the orientation of the collagen matrix, collagen fibre concentration, and hydration content in the extracellular cartilage (Mosher & Dardzinski, 2004). However, it still remains unclear whether these biochemical differences exist among novice and ME runners.

This study has several limitations that should be considered when interpreting the results. The model does not take into consideration individual cartilage geometry, foot geometry and material properties as we used a generic foot model loaded with subject-specific loading patterns. There might be a possibility ME runners have different geometry and material property adaptations when compared to novice runners and hence affect the tibiotalar cartilage stress. However, in this study we normalised for differences in foot shape and material properties and considered only the influence of the plantar pressure pattern. Secondly, this study considered only 20 participants due to the cost and feasibility of multiple MRIs, however, although we considered only ten runners in each group, we found a consistent trend of stress and T2 value modification suggesting a larger study would only further support this finding.

Chapter 9. General Discussion

9.1 Summary of Findings

The predominant aim of this thesis was to quantitatively examine the influence of cumulative loading on the tibiotalar cartilage following long-distance unshod running and identify running biomechanics to modify this response. In general, the central hypothesis was supported as I have found that T2 values were increased in novice runners, plantar pressure was shifted from the medial to the lateral aspect of the foot, and FE predicted stress of tibiotalar cartilage was reduced in marathon-experienced runners following 5km unshod running.

In this thesis, I have demonstrated the following key findings:

- Ankle kinematics were most prominently influenced by 5km unshod running, especially in female runners. However, these modified ankle kinematics did not appear to directly affect the T2 values, suggesting that kinematic changes are less associated with tibiotalar cartilage fluid development and possible inflammation **(Chapter 4 and 6).**
- Plantar loading was shifted from the medial forefoot to the lateral forefoot and midfoot after long-distance, unshod running with the most significant changes amongst novice and female runners **(Chapter 4 and 6).**
- 5km unshod running had an acute effect on the tibiotalar cartilage in novice runners, reporting an increase in T2 values in the anterior, posterior, and lateral tibiotalar

cartilage. These high T2 values indicate early stages of cartilage damage **(Chapter 6).**

- T2 increase on the lateral tibiotalar cartilage was only observed in novice runners following 5km unshod running and this was associated with elevated plantar pressure under the 5th metatarsal and lateral midfoot. This suggests plantar pressure may play a role in elevated cartilage fluid levels **(Chapter 6).**
- FE predicted tibiotalar cartilage stress patterns corresponding to T2 map patterns. Large stresses were observed in the anterior, posterior, and lateral tibiotalar cartilage and this corresponds with high T2 uptake **(Chapter 6 and 8).**
- The predicted von Mises stress in the tibiotalar cartilage was decreased in marathon-experienced runners after 5km unshod running. In contrast, novice runners maintained similar von Mises stress levels after running, leading to elevated T2 values. Marathon-experienced runners appear to reduce stress and prevent elevated fluid gathering in cartilage whereas novice runners are less experienced and appear to maintain similar stress levels after running leading to elevated T2 levels **(Chapter 6 and 8).**

9.2 Identifying the Significance of T2 maps and Plantar Pressure following Long-Distance Unshod Running

The running biomechanics described in **Chapter 4 and 8** together with radiologic findings in **Chapter 6** suggest that long-distance unshod running have an acute effect on increasing hydration in tibiotalar cartilage, and plantar pressure likely has a mechanical role in this fluid development (T2 values). Previous MR studies also demonstrated similar results, reporting a significant T2 elevation in the knee cartilage after a marathon race (Mosher et al., 2005; Stehling et al., 2011) and a significant T2* elevation over an ultra-marathon race in the tibiotalar cartilage (Schutz et al., 2014). Alteration of plantar pressure after long-distance shod running has been also reported in the literature (Alfuth & Rosenbaum, 2011; Bisiaux & Moretto, 2008; Karagounis et al., 2009; Nagel et al., 2008; Willems et al., 2012). Furthermore, it has been reported that professional ballet dancers revealed higher tibiotalar cartilage T2 values in comparison with non-dancers (Cha et al., 2015) and that professional dancers demonstrated higher plantar pressure in the medial forefoot during walking compared with non-dancers (Prochazkova et al., 2014). Although there are no studies examining whether T2 values correspond to the modified plantar pressure, we proposes the significant plantar pressure alteration may lead to a T2 elevation.

In this thesis, the loading under the medial toes and forefoot were shown to be significantly decreased, shifting to the lateral forefoot after running, and this loading elevation under the lateral forefoot may contribute to increasing T2 values in the lateral tibiotalar cartilage in novice runners. This thesis, therefore, suggests that T2 elevation may be in part related with alteration of plantar pressure. However, closer analysis investigating the association between T2 values and plantar pressure should be required for a further study.

One of the major findings in this thesis was that the unshod running does reduce the stress level in tibiotalar cartilage, especially in marathon-experienced runners **(Chapter 8)**. After running, only marathon-experienced runners demonstrated a reduction in peak force under the forefoot. This difference in foot loading suggests a different coping mechanism where marathon-experienced runners were able to limit the loading experienced in the tibiotalar cartilage after running, leading to maintenance of a similar level of T2 values pre and post-run. Similar results were also reported from the previous study, although they investigated the knee joint; Bonacci et al. (2014) found a significant stress level reduction in patellofemoral joint in response to unshod running in highly trained runners when compared to shod running. These results may in part explain why unshod running has been reported to reduce running-related injuries by lowering impact force and rate (Lieberman et al., 2010).

Furthermore, this thesis demonstrates that the FE predicted tibiotalar cartilage stress patterns corresponds to T2 map patterns. Large stresses were observed in the anterior, posterior, and lateral tibiotalar cartilage and this corresponded to high T2 uptake. Therefore, tibiotalar cartilage stress may play a likely mechanical role in increasing cartilage hydration, indicating early stages of cartilage damage.

9.3 Ankle Kinematics Changes are Less Associated with Fluid Development

Among the three lower limb joints, the ankle kinematic showed significant modification after running, including decreases in peak plantarflexion and peak internal rotation, while increasing in peak inversion and peak external rotation in female runners **(Chapter 4).** This combination of the ankle kinematics possibly associates with supination of the foot. It has been reported that excessive supination is one of the risk factors of running-related injuries (Burns et al., 2005) because landing with a smaller area of the foot may cause inefficient shock absorption.

However, this significant ankle kinematic change was revealed to be insignificantly associated with MRI-derived T2 maps **(Chapter 6).** Novice runners, who showed no ankle kinematics changes, demonstrated a significant T2 elevation in the anterior, posterior, and lateral tibiotalar cartilage after running. This significant ankle kinematics modification might be associated more confidently with lowering plantarflexion moment. This thesis revealed that plantarflexion moment was significantly decreased after running, showed a strong, negative correlation with the internal rotation of ankle angle and plantar pressure, and was only observed in female runners **(Chapter 4).** Although this thesis did not evaluate electromyography (EMG) in muscles, the lowering plantarflexion may indicate fatigued plantar-flexor muscles and this might lead to modifying ankle kinematics in female runners.

9.4 Where might these Findings Apply?

This thesis reveals important information concerning ankle joint response and its relationship to running biomechanics following unshod running between novice and marathon-experienced runners, including both males and females. Many biomechanical studies have suggested that unshod running may reduce risk factors for running-related injuries by lowering collision force, impact rate and impact force (Lieberman et al., 2010). However, based on our findings, unshod running was only beneficial for marathon-experienced runners, who showed no ankle kinematic changes, no T2 values alteration, and who also importantly showed reduced tibiotalar cartilage stresses following 5km unshod running. Therefore, sports coaches may need extra caution when designing unshod exercise programs and should have different training strategies depending on the runners' running experience. Furthermore, this thesis found significant elevation of T2 values in the anterior, posterior and lateral tibiotalar cartilage, and plantar loading showed a trend of shifting the load from the medial to the lateral aspect of the foot after running. These results have important implications for the footwear industry. This combined assessment of the foot and ankle can be applied for shoe and insole designs, prosthetic designs and also injury mechanisms research. Information derived from the FE model and plantar pressure maps may provide in-depth knowledge regarding ankle response and these may be used as a useful tool in practical and clinical applications.

9.5 Strengths and Limitations of this Work

The major strength of this body of work is that it investigates the ankle joint in a multidisciplinary approach, integrating gait analysis, FE modelling of joint cartilage stress and MRI-derived T2 maps. As the ankle and foot are two of the most complex structures in the human body and are innately interlinked, the effect of repetitive loading on the ankle joint following unshod running cannot be explained by a single discipline. Thus, combining medical images with biomechanical methods in this thesis provides more in-depth knowledge of ankle joint responses. Further to this, T2 map modality allows the instant detection of cartilage damage beyond the capacity of conventional qualitative assessment. This sequence is able to provide an objective assessment of cartilage abnormality, which has led to the adoption of T2 maps in much of the scientific research in this field of study. More importantly, this multidisciplinary approach, integrating biomechanical and clinical methods, permits the association of predicted tibiotalar cartilage stress with T2 maps in response to long-distance unshod running.

