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Biomedical Engineering

Does pronation corrective heel wedging reduce the risk of diabetes forefoot ulceration by increasing the microcirculation of the plantar skin tissue?

Céline Natvig Mehta

Supervisor: Peyman Mirtaheri (OsloMet).

Co-supervisors: Rafael Borrajo (OsloMet),

Håvard Engell (GAITLINE), and Olga Korostynska (OsloMet).

Department of Mechanical, Electronic and Chemical Engineering

Faculty of Technology, Art and Design

OSLOMET

PREFACE

With this thesis I conclude my time in the master's program *Applied Computer and Information Technology* (ACIT) at OsloMet. As a student in the specialization field of Biomedical Engineering and with a background in Mechanical Engineering, I feel fortunate to have had the opportunity to research the science behind the human gait in my master's project – a field of study where the mechanical meets the biomedical. This topic was first introduced to me by my head supervisor professor Peyman Mirtaheri as part of a larger cooperation between GAITLINE AS and OsloMet University and has been a valuable learning experience for me.

I would here like to thank my external supervisor and founder of GAITLINE, Håvard Engell, for generously putting his time, equipment, and laboratory at my disposal, and for engaging in this project and enriching it with his expertise of the field. I am thankful to the team at the GAITLINE company as well for the warm welcome I received there.

I would also like to thank my OsloMet supervisors, professors Peyman Mirtaheri, Rafael Borrajo and Olga Korostynska, as well as PhD student Haroon Khan for the help and pushes they have given me along the way.

Céline Natvig Mehta

May 2022	Pilestredet 35, Oslo	Céline Mehta
Date	Place	Signature

ABSTRACT

Foot ulceration is one of the common complications of *diabetes mellitus* and is generally attributed to neuropathy and reduced blood flow through atherosclerosis. These complications cause high risk of damage and reduced healing ability in the skin of the feet. Recent studies have drawn a correlation between foot pronation and ulcers, and the role of foot pronation in the vascular function of the lower limbs has gained more attention.

The purpose of this study has been to determine whether foot pronation is a circulatory risk factor for developing foot ulceration through local or global vasoconstriction in the plantar foot and to examine whether the use of medially wedged pronation corrective footwear has a positive short- term effect on the microcirculation in the forefoot in overpronating persons. The pronation assessment in this study was limited to a measurement of the Achilles tendon angle in the frontal plane since the variable of the study is a mediolateral wedge correction.

The flux (laser doppler blood flow) response was assessed on four non-diabetic overpronating volunteers, using two single-channel Laser Doppler Flowmetry sensors on the medial and lateral sides of the right forefoot. The corrective sandals were adapted to each subject, and the flux response was compared to that of using flat and laterally wedged footwear. Flux was measured during stance in wedged sandals, immediately succeeding stance, and in the prone position after walking with sandals for 10 minutes.

The findings indicate that the relative forefoot flux (compared with the flat sole response) was higher on the medial side during stance on medial wedges (188 %, SD = 132 %), and higher on the lateral side during stance on lateral wedges (216 %, SD = 216 %). This was confirmed by a complementing mediolateral pattern in the reperfusion at rest. The response to wedged footwear did not show any significant trends when analyzed over 15 minutes.

The findings indicate a clear mediolateral flux pattern, further testing is needed to confirm the statistical significance of the patterns found, and to analyze the patterns of the flux levels compared to the flat sandal further, as the laterally wedged shoe revealed some inconsistency with the mediolateral pressure model. The medially wedged shoe seems to increase the flux on the medial side of the foot, and so reducing ulceration risk on the first metatarsal head, but at the expense of the lateral forefoot flux.

TABLE OF CONTENTS

A. LIST OF TABLES

B. LIST OF FIGURES

C. ABBREVIATIONS

BPM	Beats per minute
CNS	Central Nervous System
COP	Center of Pressure
DPN	Diabetic Peripheral Neuropathy
FFT	Fast Fourier Transform
FPI	Foot Posture Index
GL	GAITLINE
LDF	Laser Doppler Flowmetry
NSD	Norwegian Centre for Research Data
PAD	Peripheral Artery Disease
PFS	Probe Flux Standard
PNS	Peripheral Nervous System
PU	Perfusion Units
REK	The Regional Comities for Medical and Health Science Ethics
ROI	Region of interest
RP	Recovery Period
SGL	Sensory Gait Line
VMS	Vascular Monitor System

1 INTRODUCTION

1.1 AN INTRODUCTION TO THE CIRCULATORY SYSTEM

The vascular system is an elaborate system that makes out one of the body's three holistic systems together with the neural and fibrous nets (Myers, 2009). It tasks are numerous as it ensures the chemical balance in the body, regulates temperature and pH, and defends the body against pathogens and toxins. Its fluid net extends throughout the body, branching out from the arteries and carrying fluid out through smaller blood vessels called *arterioles*, leading to the *capillaries*, where the nutrients are distributed to the tissues and the waste matter is transported out to the *venules*. The activity in the capillaries produces heat in the tissues. At last, the venules join the larger *veins* as the fluid flows back towards the heart. The hemoglobin molecules in the blood are oxygenated and waste gasses are deposited as the blood passes through the capillaries of the lungs during the phase of pulmonary circulation, nutrients are supplied to the intestinal capillaries during digestion, and wastes are filtered out from the blood in the capillaries of the kidneys (Hauge, 2021). These are some of the mechanisms that enable the vascular network to fulfil its task of maintaining the chemical balance of the body.

The heart produces the pressure that generates the circulation of fluids, and this plays an important role in the temperature regulation of the body through internal heat transfer by forced convection. The capillaries reach to the dermis below the outer epidermis of 0.3-1.5 mm thickness. Here it interacts with the skin on its large surface area to ensure temperature regulation. The dermis is approximately 1.5-4 mm and here the arterioles and venules are arranged in a superficial and a deeper network of blood vessels (Holck, huden, 2021). In the glabrous skin of the hands and feet, there are numerous arteriovenous anastomoses - shunts that directly connect arterioles to venules while circumventing the capillary system and thus increasing the speed of the blood (Walløe, 2016). These anastomoses are under nervous control and dilate or constrict in accordance with the sensory information received from the skin (Holck, anastomose, 2020).

This is one example of the intricate interplay between the neural and circulatory nets. The heart's beat is initiated by a neurological signal and is Influenced by the body's communicated need of oxygenation and nutrition. The blood in turn nourishes the tissues and enables the nerve cells to perform their tasks. The thermoreceptive sensory neuron heads in the dermis sense temperature changes and inform the circulatory flow that acts to maintain thermal homeostasis. In case of injury or detection of offending agents in the body, the sensory cells signal the blood to rush in and respond. The networks are intertwined and provide one another with information. The fascial net also contributes by translating mechanical changes in the body and enhancing its reception by the neural net. When stimulus is applied to the web of connective fascia tissue, mechanoreceptors feed information from the facial net to the nervous system (Myers, 2009). The interplay between these three nets is illustrated in figure 1-1 below, using an illustration taken from the book "*Anatomy Trains"* by Thomas Meyer.

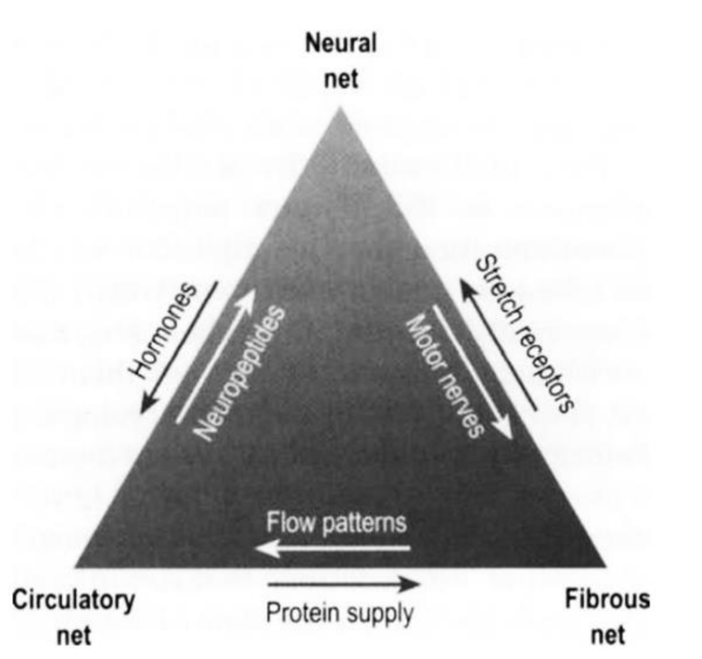

FIGURE 1-1 INTERPLAY BETWEEN THE HOLISTIC NETS, FROM "ANATOMY TRAINS" (MYERS, 2009).

What is the body's response to a disturbance in the circulatory system, and how does it connect to the other networks? As we will now see, a well-known condition such as diabetes can have many lesser-known effects on the body, as the systems are interconnected.

1.2 BLOOD FLOW, ULCERATION AND PRONATION

Insulin is a hormone responsible for reducing the level of glucose in the blood by transporting it to the cells. *Diabetes mellitus*, or simply *diabetes*, is a condition where the production of insulin in the pancreas has either stopped, as in type 1-diabetes, or where the insulin the body produces cannot be received due to a resistance to insulin, resulting in type 2-diabetes. In the US, it is estimated that 10.5 percent of the population has diabetes (NIH, 2020). The latter is the more common kind, accounting for 90 percent of all cases (Åsvold, 2021). Although diabetes type 1 and type 2 are different, the lack of received insulin results in hyperglycemia in both cases, which over time can lead to many various complications, among them: cardiovascular complications, kidney damage, neuropathy, reduced eyesight, oral infections and tooth impairment, and joint pain (Diabetesforbundet, 2021). The vascular, facial, and fibrous nets are all affected.

Diabetes type 1 and type 2 are associated with a higher likelihood of developing foot ulcers. These are pressure associated sores that develop under the feet. If they are not treated properly, foot ulcerations can lead to the need for amputation. An estimated 10 percent of all diabetics develop foot ulcers (Diabetesforbundet, 2021), and every year about 400-500 diabetics in Norway are amputated (Gürgen, Kaal, & Witsø, 2005). A previous history of foot ulcers leaves you at a high risk of developing it again (NHI.no, 2020), (Diabetesforbundet, 2021).

Foot ulceration in diabetics is attributed to two main factors. The first factor is atherosclerosis, where a build-up of plaque in the inner lining of the arteries hardens and narrows the circulatory pathway and reduces the blood flow (Diabetesforbundet, 2021). Atherosclerosis can cause a heart attack or stroke if the blood supply to the heart or brain is reduced or blocked by blood clots -pieces of plaque that can break off. But it can also cause Peripheral Artery Disease (PAD) if the blood supply is reduced to the arms and legs, a condition recognized by severe pain in the lower limbs and tissue death (Martel, 2021). Reduced supply of oxygen and nutrition undermines the skin’s ability to heal and is therefore a root cause of development of ulcers (Diabetesforbundet, 2021).

The other main complicating factor for diabetics that causes foot ulcers is neuropathy in the peripheral nervous system (PNS) that affects the sensory, autonomic, and motoric nervous systems. Diabetic peripheral neuropathy (DPN) is nerve damage due to hyperglycemia over longer periods of time and is the most common complication in diabetic patients (Diabetesforbundet, 2021). The role of the sensory nerves in the somatosensory system is to transmit the sensory information the body registers from stimuli such as temperature, touch, and vibrations to the central nervous system (CNS) (NHI, 2021). In people with diabetes who have DPN this tactile sensation is often reduced in the feet, increasing the risk of continual and unaddressed external damage to the skin of the feet. In addition, these wounds have a higher risk of infection in patients with hypoglycemia, which further increases the risk of foot ulceration (Diabetesforbundet, 2021). The risk factors described above do not then only increase the risk of ulceration but also increase the risk of accumulative complications. The described risk factors of foot ulceration are Illustrated in the diagram (figure 1-2) below in a simplified model.

