

# MOVING FORWARDS BY GOING OUTSIDE 

INERTIAL MEASUREMENT UNIT-BASED MONITORING OF RUNNING BIOMECHANICS

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## PROEFSCHRIFT

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## Contents

1 General introduction ..... 9
2 Effects of level running-induced fatigue on running kinematics ..... 25
3 Quantifying and correcting for speed and stride frequency ..... 81effects on running mechanics in fatiguing outdoor running
4 Peak tibial acceleration should not be used as indicator of tibial ..... 105
bone loading in running
5 Estimating 3D orientation of a body segment during running ..... 131 using a single gyroscope
6 Drift-free 3D orientation and displacement estimation for ..... 143quasi-cyclical movements using one inertial measurement unit
7 General discussion ..... 175
\& Summary | Samenvatting ..... 195
\& Dankwoord ..... 207
\& About the author ..... 213
\& Progress range ..... 217

# Chapter <br> 1 

General introduction

## Introduction to running

Running is an accessible leisure time activity. In 2020, running was the second most popular sport in The Netherlands, with 12 percent of Dutch people participating in weekly running sessions ${ }^{1,2}$. Running has many health benefits for the cardiovascular, metabolic, neuropsychiatric, and musculoskeletal systems and runners have a $30-45 \%$ lower risk of all-cause mortality ${ }^{3}$. However, runners are at risk for developing running-related injuries such as medial tibial stress syndrome (i.e., shin splints), tibial stress fractures, patellofemoral pain syndrome (i.e., runner's knee), Achilles tendinopathy, plantar fasciitis and iliotibial band syndrome ${ }^{4}$. The incidence of lower extremity running injuries is alarming, with values of up to $79 \%$, depending on the population investigated and the exact definition of an injury ${ }^{5}$. Most running injuries are overuse related and are assumed to be caused by training load errors (i.e., too fast and too far) and running biomechanics ${ }^{6,7}$, see Intermezzo "Definitions in motion analysis". A small number of prospective studies have been conducted and found biomechanical differences between runners who acquired an injury and those who remained injury free ${ }^{6,8,9}$. This link between running biomechanics and injuries sparks our interest in measuring running biomechanics and understanding the etiology of running-related injuries.

## Intermezzo: Definitions in motion analysis

## Biomechanics, kinematics, and kinetics

Biomechanics refers to "the study of biological systems, particularly their structure and function, using methods derived from mechanics, which is concerned with the effect that forces have on the motion of bodies" ${ }^{10}$. Biomechanics is typically subdivided into kinematics and kinetics. Kinematics refer to the study of the description of motion (e.g., position, joint angles, velocity, and acceleration), while kinetics involves the various forces that result in motions (e.g., ground reaction force and torque).

## Running gait

Running gait is divided into gait cycles for more straightforward analysis and visualization.
A gait cycle starts when a foot first makes contact with the ground (i.e., initial contact) and ends shortly before the same foot makes contact with the ground again, see Figure 1.1. Depending on the strike pattern of a runner, initial contact occurs with the rearfoot, midfoot, or forefoot, of which a rearfoot strike is most common (75-95\%) ${ }^{11}$.

Gait cycles are further divided into stance and swing phases. The stance phase starts with initial contact (Figure 1.1A) and ends when the foot loses contact with the ground (i.e., toe-off, Figure 1.1D). The swing phase starts with toe-off and ends with initial contact.


Figure 1.1: Visualization of a running gait cycle for the right leg. The right leg and arm are shown in blue. The text above the figure shows different moments in the gait cycle. Blocks below the figure show different phases of the gait cycle.

## Running biomechanics

During running, each foot hits the ground around 85 times per minute ${ }^{12,13}$. Every time, ground reaction forces of about 2.5 times body weight are exerted on the body ${ }^{14}$, see Figure 1.2. These impact forces cause a rapid deceleration of the foot following initial contact, shortly followed by deceleration of the lower leg, upper leg, pelvis, and upper body. Running kinematics influence these impact forces on the body. A more flexed knee and a smaller angle between the lower leg and vertical axis at initial contact result in smaller peak impact forces ${ }^{15}$. High impact forces and steep increases in impact forces are thought to reflect an increased injury risk ${ }^{16-18}$. Accelerometers can measure acceleration of body segments following initial contact and thereby quantify the decelerating effects of impact forces on body segments.

A commonly reported impact quantity is peak tibial acceleration (PTA) ${ }^{19}$, see Figure 1.2. PTA is defined as the peak axial (i.e., in the direction of the long axis of the tibia bone) acceleration typically measured with an accelerometer (or inertial measurement unit (IMU) containing an accelerometer) on the lower leg immediately after initial contact. Typical PTA values during running reach values from (mean (standard deviation)) 5.6 (1.3) to 13.3 (3.4) times the gravitational acceleration $(\mathrm{g})^{20}$. Accelerometers can also quantify peak accelerations of the foot, pelvis, and head ${ }^{21,22}$. The body is expected to minimize proximal accelerations to prevent disturbances of the vestibular and visual systems ${ }^{23,24}$. Shocks, as a consequence of impact forces, are attenuated passively through shoe soles, the Achilles' tendon, plantar fascia, and
bones and actively through muscles and joint kinematics ${ }^{25,26}$. Due to shock attenuation, peak accelerations in the body typically decrease from distal to proximal segments, see Figure 1.2. Shock attenuation is computed from peak accelerations of at least two different body segments as the percentual reduction in peak accelerations. Decreased shock attenuation could indicate that a runner is less able to attenuate impact forces, which is assumed to cause higher forces on biological structures in the body and, therefore, an increased risk of overuse-related running injuries ${ }^{22,27}$.

Shock attenuation can change by factors such as fatigue, often encountered when running for prolonged periods of time ${ }^{28}$. With fatigue, the body is hypothesized to move to shock attenuation strategies that rely more heavily on passive structures such as tendons and bones instead of active strategies mainly based on joint angle modulations through coordinated muscle contractions which are energetically costly ${ }^{15,29,30}$. Repetitive loading of tendons and bones is expected to cause overuse-related running injuries ${ }^{17}$. For instance, due to disrupted bone formation and resorption caused by impact forces resulting in accumulation of microfractures in the tibia bone and tibial stress fractures ${ }^{31}$ or possibly through muscle traction-related bone resorption in medial tibial stress syndrome ${ }^{32}$. To better understand the link between running-induced fatigue and overuse-related injuries, it is essential to know how running kinematics change due to fatigue.

Research question Chapter 2
How do running kinematics change due to running-induced fatigue?


Figure 1.2: Forces and accelerations during the stance phase of running. Top figure: Visualization of a rearfoot (RF) striking runner at A) initial contact, B-C) midstance, D) toe-off. Central figure: Vertical ground reaction forces (GRF) during the stance phase of running for a RF and non-rearfoot (NRF) striking runner. Letters refer to the gait events presented in the top figure. Bottom figure: Acceleration in the superior direction of the tibia and pelvis segments during the stance phase of running. $N=$ Newton, $B W=$ body weight, $G R F=$ vertical ground reaction force, $R F=$ rearfoot striking runner, $N R F=$ non-rearfoot striking runner, $g=$ gravitational acceleration.

PTA is one of the most popular quantities to measure when analyzing running gait with IMUs ${ }^{33}$. PTA is often considered a proxy measure for impact forces experienced at the tibia ${ }^{19}$. Higher impact forces are assumed to represent more tibial bone loading and increase the risk of particularly tibial microfractures ${ }^{34}$. Without sufficient rest and recovery, these microfractures result in tibial stress fractures ${ }^{35}$. Prospective preliminary data suggests that runners with a tibial stress fracture tended to have higher PTA values than healthy matched controls before they got injured ${ }^{36}$. Multiple studies found higher PTA values in injured compared to uninjured runners ${ }^{16,37}$ and in injured compared to uninjured legs ${ }^{38}$. In some studies, PTA increased with running-induced fatigue, which is thought to reflect an increased injury risk due to higher loads on the body ${ }^{29,39,40}$. PTA is incorporated in multiple commercial products for runners ${ }^{41-43}$ and is used as a bio-feedback variable to change the running pattern of runners with high PTA values, with the idea of decreasing their risk of injuries ${ }^{44-46}$. However, tibial bone loading is not only caused by impact forces but is a summation of the (effect of) impact forces and compressive forces from muscle contractions ${ }^{47,48}$. The effect of impact forces compromises no more than $18 \%$ of the total tibial compression forces during the stance phase, while muscle contractions of the calf muscles make up $82 \%{ }^{47}$. The small contribution of impact-related quantities to tibial compression forces questions the widespread scientific and commercial use of PTA and its assumed relationship with tibial bone loading.

## Research Question Chapter 3

How to quantify and correct for the subject-specific effects of changes in running speed and stride frequency on impact-related running mechanics during a fatiguing outdoor run?

## From the laboratory to the outside world

Running kinematics and the effect of running-induced fatigue on running kinematics is typically measured in a laboratory setting with optoelectronic systems while running on a treadmill ${ }^{49-52}$. Such a controlled environment allows researchers to eliminate or minimize the effects of possible confounding factors, such as running speed ${ }^{53}$, running surface ${ }^{54}$, and inclination ${ }^{55}$. However, these measurements have many downsides, such as an imposed running speed, long processing times, and marker occlusion, which limits the calculation of kinematics. But most importantly, there is no evidence that changes in running kinematics due to fatigue in a controlled environment are similar to those in an uncontrolled environment.

Treadmill running induces more regularity, less variability, and more significant constraints than overground running ${ }^{56,57}$. These differences could result in a poor agreement for multiple kinematic quantities between running in a constrained and unconstrained environment ${ }^{58}$. PTA was shown to differ between treadmill and track running on multiple occasions ${ }^{54,59}$. There is an increasing amount of evidence suggesting that running gait patterns should be measured in a relatively uncontrolled sport-specific setting ${ }^{33}$. However, while controlled settings have their limitations, new limitations arise for uncontrolled settings. Running speed is typically imposed in treadmill running but tends to decrease towards the end of an outdoor fatiguing protocol ${ }^{11,60,61}$. Running speed and stride frequency significantly influences many aspects of the running gait pattern ${ }^{53,62}$. Changes in running kinematics during a fatiguing protocol in a sport-specific setting can be caused by fatigue or a change in speed or stride frequency. Hence, it is necessary to investigate the effect of running speed and stride frequency on changes in running kinematics during a fatiguing protocol in a sport-specific setting such as a marathon.

## Research Question Chapter 4

What is the strength of the relationship between peak tibial acceleration and maximal tibial compression force in running?

## Intermezzo: Inertial Measurement Units (IMUs)

Measuring running-related quantities with wearable sensors is very popular in the scientific world ${ }^{33}$. In the last decade, the experience of "going for a run" has also changed for many recreational runners. Runners are using more and more technology to track their progress ${ }^{63}$. In 2014, 86\% of competitive half marathon runners reported using a device to monitor how they ran the previous year ${ }^{64}$. Global positioning system (GPS) based devices (e.g., mobile phones and sports watches) are the most popular and can be used to monitor training load. GPS-based devices allow runners to analyze how far, how fast, and how often they run. However, they do not provide information about running biomechanics and injury risks related to running biomechanics. Wearable sensors such as inertial measurement units (IMUs) are affordable and relatively easy to use. IMUs are suitable for monitoring running biomechanics in a sport-specific environment for scientists, competitive and recreational runners.

IMUs consist of three-dimensional (3D) accelerometers and 3D rate gyroscopes and are often combined with 3D magnetometers. These sensors measure the total acceleration (including gravity), angular velocity, and magnetic field in a sensor-fixed coordinate system, respectively. Sensor orientation can be computed through strapdown inertial navigation based on numerical integration of the angular velocity. However, this process is prone to integration drift ${ }^{65}$. Alternatively, data from the rate gyroscope can be combined with accelerometer and magnetometer data for inclination (orientation with respect to vertical) and heading information and be used as input for sensor fusion algorithms to estimate sensor orientation in an Earth-fixed coordinate system (for example ${ }^{66}$ ). With the orientation of a sensor in an Earth-fixed coordinate system, sensor total acceleration (including gravity) can be rotated from a sensor-fixed to an Earth-fixed coordinate system, in which the gravity component of the total acceleration measured by the accelerometer is always in the same direction. Subtracting gravity from the acceleration signal in the Earth-fixed coordinate system results in the free acceleration, which can be integrated once to obtain change in velocity or twice to obtain change in position. Also these integration operations are prone to drift, which can be reduced by applying supplementary distance measurements or assumptions about the performed movements.

In motion analysis, we are typically interested in data expressed in a coordinate system with functional meaning. Depending on the orientation of a sensor on a body segment, a sensor coordinate system may not have functional meaning while a segment coordinate system is designed to have functional meaning. For example, for the tibia, the first axis of the segment coordinate system can be chosen to be directed in the longitudinal direction of the tibia bone while a second axis can be perpendicular to the flexion-extension rotation axis of the tibia during walking or running. The sensor signals that are measured in the sensor coordinate system can be expressed in the chosen segment coordinate system through a process called sensor-to-segment calibration. When time-synchronized segment orientations of two linked body segments are available, the 3D joint angle between these segments can be computed.

## How to measure in the outside world?

Data from IMUs can be used directly (e.g., PTA), or quantities can be computed following multiple processing steps based on the sensor output. For many kinematic quantities of interest, the orientation of body segments is required, such as the orientation of the foot and lower leg at initial contact or for computation of joint angles throughout the gait cycle 29,50,52. Currently, sensor orientation estimation often relies on the integration of sensor angular velocities. This process is prone to errors and is typically combined with sensor fusion and error modeling, as demonstrated in extended Kalman filtering ${ }^{67}$. Drift reduction and orientation estimation become more challenging during highly dynamic movements or prolonged measurements ${ }^{67}$. Additionally, sensor orientation estimation often relies on extensive calibration procedures and multi-sensor setups. An alternative for Kalman filtering is to use domain-specific assumptions about the movement of interest to correct for drift in orientation estimation. A well-known example is the zero-velocity update method in walking ${ }^{68}$. The foot is assumed to be horizontal and to have zero velocity during the stance phase. This assumption allows for drift corrections in orientation estimation since the foot's orientation during the stance phase is known.

However, these assumptions are not necessarily fulfilled in running. The stance phase in running is short, and runners with a forefoot strike do not always reach a fully horizontal foot position during the stance phase. The difficulties in estimating foot orientations in running through existing domain-specific assumptions make it even harder to estimate orientations of more proximal segments, such as the tibia, as these do not have zero-velocity points. Since running is a quasi-cyclical motion, a new set of domain-specific assumptions based on quasi-cyclical motions can be created to estimate sensor orientation and displacement without many of the previously stated drawbacks.

## Research Question Chapter 5

Can the cyclical nature of running be used to acquire drift-free 3D orientation of a body segment using a single gyroscope?

## Research Question Chapter 6

How to estimate 3D orientation and displacement of a single IMU on the lower leg using the quasi-cyclical nature of running?

## General aims and outline of the thesis

This thesis aims to increase our understanding of running biomechanics as measured in and outside the laboratory and explore the challenges regarding wearable motion analysis during running in a sport-specific setting.

Based on this general aim, this thesis aims to answer the following research questions:
Chapter 2 How do running kinematics change due to running-induced fatigue?
Chapter 3 How to quantify and correct for the subject-specific effects of changes in running speed and stride frequency on impact-related running mechanics during a fatiguing outdoor run?

Chapter 4 What is the strength of the relationship between peak tibial acceleration and maximal tibial compression force in running?

Chapter 5 Can the cyclical nature of running be used to acquire drift-free 3D orientation of a body segment using a single gyroscope?

Chapter 6 How to estimate 3D orientation and displacement of a single IMU on the lower leg using the quasi-cyclical nature of running?

Finally, the results of the presented studies and possibilities for future research are discussed in Chapter 7.

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## Chapter 2

## Effects of level running-induced fatigue on running kinematics

A systematic review and meta-analysis

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#### Abstract

Background: Runners have a high risk of acquiring a running-related injury. Understanding the mechanisms of impact force attenuation into the body when a runner fatigues might give insight into the role of running kinematics on the aetiology of overuse injuries.

Research questions: How do running kinematics change due to running-induced fatigue? And what is the influence of experience level on changes in running kinematics due to fatigue?


Methods: Three electronic databases were searched: PubMed, Web of Science, and Scopus. This resulted in 33 articles and 19 kinematic quantities being included in this review. A quality assessment was performed on all included articles and meta-analyses were performed for 18 kinematic quantities.

Results and significance: Main findings included an increase in peak acceleration at the tibia and a decrease in leg stiffness after a fatiguing protocol. Additionally, level running-induced fatigue increased knee flexion at initial contact and maximum knee flexion during swing. An increase in vertical centre of mass displacement was found in novice but not in experienced runners with fatigue. Overall, runners changed their gait pattern due to fatigue by moving to a smoother gait pattern (i.e., more knee flexion at initial contact and during swing, decreased leg stiffness). However, these changes were not sufficient to prevent an increase in peak accelerations at the tibia after a fatigue protocol. Large inter-individual differences in responses to fatigue were reported. Hence, it is recommended to investigate changes in running kinematics as a result of fatigue on a subject-specific level since group-level analysis might mask individual responses.

## Introduction

Running is a popular sport worldwide. With up to $79 \%$ of runners acquiring a running-related injury in the lower extremity, runners are likely to get injured ${ }^{1}$. Most injuries are overuse related and assumed to be caused by training load errors (i.e., too fast and too far) and running kinematics ${ }^{2-4}$. During running, the body repetitively endures high-impact forces caused by the feet colliding with the ground. High impact forces on the body and changes in attenuation of these forces with fatigue are expected to result in overuse-related injuries such as tibial stress fractures ${ }^{5}$.

Understanding the mechanisms of impact force attenuation into the body when a runner fatigues might give insight into the role of running kinematics on the etiology of overuse injuries. Running kinematics largely influence peak impact forces during running ${ }^{6-9}$, possibly by modulating the stiffness of the lower body. Peak accelerations of body segments during running are mostly caused by impact forces and can be used as measures for loading on the body. Peak accelerations can quantify how well the body can attenuate impact forces ${ }^{10}$. A general idea is that higher peak accelerations due to fatigue indicate a higher load on the body and therefore increase the risk of overuse injuries, although this relationship needs further investigation ${ }^{11,12}$. Multiple studies showed an increase in peak accelerations and change in joint angles due to running-induced fatigue, although there is not yet a consensus about the exact effect of fatigue on peak accelerations and joint angles in running ${ }^{13-15}$.

The effect of fatigue on running kinematics was previously investigated in three literature reviews. Winter et al. ${ }^{16}$ summarized the effects of fatigue on kinematics and kinetics during overground running, while Kim et al. ${ }^{17}$ summarized the effects of fatigue on foot plantar pressure and associated kinematic quantities. Apte et al. ${ }^{18}$ investigated the effect of fatigue, the severity of fatigue, and the influence of running surfaces on a total of 42 quantities. From these literature reviews, it can be concluded that the maximal vertical ground reaction force ( $F_{z, \max }$ ) generally decreases after a fatigue protocol. Spatiotemporal changes with fatigue were dependent on the running surface, and plantar pressure measurements showed that the loading under the metatarsal area was increased after a fatigue protocol. Winter et al. ${ }^{16}$, Kim et al. ${ }^{17}$ and Apte et al. ${ }^{18}$ concluded that it was difficult to compare kinematic results from studies due to small numbers of studies investigating some quantities, differences in subject characteristics (i.e., experience level, familiarity with fatigue protocols, lack of information) and fatigue protocols (i.e., speed, duration, stopping criteria). All three of these literature
reviews do not give us insight into the amount of change in kinematic quantities to expect after a fatiguing protocol. Additionally, Apte et al. ${ }^{18}$ mentioned that combining results of runners with different skill levels might lead to confounding effects. Hence, there is a need for a systematic literature review in combination with meta-analyses on the effect of running-induced fatigue on running kinematics, which also takes subject characteristics into account.

The primary aim of this study was therefore to provide an overview of kinematic changes due to running-induced fatigue. The secondary aim was to investigate the influence of experience level on kinematic changes with fatigue.

Many quantities related to running biomechanics have been proposed in the literature. This review focussed on a selection of intertwined quantities related to peak accelerations and shock attenuation because of the assumed link with the development of running-related injuries ${ }^{11,12}$. Quantities included in this review were:

- Peak accelerations
- Shock attenuation
- Vertical and leg stiffness
- Vertical COM displacement $\left(\Delta C O M_{z}\right)$
- Lower body joint angles

It is hypothesized that fatigued runners adopt a stiffer gait pattern to save energy ${ }^{19}$, at the cost of higher impact forces on the body. A stiffer gait pattern would result in increased peak accelerations, decreased shock attenuation, decreased $\Delta C O M_{z}$ and decreased joint flexion angles. Experienced runners are hypothesized to show smaller changes in kinematics due to fatigue since they are more familiar with, and accustomed to, running-induced fatigue.

## Methods

## Search strategy

For this systematic review, three electronic databases were searched: PubMed, Web of Science, and Scopus. The search terms used can be found in Table 2.1, and the search strings can be found in Appendix 2.A. The first literature search was performed in May 2019 (without time constraints), the literature search was repeated in April 2020 (period: 2019-01-01 till 2020-12-31) to ensure no relevant new studies were missing.

## Selection criteria

Two researchers independently performed a screening of titles, abstracts, and full-text articles. Disagreements between researchers were solved in a consensus meeting with a third independent researcher when necessary. For a more homogeneous literature review, only studies investigating runners (i.e., people engaging in running-related activities) without injuries and continuously running on a relatively flat surface for a minimum of 3 km were included. A minimum distance of 3 km was chosen to impose a lower threshold for the fatigue protocol and to comply with the definition of long-distance running ${ }^{21}$. To exclude the effect of running speed on running kinematics, only studies in which the running speed during the pre-and post-fatigue measurement was controlled or intended to be similar were included. Exclusion criteria are provided in Table 2.2.

Table 2.1: Search terms

## Keywords for inclusion

(run OR running OR runner* OR marathon)
AND
(exhaust* OR exert* OR prolong* OR fatigue*)
AND
(kinemat* OR kinet* OR biomechanic* OR mechanic* OR acceler* OR centre of mass OR centre of mass OR center of gravity OR centre of gravity OR ground reaction OR angle OR angular OR force OR moment* OR impact OR shock OR inertia* OR pressure)

Table 2.2: Exclusion criteria

## Exclusion criteria

- Runners (i.e., people engaging in running-related activities) were not the main subject group
- Runners were injured shortly before or at the time of measurement (healthy control groups were included)
- The fatigue protocol did not satisfy all of the following conditions:
- Minimum distance covered of 3 km
- Continuous running (no interval training)
- Relatively flat surface (no uphill/downhill running, 1\% inclination on a treadmill was allowed)
- No imposed step frequency/strike pattern
- Speed during pre- and post-fatigue measurement was controlled/intended to be similar
- No quantities of interest were measured at two time points (pre- \& post-fatigue):

Exclude if simulations were performed based on a model about fatigue

- The aim of the study was the effect of footwear (including insoles) on the gait pattern
- No full-text article in English was available


## Quality assessment

To assess the quality of included studies, 13 out of the 27 questions from the Downs and Black quality assessment checklist ${ }^{20}$ were used, resulting in a maximal quality score of 14 , see Table 2.3. A description for all included questions and a justification for all excluded questions, and a change in scoring for one question are provided in Appendix 2.B. Quality labels based on the quality score were based on Hooper et al. ${ }^{22}$. A score between 0 and 7 points indicated a study of "Poor" quality, a score of 8 or 9 a study of "Fair" quality, a score of 10 till 12 a study of "Good" quality and a score of 13 or 14 a study of "Excellent" quality.

Table 2.3: Quality assessment items. Questions for the quality assessment were adapted from the Downs and Black quality assessment checklist ${ }^{20}$ and kept the original numbering (first column). A more extensive description of the quality assessment questions and all alterations to the original Downs and Black quality assessment checklist can be found in Appendix 2.B. UTD = unable to determine.

| Quality assessment items |  |  |
| :---: | :---: | :---: |
| \# | Question | Scoring |
| Q1 | Is the hypothesis/aim/objective of the study clearly described? | 0/1 |
| Q2 | Are the main outcomes to be measured clearly described in the Introduction or Methods section? | 0/1 |
| Q3 | Are the characteristics of the subjects included in the study clearly described? | 0/1 |
| Q4 | Is the fatigue protocol clearly described? | 0/1 |
| Q6 | Are the main findings of the study clearly described? | 0/1 |
| Q7 | Does the study provide estimates of the random variability in the data for the main outcomes? | 0/1 |
| Q10 | Have actual probability values been reported (e.g. 0.035 rather than $<0.05$ ) for the main outcomes except where the probability value is less than 0.001 ? | 0/1 |
| Q11 | Were the subjects asked to participate in the study representative of the entire population from which they were recruited? | 0/1/UTD |
| Q13 | Was the setting of the fatiguing protocol representative for a typical run? | 0/1/UTD |
| Q16 | If any of the results of the study were based on "data dredging", was this made clear? | 0/1/UTD |
| Q18 | Were the statistical tests used to assess the main outcomes appropriate? | 0/1/UTD |
| Q20 | Were the main outcome measures used accurate (valid and reliable)? | 0/1/UTD |
| Q27 | Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5\%? | 0/1/2/UTD |

## Quantities of interest

Quantities of interest for this review were related to peak accelerations and shock attenuation in running. To prevent general conclusions based on a small number of findings, only quantities that were investigated in a minimum of two studies were included.

- Peak accelerations: Maximum amplitude in the acceleration signal in the axial direction of a body segment (i.e., approximately upward in neutral standing).
- Peak tibial acceleration
- Peak sacral acceleration
- Peak head acceleration
- Shock attenuation: Percent reduction in peak acceleration between a distal and proximal location on the body (Equation 2.1).
- Shock attenuation between the tibia and head
- Shock attenuation between the tibia and sacrum

$$
\begin{equation*}
\text { shock attenuation }=\left(1-\frac{\text { Peak proximal acceleration }}{\text { Peak distal acceleration }}\right) * 100 \tag{2.1}
\end{equation*}
$$

- Vertical and leg stiffness: Ratio between the peak vertical ground reaction force ( $F_{z, \max }$ ) and a measure of compression of the lower body during the stance phase.
- Vertical stiffness $\left(K_{\text {vert }}\right)$ (Equation 2.2): Ratio between $F_{z, \max }$ and the maximum COM displacement in de stance phase $\left(\Delta C O M_{z, \text { stance }}\right)^{23}$
- Leg stiffness $\left(K_{l e g}\right)$ (Equation 2.3): Ratio between $F_{z, \max }$ and the maximum estimated leg compression in the stance phase $\left(\Delta L_{\text {stance }}\right)^{24}$

$$
\begin{align*}
K_{v e r t} & =\frac{F_{z, \max }}{\Delta C O M_{z, \text { stance }}}  \tag{2.2}\\
K_{\text {leg }} & =\frac{F_{z, \text { max }}}{\Delta L_{\text {stance }}} \tag{2.3}
\end{align*}
$$

- Vertical COM displacement $\left(\Delta C O M_{z}\right)$ : Maximal vertical COM displacement during either the stance phase or full gait cycle.
- Lower body joint angles: Sagittal plane joint angles of the lower body. Joint angles in the transversal and frontal plane were excluded because their range of motion (ROM) in running is small, while they have a relatively large measurement error ${ }^{25}$.
- Ankle dorsi-/plantarflexion angle
- Knee flexion/extension angle
- Hip flexion/extension angle


## Data extraction

For all quantities of interest, initial (i.e., unfatigued) and final (i.e., fatigued) values were extracted. Obtained data were converted to the same units and recalculated to describe joint angles similarly. When absolute values were not provided, these were estimated from figures using WebPlot Digitizer (Web Plot Digitizer, version 4.5, USA) by two researchers; differences were solved in a consensus meeting. When a study was described in multiple articles, results of the study were included once, although methodological information was extracted from all articles. If two out of three quantities of speed, distance, and time were provided, the third was computed. Additional information about subject characteristics, fatigue protocols, rate of perceived exertion (RPE) ${ }^{26}$, measurement systems, and data analyses were extracted from all included articles.

## Data analysis

To investigate the effect of fatigue on kinematic quantities, multiple meta-analyses were performed. When absolute initial and final values or the mean difference (MD) for a quantity were provided for two or more studies, a random-effects meta-analysis was performed using the Metafor statistical package in R software (version 4.2.0, R Foundation for Statistical Computing). MDs (fatigued versus unfatigued) were weighted based on their inverse variance. $95 \%$ Confidence intervals (CI) of MDs were computed based on p-values when provided. Otherwise, the standard deviation (SD) of the fatigued measurement was used as the SD of the MD ${ }^{27,28}$. P -values provided as " $\mathrm{p}<0.05$ " or similar were assumed to be equal to the right-hand operand of the inequality sign. $P$-values provided as " $p>0.05$ " were treated as if no $p$-value was provided. In the case of repeated measures analysis of variance, only $p$-values from post hoc tests between the first and last stage of running, and not from main effects, were used to calculate Cl . When a study provided data for multiple independent subgroups, both groups were included for analysis. In the case of dependent subgroups (same runners on different undergrounds ${ }^{29}$ or data from both legs ${ }^{30}$ ), the subgroup most similar to the conditions of all other studies was included for analysis. The percentage variation in estimated
pooled effects due to differences between studies rather than chance (i.e., heterogeneity) was estimated using $I^{2}$ ( $I^{2}<25$ was considered small, $I^{2}=25-49 \%$ as moderate and $I^{2} \geq$ $50 \%$ as high $)^{31}$. High heterogeneity is an indication that the results of studies are inconsistent, for instance, due to differences in the fatigue protocol or subject characteristics. Statistical significance was defined as $p<0.05$.

## Results

An overview of the literature search process is shown in Figure 2.1. Details about the subject characteristics, fatigue protocols, measurement systems, and data analyses can be found in Table 2.4. The mean quality assessment score was 10 (SD: 1 , range: $6-12$ ) out of 14 , indicating an overall good quality. Heterogeneity was high for most kinematic quantities, indicating that the variation in results between studies is larger than expected by chance ${ }^{31}$. All quality assessment scores can be found in Table 2.5. Results for all included quantities are presented in Table 2.6 and Table 2.7, where single values between parentheses represent SDs ${ }^{32-58}$.

Table 2.4: Study characteristics for all included studies. "Measure" and "Fatigue" refer to a different setting or speed for the measurement and the fatigue protocol. An asterisk $\left(^{*}\right.$ ) indicates that results were not included for meta-analyses. NP = not provided; $M=$ male; $F=$ female; nov = novice runners; com = competitive runners; rec = recreational runners; PTA = peak tibial acceleration; PSA = peak sacral acceleration; PHA = peak head acceleration; COM = centre of mass; FCA = foot contact angle; IMU = inertial measurement unit; uni = unilateral; bil = bilateral; IC = initial contact; MS = midstance; TO = toe-off; cal. = calibration only; IQR = inter quartile range; $H R=$ heart rate; HRmax = maximum $H R ; V O 2$ max = maximum rate of oxygen consumption; VVO2max = running speed at VO2max; VO2peak = surrogate of VO2max measured during a submaximal exercise; PETCO2 = end tidal carbon dioxide pressure; RPE = rate of perceived exertion.

| 1/7 | Abt et al. ${ }^{32}$ | Avogadro et al. ${ }^{33}$ | Bazett-Jones et al. ${ }^{34}$ | Bigelow et al. ${ }^{35}$ |
| :---: | :---: | :---: | :---: | :---: |
| Subject information |  |  |  |  |
| Subject population | Competitive distance runners | Runners or triathletes | Runners or doing running-related activities | Physically active subjects |
| Subjects (sex), Age (years), Height (cm), Weight (kg) | $\begin{aligned} & 12(M+F), 25(4), 174(9), 65 \\ & (10) \end{aligned}$ | 10 (M), 22 (2), 178 (5), 68 (4) | $\begin{aligned} & 19 \text { (10M+9F), } 24 \text { (4), } 174 \text { (9), } \\ & 70 \text { (11) } \end{aligned}$ | 12, 33 (10), 167 (9), 60 (5) |
| Training information | Min 3 years, Min 48 km/week, Min 10.7 km/h, No injuries last 3 months | VO2max $=69$ ( 8 ) $\mathrm{ml} / \mathrm{kg} / \mathrm{min}$, VVO2max $=18.2 \mathrm{~km} / \mathrm{h}$ | Min 10 (8) hours/week, No injuries last 6 months | Min 6 weeks, Min 3 hours/ week, <br> Never had an injury |
| Fatigue protocol |  |  |  |  |
| Duration protocol | 17.8 (5.7) min | 13.8 (2.8) min | 36.3 (22.7) min |  |
| Measure of fatigue |  | Lactate + respiratory data | RPE : 16.6 (1.3) |  |
| Other information |  |  | RPE matched to patient group |  |


| 1/7 | Abt et al. ${ }^{32}$ | Avogadro et al. ${ }^{33}$ | Bazett-Jones et al. ${ }^{34}$ | Bigelow et al. ${ }^{35}$ |
| :---: | :---: | :---: | :---: | :---: |
| Measurement system |  |  |  |  |
| Specifications: marker model, sampling frequency, location, axes, operating range, weight | Optical: Plug-in Gait, 120 Hz IMU: forehead, proximal tibia, 3D, $1200 \mathrm{~Hz}, 25 \mathrm{~g}, 21 \mathrm{gram}$ | Other: treadmill with 3D forceplate, 1000 Hz | Optical: cluster + anatomical (cal.), 200 Hz | IMU: sacrum, 3D, 1000 Hz , $18 \mathrm{~g}, 55$ gram |
| Data analysis |  |  |  |  |
| When was data collected | During fatigue protocol: <br> First and last minute | During fatigue protocol: Minute 3 and last minute | Separate trials: <br> Before and after fatiguing run | During fatigue protocol: <br> Continuous |
| Amount of data analysed | $2 \times 5$ seconds | $2 \times 20$ seconds | $2 \times 5$ strides | $16 \times 400$ meter |
| Uni-/bilateral data | Uni: dominant leg | Bil: data combined | Uni: matched to patient group | NA |
| Filtering of data | Markers: low-pass 16 Hz |  | low-pass 12 Hz |  |
| Quantities |  |  |  |  |
| Peak accelerations | PTA, PHA |  |  | PSA |
| Shock attenuation | PTA/PHA |  |  |  |
| Stiffness (vertical/leg) |  | Leg stiffness* |  |  |
| Vertical COM displacement |  |  |  |  |
| Ankle angles |  |  |  |  |
| Knee angles | max flexion stance |  | max flexion stance |  |
| Hip angles |  |  | max flexion |  |
| Quality assessment | 11-Good | 8- Fair | 11-Good | 10-Good |


| 2/7 | Clansey et al. ${ }^{5}$ | Derrick et al. ${ }^{13}$ | Dierks et al. ${ }^{36,37}$ | Dutto and Smith ${ }^{38}$ |
| :---: | :---: | :---: | :---: | :---: |
| Subject information |  |  |  |  |
| Subject population | Highly trained distance runners | Recreational runners | Recreational runners | Well-trained runners |
| Subjects (sex), Age (years), Height (cm), Weight (kg) | 21 (M), 36 (13), 180 (8), 75 (12) | 10, 26 (7), NP, 71 (10) | $\begin{aligned} & 20 \text { ( } 5 M+15 F), 23(6), 170(10) \text {, } \\ & 63 \text { (9) } \end{aligned}$ | 15 (11M+4F), 28 (7), NP, 68 (11) |
| Training information | 72 (37) km/week, Free of injuries now | Free of injuries now | 25 (10) km/week, <br> Free of injuries now | Min $40 \mathrm{~km} /$ week |
| Fatigue protocol |  |  |  |  |
| Speed based on | 3.5 mM blood lactate concentration | 3.2 km time trial | Self-selected (typical traning pace) | 80\% VO2peak |
| Speed | Measure: relatively constant at $16.2(0.8) \mathrm{km} / \mathrm{h}$, Fatigue: constant at 13.8 (2.1) km/h | Constant at 12.2 (1.4) km/h | Constant at 9.5 (1.3) km/h | Constant at 14.5 (1.3) km/h |
| Setting | Measure: overground Fatigue: treadmill | Treadmill | Treadmill | Treadmill |
| Stopping criteria | Time | Feeling: unable to continue | Feeling: RPE $=17$ or $H R:>85 \%$ of HRmax | Feeling: unable to continue |
| Distance covered | 9.2 km | 3.2 km | 7.1 km | 13.8 km |
| Duration protocol | 40 min | 15.7 min | 45 (12) min | 57 (19) min |
| Measure of fatigue | RPE: 17.4 (1.5) |  | RPE: >15 |  |
| Other information | Treadmill with 1\% inclination |  | Stopped due to: $R P E=14, H R=6$ |  |


| 2/7 | Clansey et al. ${ }^{5}$ | Derrick et al. ${ }^{13}$ | Dierks et al. ${ }^{36,37}$ | Dutto and Smith ${ }^{38}$ |
| :---: | :---: | :---: | :---: | :---: |
| Measurement system |  |  |  |  |
| Specifications: marker model, sampling frequency, location, axes, operating range, weight | Optical: cluster + anatomical (cal.), 200 Hz IMU: forehead, distal tibia, 2D, $1500 \mathrm{~Hz}, 16 \mathrm{~g}$ | IMU: forehead, distal tibia, 1D, $1000 \mathrm{~Hz}, 1.8$ gram Other: electrogoniometer, 1000 Hz | Optical: cluster + anatomical (cal.), 120 Hz IMU: distal tibia, 1D, 1080 Hz | Other: treadmill with 3D forceplate, 1000 Hz |
| Data analysis |  |  |  |  |
| When was data collected | Separate trials: Before, middle, after | During fatigue protocol: First, middle and last minute | During fatigue protocol: First and last minute | During fatigue protocol: <br> 0, 25, 50, $75,100 \%$ of duration |
| Amount of data analysed | $3 \times 6$ strides | $3 \times 16$ seconds | $2 \times 20$ strides | $5 \times 35-40$ steps |
| Uni-/bilateral data |  | Uni: right leg | Uni: random | Bil: combined |
| Filtering of data | PHA/PTA: low-pass $30 / 60 \mathrm{~Hz}$ Markers: low-pass 12 Hz | Markers: low-pass 18 Hz | IMU: low-pass 75 Hz <br> Markers: low-pass 8 Hz |  |
| Quantities |  |  |  |  |
| Peak accelerations | PTA, PHA | PTA, PHA | PTA |  |
| Shock attenuation |  | PTA/PHA |  |  |
| Stiffness (vertical/leg) |  |  |  | vertical \& leg stiffness |
| Vertical COM displacement |  |  |  |  |
| Ankle angles | IC |  |  |  |
| Knee angles | IC + max flexion stance | IC + max flexion stance | max flexion stance |  |
| Hip angles | IC + MS |  |  |  |