Limitations have been addressed in previous chapters reporting each study. Here six general but important limitations were addressed which should be acknowledged when interpreting the results of this thesis. First, care must be taken when interpreting our results with different ethnicities in mind as all the work in this thesis was conducted on Caucasian participants. This is due to previous studies reporting differences in foot pressure between Caucasian, Asian, and Indian feet due to known differences in foot morphology (Hawes et al., 1994; Putti et al., 2010). It would have been desirable to have other ethnic groups, and comparison of two groups would enhance the external validity of our study. However, considering the available resources this was not feasible for this thesis. Second, all work in this thesis was conducted recording only one immediate follow-up test. There was no further monitoring of gait and T2 values in the tibiotalar cartilage after 5km unshod running beyond the immediate post-run evaluation. As T2 values may be non-specific and resolve spontaneously, the elevation of T2 values may return to the normal level after a rest period. However, it has been reported that $T1_p$ remained at a high level in response to a marathon race after a three-month rest period in meniscus compartments (Stehling et al., 2011). Although T2 maps and $T1_p$ are different, (i.e. $T1_p$ assess can collagen network and glycosaminoglycans in collagen-proteoglycan matrix, while T2 map can assess the extracellular water content and collagen degradation), both sequences are able to quantify biochemical composition, thereby detecting the earliest changes of cartilage damage. Since this thesis found ankle kinematic changes as well as stress and T2 level changes in the tibiotalar cartilage after unshod running, a closer analysis of the ankle should be required for further study. Third, subject selection bias should also be considered; if runners are suffering from joint pain or injuries, they are likely to stop exercise. A previous study reported less osteoarthritis in experienced runners compared with age-matched controls. This is possibly because when the subjects were asked to describe their running level (either runner or non-runner groups), runners who have injuries or pain may select non-runner control group (Willick & Hansen, 2010). However, this thesis recruited only healthy and injury-free individuals and also adopted the Tegner scale (Tegner & Lysholm, 1985) to objectively discriminate runners' fitness level. Fourth, the absence of a control intervention would be a limitation on the study design. Some of the results may be simply due to the fact we have shod people running barefoot. We did not include a control group of naturally barefoot people running barefoot. However, we used the pre 5km run as a base control for each person and tested against their post 5km run. Thus, the absence of a control intervention may not affect this thesis conclusions. Fifth, some caution is warranted in using a systematic review approach to determine how we might conduct a new analysis, as what people have done in the past is not necessarily a good indication of how things should be done in the future. In this thesis, literature reviews were conducted in a systematic review manner to provide a background knowledge regarding running biomechanics and ankle cartilage quantification in response to long-distance unshod running. This means that we did not solely rely on the systematic reviews for deciding our methodologies. We have conducted pilot tests for the details of our methodologies, have consulted with radiologists for MR sequences, and have consulted with a statistician for study design. Lastly, although we have a small sample size, a large number of variables were assessed in this thesis and this may increase the risk of type I error. To control this error, the effect size was reported to provide readers an appreciation for the sample size on our findings. This small sample size is potentially limited, but this thesis was able to detect a significant effect on running biomechanics, plantar pressure distribution, T2 values, and FE predicted stress in ankle cartilage. This thesis may allow future study to be powered at clinical and statistical level of significance.

9.6 Concluding Remarks

This thesis expands significantly on our understanding of the effect of repetitive and high rate loading on the ankle cartilage and its relationship to running biomechanics following long-distance unshod running. 5km unshod running does modify ankle kinematics, T2 values of tibiotalar cartilage, and FE predicted tibiotalar cartilage stress **(Chapters 4, 6, and 8)**. Significant modification of ankle kinematics are observed after running **(Chapter 4)**, but this may not play a mechanical role in fluid development in the tibiotalar cartilage (T2 maps) **(Chapter 6).** 5km unshod running may have an acute effect on T2 values of tibiotalar cartilage in the anterior, posterior and lateral tibiotalar cartilage in novice runners, suggesting that these regions may have important mechanical contributions during unshod running. These high T2 values in novice runners indicate potential tibiotalar cartilage damage, but longitudinal monitoring of T2 would be essential for a further study and confirmation of this. Plantar loading elevation in the lateral aspect of the foot also emphasises that unshod running is functionally demanding for the lateral aspect, especially in novice and female runners. Unshod running may be in part beneficial only for marathon-experienced runners, who showed a significant reduction of von Mises stress in the tibiotalar cartilage **(Chapter 8)** and who maintained similar T2 levels post-run **(Chapter 6).**

In addition to contributing to our understanding of the effects of long-distance unshod running on the ankle cartilage and running biomechanics, this thesis also demonstrates the connection between ankle biomechanics and T2 maps. As the patterns of plantar loading and FE predicted stress of tibiotalar cartilage corresponds to high T2 uptake, tibiotalar cartilage stress and plantar loading may likely play a mechanical role in hydration build-up and possible inflammation, supported by high T2 uptake. Ankle kinematics on the other hand did not appear to directly affect the T2 levels. Information derived from the FE model and plantar pressure may provide in-depth knowledge regarding ankle responses which can be used in practical and clinical applications.

References

Abt, J. P., Sell, T. C., Chu, Y., Lovalekar, M., Burdett, R. G., & Lephart, S. M. (2011). Running kinematics and shock absorption do not change after brief exhaustive running. *Journal of Strength and Conditioning Research / National Strength & Conditioning Association, 25*(6), 1479-1485. doi:10.1519/JSC.0b013e3181ddfcf8 [doi]

Adams, D., & Swanson, S. A. (1985). Direct measurement of local pressures in the cadaveric human hip joint during simulated level walking. *Annals of the Rheumatic Diseases, 44*(10), 658-666.

Alfuth, M., & Rosenbaum, D. (2011). Long distance running and acute effects on plantar foot sensitivity and plantar foot loading. *Neuroscience Letters, 503*(1), 58-62.

Anderson, T. (1996). Biomechanics and running economy. *Sports Medicine, 22*(2), 76-89.

Arndt, A., Ekenman, I., Westblad, P., & Lundberg, A. (2002). Effects of fatigue and load variation on metatarsal deformation measured in vivo during barefoot walking. *Journal of Biomechanics, 35*(5), 621-628.

Baur, H., Hirschmüller, A., Müller, S., Gollhofer, A., & Mayer, F. (2007). Muscular activity in treadmill and overground running. *Isokinetics and Exercise Science, 15*(3), 165-171.

Becker, J., Howey, R., Osternig, L., James, S., & Chou, L. (2012). Plantar pressure differences between rearfoot and midfoot striking runners during shod running. Paper presented at the *The 2012 ASB Annual Meeting, Gainesville, FL.*

Bergstra, S., Kluitenberg, B., Dekker, R., Bredeweg, S., Postema, K., Van den Heuvel, E., . . . Sobhani, S. (2015). Running with a minimalist shoe increases plantar pressure in the forefoot region of healthy female runners. *Journal of Science and Medicine in Sport, 18*(4), 463-468.

Beynnon, B. D., Renström, P. A., Alosa, D. M., Baumhauer, J. F., & Vacek, P. M. (2001). Ankle ligament injury risk factors: A prospective study of college athletes. *Journal of Orthopaedic Research, 19*(2), 213-220.

Bishop, M., Fiolkowski, P., Conrad, B., Brunt, D., & Horodyski, M. (2006). Athletic footwear, leg stiffness, and running kinematics. *Journal of Athletic Training, 41*(4), 387-392.

Bisiaux, M., & Moretto, P. (2008). The effects of fatigue on plantar pressure distribution in walking. *Gait & Posture, 28*(4), 693-698.

Bonacci, J., Saunders, P. U., Hicks, A., Rantalainen, T., Vicenzino, B. T., & Spratford, W. (2013). Running in a minimalist and lightweight shoe is not the same as running barefoot: A biomechanical study. *British Journal of Sports Medicine, 47*(6), 387-392. doi:10.1136/bjsports-2012-091837

Bonacci, J., Vicenzino, B., Spratford, W., & Collins, P. (2014). Take your shoes off to reduce patellofemoral joint stress during running. *British Journal of Sports Medicine, 48*(6), 1-5.

Boocock, M., McNair, P., Cicuttini, F., Stuart, A., & Sinclair, T. (2009). The short-term effects of running on the deformation of knee articular cartilage and its relationship to biomechanical loads at the knee. *Osteoarthritis and Cartilage, 17*(7), 883-890.

Brown, T. D., Anderson, D. D., Nepola, J. V., Singerman, R. J., Pedersen, D. R., & Brand, R. A. (1988). Contact stress aberrations following imprecise reduction of simple tibial plateau fractures. *Journal of Orthopaedic Research, 6*(6), 851-862.

Brown, T. D., & Shaw, D. T. (1983). In vitro contact stress distributions in the natural human hip. *Journal of Biomechanics, 16*(6), 373-384.

Buckwalter, J. (2002). Articular cartilage injuries. *Clinical Orthopaedics and Related Research*, *402*, 21-37.

Buckwalter, J. A., & Lane, N. E. (1997). Athletics and osteoarthritis. *The American Journal of Sports Medicine*, *25*(6), 873-881.

Burns, J., Keenan, A., & Redmond, A. (2005). Foot type and overuse injury in triathletes. *Journal of the American Podiatric Medical Association, 95*(3), 235-241.

Bus, S. A., Maas, M., de Lange, A., Michels, R. P., & Levi, M. (2005). Elevated plantar pressures in neuropathic diabetic patients with claw/hammer toe deformity. *Journal of Biomechanics*, *38*(9), 1918-1925.

Bygrave, C., & Betts, R. (1993). The plantar tissue thickness in the foot: A new ultrasound technique for loadbearing measurements and a metatarsal head depth study. *The Foot, 3*(2), 71-78.

Caravaggi, P., Pataky, T., Günther, M., Savage, R., & Crompton, R. (2010). Dynamics of longitudinal arch support in relation to walking speed: Contribution of the plantar aponeurosis. *Journal of Anatomy, 217*(3), 254-261.