Diabetes and Foot Ulcers

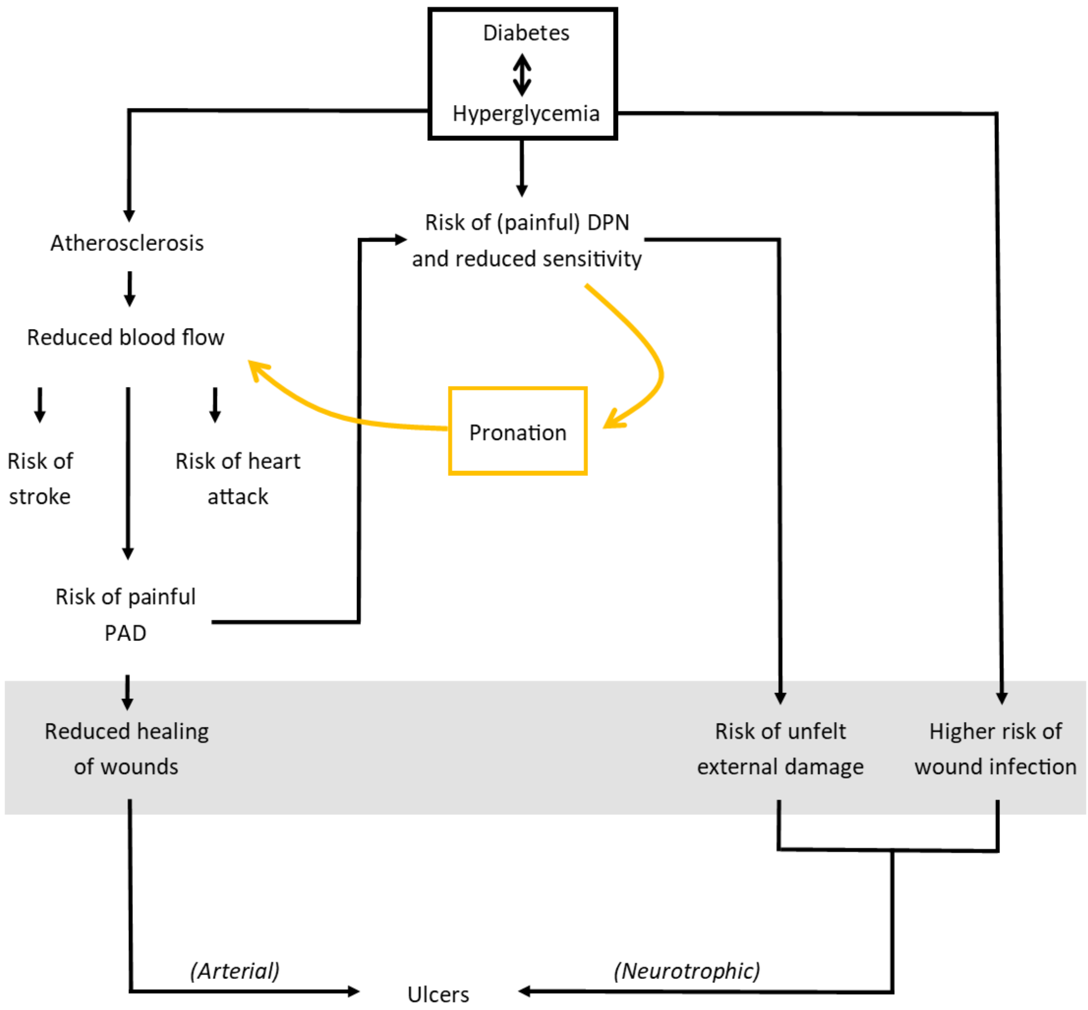

FIGURE 1-2 ULCERATION RISK FACTORS IN PEOPLE WITH DIABETES COMPLICATIONS

There are further associated complications that increase the risk of ulceration, such as reduced vision, which can leave external damage to the skin or early-stage ulceration undetected, dried skin caused by autonomous neuropathy affecting the sweat glands giving room for bacteria, and joint problems and motoric neuropathy that can cause postural changes and shifts in the pattern of pressure application under the feet (Furenes & Robberstad, u.d.).

It is the mechanical risk factors linked to posture that is the focus of this study, as indicated by the yellow curved lines in the diagram of figure 1-2. A study performed by García-Álvarez et al. in 2013 showed that a pronated foot is associated with higher body mass index (BMI), diabetes of long duration, and neuropathy (García-Álvarez, et al., 2013), drawing a link between pronation and the diabetic foot and, and between pronation and DPN. The aim of this research study is to better understand the relationship between pronation and plantar circulation, and its associated ulceration risk.

1.3 BALANCE AND PRONATION

There are several systems in the body that enable us to maintain balance while standing upright. Eyesight, proprioceptors in the muscles, joints and tendons, mechanoreceptors in the skin, and the vestibular system in the inner ear are important sensing mechanisms that work together to collect the data needed. The mechanoreceptors in the skin under the foot register the pressure differential throughout the sole and so register the location of the center of mass of the body. Similarly, proprioceptors are muscle spindles that contribute to postural control by detecting the change of length in our muscles (Brodal, 2004). As this sensory data is collected, the muscles are employed to continually adjust the stance. Complications associated with diabetes do not lend themselves to postural stability.

It is important to have a dependable balance strategy to avoid fall injury, but it is also important to implement strategies for everyday life that prevent damage and discomfort in the body over time. *Pronation* movement and its countermovement, *supination*, are both necessary and normal parts of the human gait cycle that play important roles in the foot stabilization and shock absorption. Excessive pronation (often called *overpronation* or simply *pronation*) and supination (also called *underpronation*) are however associated with negative postural compensation patterns and injury risk such as Achilles tendinopathy, plantar fasciitis, exercise related pain to the lower legs, and anterior knee pain (Willems, Ley, Goetghebeur, Theisen, & Malisoux, 2021).

The terminology surrounding foot pronation and the assessment thereof varies from study to study. It is therefore necessary to define the term as it will be used here and be attentive to its definition in publications. Pronation of the foot is a combined rotational motion about all three planes during gait, comprising of a simultaneous abduction, eversion, and dorsiflexion movement (Wezenbeek, et al., 2017). This resulting rotational motion can more simply be defined using the definition of Nigg, Behling and Hamill in their paper *"Foot pronation"* from 2019 as a rotational motion about the *subtalar joint axis* (Nigg, Behling, & Hamill, 2019). This axis runs along the *subtalar joint*, between the calcaneus and talus bones in the rearfoot, inclining about 42 degrees as from posterior lateral side of the foot to the anterior medial side of the foot, as illustrated in figure 1-3.

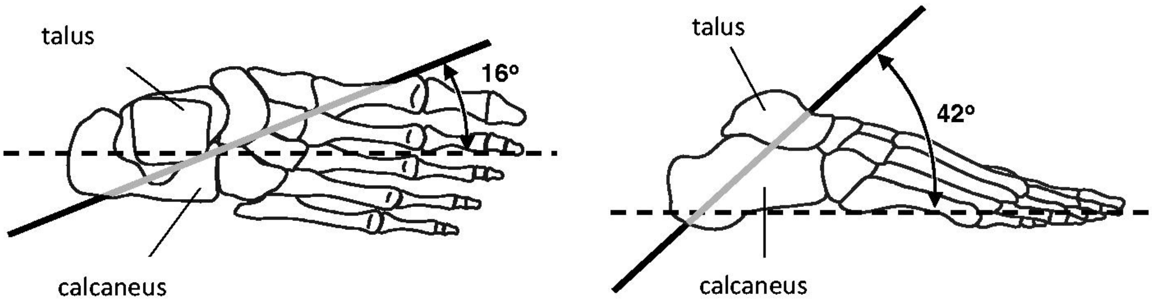

FIGURE 1-3 ILLUSTRATION OF THE SUBTALAR JOINT AXIS, TAKEN FROM "*FOOT PRONATION*" (NIGG, BEHLING, & HAMILL, 2019).

How large the degree of rotation or angle deviation of the foot along this axis must be before the foot is considered to be overpronated is not standardized. In this study, the quantization of foot pronation will be simplified down to an analysis of the Achilles tendon in the frontal plane, assessed during static stance. This is one of the most measures of pronation used (Nigg, Behling, & Hamill, 2019). The differentiation between a pronating foot, a neutral foot and a supinating foot is in this study set using a limit of 6° deviation from the vertical axis in both directions. The term *overpronation* will be applied to subjects displaying an eversion of more than 6°, and the term *supination* to the subjects with an inversion of more than 6° in the frontal plane. This is a simplified model that focuses on one measurand of a rotational movement that is in reality a more complex movement in three dimensions.

In response to the negative postural patterns associated with pronation, a Norwegian company called GAITLINE has developed footwear using Sensory Gait Line (SGL) technology that guides the foot and ankle to distribute the forces applied to the bones and joints of the feet optimally and lay a good foundation for the posture in the rest of the body. Their shoes are designed for comfort and balance with a sole that supports the foot's natural arch, and are made with materials that keep their original shape (Gaitline AS, 2021). An important feature of the SGL-footwear is the rearfoot medial wedge designed to encourage the heelbones to move in a less everted position by straightening the angle of the Achilles tendon in overpronating persons. The circulatory effect of the SGL-technology has not been mapped out yet.

1.4 RESEARCH QUESTIONS, HYPOTHESIS AND GOALS

It is the connection to the circulatory response to pronation and pronation correction using SGL-technology which is the focus of this study. If corrective footwear upholds a higher superficial circulation than other footwear it could be a step towards uncovering a useful tool for diabetics to prevent ulceration of the feet. The main research question that is being addressed in this project is:

Main Research Question:

"Does medially wedged corrective footwear improve the short- term medial and lateral superficial plantar microcirculation of the forefoot in overpronating subjects when compared to flat and laterally wedged footwear?"

The stimuli in question here is one adopting the wedge feature of SGL technology footwear alone - wedging the heelbone on the medial side so that the foot is inverted and the Achilles tendon aligned in the frontal plane. The degree of correction applied is adapted to each subject. Overpronating subjects are defined as subjects in need of more than 6° wedge correction. Other foot types are excluded from participation. The footwear of comparison in this study is a neutral flat sole and an oppositely wedged sole – a sole wedged on the lateral side to aggravate the degree of pronation. The wedges used are medical grade wedges covering only the area of the hindfoot and are designed not to deform easily. The choice of subjects and test soles will be discussed further in the methodology section. The three test situations are illustrated below on a right foot heel as seen from the back.

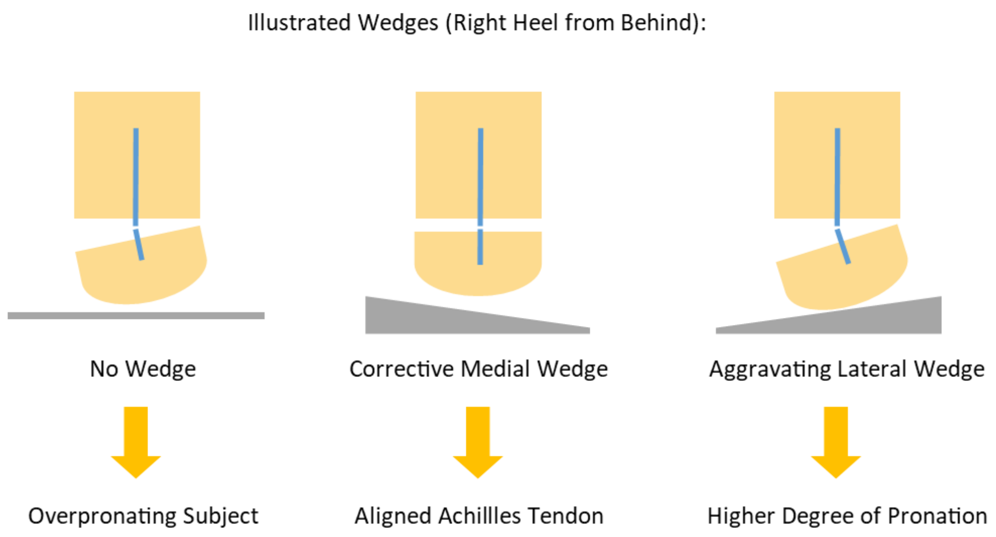

FIGURE 1-4 WEDGE CONDITIONS FOR TESTING ILLUSTRATED

The improvement under evaluation in the main research question is a heightened flux response when using the corrective soles when compared with the flat or laterally wedged footwear within the first seconds and minutes of stimuli. The LDF-sensor that will be employed has an approximate depth of 1 mm (Moor Instruments, u.d.), which will be placed on the forefoot skin under the metatarsal heads - an area associated with a higher risk of ulceration in the superficial skin for diabetics (Oyibo, et al., 2000).

This primary research question is divided into four specific research questions:

Research Question 1:

> ***"Is the forefoot flux greater while standing on corrective soles than standing on flat or laterally wedged soles?"***

Research Question 2:

> ***"Is the forefoot flux response at rest greater after having stood on corrective soles compared to having stood on flat or laterally wedged soles?"***

Research Question 3:

> ***"Is the forefoot flux response at rest greater after having walked with corrective shoes for 10 minutes compared to having walked on flat or oppositely wedged woot wear?"***

Research Question 4:

"Does the flux response across trials correlate with the subject's weight or needed degree of correction?"

Based on the literature review, which will be presented in section 2, the experimental study hypothesis is that the circulation of pronating subjects is poorer on both medial and lateral sides in response to and while using laterally wedged footwear compared to the response to and measurement during stance on flat footwear, and conversely better as a response to and while using medially wedged corrective footwear. The expectation is that the difference will correlate to the force applied to the soles, and therefore the subject's weight and degree of wedge correction, so that a perfusion response at rest will be greater for subjects in laterally wedged shoes as a result of a higher reperfusion caused by vascular constriction during rest. The communication between the neural, fibrous, and circulatory nets innkeeping with this hypothesis is illustrated in the triangle below using the Thomas W. Meyer's "Anatomy Trains" model.