[^0]| 3/7 | Fuhr et al. ${ }^{39}$ | García-Pérez et al. ${ }^{29}$ | García-Pinillos et al. ${ }^{40}$ | Hanley and Mohan ${ }^{41}$ |
| :---: | :---: | :---: | :---: | :---: |
| Subject information |  |  |  |  |
| Subject population | Runners | Recreational runners | Trained endurance runners | Competitive distance runners |
| Subjects (sex), Age (years), Height (cm), Weight (kg) | $9(F), 32(4), 167$ (7), 58 (7) | $\begin{aligned} & 20 \text { (11M+9F), } 34 \text { (8), } 172 \text { (8), } \\ & 64 \text { (8) } \end{aligned}$ | 22 (M), 34 (8), 176 (4), 71 (6) | 15 (M), 32 (7), 178 (7), 65 (7) |
| Training information | Min 3 years, 10 km : 35-48 min, Free of injuries now | 10 (6) years, 50 (18) km/week, 4 (1) days/week, Stated to be healthy | $10 \mathrm{~km}: 37$ (1) min, No injuries last 6 months | $10 \mathrm{~km}: 30-35 \mathrm{~min}$, Free of injuries now |
| Fatigue protocol |  |  |  |  |
| Speed based on | 95\% of 10 km time trial | 85\% of 5 min time trial speed | Self-selected ( 60 min time trial) | 103\% of 10 km race |
| Speed | Constant at $13.2 \mathrm{~km} / \mathrm{h}$ | Measure: constant at 14.4 $\mathrm{km} / \mathrm{h}$, Fatigue: constant at 13.7 (1.4) km/h | Measure: constant at 12.0 $\mathrm{km} / \mathrm{h}$, Fatigue: Variable around 15.1 ( 0.6 ) km/h | Constant at 17.5 (0.6) km/h |
| Setting | Treadmill | Treadmill | Treadmill | Treadmill |
| Stopping criteria | Feeling: unable to continue | Time | Time | Distance |
| Distance covered | 10 km | 6.9 km | 15.1 km | 10 km |
| Duration protocol | 45.3 min | 30 min | 60 min | 34.3 min |
| Measure of fatigue | RPE: 19 (1) |  | RPE: 19.3 (0.9) | RPE: start 11 (1), end: 18 (3) |
| Other information |  | All rearfoot strikers |  | 11 rearfoot strikers +4 midfoot strikers |


| 3/7 | Fuhr et al. ${ }^{39}$ | García-Pérez et al. ${ }^{29}$ | García-Pinillos et al. ${ }^{40}$ | Hanley and Mohan ${ }^{41}$ |
| :---: | :---: | :---: | :---: | :---: |
| Measurement system |  |  |  |  |
| Specifications: marker model, sampling frequency, location, axes, operating range, weight | Optical: cluster + anatomical (cal.), 120 Hz | IMU: forehead, proximal tibia, 1D, $100 \mathrm{~Hz}, 55 \mathrm{~g}$ | Optical: OptoGait (for spatiotemporal parameters), 1000 Hz | Other: high speed camera, $250 \mathrm{~Hz}$ |
| Data analysis |  |  |  |  |
| When was data collected | During fatigue protocol: Every 1500 m | Separate trials: Before and after | Separate trials: Before and after | During fatigue protocol: 1.5 and 9.5 km |
| Amount of data analysed | $8 \times 5$ strides | $2 \times 3$ strides | $2 \times 3$ minutes | $2 \times 30$ seconds |
| Uni-/bilateral data |  | Uni: right leg | Bil: combined | Bil: combined |
| Filtering of data |  |  |  | low-pass 10 Hz |
| Quantities |  |  |  |  |
| Peak accelerations |  | PTA, PHA |  |  |
| Shock attenuation |  | PTA/PHA |  |  |
| Stiffness (vertical/leg) |  |  | vertical \& leg stiffness |  |
| Vertical COM displacement |  |  |  |  |
| Ankle angles |  |  |  | IC + TO |
| Knee angles | max flexion + max extension |  |  | IC |
| Hip angles | max flexion |  |  | IC + TO |
| Quality assessment | 10-Good | 9- Fair | 9- Fair | 11-Good |


| 4/7 | Jewell et al. ${ }^{42}$ | Koblbauer et al. ${ }^{30}$ | Lucas-Cuevas et al. ${ }^{14}$ | Maas et al. ${ }^{43}$ |
| :---: | :---: | :---: | :---: | :---: |
| Subject information |  |  |  |  |
| Subject population | Recreational active runners | Novice runners | Recreational runners | Competitive (com) and novice (nov) runners |
| Subjects (sex), Age (years), Height (cm), Weight (kg) | $\begin{aligned} & 14 \text { (8M+6F), } 27 \text { (9), } 173 \text { (10), } \\ & 68 \text { (8) } \end{aligned}$ | $\begin{aligned} & 17 \text { (7M+10F), } 26 \text { (3), } 172 \text { (10), } \\ & 67 \text { (11) } \end{aligned}$ | $\begin{aligned} & 40(20 M+20 F), 28(6), 173(10), \\ & 68(10) \end{aligned}$ | ```30 (com:10M+5F, nov:9M+6F), com: }22\mathrm{ (4), nov: 21 (1), com: }179\mathrm{ (8), nov: }177\mathrm{ (8), com: }64\mathrm{ (6), nov: 69 (6)``` |
| Training information | 50 (25) km/week, No injuries last year | Max 10 km/run, Max 2-3 runs/week | 27 (4) km/week, <br> No injuries last year, No surgery last 3 years | com: 10 (3) years, com: 77 (17) km/week, nov: max 10 km/ week, nov: able to do a 3.2 km run, No injuries last 6 months |
| Fatigue protocol |  |  |  |  |
| Speed based on | Self-selected <br> (able to run 15 but not 20 min ) | RPE 13 | $80 \%$ of 5 min time trial | 3.2 km time trial |
| Speed | Constant at 14.0 (2.2) km/h | Constant at 9.4 (5.8) km/h | Constant at 12.6 (1.1) km/h | Constant, com: measure: 12.0 $\mathrm{km} / \mathrm{h}$, fatigue: 17.6 (2.1) km/h, nov: measure: 9.9 (1.8) km/h, fatigue: 9.9 (1.8) km/h |
| Setting | Treadmill | Treadmill | Treadmill | Treadmill |
| Stopping criteria | Feeling: unable to continue | Feeling: RPE = 17 or HR: >90\% of HRmax | Time | Feeling: unable to continue |
| Distance covered | 3.6 km | 3.1 km | 6.3 km | com: 4.6 km , nov: 4.7 km |
| Duration protocol | 15.4 (2.2) min | 19.7 (7.8) min | 30 min | com: 15.8 (4.7) min nov: 28.2 (9.8) min |
| Measure of fatigue | RPE: 18-19 |  | RPE: 17.1 (0.6) | RPE: $\min 17$ |
| Other information | Forefoot strikers |  | Placebo group included |  |


| 4/7 | Jewell et al. ${ }^{42}$ | Koblbauer et al. ${ }^{30}$ | Lucas-Cuevas et al. ${ }^{14}$ | Maas et al. ${ }^{43}$ |
| :---: | :---: | :---: | :---: | :---: |
| Measurement system |  |  |  |  |
| Specifications: marker model, sampling frequency, location, axes, operating range, weight | Optical: cluster + anatomical + foot model, 200 Hz | Optical: cluster + anatomical probing, 100 Hz | IMU: forehead, proximal tibia, 3D, $500 \mathrm{~Hz}, 2.5$ gram | $\begin{aligned} & \text { Optical: cluster + anatomical, } \\ & 150 \mathrm{~Hz} \end{aligned}$ |
| Data analysis |  |  |  |  |
| When was data collected | During fatigue protocol: First and last minute | During fatigue protocol: First and last minute | During fatigue protocol: Every 5th minute | During fatigue protocol: Second and last minute |
| Amount of data analysed | $2 \times 5$ strides | 20 strides | $7 \times 15$ seconds | $2 \times 10$ seconds |
| Uni-/bilateral data | Uni: right leg | Bil | Uni:- | Bil: independent legs |
| Filtering of data | low-pass 12 Hz | low-pass 15 Hz | low-pass 50 Hz | low-pass 15 Hz |
| Quantities |  |  |  |  |
| Peak accelerations |  |  | PTA, PHA |  |
| Shock attenuation |  |  | PTA/PHA |  |
| Stiffness (vertical/leg) |  |  |  |  |
| Vertical COM displacement |  |  |  |  |
| Ankle angles | IC + TO + max dorsiflexion | max dorsiflexion |  | max dorsiflexion |
| Knee angles | IC + max flexion stance + max extension | max flexion + max extension |  | max flexion stance |
| Hip angles |  | max flexion |  |  |


| 5/7 | Mizrahi et al. ${ }^{15,44,45,46}$ | Murray et al. ${ }^{47}$ | Nicol et al. ${ }^{48}$ | Paquette et al. ${ }^{49}$ |
| :---: | :---: | :---: | :---: | :---: |
| Subject information |  |  |  |  |
| Subject population | Recreational runners | Recreational competitive runners | Experienced endurance runners | Runners |
| Subjects (sex), Age (years), Height (cm), Weight (kg) | 14 (M), 24 (4), 176 (6), 73 (8) | $\begin{aligned} & 24(15 \mathrm{M}+9 \mathrm{~F}), 36.5(11.2), \\ & 172 \text { (9), } 73.6 \text { (12.5) } \end{aligned}$ | $\begin{aligned} & 8 \text { (7M+1F), 30, } 177 \text { (168-190), } \\ & 68 \text { (59-93) } \end{aligned}$ | $\begin{aligned} & 21 \text { (14M+7F), } 32 \text { (8), } 176 \text { (11), } \\ & 70 \text { (11) } \end{aligned}$ |
| Training information | Min 3 months, 8-10 km/week, Min 2 days/week, Around 12 km/h, Never had an injury | 5 years (IQR:1-10), 3 runs/week (IQR: 3-5), Goal: 12 km < 75 min, Free of injuries now |  | 12 (6) years, 56 (21) km/week, No injuries last year |
| Fatigue protocol |  |  |  |  |
| Speed based on | 105\% of anaerobic threshold | Race pace 12 km | Training status + last performance | $75 \%$ of 10 km personal best |
| Speed | Constant at 12.7 (0.7) km/h | Measure: relatively constant at 15.3 (2.0) km/h, Fatigue: variable around $11.8 \mathrm{~km} / \mathrm{h}$ | Measure: constant at 14.4 $\mathrm{km} / \mathrm{h}$, Fatigue: relatively constant at $13.9 \mathrm{~km} / \mathrm{h}$ | Constant at $10.8 \mathrm{~km} / \mathrm{h}$ |
| Setting | Treadmill | Outdoor race | Measure: treadmill Fatigue: outdoor | Treadmill |
| Stopping criteria | Time | Distance | Distance | Time |
| Distance covered | 6.4 km | 12 km | 42.2 km | 7.2 km |
| Duration protocol | 30 min | 61 (8) min | 3.0 hours | 40 min |
| Measure of fatigue | Decrease in PETCO2 | RPE: median: 17, IQR: 15-18 |  |  |
| Other information |  | All rearfoot strikers |  | Rearfoot and non-rearfoot strikers |


| 5/7 | Mizrahi et al. ${ }^{15,44,45,46}$ | Murray et al. ${ }^{47}$ | Nicol et al. ${ }^{48}$ | Paquette et al. ${ }^{49}$ |
| :---: | :---: | :---: | :---: | :---: |
| Measurement system |  |  |  |  |
| Specifications: marker model, sampling frequency, location, axes, operating range, weight | IMU: sacrum, proximal tibia, 1D, $1667 \mathrm{~Hz}, 4.2$ gram Other: video camera, 50 Hz | Other: camera, 240 Hz | Other: Video camera, 100 Hz, electric goniometer | Optical: cluster + anatomical, $240 \mathrm{~Hz}$ |
| Data analysis |  |  |  |  |
| When was data collected | During fatigue protocol: Every 5th km | Separate trials: Before and after | Separate trials: Before and after | During fatigue protocol: Every 10 minutes |
| Amount of data analysed | $7 \times 20$ seconds | $2 \times 3$ strides | $2 \times 1$ stride | $4 \times 5$ steps |
| Uni-/bilateral data | Uni: right leg | Uni: right leg | Uni: left leg | Uni: right leg |
| Filtering of data | Markers: low-pass 40 Hz |  |  | low-pass 8 Hz |
| Quantities |  |  |  |  |
| Peak accelerations | PTA, PSA |  |  |  |
| Shock attenuation | PTA/PSA |  |  |  |
| Stiffness (vertical/leg) |  |  |  |  |
| Vertical COM displacement | $X^{*}$ |  | X* |  |
| Ankle angles |  | FCA | IC* + TO* | FCA |
| Knee angles | IC + max flexion stance* + max extension |  | IC |  |
| Hip angles |  |  | IC* |  |
| Quality assessment | 9- Fair | 12-Good | 9- Fair | 11-Good |


| 6/7 | Paquette and Melcher ${ }^{50}$ | Rabita et al. ${ }^{51}$ | Reenalda et al. ${ }^{52}$ | Sanno et al. ${ }^{53}$ |
| :---: | :---: | :---: | :---: | :---: |
| Subject information |  |  |  |  |
| Subject population | Trained runners | Elite triathletes | Well-trained runners | Recreational (rec) and competitive (com) long distance runners |
| Subjects (sex), Age (years), Height (cm), Weight (kg) | 12 (M), 33 (10), 180 (8), 74 (12) | $\begin{aligned} & 9(6 M+3 F), \text { M: } 23(3), \text { F: } 25(4), \\ & \text { M: } 182(2), \text { F: } 167(4), \\ & \text { M: } 68(5), \text { F: } 58 \text { (3) } \end{aligned}$ | 10 (M), 31 (5), 183 (3), 76 (9) | $\begin{aligned} & 25 \text { (rec: } 13 \mathrm{M} \text { + com: 12M), } \\ & \text { rec: } 24(3) \text {, com: } 25(4), \\ & \text { rec: } 184(5), \text { com: } 182(6) \text {, } \\ & \text { rec: } 81(7) \text {, com: } 73(8) \end{aligned}$ |
| Training information | 9 (5) years, 77 (21) km/week, Long run: 19 (5) km, Free of injuries now | $\begin{aligned} & 55-75 \mathrm{~km} / \text { week, } \\ & \text { VO2 } \mathrm{max}=72(7) \mathrm{ml} / \mathrm{min} / \mathrm{kg} \text {, } \\ & \text { VVO } 2 \mathrm{max}=18 \mathrm{~km} / \mathrm{h} \end{aligned}$ | Min 40 km/week, No injuries last 6 months | 10 km : rec: >47.5 min, 10 km : com: < 37.5 min |
| Fatigue protocol |  |  |  |  |
| Speed based on | Self-selected at long run pace | 95\% VVO2max | 96\% of 10 km personal best | 105\% of season's best 10 km |
| Speed | Measure: relatively constant at 12.2 km/h <br> Fatigue: constant at $12.2 \mathrm{~km} / \mathrm{h}$ | Relatively constant at $18.3 \mathrm{~km} / \mathrm{h}$ | Relatively constant at 15.8 (1.4) km/h | rec: constant at $11.5 \mathrm{~km} / \mathrm{h}$, com: constant at $15.8 \mathrm{~km} / \mathrm{h}$ |
| Setting | Measure: overground Fatigue: treadmill | Indoor synthetic track | Outdoor track | Treadmill |
| Stopping criteria | Distance | Feeling: unable to continue | Time | Distance |
| Distance covered | 19.2 km | 3.3 (0.8) km | 5.3 km | 10 km |
| Duration protocol | 94.2 min | 10.7 (2.6) min | 20 min | rec: 52.8 (2.4) min com: 37.5 (1.3) min |
| Measure of fatigue |  |  |  | RPE: rec: 16.9 (1.3) com: 17.1 (1.2) |
| Other information | Rearfoot strikers |  |  |  |


| 6/7 | Paquette and Melcher ${ }^{50}$ | Rabita et al. ${ }^{51}$ | Reenalda et al. ${ }^{52}$ | Sanno et al. ${ }^{53}$ |
| :---: | :---: | :---: | :---: | :---: |
| Measurement system |  |  |  |  |
| Specifications: marker model, sampling frequency, location, axes, operating range, weight | Optical: cluster + anatomical (cal.), 240 Hz | Other: force platform, 500 Hz | IMU: sacrum, proximal tibia, 3D, $100 \mathrm{~Hz}, 18$ g, 30 gram | Optical: anatomical, 250 Hz |
| Data analysis |  |  |  |  |
| When was data collected | Separate trials: Before and after | During fatigue protocol: $10,33,67,100 \%$ of total time | During fatigue protocol: Minute 3 and 18 | During fatigue protocol: $0.2 \mathrm{~km}, 0.5 \mathrm{~km}$, and every km |
| Amount of data analysed | $2 \times 5$ stance phases | $4 \times 4-6$ steps | $2 \times 20$ strides | $13 \times 20$ stance phases |
| Uni-/bilateral data | Uni: right leg | Bil: combined | Uni: right leg | Uni: right leg |
| Filtering of data | low-pass 8 Hz |  |  | low-pass 20 Hz |


| Quantities |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
| Peak accelerations |  |  | PTA, PSA |  |
| Shock attenuation |  |  | PTA/PSA |  |
| Stiffness (vertical/leg) |  | vertical \& leg stiffness |  |  |
| Vertical COM displacement |  | $X^{*}$ |  | $X^{*}$ |
| Ankle angles |  |  |  | IC + TO + max dorsiflexion |
| Knee angles | max flexion stance |  | IC + max flexion stance | IC + max flexion stance |
| Hip angles |  |  | $I C+M S$ | MS |
| Quality assessment | 11-Good | 11-Good | 9- Fair | 9- Fair |


| 7/7 | Schütte et al. ${ }^{54}$ | Siler and Martin ${ }^{55}$ | Strohrmann et al. ${ }^{56}$ | Voloshin et al. ${ }^{57}$, Verbitsky et al. ${ }^{58}$ |
| :---: | :---: | :---: | :---: | :---: |
| Subject information |  |  |  |  |
| Subject population | Novice to experienced runners | Regularly training runners (split into fast and slow runners) | Runners of different skill levels | Non-professional runners |
| Subjects (sex), Age (years), Height (cm), Weight (kg) | 20 (12+8F), 21 (2), 177 (8), 66 (6) | 19 (M), fast: 29 (4), slow: 30 (5), fast: 174 (6), slow: 176 (8), fast: 67 (5), slow: 74 (9) | 21, NP, NP, NP | 22 (M), 31 (5), 174 (7), 70 (9) |
| Training information | 48 (36) km/week, No injuries last 6 months | fast: 5 (2), slow: 4 (3) years, fast: 73 (21), slow: 32 (16) km/week, 10 km : fast<36, slow>40 min, Free of injuries now | 0-45 km/wk | Min 2 days/week, Never had an injury |
| Fatigue protocol |  |  |  |  |
| Speed based on | 3.2 km time trial | fast: 87\% of VVO2max, slow: 81\% of VVO2max | 85\% of 1 min max speed | Anaerobic threshold |
| Speed | Measure: constant at max 12.0 $\mathrm{km} / \mathrm{h}$, Fatigue: constant at 14.0 (4.5) km/h | fast: constant at $17.0(0.9) \mathrm{km} / \mathrm{h}$, slow: constant at $13.0(0.4) \mathrm{km} / \mathrm{h}$ | Constant, Beginner: 9-10.5 <br> km/h, Intermediate: 10.5-12 <br> $\mathrm{km} / \mathrm{h}$, Advanced: 12-14.5 <br> km/h, Expert: $14.5-17.8 \mathrm{~km} / \mathrm{h}$ | Fatigued: constant at 9.9 (1.0) $\mathrm{km} / \mathrm{h}$, Unfatigued: constant at 9.9 (1.7) km/h |
| Setting | Treadmill | Treadmill | Treadmill | Treadmill |
| Stopping criteria | Feeling: unable to continue or RPE $=17$ | Feeling: unable to continue | Time | Time |
| Distance covered | 4.8 km | fast: 8.4 km , slow: 9.6 km | $6.8-13.4 \mathrm{~km}$ | 5.0 km |
| Duration protocol | 20.5 (6.9) min | fast: 29.5 (5.8) min, slow: 44.2 (7.6) min | 45 min | 30 min |
| Measure of fatigue | RPE: >17 | RPE: fast: 18.9 (0.3), slow: 19.2 (0.4) |  | PETCO2 |
| Other information |  |  |  | Split in fatigued and unfatigued group based on PETCO2 |


| 7/7 | Schütte et al. ${ }^{54}$ | Siler and Martin ${ }^{55}$ | Strohrmann et al. ${ }^{56}$ | Voloshin et al. ${ }^{57}$, Verbitsky et al. ${ }^{58}$ |
| :---: | :---: | :---: | :---: | :---: |
| Measurement system |  |  |  |  |
| Specifications: marker model, sampling frequency, location, axes, operating range, weight | Optical: anatomical, 150 Hz | Optical: anatomical, 100 Hz | IMU: sacrum, 3D, $100 \mathrm{~Hz}, 6 \mathrm{~g}$, 22 gram | IMU: sacrum, proximal tibia, 1D, 1667 Hz, 2.3 gram |
| Data analysis |  |  |  |  |
| When was data collected | Varied: <br> First and last minute | During fatigue protocol: Minute 5 and every $10 \%$ of total time | During fatigue protocol | During fatigue protocol: Every 5th minute |
| Amount of data analysed | $2 \times 20$ steps | $10 \times 2$ strides | 2 measurement points | $7 \times 20$ seconds |
| Uni-/bilateral data | NA | Uni: left leg | NA | Uni: right leg |
| Filtering of data | low-pass 15 Hz | low-pass $5.5-7.5 \mathrm{~Hz}$ <br> (different for each marker) |  |  |



Table 2.5: Quality assessment scores for all included articles. A more extensive description of the questions can be found in Table 2.3 and Appendix 2.B. UTD = Unable to determine.

|  | Reporting |  |  |  |  |  |  | Validity |  |  |  |  | $\begin{aligned} & \text { 20 } \\ & 3_{0}^{0} \end{aligned}$ |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  |  |  | External |  | Internal |  |  |  |  |  |
|  | $\begin{aligned} & \underset{i}{E} \\ & i \end{aligned}$ |  | 3. Subject characteristics |  |  |  |  | 11. Subjects representative | 13. Protocol representative |  | 18. Appropriate statistics |  |  |  | $\begin{aligned} & \frac{\lambda}{2} \\ & \frac{\pi}{0} \\ & 0 \end{aligned}$ |
| Abt et al. ${ }^{32}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 11 | Good |
| Avogadro et al. ${ }^{33}$ | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | UTD | 8 | Fair |
| Bazett-Jones et al. ${ }^{34}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | UTD | 11 | Good |
| Bigelow et al. ${ }^{35}$ | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | UTD | 10 | Good |
| Clansey et al. ${ }^{5}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | UTD | 10 | Good |
| Derrick et al. ${ }^{13}$ | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | UTD | 9 | Fair |
| Dierks et al. ${ }^{36,37}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 10 | Good |
| Dutto and Smith ${ }^{38}$ | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | UTD | 8 | Fair |
| Fuhr et al. ${ }^{39}$ | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | UTD | 10 | Good |
| García-Pérez et al. ${ }^{29}$ | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | UTD | 9 | Fair |
| García-Pinillos et al. ${ }^{40}$ | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | UTD | 9 | Fair |
| Hanley and Mohan ${ }^{41}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | UTD | 11 | Good |
| Jewell et al. ${ }^{42}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 11 | Good |
| Koblbauer et al. ${ }^{30}$ | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | UTD | 10 | Good |
| Lucas-Cuevas et al. ${ }^{14}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | UTD | 10 | Good |
| Maas et al. ${ }^{43}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 2 | 12 | Good |
| Mizrahi et al. ${ }^{15,44,45,46}$ | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | UTD | 9 | Fair |
| Murray et al. ${ }^{47}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | UTD | 12 | Good |
| Nicol et al. ${ }^{48}$ | 1 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | UTD | 9 | Fair |
| Paquette et al. ${ }^{49}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 11 | Good |
| Paquette and Melcher ${ }^{50}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 11 | Good |
| Rabita et al. ${ }^{51}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | UTD | 11 | Good |
| Reenalda et al. ${ }^{52}$ | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | UTD | 9 | Fair |
| Sanno et al. ${ }^{53}$ | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | UTD | 9 | Fair |
| Schütte et al. ${ }^{54}$ | 1 | 1 | 1 | 1 | 1 | 1 | 1 |  | 0 | 1 | 1 | 1 | UTD | 11 | Good |
| Siler and Martin ${ }^{55}$ | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | UTD | 10 | Good |
| Strohrmann et al. ${ }^{56}$ | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | UTD | 1 | 1 | UTD | 6 | Poor |
| Voloshin et al. ${ }^{57}$ Verbitsky et al. ${ }^{58}$ | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | UTD | 7 | Poor |
| Total of all studies | 28 | 28 | 23 | 27 | 22 | 27 | 17 | 11 | 2 | 26 | 28 | 28 | 7 |  |  |

## Peak accelerations

Peak tibial acceleration increased on average $0.39 \mathrm{~g}(\mathrm{Cl}:[0.16,0.62], \mathrm{p}=0.001)$ after a fatigue protocol, see Table 2.6. There was no significant pooled effect of fatigue on peak sacral acceleration (MD: $0.44 \mathrm{~g}, \mathrm{Cl}:[-0.07,0.95], \mathrm{p}=0.09$ ) and peak head acceleration (MD: $0.08 \mathrm{~g}, \mathrm{Cl}$ : $[-0.05,0.21], p=0.22$ ). From the study of Bigelow et al. ${ }^{52}$, only results for trials on the treadmill fulfilled the inclusion criteria and were included in this literature review. García-Pérez et al. ${ }^{29}$ investigated peak tibial accelerations both during treadmill and overground running. Only treadmill running was included in the meta-analysis to prevent dependent inputs. They found no significant effect of fatigue on peak tibial acceleration during overground running (pre-fatigue: 24.6 (10.8) g, post-fatigue: 22.2 (10.3) g)). Findings of the study of Voloshin et al. ${ }^{50}$ and Verbitsky et al. ${ }^{51}$ were not included in meta-analyses because they lacked absolute values. However, they classified the group of runners into a "fatigued" and "unfatigued" group based on end-tidal carbon dioxide pressure after a fatigue protocol. They found a significant increase of $62(32) \%(p<0.05)$ in peak tibial acceleration in the group of runners classified as "fatigued" but not in the group of runners classified as "unfatigued" (-1 (14)\%, $p>0.05)$. The normalized peak sacral acceleration also significantly increased in the group of "fatigued" runners (37 (30)\%, p < 0.05) but not in the group of "unfatigued" runners (22 (31) \%, p > 0.05). Note that there was small to high heterogeneity for peak accelerations, indicating variable results between studies.

## Shock attenuation

Fatigue resulted in no pooled significant changes in shock attenuation between the tibia and head (MD: 2.10\%, CI: [-0.67, 4.87], $p=0.14$ ) and between the tibia and sacrum (MD: 4.65\%, Cl: [-3.34, 12.64], $p=0.25)$, see Table 2.6.

## Vertical and leg stiffness

After a fatigue protocol, a significant pooled decrease in $K_{l e g}$ was found (MD:- $0.73 \mathrm{kN} / \mathrm{m}, \mathrm{Cl}$ : $[-1.20,-0.25], p=0.003)$, see Table 2.6. The meta-analysis did not show a significant pooled effect of fatigue on $K_{\text {vert }}$ (MD:-0.17 kN/m, Cl: [-0.59, 0.25], $\mathrm{p}=0.43$ ). Results of Avogadro et al. ${ }^{33}$ for $K_{l e g}$ were not included in the meta-analysis because of a different computation, however, they did not find a significant effect of fatigue on $K_{l e g}$ (pre-fatigue:15.12 (3.33) $\mathrm{kN} / \mathrm{m}$; post-fatigue: 15.82 (3.52) kN/m, $\mathrm{p}=0.24$ ).
Table 2.6: Random-effects meta-analyses for the effect of running-induced fatigue on peak accelerations, shock attenuation and stiffnesses. An asterisk (*) before the name of the authors indicates that a significant change with fatigue was found in that study. $S D=$ standard deviation; Cl = confidence interval; TM = treadmill.




## Vertical COM displacement

A total of six studies investigated $\Delta C O M_{z}^{15,36,40,43,46,47,49}$, findings were not included in a meta-analysis because the definition of $\Delta C O M_{z}$ differed between studies. Strohrmann et al. ${ }^{49}$ found an increase in $\Delta C O M_{z}$ during the complete gait cycle in novice (MD: 8.12\%, $p=0.041$ ) but not in more experienced runners (data not provided). Similarly, Sanno et al. ${ }^{46}$ found a significant decrease in the COM height at initial contact in recreational runners (pre-fatigue: 1.053 ( 0.033 ) m, post-fatigue: 1.047 ( 0.033 ) m, $\mathrm{p}<0.05$ ) but not in competitive runners (pre-fatigue: 1.043 ( 0.041 ) m, post-fatigue: 1.039 ( 0.043 ) $\mathrm{m}, \mathrm{p}>0.05$ ). They also found a significant decrease in the minimum COM height in recreational runners (pre-fatigue: 0.988 (0.031) m, post-fatigue: $0.980(0.029) \mathrm{m}, \mathrm{p}<0.01$ ) but not in competitive runners (pre-fatigue: 0.982 ( 0.039 ) m, post-fatigue: $0.977(0.040) \mathrm{m}, \mathrm{p}>0.05$ ). Rabita et al. ${ }^{43}$ found a decrease in $\Delta C O M_{z}$ during the stance phase (pre-fatigue: $0.045(0.004) \mathrm{m}$, post-fatigue: 0.040 ( 0.006 ) $\mathrm{m}, \mathrm{p}=0.025$ ). A surrogate for $\Delta C O M_{z}$ (i.e., hip excursion) was investigated by Mizrahi et al. ${ }^{15,36}$. They found an increase in hip excursion between the moment of maximum hip height and the moment of peak tibial acceleration (shortly after initial contact) (pre-fatigue: 0.051 ( 0.015 ) m, post-fatigue: $0.062(0.012) \mathrm{m}, \mathrm{p}<0.05)$. They found no significant effect of fatigue on hip excursion between the moment of peak acceleration and the minimum hip height (pre-fatigue: $0.022(0.009) \mathrm{m}$, post-fatigue: $0.019(0.009) \mathrm{m}, \mathrm{p}>0.05$ ) or the maximum hip height, minimum hip height or hip height at the moment of peak tibial acceleration (data not provided). No significant effects of fatigue on $\Delta C O M_{z}$ during the full gait cycle were found by Schütte et al. ${ }^{47}$ (pre-fatigue: 0.107 ( 0.013 ) m, post-fatigue: $0.110(0.014) \mathrm{m}, \mathrm{p}=0.33$ ) and Nicol et al. ${ }^{40}$ (no data provided).

The effect of experience level on $\Delta C O M_{z}$ was qualitatively investigated. Two studies measured runners with different experience levels and found significant changes in $\Delta C O M_{z}$ only in novice or recreational runners but not in more experienced runners ${ }^{46,49}$. Additionally, Mizrahi et al. ${ }^{15,36}$ included only recreational runners (i.e., low experience level) and found a significant increase in the change in hip height (i.e., surrogate for $\Delta C O M_{z}$ ) between the moment of maximal hip height and peak tibial acceleration. Another study included only elite athletes (i.e. high experience level) and found a significant decrease in $\Delta C O M_{z}$ with fatigue ${ }^{43}$.

## Lower body joint angles

## Ankle angles

No significant pooled effect of fatigue on ankle angles at initial contact (MD:-0.06 ${ }^{\circ}$, $\mathrm{Cl}:[-1.92$, $1.80], \mathrm{p}=0.95$ ), ankle angles at toe-off (MD:-0.05 ${ }^{\circ}$, $\mathrm{Cl}:[-1.43,1.33], \mathrm{p}=0.95$ ) or maximum dorsiflexion angles (MD: $-0.31^{\circ}$, CI: $[-0.75,0.13], \mathrm{p}=0.17$ ) were found, see Table 2.7. No significant pooled effect of fatigue was found for the foot contact angle (i.e., sagittal plane angle between foot and ground at initial contact) (MD: $0.50^{\circ}, \mathrm{Cl}:[-1.12,2.12], \mathrm{p}=0.54$ ). Results of Nicol et al. ${ }^{40}$ were excluded from meta-analyses since they did not provide actual values, however, they reported no significant effect of fatigue on ankle angles at initial contact or toe-off ( $p>0.05$ ).

## Knee angles

After a fatigue protocol, knee flexion angles at initial contact increased by $1.64{ }^{\circ}$ (Cl: [0.61, 2.66], $\mathrm{p}=0.002$ ) and maximum knee flexion during swing increased with $2.92^{\circ}$ ( Cl : [0.80, 5.04], $p=0.007]$ ), see Table 2.7. No significant pooled effect of fatigue was found on maximum knee flexion angles during stance (MD: $0.36^{\circ}$, $\mathrm{Cl}: ~[-0.34,1.06], \mathrm{p}=0.31$ ) or maximum knee extension (MD: $0.37^{\circ}, \mathrm{Cl}:[-0.90,1.65], \mathrm{p}=0.57$ ). Results of Mizrahi et al. ${ }^{36}$ were excluded from meta-analyses since they did not report actual values, however, they stated that the maximum knee flexion angle during stance did not significantly change after a fatigue protocol ( $\mathrm{p}>0.05$ ).