Carroll, M., Parmar, P., Dalbeth, N., Boocock, M., & Rome, K. (2015). Gait characteristics associated with the foot and ankle in inflammatory arthritis: A systematic review and meta-analysis. *BMC Musculoskeletal Disorders, 16*(1), 1.

Cha, J. G., Yi, J. S., Han, J. K., & Lee, Y. K. (2015). Comparison of quantitative cartilage T2 measurements and qualitative MR imaging between professional ballet dancers and healthy volunteers. *Radiology, 276*(1), 199-206.

Chen, W., Tang, F., & Ju, C. (2001). Stress distribution of the foot during mid-stance to push-off in barefoot gait: A 3-D finite element analysis. *Clinical Biomechanics, 16*(7), 614-620.

Chen, W., Lee, T., Lee, P. V., Lee, J. W., & Lee, S. (2010). Effects of internal stress concentrations in plantar soft-tissue—a preliminary three-dimensional finite element analysis. *Medical Engineering & Physics, 32*(4), 324-331.

Cheung, J. T., Zhang, M., & An, K. (2004). Effects of plantar fascia stiffness on the biomechanical responses of the ankle–foot complex. *Clinical Biomechanics, 19*(8), 839-846.

Chuckpaiwong, B., Nunley, J. A., Mall, N. A., & Queen, R. M. (2008). The effect of foot type on in-shoe plantar pressure during walking and running. *Gait & Posture, 28*(3), 405-411.

Coleman, J. L., Widmyer, M. R., Leddy, H. A., Utturkar, G. M., Spritzer, C. E., Moorman, C. T., . . . DeFrate, L. E. (2013). Diurnal variations in articular cartilage thickness and strain in the human knee. *Journal of Biomechanics, 46*(3), 541-547.

Crema, M. D., Roemer, F. W., Marra, M. D., Burstein, D., Gold, G. E., Eckstein, F., . . . Guermazi, A. (2011). Articular cartilage in the knee: Current MR imaging techniques and applications in clinical practice and research. *Radiographics, 31*(1), 37-61.

D'AoÛt, K., Pataky, T. C., De Clercq, D., & Aerts, P. (2009). The effects of habitual footwear use: Foot shape and function in native barefoot walkers. *Footwear Science, 1*(2), 81-94.

Davis, I. S., Rice, H. M., & Wearing, S. C. (2017). Why forefoot striking in minimal shoes might positively change the course of running injuries. *Journal of Sport and Health Science, 6*(2), 154-161.

Davis, I., Milner, C. E., & Hamill, J. (2004). Does increased loading during running lead to tibial stress fractures? A prospective study. *Med Sci Sports Exerc, 36*(5), S58.

Davis, I., Bowser, B., & Mullineaux, D. (2010). (2010). Do impacts cause running injuries? A prospective investigation. Paper presented at the *Annual Meeting of the American Society of Biomechanics,* De Clercq, D., Aerts, P., & Kunnen, M. (1994). The mechanical characteristics of the human heel pad during foot strike in running: An in vivo cineradiographic study. *Journal of Biomechanics, 27*(10), 1213-1222.

De Wit, B., De Clercq, D., & Aerts, P. (2000). Biomechanical analysis of the stance phase during barefoot and shod running. *Journal of Biomechanics, 33*(3), 269-278. doi:10.1016/S0021-9290(99)00192-X

Deeks, J., Dinnes, J., D'amico, R., Sowden, A., Sakarovitch, C., Song, F., . . . Altman, D. (2003). Evaluating non-randomised intervention studies. *Health Technology Assessment (Winchester, England), 7*(27), iii-x, 1-173.

Degache, F., Guex, K., Fourchet, F., Morin, J. B., Millet, G. P., Tomazin, K., & Millet, G. Y. (2013). Changes in running mechanics and spring-mass behaviour induced by a 5-hour hilly running bout. *Journal of Sports Sciences, 31*(3), 299-304.

Dekel, S., & Weissman, S. (1978). Joint changes after overuse and peak overloading of rabbit knees in vivo. *Acta Orthopaedica Scandinavica, 49*(6), 519-528.

Derrick, T. R., Dereu, D., & McLean, S. P. (2002). Impacts and kinematic adjustments during an exhaustive run. *Medicine and Science in Sports and Exercise, 34*(6), 998-1002.

Derrick, T. R. (2004). The effects of knee contact angle on impact forces and accelerations. *Medicine and Science in Sports and Exercise, 36*(5), 832-837. doi:00005768-200405000-00015 [pii]

Derrick, T. R., Hamill, J., & Caldwell, G. E. (1998). Energy absorption of impacts during running at various stride lengths. *Medicine and Science in Sports and Exercise, 30*(1), 128-135.

Dierks, T. A., Davis, I. S., & Hamill, J. (2010). The effects of running in an exerted state on lower extremity kinematics and joint timing. *Journal of Biomechanics, 43*(15), 2993-2998.

Dillman, C. J. (1975). Kinematic analyses of running. *Exercise and Sport Sciences Reviews, 3*(1), 193-218.

Divert, C., Mornieux, G., Freychat, P., Baly, L., Mayer, F., & Belli, A. (2008). Barefoot-shod running differences: Shoe or mass effect? *International Journal of Sports Medicine, 29*(06), 512-518.

Dowling, G. J., Murley, G. S., Munteanu, S. E., Smith, M. M. F., Neal, B. S., Griffiths, I. B., . . . Collins, N. J. (2014). Dynamic foot function as a risk factor for lower limb overuse injury: A systematic review. *Journal of Foot and Ankle Research, 7*, 53. doi:10.1186/s13047-014-0053-6

Downs, S. H., & Black, N. (1998). The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *Journal of Epidemiology and Community Health, 52*(6), 377-384.

Dunn, T. C., Lu, Y., Jin, H., Ries, M. D., & Majumdar, S. (2004). T2 relaxation time of cartilage at MR imaging: Comparison with severity of knee osteoarthritis 1. *Radiology, 232*(2), 592-598.

Fellin, R. E., Manal, K., & Davis, I. S. (2010). Comparison of lower extremity kinematic curves during overground and treadmill running. *Journal of Applied Biomechanics, 26*(4), 407-414.

Ferber, R., Hreljac, A., & Kendall, K. D. (2009). Suspected mechanisms in the cause of overuse running injuries: A clinical review. *Sports Health, 1*(3), 242-246. doi:10.1177/1941738109334272 [doi]

Fernandez, J. W., Haque, M. Z. U., Hunter, P. J., & Mithraratne, K. (2012). Mechanics of the foot part 1: A continuum framework for evaluating soft tissue stiffening in the pathologic foot. *International Journal for Numerical Methods in Biomedical Engineering, 28*(10), 1056-1070. doi:10.1002/cnm.2494

Fleming, N., Walters, J., Grounds, J., Fife, L., & Finch, A. (2015). Acute response to barefoot running in habitually cross mark shod males. *Human Movement Science, 42*, 27-37. doi:10.1016/j.humov.2015.04.008

Franz, J. R., Wierzbinski, C. M., & Kram, R. (2012). Metabolic cost of running barefoot versus shod: Is lighter better. *Med Sci Sports Exerc, 44*(8), 1519-1525.

Freund, W., Billich, C., Brambs, H., Weber, F., & Schutz, U. H. (2011). [MRI changes of achilles tendon and hindfoot in experienced runners and beginners during training and after a (half)-marathon competition]. [MR-tomografische Veranderungen an

Achillessehne und Ruckfus von Laufanfangern und Lauferfahrenen im Trainingsverlauf und nach einem (Halb-)Marathon.] *Zeitschrift Fur Orthopadie & Unfallchirurgie, 149*(4), 407-417. doi:http://dx.doi.org/10.1055/s-0030-1271074

Freund, W., Weber, F., Billich, C., & Schuetz, U. H. (2012). The foot in multistage ultra-marathon runners: Experience in a cohort study of 22 participants of the trans europe footrace project with mobile MRI. *Bmj Open, 2*(3), e001118. doi:10.1136/bmjopen-2012-001118

García-Pérez, J. A., Pérez-Soriano, P., Llana, S., Martínez-Nova, A., & Sánchez-Zuriaga, D. (2013). Effect of overground vs treadmill running on plantar pressure: Influence of fatigue. *Gait & Posture, 38*(4), 929-933.

García-Pérez, J. A., Pérez-Soriano, P., Llana Belloch, S., Lucas-Cuevas, Á G., & Sánchez-Zuriaga, D. (2014). Effects of treadmill running and fatigue on impact acceleration in distance running. *Sports Biomechanics, 13*(3), 259-266.

Garcia-Perez, J. A., Perez-Soriano, P., Llana, S., Martinez-Nova, A., & Sanchez-Zuriaga, D. (2013). Effect of overground vs treadmill running on plantar pressure: Influence of fatigue. *Gait & Posture, 38*(4), 929-933. doi:10.1016/j.gaitpost.2013.04.026

Gefen, A., Megido-Ravid, M., Itzchak, Y., & Arcan, M. (2000). Biomechanical analysis of the three-dimensional foot structure during gait: A basic tool for clinical applications. *Journal of Biomechanical Engineering, 122*(6), 630-639.

Gefen, A. (2002). Stress analysis of the standing foot following surgical plantar fascia release. *Journal of Biomechanics, 35*(5), 629-637.