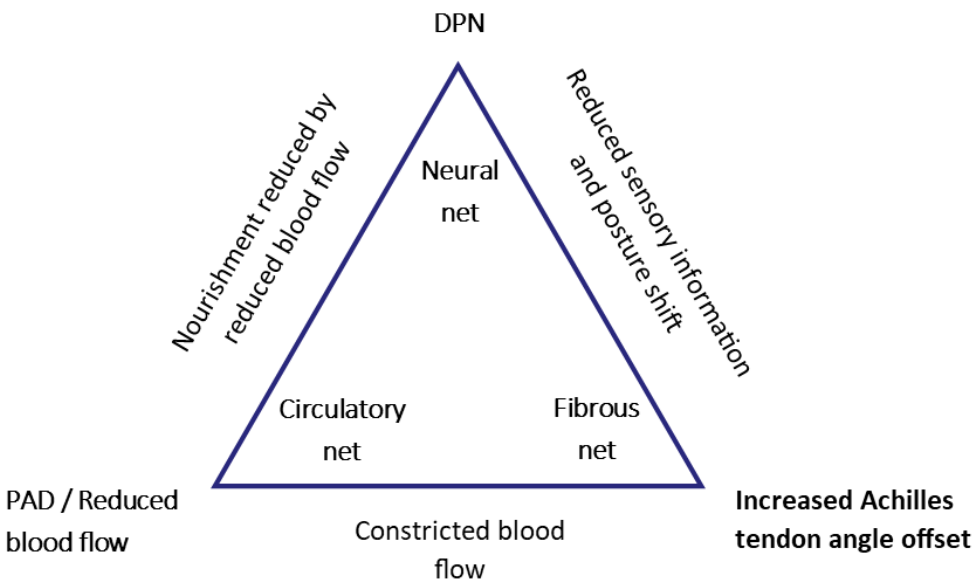

FIGURE 1-5 HYPOTHESIS OF HOW PRONATION CONNECTS TO DIABETIC COMPLICATIONS. ILLUSTRATION INSPIRED BY ILLUSTRATION IN "ANATOMY TRAINS" BY THOMAS W. MEYER (MYERS, 2009).

1.5 TOOLS

The tool employed to answer the research questions above is a single channel Laser Doppler Flowmetry sensor (LDF), called *Standard moorVMS-LDF1*. This optical instrument is used to monitor laser doppler blood flow or *flux*, tissue temperature, moving blood volume and light intensity, depending on the probe accessories used. The depth of the measurement is approximately 1mm (Moor Instruments, u.d.), but is dependent on the probe head used and skin tissue characteristics. It is, therefore, suitable for measurement of the peripheral tissue perfusion.

FIGURE 1-6 LOW-PROFILE PROBE HEAD

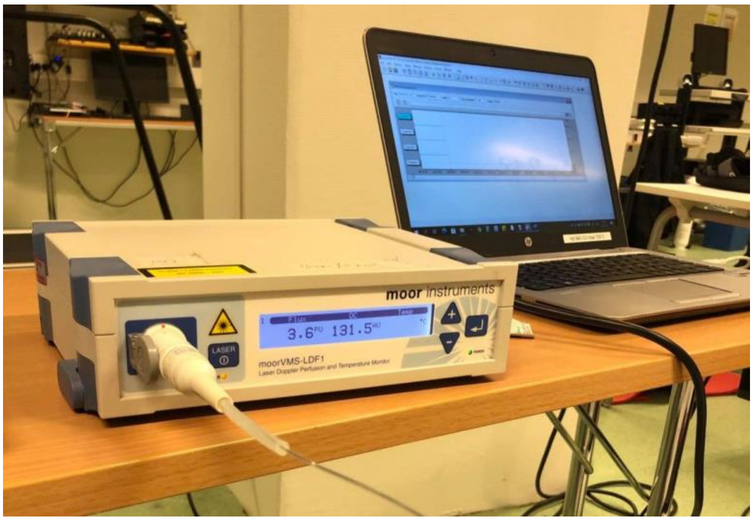

FIGURE 1-7 THE LDF-SENSOR: STANDARD MOORVMS-LDF1

To measure the blood flow the probe emits infra-red light onto the skin tissue via flexible glass optic fibre. As explained in the moor-VMS user manual, this light is then scattered by skin tissue and moving blood cells in the capillaries, arterioles, and venules, and is then partly reflected and transmitted back to a photo detector in the LDF sensor through the fibre optics. The ´reflection of the LDF-sensor is illustrated in figure 1-8, taken from the *moor instruments* user manual (Moor Instruments, u.d.). The light reflected of a moving blood cell undergoes a *Doppler* frequency shift, which is dependent on the speed of the object. This light component is then compared to the non-frequency shifted light reflected by the static tissue and used to calculate the flux and concentration of the blood flow in perfusion units, PU (moor instruments, 2015) (Moor Instruments, u.d.).

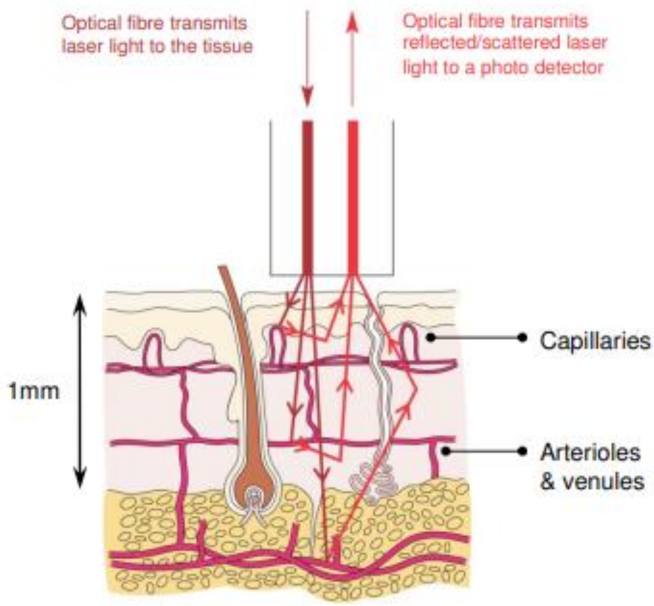

FIGURE 1-8 THE FUNCTION OF THE LDF-SENSOR, FROM MOOR INSTRUMENTS USER MANUAL (MOOR INSTRUMENTS, U.D.)

The flux is calculated using equation 1 below, where *DC* is the light intensity, ω_1 and ω_2 are lower and upper bandwidth limits, *P*(ω) is the optical power density at Doppler frequency shift ω, and k_1 and k_2 are scaling constants used in calibration (Moor Instruments, u.d.). The displayed signal will be partly signal from blood flow and partly noise, as the influence of movement and external light can affect the true blood flow readings.

$$flux = k_1 \cdot \int_{\omega_1}^{\omega_2} \frac{\omega \cdot P(\omega) \cdot d\omega}{DC^2} - noise \qquad (Equation\ 1)$$

The probes used in this research project are low-profile non-invasive VP8c-Suturable probes, 90°-angled with titanium disc probe heads. These probes do not monitor temperature changes in the skin but are in turn well suited for measurement to the skin in areas that are difficult to access. They also reduce the probe’s pressure applied to the skin in cases where the probe is covered, which is an advantage in a setup where the sensor is to be used while wearing sandals or be held in place using adhesive tape.

The circulatory system has a slower initial response time than that of the neural net and the immediate response of the facial net, where a red blood cell spends approximately 1.5 minutes before it returns to the heart (Myers, 2009). The experimental protocol must allow for time corresponding to the duration and speed of response of the physiological changes involved. The LFD-sensor is suited for an analysis of both the short and longer-term effects of wedged shoes in percental change and analysis in frequency domain. The LDF-sensor captures these changes in real time with a sampling rate of up to 40 samples per second. The changes are then logged using the corresponding recording and analysis software, called *moorVMS-PC V3.1* (Vascular Monitor System).

2 LITERATURE REVIEW

This literature survey seeks to place this study within a larger context and assess the current knowledge of the field. The articles presented illustrate the attention that circulatory net has regarding pronation, and what the consensus is on the measurement and effects of pronation today.

2.1 MEASUREMENT OF PRONATION

As introduced earlier, pronation is a complex triplanar movement of the foot and presents challenges when it comes to its quantization. Different tools have been employed to measure pronation in one, two or three dimensions, during dynamic gait or in a static context.

One advanced method to analyze gait is to use a 3D-motion capture system, such as *Qualisys*. Here reflective markers are placed strategically (on for example the foot and lower leg) and the gait is analyzed in a dynamic context through numerous digitized shots captured throughout the gait cycle, as done by Horsak and Baca in 2013 in assessment of balance when using instability inducing shoes (Horsak & Baca, 2013), and by Gomez et al. in 2019 in an analysis of mechanical midfoot resistance related to foot pronation (Gomes, Souza, Paes, Magalhães, & Gontijo, 2019). This method can also be applied in a two-dimensional analysis of the deconstructed rotational movements in pronation. This method was used by Reinschmidt et al. in a motion capture analysis of tibiocalcaneal motion in all three rotational planes (Reinschmidt, Bogert, Murphy, Lundberg, & Nigg, 1997). It was also used by Wezenbeek et al. in their study from 2017 in order to determine its correlation with the blood flow in the Achilles tendon. In their study the eversion of the heelbone in the frontal plane and dorsiflexion in the sagittal plane are analyzed separately (Wezenbeek, et al., 2017).

Pronation can also be assessed using the navicular drop test, as Cote, Brunet, Gansneder and Shultz did in their 2005 study where the relationship between foot type and postural stability was under study (Cote, Brunet, Gansneder, & Shultz, 2005). With this method the distance from the navicular tubercle, a rounded prominence in the navicular bone of the foot, to the floor is measured in weight baring (or relaxed) conditions and neutral position using a ruler. This can also be measured using a motion capture systems. The difference is given in millimeters. A more common clinical assessment of pronation is an analysis of the Achilles tendon angle in the frontal plane (Nigg, Behling, & Hamill, 2019) which can be analyzed using motion capture system as described above, or in a static context using for example a goniometer.

A tool developed by Redmond et al. in 2005 is the *foot posture index* (FPI-6), which has since become a standardized and clinically validated assessment tool (Keenan, Redmond, Horton, G.Conaghan, & Tennant, 2005). This tool is made to simplify an evaluation and categorization of the foot in a supinating, pronating or neutral type based on six evaluations, combining several assessment methods described above in one the total score (Redmond, Crosbie, & Ouvrier, 2005). One of the rearfoot evaluations in the FPI is the calcaneal position in the frontal plane, where a 5° deviation is the set divide between the foot types. This tool was used by García-Álvarez, et al. in a morphological study of neuropathic diabetics, which will be expunden on below (García-Álvarez, et al., 2013).

In this study, the quantization of foot pronation is an analysis of the Achilles tendon angle (or calcaneal position) in the frontal plane, assessed during static stance. Since the variable of this study is the angle of the mediolateral wedges applied to footwear, it is no disadvantage to limit pronation assessment to this evaluation.

2.2 PRONATION LINKED TO PERFUSION

As illustrated above, there have been several topics of interest within the study of pronation, exploring its connection to morphology, balance and stability, mechanical resistance, and medical diagnoses. The link to the circulatory net has also been looked in to from a few angles.

2.2.1 THE WRINGING EFFECT

In the 2017 study performed by E. Wezenbeek et al. introduced above, the correlation between pronation and blood flow patterns in the Achilles tendon was examined. The theory underlying this study is the *whipping phenomenon* first presented in 1984 by Clement et al., which claims that the pronated foot movement from an inverted to an excessively everted position during stride from heel strike to midstance causes simultaneous pronation and knee extension - conflicting rotary forces that “wrings out” the Achilles tendon and causes blanching, a temporary vascular constriction, in the tendon (Clement, Taunton, & Smart, 1984). In the 2017 study, blood flow was determined using an oxygen-to-see LDF-sensor (LEA Medizintechnik, Giessen, Germany) and was measured in the prone position initially after a 10-minute rest, and again immediately post-running in the same position. The study revealed that a greater eversion excursion in the Achilles tendon, here defined as the difference between tendon angle the maximal inversion and at maximal eversion during gait, was correlated with a lower increase in blood flow in the Achilles tendon after shod running for the duration of 10 minutes (Wezenbeek, et al., 2017). Their conclusion is that the whipping theory is supported, and that anti-pronation measures could be beneficial for prevention and treatment of Achilles tendinopathy. The same conclusion was drawn in a similar study performed by Karzis et al. in 2016, where the blood flow was measured during in a static condition using power Doppler ultrasonography in non-weight bearing stance, bipedal stance, and monopedal stance. They found that the blood flow was particularly affected in the mid-tendon, and that it may be an injury risk factor (Karzis, et al., 2016). Does vasoconstriction due to a wringing effect in the lower leg translate to the plantar circulation?

2.2.2 The Foot Pump model

In 1983, Gartner and Fox presented a model were the dynamic compressions of the foot during gait are demonstrated to function as a pump that plays an important role for veinous return in the foot. The study was performed with venography using radiographic contrast media in weight bearing and non-weightbearing standing positions (Gardner & Fox, 1983). Horwood expanded on this model in 2019. He writes that a pumping action is generated as soon as the heel strikes, and that the supply of blood vessels in the veins in the heel pad are compressed during the progressive deformation from lateral posterior to anterior medial position. The veinous return is then driven by repeated compression to the feet during gait to a circulatory system that flows in one direction due to venous valves that only allow return flow. The change of the foot profile as the forefoot is loaded is, he writes, associated with foot pronation and could be important to maximize the foot pump effect, as it allows for more soft tissue deformation. This model challenges the widely held negative association with foot pronation when considering its circulatory effects. However, this model is less elaborated on in literature, and Horwood writes that it may be more relevant to consider the compliance and stiffening of the foot as the true variables at play (Horwood, 2019). If this model holds, a higher blood flow could be expected as a response to using soles that increase pronation and surface contact area at impact.