## Hip angles

Meta-analyses showed no significant pooled effects of fatigue on hip angles at initial contact (MD:-0.77 ${ }^{\circ}$, $\mathrm{Cl}:[-3.32,1.78], \mathrm{p}=0.55$ ), midstance (MD:-1.71 ${ }^{\circ}$, $\mathrm{Cl}:[-3.93,0.51], \mathrm{p}=0.13$ ) or maximum hip flexion (MD: $0.57^{\circ}$, $\mathrm{Cl}:[-0.51,1.65], \mathrm{p}=0.30$ ), see Table 2.7. Results of Nicol et al. ${ }^{40}$ were excluded from meta-analyses since they did not report actual values, however, they found no significant differences in the hip angles at initial contact after a fatiguing protocol ( p $>0.05$ ). It should be noted that most quantities related to hip angles were investigated by a small number of studies.
Table 2.7: Random-effects meta-analysis for the effect of running-induced fatigue on joint angles. An asterisk (*) before the name of the authors indicates that a significant change with fatigue was found in that study. Comp = competitive runners; Recr = recreational runners; Nov = Novice runners; Dom = dominant leg; Fast = group of faster runners; Slow = group of slower runners; SD = standard deviation; Cl = confidence interval.




| Knee angle <br> max flexion stance | Unfatigued <br> mean (SD) <br> [deg] | Fatigued <br> mean (SD) [deg] | Subjects |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | Weight | Mean difference |
| :--- |
| $[95 \% \mathrm{Cl}]$ |


| Knee angle max flexion swing | Unfatigued mean (SD) [deg] | Fatigued mean (SD) [deg] | Subjects | Weight | Mean difference [95\% CI] | Mean difference, $95 \% \mathrm{Cl}$ decrease $\leftarrow \rightarrow$ increase |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| * Fuhr et al. ${ }^{39}$ | 97.4 (6.6) | 101.7 (9.3) | 9 | 34.0\% | 4.27 [0.64, 7.90] |  |  |  |  |  |
| Koblbauer et al. ${ }^{30}$ Dom | 89.0 (10.2) | 92.2 (12.7) | 15 | 40.0\% | 3.20 [-0.15, 6.55] |  |  |  |  |  |
| Siler and Martin ${ }^{55}$ Fast | 120.5 (10.2) | 121.9 (9.3) | 9 | 12.5\% | 1.40 [-4.58, 7.38] |  |  |  |  |  |
| Siler and Martin ${ }^{55}$ Slow | 103.8 (11.8) | 103.9 (9.3) | 10 | 13.5\% | 0.10 [-5.66, 5.86] |  |  |  |  |  |
| Total (95\% CI) |  |  | 43 | 100.0\% | 2.92 [0.80, 5.04] |  |  |  |  |  |
| Heterogeneity: $1^{2}=0 \%$ |  |  |  |  |  |  |  |  |  |  |
| Test for overall effect: $Z=2.71(p=0.007)$ |  |  |  |  |  | -10 | -5 | 0 | 5 | 10 |




## Discussion

The primary aim of this study was to provide an overview of kinematic changes due to running-induced fatigue. The main changes in kinematics due to fatigue included an increase in peak accelerations at the tibia, decreased leg stiffness, an increase in knee flexion at initial contact and maximum knee flexion, and an increase in $\Delta C O M_{z}$ in novice, but not in experienced runners. The hypothesis that the lower body would behave stiffer with fatigue was not supported by the results of this literature review. Since most included kinematic quantities are intertwined (i.e., a decrease in stiffness is likely to result in an increase in knee flexion and shock attenuation), the results of this literature review did not support most of the hypotheses. The secondary aim of this study was to investigate the influence of experience level on kinematic changes with fatigue. The hypothesis that experienced runners show smaller changes in kinematics due to fatigue was supported by the finding that $\Delta C O M_{z}$ increased in novice but not in experienced runners with fatigue.

Results from this literature review with meta-analyses were generally in line with results from Apte et al. ${ }^{18}$, who investigated seven of the eighteen quantities included in the meta-analyses. They found an increase in PTA, decrease in $K_{\text {vert }}$ and $K_{\text {leg }}$, increased knee flexion at initial contact and maximum knee flexion during swing and an increase in ankle dorsiflexion at initial contact ${ }^{18}$. The decrease in $K_{v e r t}$ and increase in ankle dorsiflexion were not supported by the meta-analyses which can be explained by different exclusion criteria such as including fatigue protocols with a constant versus an uncontrolled running speed. The differences in effects of fatigue between literature reviews emphasize the importance of confounding factors when comparing studies.

## Peak accelerations

Peak accelerations at the tibia significantly increased with fatigue. There was no pooled effect of fatigue on peak accelerations at the sacrum and head. An explanation for higher peak tibial accelerations with fatigue could be that in a fatigued state, the body is less capable of coordinating the activation of musculature around the ankle, knee, and hip joints. Decreased coordination might negatively affect the spreading of the impact force impulse over time, resulting in higher peak accelerations ${ }^{59}$. Another explanation for higher peak tibial accelerations is a change in effective mass. The effective mass is the proportion of the body mass that is accelerated during impact and decreases with an increase in knee flexion at initial contact ${ }^{13}$. Since \F=ma, a decrease in effective mass results in an increase in acceleration when
forces remain constant. Since knee flexion angles at initial contact were shown to increase in this literature review, the increase in peak tibial acceleration can partly be explained by a decrease in effective mass.

## Shock attenuation

Fatigue resulted in no significant pooled changes in shock attenuation between the tibia and sacrum and the tibia and head. Shock attenuation was expected to increase based on several reasons. Firstly, due to a pooled increase in peak tibial acceleration without a pooled increase in peak sacral and peak head accelerations after a fatigue protocol. Secondly, because of an increase in knee flexion at initial contact ${ }^{19}$. And finally, as a way to keep proximal accelerations low to prevent disturbances of the vestibular and visual systems ${ }^{60}$. It should be noted that the number of included studies for both shock attenuation quantities was limited, and high heterogeneity was present, probably resulting in underpowered meta-analyses.

## Vertical and leg stiffness

Vertical and leg stiffness refers to how compliant, respectively, the whole lower body and the lower leg are to the exerted $F_{z, \max }$. After a fatigue protocol, $K_{\text {leg }}$ decreased while $K_{v e r t}$ did not significantly change. The number of studies investigating $K_{v e r t}$ and $K_{l e g}$ is limited and heterogeneity was small for $K_{\text {vert }}$ and high for $K_{\text {leg }}$. It is unknown if the decrease in $K_{\text {leg }}$ was caused by a decrease in $F_{z, \max }$ or an increase in $\Delta L_{\text {stance }}$. However, a decrease in $K_{l e g}$ implies a more compliant lower body with a decreased tolerance for impact forces after a fatigue protocol. Apte et al. ${ }^{18}$ found a decreasing trend for $K_{\text {vert }}$ which was not shown in this meta-analysis. This difference is likely the result of the methods used to define a trend (median and median absolute deviation versus MD and Cl ).

## Vertical COM displacement

Qualitative subgroup analysis showed that $\Delta C O M_{z}$ increased with fatigue in novice, but not in more experienced runners. Differences in responses to fatigue based on experience level might be caused by a better ability of experienced runners to adopt an energetically efficient gait pattern with smaller $\Delta C O M_{z}{ }^{61,62}$. A larger $\Delta C O M_{z}$ in novice runners might be caused by an increase in knee flexion because of more pronounced knee extensor strength loss with fatigue ${ }^{40,63}$.

## Lower body joint angles

Fatigue significantly increased knee flexion angles at initial contact and maximum knee flexion angles during the swing phase. An increase in knee flexion at initial contact increases the oxygen cost of running and is energetically costly ${ }^{19}$. This increase in knee flexion could be caused by knee extensor strength loss and decreased tolerance to imposed stretch loads with fatigue ${ }^{40,63}$. Other explanations for more knee flexion at initial contact include a decrease in the effective mass or an increase in active shock absorption ${ }^{13}$. An increase in maximum knee flexion angles during the swing phase could indicate that runners tried to decrease the moment of inertia of the leg about the hip joint, making it easier to swing the leg forward by decreasing required hip flexor torques while possibly increasing activation and metabolic costs of hamstrings and calf muscles ${ }^{56,64}$. None of the other investigated joint angles showed a pooled significant effect of fatigue. This lack of significant findings might be caused by conflicting significant changes in joint angles with fatigue or due to small sample sizes. Heterogeneity was moderate to high for multiple joint angles. Hence, it is likely that there is an additional confounding factor that could explain the conflicting findings for many joint angles. Possible confounding factors include the effect of foot strike pattern, experience level, running surface, shoe wear, sex, and familiarity with running till exhaustion. However, not enough information was available to perform subgroup analyses for the aforementioned factors.

## Effect of different fatigue protocols

Fatigue protocols can differ in terms of distance, duration, speed, running surface, stopping criteria, etcetera. The speed of a fatigue protocol influences both kinematics ${ }^{65}$ and the presence of kinematic changes after a fatigue protocol. Voloshin et al. ${ }^{50}$ and Verbitsky et al. ${ }^{51}$ split their subjects into a "fatigued" and "unfatigued" group based on their end-tidal carbon dioxide pressure after a fatigue protocol with a fixed speed. They found a significant increase in both peak tibial and peak sacral accelerations for the "fatigued" group but not for the "unfatigued" group. One subject who fell into the "unfatigued" group repeated the fatigue run on a different day and at a slightly higher fixed speed. During the second fatigue protocol, he was classified for the "fatigued" group and showed an increase in peak tibial acceleration. These findings strengthen the idea that there is a subject-specific threshold above which kinematic changes occur due to fatigue. This subject-specific threshold is expected to apply to running distance and duration as well. Studies typically did not provide enough information to determine if all runners reached their subject-specific threshold and were, therefore, truly
fatigued. The distance of each fatigue protocol needed to be at least 3 km to impose a lower threshold on running-induced fatigue and to comply with the definition of long-distance running ${ }^{21}$. The assumption was made that all runners in all studies were fatigued after the fatigue protocol and that kinematic changes caused by running-induced fatigue did not differ between runs of different distances, speeds, or durations.

A measure of fatigue was provided by sixteen studies. Most studies reported RPE scores that were always 15 or higher, indicating that runners experienced the fatigue protocol from "hard" to "very, very hard" ${ }^{26}$. When subjects could decide to terminate the fatigue protocol, subjects were instructed to either run to volitional exhaustion or until a certain RPE score was achieved ${ }^{26}$. When RPE scores were used as a stopping criterion, none of the included quantities showed significant effects of fatigue ${ }^{35,44,47,53,54}$. This implies that terminating a fatigue protocol based on an RPE score below volitional exhaustion might not be sufficient to reach the subject-specific fatigue threshold for kinematic quantities included in this review.

Running kinematics have been shown to be largely comparable between treadmill and overground running ${ }^{66}$. However, one of the included studies investigated the effect of running surfaces on fatigue ${ }^{29}$. Peak tibial and head accelerations were found to be significantly lower on a treadmill versus an athletic track in an unfatigued state but not in a fatigued state. These differences in an unfatigued state might be related to lower reaction forces and alterations in the effective mass ${ }^{29}$. For this literature review, subgroup analysis for running surface was not possible since only six studies performed the pre-and post-fatigue measurements overground $5,29,39,42,43,45$. For two quantities, running surfaces tended to result in different effects of fatigue. The maximum knee angle during stance tended to decrease or show no change in overground measurements ${ }^{5,42,44,45}$ while it tended to show no change or increase in treadmill measurements ${ }^{13,32,34,35,46,53}$. Additionally, the hip angle at midstance decreased in overground measurements ${ }^{5,45}$ while it remained the same or increased in treadmill measurements ${ }^{46}$. It is unclear if these differences are truly caused by a difference in running surface or by other confounding factors, but it is recommended to more thoroughly investigate the effect of running surface on running kinematics in future research.

## Effect of subject characteristics

Investigation of the effect of subject characteristics on kinematic changes due to fatigue heavily depended on the provided information from articles and was therefore limited to $\triangle C O M_{z}$ . As a response to fatigue, novice runners increased $\triangle C O M_{z}$ while more experienced
runners did not show a significant change on a group level. Less experienced runners showed larger kinematic changes due to fatigue than more experienced runners ${ }^{49}$. Multiple studies reported differences between less and more experienced runners. More experienced runners showed less maximal ankle plantarflexion after a fatigue protocol ${ }^{35}$ while less experienced runners showed more $\Delta C O M_{z}$, a smaller maximum ankle dorsiflexion angle, less ankle plantarflexion at toe-off and more maximum knee flexion during stance ${ }^{46,48,49}$. Since there are differences in responses to fatigue for runners with different experience levels, the training history of subjects should be reported, and the results of a fatigue study cannot easily be generalized to the total population of runners.

Most studies analyzed changes in kinematic quantities on a group level. However, inter-individual differences in running kinematics were already present in an unfatigued state ${ }^{40,49,55}$ and became even more apparent in a fatigued state $40,43,48,49,55$. Especially changes in kinematics in opposite directions were often mentioned to result in a lack of significant findings on a group level. Siler and Martin ${ }^{48}$ found that changes in maximal knee extension due to fatigue ranged from an increase of $7.8^{\circ}$ to a decrease of $11.1^{\circ}$. Hence, already in 1991 , it was proposed by Siler and Martin that future research should be sensitive to individual responses to fatigue. Running kinematics are unique for a runner, as well as the way they change with fatigue. Hence, it is recommended to investigate changes in running kinematics as a result of fatigue on a subject-specific level since group-level analysis might mask individual responses.

## Limitations and future research

Studies often consisted of small sample sizes, had different fatigue protocols, and some kinematic quantities were investigated by a limited number of studies. All these factors increase heterogeneity and variability in the results. Many studies were likely underpowered, resulting in non-significant pooled findings. In multiple cases, conflicting significant changes for a quantity were reported. Part of the conflicting findings might be caused by confounding factors such as not reaching a subject-specific fatigue threshold, running surface, foot strike pattern, covered distance, experience level, or stopping criterium. For future studies, it is advised to investigate the possible influence of these factors or at least clearly report the fatigue protocol and subject characteristics. Heterogeneity of results was variable for the pooled significant findings that were found in this literature review, indicating some inconsistent results between studies. Hence, results of individual studies should be interpreted with caution, and results from this review should be treated carefully.

Multiple studies did not report exact p-values of statistical tests but only reported that the p-value was below or above a certain threshold, typically 0.05 . The CI of MD was computed based on p-values when these were available. A conservative approach was used when $p$-values were reported to be below a defined threshold by assuming that the p-value was equal to that threshold. When p-values were actually lower than that threshold, this would result in a smaller standard error and Cl and increase the weight of that particular study since the weight is based on the inverse variance. Hence, multiple studies finding significant differences without reporting the exact p-values were assigned lower weights in these meta-analyses, possibly underestimating the true effect of fatigue on multiple kinematic quantities.

There are many possible kinematic quantities to investigate when analyzing running gait, increasing the risk of reporting and publication bias. The risk of bias was minimized by performing a quality assessment and by estimating the heterogeneity between studies. The quality assessment showed that the mean quality was good, although studies scored poorly on questions related to external validity and power calculations. Heterogeneity was large for most kinematic quantities, indicating inconsistent findings based on $I^{2}$, supported by conflicting findings for multiple quantities. Results for kinematic quantities that did not significantly change with fatigue were often published, implying a small effect of reporting and publication bias. The effect of bias on this literature review was assumed to be limited and results were assumed to be valid for the investigated kinematic quantities.

The unfatigued and fatigued states were defined differently across studies. Some studies performed separate measurements before and after a fatigue protocol while others measured quantities during a fatigue protocol. Studies included different amounts of steps in their analyses and applied different filters to their data. Since this review focused on changes in kinematic quantities due to fatigue rather than the absolute values across studies, differences in data acquisition and processing are expected to have a similar influence on unfatigued and fatigued values and, therefore, a small influence on the result of this literature review.

To prevent general conclusions based on a small number of findings, only quantities that were investigated in a minimum of two studies were included. Hence, possible relevant findings mentioned in just one study were not taken into account, for example, studies investigating knee stiffness. Furthermore, $F_{z, \max }$ and especially the impulse of $F_{z, \max }$ were not included
in this review. Based on the results of this review, it is thought that ground reaction force variables in combination with shock attenuation, will provide additional insight into changes in shock attenuation mechanisms with fatigue and should be investigated in the future.

To limit the number of included kinematic quantities, joint angles in the frontal and transversal planes were not included in this review. Frontal and transversal plane joint angles have relatively large errors with respect to their ROM and their contribution to shock attenuation is expected to be smaller than for sagittal plane kinematics. However, Pratt ${ }^{59}$ showed that ankle pronation also contributes to shock attenuation and it is therefore recommended to further investigate the effect of fatigue on frontal and transversal plane kinematics in future research.

## Conclusions

This literature review showed that running kinematics change as a result of running-induced fatigue. As a consequence of fatigue, peak accelerations at the tibia increased, leg stiffness decreased, knee flexion at initial contact and maximum knee flexion increased and $\Delta C O M_{z}$ increased in novice but not in experienced runners. In addition, large inter-individual differences in responses to fatigue were found. Changes in running kinematics due to fatigue might be explained by a decrease in the tolerance of knee extensors to imposed stretch loads or a decrease in the neuromuscular control resulting in less spreading of the impact force impulse over time.

## Recommendations

- Investigate kinematic changes due to fatigue on an individual instead of a group level
- Clearly report training history of subjects since results of runners with a certain experience level cannot be generalized to the total population of runners
- Investigate additional confounding factors to explain contradicting findings, especially concerning joint angles
- Investigate the effect of fatigue on joint angles in the frontal and transversal plane
- Investigate the effect of spreading of impact force impulses over time on peak accelerations


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## Appendix 2.A: Search strategy

This appendix provides an overview of search strings and additional limitations used for the different included databases (i.e., PubMed, Web of Science, Scopus). Note that "Marathon" was included in the search terms while other distances were not included in the search terms. Since "Marathon" is implicitly connected to running, the modality is not always mentioned together with "Marathon". To be sure that articles investigating Marathon running wouldn't be missed, "Marathon" was added to the search terms referring to the modality.

For PubMed, the MeSH term "Humans" was required and the full-text article needed to be available.

For Web of Science, titles, abstracts and keywords were searched. Additionally, results needed to be categorized as "article" and belong to one of the four following Web of Science categories; "Sport sciences", "Engineering biomedical", "Orthopaedics", "Biophysics".

For Scopus, titles and abstracts were searched. Results needed to be categorized as "article" or "article in press". The MedLine database was excluded from the Scopus search (MedLine was already included in the PubMed search). Furthermore, results needed to belong to one of the three following subject areas: "Engineering", "Medicine", "Health professions" and one of the following keywords needed to present; "running", "exercise", "fatigue", "exertion", "athlete", "endurance", "biomechanics". Results containing the keyword; "fatigue of materials" were excluded.

## PubMed search string

((()(run[Title/Abstract] OR running[Title/Abstract] OR runner*[Title/Abstract] OR marathon[Title/Abstract])) AND (exhaust*[Title/Abstract] OR exert*[Title/Abstract] OR prolong*[Title/ Abstract] OR fatigue*[Title/Abstract])) AND (kinemat*[Title/Abstract] OR kinet*[Title/Abstract] OR biomechanic*[Title/Abstract] OR mechanic*[Title/Abstract] OR acceler*[Title/Abstract] OR centre-of-mass[Title/Abstract] OR center-of-mass[Title/Abstract] OR center-of-gravity[Title/Abstract] OR centre-of-gravity [Title/Abstract] OR ground-reaction[Title/Abstract] OR angle[Title/Abstract] OR angular[Title/Abstract] OR force[Title/Abstract] OR moment*[Title/ Abstract] OR impact[Title/Abstract] OR shock[Title/Abstract] OR inertia*[Title/Abstract] OR pressure[Title/Abstract]))) AND (full text[sb] AND Humans[Mesh])

## Web of Science search string

(TS=((run OR running OR runner* OR marathon) AND (exhaust* OR exert* OR prolong* OR fatigue*) AND (kinemat* OR kinet* OR biomechanic* OR mechanic* OR acceler* OR centre-of-mass OR center-of-mass OR center-of-gravity OR centre-of-gravity OR ground-reaction OR angle OR angular OR force OR moment* OR impact OR shock OR inertia* OR pressure))) AND DOCUMENT TYPES: (Article)

Refined by: WEB OF SCIENCE CATEGORIES: ( SPORT SCIENCES OR ENGINEERING BIOMEDICAL OR ORTHOPEDICS OR BIOPHYSICS )

Timespan: All years. Indexes: SCI-EXPANDED, SSCI, A\&HCI, CPCI-S, CPCI-SSH, ESCI.

## Scopus search string

TITLEABS ( ( run OR running OR runner* OR marathon ) AND ( exhaust* OR exert* OR prolong* OR fatigue* ) AND ( kinemat* OR kinet* OR biomechanic* OR mechanic* OR acceler* OR centre-of-mass OR center-of-mass OR center-of-gravity OR centre-of-gravity OR ground-reaction OR angle OR angular OR force OR moment* OR impact OR shock OR inertia* OR pressure ) ) AND KEY ( running OR exercise OR fatigue OR exertion OR athlete OR endurance OR biomechanics ) AND NOT KEY ( fatigue-of-materials ) AND NOT DBCOLL ( medl ) AND ( LIMIT-TO ( DOCTYPE , "ar" ) OR LIMITTO ( DOCTYPE, "ip" ) ) AND ( LIMITTO ( SUBJAREA , "MEDI" ) OR LIMIT-TO ( SUBJAREA , "ENGI" ) OR LIMIT-TO ( SUBJAREA, "HEAL" ) )

## Appendix 2.B: Quality assessment

The quality assessment checklist (see Table 2.3 (short version) and Table 2.8) is based on 13 out of 27 items of the Downs and Black quality assessment checklist ${ }^{20}$. Fourteen items of the original Downs and Black quality assessment checklist were removed because they applied to intervention studies, comparison studies, follow-up measurements or adverse events and did not apply to the aim of this review. Three questions were adapted for the scope of this review. In question 3 of the original Downs and Black quality assessment checklist, "patients" was replaced by "subjects". In question 4, "Interventions of interest" was replaced by "Fatigue protocol". Question 13 ("were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?") was replaced by "Was the setting of the fatiguing protocol representative for a typical run (i.e., overground and with a self-selected speed)?". The adapted Downs and Black quality assessment checklist consists of 13 questions compared to the 27 questions from the original checklist.

In the original Downs and Black quality assessment checklist, question 27 is about the statistical power calculation. A study could score between zero and five points for their power calculation, out of a total of 32 possible points for the complete checklist. The weight factor of question 27 in the original checklist is therefore $16 \%(10)^{*}(5 / 32)$ ). Since fourteen items were removed from the adapted quality checklist, a maximum of five points for question 27 would increase the weight of question 27 to $29 \%$ ( $100 *(5 / 17)$ ). Hence, the scoring of question 27 was adapted to keep the weight of question 27 around $15 \%$ by adjusting the maximum score for this question to two points instead of five $\left(100^{*}(2 / 14)=14 \%\right)$. Studies received 0 points if they had a power below $80 \%$ or when no power calculation was performed or reported. Studies with a power between $80 \%$ and $89 \%$ received 1 point. Studies with a power of $90 \%$ or higher received 2 points. Because of the new scoring of question 27, the maximum number of points that a study can score for the adapted Downs and Black quality assessment checklist is 14 .

Quality labels were matched with quality scores based on the scoring of Hooper et al. ${ }^{22}$. This resulted in the following cut-off scores. A quality score between 0 and 7 points indicated a study of "Poor" quality, a score of 8 or 9 a study of "Fair" quality, a score of 10 till 12 a study of "Good" quality and a score of 13 or 14 a study of "Excellent" quality."

Table 2.8: Quality assessment checklist based on the Downs and Black quality assessment checklist ${ }^{20}$. UTD = Unable to determine.

| Quality assessment checklist | Scoring |  |
| :--- | :--- | :---: |
| \# | Question | $0 / 1$ |
| Q1 | Is the hypothesis/aim/objective of the study clearly described? | $0 / 1$ |
| Q2 | Are the main outcomes to be measured clearly described in the Introduction <br> or Methods section? (If the main outcomes are first mentioned in the Results <br> section, the question should be answered no) | $0 / 1$ |
| Q3 | Are the characteristics of the subjects included in the study clearly described? <br> (Inclusion and/or exclusion criteria should be given. Some information regarding <br> training history should be given (km/week, hr/week, years of training, 5k or 10k <br> time)) | $0 / 1$ |
| Q4 | Is the fatigue protocol clearly described? (Duration, distance and speed (two <br> out of three) should be reported. Stopping criteria and setting of the fatigue <br> protocol should be given) |  |

Q6 Are the main findings of the study clearly described? (Simple outcome data (including denominators and numerators) should be reported for all major findings. This question does not cover statistical tests)

Q7 Does the study provide estimates of the random variability in the data for the main outcomes? (In non-normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered yes)

Q10 Have actual probability values been reported (e.g. $\mathbf{0 . 0 3 5}$ rather than <0.05) for 0/1 the main outcomes except where the probability value is less than 0.001 ?

Q11 Were the subjects asked to participate in the study representative of the entire population from which they were recruited? (The study must identify the source population/how subjects were recruited/how subjects were selected. The subject population that is included should be described (competitive, novice, experienced, marathon runners, etcetera))

Q13 Was the setting of the fatiguing protocol representative for a typical run (i.e. 0/1/UTD overground and with a self-selected speed)? (For the question to be answered yes the study should mimic a typical run (free to adapt running speed and running overground))

Q16 If any of the results of the study were based on "data dredging", was this 0/1/UTD made clear?
Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.

| Quality assessment checklist | Scoring |  |
| :--- | :--- | :--- |
| $\#$ | Question | $0 / 1 /$ UTD |
| Q18 | Were the statistical tests used to assess the main outcomes appropriate? (The <br> statistical techniques used must be appropriate to the data. For example, non- <br> parametric methods should be used for small sample sizes. Where little statistical <br> analysis has been undertaken but where there is no evidence of bias, the <br> question should be answered yes. If the distribution of the data (normal or not) is <br> not described it must be assumed that the estimates used were appropriate and <br> the question should be answered yes) |  |
| Q20 | Were the main outcome measures used accurate (valid and reliable)? (For <br> studies where the outcome measures are clearly described, the question should <br> be answered yes. For studies that refer to other work or that demonstrates the <br> outcome measures are accurate, the question should be answered as yes) | 0/1/UTD |
| Q27 | Did the study have sufficient power to detect a clinically important effect <br> where the probability value for a difference being due to chance is less than <br> 5\%? (Sample sizes have been calculated to detect a difference of x\% and y\%. | $0 / 1 / 2 /$ |
| 70\% (power of 0.7) $=0$ points, $80-89 \%$ (power of 0.8-0.89) $=1$ point, $90-99 \%$ | UTD |  |
| (power of 0.9-0.99) = 2 points) |  |  |

## Chapter <br> 3

## Quantifying and correcting for speed and stride frequency effects on running mechanics in fatiguing outdoor running

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The data presented in this study will be openly available in 4TU.ResearchData.


#### Abstract

Background: Real-time feedback on impact-related quantities in running is of interest to prevent injuries. Many quantities are typically measured in a controlled laboratory setting, even though most runners run in uncontrolled outdoor environments. While monitoring running mechanics in an uncontrolled environment, a decrease in speed or stride frequency can mask fatigue-related changes in running mechanics.


Aim: This study aimed to quantify and correct for the subject-specific effects of running speed and stride frequency on changes in impact-related running mechanics during a fatiguing outdoor run.

Methods: Nine runners ran a competitive marathon while peak tibial acceleration and knee angles were measured with inertial measurement units. Running speed was measured through GPS-based sports watches. Median values over segments of 25 strides throughout the marathon were computed and used to create subject-specific multiple linear regression models. These models predicted peak tibial acceleration, knee angles at initial contact, and maximum stance phase knee flexion based on running speed and stride frequency. Data for all subjects were corrected for individual speed and stride frequency effects during the marathon. The speed and stride frequency corrected and uncorrected data were divided into ten stages to investigate the effect of marathon stage on mechanical quantities.

Results and significance: Running speed and stride frequency explained on average 20\% to $30 \%$ of the variance in peak tibial acceleration, knee angles at initial contact, and maximum stance phase knee angles while running in an uncontrolled setting. Regression coefficients for speed and stride frequency varied strongly between subjects. Speed and stride frequency corrected peak tibial acceleration and maximum stance phase knee flexion increased throughout the marathon. At the same time, uncorrected values showed no significant differences between marathon stages due to a decrease in running speed. Hence, subjectspecific effects of changes in speed and stride frequency on running mechanics should be corrected for when interpreting or providing feedback on the gait pattern in uncontrolled environments.

## Introduction

Motion analysis in running provides objective information about running technique. This information can be used to improve running performance ${ }^{1,2}$, monitor effects of fatigue on the gait pattern ${ }^{3,4}$, and possibly reduce injury risk through real-time feedback on mechanical quantities ${ }^{5,6}$. The repetitiveness of impact forces during running is thought to be related to the development of running injuries ${ }^{7,8}$. Impact forces cause a rapid deceleration of the foot after initial contact, shortly followed by deceleration of the lower leg, upper leg, pelvis, and upper body ${ }^{9}$. Accelerometers can quantify the magnitude of deceleration at, for instance, the tibia (i.e., peak tibial acceleration (PTA)) and thereby reflect the effect of impact forces when force plates are unavailable. Impact forces can be modulated by controlling the knee angle ${ }^{10}$, which makes PTA and knee angles interesting quantities to monitor with respect to injury risk.

Traditionally, running mechanics were measured in a gait laboratory. A laboratory setting allows researchers to control or minimize influences on the gait pattern from, for instance, running speed, inclination, running surface, and the weather. Simultaneously, a laboratory setting is restricted to an artificial environment that is not sport-specific. Multiple mechanical quantities concerning peak accelerations and shock attenuation showed important differences between overground and treadmill running ${ }^{11-14}$. Hence, running mechanics should be analyzed in a representative environment since findings from laboratory-based treadmill studies cannot easily be generalized to overground running ${ }^{14-16}$.

One essential difference between treadmill and outdoor running is the ability to adapt running speed. Most runners lower their speed after prolonged running due to fatigue ${ }^{17,18}$. The influence of running speed and stride frequency on mechanical variables has extensively been studied in controlled environments and typically on a treadmill. PTA increases with an increase in running speed ${ }^{19}$ or a decrease in stride frequency ${ }^{20}$. PTA showed a strong significant linear regression with speed in treadmill running ${ }^{21,22}$. Individual variances in these relationships were large, highlighting the need for subject-specific analysis ${ }^{19,21}$. Additionally, maximum stance phase knee flexion increased with an increase in speed or a decrease in stride frequency ${ }^{23,24}$. No speed effect on knee flexion angles at initial contact was found over a small range of running speeds in recreational runners ${ }^{23}$. Hence, running speed and stride frequency influence PTA and some measures related to knee angles in running. Two previous studies corrected mechanical quantities during running in an uncontrolled setting for speed
by computing individual ratios (i.e., dividing by speed) ${ }^{17,18}$. This correction assumes that the relationship between speed and quantities of interest is linear and crosses the origin for all subjects. In the case of PTA, the regression equation between speed and PTA differs between foot strike patterns ${ }^{18}$, between subjects ${ }^{19}$ and the intercepts of group-based analyses do not appear to cross the origin ${ }^{18}$. Thus, individual ratios likely oversimplify the relationship between speed and quantities of interest.

Inertial measurement units (IMUs) can measure running mechanics in a sport-specific setting and open up new possibilities for real-time feedback on running technique in a representative environment ${ }^{16}$. PTA is often used as bio-feedback quantity to improve running technique and prevent injuries by providing feedback on high PTA values, both in commercial devices and in research ${ }^{25-29}$. Additionally, algorithm development allows the estimation of knee angles based on a minimal sensor set ${ }^{30}$. Feedback on running technique is often based on an arbitrary fixed threshold independent of running speed and stride frequency which can mask fatigue-related changes in running biomechanics. Without correcting for the effects of speed and stride frequency, the origin of changes is unclear, preventing appropriate interpretation and feedback on running biomechanics. Hence, this study aims to quantify and correct for the subject-specific effect of running speed and stride frequency on changes in impact-related running mechanics during a fatiguing outdoor run.

A marathon was used as an uncontrolled setting to ensure that a wide range of external influences (e.g., fatigue, different surfaces, other runners) found in typical uncontrolled outdoor running were incorporated to improve the ecological validity of relationships. We hypothesized that:

- Running speed and stride frequency decrease toward the end of the marathon
- The influence of running speed and stride frequency on PTA, knee angles at initial contact, and maximum stance phase knee flexion angles differs between subjects
- Speed and stride frequency influence the interpretation of running mechanics in uncontrolled settings


## Methods

## Participants

Nine healthy recreational runners participated in this study. Technical errors resulted in missing data for two subjects. Therefore, data from three females and four males were included (mean (standard deviation); age: 36 (11) years, height: 181 (5) cm, mass: 74 (8) kg, running experience: 7 (4) years). All subjects gave written informed consent before participating in this study. The Ethics Committee Computer and Information Science of the University of Twente approved the study protocol.

## Measurement systems

Subjects were equipped with eight IMUs (240 Hz, MVN Link, Xsens Technologies, Enschede, The Netherlands). IMUs were placed on the sternum, back of the pelvis, and bilaterally on the midportion of the lateral upper leg, proximally on the tibia, and on the midfoot. Hair on the skin was shaved to improve IMU attachment before IMUs were fixed to the skin with double-sided tape and covered with additional tape. IMUs on the midfoot were placed under the tongue of the shoes. Wires between IMUs were loosely taped to the skin to prevent entanglement, see Figure 3.1. IMUs were connected with a bodypack and battery pack. The bodypack delivered power from the battery pack to the IMUs and synchronized and stored data from the IMUs on internal memory. The bodypack and battery pack weighed 220 grams ${ }^{31}$ and were placed in a neoprene storage belt around the waist of the runners. Subjects used their personal sports watches with a global positioning system (GPS), measuring GPS coordinates with different sampling frequencies (on average $0.7(0.4) \mathrm{Hz}$ ).


Figure 3.1: One of the runners a few meters before the finish line. The bodypack and battery pack are placed in the pink belt. White tape is visible, which covers the sensors and fixates sensor wires.

## Measurement protocol

Measurements were performed during the Enschede marathon ( 42.195 km ) in the Netherlands on a typical Dutch spring day with temperatures around $10{ }^{\circ} \mathrm{C}$. The course was relatively flat, with about 170 meters of elevation. Before the marathon, multiple anthropometric values were measured (body height, hip height, hip width, knee height, ankle height, and shoe length). Sensor-to-segment calibration was performed according to the manufacturer's recommendations ${ }^{32}$. Subjects were instructed to run their marathon as planned and not to worry about the equipment.

## Data analysis

The data presented in this study will be openly available in 4TU.ResearchData.

## Data extraction and computing speed

Sensor data was extracted from the internal memory of the bodypack. Proprietary filtering based on sensor acceleration, angular velocity, and magnetometer data was used to estimate sensor orientations in the software package Xsens MVN Analyze (version 2019.2.1). A scaled biomechanical model was created based on anthropometric measurements, raw sensor data (accelerations and angular velocities), and estimated sensor orientations. Knee flexion angles were obtained from this scaled biomechanical model ${ }^{32}$. Latitude and longitude coordinates were extracted from the GPS data. Missing latitude-longitude coordinates were linearly interpolated before speed was computed as the distance between two latitude-longitude coordinates based on the Haversine formula ${ }^{33}$. Speeds above $20 \mathrm{~km} / \mathrm{h}$ were deemed extremely unlikely and replaced with spline interpolation. Speed was then resampled to 240 Hz to match the sampling frequency of the IMUs.

## Temporal synchronization

GPS and IMU data were temporally aligned based on GPS speed and speed of the pelvis IMU. Pelvis IMU speed was computed as the resultant pelvis IMU velocity obtained from the scaled biomechanical model. GPS and IMU data were then synchronized by cross-correlating GPS speed with pelvis IMU speed. Temporal alignment between both systems was visually checked at the start and end of the marathon to ensure that possible differences in internal clocks would not influence temporal alignment. Visual misalignment was present in data of one subject, for which IMU data was resampled based on cross-correlation of the first and last 20\% of the data points separately.

## Removing walking parts and segmentation

Some participants walked for short periods during the marathon to drink something or due to fatigue. PTA is higher for running than for walking ${ }^{9}$. Walking parts were detected and removed based on a minimum of two adjacent outliers in PTA of the right leg. In this case, an outlier was defined as a PTA value of more than four scaled median absolute deviations below the median over the complete marathon ${ }^{34}$. Additionally, ten strides before and after a walking part were removed to omit the effect of slowing down and increasing speed. After removing the walking parts, data were segmented into time-normalized gait cycles starting with initial contact based on right foot accelerations ${ }^{35}$.

## Extracting quantities of interest and removing outliers

Quantities of interest were computed for the right legs from all subjects. PTA was defined as the positive acceleration peak in the axial direction of the tibia in a sensor-fixed coordinate system during the first $33 \%$ of the gait cycle. Accelerations in the axial direction compared to the resultant acceleration were chosen to better represent the main direction of impact forces in the body. Knee flexion angles were defined as $0^{\circ}$ when the leg was fully extended, and flexion resulted in positive values. The knee angle at initial contact was extracted from the first sample of the time-normalized gait cycle. Maximum stance phase knee flexion was defined as the maximum knee angle during the first $33 \%$ of the gait cycle. Stride frequency (strides/minute) was based on the time between two right initial contacts. Speed was averaged over the complete gait cycle. The average foot strike angle (i.e., angle between the foot and horizon in the sagittal plane at initial contact) over the complete marathon was computed to determine the foot strike pattern of subjects ${ }^{36}$. Outliers in quantities of interest were defined as values deviating more than four scaled median absolute deviations from the moving median over a window of 500 strides. A relatively large deviation from the median value was chosen to classify outliers to prevent removal of a considerable amount of data and over-smoothing the data. All strides with an outlier in any of the quantities of interest were removed from further analyses.

Median values over segments of 25 strides were computed, and outliers were removed (>4 scaled median absolute deviation from moving median over a window of 500 segments) to improve data stability and reduce the amount of data ${ }^{37}$. The marathon was divided into ten stages to investigate the effect of marathon stage; each stage was roughly equal to 4 km of running data. Mean values for each stage of the marathon were computed from the earlier defined median values, see Figure 3.2.