Gerlach, K. E., White, S. C., Burton, H. W., Dorn, J. M., Leddy, J. J., & Horvath, P. J. (2005). Kinetic changes with fatigue and relationship to injury in female runners. *Medicine and Science in Sports and Exercise, 37*(4), 657-663. doi:00005768-200504000-00019 [pii]

Giuliani, J., Masini, B., Alitz, C., & Owens, L. B. D. (2011). Barefoot-simulating footwear associated with metatarsal stress injury in 2 runners. *Orthopedics, 34*(7), e320-e323.

Grimston, S. K., & Zernicke, R. F. (1993). Exercise-related stress responses. *Journal of Applied Biomechanics, 9*, 2.14.

Hadley, N. A., Brown, T. D., & Weinstein, S. L. (1990). The effects of contact pressure elevations and aseptic necrosis on the long-term outcome of congenital hip dislocation. *Journal of Orthopaedic Research, 8*(4), 504-513.

Haglund-Åkerlind, P. Y., & Eriksson, E. (1993). Range of motion, muscle torque and training habits in runners with and without achilles tendon problems. *Knee Surgery, Sports Traumatology, Arthroscopy, 1*(3-4), 195-199.

Hamill, J., Russell, E. M., Gruber, A. H., & Miller, R. (2011). Impact characteristics in shod and barefoot running. *Footwear Science, 3*(1), 33-40.

Hanson, N., Berg, K., Deka, P., Meendering, J., & Ryan, C. (2011). Oxygen cost of running barefoot vs. running shod. *International Journal of Sports Medicine, 32*(06), 401-406.

Hasegawa, H., Yamauchi, T., & Kraemer, W. J. (2007). Foot strike patterns of runners at the 15-km point during an elite-level half marathon. *Journal of Strength and Conditioning Research, 21*(3), 888-893. doi:10.1519/R-22096.1

Hatala, K. G., Dingwall, H. L., Wunderlich, R. E., & Richmond, B. G. (2013). Variation in foot strike patterns during running among habitually barefoot populations. *PLoS One, 8*(1), e52548.

Hawes, M. R., Sovak, D., Miyashita, M., Kang, S., Yoshihuku, Y., & Tanaka, S. (1994). Ethnic differences in forefoot shape and the determination of shoe comfort. *Ergonomics, 37*(1), 187-196.

Hinterwimmer, S., Feucht, M. J., Steinbrech, C., Graichen, H., & von Eisenhart-Rothe, R. (2014). The effect of a six-month training program followed by a marathon run on knee joint cartilage volume and thickness in marathon beginners. *Knee Surgery, Sports Traumatology, Arthroscopy, 22*(6), 1353-1359. doi:10.1007/s00167-013-2686-6

Ho, I. -., Hou, Y., Yang, C., Wu, W., Chen, S., & Guo, L. (2010). Comparison of plantar pressure distribution between different speed and incline during treadmill jogging. *Journal of Sports Science and Medicine, 9*(1), 154-160.

Hohmann, E., Reaburn, P., Tetsworth, K., & Imhoff, A. (2016). Plantar pressures during long distance running: An investigation of 10 marathon runners. *Journal of Sports Science & Medicine, 15*(2), 254-262.

Hohmann, E., Wortler, K., & Imhoff, A. B. (2004). MR imaging of the hip and knee before and after marathon running. *The American Journal of Sports Medicine, 32*(1), 55-59.

Hong, Y., Wang, L., Li, J. X., & Zhou, J. H. (2012). Comparison of plantar loads during treadmill and overground running. *Journal of Science and Medicine in Sport, 15*(6), 554-560. doi:10.1016/j.jsams.2012.01.004

Hreljac, A., Marshall, R. N., & Hume, P. A. (2000). Evaluation of lower extremity overuse injury potential in runners. *Medicine and Science in Sports and Exercise, 32*(9), 1635-1641.

Iglic, A., Iglic, V. K., Antolic, V., Srakar, F., & Stanic, U. (1993). Effect of the periacetabular osteotomy on the stress on the human hip joint articular surface. *IEEE Transactions on Rehabilitation Engineering, 1*(4), 207-212.

Jacob, H. A., & Zollinger, H. (1992). Biomechanics of the foot--forces in the forefoot during walking and their clinical relevance. [Zur Biomechanik des Fusses--Krafte beim Gehen im Vorfuss und ihre klinische Relevanz] *Der Orthopade, 21*(1), 75-80.

Jacobs, S. J., & Berson, B. L. (1986). Injuries to runners: A study of entrants to a 10,000 meter race. *The American Journal of Sports Medicine, 14*(2), 151-155.

Jenkins, D. W., & Cauthon, D. J. (2011). Barefoot running claims and controversies: A review of the literature. *Journal of the American Podiatric Medical Association, 101*(3), 231-246.

Jepsen, J. R., Laursen, L. H., Hagert, C., Kreiner, S., & Larsen, A. I. (2006). Diagnostic accuracy of the neurological upper limb examination I: Inter-rater reproducibility of selected findings and patterns. *BMC Neurology, 6*(1), 1.

Jokl, P., Sethi, P. M., & Cooper, A. J. (2004). Master's performance in the new york city marathon 1983-1999. *British Journal of Sports Medicine, 38*(4), 408-412. doi:10.1136/bjsm.2002.003566 [doi]

Kafka, V. (2002). Surface fissures in articular cartilage: New concepts, hypotheses and modeling. *Clinical Biomechanics, 17*(1), 73-80.

Karagounis, P., Prionas, G., Armenis, E., Tsiganos, G., & Baltopoulos, P. (2009). The impact of the spartathlon ultramarathon race on athletes' plantar pressure patterns. *Foot & Ankle Specialist, 2*(4), 173-178. doi:10.1177/1938640009342894 [doi]

Kasmer, M. E., Ketchum, N. C., & Liu, X. (2014). The effect of shoe type on gait in forefoot strike runners during a 50-km run. *Journal of Sport and Health Science, 3*(2), 122-130.

Kennedy J.G., Knowles B., Dolan M., & Bohne, W. (2005). Foot and ankle injuries in the adolescent runner. *Current Opinion in Pediatrics, 17*(1), 34-42.

Kerrigan, D. C., Franz, J. R., Keenan, G. S., Dicharry, J., Della Croce, U., & Wilder, R. P. (2009). The effect of running shoes on lower extremity joint torques. *Pm&r, 1*(12), 1058-1063.

Kersting, U., Stubendorff, J., Schmidt, M., & Bruggemann, G. (2005). Changes in knee cartilage volume and serum COMP concentration after running exercise. *Osteoarthritis and Cartilage, 13*(10), 925-934. doi:10.1016/j.joca.2005.06.005

Kessler, M., Glaser, C., Tittel, S., Reiser, M., & Imhoff, A. (2006). Volume changes in the menisci and articular cartilage of runners - an in vivo investigation based on 3-D magnetic resonance imaging. *American Journal of Sports Medicine, 34*(5), 832-836. doi:10.1177/0363546505282622

Kessler, M. A., Glaser, C., Tittel, S., Reiser, M., & Imhoff, A. B. (2008). Recovery of the menisci and articular cartilage of runners after cessation of exercise - additional aspects of in vivo investigation based on 3-dimensional magnetic resonance imaging. *American Journal of Sports Medicine, 36*(5), 966-970. doi:10.1177/0363546507313093

Kim, H. K., Fernandez, J., & Mirjalili, S. A. (2017). Evaluation of MR images of the ankle and foot in response to long- distance running: A systematic review. *Advanced Techniques in Biology & Medicine, 5:2* doi:10.4172/2379-1764.1000222

Kim, H. K., Mirjalili, S. A., & Fernandez, J. (2017). Gait kinetics, kinematics, spatiotemporal and foot plantar pressure alteration in response to long-distance running: Systematic review. *Human Movement Science,*

Kim, W., & Voloshin, A. S. (1995). Role of plantar fascia in the load bearing capacity of the human foot. *Journal of Biomechanics, 28*(9), 1025-1033.

Koff, M., Amrami, K., & Kaufman, K. (2007). Clinical evaluation of T2 values of patellar cartilage in patients with osteoarthritis. *Osteoarthritis and Cartilage, 15*(2), 198-204.

Kongsgaard M., Aagaard P., Kjaer M., & Magnusson, S. P. (2005). Structural achilles tendon properties in athletes subjected to different exercise modes and in achilles tendon rapture patients. *Journal of Applied Physiology, 99*(5), 1965-1971.

Kornaat, P. R., Ceulemans, R. Y., Kroon, H. M., Riyazi, N., Kloppenburg, M., Carter, W. O., . . . Bloem, J. L. (2005). MRI assessment of knee osteoarthritis: Knee osteoarthritis scoring system (KOSS)—inter-observer and intra-observer reproducibility of a compartment-based scoring system. *Skeletal Radiology, 34*(2), 95-102.

Kornaat, P. R., & Van de Velde, S. K. (2014). Bone marrow edema lesions in the professional runner. *American Journal of Sports Medicine, 42*(5), 1242-1246. doi:10.1177/0363546514521990

Krampla, W., Mayrhofer, R., Malcher, J., Kristen, K. H., Urban, M., & Hruby, W. (2001). MR imaging of the knee in marathon runners before and after competition. *Skeletal Radiology, 30*(2), 72-76. doi:10.1007/s002560000296

Krampla, W. W., Newrkla, S. P., Kroener, A. H., & Hruby, W. F. (2008). Changes on magnetic resonance tomography in the knee joints of marathon runners: A 10-year longitudinal study. *Skeletal Radiology, 37*(7), 619-626. doi:10.1007/s00256-008-0485-9

Kursunoglu-Brahme, S., Schwaighofer, B., Gundry, C., Ho, C., & Resnick, D. (1990). Jogging causes acute changes in the knee joint: An MR study in normal volunteers. *AJR.American Journal of Roentgenology, 154*(6), 1233-1235. doi:10.2214/ajr.154.6.2110734 [doi]

Kyröläinen, H., Pullinen, T., Candau, R., Avela, J., Huttunen, P., & Komi, P. (2000). Effects of marathon running on running economy and kinematics. *European Journal of Applied Physiology, 82*(4), 297-304.