2.2.3 Areas of Local Pressure

Ulceration is associated with areas of pressure, with a prevalence under the forefoot region (Oyibo, et al., 2000). Therefore, offloading through use of orthopedic footwear such as the knee-high device, or use of wheelchair or crutches or plaster treatment is often recommended for diabetics with onset ulceration (Furenes & Robberstad, u.d.). According to the systematic review of offloading interventions by Bus et al. from 2015, when it comes to offloading using orthopedic footwear there is however only good support for the use of non-removable offloading devices and the evidence to support the use other offloading interventions is insufficient (Bus, et al., 2015).

In a study performed by Sundby et al. in 2016 the microcirculation in the lower leg was assessed when exposed to intermittent negative pressure (INP). The negative pressure, or vacuum, was achieved by attaching a rigid boot to a pressure control system and sealing it below the knee. The microcirculation in the plantar skin was assessed in the Hallux using laser Doppler flowmetry (LDF; Periflux PF 4000; Perimed AB, Järfälla, Sweden). The study revealed that INP gives an increased foot perfusion, with an attained maxima at approximately 2 sec. after onset pressure (Sundby, et al., Application of intermittent negative pressure on the lower extremity and its effect on macro- and microcirculation in the foot of healthy volunteers, 2016). A follow up paper treated four patients with advanced foot ulceration applying INP throughout an 8-week period. The treatment improved all four ulcerated patients, with one complete recovery. The conclusion of the study is that an improved flow provided by INP improves circulation in the small vessels of the skin and assists wound healing (Sundby, et al., The effects of intermittent negative pressure on the lower extremities' peripheral circulation and wound healing in four patients with lower limb ischemia and hard-to-heal leg ulcers: a case report, 2016).

Another study was performed in 2016 by Molines-Barroso, et al. where 258 feet of neuropathic diabetics were analyzed using FPI-6, whereof 104 had a previous history of previous foot ulceration (Molines-Barroso, et al., 2016). Their multivariate analysis revealed that forefoot ulceration is a higher risk in neuropathic diabetics with pronated feet than in neuropathic diabetics with supinated feet. The risk between supinated and neutral feet were negligable.

These studies indicate that an *offloading*, even an intermittent one, is beneficial for ulcer treatment. The higher ulceration risk in pronated diabetics found by Molines-Barrasso et al. suggests that an offloading that specifically counteracts the plantar pressure pattern in pronated feet is beneficial. Does the medially wedged sole in this experiment provide such an offloading effect? In contrast to the earlier studies looked at, these last studies presented attribute the ulceration risk in diabetics to to a local pressure pattern, and do not consider a general circulatory flow reduction caused by for exaple a wringing effect in the Achilles tendon or reduced pumping effect. Does pronation cause a local or a general vasoconstrivtion in the plantar skin of the foot?

3 METHODOLOGY

3.1 ETHICAL CONSIDERATIONS

This project has been approved by REK (The Regional Comities for Medical and Health Science Ethics). The experimental work has been developed in keeping with the ethical guidelines of REK and NSD (Norwegian Centre for Research Data) concerning participation and data storage.

Before participating, volunteers are required to sign a consent form and submit a preliminary questionnaire. In the consent form, volunteers are provided with information concerning their role as a participant in this project and concerning the storage of their personal data. The data collected in this project will only be used in this project and further research projects in collaboration with OsloMet University and GAITLINE. Volunteers may withdraw their participation at any time without stating a reason. The information collected during the laboratory experiments will be stored separately from their personal information, published anonymously, and not referenced in any way that could identify them. The volunteers are also given an opportunity to request special considerations to be made when performing their laboratory experiments, such as requests concerning privacy or dress.

The preliminary questionnaire is a short demographic analysis of the participants, where information such as age, height, weight, and walking habits are collected. The subjects are also asked to assess the frequency at which they experience unprovoked pain in the regions of the back, hips, and lower limbs. This data is collected for further analysis and discussion of the results found.

The LDF-equipment used in this experiment is not harmful to the skin. The *Standard moorVMS-LDF1* has a maximum power of 2.5mW, but a typical power output of 0.5 to 1.2mW. The device classifies as a class 1 laser product according to the International Electrotechnical Commission (IEC) safety standard *IEC 60825-1:2007*, and safety goggles are, according to the moorVMS-LDF user manual, not required for the operator nor the subject. Unnecessary direct viewing of the laser beam should however be avoided (moor instruments, 2015).

3.2 PRINCIPLES FOR TESTING

Before presenting the experimental protocol in section 3.3, some of the choices made beforehand in the experimental design are presented here, such as participation criteria for subjects, choice of footwear, and considerations regarding the protocol design.

3.2.1 SUBJECTS AND EXCLUSION CRITERIA

When choosing a sample subject group, it must be selected and recruited so as to ensure that it properly represents the population under study. The GAITLINE shoes are intended primarily for urban pedestrians, and it is therefore no disadvantage to recruit volunteers among students at a metropolitan university. This study is designed for application and further testing on diabetic persons. In this thesis however, the goal is to first investigate the circulatory patterns generated by use of wedges on healthy subjects, without introducing additional variables that are inevitable when testing on diabetics. Complications such as foot deformities, change in gait pattern, changed pressure distribution, reduced pulse in foot, and reduced capillary refill time (CRT), as often seen in diabetic feet with complications (Furenes & Robberstad, u.d.), can significantly influence the outcome of the LDF experiment and complicate an analysis of the correlation to wedge influence.

Additional exclusion criteria are applied for participation, to represent the statistical population of interest. The main research question posed in section 1.4 addresses the microcirculatory response to pronation corrective footwear in overpronators. A neutral or supinating foot type were therefore grounds for exclusion. The limit applied in this study was a minimum pronation of 6°, which closely resembles the 5° standard limit for neutral calcaneal eversion in one of the FPI-6 assessments (Redmond, Crosbie, & Ouvrier, 2005). Persons with a history of severe injury to the back or lower limbs, as well as persons with a circulatory disease or history of previous foot ulceration were also excluded from participation.

The age limit for subjects was set to 17-40 years to avoid aging influence, as factors such as plantar foot sensitivity and pressure distribution varies between young adults and elderly, as demonstrated by Machando et al. in 2015 (Machado, Bombach, Duysens, & Carpes, 2015), as well as sensory information processing ability (Brodal, 2004).

3.2.2 PRONATION ASSESSMENT

The foot type in each subject taking part in the experiment was first assessed visually in a preliminary evaluation to exclude non-overpronating candidates at an early stage. The foot type was confirmed, and the degree of pronation determined in the beginning of each experimental trial with the help of the trained eye of Håvard Engell, the founder of GAITLINE, using the *Achilles laser* and *Achilles marker*.

The Achilles marker, illustrated in figure 3-1, is a custom-made GAITLINE tool designed to mark the centerline of the Achilles tendon. This is carried out while the subject is lying in prone position without support under the feet as shown in figure 3-2. The subject is then instructed to stand upright in a relaxed bipedal stance. In this position the marked centerline of the tendon is compared to the vertical laser beam of the GAITLINE Achilles laser. This tool is a frame placed around the foot of the subject that indicates the vertical axis along the leg in the frontal plane. The heel of the overpronating subject is wedged medially until the centerline marked with the Achilles marker is aligned with the vertical axis. The degree of the wedges needed to correct the everted foot angle is thus determined for both feet. The use of the Achilles laser is illustrated in figure 3-3.

FIGURE 3-1 THE ACHILLES MARKER, AND FIGURE 3-2 MARKING THE CENTERLINE OF THE ACHILLES TENDON WITH THE ACHILLES MARKER.

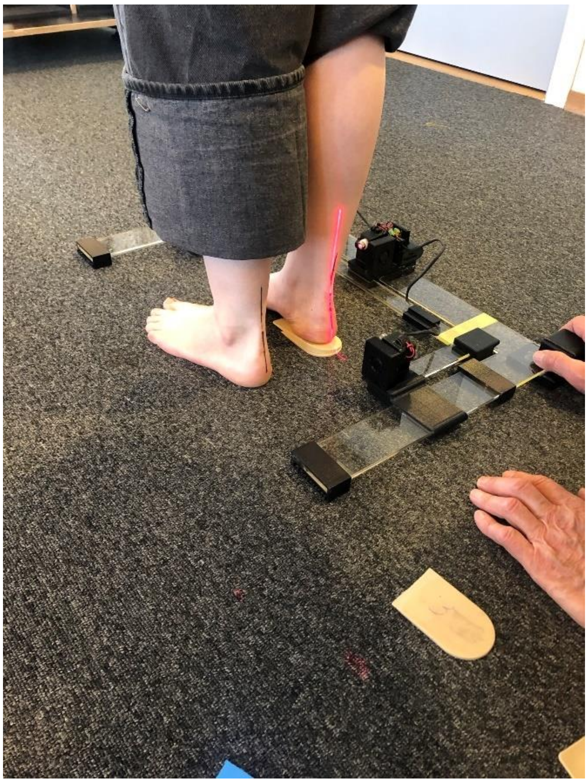

FIGURE 3-3 DEMONSTRATED USE OF THE ACHILLES LASER. WEDGES ARE ADDED AS NEEDED.

The stimuli comparison in the main research question is using medially wedged soles compared using flat and laterally wedged soles. The laterally wedged footwear used as a comparison is a wedge that aggravates the subject's degree of pronation. The size of the wedge applied in this case is chosen so as to result in an equally exaggerated degree of pronation on both feet, amounting to 20° in all subjects. The degree of rotational freedom may vary from subject to subject.

The three wedge conditions are explained in figure3-4 below using the right foot of subject B as an illustration. This foot had a pronation degree of 12° when measured using the Achilles marker and laser. This subject was therefore equipped with a 12° wedge to correct pronation and align the tendon. The lateral wedge for comparison was a 6° wedge, resulting in a hightened degree of pronation of 20°.

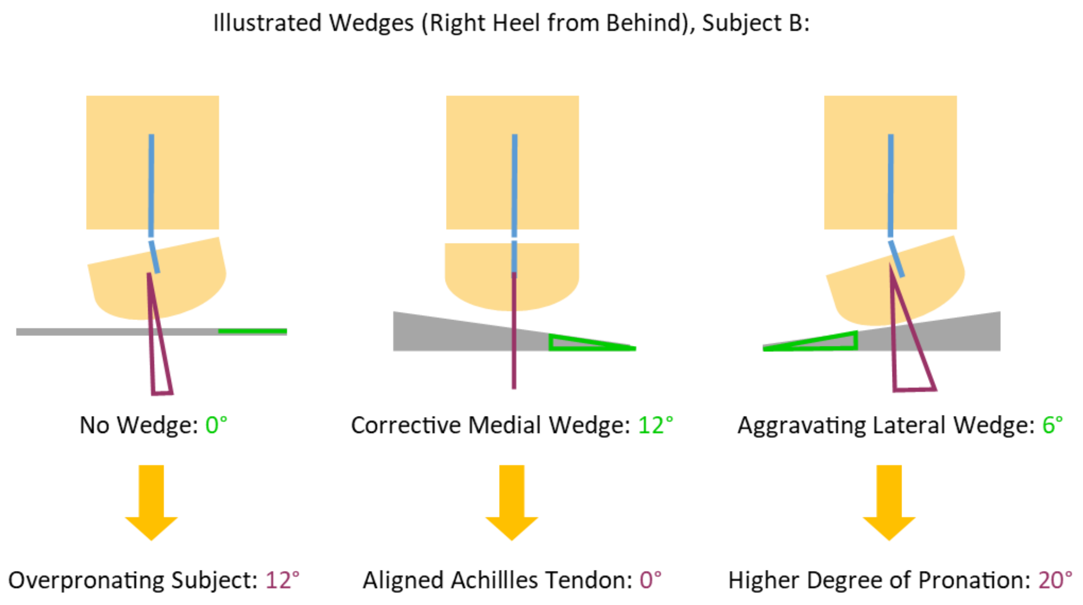

FIGURE 3-4 ILLUSTRATION OF WEDGE ANGLES USED ON SUBJECT B.

3.2.3 CHOICE OF FOOTWEAR BASE

The wedges applied are, as explained above, adapted to the subject's individual need of pronation correction. These wedges are independent and can be inserted under the insole of most shoes, placed directly on the floor, or added to the surface of the sole of a sandal using thin double-sided adhesive tape. That presents the question: what footwear provides the best base for a wedge stimuli comparison?

One option is to let the subject walk barefoot on the floor when testing the flat soled condition. The advantage here is that it is the condition in which the subject's degree of pronation is initially assessed, and thus allows for the most unchanged position and movement of the foot. The wedges can easily be placed on the base floor and allow for static step tests with immediate measurement and eliminate any transition time in taking off test shoes before measurement. It does not however allow for walking tests in with wedges. Using GL-shoes is also an option that does allow for walking tests with corrective wedge. It does however also introduce added SLG-features, such as the *Arch-Roller* that supports the arch of the foot (Gaitline AS, 2021), which is not a variable included in this study design.