Tibial acceleration


Figure 3.2: Data extraction shown for peak tibial acceleration (PTA). The top figure shows the tibial acceleration of one subject during the full marathon. Walking parts are labeled red and removed from further analysis. The middle figure shows a snapshot of the tibial acceleration signal in which PTAs are shown with green dots. Vertical grey lines show segments of 25 strides from which the median PTA is computed and shown as a pink dot. The bottom figure shows all median PTA values during the marathon. The full marathon duration is divided into ten stages for group-based statistical analyses.

## Statistical analysis

Group-based one-way repeated measures ANOVAs were performed to test whether running speed, stride frequency, PTA, knee angles at initial contact, and maximum stance phase knee flexion changed over the different stages of the marathon. The ANOVAs had ten levels (stages of the marathon), and the mean values for each subject for all ten stages were used as input. When a significant effect of marathon stage on one of the quantities of interest was found, post hoc tests were used to test which marathon stages differed from each other.

Subject-specific multiple linear regression models were created to test if running speed and stride frequency could predict PTA, knee angles at initial contact, and maximum stance phase knee flexion angles. Median values for all 25 stride segments were used as input for the regression models, and no distinction for marathon stage was made. Intercepts and coefficients from the subject-specific regression equations were used to correct PTA and knee angles for the subject-specific effect of changes in speed and stride frequency.

Speed and stride frequency corrected quantities were computed by subtracting the product of the coefficient for speed with the deviation from the mean speed and by subtracting the product of the coefficient for stride frequency with the deviation from the mean stride frequency for all median values. Effectively, this creates a signal in which speed and stride frequency are equal to the average speed and stride frequency during the whole marathon. Group-based one-way repeated measures ANOVAs (10-levels) were repeated to test whether speed and stride frequency corrected PTA, knee angles at initial contact, and maximum stance phase knee flexion changed over the different stages of the marathon.

An alpha level of 0.05 was used to determine statistical significance. When applicable, Holm-Bonferroni corrections were applied for all possible 45 post hoc pairwise comparisons. Correlations were interpreted as very strong $r=(0.90,1.00)$, strong for $r=(0.70,0.89)$, moderate for $r=(0.40,0.69)$, weak for $r=(0.20,0.39)$ and very weak for $r=(0.00,0.19)^{38}$.

## Results

Subjects finished the marathon in 3 hours and 55 minutes ( 30 minutes), with an average speed of 11.0 (1.5) km/h and an average stride frequency of 85.6 (2.9) strides/minute. Walking parts resulted in the removal of 2.7 (2.1)\% of all data points. An average of 19383 (2073) gait cycles were measured per runner, of which 8.8 (2.4)\% was removed due to outliers. Runners 1 and 5 were classified as non-rearfoot strikers based on a foot contact angle smaller than $8^{\circ}{ }^{36}$.

## Speed and stride frequency

There was a statistically significant effect of marathon stage on speed on a group level, $F(9,54)$ $=5.766, p<0.001$, see Figure 3.3. Running speed decreased from 11.5 (1.8) km/h to 10.3 (1.4) km/h between the first and last stages of the marathon. Post-hoc analyses showed that speed during the last two stages was lower than in the first four stages of the marathon. No significant effect of marathon stage on stride frequency was found on a group-level, $F(9,54$ ) $=0.725, p=0.684$. Speed and stride frequency were weakly correlated on a group level, $r=$ 0.21 (0.18).


Figure 3.3: Mean speed and stride frequency for every runner during all marathon stages. The solid red lines show the group means. A significant effect of marathon stage on speed was found. Significant results from post hoc analyses are shown by an asterisk at the top of the figure.

## Peak tibial acceleration

On a group level, PTA had a moderate positive correlation with speed ( $r=0.40(0.24)$ ) and a very weak negative correlation with stride frequency ( $r=-0.09(0.20)$ ), see Table 3.1. Subject-specific multiple linear regression equations to predict PTA based on speed and stride frequency were significant for all subjects and explained 26 (18)\% of the variance in PTA, see Figure 3.4. Speed was a significant predictor of PTA for all runners while stride frequency was a significant predictor for all but one runner. On a group level, there was a statistically significant effect of marathon stage on PTA both for uncorrected $(F(9,54)=2.786$, $p=0.009)$ and speed and stride frequency corrected values $(F(9,54)=2.316, p=0.028)$. However, post hoc analyses only showed significant differences in PTA between marathon stages after correcting for speed and stride frequency, see Figure 3.5. PTA corrected for speed and stride frequency was higher in the third ( $\left.77.5(17.3) \mathrm{m} / \mathrm{s}^{2}\right)$ compared to the first stage of the marathon ( $\left.71.0(17.5) \mathrm{m} / \mathrm{s}^{2}\right)$.

Table 3.1: Left side of table: Individual correlations of peak tibial acceleration (PTA) with speed and stride frequency (SF). Right side of table: Individual regression equations to predict PTA based on speed and stride frequency together with the adjusted R-squared value (i.e., explained variance of regression equation). $r=$ Pearson's correlation coefficient, $S D=$ standard deviation, $n s=n o n$-significant finding, NRF = non-rearfoot striking subject.

| PTA | Correlation |  | Regression |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Speed (r) | SF (r) | Intercept | Coefficient speed $\left(\frac{m / s^{2}}{k m / h}\right)$ | Coefficient SF $\left(\frac{m / s^{2}}{\text { strides } / \min }\right)$ | Adjusted $\mathrm{R}^{2}$ |
| Runner $1^{\text {NRF }}$ | 0.48 | -0.22 | 148.18 | 4.14 | -1.37 | 0.31 |
| Runner 2 | 0.33 | 0.11 | 65.78 | 3.75 | -0.31 ns | 0.11 |
| Runner 3 | 0.55 | 0.11 | 106.14 | 4.83 | -0.77 | 0.32 |
| Runner 4 | 0.17 | -0.21 | 115.32 | 1.45 | -0.93 | 0.08 |
| Runner 5 NRF | 0.79 | 0.12 | $23.27{ }^{\text {ns }}$ | 7.76 | -0.43 | 0.62 |
| Runner 6 | 0.44 | -0.17 | 114.41 | 2.00 | -0.89 | 0.21 |
| Runner 7 | 0.06 ns | -0.39 | 479.17 | 1.53 | -4.92 | 0.16 |
| Mean (SD) | 0.40 (0.24) | -0.09 (0.20) | 150.32 (150.50) | 3.64 (2.26) | -1.37 (1.60) | 0.26 (0.18) |



Figure 3.4: Scatterplot of individual peak tibial acceleration and knee angle values as a function of speed. Each dot represents the median value over a segment of 25 strides during the marathon. Subjectspecific linear regressions are shown as solid lines.

Peak tibial acceleration: Uncorrected and speed \& SF corrected


Figure 3.5: Individual mean peak tibial accelerations during all marathon stages. Dotted lines show uncorrected PTA values (i.e., as measured during the marathon). Solid lines represent speed and stride frequency corrected PTA values. Grey lines show the group means. Significant effects of running duration are shown with an asterisk and black lines. Solid black lines represent significant differences in corrected PTA values.

## Knee angle at initial contact

On a group level, knee angles at initial contact showed a weak negative correlation with speed ( $r=-0.24(0.30)$ ) and a very weak negative correlation with stride frequency ( $r=-0.03$ (0.28)), see Table 3.2. Subject-specific multiple linear regression equations to predict knee angles at initial contact based on speed and stride frequency were significant for all subjects and explained 20 (10)\% of the variance in knee angles at initial contact, see Figure 3.6. Speed was a significant predictor of knee angles at initial contact for all runners while stride frequency was a significant predictor for all but two runners. On a group level, there was a statistically significant effect of marathon stage on both corrected (F(9,54) = 5.136, p < 0.001) and uncorrected knee angles at initial contact $(F(9,54)=7.227, p<0.001)$. Knee angles at initial contact during later stages of the marathon were significantly higher than during the first stages of the marathon.

Table 3.2: Left side of table: Individual correlations of knee angles at initial contact (IC) with speed and stride frequency (SF). Right side of table: Individual regression equations to predict knee angles at IC based on speed and stride frequency together with the adjusted $R$-squared value (i.e., explained variance of regression equation). $r=$ Pearson's correlation coefficient, $S D=$ standard deviation, ns = nonsignificant finding, $N R F=$ non-rearfoot striking subject.

| Knee IC | Correlation |  | Regression |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | Speed (r) | SF (r) | Intercept | Coefficient speed <br> $\left(\frac{d e g}{k m / h}\right)$ | Coefficient SF <br> $\left(\frac{d e g}{\text { strides } / \mathrm{min}}\right)$ | Adjusted R² |
| Runner 1 NRF | 0.37 | 0.02 ns | 10.08 | 0.83 | -0.05 ns | 0.13 |
| Runner 2 | -0.44 | -0.24 | 44.34 | -1.52 | -0.16 ns | 0.19 |
| Runner 3 | -0.29 | $0.06^{\mathrm{ns}}$ | 2.04 ns | -0.91 | 0.33 | 0.12 |
| Runner 4 | -0.15 | -0.42 | 78.54 | -0.25 | -0.64 | 0.18 |
| Runner 5 NRF | -0.51 | 0.19 | -17.90 | -0.93 | 0.45 | 0.36 |
| Runner 6 | -0.43 | 0.40 | -45.22 | -0.70 | 0.83 | 0.32 |
| Runner 7 | -0.25 | -0.21 | 67.32 | -0.71 | -0.51 | 0.09 |
| Mean (SD) | $-0.24(0.30)$ | $-0.03(0.28)$ | $19.89(45.40)$ | $-0.60(0.73)$ | $0.04(0.53)$ | $0.20(0.10)$ |



Figure 3.6: Individual mean knee angles during all marathon stages. The left figure shows knee angles at initial contact, while the right figure shows maximum stance phase knee flexion angles. Dotted lines show uncorrected knee angles (i.e., as measured during the marathon). Solid lines represent speed and stride frequency corrected knee angles. Dotted black lines represent significant differences in uncorrected knee angles while solid black lines represent significant differences in knee angles corrected for the effect of changes in speed and stride frequency. Grey lines show the group means. Significant effects of marathon stage are shown with an asterisk and black lines.

## Maximum stance phase knee angles

On a group level, maximum stance phase knee angles had a weak positive correlation with speed ( $r=0.32(0.27)$ ) and a weak negative correlation with stride frequency ( $r=-0.21(0.28)$ ), see Table 3.3. Subject-specific multiple linear regression equations to predict maximum stance phase knee angles based on speed and stride frequency were significant for all subjects and explained $30(20) \%$ of the variance in maximum stance phase knee angles, see Figure 3.6. Speed was a significant predictor for maximum stance phase knee angles for all runners while stride frequency was a significant predictor for all but one runner. On a group level, marathon stage had no statistically significant effect on maximum stance phase knee flexion (F(9,54) = $1.770, p=0.096$ ). After correcting knee angles for subject-specific effects of speed and stride frequency, a significant effect of marathon stage on maximum stance phase knee flexion was found $(F(9,54)=2.294, p=0.029)$. Maximum stance knee flexion corrected for speed and stride frequency was significantly higher in the third (43.4 (4.9)) compared to the first stage of the marathon (41.8 (4.0)).

Table 3.3: Left side of table: Individual correlations of maximum stance phase knee angles with speed and stride frequency (SF). Right side of table: Individual regression equations to predict maximum stance phase knee angles based on speed and stride frequency together with the adjusted $R$-squared value (i.e., explained variance of regression equation). $r=$ Pearson's correlation coefficient, SD $=$ standard deviation, $n s=$ non-significant finding, $N R F=$ non-rearfoot striking subject.

| Knee stance | Correlation |  | Regression |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Speed (r) | SF (r) | Intercept | Coefficient speed $\left(\frac{\operatorname{deg}}{k m / h}\right)$ | Coefficient SF $\left(\frac{\operatorname{deg}}{\text { strides } / \min }\right)$ | Adjusted R ${ }^{2}$ |
| Runner $1^{\text {NRF }}$ | 0.59 | -0.27 | 76.58 | 2.37 | -0.80 | 0.48 |
| Runner 2 | 0.31 | 0.25 | 25.13 | 0.45 | 0.19 | 0.11 |
| Runner 3 | 0.22 | -0.22 | 62.92 | 0.45 | -0.27 | 0.17 |
| Runner 4 | $0.03{ }^{\text {ns }}$ | -0.69 | 152.86 | 0.44 | -1.27 | 0.49 |
| Runner 5 NRF | 0.69 | -0.08 | 63.90 | 1.67 | -0.48 | 0.54 |
| Runner 6 | 0.42 | -0.17 | 48.46 | 0.30 | -0.14 | 0.20 |
| Runner 7 | $-0.04{ }^{\text {ns }}$ | -0.30 | 89.40 | 0.01 ns | -0.49 | 0.09 |
| Mean (SD) | 0.32 (0.27) | -0.21 (0.28) | 74.18 (40.27) | 0.81 (0.86) | -0.47 (0.47) | 0.30 (0.20) |

## Discussion

This research aimed to quantify and correct for the subject-specific effect of changes in running speed and stride frequency on impact-related running mechanics during a fatiguing outdoor run. Mostly in line with our hypothesis, speed decreased throughout the marathon while no effect of marathon stage on stride frequency was found. PTA and maximum stance phase knee flexion corrected for changes in speed and stride frequency increased throughout the marathon, while uncorrected values showed no significant change. Running speed and stride frequency explained, on average 20 to $30 \%$ of the variance in PTA, knee angles at initial contact, and maximum stance phase knee flexion while running in an uncontrolled setting. Regression coefficients for speed and stride frequency varied strongly between subjects. Hence, the subject-specific effects of changes in speed and stride frequency on running mechanics should be corrected for when interpreting or providing feedback on the gait pattern in uncontrolled environments.

## Speed and stride frequency

Running speed significantly decreased during the marathon. A decrease in speed during a marathon is typically found ${ }^{17,18,39,40}$ and is likely caused by fatigue, although race strategy can also play a role. Stride frequency did not show a significant effect of marathon stage and was
weakly correlated with speed, indicating that, similar to previous studies, the speed reduction is generally caused by a decrease in stride length instead of stride frequency ${ }^{17,41}$. The significance of predictors, regression equations, and explained variances differed between subjects. Differences might be caused by differences in body weight, ankle angle at initial contact ${ }^{10}$, foot strike pattern ${ }^{18}$, individual differences in adaptations to speed by increasing step length versus stride frequency, differences in the tolerance to effects of fatigue and differences in the capacity to sustain a stable gait pattern over a range of speeds. Even though stride frequency did not change on a group level, adding stride frequency to the regression models resulted in significantly better predictions for almost all runners, emphasizing the benefits of subject-specific analysis versus group-based analysis.

## Peak tibial acceleration

Average group-based PTA values showed a significant main effect of marathon stage, although post hoc analyses showed no differences between marathon stages for uncorrected values. PTA values were within the range found in literature ${ }^{18,19,42}$. The correlations between PTA and speed ( $r=0.40(0.24))$ during a marathon were similar to the correlations between resultant PTA and speed in controlled settings $(r=0.42)^{19}$. Subject-specific multiple linear regressions showed that, on average, PTA increased with $3.6 \mathrm{~m} / \mathrm{s}^{2}$ for every $1 \mathrm{~km} / \mathrm{h}$ increase in speed, although subject-specific coefficients ranged from $1.5 \mathrm{~m} / \mathrm{s}^{2}$ to $7.8 \mathrm{~m} / \mathrm{s}^{2}$. The speed coefficient of PTA was between $4.1 \mathrm{~m} / \mathrm{s}^{2}$ and $6.7 \mathrm{~m} / \mathrm{s}^{2}$ in controlled settings ${ }^{19,22}$. The speed coefficient to predict PTA in our study was generally lower than in laboratory-based studies, possibly due to the inclusion of stride frequency or external influences like fatigue. Foot strike pattern has been shown to influence the speed coefficient of PTA during a marathon. Rearfoot striking runners showed higher speed coefficients ( $12.8 \mathrm{~m} / \mathrm{s}^{2}$ ) than midfoot striking runners ( $7.0 \mathrm{~m} /$ $\mathrm{s}^{2}$ ), while no significant speed coefficient was found for forefoot striking runners ${ }^{18}$. In our study, the two non-rearfoot striking runners (subjects 1 and 5) had amongst the highest speed coefficients, which is possibly an effect of group- versus subject-based analysis. The regression equation explained, on average, 26 (18)\% of the variance in PTA. Although relatively low, it is higher than the $19 \%$ of explained variance in resultant PTA found in labora-tory-based studies ${ }^{19}$. To accurately predict PTA in outdoor environments, more variables are needed in the multiple linear regression equation (e.g., knee angle at initial contact), but for the scope of this paper, we were solely interested in the explained variance by speed and stride frequency. After correcting PTA for the subject-specific effects of speed and stride frequency, a significant increase in PTA between the first and third stages of the marathon was found. An increase in PTA corrected for changes in speed and stride frequency could
indicate a decrease in the runner's capacity to attenuate shocks. Alternatively, the effective mass (i.e., the portion of body mass that is decelerated upon ground contact ${ }^{43}$ ) can decrease with increased knee flexion at initial contact (as shown during the marathon), which results in higher leg accelerations when similar ground reaction forces are applied. To conclude, PTA and its interpretation are influenced by subject-specific effects of changes in speed and stride frequency during a fatiguing run.

## Knee angles

Average knee angles at initial contact $\left(16.1(2.5)^{\circ}\right)$ and maximum stance phase knee angles (42.9 (5.1) $)^{\circ}$ ) were within the range reported in literature ${ }^{4,23,43-45}$. Knee angles at initial contact showed a negative weak and very weak correlation with speed and stride frequency, indicating more knee extension with higher speeds and stride frequencies. Previously, the knee flexion angle at initial contact remained similar ${ }^{23}$ or increased with speed ${ }^{46}$, although the range of speeds included was drastically higher than those found during the marathon. A decrease in knee angle at initial contact with an increase in speed might be a strategy to increase stride length by increasing leg extension. Knee angles at initial contact corrected for subject-specific effects of changes in speed and stride frequency showed a similar increasing pattern during the marathon compared to uncorrected values. Knee angles at initial contact have been found to increase with fatigue in controlled settings ${ }^{43,45,47}$, possibly to decrease vertical ground reaction forces ${ }^{10}$ at a higher metabolic cost ${ }^{48}$. Hence, the increase in knee angles at initial contact during a marathon is not solely an effect of changes in speed and stride frequency but is likely a result of fatigue.

Maximum stance phase knee angles had a weak positive correlation with speed and a weak negative correlation with stride frequency, indicating that the stance phase shortens at higher stride frequencies, resulting in less knee flexion during stance ${ }^{24}$. An increase in knee flexion with an increase in speed has been shown previously ${ }^{23}$ and might be caused by higher forces on the body that need to be absorbed at higher speeds. However, it seems counterintuitive since more flexion during the stance phase typically increases the stance phase, while shorter contact times are expected at higher speeds ${ }^{23,40}$. The average increase in maximum stance phase knee flexion of $0.8^{\circ}$ for every $1 \mathrm{~km} / \mathrm{h}$ increase in speed is similar to previous findings in controlled settings $\left(0.7^{\circ}\right)^{23}$. Maximum stance phase knee flexion angles corrected for changes in speed and stride frequency reveal a significant increase between the first and third stages of the marathon that is not present in uncorrected values. An increase in maximal stance knee flexion could indicate an increase in stride length ${ }^{49}$, knee extensor
strength loss, or a reduced tolerance to imposed stretch loads with fatigue ${ }^{40,50}$. Despite relatively small explained variances of regression equations for knee angles, subject-specific corrections for changes in speed and stride frequency on knee angles significantly influenced the interpretation of mechanical changes during a marathon.

## Fatigue

Subjects likely experienced high levels of fatigue toward the end of the marathon. Runninginduced fatigue typically increases PTA ${ }^{47}$, knee flexion at initial contact ${ }^{47}$ and tends to increase maximal stance phase knee flexion ${ }^{43,45,51}$. Both speed and fatigue are positively associated with PTA and maximum stance phase knee angles. Fatigue might have caused lower speed coefficients for PTA and maximum stance phase knee angles than expected without the influence of fatigue. Since subjects generally ran slower at the end of the marathon, PTA and maximum knee angles possibly decreased less with a decrease in speed towards the end of the marathon due to fatigue. Therefore, the influence of speed and stride frequency on running mechanics in an uncontrolled environment might be larger than shown in this study. To omit the effect of fatigue, we could have taken data from the start of the marathon, defined linear regression equations from data in an unfatigued state, and applied a correction to the remainder of the data, similar to ${ }^{52}$. However, most runners will experience some level of fatigue during their runs, making relationships solely based on unfatigued data invalid. Hence, we deliberately included data from an unfatigued to a fully fatigued state to create subject-specific relationships with better ecological validity.

## Limitations

Collecting data in an uncontrolled environment is both a benefit and a shortcoming of this study. The benefit is that runners were measured in the actual environment where they typically run without any constrictions that a laboratory setting or a treadmill would impose on their gait pattern. However, we investigated the effects of speed and stride frequency on multiple mechanical quantities. At the same time, many other external influences could have played a role, such as running surface, fatigue, other runners, or distractions. The explained variance of quantities of interest can be improved by incorporating additional variables into the regression equation. However, for the scope of this paper, we were only interested in how much of the variance in included quantities could be explained by changes in speed and stride frequency.

## Practical implications

This study showed that running speed and stride frequency have a subject-specific relationship with PTA, knee angles at initial contact, and maximum stance phase knee flexion. Correcting for these relationships influences the interpretation of changes in mechanical quantities while running in an uncontrolled environment. Many wearable devices provide feedback on peak accelerations to reduce injury risk ${ }^{25-27}$. Since a decrease in speed or an increase in stride frequency can mask an increase in PTA due to fatigue, it would be relevant from an injury perspective to provide feedback on changes in quantities caused by fatigue rather than by changes in speed or stride frequency. We advise investigating and correcting for subject-specific regression equations for all quantities of interest when measuring and providing feedback on running mechanics in an uncontrolled environment.

## Conclusions

In this study, we quantified and corrected for the subject-specific effect of changes in running speed and stride frequency on impact-related running mechanics during a fatiguing outdoor run. Subject-specific corrections through multiple linear regression equations revealed a significant effect of marathon stage on PTA and maximal stance phase knee flexion, which was previously masked by changes in speed and stride frequency. The effect of marathon stage on knee angles at initial contact changed after correcting for changes in speed and stride frequency. Hence, speed and stride frequency influence the interpretation of changes in mechanical quantities in a subject-specific manner when running in an uncontrolled environment. Subject-specific effects of speed and stride frequency on quantities of interest should be investigated and corrected when interpreting, or providing feedback on, running mechanics in an uncontrolled environment.

## Data availability statement

The data presented in this study will be openly available in 4TU.ResearchData.

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## Chapter 4

## Peak tibial acceleration should not be used as indicator of tibial bone loading during running

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#### Abstract

Peak tibial acceleration (PTA) is a widely used indicator for tibial bone loading. Indirect bone loading measures are of interest to reduce the risk of stress fractures during running. However, tibial compressive forces are caused by both internal muscle forces and external ground reaction forces. PTA might reflect forces from outside the body, but likely not the compressive force from muscles on the tibial bone. Hence, the strength of the relationship between PTA and maximum tibial compression forces in rearfoot-striking runners was investigated. Twelve runners ran on an instrumented treadmill while tibial acceleration was captured with accelerometers. Force plate and inertial measurement unit data were spatially aligned with a novel method based on the center of pressure crossing a virtual toe marker. With spatially aligned data, the ground reaction force moment arm with respect to the ankle joint center, the sagittal plane ankle moment, and maximum tibial compression forces were computed. The correlation coefficient between maximum tibial compression forces and PTA was $0.04 \pm 0.14$ with a range of -0.15 to +0.28 . On a group level, this study showed a very weak and non-significant correlation between PTA and maximum tibial compression forces while running on a level treadmill at a single speed. Hence, PTA as an indicator for tibial bone loading should be reconsidered, as PTA does not provide a complete picture of both internal and external compressive forces on the tibial bone.


## Introduction

Runners are at high risk of developing bone stress fractures. Stress fractures account for 3\% to $14 \%$ of running injuries ${ }^{1-3}$ and are most prevalent in the distal part of the tibial bone ( $20 \%$ to $53 \%)^{4,5}$. Stress fractures are the result of prolonged and repetitive forces on the bone without enough rest for bone remodelling ${ }^{6,7}$. Stress fracture risk is influenced by both fixed factors, such as sex, skeleton alignment, bone geometry, bone remodelling, and bone mineral density, and variable factors, such as training intensity, training frequency, training surface, footwear, running incline, and running kinematics ${ }^{6-10}$. Forces on the tibia and subsequent tibial bone deformation can only be directly measured in vivo after an invasive surgery ${ }^{11-13}$. Hence, there is a lot of interest in indirect measures of tibial bone forces.

Ground reaction forces (GRFs) and peak tibial accelerations (PTAs) are often used as surrogate measures for tibial bone loading and injury risk in running ${ }^{14-21}$. GRF is the force exerted by the ground on the body to support the body weight (BW) and, in addition, results in acceleration and deceleration of the body's center of mass during the stance phase of running. The collision of the foot with the ground causes an impact shock that travels through the body ${ }^{20}$. PTA reflects this impact shock at the surface of the skin near the tibia bone ${ }^{22}$. PTA occurs shortly after initial contact and negligibly to moderately correlates with the slope of the vertical GRF and GRF impact peak shortly after initial contact ${ }^{23,24}$. The benefit of PTA compared to GRF metrics is that PTA can be easily measured outside of the lab with a wearable accelerometer. Multiple studies link high PTA values to retrospective running injuries ${ }^{10,14,25}$. Prospective preliminary data of five runners suggest that runners with a tibial stress fracture tended to have higher PTA values $(9.1 \mathrm{~g})$ compared to matched controls ( $4.7 \mathrm{~g} ; \mathrm{p}=0.06$ ) before they sustained an injury ${ }^{26}$. PTA is often used as a biofeedback variable to decrease impacts and risk of tibial stress fractures in runners ${ }^{27-29}$ and is even applied in commercially available sensors as an indicator of running injury risk ${ }^{30}$. Hence, many findings support the idea of using PTA as a surrogate measure for tibial bone forces in running.

Compression forces acting on the tibial bone $\left(F_{\text {tibia }}\right)$ can be divided into external forces ( $F_{\text {ext }}$ ) caused by the foot contacting the ground and internal forces ( $F_{\text {int }}$ ) caused by the pull of muscles ${ }^{5,31}$. $F_{\text {tibia }}$ in the distal tibia can reach values of 10.3 up to 14.3 times BW during running, of which only $18 \%$ is caused by $F_{\text {ext }}{ }^{31}$. Most of $F_{\text {tibia }}$ is therefore caused by internal forces which reach their maximum compressive action around midstance during running ${ }^{24,31-34}$. Matijevich and colleagues investigated the commonly assumed relationship
between GRF metrics (peak vertical GRF around impact and midstance, slope of vertical GRF and GRF impulse) and maximum tibial compression forces ( $F_{\text {tibia,max }}$ ) during running ${ }^{24}$. Since GRF does not account for compressive muscle forces, no strong group-level correlation with $F_{\text {tibia }}$ was found, although there was high inter-subject variability. Hence, GRF metrics should not be used as indicator of tibial bone forces in running.

Despite the widespread use of PTA as a measure for tibial bone loading and injury risk, PTA (occurring shortly after initial contact) and $F_{\text {tibia, max }}$ (occurring around midstance) do not coincide in time. PTA is expected to reflect the contribution of GRF around initial contact to $F_{t i b i a}$, however, $F_{e x t}$ is only $18 \%$ of $F_{\text {tibia, } \max }{ }^{31}$. Hence, there is reason to doubt the commonly used PTA as a surrogate for tibial bone loading in running. Therefore, the research question of this study is: How strong is the relationship between PTA and $F_{\text {tibia,max }}$ in rearfoot-striking runners during level running at a single speed? It is hypothesized that PTA does not reflect the contribution of $F_{\text {int }}$ (i.e., muscle contractions) to $F_{\text {tibia, max }}$ and therefore that there are no statistically significant correlations between PTA and $F_{\text {tibia,max }}$.

## Methods

## Participants

Thirteen recreational runners participated in this study. Since internal forces tend to be different for non-rearfoot striking runners, only rearfoot striking runners were included in this study ${ }^{35-37}$. Inclusion criteria were: 1) Able to run for 5 minutes at $14 \mathrm{~km} / \mathrm{h}$ to prevent possible effects of fatigue; 2) Injury-free for at least six months; 3) Self-reported rear-foot strike pattern. One subject was retrospectively excluded from analysis because of a non-rearfoot strike pattern. Data from 4 females and 8 males were included (age: $36.7 \pm 12.2$ years, height: $178.7 \pm 9.6 \mathrm{~cm}$, mass: $74.2 \pm 17.7 \mathrm{~kg}$ ). Subjects ran on average $29.9 \pm 19.9 \mathrm{~km}$ per week with $15.0 \pm 14.9$ years of running experience. All participants gave written informed consent before participating in this study. The study protocol was approved by the Ethics Committee Computer and Information Science of the University of Twente (EC-CIS, ref.:RP2021-117).

## Measurement systems

Subjects ran on one belt of a dual-belt treadmill with an integrated three-dimensional (3D) force plate (custom Y-mill, Motekforce-Link, Culemborg, The Netherlands). 3D GRFs and ground reaction moments were captured at 2048 Hz . Subjects were equipped with eight IMU sensors (MVN Link, Xsens, Enschede, The Netherlands) capturing at 240 Hz , measuring acceleration ( $\pm 16 \mathrm{~g}$ ), angular velocity ( $\pm 2000 \mathrm{deg} / \mathrm{s}$ ), and the Earth magnetic field ( $\pm 1.9$ Gauss).

Sensors were placed on the sternum and pelvis and bilaterally on the lateral midportion of the thigh, medial surface of the proximal tibia, and on top of the midfoot in the shoes. All sensors had one axis aligned with the longitudinal direction of the associated segment. Sensors were attached to the skin with double-sided tape and covered with stretchable tape ${ }^{19}$. Subjects wore slightly compressing sleeves to firmly fix the sensors on the tibia to the lower leg.

## Measurement protocol

Multiple anthropometric values were measured (body height, hip height, hip width, knee height, ankle height, and shoe length). Subjects wore their own running shoes throughout the experiment. Subjects performed a five-minute warming-up at a self-selected speed on an instrumented treadmill. After the warming-up, an IMU sensor-to-segment calibration was performed according to the manufacturer's instructions ${ }^{38}$.

Subjects performed a ninety-second running trial at their self-selected step frequency at 12 $\mathrm{km} / \mathrm{h}$. Trials started and ended with three jumps on the treadmill to time-synchronize the force plate and IMU data (see section: "Temporal synchronization and spatial alignment") ${ }^{39}$. Since this study was part of a larger experiment, each subject performed a total of nine running trials of ninety seconds at different speeds ( 10,12 , and $14 \mathrm{~km} / \mathrm{h}$ ) in random order and with different step frequencies (self-selected and imposed), of which data was not included in further analysis. Subjects had a three-minute break after every trial to minimize possible effects of fatigue.

## Data processing

Unless stated otherwise, data were expressed in the global force plate coordinate system ( $\psi^{g l, f p}$ ) with the X-axis pointing in the running direction, the $Y$-axis upwards, and the $Z$-axis to the right. The stance phase of running was defined as the period where the vertical GRF was larger than $20 \mathrm{~N}^{40}$. The stance phase started with initial contact and ended with toe-off. Data were normalized for BW and expressed as a percentage of the stance phase. To exclude effects of adapting to the treadmill speed, 50 right leg stance phases between the $40^{\text {th }}$ and $80^{\text {th }}$ second of the running trial were used for analysis. To check if all runners had a rearfoot striking pattern, the mean foot contact angle (i.e., angle between sagittal plane orientation of the foot and the global vertical axis as provided by the IMU-based biomechanical model) at initial contact was computed for each subject. A mean foot contact angle smaller than 8 degrees (less dorsiflexion results in a smaller angle) was interpreted as a non-rearfoot strike pattern, and these subjects were excluded from further analysis ${ }^{41}$. Data processing and statistics were performed in MATLAB (MathWorks Inc., MA, USA, version 2022a).

## IMU data

Sensor orientations were estimated with proprietary filtering based on acceleration, angular velocity, and magnetometer data from the IMUs in the software package Xsens MVN Analyze (version 2020.0.2). Sensor orientations, together with anthropometric measurements, were used to create a scaled biomechanical model of each subject in the same software. Lower body kinematics, 3D coordinates of joint centers, and locations of virtual anatomical landmarks with respect to joint centers were obtained from the scaled biomechanical model ${ }^{38}$. These IMU-derived data were expressed in either a global IMU-based coordinate system $\left(\psi^{g l, i m u}\right)$ or a sensor-fixed coordinate system $\left(\psi^{s}\right)$. The forward direction (X-axis) of $\psi^{g l, i m u}$ was determined during the sensor-to-segment calibration and was roughly similar to the running direction in $\psi^{g l, f p}$.

## Force plate data

GRF, ground reaction moments, and center of pressure (COP) as measured by the force plate (in $\psi^{g l, f p}$ ) were low-pass filtered with a third-order recursive Butterworth filter of $15 \mathrm{~Hz}{ }^{24}$. Force plate data were then linearly downsampled to 240 Hz to match the sampling frequency of IMU data.

## Temporal synchronization and spatial alignment

A rough estimate of the vertical ground reaction force in running can be made by multiplying vertical pelvis acceleration with BW ${ }^{39}$. Force plate and IMU data can then be time-synchronized by cross-correlating the vertical acceleration of the pelvis segment with the vertical GRF during the first three jumps on the treadmill ${ }^{39}$. Note that BW only functions as a scaling factor and is not necessary for time synchronization.

To compute $F_{\text {tibia }}$, the sagittal plane ankle moment ( $M_{\text {ankle }}$ ) and the GRF moment arm with respect to the ankle joint center was required (see Section "Tibial compression force"). To compute the GRF moment arm, IMU-derived data (expressed in $\psi^{g l, i m u}$ ) needed to be transformed to $\psi^{g l, f p}$. First, the orientation of $\psi^{g l, i m u}$ was rotated to match the orientation of $\psi^{g l, f p}$ using the running direction (positive X-axis). The IMU-based biomechanical model cannot distinguish between stationary (i.e., on a treadmill) and overground running, which resulted in a displacement of the pelvis segment in $\psi^{g l, i m u}$ of about 250 m during each trial, predominantly in the $X$-axis. A least-squares line was fitted through the forward and sideward pelvis displacement in $\psi^{g l, i m u}$ and the angle between these lines was used to rotate all IMU-derived data from $\psi^{g l, i m u}$ to $\psi^{g l, f p}$.

The origin of $\psi^{g l, i m u}$ was then translated to match $\psi^{g l, f p}$ during each step to be able to estimate the GRF moment arm and compute $M_{\text {ankle }}$. Since $F_{\text {tibia }}$ is computed with a 2D model, only spatial alignment of data in the forward direction ( X -axis) was required. The COP trajectory was provided by the force plate in $\psi^{g l, f p}$. In rearfoot striking runners on a treadmill, the forward trajectory of COP $\left(C O P_{x}\right)$ over the surface of the foot was expected to be similar. Therefore, it was assumed that the percentage of the stance phase at which $C O P_{x}$ crossed the fifth metatarsal marker ( $M T 5_{x}$ ) would be similar between strides and subjects. The IMU-based scaled biomechanical model provided virtual marker locations of the heel and MT5 with respect to the ankle joint center. These virtual marker locations were modeled based on the foot length of participants. The mean percentage of the stance phase at which $C O P_{x}$ crossed $M T 5_{x}$ in rearfoot runners was then used to spatially align $\psi^{g l, i m u}$ with $\psi^{g l, f p}$ in the X-direction during each stride, see Figure 4.1. A published dataset of six rearfoot striking runners running at eight different speeds was used to test this method and to obtain the mean percentage of the stance phase at which $C O P_{x}$ crossed $M T 5_{x}{ }^{24}$. This mean percentage at which $C O P_{x}$ crossed $M T 5_{x}$ was then applied to all steps from all subjects from the online dataset. The error of this alignment method was quantified by computing the absolute distance between $M T 5_{x}$ and $C O P_{x}$ at the group-mean percentage of the stance phase were $M T 5_{x}$ crossed $C O P_{x}$. A full description of the analyses of the online dataset can be found in Appendix 4.


Figure 4.1: Visualization of spatial alignment method for $\psi^{g l, i m u}$ and $\psi^{g l, f p}$ for a representative subject. The mean percentage of the stance phase at which the center of pressure (COP) crosses the fifth metatarsal marker (MT5) in the forward direction (X-axis) is used to align $\psi^{g l, i m u}$ and $\psi^{g l, f p}$. COP and MT5 positions with respect to the heel marker are shown. COP data was downsampled for visualization purposes and only the forward position of COP is aligned and shown. This figure was inspired by Figure 1 of ${ }^{58}$.