Lafortune, M., Hennig, E., & Milani, T. (1994). (1994). Comparison of treadmill and overground running. Paper presented at the *Proceedings, Eighth Biennial Conference, Canadian Society for Biomechanics, Calgary August 18, , 20* 90-91.

Larson, P., Higgins, E., Kaminski, J., Decker, T., Preble, J., Lyons, D., . . . Normile, A. (2011). Foot strike patterns of recreational and sub-elite runners in a long-distance road race. *Journal of Sports Sciences, 29*(15), 1665-1673.

Lieberman, D. E., Venkadesan, M., Werbel, W. A., Daoud, A. I., D'Andrea, S., Davis, I. S., . . . Pitsiladis, Y. (2010). Foot strike patterns and collision forces in habitually barefoot versus shod runners. *Nature, 463*(7280), 531-535.

Liess, C., Lusse, S., Karger, N., Heller, M., & Gluer, C. C. (2002). Detection of changes in cartilage water content using MRI T2-mapping in vivo. *Osteoarthritis and Cartilage, 10*(12), 907-913. doi:S1063458402908472 [pii]

Lin, S., Chen, C. P., Tang, S. F., Chen, C., Wang, J., Hsu, C., . . . Chen, W. (2014). Stress distribution within the plantar aponeurosis during walking—a dynamic finite element analysis. *Journal of Mechanics in Medicine and Biology, 14*(04), 1450053.

Lohman, M., Kivisaari, A., Vehmas, T., Kallio, P., Malmivaara, A., & Kivisaari, L. (2001). MRI abnormalities of foot and ankle in asymptomatic, physically active individuals. *Skeletal Radiology, 30*(2), 61-66.

Luke, A. C., Stehling, C., Stahl, R., Li, X., Kay, T., Takamoto, S., . . . Link, T. (2010). High-field magnetic resonance imaging assessment of articular cartilage before and after marathon running does long-distance running lead to cartilage damage? *American Journal of Sports Medicine, 38*(11), 2273-2280. doi:10.1177/0363546510372799

Lussiana, T., Hébert-Losier, K., Millet, G. P., & Mourot, L. (2016). Biomechanical changes during a 50-minute run in different footwear and on various slopes. *Journal of Applied Biomechanics, 32*(1), 40-49.

Macintyre, J., Taunton, J., Clement, D., Lloyd-Smith, D., McKenzie, D., & Morrell, R. (1991). Running injuries: A clinical study of 4,173 cases. *Clinical Journal of Sport Medicine, 1*(2), 81-87.

Marti, B., Vader, J. P., Minder, C. E., & Abelin, T. (1988). On the epidemiology of running injuries. the 1984 bern grand-prix study. *The American Journal of Sports Medicine, 16*(3), 285-294.

Matheson, G. O., Clement, D. B., McKenzie, D. C., Taunton, J. E., Lloyd-Smith, D. R., & MacIntyre, J. G. (1987). Stress fractures in athletes. A study of 320 cases. *The American Journal of Sports Medicine, 15*(1), 46-58.

Matsas, A., Taylor, N., & McBurney, H. (2000). Knee joint kinematics from familiarised treadmill walking can be generalised to overground walking in young unimpaired subjects. *Gait & Posture, 11*(1), 46-53.

Maxian, T. A., Brown, T. D., & Weinstein, S. L. (1995). Chronic stress tolerance levels for human articular cartilage: Two nonuniform contact models applied to long-term follow-up of CDH. *Journal of Biomechanics, 28*(2), 159-166.

McGinley, J. L., Baker, R., Wolfe, R., & Morris, M. E. (2009). The reliability of three-dimensional kinematic gait measurements: A systematic review. *Gait & Posture, 29*(3), 360-369. doi:10.1016/j.gaitpost.2008.09.003 [doi]

Mei, Q., Fernandez, J., Fu, W., Feng, N., & Gu, Y. (2015). A comparative biomechanical analysis of habitually unshod and shod runners based on a foot morphological difference. *Human Movement Science, 42,* 38-53. doi:10.1016/j.humov.2015.04.007

Mercer, J., Bates, B., Dufek, J., & Hreljac, A. (2003). Characteristics of shock attenuation during fatigued running. *Journal of Sports Science, 21*(11), 911-919.

Mercer, J. A., DeVita, P., Derrick, T. R., & Bates, B. T. (2003). Individual effects of stride length and frequency on shock attenuation during running. *Medicine and Science in Sports and Exercise, 35*(2), 307-313.

Meyer, S., Karttunen, A. H., Thijs, V., Feys, H., & Verheyden, G. (2014). How do somatosensory deficits in the arm and hand relate to upper limb impairment, activity, and participation problems after stroke? A systematic review. *Physical Therapy, 94*(9), 1220-1231. doi:10.2522/ptj.20130271 [doi]

Millet, G. Y., Morin, J., Degache, F., Edouard, P., Feasson, L., Verney, J., & Oullion, R. (2009). Running from paris to beijing: Biomechanical and physiological consequences. *European Journal of Applied Physiology, 107*(6), 731-738.

Mitchell, S. (2002). A technical history of hexahedral mesh generation. *Proceedings of the 11th International Meshing Roundtable, Ithaca,*

Mizrahi, J., Verbitsky, O., & Isakov, E. (2001). Fatigue-induced changes in decline running. *Clinical Biomechanics, 16*(3), 207-212.

Mizrahi, J., Verbitsky, O., Isakov, E., & Daily, D. (2000). Effect of fatigue on leg kinematics and impact acceleration in long distance running. *Human Movement Science, 19*(2), 139-151.

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Annals of Internal Medicine, 151*(4), 264-269.

Moore, I. S., & Dixon, S. J. (2014). Changes in sagittal plane kinematics with treadmill familiarization to barefoot running. *Journal of Applied Biomechanics, 30*(5), 626-631. doi:10.1123/JAB.2013-0239

Morag, E., & Cavanagh, P. (1999). Structural and functional predictors of regional peak pressures under the foot during walking. *Journal of Biomechanics, 32*(4), 359-370.

Morin, J., Tomazin, K., Edouard, P., & Millet, G. (2011). Changes in running mechanics and spring–mass behavior induced by a mountain ultra-marathon race. *Journal of Biomechanics, 44*(6), 1104-1107.

Morin, J., Samozino, P., & Millet, G. Y. (2011). Changes in running kinematics, kinetics, and spring-mass behavior over a 24-h run. *Med Sci Sports Exerc, 43*(5), 829-836.

Mosher, T. J., & Dardzinski, B. J. (2004). Cartilage MRI T2 relaxation time mapping: Overview and applications. Paper presented at the *Seminars in Musculoskeletal Radiology, , 8*(04) 355-368.

Mosher, T. J., Liu, Y., & Torok, C. M. (2010). Functional cartilage MRI T2 mapping: Evaluating the effect of age and training on knee cartilage response to running. *Osteoarthritis and Cartilage, 18*(3), 358-364.

Mosher, T. J., Smith, H. E., Collins, C., Liu, Y., Hancy, J., Dardzinski, B. J., & Smith, M. B. (2005). Change in knee cartilage T2 at MR imaging after running: A feasibility study 1. *Radiology, 234*(1), 245-249.

Mow, V., & Rosenwasser, M. (1988). Articular cartilage: Biomechanics. *Injury and Repair of the Musculoskeletal Soft Tissues, 1,* 427-463.

Mueller, M. J., Hastings, M., Commean, P. K., Smith, K. E., Pilgram, T. K., Robertson, D., & Johnson, J. (2003). Forefoot structural predictors of plantar pressures during walking in people with diabetes and peripheral neuropathy. *Journal of Biomechanics, 36*(7), 1009-1017.

Nagel, A., Fernholz, F., Kibele, C., & Rosenbaum, D. (2008). Long distance running increases plantar pressures beneath the metatarsal heads: A barefoot walking investigation of 200 marathon runners. *Gait & Posture, 27*(1), 152-155.

Nakamura, S., Crowninshield, R. D., & Cooper, R. R. (1981). An analysis of soft tissue loading in the foot--a preliminary report. *Bulletin of Prosthetics Research, 10-35*, 27-34.

Napier, C., Cochrane, C. K., Taunton, J. E., & Hunt, M. A. (2015). Gait modifications to change lower extremity gait biomechanics in runners: A systematic review. *British Journal of Sports Medicine, 49*(21), 1382-1388. doi:10.1136/bjsports-2014-094393 [doi]

Nicholson, C. W., Berlet, G. C., & Lee, T. H. (2007). Prediction of the success of nonoperative treatment of insertional achilles tendinosis based on MRI. *Foot & Ankle International, 28*(4), 472-477. doi:956376 [pii]

Nigg, B. M. (1985). Biomechanics, load analysis and sports injuries in the lower extremities. *Sports Medicine, 2*(5), 367-379.