A third option is to compare the different wedge stimuli by using the participants own everyday shoes with added wedges placed inside. This provides a similar base for comparison for the three wedge conditions within each subject trial. On the other hand, these shoes are not comparable across subjects, and can introduce new variables due to shoe design and wear pattern affected by the pronation degree of the subject.

The last option considered and selected was using custom-made neutral sandals (shown in figure 3-7), produced by GAITLINE in a range of sizes for testing. These sandals can easily be equipped with wedges (see figure 3-7) and provide a good ground of comparison across wedge comparisons and across subject trials. The soles of these sandals are fully flat and designed so as to not change shape by forming to the subject's foot. The rims of the sandals can also be removed, which allows for both walking tests and step tests. Below is table 3-1, illustrating the considerations made when choosing the footwear base. The footwear is illustrated in figure 3-5.

FIGURE 3-5 FROM THE LEFT: SUBJECT'S WALKING SHOES, GAITLINE SHOES, TEST SANDALS (HERE WITH ATTACHED WEDGES) AND BAREFOOT.

TABLE 3-1 ASSESSMENT OF FOOTWEAR BASE

Desired criteria	Footwear considered			
	GL-shoes	Subject's own shoes	Barefoot	Flat test sandals
Available in all relevant sizes	Yes.	Yes.	Yes.	Yes. Had to be made.
Provides flat initial base	No. Wedge is integrated.	No. Some variations can occur.	Yes.	Yes.
Similar base in all three wedge conditions	No. Cannot be used for flat or oppositely wedged conditions.	Yes.	Yes. Floor is base.	Yes.
Similar base across all subjects	Yes.	No. Wear and design variations in subject shoes occur.	Yes.	Yes.
No additional variables introduced	No. Ex. Arch-Roller support is added.	No. Ex: Dampening, and heel elevation can occur.	Yes.	Yes.
Suited for walking tests	Yes.	Yes.	No. wedges are not attached to a mobile base.	Yes. Can be uncomfortable at length.
Suited for single step tests	No. Shoe is closed.	No. Shoe is closed.	Yes.	Yes. Sandal rims can be removed.

FIGURE 3-7 GAITLINE TEST SANDALS IN A RANGE OF SIZES.

FIGURE 3-6 WEDGE PLACED ON FLAT SANDAL BASE

3.2.4 SENSOR PLACEMENT

The sensor placement is chosen with regards to the application of the study on diabetic patients with ulceration risk. This area shows a prevalence of ulcer location in the plantar foot (Oyibo, et al., 2000). The LDF-sensors are attached under the 1st and 4th metatarsal heads in this experimental design, measuring the medial and lateral sides of the forefoot. The measurement is performed consistently on the right foot of each subject. The sensor placement is illustrated in figure 3-9. At the beginning of each test, the subject's right foot is marked to indicate the placement of the LDF-probes and so ensure comparable recordings between activities when reattaching the probes. Sensor placement on visible peripheral blood vessels was avoided. The placement was traced while keeping marker ink clear of the area in the direct trajectory of the LDF laser beam.

FIGURE 3-9 PRE-MARKED PLACEMENT OF THE LDF-PROBES

FIGURE 3-8 ATTACHED LDF-SENSORS MEDIALLY AND LATERALLY TO PRE-MARKED MEASUREMENT SITES

The low-profile LSD probes were attached using adhesive tape, as shown in figure 3-8, and the probe leads were placed and attached when necessary to avoid movement artefact or damagingly low radii of the optical fibre. A thin film of optical coupling gel (ultrasound gel) was applied between the probe head and skin to reduce any laser reflection on the skin surface (Moor Instruments, u.d.).

3.2.5 VARIABLES AND CONSTANTS

The controlled variables that are compared in this experiment is the wedge condition applied - whether medially wedged, flat, or laterally wedged - and the degree of correction needed from subject to subject. The other parameters that influence the measurements should be kept as constant as possible in order to clearly identify the cause of the change observed when footwear stimulus is introduced, without artefacts or systematic sources of error.

The temperature and humidity of the room can affect the participants blood flow (Moor Instruments, u.d.). To maintain stable surrounding conditions, the test protocol is carried out in the same location and at the same time of day, with the same setup. The lab used for testing is a large open area with regulated heating. The surrounding conditions are monitored to ensure that the requirements are met.

The condition of the subject also influences the measurements. The Moor LDF manual recommends a period of 15 min before the experiment starts in order to let the participant acclimatize to the test room (moor instruments, 2015). The subject is also instructed to abstain from exercise, food, and stimulants such as caffeine and alcohol in the hours preceding the experiment. During LDF measurement in the experimental run, the subjects are instructed to breathe normally, refrain from talking, and relax. The auditive and visual external stimuli are kept to a minimum during recording. This is to ensure minimum movement artifact and minimum changes in the blood flow caused by respiration or mental state.

The measurement site is covered by a blanket when measurement is performed at rest to eliminate any light artefact from the surroundings, and to insulate the bare feet of the subject from significant temperature changes during more extended measurements. The order in which the test activities of the laboratory experiments are performed is randomized for each participant to eliminate any systematic sources of error.

3.2.6 Considerations in Protocol design

The protocol, presented next in section 3.3, was shaped by the research questions, and the considerations that were made in its design. As the sub-research questions stated in section 1.4, the perfusion response to the wedged footwears will be compared in three different contexts:

a) *when standing* on the wedges,
b) *after standing* on the wedges, and
c) *after walking* with the wedged footwear for 10 min.

Perfusion measurement *during* gait was not pursued, as dynamic testing presents considerable limitations. The movement of the probes and optical fibers during gait causes unacceptable movement artefact, causing artificially high blood flow readings. The pressure application to the LDF- probes, on the other hand, reduces the signal readings. The LDF moor manual warns that pressure application from the probe head to the skin reduces the blood flow and can give inaccurate readings in LDF experiments (moor instruments, 2015). In our experiment however, the influence from pressure application is welcome, as it is this reduced blood flow that is of interest here.

This movement artefact was confirmed in a preliminary dynamic experiment. In this study, time periods of 10 sec. were repeated five times for intermittent rest and activity. During the activity period, the subject was to step forward onto the right foot and back repeatedly. This protocol was performed multiple times on all three wedge conditions. The dynamic experiment revealed that the signal to noise was too high in a dynamic test situation, as the pulse frequency, which is one of the principal influencers of the Doppler measurement was undetectable among the high reading at dynamic phase. The movement created noise and displayed artificially high readings. Mock tests were also performed in the dynamic experiment, where the probes were attached to the sandal sole instead of the skin. These tests also displayed high readings during dynamic phases, which could be explained by large movement artefact or change in the LDF backscattered reflection from the rubber sole during compression. Although there is here no comparison to the signal of interest, the signal displayed by the movement alone could further indicate unacceptably large movement artefact. The diagrams of one of the flat sandaled dynamic tests is shown below in figure 3-10 together with one of the mock tests in figure 3-11. The five signal bulks represent the activity periods.

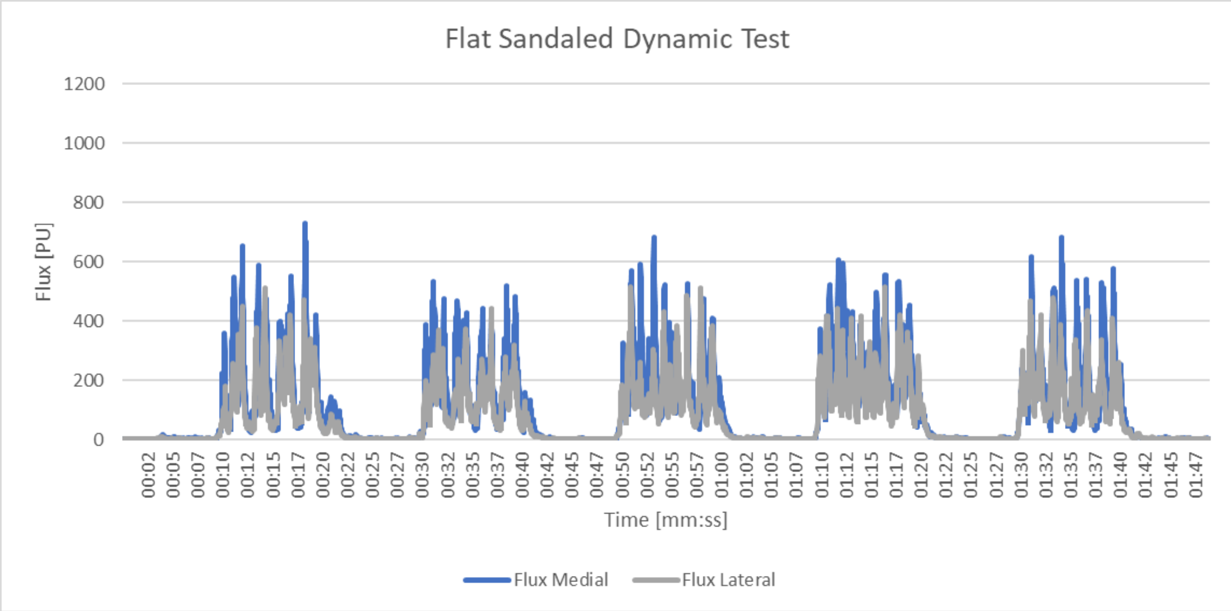

FIGURE 3-10 FLAT SANDALED PRELIMINARY DYNAMIC TEST (RIGHT FOOT).

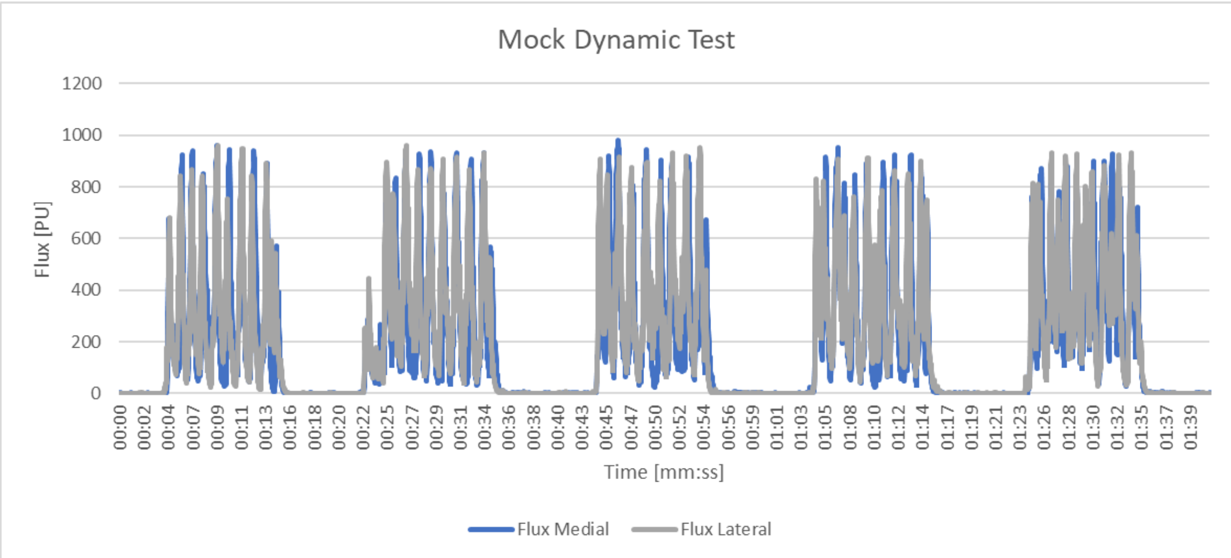

FIGURE 3-11 PRELIMINARY DYNAMIC MOCK TEST (RIGHT FOOT). PROBE IS NOT ATTACHED TO SKIN.

Instead of dynamic testing, the protocol was shaped to measure perfusion either at rest during static activity (stance), or before and after dynamic activity (walk). This is in line with the literature, where perfusion is often measured before and after an introduced stimulus and is then compared, or initial post-activity response is compared to the response after a recovery period (RP). This is usually done when the stimulus of the experiment is physical activity, where access to the measurement site is needed between measurements, or when a site is monitored over time.

This was the case in the study by Wezenbeek, et al. discussed earlier, where the flow in the Achilles tendon was evaluated before and after barefoot and shod running and compared in percental change with the degree of pronation (Wezenbeek, et al., 2017). This was also the method Fu-Lien Wu et al. used in 2020, where LDF was measured before and after running activities to study the effects of walking speeds and durations on plantar skin blood flow responses. (Wu, et al., 2020). A study from 2020 by Hou et al. researched the response to cupping therapy on the control mechanisms for peripheral blood flow in the skin. Here the blood flow was measured for ten minutes before and after variations of cupping therapy procedures and analyzed using a wavelet frequency analysis (Hou, et al., 2020). An example of a study where the perfusion was monitored over time over time is a pulp vitality test performed by Ercahan et al. in 2018, where the vitality subjects' teeth were monitored using LDF for months after trauma. Here, the data was analyzed in PU values after a phase signal analysis. To obtain a repeatable measurement site, a custom-made splint was fabricated to secure the probe (Ersahan, Sabuncuoglu, & Oktay, 2018).