## Tibial compression force

$F_{\text {tibia }}$ was defined as the axial compression force on the distal end of the tibia and is equal to the ankle compression force ${ }^{24,31,32,42}$, see Figure 4.2. $F_{\text {tibia }}$ is computed according to a 2D (sagittal plane) lower limb model which sums the ankle joint reaction force caused by GRF $\left(F_{\text {ext }}\right)$ and an estimate of compression forces on the tibia exerted by the soleus, gastrocnemius medialis, and lateralis plantar flexor muscles ( $F_{\text {int }}$ ) while ignoring contributions of other muscles ${ }^{31}$.

$$
\begin{equation*}
F_{t i b i a}(t)=F_{\text {ext }}(t)+F_{\text {int }}(t) \tag{4.1}
\end{equation*}
$$

The mass and inertia of the foot were assumed to be negligible ${ }^{24,31,42} . F_{\text {ext }}$ was therefore set equal to GRF in the axial direction of the tibia, but GRF was low-pass filtered with a 45 Hz ( $\overrightarrow{G R F}^{*}$ ) instead of a 15 Hz cut-off frequency to allow representation of the heel impact in $F_{\text {ext }}{ }^{24,31}$ :

$$
\begin{equation*}
F_{e x t}(t)=\left|\overrightarrow{G R F}^{*}(t)\right| * \cos \beta(t) \tag{4.2}
\end{equation*}
$$

Where $\beta$ represents the angle between $\overrightarrow{G R F}^{*}$ and the orientation of the tibial segment (obtained from IMU-based biomechanical model) in the sagittal plane. $F_{\text {int }}$ is computed as $M_{\text {ankle }}$ divided by the Achilles tendon moment arm relative to the ankle joint center $\left(r_{a t}\right)$, which was assumed to be constant and $0.05 \mathrm{~m}^{24,42-44}$ :

$$
\begin{equation*}
F_{\text {int }}(t)=\frac{M_{\text {ankle }}}{r_{a t}}=\frac{C O P_{x, \text { ankle }} * G R F_{z}(t)}{0.05} \tag{4.3}
\end{equation*}
$$

Where $C O P_{x, \text { ankle }}$ represent the forward COP position with respect to the ankle joint center obtained from the scaled biomechanical model and is an estimate of the GRF moment arm relative to the ankle joint center. $M_{\text {ankle }}$ was estimated by multiplying $C O P_{x, \text { ankle }}$ with the vertical $\operatorname{GRF}\left(G R F_{z}\right)$. This computation of $M_{\text {ankle }}$ assumes that solely the plantar flexors contribute to $F_{\text {int }}$ during the stance phase and that there is no co-contraction between plantar and dorsi flexors during the stance phase ${ }^{24,31,42}$.

## Peak tibial acceleration

The acceleration of the tibial sensor, including gravity ( $\vec{a}_{\text {tibia }}$ ) expressed in $\psi^{s}$, was filtered with a fourth-order Butterworth recursive lowpass filter of 60 Hz to minimize noise ${ }^{22}$. PTA was defined as the peak acceleration in the axial direction of the tibial sensor in the local tibial sensor coordinate system, similar to ${ }^{18,29,45}$.


Figure 4.2: Visualization of the 2D lower leg model to estimate tibial compression forces. Calf muscle = combination of the soleus, gastrocnemius medialis and lateralis muscles; $r_{a t}=$ Achilles tendon moment arm relative to the ankle joint center; GRF = ground reaction force; Center of rotation = center of rotation of the ankle joint; Angle $\beta=$ Angle between long axis of tibia and ground reaction force vector in the sagittal plane.

## Statistical analysis

To test if PTA correlates with $F_{\text {tibia,max }}$ in running on level ground at a single speed, Pearson's correlation coefficients ( $r$ ) were computed for each participant independently, after which the group mean correlation was computed. Correlation coefficients were based on 50 right leg PTA and $F_{\text {tibia, max }}$ values for each subject. Correlations were interpreted as very strong $r= \pm(0.90,1.00)$, strong for $r= \pm(0.70,0.89)$, moderate for $r= \pm(0.40,0.69)$, weak for $r= \pm(0.20,0.39)$ and very weak for $r= \pm(0.00,0.19)^{46}$. The level of statistical significance was set to an alpha of 0.05 . The influence of an offset in aligning $\psi^{g l, i m u}$ with $\psi^{g l, f p}$ on the conclusion of this study was assessed by introducing an additional error of 10,20 , and 30 mm to the alignment of $\psi^{g l, i m u}$ and $\psi^{g l, f p}$ and recomputing the correlation between PTA and $F_{t i b i a, \max }$ with these offsets.

## Results

$F_{\text {tibia, } \max }$ was estimated to be, on average $7.6 \pm 0.6 \mathrm{BW}$ with a range of 6.5 to 8.7 BW , see Table 4.1 and Figure 4.3. The within-subject range of $F_{t i b i a, \max }$ was on average 1.6 BW. Mean PTA was $7.8 \pm 1.6 \mathrm{~g}$ and ranged from 4.9 up to 10.1 g . The within-subject range of PTA was on average 3.3 g . On a group level, PTA and $F_{\text {tibia, } \max }$ showed a very weak correlation coefficient of $0.04 \pm 0.14$ with a range of -0.15 up to 0.28 (very weak to weak). No significant correlations between PTA and $F_{\text {tibia,max }}$ were found for any of the runners, see Figure 4.4.

Table 4.1: Mean maximum values. Range refers to the minimum and maximum average subject values (coloured dots in Figure 4.4). GRF $\max =$ Maximum vertical ground reaction force; $M_{\text {ankle }, \max }=$ Maximum ankle moment; $F_{\text {ext,max }}=$ Maximum external force; $F_{\text {int }, \text { max }}=$ Maximum internal force; $F_{\text {tibia,max }}=$ Maximum tibial force; PTA = Peak tibial acceleration; $r=$ correlation coefficient; BW = body weight; $g$ = gravitational acceleration; SD = standard deviation.

|  | Mean $\pm$ SD | Range |
| :--- | :--- | :--- |
| $G R F_{\max }(\mathrm{BW})$ | $2.4 \pm 0.2$ | $2.1-2.7$ |
| $M_{\text {ankle, } \max \left(\frac{\mathrm{Nm}}{\mathrm{kg}}\right)}$ | $0.3 \pm 0.0$ | $0.2-0.3$ |
| $F_{\text {ext, max }}(\mathrm{BW})$ | $2.4 \pm 0.2$ | $2.1-2.8$ |
| $F_{\text {int }, \max }(\mathrm{BW})$ | $5.3 \pm 0.6$ | $4.5-6.2$ |
| $F_{\text {tibia, max }}(\mathrm{BW})$ | $7.6 \pm 0.6$ | $6.5-8.7$ |
| PTA (g) | $7.8 \pm 1.6$ | $4.9-10.1$ |
| Correlation | $0.04 \pm 0.14$ | $-0.15-+0.28$ |
| PTA- $F_{\text {tibia }}(\mathrm{r})$ |  |  |

Tibial compression forces



Figure 4.3: Group average estimated tibial forces (top figure) and axial tibial acceleration (bottom figure) as a percentage of the stance phase. Dots represent maximum values for estimated tibial forces and tibial acceleration during the stance phase. Shaded areas represent the standard deviation around the group mean. $F_{\text {tibia }}=$ tibial compression force; $F_{\text {int }}=$ Internal component of tibial compression force (i.e., caused by muscle contractions); $F_{\text {ext }}=$ external component of tibial compression force (i.e., caused by ground reaction force); $a_{\text {tibia }}=$ tibial acceleration in the axial direction of the tibial sensor; $B W=$ body weight; $g=$ gravitational acceleration.


Figure 4.4: scatterplot of PTA and estimated $F_{\text {tibia,max }}$ values for all 50 strides of all subjects (light grey dots). Coloured dots represent the mean PTA and $F_{\text {tibia, max }}$ for each subject. Coloured ellipses represent the standard deviation ellipse for all individual runners. The legend shows the correlation coefficients (r) between PTA and $F_{\text {tibia,max }}$.

To validate the method to spatially align $\psi^{g l, i m u}$ with $\psi^{g l, f p}$ during each step, to be able to compute the GRF moment arm, an online dataset was used ${ }^{24}$. On average, COP crossed the MT5 marker in the forward direction at $62 \pm 12 \%$ of the gait cycle with a range of $47 \%$ to $85 \%$, see Table 4.2. Within-subject variability was small, while between-subject variability was larger. The mean absolute error introduced by this alignment method was $12 \pm 15 \mathrm{~mm}$ with a range of 4 to 28 mm .

The effect of a possible error in tibial force estimates caused by the alignment method of $\psi^{g l, i m u}$ with $\psi^{g l, f p}$ on the conclusion of this study was investigated by applying an additional alignment offset in the forward direction impacting the GRF moment arm estimate, see Table 4.3. An additional alignment offset influenced the estimation of $F_{\text {int }}$ and $F_{\text {tibia, max }}$ , however the correlation between $F_{\text {tibia,max }}$ and PTA remained very weak for all imposed offsets.

Table 4.2: Results from validating the spatial alignment method on an online dataset. The second column shows the percentage of the stance phase at which the center of pressure in the forward direction $\left(C O P_{x}\right)$ crossed the marker of the fifth metatarsal $\left(M T 5_{x}\right)$. The third column shows the absolute mean error in spatial alignment introduced by assuming that $C O P_{x}$ always crossed $M T 5_{x}$ at $62 \%$ of the stance phase.

| Subject | COP crossing MT5 <br> (\% stance phase) | Absolute mean <br> error (mm) |
| :--- | :--- | :--- |
| 1 | $47 \pm 2$ | $28 \pm 3$ |
| 2 | $59 \pm 3$ | $4 \pm 3$ |
| 4 | $85 \pm 10$ | $16 \pm 3$ |
| 5 | $56 \pm 4$ | $9 \pm 5$ |
| 6 | $68 \pm 3$ | $5 \pm 2$ |
| 7 | $68 \pm 6$ | $14 \pm 9$ |
| 10 | $56 \pm 2$ | $8 \pm 3$ |
| Group mean | $62 \pm 12$ | $12 \pm 15$ |

Table 4.3: Influence of additional alignment offset between $\psi^{g l, i m u}$ and $\psi^{g l, f p}$ on estimated tibial forces and the correlation between PTA and $F_{\text {tibia, max }}$. Columns represent the introduced translation error in the forward direction of $\psi^{g l, i m u}$ with respect to $\psi^{g l, f p}$ for each step.

|  | $\mathbf{- 3 0} \mathbf{~ m m}$ | $\mathbf{- 2 0} \mathbf{~ m m}$ | $\mathbf{- 1 0} \mathbf{~ m m}$ | $\mathbf{0} \mathbf{~ m m}$ | $\mathbf{+ 1 0} \mathbf{~ m m}$ | $\boldsymbol{+ 2 0} \mathbf{~ m m}$ | $\boldsymbol{+ 3 0} \mathbf{~ m m}$ |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| $F_{\text {ext, } \max }$ (BW) | $2.4 \pm 0.2$ | $2.4 \pm 0.2$ | $2.4 \pm 0.2$ | $2.4 \pm 0.2$ | $2.4 \pm 0.2$ | $2.4 \pm 0.2$ | $2.4 \pm 0.2$ |
| $F_{\text {int, } \max }$ (BW) | $4.0 \pm 0.5$ | $4.4 \pm 0.5$ | $4.9 \pm 0.6$ | $5.3 \pm 0.6$ | $5.8 \pm 0.6$ | $6.3 \pm 0.6$ | $6.8 \pm 0.6$ |
| $F_{\text {tibia, } \max }$ (BW) | $6.2 \pm 0.6$ | $6.6 \pm 0.6$ | $7.1 \pm 0.6$ | $7.6 \pm 0.6$ | $8.1 \pm 0.6$ | $8.5 \pm 0.6$ | $9.0 \pm 0.7$ |
| Correlation | $0.04 \pm$ | $0.04 \pm$ | $0.04 \pm$ | $0.04 \pm$ | $0.04 \pm$ | $0.04 \pm$ | $0.05 \pm$ |
| PTA- $F_{\text {tibia, } \max }$ (r) | 0.14 | 0.14 | 0.14 | 0.14 | 0.15 | 0.15 | 0.15 |

## Discussion and implications

This research aimed to investigate the strength of the relationship between PTA, a commonly used measure for tibial bone loading, and estimated $F_{\text {tibia,max }}$ during treadmill running. This study showed a very weak correlation ( $r=0.04 \pm 0.14$ ) between PTA and $F_{\text {tibia, max }}$ in rearfoot striking runners on a treadmill at a single running speed. The hypothesis that there would be no statistically significant correlations between PTA and $F_{\text {tibia,max }}$ was accepted. On a group level, the very weak correlation between PTA and $F_{\text {tibia, max }}$ cannot be considered relevant for estimating tibial bone loading based on PTA. The weak correlations between PTA and $F_{\text {tibia,max }}$ are expected to be caused by the inability of PTA to reflect internal compressive forces from muscle contractions and the mis-timing between PTA (shortly after initial contact) and $F_{\text {tibia, max }}$ (around midstance). The use of PTA as a surrogate measure for $F_{t i b i a, \max }$ during treadmill running is therefore not supported by the findings of this study.

PTA and GRF reflect the effect of external forces on the body during running. GRF represents the effect of external forces during the complete stance phase, while PTA mostly reflects the impact peak that travels up the leg caused by the foot hitting the ground at the start of the stance phase. The contribution of $F_{\text {ext }}$ to $F_{\text {tibia, max }}$ is only about $18 \%-30 \%$, while the remainder is caused by $F_{\text {int }}{ }^{31}$. PTA, GRF loading rate, and GRF impact peak are often used as surrogate measures for each other and for tibial bone loading ${ }^{14-21}$. Previously, Matijevich et al. ${ }^{24}$ showed that the slope of the vertical GRF and impact peak did not strongly correlate with $F_{\text {tibia }}$. Hence, the contribution of the high impact peak shortly after initial contact towards tibial stress fracture injury risk has been challenged before ${ }^{47,48}$ but not in relation to PTA assessed using an IMU on the tibia, although this relation has been often assumed ${ }^{14-21}$. No strong correlations between the slope of the vertical GRF, GRF impact peak, PTA, and tibial bone loading have been found in this study or in other literature ${ }^{23,24}$, indicating that these metrics should not be used as surrogate measures for each other.

A group mean value for PTA of $7.8 \pm 1.6 \mathrm{~g}$ was found, which is well within the expected range when running at $12 \mathrm{~km} / \mathrm{h}^{22,23,49} . F_{\text {tibia, max }}$ in this study was estimated to be $7.6 \pm$ 0.6 BW on average, which is similar to studies in which subjects ran at a similar speed ${ }^{42}$ and falls between values reported for lower ${ }^{36}$ and higher speeds ${ }^{31-33}$. $F_{\text {tibia, max }}$ increases with running speed ${ }^{50}$. Values for $F_{\text {int, max }}$, also called plantar flexor forces or Achilles tendon forces, reported in literature were similar to our findings, respectively $5.7 \pm 1.5$ versus 5.3
$\pm 0.6 \mathrm{BW}{ }^{51}$. Comparable values for $F_{\text {int }}$ of $5.1 \pm 0.9 \mathrm{BW}{ }^{52}$ when running at $14.4 \mathrm{~km} / \mathrm{h}$ and $6.1 \pm 0.6^{35}$ when running at $13 \mathrm{~km} / \mathrm{h}$ were found in literature. In vivo values for $F_{\text {int }, \text { max }}$ of 3750 N at $14 \mathrm{~km} / \mathrm{h}$ were found with a buckle transducer ${ }^{11}$. These findings are only slightly lower than what we found ( $3914 \pm 1094 \mathrm{~N}$ ). Values for $F_{\text {ext, max }}$ from our study $(2.4 \pm 0.2$ BW) where higher than found in literature (1.6-2.0 BW) ${ }^{31,32}$ at similar speeds. Overall, PTA and estimated tibial force values of this study are in line with literature.

A simple 2D lower leg model was used to estimate $F_{\text {tibia }}$ of the distal third of the tibial bone ${ }^{31}$. This model assumes that only the gastrocnemius medialis, lateralis, and soleus contribute to $F_{\text {int }}$, that there is no co-activation of dorsiflexor muscles or other plantarflexor muscles, no influence of bi-articular muscles and neglects the mass and inertia of the foot. These assumptions likely result in an underestimation of true $F_{i n t}$ at similar speeds due to co-activation of dorsiflexor muscles and contribution of smaller plantarflexor muscles. $F_{\text {ext }}$ is likely overestimated in the simple 2D lower leg model since the mass and inertia of the foot dampens GRF while the model assumes that the full GRF acts on the ankle joint. Multiple studies used more elaborate models to estimate $F_{\text {tibia }}$ that included dorsiflexor muscles and smaller plantarflexor muscles $32,33,51$. They found that during $20 \%$ - $90 \%$ of the stance phase, mostly the gastrocnemius medialis, lateralis, and soleus were active with only little contributions (max 0.3 BW per muscle) from other plantar or dorsiflexor muscles ${ }^{32}$. When co-activation occurred, this was mostly during the start and end of the stance phase while $F_{\text {tibia, max }}$ occurs around midstance. The simple 2D lower leg model has been shown to provide $F_{\text {int, max }}$ in running that were similar to an extensive musculoskeletal model using 300 muscles with static optimization, respectively $5.7 \pm 0.6$ and $5.5 \pm 1.4 \mathrm{BW}{ }^{51}$. A 2D versus a 3D lower leg model to compute $F_{t i b i a, \max }$ and $F_{i n t, \max }$ provided similar results for both models ${ }^{33}$. Hence, using a simple or more elaborate model of the lower leg to estimate $F_{\text {tibia }}$ is not expected to influence the conclusion of this study.

A new method was developed, validated, and applied to spatially align force plate and IMU data in the forward direction to be able to estimate the GRF moment arm relative to the ankle joint center. Validation was performed on an online dataset and showed an absolute misalignment error of $12 \pm 15 \mathrm{~mm}$ in the forward direction ${ }^{24}$. To ascertain that an error of this magnitude would not affect the conclusion of this study, an additional offset between $\psi^{g l, i m u}$ and $\psi^{g l, f p}$ was added (i.e., affecting the GRF moment arm relative to the ankle joint center and thus $M_{a n k l e}, F_{i n t}$ and $F_{t i b i a}$ and the correlation between PTA and $F_{\text {tibia, max }}$
was computed. This analysis showed that despite some uncertainty regarding the exact alignment of $\psi^{g l, i m u}$ and $\psi^{g l, f p}$, all alignment offsets (of up to 30 mm ) resulted in a very weak correlation ( $r=0.04-0.05$ ) and did not influence the conclusion of this study.

This study focussed on the relationship between tibial compression forces and 1-dimensional axial tibial sensor acceleration. Besides compression forces, bending and shear forces on the tibia might play a role in the development of stress fractures ${ }^{31-34}$. However, there is no reason to expect that PTA, measured in the axial direction of the tibial bone, would correlate better with bending or shear forces than with axial compression forces. Additionally, these bending and shear forces are of a smaller magnitude (max 1.2 BW) and work in different directions than maximum axial compression forces ${ }^{32}$. The axial compared to the resultant tibial acceleration was investigated in this study due to its demonstrated relationship with injuries ${ }^{22}$ and possibly a stronger correlation with tibial compression forces. The difference between axial and resultant PTA is caused by acceleration components in the forward and sideward direction, while these are not expected to contribute to axial compression forces. Hence, the correlation between the resultant PTA and $F_{\text {tibia,max }}$ is expected to be lower than between the axial PTA and $F_{\text {tibia,max }}$.

The results of this study are based on a relatively small sample of twelve subjects. None of the runners showed a significant correlation between PTA and $F_{\text {tibia,max }}$. Increasing the sample size of this study would likely not affect the conclusion that there is no clinically relevant correlation between PTA and $F_{\text {tibia, max }}$ on a group level.

Measurements were performed on an indoor instrumented treadmill. However, the effect of running surface on PTA is unclear ${ }^{17,49,53,54}$. In-vivo axial tibial compression strains were lower ${ }^{55}$ while modeled $F_{\text {int }}$ were higher in treadmill versus overground running ${ }^{56}$. Without further understanding of the effect of running surface on PTA and tibial forces, the results of this study cannot be generalized to overground running without additional validation.

This study showed that there is only a very weak and non-significant correlation between PTA and $F_{\text {tibia,max }}$ during treadmill running in rearfoot-striking runners, which cannot be considered relevant for estimating tibial bone loading based on PTA. Hence, PTA as an indicator for $F_{\text {tibia, max }}$ and tibial stress fractures, as often used in literature and commercial products, is not supported by scientific data. PTA might be an indicator of other running-related injuries, although the relation between PTA and tibial stress fracture risk is
most referred to in literature ${ }^{14,27,29}$. Future research should focus on a surrogate measure for tibial bone loading, which includes the contribution of $F_{\text {int }}$. The plantar flexor muscles are the largest contributors to $F_{\text {tibia }}{ }^{51}$ and the magnitude of ankle power generation is directly related to running speed ${ }^{57}$. Therefore, 3D acceleration of the pelvis (i.e., close to the center of mass) might reflect plantar flexor forces during running, and thus the contribution of $F_{\text {int }}$ to $F_{t i b i a}$.

## Conclusion

A very weak but non-relevant correlation between PTA and $F_{\text {tibia,max }}$ in treadmill running at a single speed on level ground was found for rearfoot-striking runners. Compression forces on the tibia are composed of both $F_{\text {int }}$ (i.e., muscle contractions) and $F_{\text {ext }}$ (i.e., GRF). PTA is unable to reflect the contribution of muscle contractions to $F_{\text {tibia }}$. Hence, the assumed link between PTA and tibial bone loading $F_{\text {tibia, max }}$, and between PTA and the risk of tibial stress fractures during treadmill running is not supported by the results of this study. Further research should focus on validating these findings in overground running and the development of a surrogate measure for $F_{\text {tibia }}$ which reflects both $F_{\text {int }}$ and $F_{\text {ext }}$.

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## Appendix 4

This appendix describes the analysis of an online dataset ${ }^{24}$ to develop and validate a method to spatially align IMU-derived data expressed in a global IMU-based coordinate system $\left(\psi^{g l, i m u}\right)$, with force plate data expressed in a global force plate-based coordinate system $\left(\psi^{g l, f p}\right)$.

Force plate and optical motion analysis data of ten runners running at eight different speeds (ranging from 9.4-14.4 km/h) on a level treadmill were extracted from an online dataset ${ }^{24}$. More details about the study protocol can be found in the original article accompanying the online dataset ${ }^{24}$.

The stance phase of running was defined as the period where the vertical GRF was larger than $20 \mathrm{~N}^{40}$. The stance phase started with initial contact and ended with toe-off. To be representative of the population used in the main study, only rearfoot striking runners were included. A rearfoot strike was defined as a mean foot contact angle at initial contact of 8 degrees or more ${ }^{41}$. The mean foot contact angle was defined as the sagittal plane angle between a line from the right heel to the right toe marker and the horizontal at initial contact ${ }^{41}$. Four out of ten runners had a foot contact angle smaller than 8 degrees and were classified as non-rearfoot strikers and excluded from further analysis.

Ground reaction forces (GRF) and ground reaction moments (GRM) were filtered with a thirdorder recursive Butterworth filter of $15 \mathrm{~Hz}{ }^{24}$. The center of pressure (COP) in the running direction $\left(C O P_{x}\right)$ was computed:

$$
\begin{equation*}
C O P_{x}=\frac{G R M_{z}}{G R F_{y}} \tag{4.4}
\end{equation*}
$$

Where $G R M_{z}$ represents GRM around the Z-axis (sidewards) of $\psi^{g l, f p}$ and where $G R F_{y}$ represents the vertical GRF in $\psi^{g l, f p}$.

Positions of the right heel, right toe, and fifth metatarsal marker (MT5) marker were extracted and filtered with a third-order recursive Butterworth filter of $10 \mathrm{~Hz}^{24}$. In one subject, the right toe marker was not present; in this case, the position of the right first metatarsal marker (MT1) was extracted and filtered instead of MT5 to compute the foot contact angle.

The first 24 strides for each speed of all included subjects were used for analysis since each trial consisted of at least 24 strides. $C O P_{x}$ and the forward position of the MT5 marker $\left(M T 5_{x}\right)$ were normalized to the percentage of the stance phases. The percentage of the stance phase at which $C O P_{x}$ crossed $M T 5_{x}$ was computed and averaged for all steps. On average, $C O P_{x}$ crossed $M T 5_{x}$ at $62 \pm 12 \%$ of the stance phase, see Table 2 of the manuscript.

To quantify the error introduced by assuming that $C O P_{x}$ crossed $M T 5_{x}$ at $62 \%$ of the stance phase in all rearfoot striking runners, the positional difference between $C O P_{x}$ and $M T 5_{x}$ for all subjects, and speeds at $62 \%$ of the stance phase were computed. This error was, on average $12 \pm 15 \mathrm{~mm}$, see Table 4.2.

## Chapter 5

## Estimating 3D orientation of a body segment during running using a single gyroscope

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#### Abstract

Long distance running has a high incidence of injuries. Wearable sensors are suitable to monitor running technique (i.e., joint angles based on segment orientations) and provide feedback to runners, potentially contributing to reducing injury risk. Wearable sensors often consist of accelerometers, gyroscopes and are typically combined with magnetometers. Threedimensional (3D) orientation estimation of a body segment based on just a single gyroscope could limit computational load and increase battery life but is prone to errors. Currently, there is no drift-free 3D orientation estimation for running based on a single gyroscope. The aim of this study was to test two new methods for 3D orientation drift reduction, based on the assumption that running is quasi-cyclical. Method 1 is based on zero-mean corrected angular velocities before estimating orientation. Method 2 is based on a coordinate transformation, reducing tibia rotations to a quasi-1D rotation in a new coordinate system. These methods were tested during treadmill running. Zero-mean correction did not reduce drift; however, a coordinate transformation reducing tibia rotations to a quasi-1D rotation in a new coordinate system strongly reduced drift in 3D orientation estimation.


## Introduction

Long distance running is associated with high risks of lower extremity injuries ${ }^{1}$. Improper running technique and changes in running technique due to fatigue are expected to contribute to the aetiology of these injuries. When the running technique can be measured easily in real-life settings, runners can be informed in real-time about their current technique and can make corrections to their technique or training to reduce injury risk.

There are a number of sensor systems that can be used to measure running technique (e.g., joint angles based on segment orientations) in a real-life setting. Such sensor systems frequently consist of inertial measurement units (IMUs), which are composed of accelerometers, gyroscopes and often combined with magnetometers. Previous research from our group showed the possibility of an 8 IMU sensor setup to track changes in running technique during a marathon ${ }^{2}$. This required heavy computations afterwards. In order to reduce computational load, a single IMU can be used to calculate 3D orientation, acceleration, velocity and position of selected body segments based on a strapdown inertial navigation algorithm (i.e., sensor fusion) ${ }^{3}$. This algorithm uses the angular velocity to estimate 3D orientation based on numerical integration, although this is prone to integration drift. Gyroscopes are also subject to errors (e.g., bias and thermo-mechanical white noise) ${ }^{3}$. When integrated, most errors become significant as they add up over time ${ }^{4}$. Drift in the estimated 3D orientation should be minimized as it affects the estimated acceleration rotated to the global coordinate system. Orientation drift corrections can be based on sensor fusion or domain-specific assumptions. Downsides of sensor fusion include; requiring multiple sensors, computationally heavy algorithms, and (often) an extensive calibration procedure. All of these can be a burden to runners. A domain-specific assumption often used during walking is the zero velocity update, which assumes the velocity of the foot to be zero during the stance phase ${ }^{5,6}$. This method is less suitable for running at higher velocities, as the stance phase is too short. A domain-specific assumption for orientation drift reduction in running based on a single gyroscope would equip us with a small sensor and a relatively simple algorithm to provide drift-free 3D orientation of a body segment during running without the need for an extensive calibration procedure.

Hence, the aim of this study was to investigate if the quasi-cyclical nature of running can be used to acquire drift-free 3D orientation of a body segment using a single gyroscope. Two methods for drift reduction are proposed and tested. Both methods depend on the assump-
tion that constant speed running in a straight line is quasi-cyclical and that consecutive gait cycles and their parameters (e.g., orientation) are therefore similar. Method 1 corrects the angular velocity to have a zero-mean before estimating orientation. Method 2 rotates angular velocities to a partly functional coordinate system, which reduces the motion of the tibia to a quasi-1D rotation before estimating orientation. We hypothesize that Method 2 will work best because 3D orientations are non-commutative and, therefore, the mean angular velocity does not need to be zero for a cyclical 3D movement.

## Material and Methods

## Orientation estimation

The orientation of the sensor coordinate system $\left(\psi^{s}\right)$ at any time with respect to the initial sensor coordinate system ( $\psi^{s, \text { init }}$ ) depends on the previous sensor orientation and the angular velocities measured in all three axes (Equation 5.1) ${ }^{7}$. The time-dependent rotation matrix $R_{s}^{s, i n i t}$ expresses the rotation from $\psi^{s}$ to $\psi^{s, i n i t}$. $\dot{R}_{s}^{s, i n i t}$ is the time derivative of $R_{s}^{s, \text { init }} . \tilde{\omega}_{s}$ is a skew-symmetric matrix consisting of the components of the angular velocity vector as measured in the sensor coordinate system $\psi^{s}$ (Equation 5.2) ${ }^{7} . R_{s}^{s, \text { init }}$ can then be transformed to quaternions to visualize orientations.

$$
\begin{align*}
& \dot{R}_{s}^{s, \text { init }}=R_{s}^{s, \text { init }} * \tilde{\omega}_{s}  \tag{5.1}\\
& \tilde{\omega}_{s}=\left[\begin{array}{ccc}
0 & -\omega_{z} & \omega_{y} \\
\omega_{z} & 0 & -\omega_{x} \\
-\omega_{y} & -\omega_{x} & 0
\end{array}\right] \tag{5.2}
\end{align*}
$$

## Errors and drift

A gyroscope can be modeled as Equation 5.3, where the relation between the estimated angular velocity $\hat{\omega}_{s}$ is based on the measurement of its actual value $\omega_{s}$ and is influenced by an estimated bias $\hat{b}$ and stochastic component $\sigma$, assuming that the gain is correct. The estimated bias $\hat{b}$ is assumed to be the actual bias $b$ plus a bias error $b_{e}$ (Equation 5.4).

$$
\begin{align*}
& \hat{\omega}_{s}=\omega_{s}+\hat{b}+\sigma  \tag{5.3}\\
& \hat{b}=b+b_{e} \tag{5.4}
\end{align*}
$$

It is expected that $b_{e}$ has the largest influence on orientation estimation drift since its effect grows linearly over time if the actual orientation is not changing. The effect of the stochastic component $\sigma$ is assumed to be minimal. If $b_{e}$ is the only major influence on the drift in the orientation estimation, the effect of $b_{e}$ on the orientation can be analyzed using Equation 5.2 and 5.1. Please note that errors in angular velocity components impact the derivative of the orientation matrix $\dot{R}_{s}^{s, \text { init }}$ in other axes (Equation 5.2).

## Method 1: Zero-mean

We assume that during constant speed running in a straight line, consecutive gait cycles and their parameters (e.g., orientation) are similar, and that $b_{e}$ would result in a drift in the orientation estimation. Furthermore, we assume that the quasi-cyclical movement is such that the mean angular velocity in each axis over a complete number of gait cycles is zero. Therefore, Method 1 consists of correcting for drift in orientation estimation by subtracting the mean angular velocity (assumed to be equal to $b_{e}$ ) of a complete number of gait cycles in each axis to acquire a zero-mean angular velocity $\omega_{s(z e r o-m e a n)}$.

## Method 2: Transformed coordinate system

Furthermore, we assume that rotations of the tibia during running are quasi-1D since they predominantly occur around the flexion/extension rotation axis perpendicular to the sagittal plane. Hence, Method 2 first rotates $\psi^{s}$ to a partly functional coordinate system $\psi^{p f}$, of which one axis is approximately perpendicular to the sagittal plane. Thereby we ensure that the angular velocity around this axis is considerably larger than the angular velocities around the other axes, thus, creating quasi-1D angular velocities. Principal component analysis is used to determine the axis around which most rotation occurs (Equation 5.5). This axis, the first principal component (PC1), is used to create the rotation matrix $R_{s}^{p f}$ (Equations 5.6 and 5.7) ${ }^{7}$. In Method 2, $R_{s}^{p f}$ is used to rotate the angular velocity from $\psi^{s}$ to $\psi^{p f}$, resulting in $\omega_{p f}$.

$$
\begin{align*}
& z_{s}^{p f}=P C 1 \times\left[\begin{array}{lll}
0 & 1 & 0
\end{array}\right]  \tag{5.5}\\
& y_{s}^{p f}=z_{s}^{p f} \times P C 1  \tag{5.6}\\
& R_{s}^{p f}=\left[\begin{array}{lll}
P C 1 ; & \frac{y_{s}^{p f}}{\left\|y_{s}^{p f}\right\|} ; & \frac{z_{s}^{p f}}{\left\|z_{s}^{p f}\right\|}
\end{array}\right] \tag{5.7}
\end{align*}
$$

For both methods, orientations are estimated with Equations 5.2 and 5.1. Orientations estimates of Method 1 are rotated to $\psi^{p f}$ with $R_{s}^{p f}$ to be able to compare them with the results of Method 2. Additionally, Methods 1 and 2 are combined by zero-mean correction of $\omega_{p f}$, resulting in $\omega_{p f(z e r o-m e a n), ~ b e f o r e ~ o r i e n t a t i o n ~ e s t i m a t i o n ~ w i t h ~ E q u a t i o n s ~} 5.2$ and 5.1.

## Participants and measurement setup

The measurement was performed with one healthy male subject with running experience (age: 22 years, mass: 70.0 kg , height: 1.76 m ). The subject signed informed consent and the measurements were conducted in accordance with the Declaration of Helsinki. The subject ran for 90 seconds at $12 \mathrm{~km} / \mathrm{h}$ on a treadmill (ForceLink, Culemborg, the Netherlands). Angular velocities were collected with a wireless IMU (MTw Awinda, Xsens Technologies B.V., the Netherlands) with a sampling frequency of 100 Hz . The weight of the sensor was 16 grams and the signal range of the gyroscope $\pm 2000 \mathrm{deg} / \mathrm{s}$. The IMU was placed on the medial proximal side of the right tibia and fixated with double-sided tape between the skin and the sensor and adhesive tape over the sensor.

## Data analysis

Complete trials were cut into time-normalized gait cycles. Gait cycles started and ended with a falling edge zero crossing of $\omega_{s, y}$. This moment occurs just before initial contact. Quaternions were used to visualize rotations with respect to the initial orientation (i.e., first falling edge zero crossing of $\omega_{s, y}$ during the trial). A quaternion consists of a scalar $q_{0}$ and a vector part $\mathbf{q}$ (Equation 5.8) ${ }^{8}$. With the scalar part, the magnitude of the rotation between the initial orientation and another orientation can be shown. If $q_{0}=1$ this indicates that there is no orientation difference while $q_{0}=0$ indicates a rotation of $180^{\circ}$ with respect to the initial orientation. The amount of orientation drift for the different methods is visually compared based on the scalar part of the quaternion and the (mean) standard deviation of the vector part of the quaternion. Data were analyzed offline in MATLAB R2016b.

$$
\begin{equation*}
q=q_{0}+\mathbf{q}=q_{0}+\left(i q_{1}+j q_{2}+k q_{3}\right) \tag{5.8}
\end{equation*}
$$

## Results

The angular velocity without drift reduction shows a small standard deviation (Figure 5.1). Scalar and vector parts of the quaternions for the drift reduction methods are shown in Figure 5.2 and Figure 5.3. If the estimated 3D rotations were exactly cyclical, the quaternion scalar part would reach a value of approximately 1 during each gait cycle and the standard deviation of the vector part of the quaternion would be small. Mean standard deviations of the quaternion vector parts are shown in Table 5.1.


Figure 5.1: Mean angular velocity in $\psi^{s}$ as a function of the gait cycle. Shaded areas represent standard deviations around the mean.


Figure 5.2: The scalar part of the quaternions as a function of time. $A, B$ and $C$ show respectively the results with no drift reduction, zero-mean (Method 1), and transformation to a partly functional coordinate system (CS) $\psi^{f}$ (Method 2).