Obrien, D. L., & Tyndyk, M. (2014). Effect of arch type and body mass index on plantar pressure distribution during stance phase of gait. *Acta of Bioengineering and Biomechanics, 16*(2)

Paulson, S., & Braun, W. (2014). Mechanical and physiological examination of barefoot and shod conditions in female runners. *International Journal of Sports Medicine, 35*(09), 789-793.

Peltonen, J., Cronin, N. J., Stenroth, L., Finni, T., & Avela, J. (2012). Achilles tendon stiffness is unchanged one hour after a marathon. *The Journal of Experimental Biology, 215*(Pt 20), 3665-3671. doi:215/20/3665 [pii]

Perl, D. P., Daoud, A. I., & Lieberman, D. E. (2012). Effects of footwear and strike type on running economy. *Medicine & Science in Sports & Exercise, 44*(7), 1335-1343.

Prochazkova, M., Tepla, L., Svoboda, Z., Janura, M., & Cieslarová, M. (2014). Analysis of foot load during ballet dancers' gait. *Acta of Bioengineering and Biomechanics, 16*(2), 41--45.

Pugh, Lewis Griffith Cresswell Evans. (1970). Oxygen intake in track and treadmill running with observations on the effect of air resistance. *The Journal of Physiology, 207*(3), 823-835.

Putti, A., Arnold, G., & Abboud, R. (2010). Differences in foot pressures between caucasians and indians. *Foot and Ankle Surgery, 16*(4), 195-198.

Queen, R. M., Abbey, A. N., Wiegerinck, J. I., Yoder, J. C., & Nunley, J. A. (2010). Effect of shoe type on plantar pressure: A gender comparison. *Gait & Posture, 31*(1), 18-22.

Repo, R. U., & Finlay, J. B. (1977). Survival of articular cartilage after controlled impact. *The Journal of Bone and Joint Surgery.American Volume, 59*(8), 1068-1076.

Ridge, S. T., Johnson, A. W., Mitchell, U. H., Hunter, I., Robinson, E., Rich, B., & Brown, S. D. (2013). Foot bone marrow edema after 10-week transition to minimalist running shoes. *Med Sci Sports Exerc, 45*(7), 1363-1368.

Riley, P. O., Dicharry, J., Franz, J., Croce, U. D., Wilder, R. P., & Kerrigan, D. C. (2008). A kinematics and kinetic comparison of overground and treadmill running. *Medicine and Science in Sports and Exercise, 40*(6), 1093.

Saltzman, C. L., & Nawoczenski, D. A. (1995). Complexities of foot architecture as a base of support. *Journal of Orthopaedic & Sports Physical Therapy, 21*(6), 354-360.

Savelberg, H. H., Vorstenbosch, M. A., Kamman, E. H., van de Weijer, Jolanda GW, & Schambardt, H. C. (1998). Intra-stride belt-speed variation affects treadmill locomotion. *Gait & Posture, 7*(1), 26-34.

Schache, A. G., Blanch, P. D., Rath, D. A., Wrigley, T. V., Starr, R., & Bennell, K. L. (2001). A comparison of overground and treadmill running for measuring the three-dimensional kinematics of the lumbo–pelvic–hip complex. *Clinical Biomechanics, 16*(8), 667-680.

Schieb, D. A. (1986). Kinematic accommodation of novice treadmill runners. *Research Quarterly for Exercise and Sport, 57*(1), 1-7.

Schubert, A. G., Kempf, J., & Heiderscheit, B. C. (2014). Influence of stride frequency and length on running mechanics: A systematic review. *Sports Health, 6*(3), 210-217.

Schueller-Weidekamm, C., Schueller, G., Uffmann, M., & Bader, T. (2006). Does marathon running cause acute lesions of the knee? evaluation with magnetic resonance imaging. *European Radiology, 16*(10), 2179-2185.

Schutz, U. H. W., Ellermann, J., Schoss, D., Wiedelbach, H., Beer, M., & Billich, C. (2014). Biochemical cartilage alteration and unexpected signal recovery in T2* mapping observed in ankle joints with mobile MRI during a transcontinental multistage footrace over 4486 km. *Osteoarthritis & Cartilage, 22*(11), 1840-1850. doi:http://dx.doi.org/10.1016/j.joca.2014.08.001

Shellock, F. G., & Mink, J. H. (1991). Knees of trained long-distance runners: MR imaging before and after competition. *Radiology, 179*(3), 635-637. doi:10.1148/radiology.179.3.2027965 [doi]

Sinclair, J., Richards, J., Taylor, P. J., Edmundson, C. J., Brooks, D., & Hobbs, S. J. (2013). Three-dimensional kinematic comparison of treadmill and overground running. *Sports Biomechanics, 12*(3), 272-282.

Soila, K., Karjalainen, P. T., Aronen, H. J., Pihlajamaki, H. K., & Tirman, P. J. (1999). High-resolution MR imaging of the asymptomatic achilles tendon: New observations. *AJR.American Journal of Roentgenology, 173*(2), 323-328. doi:10.2214/ajr.173.2.10430128 [doi]

Spears, I. R., Miller-Young, J. E., Waters, M., & Rome, K. (2005). The effect of loading conditions on stress in the barefooted heel pad. *Medicine and Science in Sports and Exercise, 37*(6), 1030-1036. doi:10.1249/01.mss.0000171620.07016.6d

Squadrone, R., Rodano, R., Hamill, J., & Preatoni, E. (2015). Acute effect of different minimalist shoes on foot strike pattern and kinematics in rearfoot strikers during running. *Journal of Sports Sciences, 33*(11), 1196-1204.

Squadrone, R., & Gallozzi, C. (2009). Biomechanical and physiological comparison of barefoot and two shod conditions in experienced barefoot runners. *Journal of Sports Medicine and Physical Fitness, 49*(1), 6-13.

Stahl, R., Luke, A., Ma, C. B., Krug, R., Steinbach, L., Majumdar, S., & Link, T. M. (2008). Prevalence of pathologic findings in asymptomatic knees of marathon runners before and after a competition in comparison with physically active subjects—a 3.0 T magnetic resonance imaging study. *Skeletal Radiology, 37*(7), 627-638.

Stehling, C., Luke, A., Stahl, R., Baum, T., Joseph, G., Pan, J., & Link, T. M. (2011). Meniscal T1rho and T2 measured with 3.0T MRI increases directly after running a marathon. *Skeletal Radiology, 40*(6), 725-735. doi:10.1007/s00256-010-1058-2

Subburaj, K., Kumar, D., Souza, R. B., Alizai, H., Li, X., Link, T. M., & Majumdar, S. (2012). The acute effect of running on knee articular cartilage and meniscus magnetic resonance relaxation times in young healthy adults. *American Journal of Sports Medicine, 40*(9), 2134-2141. doi:10.1177/0363546512449816

Tadepalli, S. C., Erdemir, A., & Cavanagh, P. R. (2011). Comparison of hexahedral and tetrahedral elements in finite element analysis of the foot and footwear. *Journal of Biomechanics, 44*(12), 2337-2343.

Taunton, J. E., Ryan, M. B., Clement, D. B., McKenzie, D. C., Lloyd-Smith, D. R., & Zumbo, B. D. (2002). A retrospective case-control analysis of 2002 running injuries. *British Journal of Sports Medicine, 36*(2), 95-101.

Taunton, J. E., Ryan, M. B., Clement, D. B., McKenzie, D. C., Lloyd-Smith, D. R., & Zumbo, B. D. (2003). A prospective study of running injuries: The vancouver sun run "in training" clinics. *British Journal of Sports Medicine, 37*(3), 239-244.

Tegner, Y., & Lysholm, J. (1985). Rating systems in the evaluation of knee ligament injuries. *Clinical Orthopaedics and Related Research, 198,* 42-49.

Thijs, Y., De Clercq, D., Roosen, P., & Witvrouw, E. (2008). Gait-related intrinsic risk factors for patellofemoral pain in novice recreational runners. *British Journal of Sports Medicine, 42*(6), 466-471. doi:10.1136/bjsm.2008.046649 [doi]

Trappeniers, L., De Maeseneer, M., De Ridder, F., Machiels, F., Shahabpour, M., Tebache, C., . . . Osteaux, M. (2003). Can bone marrow edema be seen on STIR images of the ankle and foot after 1 week of running?. *European Journal of Radiology, 47*(1), 25-28.

Verbitsky, O., Mizrahi, J., Voloshin, A., Treiger, J., & Isakov, E. (1998). Shock transmission and fatigue in human running. *Journal of Applied Biomechanics, 14,* 300-311.

Vickers, A. J., & Altman, D. G. (2001). Statistics notes: Analysing controlled trials with baseline and follow up measurements. *BMJ (Clinical Research Ed.), 323*(7321), 1123-1124.

Wang, Y., Wong, D. W., & Zhang, M. (2016). Computational models of the foot and ankle for pathomechanics and clinical applications: A review. *Annals of Biomedical Engineering, 44*(1), 213-221.

Wank, V., Frick, U., & Schmidtbleicher, D. (1998). Kinematics and electromyography of lower limb muscles in overground and treadmill running. *International Journal of Sports Medicine, 19*(7), 455-461. doi:10.1055/s-2007-971944 [doi]

Weierink, L., Vermeulen, R. J., & Boyd, R. N. (2013). Brain structure and executive functions in children with cerebral palsy: A systematic review. *Research in Developmental Disabilities, 34*(5), 1678-1688.