Some experimental paradigms allow for continuous measurement during the introduction of stimuli given that the stimulus causes minimal movement artefact and respiratory variation, such as use if a pharmaceutical drug, occlusion, or environmental changes in temperature or local atmospheric pressure. The INP-study discussed above by Sundby et al. in 2016 measured the microcirculation in the lower leg continously, as the custom boot exposed the leg to intermittant patterns of negative pressure (Sundby, et al., Application of intermittent negative pressure on the lower extremity and its effect on macro- and microcirculation in the foot of healthy volunteers, 2016). Mizeva et al. also atlered surrounding conditions by exposing the skin of the foot to stages of cooling and heating for the duration of 22 minutes. This was to study its effect on the flow frequency patterns in the feet of patients with diabetes mellitus (Mizeva, et al., 2018). A continuous measurement was also possible in a 2019 study by Wenzu et al. where Pulsinelli's four-vessel occlusion model was researched as the decline of blood flow in the bilateral vertebral arteries of rats were measured with LDF during electrocoagulation and analyzed in percental change (Wenzhu, et al., 2019).

Since our stimuli are dynamic, we adopt the former method of measurement, by measuring flow before and after activity in a standing or supine position. A supine measurement allows easy probe attachment, and minimal movement artefact during extended measurements.

Walking tests were performed in a pattern-eight *infinity walk*, in favor of a circular walking path to avoid mediolateral asymmetries in the gait pattern. The skin blood flow to the feet increases with walking speed, as demonstrated by Fu-Lien Wu et al. in their research study *"Effects of walking speeds and durations on plantar skin blood flow responses"* using LDF-sensors (Wu, et al., 2020). The subjects are therefore instructed to walk in a moderate pace in the walking activities. The pace is kept constant using a metronome set to 95 bpm, which gives the feet a high contact-time in the stance phase of the gait.

According to Reynès, Vinet and Knapp in the study *"Minimizing the duration of laser Doppler flowmetry recordings while maintaining wavelet analysis quality: a methodological study"* an LDF recording must last for 13 minutes to allow for a quality assessment of the neurogenic and endothelial bands, which constitute the lower frequency bands (Reynès, Vinet, & Knapp, 2020). Therefore, the duration of the measurements was kept above 13 min. in the measurements that were performed in prone positions and so allow for this. This also allows for a moorVMS software *trend analysis* of the lower frequencies, which requires a minimum recording of 10 min (Moor Instruments, 2011).

3.3 TEST PROTOCOL

To answer the research questions posed in section 1.4, the test protocol has been designed to assess the perfusion response performing two tests:

I. **The Step Perfusion Test** (static activity period)
II. **The Static Postambulatory Perfusion Test** (dynamic activity period)

These are tests are carried out on all subjects using flat soles, medially wedged soles, and laterally wedged soles.

3.3.1 EXPERIMENTAL RUN

The *Step Perfusion Test* is a protocol where the subject is applying pressure to each sole in in turn from a standing position for a duration of 30 seconds, followed by a 30 second rest where the foot is elevated with the heel resting on a small platform to minimize movement artefact. This test allows for an immediate response analysis, since the LDF-sensor is attached during stance and foot elevation, with no transition time needed. Its main limitations are that its measurement duration is too short to provide a quality frequency analysis, and that the protocol leads to a brief signal noise in the transitions between step and rest positions. The Step Perfusion Test protocol is shown in table 3-2, and the foot elevation and setup are illustrated in figure 3.12.

TABLE 3-2 PROTOCOL FOR THE STEP PERFUSION TEST

Step Perfusion Test	**Series Information**	
	Duration	***Condition***
Wait	10 sec	Get ready
Initial rest	30 sec	Foot elevated
1st footwear	30 sec	Stand
	30 sec	Foot elevated
2nd footwear	30 sec	Stand
	30 sec	Foot elevated
3rd footwear	30 sec	Stand
	30 sec	Foot elevated
Final rest	30 sec	Foot elevated

FIGURE 3-12 FOOT ELEVATION DURING STEP PERFUSION TEST

The subject is in this test given instructions on a screen where the actions (*wait/ rest/ step*) are displayed on a timer with the help of the *moorVMS Protocol Setup* in the *moorVMS* software. This protocol setup facilitates the recording by inserting markers on selected time stamps in the LDF recording. The used protocol setup and message display are illustrated in figure 3-13.

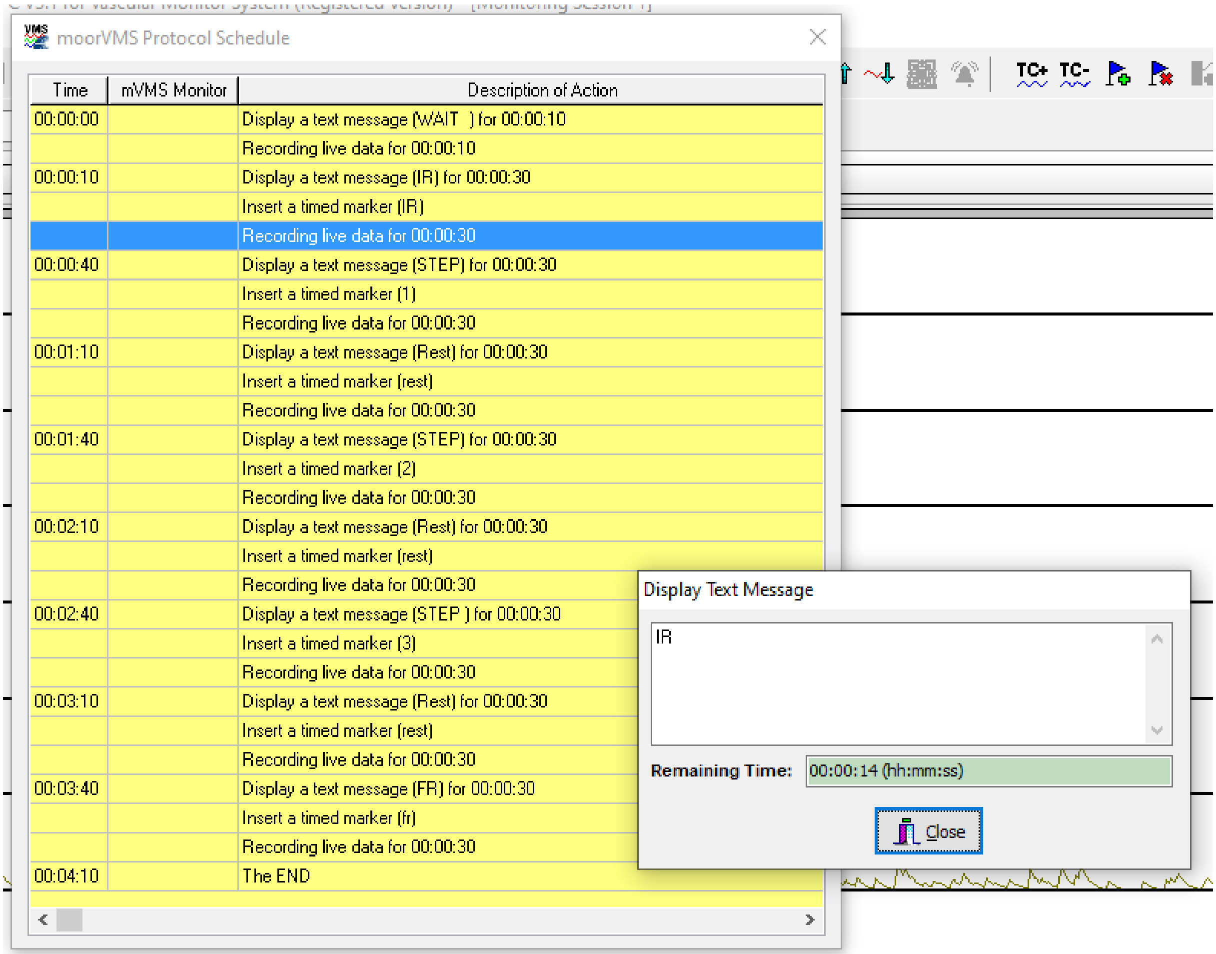

FIGURE 3-13 PROTOCOL SET UP FOR THE STEP PERFUSION TEST

The Static Postambulatory Perfusion Test, on the other hand, is a protocol where the subject walks at a constant moderate speed for 10 min while wearing the wedged or flat footwear. The walking pace is held constant using a digital metronome. The flux was then measured *postambulatory* with the subject resting in the prone position. This measurement was performed for the duration of 13 minutes, to allow for a trend and frequency analysis of the neurogenic and endothelial bands. The walk and subsequent measurement are repeated for all three footwears in randomized order.

The Static Postambulatory Perfusion Test and the Step Perfusion Test were both preceded by an initial measurement of the subject for 13 minutes in prone position. The protocol for the Static Postambulatory Perfusion Test is explained in table 3-8, and the measurement setup is illustrated in figure 3-13 where the measurement site is covered to reduce artifact due to external light sources. The two tests are compared, and their advantages and limits presented in table 3-4.

TABLE 3-3 PROTOCOL FOR THE STATIC POSTAMBULATORY PERFUSION TEST

Postambulatory Perfusion Test	**Series Information**	
	Duration	**Condition**
Initial measurement [a]	15 min	Measurement at rest in prone position
1st footwear	10 min	Walk 95 bpm
	15 min	Measurement at rest in prone position
2nd footwear	10 min	Walk 95 bpm
	15 min	Measurement at rest in prone position
3rd footwear	10 min	Walk 95 bpm
	15 min	Measurement at rest in prone position

a. Double-lined separations indicate discontinuity between footwear tests

FIGURE 3-14 MEASUREMENT SETUP DURING STATIC POSTAMBULATORY PERFUSION TEST AND INITIAL MEASUREMENT

TABLE 3-4 COMPARISON OF TEST PROTOCOLS

Comparison of test protocols	Test Protocols	
	Step perfusion test	**Postambulatory Perfusion test**
Stimuli condition	Still stance on sole	Walking with wedged shoes
Stimuli duration	30 sec. (Step)	10 min. (Walk)
Measurement condition	Standing in stance and standing with elevated foot	Prone position
Measurement duration	30+30 sec. (Step and foot elevation)	13 min. (Prone measurement)
Transition time	2 second transition time to elevate foot. Transitional noise occurs.	Approx. 15 sec.
Advantages	Vertical measurement position Low transition time	Allows for analysis after RP Allows for quality frequency analysis Allows for moorVMS trend analysis
Disadvantages	Small movement artefacts	Prone measurement position Higher transition time
Goal	Measure immediate response Measure perfusion during pressure	Measure response to realistic walking situation Measure response after RP Compare response with initial prone measurement Analyze short to long-term response Analyze low frequency patterns

3.3.2 SETUP

Below is a systematic description of the setup of the experiment, how the equipment and subjects were prepared before test run.

A. Prepare the test room
    a. Temperature should be between 20°C and 24°C (Moor Instruments, u.d.)
    b. Cover or turn off sources strong ambient light
    c. Ensure a relaxed test environment
    d. Ensure a constant humidity level in the room. This is ensured in part by the size and location of the lab.
    e. Prepare a figure-8 walking path and station for measurement at rest, where the subject can lie down in prone position on a mat in proximity to the walking path (to reduce transition time) and to the measuring equipment. See figure 3-15. Prepare cushioning support if needed.
    f. Prepare a station where standing measurements can be performed, with chairs for light balance support and a platform for foot election. This must be in proximity of the LDF-equipment and monitor software screen, where the timed protocol is displayed to the subject. See figure 3-14.
    g. Prepare ultrasound gel, wipes, cable clips, and tape next to measurement stations for low transition time.

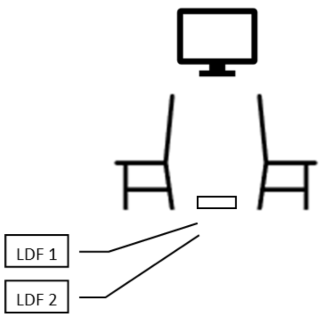

FIGURE 3-15 STATION FOR STANDING STEP TEST. CHAIRS FOR BALANCE SUPPORT DURING MEASUREMENT WITH ELEVATED FOOT

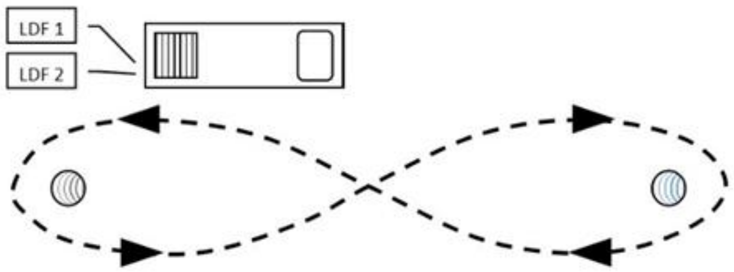

FIGURE 3-16 WALKING PATH AND MEASUREMENT STATION FOR STATIC POSTAMBULATORY PERFUSION TEST

B. Prepare instrumentation
    a. Prepare digital metronome and speaker and for walking test
    b. Prepare temperature and humidity monitor
    c. Prepare pulse monitor
    d. Check the LDF probes and probe leads for damage before use. Ensure that light is transmitted from the probe connector to the probe tip.
    e. Prepare the probe's attachment to ensure minimal delay between activity and measurement
    f. Stack, connect and turn on the two *Standard moorVMS-LDF1* single channel sensors and connect the low-profile probes. Label the probes as medial or lateral, and name corresponding channels in MoorVMS logging software.