Figure 5.3: The vector parts of the quaternions in $\psi^{p f}$ as a function of the gait cycle. $A, B$ and $C$ show respectively the results with no drift reduction, zero-mean (Method 1), and transformation to a partly functional coordinate system (CS) $\psi^{p f}$

Table 5.1: Mean standard deviation of the quaternion vector parts for the different drift reduction methods, including the combination of Method 1 and 2 (i.e., transformed coordinate system and zero-mean). CS = Coordinate system.

|  | No drift reduction | Method 1: <br> Zero-mean | Method 2: <br> Transformed CS | Method 1+2 |
| :--- | :--- | :--- | :--- | :--- |
| q1 | 0.12 | 0.12 | 0.10 | 0.12 |
| q2 | 0.22 | 0.57 | 0.04 | 0.63 |
| q3 | 0.61 | 0.41 | 0.05 | 0.29 |

## Discussion

The aim of this study was to investigate if the quasi-cyclical nature of running can be used for drift-free 3D orientation of a body segment using a single gyroscope. This study showed that orientation drift could be drastically reduced by transforming angular velocities to a different coordinate system (i.e., Method 2) before estimating 3D orientations. The assumption that running at a constant speed and in a straight line is a quasi-cyclical motion is strengthened by the small standard deviation in the angular velocity (Figure 5.1).

Method 1 assumes that the mean angular velocity during quasi-cyclical running motion should be approximately zero. Therefore, Method 1 subtracts the mean of the angular velocity from each axis over a complete number of gait cycles before estimating 3D orientation. Method 1 did not result in an orientation drift reduction, as shown by the scalar part of the quaternion moving away from 1 (Figure 5.2b) and no reduction in the standard deviation of the vector part of the quaternion compared to no drift reduction (Table 5.1, Figure 5.3b). The angular velocity contains two dominant axes $\omega_{s, y}$ and $\omega_{s, z}$ (Figure 5.1), indicating that the quasi-1D rotation of the tibia is not around a single axis in the sensor coordinate system. Since 3D rotations are non-commutative, rotations in both dominant axes influence the orientation of the sensor coordinate system, resulting in Method 1 failing to decrease drift in orientation. Please note that the errors in cyclical orientation estimation without subtraction of mean angular velocities (Figure 5.2a and Figure 5.3a) may already reduce by increasing the sampling rate of the angular velocity.

To avoid the problem with non-commutative 3D orientations, Method 2 rotates the angular velocity to a partly functional coordinate system, in which the rotation of the tibia occurs mainly around a single axis (flexion/extension). Therefore, a quasi-1D situation is created before 3D orientations are estimated. Method 2 drastically decreased the drift in orientation estimation, as shown by the quaternion scalar part remaining closer to 1 (Figure 5.2c) and the standard deviation of the quaternion vector part being smaller than with no drift reduction or with Method 1 (Table 5.1, Figure 5.3c). However, there is still drift present in the 3D orientation estimation, as shown by the tendency of the scalar part of the quaternion to move away from 1 over the duration of the trial. Additional subtraction of the mean angular velocity in $\psi^{p f}$ before integration (combination of Method 1 and 2) did not improve drift reduction but resulted in larger standard deviations of the vector parts of the quaternions (Table 5.1). This indicates that transforming to a quasi-1D situation helped in reducing orientation drift
but residual rotations around the other two axes are still present. Therefore subtraction of mean angular velocities according to Method 1 does not result in further improvement in estimating cyclical 3D rotations.

The reason for the errors in cyclical orientation estimation in Method 1 is clearly not due to an error in angular velocity bias but to the interactions of angular velocities around different axes according to Equations 5.2 and 5.1, which may reduce if a higher sampling rate would be used. This would need to be further tested. Please note that this interaction can be effectively reduced at the currently applied sampling rate by rotation to a partly functional coordinate system $\psi^{p f}$ with one axis being the principle component of the rotation, directed approximately perpendicular to the sagittal plane (Method 2). This reduced interaction is clearly seen in Equation 5.2 if only $\omega_{x}$ is assumed to be non-zero.

This study showed that transforming angular velocities to a partly functional coordinate system before integration seems to be a promising method for reducing drift in 3D orientation based on a single gyroscope in running. As such, partly functional body segment orientations can be used to define running technique with a single gyroscope instead of using an IMU consisting of an accelerometer, gyroscope, and magnetometer, and eventually contribute to reducing injury risk. In future work, the drift reduction method should be adapted such that accurate 3D orientation estimates can be made for a longer duration, and this method should be validated in a larger group of runners.

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## Chapter 6

## Drift-free 3D orientation and displacement estimation for quasi-cyclical movements using one inertial measurement unit <br> Application to running

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The data presented in this study are openly available in 4TU.ResearchData.


#### Abstract

A Drift-Free 3D Orientation and Displacement estimation method (DFOD) based on a single inertial measurement unit (IMU) is proposed and validated. Typically, body segment orientation and displacement methods rely on a constant- or zero-velocity point to correct for drift. Therefore, they are not easily applicable to more proximal segments than the foot. DFOD uses an alternative single sensor drift reduction strategy based on the quasi-cyclical nature of many human movements. DFOD assumes that the quasi-cyclical movement occurs in a quasi-2D plane and with an approximately constant cycle average velocity. DFOD is independent of a constant- or zero-velocity point, a biomechanical model, Kalman filtering or a magnetometer. DFOD reduces orientation drift by assuming a cyclical movement, and by defining a functional coordinate system with two functional axes. These axes are based on the mean acceleration and rotation axes over multiple complete gait cycles. Using this driftfree orientation estimate, the displacement of the sensor is computed by again assuming a cyclical movement. Drift in displacement is reduced by subtracting the mean value over five gait cycles from the free acceleration, velocity, and displacement. Estimated 3D sensor orientation and displacement for an IMU on the lower leg were validated with an optical motion capture system (OMCS) in four runners during constant velocity treadmill running. Root mean square errors for sensor orientation differences between DFOD and OMCS were $3.1 \pm 0.4^{\circ}$ (sagittal plane), $5.3 \pm 1.1^{\circ}$ (frontal plane), and $5.0 \pm 2.1^{\circ}$ (transversal plane). Sensor displacement differences had a root mean square error of $1.6 \pm 0.2 \mathrm{~cm}$ (forward axis), $1.7 \pm$ 0.6 cm (mediolateral axis), and $1.6 \pm 0.2 \mathrm{~cm}$ (vertical axis). Hence, DFOD is a promising 3D drift-free orientation and displacement estimation method based on a single IMU in quasicyclical movements with many advantages over current methods.


## Introduction

Activities like walking, running, swimming, rowing, and skating are all quasi-cyclical in nature. The repetitiveness of these movements, and their associated loads on the human body, can result in overuse injuries ${ }^{1}$. Repetitive movements are often studied inside movement analysis laboratories for insight into overloading of the human body and performance enhancement, among other applications. With the introduction of wearable systems, motion analysis is no longer restricted to a controlled lab setting ${ }^{2,3}$. This opens up new possibilities of analyzing movements that are difficult to measure in a lab, due to technical constraints of optical motion capture systems (OMCS).

Inertial measurement units (IMUs) are widely used in wearable motion capture systems due to their small size and ease of use ${ }^{4}$. IMUs are composed of accelerometers, gyroscopes, and are often combined with magnetometers. The acceleration, orientation, and displacement of a sensor are of interest for many motion analysis applications such as impact analyses, monitoring the range of motion (ROM), or inclination of a body segment, e.g., the lower leg ${ }^{5,6}$. To obtain orientation and displacement from sensor accelerations and angular velocities, the orientation of the sensor in the global coordinate system (CS) $\left(\psi^{g l}\right)$ is required. Displacement can then be obtained via strapdown inertial navigation, although this process is prone to errors ${ }^{7}$. Drift in estimated 3D orientations should be minimized as it strongly influences the estimated displacement in $\psi^{g l}$. Drift can be compensated for by incorporating other sensors (i.e., magnetometer). However, drift reduction and 3D orientation estimation become more challenging during highly dynamic movements, prolonged measurements, or when magnetic distortions are present ${ }^{8}$. Drift can alternatively be reduced by applying domain-specific assumptions, such as the zero-velocity update method ${ }^{9,10}$.

The zero-velocity update method assumes that the velocity of the foot is zero and the orientation of the foot is known during the stance phase. This information is used to reset drift in orientation, velocity, and position during each gait cycle ${ }^{9,10}$. Similar assumptions have been used in running in specific conditions. Bailey and Harle corrected for positional drift of an IMU on the foot by using a constant-velocity update in runners with a heel strike ${ }^{11}$. However, constant- or zero-velocity assumptions are not suitable for more proximal segments or runners with a forefoot strike, since a constant- or zero-velocity point is often not present ${ }^{12}$.

To estimate orientation and displacement using a single IMU placed on body segments without a constant- or zero-velocity point, the quasi-cyclical nature of numerous movements can be used. Kalman filtering or analytical integration of acceleration in combination with assumptions about the quasi-cyclical nature of movements have been used to estimate displacements of, for example, the pelvis during walking ${ }^{13-15}$. These studies involved relatively slow movements, required multiple sensors, a calibration procedure, or prior information about the movements. As a solution to many of these drawbacks, we propose to directly use the quasi-cyclical nature of movements to estimate 3D orientation and displacement using a single IMU without the need for Kalman filtering. Hence, the research question of this study was: How to estimate 3D orientation and displacement of a single IMU on the lower leg using the quasi-cyclical nature of running?

To answer this research question, a method is proposed in which drift-free 3D orientation and displacement of a single IMU are estimated using the quasi-cyclical nature of numerous human movements. We call this method Drift-Free Orientation and Displacement estimation (DFOD). DFOD assumes that the movement is quasi-cyclical, occurs in a quasi-2D plane, and has an approximately constant cycle average velocity. DFOD will be demonstrated in treadmill running, although it is expected to generalize to many quasi-cyclical quasi-2D movements.

## Materials and methods

Validation of DFOD was part of a larger study. For sake of clarity, only measurement systems and trials required for validation of DFOD will be described.

## Participants

Four healthy recreational runners participated in this study (2M/2F, age: $30.6 \pm 9.2$ years, height: $181 \pm 4 \mathrm{~cm}$, body mass: $65.0 \pm 5.4 \mathrm{~kg}$ ). The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of METC Twente. All participants gave written informed consent before participating in the study.

## Protocol

Subjects ran for 2 min on a level treadmill at $3.6 \mathrm{~m} / \mathrm{s}$. To validate DFOD with OMCS, a calibration procedure was performed in which subjects stood still in a neutral pose and flexed and extended their leg four times while keeping their upper leg horizontal. This calibration procedure was not required for DFOD but was used to convert the OMCS orientation and displacement estimates to the same CS as used in DFOD for comparison purposes.

## Measurement systems

Subjects ran on a treadmill (C-Mill, ForceLink, Culemborg, The Netherlands) while 3D angular velocities and accelerations were captured by a single IMU on the lower leg at 240 Hz (MVN Link, Xsens, Enschede, The Netherlands). The ranges of the accelerometer and angular velocity sensor were $\pm 16 \mathrm{~g}$ and $\pm 2000 \%$, respectively. Positional data from a cluster marker set on the lower leg were captured for reference measurements with an eightcamera optical motion capture system (OMCS) at 100 Hz (Vantage, Vicon, Oxford, UK). The cluster marker set consisted of four individual markers attached to a rigid plate. The IMU was placed medially to the tibial tuberosity and the cluster marker set was placed below the IMU, both on the flat surface of the tibia to ensure measurements of tibia motion, see Figure 6.1. Both systems were attached to the skin with double-sided tape and covered with stretched strapping tape.


Figure 6.1: Overview of $I M U$ and cluster marker set placement. "M1", "M2", and "M3" refer to the individual markers of the cluster marker set. The shown coordinate system is the functional coordinate system $\psi^{f}$. The X-axis points forward (running direction), the $Y$-axis mediolateral, and the Z-axis upward.

## Data preparation

Optical and inertial data of the left or right lower leg were selected based on minimal OMCS marker occlusion. Optical data were upsampled to 240 Hz with linear interpolation and low-pass filtered with a recursive fourth-order 20 Hz Butterworth filter ${ }^{16}$. Inertial data were not filtered.

Data were segmented into gait cycles based on falling edge angular velocity zero-crossings in the sensor $\mathrm{CS}\left(\psi^{s}\right) Y$-axis, which was directed in the global $\mathrm{CS}\left(\psi^{g l}\right)$ forward/mediolateral direction. These zero-crossings occur shortly before initial contact. Data were cropped to include all complete gait cycles during one minute of running, hereby excluding around $30-45$ s of data in which the subject increased their running speed from standing still up
to $3.6 \mathrm{~m} / \mathrm{s}$. Sensor acceleration and angular velocity in $\psi^{s}$ (i.e., input signals for DFOD) as a function of the time-normalized gait cycle for a representative subject are shown in Figure 6.2. Data analysis was performed in MATLAB R2021a.


Figure 6.2: Three-dimensional sensor acceleration (i.e., including gravity) (left figure) and sensor angular velocity (right) in $\psi^{s}$ as a function of the time-normalized gait cycle for a representative subject. Solid lines represent the mean while shaded areas represent the standard deviation around the mean over one minute of running. Note that these two signals are the input for the orientation and displacement estimation algorithm. Positive acceleration values represent an acceleration into the upward, sideward (left), and forward direction of $\psi^{s}$. Positive angular velocity values represent anti-clockwise rotations in $\psi^{s}$.

## Estimate sensor orientation in a functional CS ( $\psi^{f}$ )

The aim of DFOD is to estimate 3D orientation and displacement of a single sensor in a functional $\mathrm{CS}\left(\psi^{f}\right)$ of which the vertical and mediolateral axes are fixed and the origin moves with the body at the cycle average velocity. $\psi^{f}$ is defined in Figure 6.1 and Figure 6.3. DFOD assumes that the body segment on which the sensor is placed:

- moves quasi-cyclical (i.e., cycles are similar)
- moves in a quasi-2D plane (i.e., most movement occurs in a 2D plane)
- has an approximately constant cycle average velocity

The time- and gait cycle-dependent rotation matrix $R_{s, i}^{f}(t)$ from $\psi^{s}$ to $\psi^{f}$, representing the sensor orientation in a functional drift-free CS of which the vertical and mediolateral axes are fixed and the origin moves with the body at the cycle average velocity, can be written as three subsequent rotations as in Equation 6.1:

$$
\begin{equation*}
R_{s, i}^{f}(t)=R_{d f, i}^{f} R_{p f}^{d f}(t) R_{s}^{p f} \tag{6.1}
\end{equation*}
$$

where the sensor CS $\left(\psi^{s}\right)$ is first rotated to a sensor-fixed partly functional CS $\left(\psi^{p f}\right)$ with the time-independent rotation matrix from $\psi^{s}$ to $\psi^{p f}\left(R_{s}^{p f}\right)$. Then, $\psi^{p f}$ is rotated to a drifting partly functional $\operatorname{CS}\left(\psi^{d f}\right)$ with the time-dependent rotation matrix from $\psi^{p f}$ to $\psi^{d f}$ ( $\left.R_{p f}^{d f}(t)\right) . \psi^{d f}$ has an origin that moves with the cycle average velocity. Lastly, drift in $\psi^{d f}$ is corrected for each gait cycle $i$ by rotating to a functional drift free $\operatorname{CS}\left(\psi^{f}\right)$ with the gait cycle-dependent rotation matrix from $\psi^{d f}$ to $\psi^{f}\left(R_{d f, i}^{f}\right)$. All rotations are visualized in Figure 6.3.


Figure 6.3: Summary of DFOD (left four columns) and the validation of DFOD (right two columns). Columns represent different coordinate systems (CS). For each CS some basic information is stated: symbol, name, measurement system on which the CS is based, origin, fixed functional axes (i.e., which axes have functional meaning), and the presence of drift. Available quantities in each CS are shown in white squares (all time-dependent), rotation matrices from one CS to another are shown in blue arrows, curved arrows at the top represent the different rotations which are referred to in the text, integrations over time are shown as green arrows. At the bottom of the figure, a schematic representation of the CS with respect to the lower leg of a runner is shown, orange boxes represent the $I M U$, and blue dots represent the cluster marker set. DFOD is validated against an OMCS based on the quantities in the red squares. Note that the CSs in grey (two right columns) are only used for validation of DFOD and are not a part of DFOD. IMU = inertial measurement unit; OMCS = optical motion capture system; GCZM = gait cycle zero mean (mean value over each gait cycle is subtracted from the gait cycle); CS = coordinate system; $\vec{a}_{C S}=$ acceleration expressed in the CS in the subscript; $\vec{\omega}_{C S}=$ angular velocity expressed in the CS in the subscript; $\vec{a}_{f, f a, G C Z M}=$ free acceleration (fa) with a gait cycle zero mean average (GCZM) expressed in the functional CS (f); $R_{C S 1}^{C S 2}=$ rotation matrix from CS 1 to CS 2; $\vec{v}=$ velocity; $\vec{s}=$ displacement; $\vec{p}=$ position, $i=$ index of gait cycle.

## Rotation 1

## From sensor CS $\left(\psi^{s}\right)$ to partly functional CS $\left(\psi^{p f}\right)$

Integration error accumulation can be reduced by aligning the rotation axis of a quasi-2D movement with one axis in 3D space to create a partly functional CS $\left(\psi^{p f}\right)^{17}$. One axis has functional and anatomical meaning in $\psi^{p f}$. The functional axis ( $\vec{y}_{p f}^{s}$, the $y$-axis of the sensorfixed partly functional $\operatorname{CS}\left(\psi^{p f}\right)$ expressed in the sensor $\left.\operatorname{CS}\left(\psi^{s}\right)\right)$ is perpendicular to the plane of movement. Therefore, this axis is described by the first principal component of the angular velocity in $\psi^{s}\left(\vec{\omega}_{s}\right)$, measured by the 3D angular velocity sensor of the IMU, over one minute of running ${ }^{18}$ :

$$
\begin{equation*}
\vec{y}_{p f}^{s}=P C A 1\left(\vec{\omega}_{s}\right) \tag{6.2a}
\end{equation*}
$$

To create a rotation matrix from $\psi^{p f}$ to $\psi^{s}$, a temporary X -axis is defined by arbitrarily setting the X -axis of $\psi^{p f}\left(\vec{x}^{\prime}{ }_{p f}\right)$ to the X -axis of $\psi^{s}$ :

$$
\vec{x}_{p f}^{\prime s}=\left[\begin{array}{lll}
1, & 0, & 0 \tag{6.2b}
\end{array}\right]
$$

The Z-axis of $\psi^{p f}\left(\vec{z}_{p f}^{s}\right)$ was computed and $\vec{x}^{\prime}{ }_{p f}^{s}$ updated to ensure an orthogonal CS according to the TRIAD algorithm ${ }^{19}$ :

$$
\begin{align*}
& \vec{z}_{p f}^{s}=\vec{x}^{\prime}{ }_{p f}^{s} \times \vec{y}_{p f}^{s}  \tag{6.2c}\\
& \vec{x}_{p f}^{s}=\vec{y}_{p f}^{s} \times \vec{z}_{p f}^{s} \tag{6.2d}
\end{align*}
$$

The time-invariant orthonormal rotation matrix from $\psi^{p f}$ to $\psi^{s}$ was:

$$
R_{p f}^{s}=\left[\begin{array}{ccc}
\vec{x}_{p f}^{s}  \tag{6.2e}\\
\left\|\vec{x}_{p f}^{s}\right\| & \frac{\vec{y}_{p f}^{s}}{\left\|\vec{y}_{p f}^{s}\right\|} ; & \| \vec{z}_{p f}^{s} \\
\left\|\vec{z}_{p f}^{s}\right\|
\end{array}\right]
$$

The time-invariant rotation matrix from $\psi^{s}$ to $\psi^{p f}\left(R_{s}^{p f}\right)$ was obtained by taking the inverse of $R_{p f}^{s}$ (Equation 6.2e):

$$
\begin{equation*}
R_{s}^{p f}=R_{p f}^{s}-1 \tag{6.2f}
\end{equation*}
$$

## Rotation 2

From partly functional CS $\left(\psi^{p f}\right)$ to drifting partly functional CS $\left(\psi^{d f}\right)$
To go from a sensor-fixed CS to a drifting CS in which axes do not depend on the sensor orientation, the angular velocity in $\psi^{p f}\left(\vec{\omega}_{p f}\right)$ was integrated according to Bortz ${ }^{20,21}$. $\vec{\omega}_{p f}$ was expressed as a skew-symmetric matrix ( $\tilde{\omega}_{p f}$ ), and the differential equation was solved and used to obtain the rotation matrix from $\psi^{p f}$ to $\psi^{d f}\left(R_{p f}^{d f}\right)$ :

$$
\begin{align*}
& \tilde{\omega}_{p f}(t)=\left(\begin{array}{ccc}
0 & -\omega_{p f, z}(t) & \omega_{p f, y}(t) \\
\omega_{p f, z}(t) & 0 & -\omega_{p f, x}(t) \\
-\omega_{p f, y}(t) & -\omega_{p f, x}(t) & 0
\end{array}\right)  \tag{6.3a}\\
& \dot{R}_{p f}^{d f}(t)=R_{p f}^{d f}(t) \tilde{\omega}_{p f}(t) \tag{6.3b}
\end{align*}
$$

$\dot{R}_{p f}^{d f}(t)$ is the time-derivative of $R_{p f}^{d f}(t)$, and $R_{p f}^{d f}(t)$ at $t=0$ is the identity matrix. Note that $\psi^{d f}$ drifts, predominantly around the $y$-axis $\left(\psi_{y}^{d f}\right)$, due to accumulated integration errors from Equations 6.3a and 6.3b. This drift needs to be corrected to get a useful orientation estimate of the sensor (rotation 3 in Figure 6.3).

## Rotation 3

From drifting partly functional CS $\left(\psi^{d f}\right)$ to drift-free functional CS $\left(\psi^{f}\right)$
Following an assumption of quasi-cyclical running, the lower leg keeps rotating around the same mediolateral axis. By continuously calculating this rotation axis we can correct for integration drift from Equation 6.3a and 6.3b. The rotation axis was again based on the first principal component of the 3D angular velocity, now in $\psi^{d f}\left(\vec{\omega}_{d f}\right)$, over five complete gait cycles (Equation 6.4a). Multiple gait cycles were included to obtain a more robust estimate of $\vec{y}_{d f, i}^{f}$ (see section "Algorithm characteristics"):

$$
\begin{align*}
& \vec{y}_{d f, i}^{f}=P C A 1\left(\vec{\omega}_{d f}(t)\right) \\
& \qquad t_{0_{i}}-T_{i-1}-T_{i-2}<t<t_{0_{i}}+T i+T_{i+1}+T_{i+2} \tag{6.4a}
\end{align*}
$$

Where $t_{0_{i}}-T_{i-1}-T_{i-2}<t<t_{0_{i}}+T i+T_{i+1}+T_{i+2}$ represents the interval of five complete gait cycles, $t_{0_{i}}$ stands for the first time point of gait cycle $i, T_{i}$ stands for the duration of gait cycle $i$, and is obtained from the earlier described falling edge angular velocity
zero-crossings in $\psi_{y}^{s}$ (See section "Data preparation"). Note that the first principal component of the angular velocity is obtained twice (Equation 6.2a and Equation 6.4a). In Equation 6.2a, $\vec{y}_{s}^{p f}$ has a constant value over a longer period of time since there is no drift in $\psi^{s}$. In Equation 6.4a, the angular velocity $\left(\vec{\omega}_{d f}\right)$ is expressed in a drifting $\operatorname{CS}\left(\psi^{d f}\right)$. Therefore, $\vec{y}_{d f, i}^{f}$ differs for each gait cycle to correct for the drift in $\psi^{d f}$.

Following an assumption of approximately constant cycle average velocity running, the free acceleration in $\psi^{f}$ will be approximately zero-mean over a complete gait cycle. Hence, the mean total acceleration (i.e., including gravity) over a complete number of gait cycles represents the gravitational acceleration and is directed vertically. Therefore, the temporary Z-axis of the functional CS $\psi^{f}\left(\vec{z}^{\prime}{ }_{d f}^{f}\right)$ was based on the average total acceleration (i.e., including gravity) in $\psi^{d f}\left(\vec{a}_{d f}\right)$, over five complete gait cycles (Equation 6.4 b ). Multiple gait cycles were included to obtain a more robust estimate of $\vec{z}^{\prime}{ }_{d f}^{f}$ (see section "Algorithm characteristics"):

$$
\begin{equation*}
\vec{z}^{\prime}{ }_{d f, i}^{f}=\frac{1}{\sum_{j=-2}^{+2} T_{i+j}} \int_{t_{0_{i}}-T_{i-1}-T_{i-2}}^{t_{0_{i}}+T_{i}+T_{i+1}+T_{i+2}} \vec{a}_{d f}(\tau) d \tau \tag{6.4b}
\end{equation*}
$$

where $j$ is an index to define included gait cycles. The x-axis of $\psi^{d f}\left(\vec{x}_{d f}^{f}\right)$ was computed and $\vec{z}^{\prime}{ }_{d f, i}^{f}$ updated to ensure an orthogonal CS according to the TRIAD algorithm ${ }^{19}$ :

$$
\begin{align*}
& \vec{x}_{d f, i}^{f}=\vec{y}_{d f, i}^{f} \times \vec{z}^{\prime}{ }_{d f, i}^{f}  \tag{6.4c}\\
& \vec{z}_{d f, i}^{f}=\vec{x}_{d f, i}^{f} \times \vec{y}_{d f, i}^{f} \tag{6.4d}
\end{align*}
$$

The orthonormal drift-correcting rotation matrix from $\psi^{d f}$ to $\psi^{f}$ was:

$$
\begin{equation*}
R_{d f, i}^{f}=\left[\frac{\vec{x}_{d f, i}^{f}}{\left\|\vec{x}_{d f, i}^{f}\right\|} ; \quad \frac{\vec{y}_{d f, i}^{f}}{\left\|\vec{y}_{d f, i}^{f}\right\|} ; \quad \frac{\vec{z}_{d f, i}^{f}}{\left\|\vec{z}_{d f, i}^{f}\right\|}\right] \tag{6.4e}
\end{equation*}
$$

where $R_{d f, i}^{f}$ has a constant value within each cycle but varies over cycles to correct for drift. The drift-free 3D rotation matrix of the sensor in a functional $\mathrm{CS}\left(R_{s, i}^{f}\right)$ of which the vertical and mediolateral axes are fixed, and the origin moves with the body at the cycle average velocity was then computed with Equation 6.1.

## From sensor orientation to sensor displacement

Three-dimensional angular velocity and total (i.e., including gravity) acceleration in $\psi^{f}\left(\vec{\omega}_{f}\right.$ and $\vec{a}_{f}$ ) were obtained with Equation 6.1. Free acceleration in $\psi^{f}\left(\vec{a}_{f, f a}\right)$ was obtained by subtracting the modulus of the gravitational acceleration $\left(\vec{g}_{f}\right)$ from the total acceleration $\left(\vec{a}_{f}\right)$ :

$$
\vec{a}_{f, f a}(t)=\vec{a}_{f}(t)-\left[\begin{array}{lll}
0, & 0, & \left.\left\|\vec{g}_{f}\right\|\right] \tag{6.5a}
\end{array}\right.
$$

Following an assumption of approximately constant cycle average velocity, the free acceleration in $\psi^{f}$ will be approximately zero-mean over a complete number of gait cycles. Hence, the mean free acceleration value over a window of five gait cycle was subtracted to correct for drift:

$$
\begin{array}{r}
\vec{a}_{f, f a, G C Z M}(t)=\vec{a}_{f, f a}(t)-\frac{1}{T_{i}} \int_{t_{0_{i}}-T_{i-1}-T_{i-2}}^{t_{0_{i}}+T_{i}+T_{i+1}+T_{i+2}} \vec{a}_{f, f a}(\tau) d \tau \\
\quad t_{0_{i}} \leq t \text { and } t_{0_{i}}+T_{i}>t
\end{array}
$$

where $\vec{a}_{f, f a, G C Z M}$ is the free acceleration with a gait cycle zero-mean (GCZM). $\vec{a}_{f, f a, G C Z M}$ was numerically integrated (Figure 6.3, Column $\psi^{f}$, upper green arrow) with the trapezoidal rule to obtain the velocity $\left(\vec{v}_{f}\right)$ :

$$
\begin{equation*}
\vec{v}_{f}(t)=\int_{t_{0_{i}}}^{t} \vec{a}_{f, f a, G C Z M}(\tau) d \tau \tag{6.6a}
\end{equation*}
$$

Following an assumption of approximately constant cycle average velocity, the mean velocity in $\psi^{f}$ over a complete number of gait cycles is approximately zero in all axes since the origin of $\psi^{f}$ moves with the body at the cycle average velocity. Hence, the drift-corrected GCZM velocity was computed by subtracting the mean velocity over a window of five gait cycles:

$$
\begin{align*}
& \vec{v}_{f, G C Z M}(t)=\vec{v}_{f}(t)-\frac{1}{T_{i}} \int_{t_{0_{i}}-T_{i-1}-T_{i-2}}^{t_{0_{i}}+T_{i}+T_{i+1}+T_{i+2}} \quad \vec{v}_{f}(\tau) d \tau  \tag{6.6b}\\
& t_{0_{i}} \leq t \text { and } t_{0_{i}}+T_{i}>t
\end{align*}
$$

Sensor displacement in $\psi^{f}\left(\vec{s}_{f}\right)$ was obtained with the trapezoidal rule and numeric integration of $\vec{v}_{f, G C Z M}$ (Figure 6.3, Column $\psi^{f}$, lower green arrow):

$$
\begin{equation*}
\vec{s}_{f}(t)=\int_{t_{0_{i}}}^{t} \vec{v}_{f, G C Z M}(\tau) d \tau \tag{6.7a}
\end{equation*}
$$

Following an assumption of approximately constant cycle average velocity, the mean displacement in $\psi^{f}$ approximates zero is all directions over a complete number of gait cycles. Hence, the mean displacement over five gait cycles was subtracted and GCZM displacement ( $\vec{s}_{f, G C Z M}$ ) was computed and used as outcome measure:

$$
\begin{align*}
& \vec{s}_{f, G C Z M}(t)=\vec{s}_{f}(t)-\frac{1}{T_{i}} \int_{t_{0_{i}}-T_{i-1}-T_{i-2}}^{t_{0_{i}}+T_{i}+T_{i+1}+T_{i+2}} \quad \vec{s}_{f}(\tau) d \tau  \tag{6.7b}\\
& t_{0_{i}} \leq t \text { and } t_{0_{i}}+T_{i}>t
\end{align*}
$$

## Validation of orientation and displacement estimates

The steps described below are used to validate DFOD and are not part of DFOD. To compare the results of DFOD against OMCS, the orientation of the cluster marker set was computed and both the orientation and displacement were transformed to $\psi^{f}$.

## Rotation 4

From optical motion capture $\operatorname{CS}\left(\psi^{c l}\right)$ to functional CS $\left(\psi^{f}\right)$
The orientation of the OMCS cluster marker set in ( $\psi^{g l}$ ) was based on the relative positions of three of its individual markers according to the TRIAD algorithm ${ }^{19}$ :

$$
\begin{align*}
& \vec{z}_{c l}^{g l}(t)=\vec{p}_{g l, m 2}(t)-\vec{p}_{g l, m 1}(t)  \tag{6.8a}\\
& \vec{y}_{c l}^{\prime g l}(t)=\vec{p}_{g l, m 3}(t)-\vec{p}_{g l, m 1}(t) \tag{6.8b}
\end{align*}
$$

where $\vec{p}_{g l, m}$ refers to the position of the individual markers of the cluster marker set in $\psi^{g l}$, see Figure 6.1. $\vec{z}_{c l}^{g l}$ and $\vec{y}^{\prime}{ }_{c l}^{g l}$ represent the Z-axis and temporary $Y$-axis of the cluster marker CS $\left(\psi^{c l}\right)$ in $\psi^{g l}$. The X-axis of $\psi^{c l}\left(\vec{x}_{c l}^{g l}\right)$ was computed and $\vec{y}^{\prime}{ }_{c l}^{g l}$ updated to ensure an orthogonal CS:

$$
\begin{align*}
\vec{x}_{c l}^{g l}(t) & =\vec{y}_{c l}^{g l}(t) \times \vec{z}_{c l}^{g l}(t)  \tag{6.8c}\\
\vec{y}_{c l}^{g l}(t) & =\vec{z}_{c l}^{g l}(t) \times \vec{x}_{c l}^{g l}(t) \tag{6.8d}
\end{align*}
$$

The orthonormal rotation matrix of $\psi^{c l}$ to $\psi^{g l}\left(R_{c l}^{g l}\right)$ was:

$$
R_{c l}^{g l}(t)=\left[\begin{array}{ll}
\frac{\vec{x}_{c l}^{g l}(t)}{\left\|\vec{x}_{c l}^{g l}(t)\right\|} ; & \frac{\vec{y}_{c l}^{g l}(t)}{\left\|\vec{y}_{c l}^{g l}(t)\right\|} ; \tag{6.8e}
\end{array} \frac{\frac{z_{c l}^{g l}(t)}{\left\|\vec{z}_{c l}^{g l}(t)\right\|}}{\|}\right]
$$

To be comparable, the 3D orientation and position of the OMCS cluster marker set need to be expressed in the same functional CS as used for the sensor orientation and displacement estimate of DFOD. Therefore, the OMCS functional Y-axis $\left(\psi_{y}^{f}\right)$ in $\psi^{g l}\left(\vec{y}_{f}^{g l}\right)$ should be based on the same functional axis as in Equation 6.4a. However, differentiating $R_{c l}^{g l}(t)$ and computing the first principal component is prone to stochastic errors induced by differentiating 3D orientations. Alternatively, we estimated the rotation axis of the lower leg ( $\vec{y}_{f}^{g l}$ ) during the flexion-extension movements of the calibration trial, described in the section "Protocol" . During the flexion-extension movements, the lower leg moves approximately around the same rotation axis. This rotation axis $\left(\vec{y}_{f}^{g l}\right)$ was estimated by first dividing each of the four flexion-extension movements into seven intervals of equal duration ( $\frac{T_{i}}{7}$ ), $T_{i}$ being the duration of cycle $i$. See Section about algorithm characteristics. By using a larger time interval, the change in rotation during this interval is relatively large compared to the errors. The rotation matrix from time point $t_{j}=t_{i}+j \times \frac{T_{i}}{7}$ to the next was then computed as follows:

$$
\begin{equation*}
R_{t_{j}}^{t_{j+1}}=R_{c l}^{g l}\left(t_{j}\right)^{-1} R_{c l}^{g l}\left(t_{j+1}\right) \tag{6.9a}
\end{equation*}
$$

Subsequently, $R_{t_{j}}^{t_{j+1}}$ of cycle $i$ was transformed to a rotation axis ( $\vec{v}_{r o t, i, j}$ ) which corresponds to the vector part of a quaternion that can be derived from a rotation matrix ${ }^{22}$. $\vec{v}_{\text {rot }, i, j}$ was multiplied by a factor -1 for the extension part of each calibration movement cycle to ensure that the rotation axes were approximately equally directed for all intervals. The functional coordinate axis $\left(\vec{y}_{f}^{g l}\right)$ (i.e., the rotation axis of the lower leg during the flexion-extension movements) was subsequently determined by averaging all resulting rectified rotation axes ( $\vec{v}_{r o t, i, j}^{\prime}$ ) for all intervals $j$ and all cycles $i$ :

$$
\begin{equation*}
\vec{y}_{f}^{g l}=\frac{1}{4 \times 7} \sum_{i=1}^{4} \sum_{j=1}^{7} \vec{v}_{r o t, i, j}^{\prime} \tag{6.9b}
\end{equation*}
$$

The temporary Z-axis of $\psi^{f}\left(\vec{z}^{\prime}{ }_{f}^{g l}\right)$ was chosen to be equal to $\psi_{z}^{g l}$ :

$$
\vec{z}_{f}^{\prime g l}=\left[\begin{array}{lll}
0, & 0, & 1 \tag{6.9c}
\end{array}\right]
$$

The X-axis of $\psi^{f}\left(\vec{x}_{f}^{g l}\right)$ was computed and $\vec{z}^{\prime}{ }_{f}^{g l}$ corrected to create an orthogonal CS:

$$
\begin{align*}
& \vec{x}_{f}^{g l}=\vec{y}_{f}^{g l} \times \vec{z}_{f}^{\prime g l}  \tag{6.9d}\\
& \vec{z}_{f}^{g l}=\vec{x}_{f}^{g l} \times \vec{y}_{f}^{g l} \tag{6.9e}
\end{align*}
$$

The orthonormal time-invariant rotation matrix from $\psi^{f}$ to $\psi^{g l}\left(R_{f}^{g l}\right)$ was:

$$
R_{f}^{g l}=\left[\begin{array}{ccc}
\frac{\vec{x}_{f}^{g l}}{\left\|\vec{x}_{f}^{g l}\right\|} ; & \frac{\vec{y}_{f}^{g l}}{\left\|\vec{y}_{f}^{g l}\right\|} ; & \frac{\vec{z}_{f}^{g l}}{\left\|\vec{z}_{f}^{g l}\right\|} \tag{6.9f}
\end{array}\right]
$$

The time-dependent rotation matrix of $\psi^{c l}$ in $\psi^{f}\left(R_{c l}^{f}\right)$ was then computed and represented the orientation of the cluster marker set in $\psi^{f}$ (rotation 4 in Figure 6.3):

$$
\begin{equation*}
R_{c l}^{f}(t)=R_{f}^{g l-1} R_{c l}^{g l}(t) \tag{6.10}
\end{equation*}
$$

## Orientation and displacement validation

The sensor and cluster orientation estimates in $\psi^{f}$ of DFOD and OMCS were expressed in Euler angles (rotation order: YZX) for visualization purposes. To show the added drift-reducing benefit of DFOD in estimating sensor orientation, sensor orientation was also computed by integrating the sensor angular velocity in $\psi^{s}$, similar to Equations 6.3 a and 6.3 b without any drift reducing methods. This resulted in the sensor orientation with respect to the initial sensor orientation ( $\psi^{s, \text { init }}$ ) at the start of the first gait cycle. The position of the marker closest to the IMU was selected and displacement during each gait cycle was computed (similar procedure to Equation 6.7b). OMCS and IMU data were time-synchronized based on the GCZM displacement in the forward direction of the sensor and cluster marker set $\left(\vec{s}_{f, G C Z M, x}\right)$. Three-dimensional differences in Euler angles and displacement between DFOD and OMCS over time-normalized gait cycles were quantified as root mean square errors (RMSE) and absolute mean differences. A 1D orientation error was computed by transforming the difference in orientation between DFOD and OMCS to an axis-angle representation and using the rotation angle as an outcome ${ }^{23}$. This 1D angle represents the rotation that is necessary to align $R_{s}^{f}$ and $R_{c l}^{f}$. A 1D displacement error was defined as the root mean square of the 3D displacement errors. Additionally, differences at the first and last sample of each gait cycle, differences in minimum and maximum values, and the ROM between DFOD and OMCS for each gait cycle were computed and correlations between extrema and ROM were quantified with Pearson correlation coefficients. Correlations are interpreted as very strong for $r=(0.90,1.00)$, strong for $r=(0.70,0.89)$, moderate for $r=(0.40,0.69)$, weak for $r$ $=(0.20,0.39)$, and very weak for $r=(0.00,0.19){ }^{24}$. The mediolateral and vertical axis of DFOD (Equations 6.4a and 6.4b) were based on five gait cycles unless stated otherwise.