Weightman, B., Chappell, D. J., & Jenkins, E. A. (1978). A second study of tensile fatigue properties of human articular cartilage. *Annals of the Rheumatic Diseases, 37*(1), 58-63.

Weist, R., Eils, E., & Rosenbaum, D. (2004). The influence of muscle fatigue on electromyogram and plantar pressure patterns as an explanation for the incidence of metatarsal stress fractures. *The American Journal of Sports Medicine, 32*(8), 1893-1898.

Wilkerson, R. D., & Mason, M. A. (2000). Differences in men's and women's mean ankle ligamentous laxity. *The Iowa Orthopaedic Journal, 20*, 46-48.

Willems, T. M., De Ridder, R., & Roosen, P. (2012). The effect of a long-distance run on plantar pressure distribution during running. *Gait & Posture, 35*(3), 405-409.

Willems, T. M., De Clercq, D., Delbaere, K., Vanderstraeten, G., De Cock, A., & Witvrouw, E. (2006). A prospective study of gait related risk factors for exercise-related lower leg pain. *Gait & Posture, 23*(1), 91-98.

Williams Iii, D. S., McClay, I. S., & Hamill, J. (2001). Arch structure and injury patterns in runners. *Clinical Biomechanics, 16*(4), 341-347.

Willick, S. E., & Hansen, P. A. (2010). Running and osteoarthritis. *Clinics in Sports Medicine, 29*(3), 417-428.

Zelisko, J. A., Noble, H. B., & Porter, M. (1982). A comparison of men's and women's professional basketball injuries. *The American Journal of Sports Medicine, 10*(5), 297-299.

Zimmerman, N. B., Smith, D. G., Pottenger, L. A., & Cooperman, D. R. (1988). Mechanical disruption of human patellar cartilage by repetitive loading in vitro. *Clinical Orthopaedics and Related Research*, *229,* 302-307.

Appendices

Appendix A: A Case Report

Non-Symptomatic Diagnosed Inflammation on the Cuneiforms on T2* maps and its Relationship to Plantar Pressure: A Case Report

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This article has been prepared for publication. This study was also presented by H.K Kim as a poster presentation at the *International Society of Biomechanics*, 24th Jury 2017 Brisbane.

Preface

We accidently recruited one former dancer who sustained inflammation on her foot during a preliminary study. This chapter presents a case study reporting a former professional dancer with subtle inflammation at the base of between the middle and the lateral cuneiforms and its relationship to the plantar pressure distribution during gait.

Introduction

T2*-weighted mapping has been recently used to evaluate ultrastructural morphological alteration including extracellular fluid content, hence detecting early-stage degeneration within cartilage (Crema et al., 2011), which is not detectable on the conventional magnetic resonance (MR) images. However, it remains unclear how this subtle detection on T2* maps relates to the human gait.

Recently we rarely recruited a former female dancer who had a pre-existing non-symptomatic inflammation on the base of between the middle and the lateral cuneiforms on T2* maps, which is not easy to evaluate its relationship to the gait patterns mainly because of the ethical issues. This case report presented subtle inflammation on the distal cuneiforms detecting by T2* mapping and its relationship to the plantar pressure during gait.

Case report

We examined a 40-year-old female former dancer (63kg, 167cm, 22.59kg/m^2) who at the time was involved in recreational sports activities such as yoga and Pilates. She used to be dance professionally (contemporary dance), with over 10 years of experience, but it had been five years since she quit dancing at this level. At the time of enrolment in this study, she reported no pain and no lower limb injuries. We obtained her written informed consent form approved by the University of Auckland Human Participants Ethics Committee (reference number: 016488).

Magnetic resonance data acquisition and analysis

MR scans of the right foot and ankle (dominant foot) were acquired using a 3-Tesla MR scanner (Siemens Skyra 3T, Erlangen, Germany) with a sixteen channel foot coil while she was lying down in a natural position. The details of MR sequences were the same as detailed in the previous chapters 6 and 8. Additionally, we used a sagittal gradient-echo (GRE) pulse T2* map. All the MR scans were analysed by Osirix software Lite v.9.0.1 (Pixmeo, Geneva, Switzerland).

Based on the MR scans, subtle inflammation on the base of between the middle and the lateral cuneiforms was identified (Figure 1). However, despite this pre-existing inflammation, she had no pain or discomfort during walking or running.

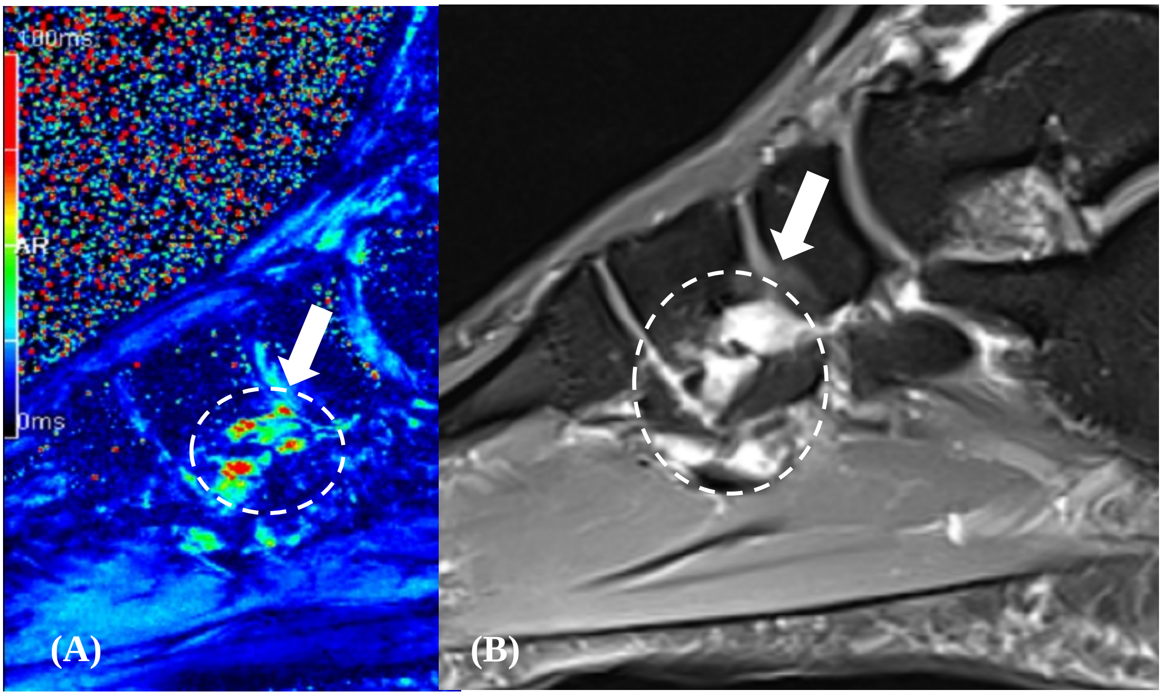

Figure 1. Sagittal view. (A) T2* mapping and (B) a sagittal PD (proton density) TSE (turbo spin-echo) spair sequence showed the pre-existing inflammation at the base of between the middle and the lateral cuneiforms.

Plantar pressure comparison against healthy subjects

To see how this non-symptomatic inflammation affects gait patterns, the plantar pressure was measured by the Novel emed® pressure platform during running unshod with natural pace. The details of plantar pressure analysis were described in the previous chapters 4, 6 and 8. Peak pressure (kPa), peak force (N), contact area (cm^2), and impulse (N s) were obtained during unshod running, and these parameters were compared against twenty (10 female and 10 male) healthy subjects investigated in the previous chapters (age: 30.1±8yrs, weight: 66.12±9.7kg, height: 1.71±0.08m). SPSS (IBM Corporation, Version 20) was employed for statistical tests. The differences in plantar pressure parameters between the case subject and the 20 healthy subjects were evaluated with a one-way T-test (two-tailed) with a significance set at $p = 0.05$.

The plantar pressure distribution (Figure 2) seemed to be very different between the case subject and the 20 healthy subjects. In the case subjects, the load underneath the medial heel (MH) and the lateral heel (LH) revealed the greatest values among the eleven ROIs during barefoot running, whereas the 20 healthy subjects showed the highest values under the first metatarsal (M1). Mean peak force and impulse also demonstrated a similar disparity, with the greatest values beneath the heel regions in the case subject while the 20 healthy subjects presented the greatest values beneath the M1. More specifically, mean peak pressure underneath MH and LH were significantly greater by 40.26% and 43.36%, respectively, in the case subject when compared with the 20 healthy subjects. The medial midfoot (MM), the lateral midfoot (LM), and the hallux (T1) also showed similar trends of significantly higher values (48.86%, 16.12%, and 16.73%, respectively) in the case subject when compared with 20 healthy subjects. Mean peak force and impulse underneath T1 (21.61%, 17.82%, respectively), MM (42.23%, 42.25%, respectively), LM (31.47%, 34.47%, respectively), and LH (23.98%, 48.68%, respectively) also presented greater values in the case subject compared with 20 healthy subjects. In contrast, all of the metatarsal regions showed lower loading in the case subject by comparison to the healthy cohort– mean peak plantar pressure underneath the second metatarsal (M2) and the third metatarsal (M3) were significantly lower in the case subject (Figure 9.2). Mean peak force and impulse underneath M1 and M2 also showed significantly lower values in the case subject. The case subject generally showed lower values in the contact area than the 20 healthy individuals, except for the LM.