C. Clean and calibrate the LDF probes to provide consistent measurements.
   This is done using *motility standard*, or *probe flux standard* (PFS), using the method described in the LDF manual.
    a. Ensure the flux standard is at a stable temperature (stored in the room used for testing). Allow at-least 30 minutes for thermal equilibration to occur before calibration (Moor Instruments, u.d.).
    b. Before using the standard, shake the vial gently for 10 seconds and then allow the standard to rest for 2 minutes before starting the calibration procedure.
    c. Inspect the ambient lighting conditions and whether they will affect calibration by checking the DC levels with lights turned off. Suitable lighting should only give a DC value change of 2 units or less (Moor Instruments, u.d.).
    d. Ensure that there is no source of knocks or vibrations during calibration, and perform calibration using the setup shown in figures 3-16 and 3-17.
    e. Perform a test measurement: Verify that flux levels are non-zero and below 1000 PU, and DC is below 1000.

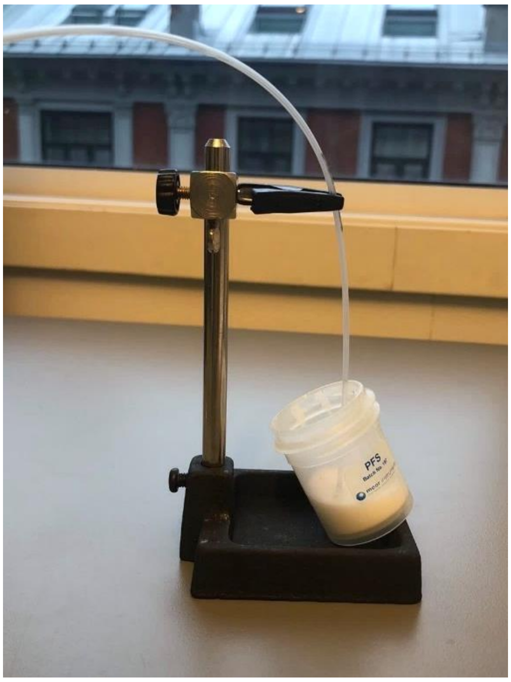

FIGURE 3-17 LDF-MONITOR CALIBRATING

FIGURE 3-18 SETUP FOR INSTRUMENT CALIBRATION

D. Prepare the subject

   The subject must, as discussed previously, prepare for testing in advance by abstaining from stimulants for the preceding hours before measurement. Upon arrival, the subjects are further prepared:

   a. Allow for subject to acclimatize to room 15 minutes or longer
   b. Assess the subject’s stance and determine the wedges needed to correct the subject’s degree of pronation using the Achilles laser and marker. Select corresponding lateral wedges and the shoes matching the subject’s size.
   c. Mark the placement of the LDF sensors with a marker on the subject.

E. Run Experiment.

   a. Static postambulatory perfusion test
   b. Step perfusion test

   Report any discomforts or anomalies during measurements along the way.

4 RESULTS

4.1 PARTICIPANT DEMOGRAPHICS AND ENVIRONMENT

The test experiments were performed on right foot of each footwear type, in randomized order. All test subjects included in the experiment were dominant in the right hand and right leg, except in one subject where the leg dominance was unknown. The perfusion was measured laterally and medially on the forefoot and logged with the moorVMS software.

The test protocol was completed on four non-diabetic overpronating volunteers. A non-pronating subject was excluded, and a subject with a blood disease was excluded. An overview of the subject demographics is presented in table 4-1 below. The demographic data was self-reported, except for the degree of pronation which was assessed in lab and the body mass index (BMI) which was calculated based on the given weight and height.

TABLE 4-1 PARTICIPANT DEMOGRAPHICS

Age, mean ± SD (y)	28 ± 6.78
Weight, mean ± SD (kg)	79.50 ± 6.03
Height, mean ± SD (m)	169.50 ± 13.30
BMI, mean ± SD (kg/m^2)	28.09 ± 5.26
Shoe size	40.75 ± 2.06
Sex	
Male, n (%)	1 (25 %)
Female, n (%)	3 (75 %)
Leg dominance	
Right dominant, n (%)	3 (75 %)
Left dominant, n (%)	0 (0%)
Unknown, n (%)	1 (25 %)
Hand dominance	
Right dominant, n (%)	4 (100 %)
Left dominant, n (%)	0 (0%)
Degree of pronation	
Left foot, mean ± SD (°)	13.75 ± 3.95
Right foot, mean ± SD (°)	13.00 ± 3.37

The subject's degree of pronation was assessed on both feet using the Achilles laser and marker. The correction needed was symmetrical in all candidates but one. The data is displayed in table 4-2.

TABLE 4-2 PARTICIPANT'S NEEDED DEGREE OF CORRECTION

	Candidates			
	A	**B**	**C**	**D**
Left foot	17°	12°	17°	9°
Right foot	14°	12°	17°	9°

The environmental conditions were monitored during the second day of testing as a verification of the test room, and the data gathered revealed a stable level of humidity, oxygen concentration and temperature throughout the experiments, as shown in figure 4-1 below. The temperature was within the ideal window of 20°-24°C according to the LDF manual (Moor Instruments, u.d.), as it varied merely from 22°C to 24°C. The stabilized environmental conditions within the first half hour, as shown on the chart, likely indicates an initial instrument acclimatization, which in turn speaks to a stable environment.

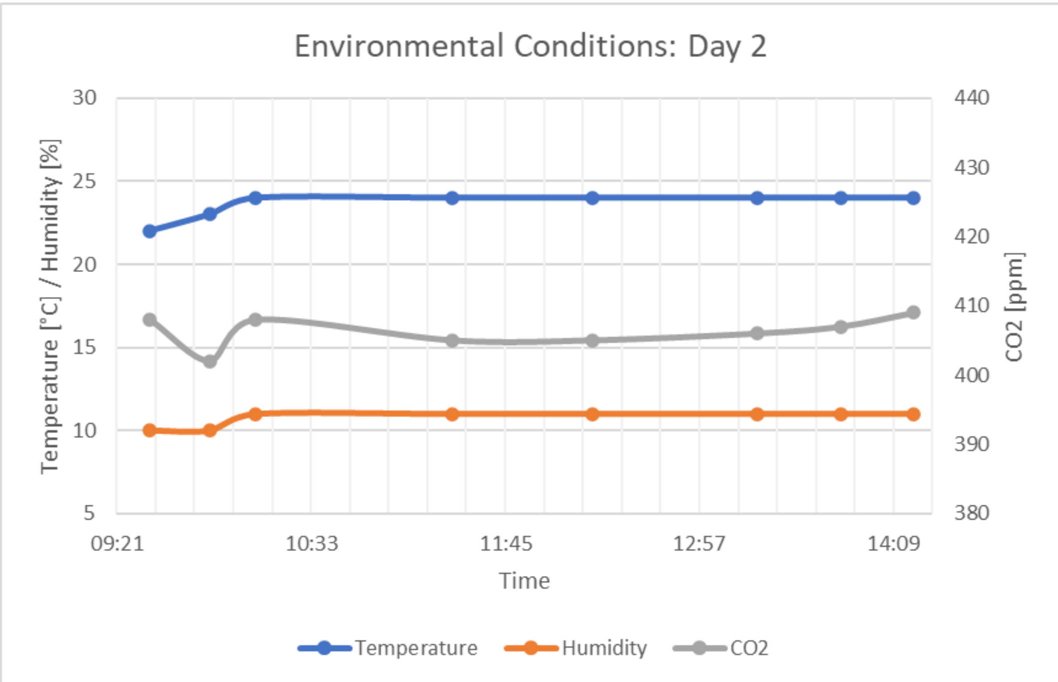

FIGURE 4-1 MONITORED ENVIRONMENTAL CONDITIONS ON DAY 2 OF TESTING

The pain assessment scale from the initial questionnaire reveals an indicative correlation between the needed degree of correction (here entered as the average between right and left foot) and the reported frequency of unprovoked pain (severe or light) in the various areas of the body between the foot sole and the back. This illustrates that the subjects were typical pronators with an associated strain pattern in agreement with the literature. The pain assessment scale used is shown in table 4-3, and the scatter plot of the submitted replies tied to each subject's need for correction is shown in figure 4-4. The points that do not appear in the diagram are here overlapping one another at point zero in the assessment scale.

TABLE 4-3 PAIN ASSESSMENT SCALE

0	"No"
1	"1-3 times a year"
2	"4-6 times a year"
3	"7-12 times a year"
4	"Several times a month"
5	"Several times a week"
6	"Ongoing pain"
Blank	"I do not know the answer/ I would rather not answer"

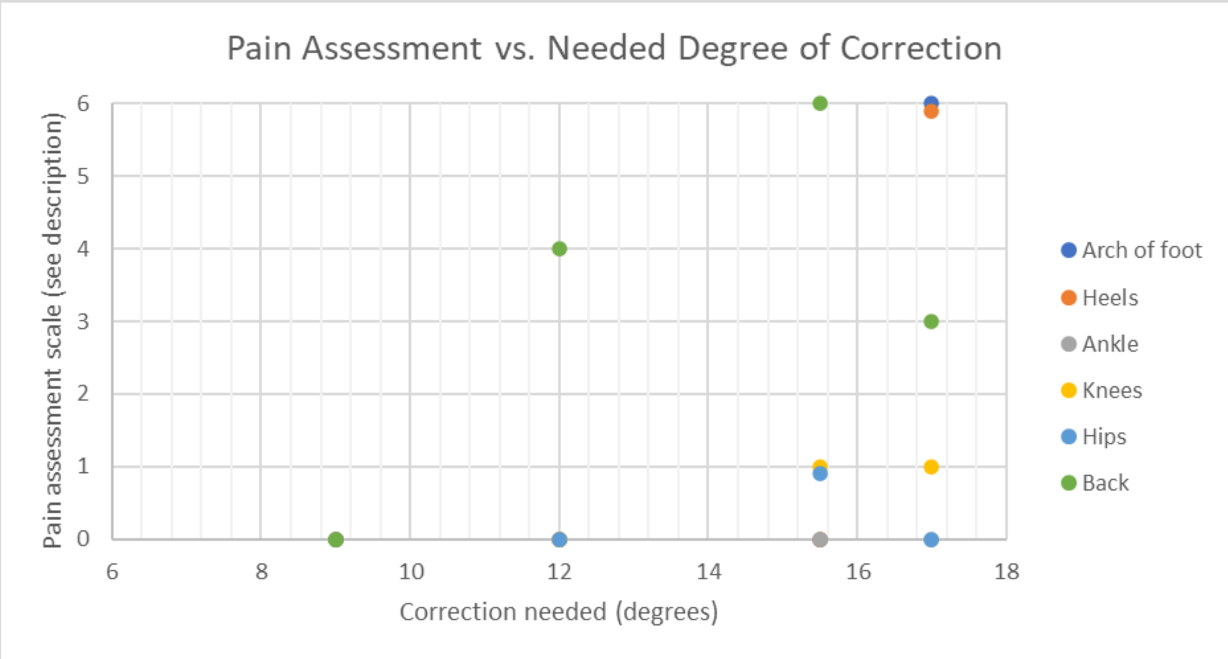

FIGURE 4-2 SCATTER DIAGRAM OF PAIN ASSESSMENT AND CORRECTION NEEDED

The data of the wedge pronation correction and weight of each subject was also used to calculate a model of the forces exerted on the heel of the foot by the wedge. The resulting force (R) of the subject's body weight was decomposed to a force component perpendicular to the wedge surface (Ry) and a force component parallel to the wedge surface (Rx), representing sheer force on the heel of the foot. This is a simplified model that does not take into account the weight distribution onto the forefoot. The purpose is to consider the influence of weight and wedge size in each subject in relation to one another for further analysis. The scales are presented in table 4-4.

Table 4-4 Forces applied to heel (simplified)

Subjects	**A**	**B**	**C**	**D**
Weight [kg]	86	76	83	73
Right foot correction [°]	14	12	17	9
Resultant force in one foot, [N]	422	373	407	358
Parallel force to sole (Rx), [N]	102	78	119	56
Perpendicular force to sole (Ry), [N]	409	365	389	354

Prints were also taken from one of the subjects in the different wedge conditions when full body pressure was applied, see figure 4-3. These prints illustrate the slightly increased contact area in a laterally wedged shoe (more marked in comparison with the medially wedged shoe), which could correlate to a more efficient foot pump effect, as discussed in the literature review of section 2.2 (Horwood, 2019).