## Algorithm characteristics

DFOD assumes that the sensor on the lower leg moves quasi-cyclically and in a quasi-2D plane. To quantify how valid these assumptions are for the lower leg motion during treadmill running, respectively the mean cycle time and standard deviation and the explained variance of the first principal component of the angular velocity in $\psi^{s}$ over one minute of running were computed.

The mediolateral (Equation 6.4a: $\vec{y}_{d f, i}^{f}$ ) and vertical axes (Equation 6.4b: $\vec{z}_{d f, i}^{f}$ ) of $\psi^{f}$ can be computed independently of each other and are not necessarily based on data of the same number of gait cycles. The effect of using data of different numbers of gait cycles to determine
these axes of $\psi^{f}$ and its error with respect to an OMCS was tested. Data of 1 up to 15 gait cycles were used to define the mediolateral and vertical axes of $\psi^{f}$, resulting in a total of 225 combinations which were tested. The outcome measure of this analysis was the 1D orientation and displacement estimate.

Full trust in the TRIAD algorithm ${ }^{19}$ was given to the mediolateral functional axis (Equation 6.4a) since this axis is not influenced by the violation of the approximately constant cycle average velocity assumption. The number of points used to estimate the rotation axis of Equations 6.9a and 6.9b was based on a trial and error procedure to obtain a small variation in the obtained axes while using as few intervals as possible. Note that the results of this trial and error process were only used to validate DFOD and were not part of DFOD.

To investigate the effect of sampling frequency on the performance of DFOD, IMU data were resampled from 240 Hz to 120 Hz and 60 Hz before DFOD was used to estimate orientation and displacement. For this analysis, the vertical and mediolateral axis of DFOD were both based on five gait cycles and the 1D orientation and displacement estimates were used as outcome measures.

## Results

An average of 79 gait cycles (range: 66-94) per subject were analyzed. When not stated otherwise, the mediolateral and vertical axes of DFOD (Equations 6.4a and 6.4b) were based on data of five gait cycles.

## Estimation of orientation

Estimated lower leg sensor orientations without drift reduction, with drift reduction according to DFOD and from an OMCS are shown in Figure 6.4. Estimated lower leg sensor orientations of DFOD were compared to an OMCS in treadmill running. Mean RMSE for orientations in the sagittal plane were $3.1 \pm 0.4^{\circ}$ while they were larger in the frontal ( $5.3 \pm 1.1^{\circ}$ ) and transversal plane ( $5.0 \pm 2.1^{\circ}$ ). The mean 1D rotation error (i.e., angle over which $R_{s}^{f}$ needs to be rotated to coincide with $R_{c l}^{f}$ was $7.5 \pm 1.7^{\circ}$. The 3D mean difference at the start and end of the gait cycle, absolute difference, and maximum and minimum difference in orientation together with the difference in ROM of DFOD and OMCS are shown in Table 6.1. Correlations between the 3D maximal angle, minimal angle, and ROM from DFOD and OMCS ranged from strong (0.77) to very strong (0.99). Mean 3D orientations of DFOD and OMCS for a representative subject are shown in Figure 6.5.


Figure 6.4: Estimated sensor (inertial) and cluster marker set (optical) orientation for a representative subject. The top figure shows estimated sensor orientation without drift reduction with respect to the initial orientation of the sensor at the start of the first gait cycle ( $\left.\psi^{s, i n i t}\right)$. The middle figure shows the estimated sensor orientation obtained with DFOD in $\psi^{f}$. The bottom figure shows the actual cluster orientation according to an optical motion capture system in $\psi^{f}$. Note that data of the top graph are shown in a different coordinate system. This figure shows the added drift-reducing benefit of DFOD compared to orientation estimation without drift reduction. Anti-clockwise rotations in $\psi^{\text {s, init }}$, (top figure), and $\psi^{f}$ (middle and bottom figure) correspond to positive angles. An angle of zero corresponds to the initial sensor orientation just before initial contact of the first gait cycle in $\psi^{s, \text { init }}$ (top figure) or $\psi^{f}$ (middle and bottom figure).

Table 6.1: Mean orientation differences between DFOD and OMCS for all subjects combined. RMSE refers to the root mean square difference in 3D orientation. "Difference start cycle" and "Difference end cycle" refer to the difference between DFOD and OCMS (OMCS-DFOD) at the first and last sample of the gait cycle. " $\Delta$ Maximal angle" and " $\Delta$ Minimal angle" refer to the differences in the estimated maximal and minimal orientation during each gait cycle between DFOD and OMCS (OMCS-DFOD). " $\Delta$ ROM" refers to the mean differences in the estimated range of motion during each gait cycle for DFOD and OMCS. Pearson correlation coefficients (r) are provided between brackets.

| Orientation <br> $\left(\psi^{f}\right)$ | RMSE | Mean <br> absolute <br> difference | Difference <br> start cycle | Difference <br> end cycle | $\Delta$ Maximal <br> angle | $\Delta$ Minimal <br> angle | $\Delta$ ROM |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| Frontal plane $5.3 \pm 1.1^{\circ}$ $4.3 \pm 0.7^{\circ}$ $-6.1 \pm 5.0^{\circ}$ $-6.2 \pm 5.1^{\circ}$ $-4.7 \pm 6.1^{\circ}$ $3.0 \pm 2.2^{\circ}$ <br> (X-axis)       |  |  |  |  | $-7.6 \pm 4.4^{\circ}$ |  |  |
| (r=0.78) | $(r=0.81)$ | $(r=0.89)$ |  |  |  |  |  |
| Sagittal plane | $3.1 \pm 0.4^{\circ}$ | $2.6 \pm 0.3^{\circ}$ | $0.3 \pm 3.7^{\circ}$ | $0.4 \pm 4.0^{\circ}$ | $-0.4 \pm 3.4^{\circ}$ | $-2.1 \pm 1.7^{\circ}$ | $1.7 \pm 3.1^{\circ}$ |
| (Y-axis) |  |  |  |  | $(r=0.95)$ | $(r=0.99)$ | $(r=0.96)$ |
| Transversal plane | $5.0 \pm 2.1^{\circ}$ | $4.5 \pm 2.1^{\circ}$ | $-3.5 \pm 3.4^{\circ}$ | $3.4 \pm 3.7^{\circ}$ | $-3.3 \pm 3.2^{\circ}$ | $2.3 \pm 5.0^{\circ}$ | $-5.6 \pm 2.1^{\circ}$ |
| (Z-axis) |  |  |  |  | $(r=0.96)$ | $(r=0.97)$ | $(r=0.81)$ |



Figure 6.5: Top figure: Mean time-normalized orientation of a sensor (DFOD, dashed line) and cluster marker (OMCS, solid line) on the lower leg (in $\psi^{f}$ ) as a function of the gait cycle. Shaded areas represent the standard deviation around the mean. Bottom figure: 1D orientation error as a function of the gait cycle. The 1D orientation error is the angle of the axis-angle representation of the difference in orientation between DFOD and OMCS ${ }^{23}$. Data are shown for a representative subject during one minute of running. Positive orientations represent anti-clockwise rotations in $\psi^{f}$.

## Estimation of displacement

Estimated lower leg sensor displacements of DFOD were compared to an OMCS in treadmill running. Mean RMSE for displacements in the forward direction were $1.6 \pm 0.2 \mathrm{~cm}$ and similar for the mediolateral ( $1.7 \pm 0.6 \mathrm{~cm}$ ) and vertical direction ( $1.6 \pm 0.2 \mathrm{~cm}$ ). The mean 1D displacement error (i.e., length of the vector between the estimated sensor position of DFOD and OMCS) was $2.7 \pm 0.4 \mathrm{~cm}$. The 3D mean difference at the start and end of the gait cycle, absolute difference, maximum difference, and minimum difference in displacement, together with the difference in ROM of DFOD and OMCS, are shown in Table 6.2. Correlations between the 3D maximal displacement, minimal displacement, and ROM were moderate ( $r$ $=0.50$ ) to strong ( $r=0.82$ ). Mean 3D displacements of DFOD and OMCS for a representative subject are shown in Figure 6.6.

Table 6.2: Mean displacement differences between DFOD and OMCS for all subjects combined. RMSE refers to the root mean square difference in 3D sensor and cluster displacement. "Difference start cycle" and "Difference end cycle" refer to the difference between DFOD and OCMS (OMCS-DFOD) at the first and last sample of the gait cycle. " $\triangle$ Maximal displacement" and " $\Delta$ Minimal displacement" refer to the differences in the estimated maximal and minimal displacement during each gait cycle between DFOD and OMCS (OMCS-DFOD). " $\triangle R O M$ " refers to the mean differences in the estimated range of motion during each gait cycle for DFOD and OMCS. Pearson correlation coefficients (r) are provided between brackets.

| Displace- <br> ment <br> $\left(\psi^{f}\right)$ | RMSE | Mean absolute difference | Difference start cycle | Difference end cycle | $\Delta$ Maximal displacement (cm) | $\Delta$ Minimal displacement (cm) | $\triangle$ ROM |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Forward (X-axis) | $1.6 \pm 0.2 \mathrm{~cm}$ | $1.4 \pm 0.2 \mathrm{~cm}$ | $2.7 \pm 0.7 \mathrm{~cm}$ | $2.8 \pm 0.6 \mathrm{~cm}$ | $\begin{aligned} & 2.4 \pm 0.7 \mathrm{~cm} \\ & (r=0.72) \end{aligned}$ | $\begin{aligned} & -1.1 \pm 0.4 \mathrm{~cm} \\ & (\mathrm{r}=0.79) \end{aligned}$ | $\begin{aligned} & 3.5 \pm 0.9 \mathrm{~cm} \\ & (r=0.81) \end{aligned}$ |
| Mediolateral (Y-axis) | $1.7 \pm 0.6 \mathrm{~cm}$ | $1.5 \pm 0.5 \mathrm{~cm}$ | $-0.3 \pm 2.1 \mathrm{~cm}$ | $-0.2 \pm 2.2 \mathrm{~cm}$ | $\begin{aligned} & -0.5 \pm 1.6 \mathrm{~cm} \\ & (r=0.51) \end{aligned}$ | $\begin{aligned} & 0.6 \pm 1.5 \mathrm{~cm} \\ & (r=0.65) \end{aligned}$ | $\begin{aligned} & -1.1 \pm 3.1 \mathrm{~cm} \\ & (r=0.59) \end{aligned}$ |
| Vertical (Z-axis) | $1.6 \pm 0.2 \mathrm{~cm}$ | $1.3 \pm 0.2 \mathrm{~cm}$ | $1.9 \pm 0.2 \mathrm{~cm}$ | $2.0 \pm 0.3 \mathrm{~cm}$ | $\begin{aligned} & 0.0 \pm 1.0 \mathrm{~cm} \\ & (r=0.50) \end{aligned}$ | $\begin{aligned} & -0.4 \pm 0.2 \mathrm{~cm} \\ & (r=0.82) \end{aligned}$ | $\begin{aligned} & 0.4 \pm 1.1 \mathrm{~cm} \\ & (r=0.71) \end{aligned}$ |



Figure 6.6: Top figure: Mean time-normalized orientation of a sensor (DFOD, dashed line) and cluster marker (OMCS, solid line) on the lower leg (in $\psi^{f}$ ) as a function of the gait cycle. Shaded areas represent the standard deviation around the mean. Bottom figure: 1D orientation error as a function of the gait cycle. The 1D orientation error is the angle of the axis-angle representation of the difference in orientation between DFOD and OMCS ${ }^{23}$. Data are shown for a representative subject during one minute of running. Positive orientations represent anti-clockwise rotations in $\psi^{f}$.

## Algorithm characteristics

Two metrics were computed to show how valid the assumptions of a quasi-cyclical and quasi-2D movements were for treadmill running. The average cycle time was $0.68 \pm 0.03$ $\mathrm{s} /$ stride and the standard deviation ranged from $0.8-1.9 \%$ of the average cycle time. The first principal component of the angular velocity explained on average $90.2 \pm 5.7 \%$ (range: 84.6-95.8\%) of the variance.

The mediolateral and vertical axes of $\psi^{f}$ (Equations 6.4a and 6.4b) are based on data of five complete gait cycles. The effect of using data of more or less gait cycles to define these axes on the mean 1D orientation error is investigated and shown in Figure 6.7. The lowest mean 1D orientation error was found when the vertical axis was based on data of 11 gait cycles and the mediolateral axis on data of 8 gait cycles (mean error: $7.5^{\circ}$ ). The highest mean orientation error was found when the vertical and mediolateral axes were both based on data of 1 gait cycle (mean error: $7.7^{\circ}$ ).


Figure 6.7: Effect of the number of gait cycles used to determine the mediolateral (Equation 6.4a) and vertical axis (Equation 6.4b) of $\psi^{f}$ on the 1D angle error. The 1D angle error represents the angle of the axis-angle representation of the difference in orientation between DFOD and OMCS.

The effect of the number of gait cycles on the mean 1D displacement error is shown in Figure 6.8. The lowest mean displacement error was found when the vertical axis was based on data of 10 gait cycles and the mediolateral axis on data of 15 gait cycles (mean error: 2.6 cm ). The highest mean displacement error was found when the vertical and mediolateral axes were both based on data of 1 gait cycle (mean error: 4.5 cm ).

To investigate the effect of sampling frequencies on DFOD, inertial data were resampled from 240 Hz to 120 Hz and 60 Hz before applying DFOD. Compared to a sampling frequency of 240 Hz , the 1D orientation error increased with $0.3^{\circ}$ for 120 Hz and $2.2^{\circ}$ for 60 Hz . The 1D displacement error increased with 1.2 cm for 120 Hz and 12.7 cm for 60 Hz .


Figure 6.8: Effect of the number of gait cycles used to determine the mediolateral (Equation 6.4a) and vertical axis (Equation 6.4b) of $\psi^{f}$ on the 1D displacement error between DFOD and OMCS.

## Discussion

A new method, called Drift-Free Orientation and Displacement estimation (DFOD), is proposed to estimate drift-free 3D sensor orientation and displacement based on a single IMU. DFOD uses the quasi-cyclical behavior of human movements and assumes a quasi-2D movement with an approximately constant cycle average velocity. The performance of DFOD for a sensor on the lower leg was validated with an optical motion capture system (OMCS) in treadmill running. Errors in estimated sensor orientation and displacement between DFOD and OMCS were comparable to errors of other orientation and displacement algorithms. However, DFOD is independent of a constant- or zero-velocity point, a biomechanical model, a magnetometer, Kalman filtering, or a calibration procedure. Hence, DFOD is a promising method for quasi-cyclical motion analysis with a single IMU and has many advantages over current methods.

## Estimation of orientation

Estimated lower leg sensor orientations of DFOD were compared to an OMCS in treadmill running. DFOD performs best for orientation estimation in the sagittal plane, possibly because the largest ROM occurs around the axis perpendicular to this plane (Equation 6.4a) in running.

To reduce drift in orientation estimation, a drift reducing rotation which was constant within each cycle, but varied over cycles, was applied (rotation 3, Figure 6.3). Orientation drift is relatively slow compared to the duration of a gait cycle (i.e., two min before $\psi^{d f}$ drifts $90^{\circ}$, or $\pm 0.5^{\circ} /$ stride, around $\psi_{y}^{f}$ ). Hence, a constant drift reducing rotation for each gait cycle seemed sufficient, although this did result in small discontinuities between gait cycles. In future work, a continuous drift reducing rotation could improve the performance of DFOD.

Since we are not aware of studies that estimated lower leg orientations during running, the results of DFOD can only be compared with studies estimating foot and thigh orientations during running and walking. Foot orientations during running have mostly been based on constant- or zero-velocity updates with an additional drift reducing component (e.g., based on joint center accelerations, filtering, or an orientation reset). At speeds similar to our study, sagittal plane foot orientations could be estimated with errors varying between $2.0^{\circ}$ and $20.8^{\circ} 11,12,25$. Frontal plane foot orientation errors differed from $2.6^{\circ}$ to $4.4^{\circ} 12,25$. Upper leg orientations during walking have been estimated with an RMSE of $1.9 \pm 0.5^{\circ}$, although the zero acceleration and angular velocity update used in that study does not apply to continuous quasi-cyclical movements like running ${ }^{26}$. Orientation errors in our study are similar or slightly larger than found in literature for other body segments, although these studies used drift reducing methods unsuitable for a sensor on the lower leg in running (i.e., based on a constant- or zero-velocity point).

Tibial orientations in the sagittal and transversal plane are commonly studied with regard to running injuries ${ }^{27-29}$. The sagittal plane orientation of the tibia at initial contact has been shown to be $4.9^{\circ}$ larger in injured than in uninjured runners and the tibia ROM in the transverse plane is around $15^{\circ}$ in running ${ }^{30}$. With a mean difference of $-0.3 \pm 3.7^{\circ}$ at the start of the gait cycle (just before initial contact) and $-5.6 \pm 2.1^{\circ}$ in the transversal plane ROM, DFOD is capable to detect meaningful changes in tibia orientations during running.

## Estimation of displacement

Estimated lower leg sensor displacements of DFOD were compared to an OMCS in treadmill running. OMCS cluster marker placement can explain some of the errors in the forward and vertical directions. The OMCS cluster marker set is placed below the IMU (see Figure 6.1). Lower placement of the cluster marker set results in a larger ROM for OMCS compared to DFOD in the forward and vertical direction. Hence, actual displacement errors in the forward and vertical direction are expected to be smaller than those reported in this study.

Since we are not aware of studies that estimated lower leg displacements during running, the results of DFOD can only be compared with studies estimating foot displacements and stride length based on IMU data during running. In literature, estimates of sagittal plane foot displacement during running at a speed similar to the speed in this study had an absolute 1D positional error of $5 \pm 2 \mathrm{~cm}$ at maximal foot height and initial contact ${ }^{11}$. The absolute 1D positional error in our study was $2.7 \pm 0.4 \mathrm{~cm}$. Previously, stride length based on an IMU in a shoe could be estimated with a mean absolute error of $7.6 \mathrm{~cm}{ }^{31}$. DFOD has a mean absolute displacement error of $1.4 \pm 0.2 \mathrm{~cm}$ in the forward direction. Hence, displacement errors of DFOD for the tibia sensor are smaller than those reported by literature for the foot segment in running.

DFOD estimates the displacement of a sensor on the lower leg. However, the displacement of each point on the tibia can be estimated based on the orientation of the sensor and the distance from the sensor to the point of interest. When the distance from the sensor to the ankle joint is known, the forward (step length) and upward (step height) displacement of the ankle can be estimated. Running velocity can then be obtained with the step length and cycle time. Hence, DFOD provides insight into the 3D trajectory of the lower leg during running and can be used to estimate step length, step height, and running velocity based on a single IMU on the lower leg.

## Algorithm characteristics

The assumptions that treadmill running is a quasi-cyclical and quasi-2D movement seem to hold based on the standard deviation of the cycle times ( $0.8-1.9 \%$ of the cycle time) and the explained variance of the first principal component for the angular velocity in $\psi^{s}$ (84.6$95.8 \%)$. The explained variance shows that DFOD is capable of accurately estimating orientation and displacement even when $15 \%$ of the angular velocity in $\psi^{s}$ occurs outside the 2D plane of a movement.

The effect of computing the functional mediolateral (Equation 6.4a) and vertical (Equation 6.4b) axes based on different numbers of gait cycles was found to be very small. The 1D orientation and displacement errors differed only $0.2^{\circ}$ and 1.9 cm between the best- and worst-performing combination of the number of included gait cycles. Hence, during indoor treadmill running at a constant velocity, the number of gait cycles for the vertical and mediolateral axes has a limited influence on the results of DFOD.

However, the goal is to apply DFOD in less controlled environments such as outdoor running. Outdoor running is likely to result in a less cyclical running pattern ${ }^{32}$. It is hypothesized that for outdoor running, a smaller number of gait cycles to compute the functional mediolateral (Equation 6.4a) and vertical (Equation 6.4b) axes is favoured over a larger number since assumptions are less likely to be violated over shorter periods. Five gait cycles to define the vertical and mediolateral axes is expected to be a reasonable trade-off between including more data to compensate for the increased variability in outdoor running while still being able to adapt to sudden changes in the gait pattern and reduce violations of assumptions. Hence, five gait cycles for both the mediolateral and vertical axes (Equations 6.4a and 6.4b) were used in this study as the default setting for DFOD.

To investigate the effect of sampling frequencies on DFOD, inertial data were resampled from 240 Hz to 120 Hz and 60 Hz before applying DFOD. Orientation and displacement errors drastically increased when IMU data resampled to 60 Hz were used as input for DFOD. These results indicate that DFOD provides satisfactory results for a sampling frequency of 240 Hz and 120 Hz , but not for 60 Hz .

## Limitations

Multiple assumptions were made to create DFOD, which can be violated by running outdoors. When runners run outside, they have a less constrained gait pattern than on a treadmill ${ }^{32}$, and can freely change their running velocity and run up or downhill, thereby violating some assumptions of DFOD. Violation of the assumption of an approximately constant cycle average velocity does not influence the mediolateral axis of $\psi^{f}$ (Equation 6.4a) since this axis is based on the first principal component of the angular velocity of the lower leg sensor. Additionally, this axis is not influenced by taking a turn or running in circles, since it moves with the body. However, the vertical axis of $\psi^{f}$ (Equation 6.4b) is influenced by a violation of the approximately constant cycle average velocity assumption. This axis is equal to the direction of the total acceleration (i.e., including gravity) over a complete number of gait
cycles when the cycle average velocity is constant. When a runner accelerates or decelerates, the free acceleration will not have a zero-mean over a complete number of gait cycles and will result in an offset in the estimated vertical axis proportional to the magnitude of the acceleration or deceleration. Since five gait cycles are included to estimate both functional axes, DFOD minimizes the effect of violated assumptions and is expected to recover from a short violation of assumptions within five gait cycles.

Similarly, the assumption of a quasi-cyclical 2D movement might be violated more often in running outdoors since impact accelerations are higher when running overground compared to a treadmill ${ }^{33}$, due to uneven terrain, stumbling, or taking a turn. DFOD will recover from short violations of the quasi-cyclical 2D movement assumption within five gait cycles. Running-induced fatigue has been shown to increase variability in the gait pattern ${ }^{34}$. This increased variability and less cyclicity might cause the assumptions of DFOD to be less valid in fatigued running, resulting in larger orientation and displacement errors. Since DFOD has an origin that moves with the body at the cycle average velocity, a change in elevation caused by running on a sloped surface will cause the origin of DFOD to move up or down with the body. An elevation change will be visible over time; however, the average displacement will still be zero.

This study aimed to propose and validate a new algorithm that makes use of the quasi-cyclical nature of many movements. The algorithm was tested on treadmill running data of four runners and provided satisfactory results for all runners. Hence, to test the idea of using the quasi-cyclical nature of many human movements to estimate orientation and displacement, a limited number of subjects is appropriate. However, before DFOD can be used to study running kinematics it should be validated in more runners and different conditions.

This study estimated sensor orientation and displacement during running while segment orientations might provide more insight for motion analysis. For a sensor to segment calibration, two axes that relate to both CSs are required. One of these axes is already defined in DFOD (Equation 6.2a). The other axis could be based on the direction of the gravitational acceleration during neutral standing, in which the tibia is assumed to be vertical. However, this sensor to segment calibration does require an additional calibration procedure.

## Future research

In future work, DFOD should be validated in a less controlled setting, such as outdoor running, in multiple body segments, and different quasi-2D movements like cycling and skating. The influence of short violations of the assumptions of DFOD, increased variability in the gait pattern (i.e., caused by fatigue), less cyclical movements, and different speeds on estimated orientations and displacement should be assessed in (outdoor) running. Additionally, the effect of continuous drift reduction instead of a drift reduction during each gait cycle (Equation 6.4 e ) could be evaluated to improve the performance of DFOD. As long as two functional axes can be defined, DFOD should be able to estimate sensor orientation and displacement. Hence, the generalized idea of DFOD could also be applied to quasi-cyclical 3D movements like swimming. For 3D movements, the validity of the functional mediolateral axis (Equation 6.4a) based on the first principal component of the angular velocity should be assessed. This component is expected to be less pronounced in 3D versus 2D movements. Finally, a sensor to segment calibration procedure could be added to enable DFOD to calculate segment orientations instead of sensor orientations.

## Conclusions

The Drift-Free Orientation and Displacement estimation method (DFOD) is proposed and validated. DFOD estimates drift-free 3D sensor orientation and displacement with a single IMU in quasi-cyclical quasi-2D plane movements with an approximately constant cycle average velocity. DFOD does not require a calibration procedure, biomechanical model, constant- or zero-velocity point, Kalman filtering, or magnetometer. Small errors in lower leg sensor orientation and displacement were found when DFOD was validated against an optical reference system in treadmill running. Hence, DFOD is a promising method for quasi-cyclical motion analysis, especially when using a minimal sensor setup.

## Data availability statement

The data presented in this study are openly available in 4TU.ResearchData. The data can be found here: [https://doi.org/10.4121/18394190] accessed on 13 December 2021.

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## Chapter 7

General discussion

The overarching aim of this thesis was to increase our understanding of running biomechanics as measured in and outside the laboratory, and to explore challenges regarding wearable motion analysis during running in a sport-specific setting. Where the previous chapters focused on specific research questions which individually contributed to this aim, the current chapter will place the combined findings in a broader perspective and critically discuss them. This chapter will start with a summary of the main findings from the individual chapters, after which a set of overarching topics about variability, moving outside the laboratory, and the future of monitoring running biomechanics will be discussed. This chapter will end with the strengths and limitations of the work presented in this thesis, general conclusions and recommendations.

## Main findings

## Increasing our understanding of running biomechanics

A systematic literature review with meta-analyses about the effect of fatigue on level-running induced fatigue showed that runners change their gait patterns due to fatigue by moving to a more compliant but less efficient gait pattern (Chapter 2). This gait pattern is characterized by decreased leg stiffness, increased knee flexion, and increased peak tibial accelerations. Interestingly, novice runners showed an increase in $\Delta C O M_{z}$ after a fatiguing protocol, while experienced runners did not. This suggests that experience level plays a role in changes in running biomechanics due to fatigue. Large differences between subjects were found, highlighting the need for subject-specific compared to group-based analyses of running biomechanics. In Chapter 3, subject-specific corrections for the effect of changes in speed and stride frequency on running mechanics were made during a fatiguing marathon. The effect of marathon stage on peak tibial acceleration and knee angles changed after correcting for speed and stride frequency changes. Hence, subject-specific effects of changes in speed and stride frequency on quantities of interest should be investigated and corrected when interpreting, or providing feedback on, running mechanics in an uncontrolled environment. The assumed link between peak tibial acceleration and tibial bone loading was tested in Chapter 4. A very weak non-significant correlation was found in rearfoot striking runners, indicating that an increase in peak tibial acceleration is not necessarily associated with an increase in tibial bone load. This non-significant correlation is caused by the inability of PTA to reflect internal compressive forces from muscle contractions and the disagreement in timing between PTA and peak tibial compression forces. Hence, the assumed link between PTA and maximal tibial compression forces and the expected associated risk of tibial stress fractures during treadmill running is not supported.

## Exploring challenges regarding wearable motion analysis

Using IMUs for wearable motion analysis in a sport-specific setting introduces challenges regarding to external influences on the gait pattern (Chapter 3) but also on how we obtain quantities of interest from raw sensor data. Laboratory based motion analysis is often based on joint angles, segment orientations and positions while these are not provided by raw IMU data. Additionally, wearable motion analysis in a sport specific setting should not form a burden to runners by relying on an extended number of sensors or on extensive sensor-tosegment calibration procedures.

In Chapter 5 and Chapter 6, we showed that the quasi-cyclical nature of running can be used to correct for drift in 3D orientation estimates of the tibia during treadmill running. Chapter 5 showed that drift could be drastically reduced by rotating angular velocities to a partly functional coordinate system in which flexion and extension of the lower leg occurred around one of the coordinate axes. However, not all drift in 3D orientation could be removed by rotating to a partly functional coordinate system. Therefore, based on the work performed in Chapter 5, additional characteristics of the quasi-cyclical nature of running were used in Chapter 6 to estimate drift-free 3D sensor orientation and displacement. An algorithm was developed to create a fully functional coordinate system based on the mean acceleration and rotation axes over multiple gait cycles. Minor errors in lower leg sensor orientation and displacement were found when the algorithm was validated against an optical reference system in treadmill running. In comparison to current methods, this new method does not require a calibration procedure, biomechanical model, constant or zero-velocity point, Kalman filtering, or magnetometer. These findings suggest that the algorithm is promising for quasi-cyclical motion analysis, especially when using a minimal sensor setup, and reduces burdens for runners to monitor their gait pattern with IMUs.

## Variability between subjects and studies

## Variability between subjects

Large differences exist in running patterns between runners performing the same task ${ }^{1-3}$. Natural within-subject variability in stride duration and PTA correspond to coefficients of variation of $3 \%$ and $7 \%$, respectively ${ }^{4,5}$. Stride time variability is highest for the preferred running speed since a given speed can be achieved by adapting both stride length and stride time. At higher and lower speeds, fewer dynamical degrees of freedom decrease stride time variability ${ }^{4}$. Less variability might reflect less flexibility to adapt to the environment
and promote repetitive overloading of specific structures or tissues ${ }^{6}$. By imposing a generic running speed on a group of runners, some might run above or below their preferred running speed, affecting their gait pattern. Individual differences in running patterns become even more prominent when runners get fatigued ${ }^{1-3,7-10}$. Fatigue-induced changes in running patterns depend, amongst others, on experience level (Chapter 2), running surface ${ }^{11,12}$, foot strike pattern ${ }^{13}$, and subject-specific fatigue thresholds ${ }^{14}$. Inter- and intra-subject variability makes it difficult to compare the gait patterns of subjects. Additionally, large inter-individual differences in group-based analyses often result in inconclusive and non-significant findings. A shift from group-based analyses to subject-specific ${ }^{8,15}$ or running-style specific ${ }^{16}$ analyses would prevent masking of individual responses in the gait pattern. Subject-specific analysis enables monitoring and feedback on deviations from a subject-specific habitual gait pattern, increasing the value of information that can be provided to runners.

## Variability between studies

Besides differences in gait patterns between runners, endless possibilities exist for creating running experiments. Variables for running experiments include experience level, injury history, shoe choice, running-induced fatigue, running surface, running speed, continuous versus interval running and running until exhaustion versus reaching a certain distance, heart rate, or perceived exertion. Additionally, choices in data processing, such as the number of strides to include, filtering specifications, and statistical methods, contribute to differences between studies ${ }^{17}$. This abundance of possible running protocols, differences in measurement devices, the number of strides analyzed, and the broad range of methods to analyze gait patterns make comparing findings of studies cumbersome.

The effect of variability between studies became apparent in Chapter 2 in the form of contradicting findings between studies. We included studies involving fatiguing protocols in meta-analyses to summarize effects of running-induced fatigue on running kinematics. Contradicting findings between studies were likely the result of differences in running protocols. A subject-specific fatigue threshold above which kinematic variables change has been shown previously ${ }^{14}$. Hence, contradicting findings in the literature review might be caused by assuming that all runners were fatigued after completing the running protocol. Additionally, relevant information about the running experience was not always provided, and studies often consisted of small sample sizes. Metabolic measurements of fatigue (e.g., based on respiratory data or blood lactate concentrations) were performed in just 3 out of 28 included studies. Despite the differences between studies investigating running-induced fatigue, in

Chapter 2, we found a general trend to a more compliant but less efficient gait pattern with fatigue, characterized by decreased leg stiffness and increased knee flexion and peak tibial accelerations.

## Moving forwards with variability

Investigating running gait patterns is a hot topic. Many papers emerge with contradicting findings, probably caused by intra- and inter-subject differences, differences in running protocols, and small sample sizes. We are convinced that the step forwards is to publish datasets that accompany an article, as demonstrated in Chapter 3 and Chapter 6. Publicly available datasets allow researchers to test their hypotheses in different populations without needing large-scale measurements. Additionally, open datasets contribute to scientific transparency, reproducibility, efficiency and are cost-saving. If publishing accompanying datasets is impossible, at a bare minimum, researchers should provide sufficient information about the running protocol and subject population and perform subject-based analyses of running gait patterns instead of group-based analyses. Additional information about subjects and running protocols allows for pinpointing sources of variability and explaining differences between studies. Due to the high variability between studies investigating effects of fatigue, it is of interest to test the reproducibility of these types of studies. Furthermore, subject-specific analysis and reporting of results contribute to a better understanding of individual differences which are often masked in group-based analyses. Finally, large variability between subjects might be something we should not try to solve but embrace in our goal to provide feedback on subject-specific deviations from a habitual gait pattern to reduce injury risk

## Moving outside

## Laboratory versus outside running biomechanics

Most studies investigating running biomechanics are conducted in a laboratory setting during overground or treadmill running. For overground running in a laboratory, subjects typically need to accelerate and decelerate on a runway of 10 to 32 meters long, while one stride is extracted per trial ${ }^{18-22}$. This process is repeated until the predefined number of successful strides is achieved. Accelerating and decelerating in a constricted volume, together with averaging over a limited number of gait cycles, brings methodological issues concerning repeatability ${ }^{23}$, generalizability to continuous (i.e., non-stop) overground running ${ }^{24}$, and picking up a natural running pattern that is appropriate for the environment ${ }^{25}$. During continuous running, runners run with flatter and more inverted feet at initial contact, have
reduced braking and propulsion forces variability, and show more variability in ankle joint variables compared to running up and down a runway ${ }^{24}$. Thus, constraints in the experimental setup influence the gait pattern.

Meta-analyses showed that treadmill running is broadly comparable with overground running from a biomechanical perspective ${ }^{26}$. However, even at similar running speeds, multiple essential differences exist with regard to shock and shock attenuation mechanisms. For instance, PTA was higher in overground compared to treadmill running in an unfatigued state but no longer in a fatigued state ${ }^{12}$ and peak foot acceleration was higher when running on grass compared to asphalt ${ }^{27}$. Most runners make the bulk of their runs outdoor ${ }^{28}$. Hence, there is a mismatch between the running environment in which most research is performed, and the actual environment where runners run. This limits the generalizability and ecological validity of findings from running studies performed in a laboratory setting.

## Measuring running biomechanics outdoors

To gain insight into running biomechanics, runners need to be measured in the environment where most runners run; outdoors. Different wearable devices can be used to monitor running biomechanics like GPS based sports watches to measure speed and location or pressure insoles to measure forces and force distribution of the feet during running. To monitor the gait pattern outdoors, IMUs can be used. IMUs are affordable and small in size, making them attractive for outdoor analyses of the gait pattern. However, the output of IMUs consists of accelerations and angular velocities, while laboratory-based measurement devices typically provide positions and position-derived joint angles. The sensor orientation needs to be estimated based on sensor data to compute similar outputs from IMU data. Sensor orientation can be obtained through different methods, such as sensor fusion or using domain-specific assumptions to correct for orientation drift.