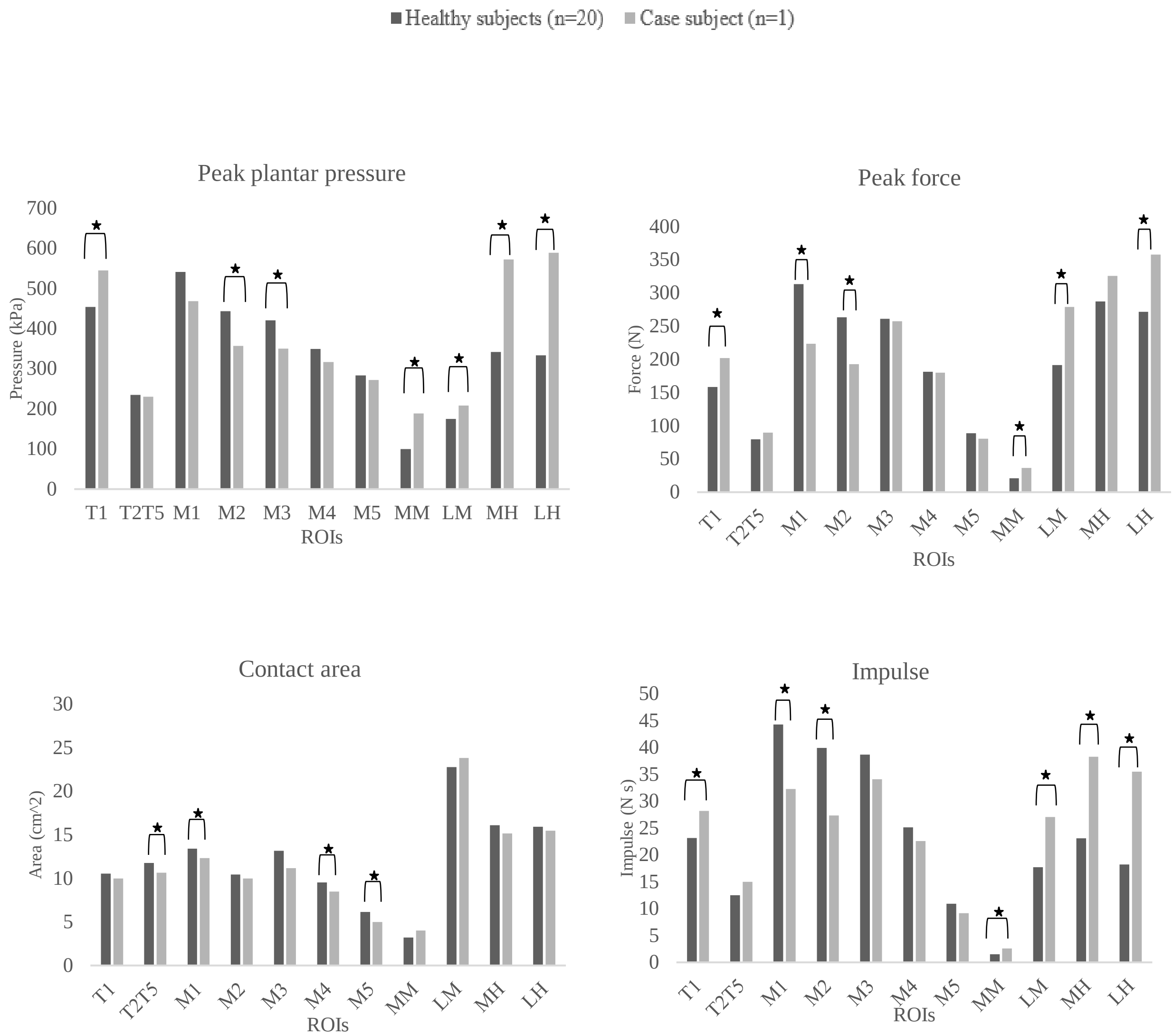

Figure 2. Peak mean plantar pressure, force, contact area, and impulse during running unshod. ***** indicates a significant (p = 0.05) difference between two groups.

Discussion

This case study shows that non-symptomatic inflammation, which was detected by T2* maps, does modify the plantar pressure distribution during natural gait. Based on the pedobarography analysis, the contribution of the heel was greatly increased in the case subject, while the healthy subjects showed greater contribution of the metatarsal regions. The results from the healthy subjects were in line with other unshod analysis studies (Bergstra et al., 2015; D'Août et al., 2009), reporting that unshod walking and/or running lead to greater loading under the forefoot regions, although it must be noted that they both had different study design, gait types, measuring devices, and shod condition. It has been well documented that barefoot runners (even first time unshod runners) likely adopt a forefoot strike techniques (Hatala et al., 2013; Lieberman et al., 2010), which results in a load increasing underneath the lateral forefoot (D'Août et al., 2009), while shod runners generally run with heel strike techniques. Heel strike landing with bare feet may cause greater deformation of the fat-pad under the calcaneus compared with a heel strike in shoes (De Clercq, Aerts, & Kunnen, 1994).

Contrary to our expectations, however, the case subject showed significantly increased loading under the heel regions during unshod running. This unexpected gait pattern was possibly due to the pre-existing inflammation at the base of her cuneiforms. Alteration of T2 and/or T2* has been associated with early-stage degeneration in cartilage (Crema et al., 2011) and a higher T2 signal was observed in severely osteoarthritic knee cartilage when compared with normal cartilage (Dunn et al., 2004). Recently, an acute alteration of T2 and/or T2* value was observed in the knee (Hesper et al., 2015; Subburaj et al., 2012) and the ankle (Schutz et al., 2014) cartilage after long-distance running. It has also been reported that female ballet dancers showed greater T2 values in the ankle cartilage when compared with age-matched healthy subjects (Cha et al., 2015). Although there is no study looking at the relationship between the T2* signal on the foot and gait pattern, the T2* values indicate changes to the cartilage that affects gait patterns to off-load the forefoot, and hence increase pressure on the heel.

Conclusions

This case study presents the evaluation of gait biomechanics in a former dancer who had pre-existing, non-symptomatic inflammation at the base of between the middle and the lateral cuneiforms. The results may suggest that the subtle inflammation, detected by T2* mapping, does modify gait and may lead to decreased involvement of metatarsal regions, while increasing involvement of heel regions when compared with healthy subjects. In the present case, the gait was altered to off-load the forefoot and metatarsals, and hence increase pressure on the heel.

Appendix B: Tegner Activity Level Scale

Please indicate in the spaces below the HIGHEST level of activity that you are currently participating.

LEVEL:________________

Level 10	Competitive sports- soccer, football, rugby (national elite)
Level 9	Competitive sports- soccer, football, rugby (lower divisions), ice hockey, wrestling, gymnastics, basketball
Level 8	Competitive sports- racquetball or bandy, squash or badminton, track and field athletics (jumping, etc.), down-hill skiing
Level 7	Competitive sports- tennis, running, motorcars speedway, handball Recreational sports- soccer, football, rugby, bandy, ice hockey, basketball, squash, racquetball, running
Level 6	Recreational sports- tennis and badminton, handball, racquetball, down-hill skiing, jogging at least 5 times per week
Level 5	Work- heavy labour (construction, etc.) Competitive sports- cycling, cross-country skiing, Recreational sports- jogging on uneven ground at least twice weekly
Level 4	Work- moderately heavy labour (e.g. truck driving, etc.)
Level 3	Work- light labour (nursing, etc.)

Level 2	Work- light labour Walking on uneven ground possible, but impossible to back pack or hike
Level 1	Work- sedentary (secretarial, etc.)
Level 0	Sick leave or disability pension because of the lower limb joint problems

(Tegner & Lysholm, 1985)

Appendix C: Consent Form

MEDICAL AND HEALTH SCIENCES
SCHOOL OF MEDICAL SCIENCES

Department of Anatomy and Medical Imaging

Faculty of Medical and Health Sciences

University of Auckland

Private Bag 92019

Auckland 1142, New Zealand

CONSENT FORM for VOLUNTEERS

This form will be held for six years.

Effect of Long-Distance Barefoot running on the ankle/foot complex

Dr Seyed Ali Mirjalili; Dr Justin Fernandez; Hyun Kyung Kim

- I have read the Participant Information Sheet (Reference Number 016488), have understood the nature of the research, and why I have been selected. I have had the opportunity to ask questions and have them answered to my satisfaction.
- I agree to voluntarily take part in this research.
- I understand that I am free to withdraw participation at any time.
- I understand that my personal details will remain confidential and will be stored on a protected server at the Department of Anatomy and Medical Imaging at the University of

Auckland for 6 years, after which they will be destroyed, and that I will not be identifiable in any publications generated from this study.

- I understand that I may request my data be withdrawn from the study up to three month after I have completed this study.
- I understand that there is a possibility to detect any clinical abnormality through examining a MRI scan on the lower limb joints. The researchers will informed of this and will be advised to consult a general practitioner or other health professional of my choice.
- I understand that if I do not wish to be informed of any abnormalities detected, then I should not participated in this project.
- I understand that there are no expected benefits to me personally from taking part, that the experiments will take up to 3 hours of my time (except for the 5km run time), and that my results will be used to understand underlying mechanisms of the lower limb joints.

I would like the researchers to send me a summary of the study results (Please circle) YES / NO

____________________	________________________	/ /
PARTICIPANT’S NAME	PARTICIPANT’S SIGNATURE	DATE
___________________	_______________________	/ /
RESEARCHER’S NAME	RESEARCHER’S SIGNATURE	DATE

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS Committee on [06.11.2015] for three years. REFERENCE NUMBER 016488.