In Chapters 5 and Chapter 6, we propose and validate a new method using the quasi-cyclical nature of running to estimate drift-free 3D sensor orientation and displacement. The benefits of this algorithm are that it requires only one IMU and does not need a biomechanical model, Kalman filtering, extensive sensor-to-segment calibration or a magnetometer. Furthermore, the sampling frequency at which satisfactory results are achieved is relatively low (i.e., 60 Hz ), making it suitable for data from low-end IMUs. Hence, this algorithm contributes to the growing interest in biomechanics from wearables using a minimal sensor setup.

The algorithms from Chapter 5 and Chapter 6 provides multiple opportunities with regard to measuring biomechanics. Although no calibration procedure is required to obtain 3D sensor orientation and displacement, one simple short measurement of a subject standing still in a neutral pose would allow computing a vertical axis in a segment fixed coordinate system. Together with the functional flexion-extension rotation axes from the algorithm, this allows for the computation of 3D segment orientation and displacement. Running speed can be calculated based on the forward displacement of the ankle joint with an additional measurement of the distance between the ankle joint center and the sensor on the lower leg. Additionally, joint angles can be computed if time-synchronized data of IMUs on two adjacent body segments are available.

Although the algorithm was tested in treadmill running, it is expected to work for other quasi-2D-cyclical motions such as cycling or rowing. The algorithm can even be applied to quasi-3D-cyclical motions if an alternative for the axis perpendicular to the plane of motion can be defined. Before the algorithm can be used in outdoor running measurements, it should be validated during continuous overground running. Especially the number of strides over which the coordinate system's functional axes are computed can differ between indoor and outdoor measurements. A validation study could be performed in a semi-controlled environment on an extensive indoor track (e.g., ${ }^{7}$ ) with an optical motion capture system or an uncontrolled environment by comparing estimated lower leg orientation and displacement from a single IMU compared to the estimated orientation output from a full-body IMU sensor setup ${ }^{29}$. The algorithms proposed in Chapter 5 and Chapter 6 brings us closer to small, affordable, and easy-to-use wearable sensors that provide drift-free 3D orientations, displacements, joint angles, and speed in sport-specific environments without the need for expensive and extensive sensor setups and software programs.

## Current use of IMUs in outdoor conditions

Despite the widespread availability of IMUs and their benefits regarding continuous analysis in a sport-specific setting, a recent scoping review showed that IMUs in running biomechanics are typically used indoors for short periods ${ }^{30}$. IMUs were used in a lab in $72 \%$ of the studies, while $67 \%$ analyzed a single step, stride, or less than 200 meters of running data ${ }^{30}$, possibly to exclude effects of fatigue or to validate or combine measurements with force plates. In outdoor settings, runners can freely change their running speed and encounter different surfaces, weather conditions, other runners, traffic, etcetera. The lack of context and the
influence of external factors when measuring in outdoor environments might play a role in the reluctance to measure outdoors. External influences on the gait pattern can burden researchers when trying to answer a research question and burden runners when comparing data of multiple runs.

In Chapter 2, PTA was shown to generally increase with fatigue at a constant running speed, indicating higher external forces on the body. However, PTA decreases with a decrease in running speed ${ }^{31}$. Since running speed typically decreases with fatigue, a possible increase in PTA due to fatigue might be masked by a decrease in PTA due to a decrease in running speed. Although a decrease in speed can be a protective mechanism of the body to keep impacts on the body low, an increase in PTA at a certain speed informs us that external forces on the body increase despite a decrease in speed. In Chapter 3, we quantified and corrected for the influence of changes in running speed and stride frequency on running mechanics during an outdoor competitive Marathon. After correcting for subject-specific effects of changes in speed and stride frequency, PTA and maximum stance phase knee angles increased during later stages of the marathon. These changes in PTA and knee angles were previously masked by changes in speed and stride frequency. Hence, subject-specific effects of changes in speed and stride frequency on quantities of interest should be investigated and corrected when interpreting, or providing feedback on, running mechanics in an uncontrolled environment.

## Moving forwards by going outside

IMUs allow for measuring outside which is important for ecological validity of running research. We believe that the most considerable burden of measuring outdoors is the lack of context and the influence of external factors. The step forwards to using IMUs in outdoor settings is gathering lots of continuous data with sufficient context to quantify the influence of multiple external factors. Although external factors might be confounding when answering research questions, it shows the important disturbances that runners encounter in sportspecific settings and increases our research's ecological validity. The proposed algorithm from Chapter 5 and Chapter 6 can be adapted to provide a range of exciting quantities of the running gait pattern indoors and outdoors (after validation).

## The future of monitoring running biomechanics and injury risk

## Running biomechanics and injury risk

A general goal of monitoring running biomechanics is to detect and provide feedback about abnormalities or changes in running biomechanics associated with increased injury risk ${ }^{32,33}$. Often, this is achieved through monitoring changes in running biomechanics due to fatigue $9,20,34$. Prospective studies identified biomechanical risk factors for different running injuries. For instance, female recreational runners who developed patellofemoral pain syndrome had increased stance phase hip adduction compared to healthy controls ${ }^{35}$. Furthermore, increased stance phase iliotibial band strain rate was found in runners who developed iliotibial band syndrome ${ }^{36}$, and reduced maximum knee flexion, lower maximal ankle dorsiflexion, and greater maximum rearfoot eversion during the stance phase were found in runners who developed Achilles tendinopathy ${ }^{37}$. Peterson and colleagues ${ }^{33}$ summarized nineteen prospective studies about musculoskeletal and biomechanical risk factors and the incidence of running injuries in meta-analyses. They found a significant effect on injury incidence for two out of twenty-five biomechanical quantities; less knee extension strength and lower hip adduction velocity. However, their meta-analyses were limited to six joint angle quantities, and they did not include hip adduction (i.e., linked to patellofemoral pain syndrome), knee angles at initial contact, and midstance (i.e., related to shock attenuation), peak accelerations or shock attenuation in their review. Especially peak accelerations and shock attenuations have been thought to be related to injury risk and can be easily measured in outdoor environments with IMUs. Hence, we recommend further investigating the relationship between peak accelerations, shock attenuation, and knee angles at initial contact and midstance with injury incidence. However, we do agree with Peterson and colleagues ${ }^{33}$ that altered running biomechanics on their own do not result in running injuries but that there is an interaction required with training characteristics, for instance, monitored as a cumulative load, when evaluating running injury risk ${ }^{38-40}$. The injury risk concerning running patterns may also be very individual and depend on factors like previous injuries, age, bone geometry, bone density, and sex ${ }^{41,42}$. Hence, differences between runners should be embraced by creating individual longitudinal datasets to investigate deviations in gait patterns on different time scales to identify and understand injury mechanisms and monitor injury risk.

## Quantities to monitor

Chapter 4 critically discussed the use of PTA as an indicator for tibial bone loading. PTA was expected to reflect impact forces on the human body and thus loading within the human body and injury risk. However, the contribution of internal forces (i.e., muscle contractions) was overlooked in this thought process. We found a non-clinically relevant relationship between PTA and tibial bone loading for rearfoot striking runners in treadmill running. Perhaps we should take one step back when investigating injury risk in runners.

The things we can observe or easily visualize tend to get our attention. When investigating running biomechanics, we often focus on running kinematics (e.g., joint angles) and external forces (e.g., ground reaction forces). To increase our understanding of running biomechanics, we must investigate the root of the kinematic changes we observe. Hence, we believe that the step forwards would be to take a step back and estimate forces and moments inside the body (i.e., kinetics) instead of their outcomes alone (i.e., kinematics) ${ }^{43,44}$. We suggest using musculoskeletal modeling ${ }^{45}$ and estimating 3D ground reaction forces based on IMU data ${ }^{46}$ to improve our understanding of biomechanical changes in sport-specific environments. Additionally, individual muscle contributions could be modeled ${ }^{47}$ and validated with wearable EMG systems to investigate further if, for instance, an increase in knee flexion at initial contact with fatigue is a consequence of unbalanced muscular fatigue between knee flexors and extensors or a different shock attenuation strategy. Finally, the impulse of tibial acceleration might provide more insight into the forces on the body compared to PTA. Since shock attenuation might cause spreading of the impact force impulse over time, a lower PTA can be found while the impulse of the acceleration during the stance phase might remain constant.

## Monitoring methods

The gait pattern differs between runners (Chapter 3). A subject-specific model of the habitual gait pattern is therefore required to monitor changes in biomechanical quantities. Since quantities can vary between runs, for instance, due to day-to-day variability or the weather ${ }^{48}$, five runs have been suggested to establish a stable subject-specific habitual running pattern when investigating multiple biomechanical quantities ${ }^{15}$. In addition, individual relationships between running speed, stride frequency, and biomechanical quantities of interest can be estimated (Chapter 3). These relationships can be used to correct quantities for changes in running speed, making individual longitudinal datasets corrected for effects of speed and
stride frequency possible. To obtain more manageable datasets and improve data stability, continuous running data can be split into bins of, for instance, 25 strides ${ }^{17}$. The median ${ }^{49}$ value for each bin with 25 strides can then be computed and corrected for running speed and stride frequency for comparison with the habitual gait pattern (Chapter 3). We presume that deviations from subject-specific habitual gait patterns provide more value to individual runners than using a rigid threshold above which a quantity is flagged as "high injury risk". Added value to the runner could be achieved by combining deviations from the habitual gait pattern with training characteristics, such as running speed (as proposed in Chapter 6), and physiological parameters, such as heart rate, to create a cumulative load. Feedback about deviations from the habitual gait pattern could help runners to change their gait pattern if desired ${ }^{50}$.

## Moving forwards with monitoring

To summarize, future (prospective) studies into the etiology of running injuries should focus on combining kinetic and kinematic quantities with training characteristics to provide a cumulative load. The biomechanical quantities to monitor during running depend on the goal for monitoring and will differ between types of running injuries. However, quantities of interest should preferably reflect forces and moments in the body and should be monitored in a sport-specific setting over more extended periods of time, for instance, with IMUs (Chapter 5 and Chapter 6). Deviations in quantities should be estimated with regard to a subject-specific habitual gait pattern established over multiple runs.

## Strengths and Limitations

Several strengths and limitations of the research presented in this thesis can be stated. One of the strengths of this thesis is that it covers a broad spectrum of running biomechanics, from fundamental research about 3D orientation estimation algorithms to applied research in the form of measuring running mechanics during an actual competitive outdoor marathon. Another strength is that we focused on measuring with IMUs, which allows for findings to be applied in a setting where runners run; outdoors. Finally, based on the findings of this thesis, we created multiple recommendations about how monitoring running biomechanics in an outdoor setting should look in the future.

A significant limitation of this thesis is that despite the clear need for outdoor analysis of running biomechanics, most studies in this thesis were based on indoor treadmill running. This was a necessary step back after the measurement during an outdoor marathon (Chapter 3) left us with fundamental questions. In Chapters 4, 5, and 6, either force plates or an optical motion capture system were required, which prevented us from performing these measurements outdoors. We strongly recommend evaluating the findings of these chapters outdoors. When performed outdoors, we suspect similar results for Chapter 4 and somewhat larger orientation and displacement differences in Chapters 5 and 6 since the gait pattern is expected to behave less cyclical in uncontrolled outdoor settings. Another limitation of this thesis is the small sample sizes in the studies. Especially Chapter $\mathbf{3}$ would benefit from a larger sample size due to variability between subjects. However, in Chapters 3 and 4, we used subject-specific analyses to reduce the effect of inter-subject variability. In Chapters 5 and 6, we introduced and validated a 3D orientation and displacement algorithm. Although this algorithm provided satisfactory results for all four runners in Chapter 6, we recommend evaluating this algorithm in more runners.

## General conclusions

Studies in this thesis have explored, evaluated, and advanced monitoring of running biomechanics, both in and outside the laboratory. The influence of fatigue and speed on running biomechanics was investigated, the link between PTA and tibial bone load was explored, and a 3D orientation and displacement algorithm was proposed. The answers to the research questions from Chapter 1 and other main conclusions from the preceding chapters in this thesis are stated below:

- Running-induced fatigue causes runners to move to a more compliant but less efficient gait pattern, characterized by decreased leg stiffness, increased knee flexion together with an increase in PTA (Chapter 2)
- The running gait pattern differs between runners, as well as the way runners react to running-induced fatigue and changes in speed and stride frequency (Chapters 2 and 3)
- Changes in PTA and knee angles were masked by changes in speed and stride frequency during a fatiguing outdoor run, subject-specific corrections were proposed in Chapter 3
- PTA should not be used as an indicator of tibial bone loading since it is unable to reflect internal compressive forces from muscles (Chapter 4)
- The quasi-cyclical nature of running can be used to estimate drift-free 3D sensor orientation and displacement with many benefits compared to other methods (Chapters 5 and 6)

Moving outside, using the methods proposed in this thesis, is the next step to increase our understanding of running biomechanics. Running biomechanics should be measured and monitored in a sport-specific setting, and the focus should shift from investigating kinematic quantities on a group level to the forces which underly them (i.e., kinetics) on a subjectspecific level.

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## Summary

Samenvatting
Dankwoord
About the author Progress range

## Summary

Running is an accessible leisure time activity. In 2020, running was the second most popular sport in The Netherlands, with 12 percent of the Dutch population participating in weekly running sessions. While running has many health benefits, runners are at high risk of developing running-related injuries like medial tibial stress syndrome (i.e., shin splints) or tibial stress fractures. The development of running-related injuries is thought to be caused by training load errors (i.e., running too fast, too far, or too often) and (changes in) the gait pattern of runners. Additionally, running-induced fatigue is believed to affect the gait pattern negatively with regard to injury risk. The link between running biomechanics and injuries sparks our interest in monitoring running biomechanics to eventually decrease the risk of running-related injuries.

Running biomechanics are often studied in a controlled laboratory setting while running on a treadmill. However, most runners run outdoors at various speeds while experiencing different levels of fatigue. Multiple differences in the gait pattern between running in a controlled laboratory setting and outdoor environments have been found, like higher peak tibial accelerations in outdoor running compared to treadmill running. These differences indicate that results from laboratory-based running experiments do not necessarily translate to running outdoors. Since most runners typically run outdoors, monitoring running biomechanics should move from the laboratory to a sport-specific environment.

The running gait pattern can be measured outside of the laboratory with wearable inertial measurement units (IMUs). Quantities like sensor orientation, knee joint angles, and peak accelerations of body segments shortly after the foot hits the ground can be computed from IMU data. However, which quantities should be used to monitor injury risk is unclear. Besides, current algorithms to extract quantities of interest from raw sensor data have many drawbacks. Hence, this thesis aimed to increase our understanding of running biomechanics as measured in and outside the laboratory and explore the challenges regarding wearable motion analysis during running in a sport-specific setting.

To accomplish these aims, the following research questions were answered in this thesis:
Chapter 2 How do running kinematics change due to running-induced fatigue?
Chapter 3 How to quantify and correct for the subject-specific effects of changes in running speed and stride frequency on impact-related running mechanics during a fatiguing outdoor run?

Chapter 4 What is the strength of the relationship between peak tibial acceleration and maximal tibial compression force in running?

Chapter 5 Can the cyclical nature of running be used to acquire drift-free 3D orientation of a body segment using a single gyroscope?

Chapter 6 How to estimate 3D orientation and displacement of a single IMU on the lower leg using the quasi-cyclical nature of running?

Chapter $\mathbf{2}$ investigated the effects of running-induced fatigue on running kinematics. Changes in the running pattern caused by fatigue are thought to reflect a deterioration in running technique and increase the risk of running-related injuries. Many contradicting findings about the effect of fatigue on running kinematics are present in the literature. Hence, we summarised and analyzed current literature about the effect of level running-induced fatigue on the running gait pattern in a systematic literature review with meta-analyses. The effect of running-induced fatigue on nineteen kinematic quantities was investigated based on thirty-three articles. Overall, running-induced fatigue resulted in a more compliant but less efficient gait pattern characterized by increased peak tibial acceleration, knee flexion at initial contact, and maximum swing phase knee flexion while leg stiffness decreased. Experience level influenced the effect of fatigue on running kinematics, as demonstrated by an increase in vertical center of mass displacement with fatigue in novice but not experienced runners. Changes in running kinematics due to fatigue might be explained by a decrease in the tolerance of knee extensors to imposed stretch loads or a decrease in the neuromuscular control resulting in less spreading of the impact force impulse over time.

Chapter 3 focussed on measuring running gait in a sport-specific environment. The running gait pattern is typically analyzed on a group level based on runs in controlled laboratory settings. However, most runners run in uncontrolled outdoor environments. Changes in speed and stride frequency, as often seen in outdoor running, influence the gait pattern and
can mask fatigue-related changes in running mechanics. We quantified and corrected for the effects of changes in running speed and stride frequency on running mechanics during a fatiguing outdoor run. The running mechanics of nine runners were analyzed with IMUs during a marathon. Subject-specific multiple linear regression models were created for speed and stride frequency effects on peak tibial acceleration, knee flexion angle at initial contact, and maximum stance phase knee flexion. These individual models were used to correct peak tibial acceleration and knee flexion angles for changes in speed and stride frequency. Regression coefficients for speed and stride frequency varied strongly between subjects, possibly caused by differences in foot strike pattern, tolerance to withstand effects of fatigue, or capacity to sustain a stable gait pattern over a range of speeds. Subject-specific corrections revealed a significant effect of marathon stage on peak tibial acceleration and knee flexion angles, which was previously masked by speed and stride frequency changes. Hence, speed and stride frequency influence the interpretation of changes in mechanical quantities in a subject-specific manner and should be corrected for when interpreting or providing feedback on running mechanics in an uncontrolled environment.

Chapter 4 focussed on investigating the relationship between peak tibial acceleration and tibial compression forces. Peak tibial acceleration is commonly used as a surrogate measure for tibial bone loading and is assumed to be related to tibial stress fracture risk. However, tibial compressive forces are caused by both internal muscle forces and the effect of external ground reaction forces. Peak tibial acceleration is expected to reflect the effect of forces from outside the body on the tibia bone but not the effect of compressive muscle forces. Hence, we investigated the strength of the relationship between peak tibial acceleration and maximum tibial compression forces in rearfoot-striking runners. Twelve runners ran on a treadmill while tibial acceleration was captured with accelerometers. Maximum tibial compression forces were computed with a lower leg model and individually correlated with peak tibial acceleration. The correlation coefficient was, on average, very weak ( $0.04 \pm 0.14$ ) and non-significant, and therefore deemed non-relevant. Peak tibial acceleration does not provide a complete picture of both internal and external compressive forces on the tibial bone. Hence, the assumed link between peak tibial acceleration and peak tibial compression forces and the expected associated risk of tibial stress fractures during treadmill running is not supported by the results of this study.

From Chapter 3, it is clear that running biomechanics should be measured in a representative natural environment. With IMUs, we can measure sensor acceleration and angular velocity outside the laboratory. However, we are typically also interested in body segment orientations and joint angles, for which sensor orientation is required. Sensor orientation can be estimated by integrating angular velocity while correcting for integration drift. Many sensor orientation estimation algorithms rely on computationally heavy Kalman filters, magnetometers, multiple IMUs, or extensive calibration procedures, which can burden runners to use IMUs to monitor their gait pattern easily. Alternatively, sensor orientation can be estimated based on domainspecific assumptions to reduce integration drift.

The aim of Chapter 5 was to investigate if the quasi-cyclical nature of running could be used to define a new set of domain-specific assumptions to acquire drift-free 3D sensor orientation of the lower leg during running based on a single gyroscope. We transformed 3D angular velocities into a new partly functional coordinate system to reduce integration drift during orientation estimation. The rotation axis of the lower leg was aligned with an axis of the partly functional coordinate system, giving one axis a functional meaning. We then estimated the change in sensor orientation for a single runner on a treadmill for 90 seconds. Drift in sensor orientation estimation was drastically reduced after transforming 3D angular velocities to the new partly functional coordinate system compared to the "old" sensor coordinate system. Hence, transforming 3D angular velocities to a partly functional coordinate system before estimating the change in sensor orientation seems promising to reduce drift in 3D orientation based on a single gyroscope in quasi-cyclical and quasi-2D motions like running.

Chapter 6 elaborated on the results of Chapter 5 and proposed a fully functional coordinate system in which all axes have functional meaning. This method used the quasi-cyclical and quasi-2D nature of many human movements. Additionally, it assumed that the velocity over multiple complete gait cycles was approximately constant, which is often the case for running. Angular velocity was expressed in the functional coordinate system before integration to obtain the change in sensor orientation. The sensor displacement was then computed by assumptions based on a quasi-cyclical movement. 3D sensor orientation and displacement for an IMU on the lower leg were validated with an optical motion capture system in four runners during constant velocity treadmill running. Errors in orientation and displacement were relatively small and comparable to other orientation and displacement algorithms. However, this new method has many advantages over current methods since it does not rely on a constant- or zero-velocity point, a biomechanical model, Kalman filtering, or a
magnetometer, and can, therefore, easily be used by runners to measure their gait pattern with a single sensor or minimal sensor setup. Although this method was validated on the lower leg in treadmill running, it is expected to work for other segments and quasi-cyclical movements.

In Chapter 7, the main findings of all chapters in this thesis were integrated and discussed. Especially the effect of variability between subjects and studies, differences between running in a laboratory compared to outdoors, and the future of monitoring running biomechanics and injury risk were discussed. Based on the findings of this thesis, we concluded that running-induced fatigue, speed, and stride frequency influence the gait pattern in a subjectspecific manner. Additionally, peak tibial acceleration is not an appropriate indicator of tibial bone loading since it does not provide a complete picture of both internal and external compressive forces on the tibial bone. Finally, we concluded that the quasi-cyclical and quasi-2D nature of running could be used to estimate drift-free 3D sensor orientation and displacement with many benefits compared to other methods. We recommend monitoring running biomechanics in a sport-specific setting and shifting the focus from investigating kinematic quantities on a group level to the forces underlying them on a subject-specific level.

## Samenvatting

Hardlopen is een toegankelijke vrijetijdsbesteding. In 2020 was hardlopen de op één na populairste sport in Nederland: 12\% van de Nederlandse bevolking liep wekelijks hard. Hoewel hardlopen veel voordelen heeft voor de gezondheid, lopen hardlopers een hoog risico op het ontwikkelen van blessures zoals het mediaal tibiaal stresssyndroom (d.w.z. shin splints) of tibiale stressfracturen. Het ontstaan van hardloopblessures wordt vermoedelijk veroorzaakt door fouten in de trainingsbelasting (te snel, te ver of te vaak hardlopen) en (veranderingen in) het hardlooppatroon. Bovendien wordt aangenomen dat vermoeidheid het looppatroon negatief beïnvloed wat het risico op blessures vergroot. Het verband tussen biomechanica en blessures wekt onze belangstelling voor het monitoren van hardloopbiomechanica om uiteindelijk het risico op loopblessures te verminderen.

Hardloopbiomechanica wordt vaak onderzocht tijdens hardlopen op een loopband in een gecontroleerde laboratoriumomgeving. De meeste hardlopers lopen echter buiten op verschillende snelheden en met verschillende mate van vermoeidheid. Er zijn meerdere verschillen gevonden in het looppatroon tussen hardlopen in een gecontroleerde laboratoriumomgeving en buiten, zoals hogere piekversnellingen van het scheenbeen bij het lopen buiten ten opzichte van een loopband. Deze verschillen wijzen erop dat de resultaten van hardloopexperimenten in het laboratorium niet noodzakelijkerwijs te vertalen zijn naar hardlopen in de buitenlucht. Aangezien de meeste hardlopers gewoonlijk buiten lopen, moet het monitoren van hardloopbiomechanica verplaatst worden van het laboratorium naar een sport specifieke omgeving.

Het looppatroon kan buiten het laboratorium worden gemeten met 'Inertial measurement units' (IMU's). Uit IMU data kunnen grootheden als sensororiëntatie, kniegewrichtshoeken en piekversnellingen van lichaamsdelen kort nadat de voet de grond raakt, worden berekend. Het is echter onduidelijk welke grootheden moeten worden gebruikt om het blessurerisico te monitoren. Bovendien hebben de huidige algoritmen om interessante grootheden uit ruwe sensordata te halen veel nadelen. Daarom was dit proefschrift gericht op het vergroten van ons begrip van de hardloopbiomechanica, zoals gemeten binnen en buiten het laboratorium en het verkennen van de uitdagingen met betrekking tot draagbare bewegingsanalyse tijdens hardlopen in een sport specifieke setting.

Om deze doelen te bereiken zijn in dit proefschrift de volgende onderzoeksvragen beantwoord:

Hoofdstuk 2 Hoe verandert de hardloopkinematica als gevolg van hardloopgeïnduceerde vermoeidheid?

Hoofdstuk 3 Hoe kan het persoon-specifieke effect van veranderingen in loopsnelheid en stapfrequentie op impact-gerelateerde loopmechanica gekwantificeerd en gecorrigeerd worden tijdens een vermoeiende buitenloop?

Hoofdstuk 4 Hoe sterk is de relatie tussen piek tibiale versnelling en maximale tibiale compressiekracht tijdens hardlopen?

Hoofdstuk 5 Kan het quasi-cyclische karakter van hardlopen gebruikt worden om driftvrije 3-dimensionale (3D) oriëntatie van een lichaamssegment te schatten op basis van één gyroscoop?

Hoofdstuk 6 Hoe kan de 3D oriëntatie en verplaatsing van één IMU op het onderbeen worden geschat op basis van het quasi-cyclische karakter van hardlopen?

Hoofdstuk 2 onderzocht de effecten van vermoeidheid op de hardloopkinematica. Van veranderingen in het looppatroon als gevolg van vermoeidheid wordt aangenomen dat zij de looptechniek verslechteren en het risico op loopblessures vergroten. De literatuur bevat veel tegenstrijdige bevindingen over het effect van vermoeidheid op de loopkinematica. Daarom hebben wij de huidige literatuur over het effect van hardloop-geïnduceerde vermoeidheid op het looppatroon samengevat en geanalyseerd in een systematisch literatuuroverzicht met meta-analyses. Het effect van vermoeidheid op negentien kinematische grootheden werd onderzocht op basis van drieëndertig artikelen. In het algemeen resulteerde hardloopgeïnduceerde vermoeidheid in een soepeler maar minder efficiënt looppatroon, gekenmerkt door verhoogde piekversnelling van het scheenbeen, een grotere knieflexie bij het eerste grondcontact en meer maximale knieflexie in de zwaaifase, terwijl de beenstijfheid afnam. Het ervaringsniveau beïnvloedde het effect van vermoeidheid op de loopkinematica, zoals bleek uit een toename van de verticale verplaatsing van het massamiddelpunt met vermoeidheid bij beginnende, maar niet bij ervaren lopers. Veranderingen in de loopkinematica als gevolg van vermoeidheid zouden verklaard kunnen worden door een afname in tolerantie van de kniestrekkers voor opgelegde strekbelasting of een afname van de neuromusculaire controle, waardoor de impuls van de botskracht van de voet met de grond minder goed verspreidt wordt over de tijd.

Hoofdstuk 3 richtte zich op het meten van het looppatroon in een sportspecifieke omgeving. Het looppatroon wordt vaak onderzocht op groepsniveau in een gecontroleerde laboratoriumomgeving. De meeste hardlopers lopen echter in een ongecontroleerde buitenomgeving. Veranderingen in snelheid en stapfrequentie, zoals die vaak voorkomen bij buitenlopen, beïnvloeden het looppatroon en kunnen vermoeidheid gerelateerde veranderingen in de looptechniek maskeren. In dit hoofdstuk kwantificeerden en corrigeerden wij voor effecten van veranderingen in loopsnelheid en stapfrequentie op de looptechniek tijdens een vermoeiende buitenloop. De looptechniek van negen lopers werd geanalyseerd met IMU's tijdens een marathon. Persoon-specifieke meervoudige lineaire regressiemodellen werden gemaakt voor effecten van veranderingen in snelheid en stapfrequentie op piek tibiale versnelling, knie flexie hoek bij het eerste grondcontact, en maximale knie flexie hoek tijdens de standfase. Deze individuele modellen werden gebruikt om de piek tibiale versnelling en knieflexiehoeken te corrigeren voor veranderingen in snelheid en stapfrequentie. Regressiecoëfficiënten voor snelheid en stapfrequentie varieerden sterk tussen proefpersonen, deze variatie werd mogelijk veroorzaakt door verschillen in landingspatroon, tolerantie voor effecten van vermoeidheid, of vermogen om een stabiel looppatroon aan te houden over een reeks snelheden. Persoon-specifieke correcties toonden een significant effect van de fase van de marathon op de piekversnelling van het scheenbeen en de knieflexiehoeken, dat eerder werd gemaskeerd door veranderingen in snelheid en stapfrequentie. Snelheid en stapfrequentie beïnvloeden dus de interpretatie van veranderingen in mechanische grootheden op een persoon-specifieke manier. Daar moet voor gecorrigeerd worden bij het interpreteren of geven van feedback op loopmechanica in een ongecontroleerde omgeving.

Hoofdstuk 4 richtte zich op het onderzoeken van de relatie tussen de piekversnelling van het scheenbeen en de compressiekrachten op het scheenbeenbot. De piekversnelling van het scheenbeen wordt gewoonlijk gebruikt als een surrogaatmaat voor de belasting op het scheenbeenbot en er wordt aangenomen dat deze verband houdt met het risico op tibiale stressfracturen. Tibiale compressiekrachten worden echter veroorzaakt door zowel interne spierkrachten als door het effect van externe grondreactiekrachten. De piekversnelling van het scheenbeen weerspiegelt naar verwachting het effect van krachten van buiten het lichaam op het scheenbeenbot, maar niet het effect van compressiekrachten van spieren. Daarom onderzochten wij de sterkte van het verband tussen de maximale tibiale versnelling en de maximale tibiale compressiekrachten bij hardlopers met een haklanding. Twaalf lopers liepen op een loopband terwijl de tibiale versnelling werd gemeten met versnellingsmeters.

De maximale tibiale compressiekrachten werden berekend met een onderbeenmodel en individueel gecorreleerd met de maximale tibiale versnelling. De correlatiecoëfficiënt was gemiddeld zeer zwak ( $0.04 \pm 0.14$ ) en niet-significant en werd vandaar niet relevant geacht. De piekversnelling van het scheenbeen geeft dus geen volledig beeld van zowel de interne als de externe compressiekrachten op het scheenbeenbot. Daarom wordt het veronderstelde verband tussen piekversnelling van het scheenbeen en piekcompressiekrachten op het scheenbeenbot en daarmee waarschijnlijk het risico op tibiale stressfracturen tijdens loopband lopen niet ondersteund door de resultaten van deze studie.

Uit hoofdstuk 3 bleek duidelijk dat de biomechanica van het hardlopen moet worden gemeten in een representatieve natuurlijke omgeving. Met IMU's kunnen we versnellingen en hoeksnelheden buiten het laboratorium meten. Meestal zijn we echter ook geïnteresseerd in lichaamssegmentoriëntaties en gewrichtshoeken, waarvoor sensor oriëntatie nodig is. Sensor oriëntatie kan worden geschat door de hoeksnelheid te integreren en te corrigeren voor integratiedrift. Veel algoritmen voor het schatten van sensor oriëntatie zijn afhankelijk van computationeel zware Kalman-filters, magnetometers, meerdere IMU's of uitgebreide kalibratieprocedures. Dit kan het voor hardlopers moeilijk maken om hun looppatroon te monitoren met IMU's. Als alternatief kan de sensor oriëntatie worden geschat op basis van domein specifieke aannames om voor integratiedrift te corrigeren.

Het doel van hoofdstuk 5 was om te onderzoeken of het quasi-cyclische karakter van hardlopen kan worden gebruikt om een nieuwe set domein specifieke aannames te definiëren om driftvrije 3D-sensor oriëntatie van het onderbeen tijdens hardlopen te bepalen op basis van één gyroscoop. Hiervoor transformeerden we 3D hoeksnelheden naar een nieuw gedeeltelijk functioneel coördinatensysteem om de integratiedrift tijdens de oriëntatieschatting te verminderen. De rotatie-as van het onderbeen werd uitgelijnd met een as van het deels functionele coördinatenstelsel, waardoor één as een functionele betekenis kreeg. Vervolgens schatten we de verandering in sensor oriëntatie voor een enkele loper op een loopband gedurende 90 seconden. De afwijking in de schatting van de sensor oriëntatie ten opzichte van een optisch meetsysteem werd drastisch verminderd na transformatie van de 3D-hoeksnelheden naar het nieuwe gedeeltelijk functionele coördinatensysteem in vergelijking met het "oude" sensorcoördinatensysteem. Het transformeren van 3D hoeksnelheden naar een gedeeltelijk functioneel coördinatensysteem voordat de verandering in sensor oriëntatie wordt geschat, lijkt dus veelbelovend om drift in 3D-oriëntatie op basis van één gyroscoop te verminderen bij quasi-cyclische en quasi-2D bewegingen zoals hardlopen.

Hoofdstuk 6 bouwde verder op de resultaten van hoofdstuk 5 en stelde een volledig functioneel coördinatensysteem voor waarin alle assen een functionele betekenis hebben. Deze methode maakte gebruik van de quasi-cyclische en quasi-2D aard van veel menselijke bewegingen. Bovendien werd aangenomen dat de snelheid over meerdere volledige loopcycli ongeveer constant was, wat vaak het geval is bij hardlopen. De hoeksnelheid werd uitgedrukt in het functionele coördinatensysteem vóór integratie om de verandering in de sensororiëntatie te verkrijgen. De sensorverplaatsing werd vervolgens berekend door aannames gebaseerd op een quasi-cyclische beweging. 3D sensor oriëntatie en-verplaatsing voor een IMU op het onderbeen werden gevalideerd met een optisch meetsysteem bij vier lopers tijdens het lopen op een loopband met constante snelheid. De fouten in oriëntatie en verplaatsing waren relatief klein en vergelijkbaar met andere oriëntatie- en verplaatsingsalgoritmen. Deze nieuwe methode heeft echter veel voordelen ten opzichte van huidige methoden. Dit omdat zij niet afhankelijk is van een punt of lichaamssegment dat stilstaat of een constante snelheid heeft, een biomechanisch model, Kalman filter of een magnetometer, en daarom gemakkelijk door lopers kan worden gebruikt om hun looppatroon te meten met één sensor of een minimale sensorset. Hoewel deze methode werd gevalideerd op het onderbeen bij hardlopen op een loopband, wordt verwacht dat zij ook werkt voor andere lichaamssegmenten en quasi-cyclische bewegingen.

In hoofdstuk 7 werden de belangrijkste bevindingen van alle hoofdstukken in dit proefschrift geïntegreerd en besproken. Daarbij werd met name het effect van variabiliteit tussen proefpersonen en studies, verschillen tussen binnen en buiten een laboratorium hardlopen en de toekomst van het monitoren van hardloopbiomechanica en het blessurerisico besproken. Op basis van de bevindingen van dit proefschrift concludeerden wij dat vermoeidheid, snelheid en stapfrequentie het looppatroon op een persoon-specifieke manier beïnvloeden. Bovendien is de piekversnelling van het scheenbeen geen geschikte indicator voor de belasting van het scheenbeenbot, omdat zij geen volledig beeld geeft van zowel de interne als de externe compressiekrachten op het scheenbeenbot. Ten slotte concludeerden wij dat de quasi-cyclische en quasi-2D aard van hardlopen kan worden gebruikt om driftvrije 3D sensororiëntatie en verplaatsing te schatten, met vele voordelen ten opzichte van andere methoden. Wij bevelen aan de hardloopbiomechanica in een sport specifieke omgeving te monitoren en de aandacht te verleggen van het onderzoeken van kinematische grootheden op groepsniveau naar de onderliggende krachten op een persoon-specifiek niveau.

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## About the author

Marit Zandbergen was born in 's-Hertogenbosch, The Netherlands on July $3^{\text {th }}$ 1995. Marit obtained her bachelor's degree Human Movement Sciences with Cum Laude in 2016 at the Vrije Universiteit Amsterdam. She also completed the Honours programme during her bachelor. In 2018, Marit obtained her Research Master's degree in Human Movement Sciences with Cum Laude at the Vrije Universiteit Amsterdam. During her studies, Marit was fascinated by human movement. Why can seemingly simple movements like walking or running be so challenging for some poeple? This interest was reflected in her bachelor and master theses about human movement analysis.

Immediatly after obtaining her master's degree, Marit started as a junior researcher and PhD candidate at Roessingh Research and Development in Enschede. Marit was involved in the runner assist project, where she was responsible for developing and evaluating algorithms to provide real-time feedback on running biomechanics to prevent injuries and improve running performance.

In February 2022, Marit started working as a movement technician at OCON in Hengelo and finished her PhD thesis in parallel.

## Awards

- American College of Sports Medicine Biomechanics Interest Group student award 2020
- Society for Movement Analysis Laboratories in the Low Lands award 2018
- Gerrit-Jan van Ingen-Schenau Promising young scientist award 2017
- Student price of the Amsterdam Movement Sciences Innovation Call 2017


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The following publications have been published in the Progress range by Roessingh Research and Development, Enschede, the Netherlands. Copies can be ordered, when available, via info@rrd.nl.

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