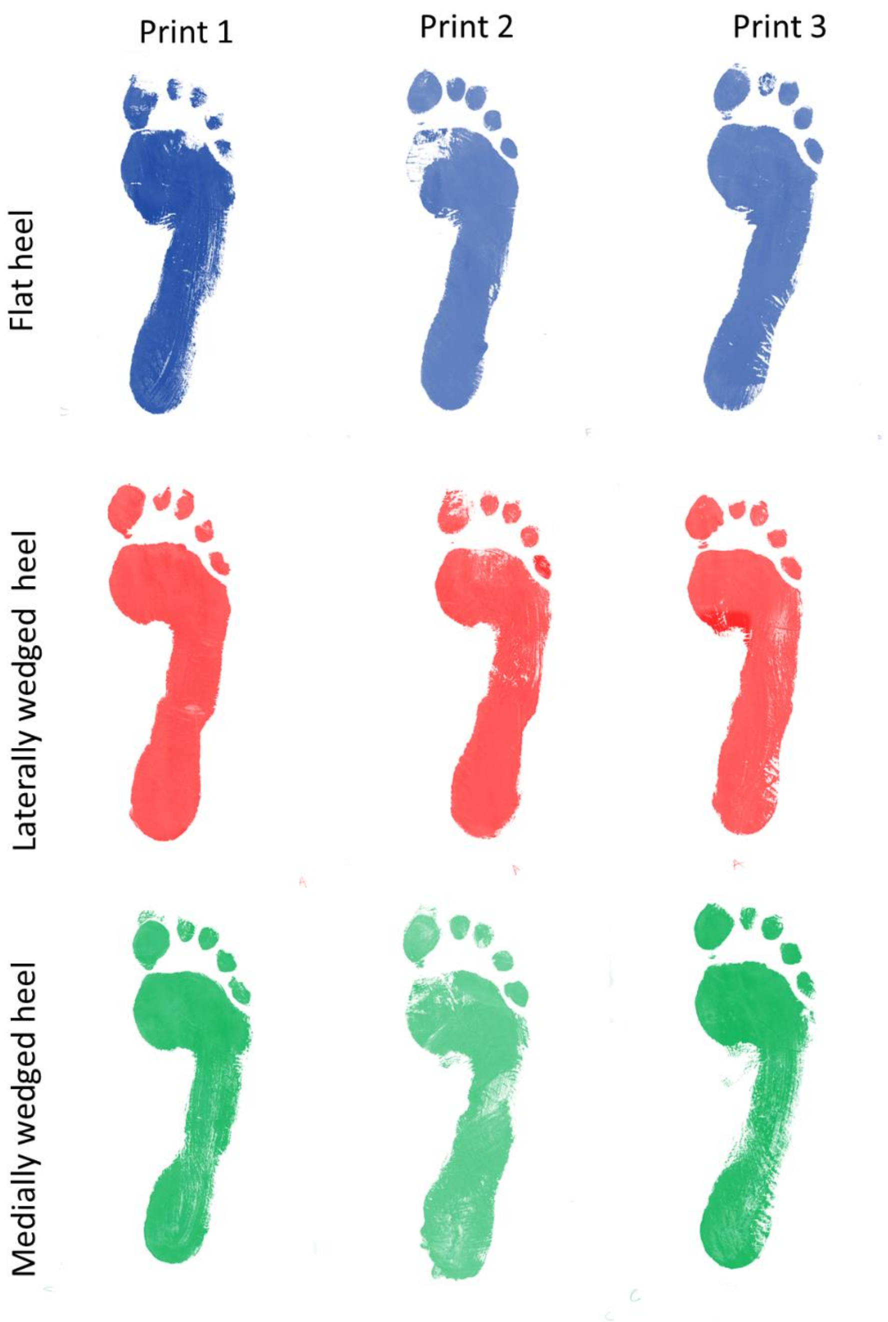

FIGURE 4-3 PRINTS OF SUBJECT D IN ALL THREE WEDGE CONDITIONS INDICATING CONTACT AREA

4.2 FINDINGS FROM THE STEP PERFUSION TEST

The Step Perfusion Test was conducted twice on candidates A-D in randomized order, with LDF measurements on medial and lateral side. When plotted, the protocol can be divided into three periods of *step* and *rest* between the initial and final rests (IR/ FR). These three periods are characterized by a low flux level for 30 seconds as the subject applies pressure to the sole, followed by an increased flux level at reperfusion of the forefoot during subsequent rest period when the foot is elevated for 30 seconds. During this rest period, the flux level slightly decreases over time. The spikes between rest and activity conditions are signs of movement artifact in the transition of foot position. The performed flux measurements are plotted in randomized order in figure 4-2 below. The final rest was interrupted in some trials, and therefore show high PU readings.

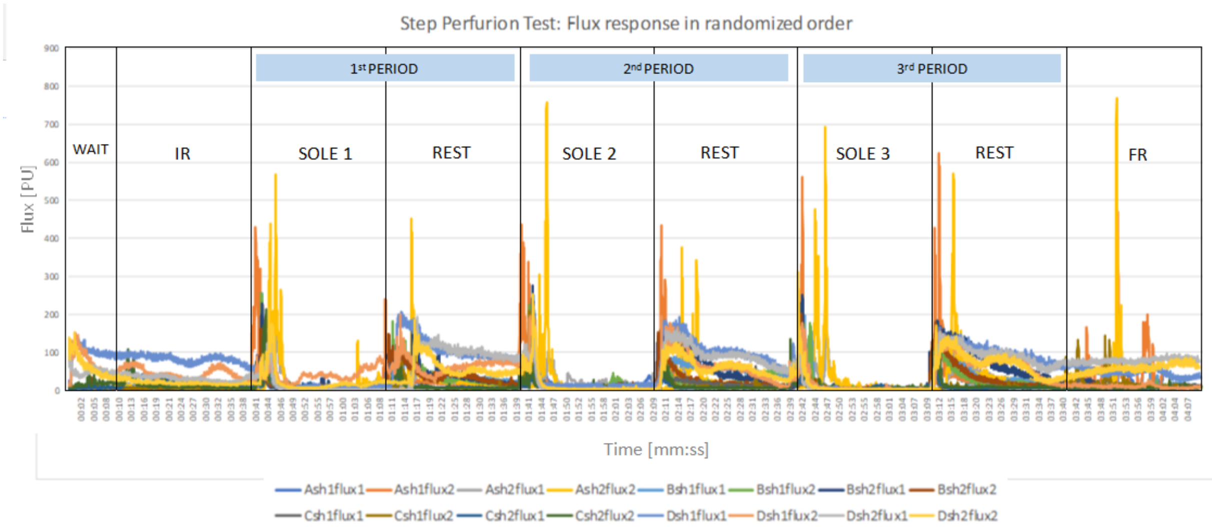

FIGURE 4-4 STEP PERFUSION TEST: FLUX MEASUREMENT IN RANDOMIZED ORDER

When sorting the trial periods according to footwear, the graphs illustrating flux response to flat, medially wedged and laterally wedged sole can more easily be read in figures 4-4, 4-5, and 4-6, on candidates (A-D), short test one and two (sh1 and sh2), on medial and lateral sides of the foot (flux1 and flux2).

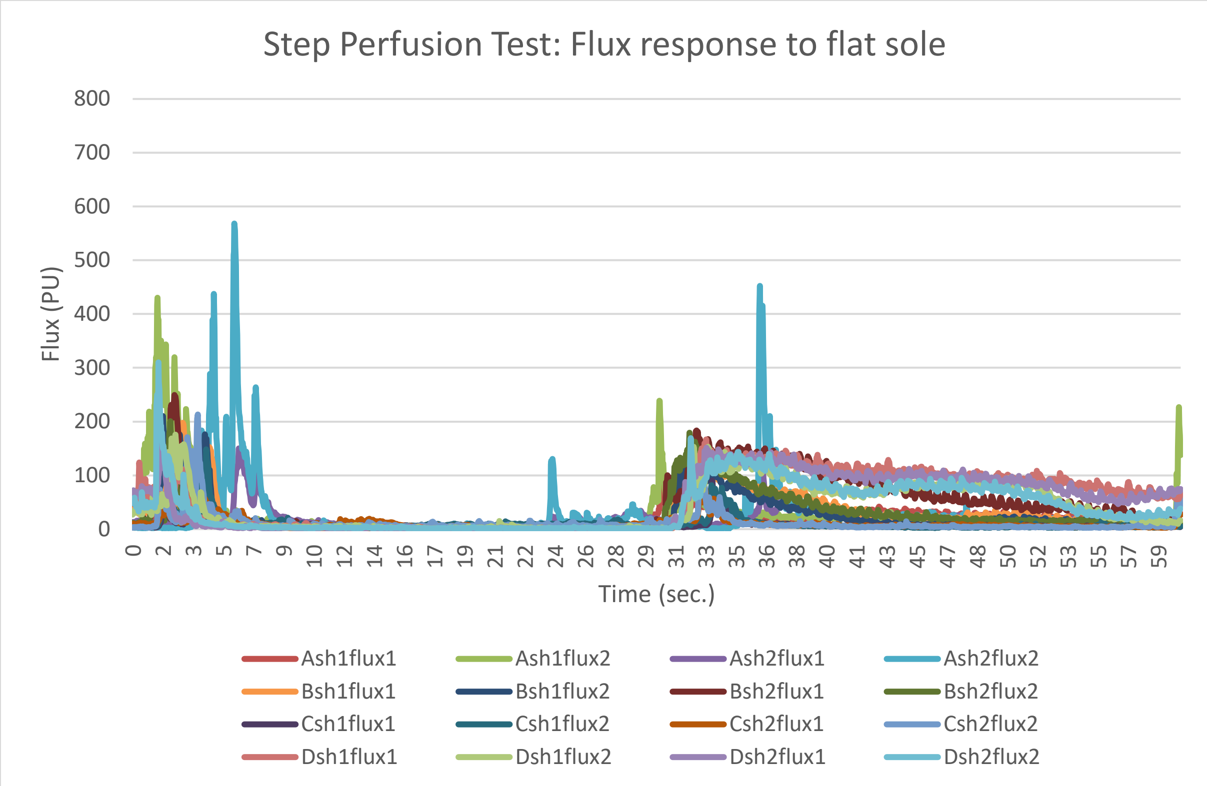

FIGURE 4-5 STEP PERFUSION TEST: FLAT SOLE

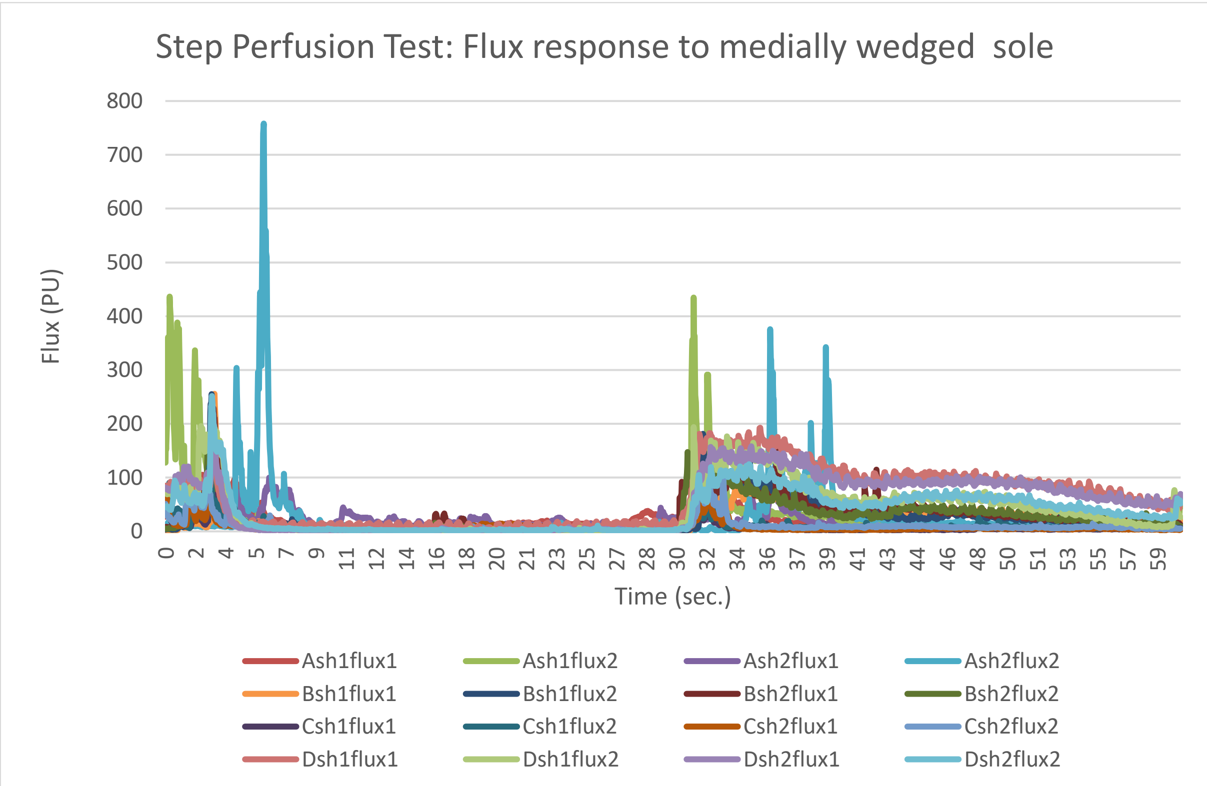

FIGURE 4-6 STEP PERFUSION TEST: CORRECTIVE SOLE

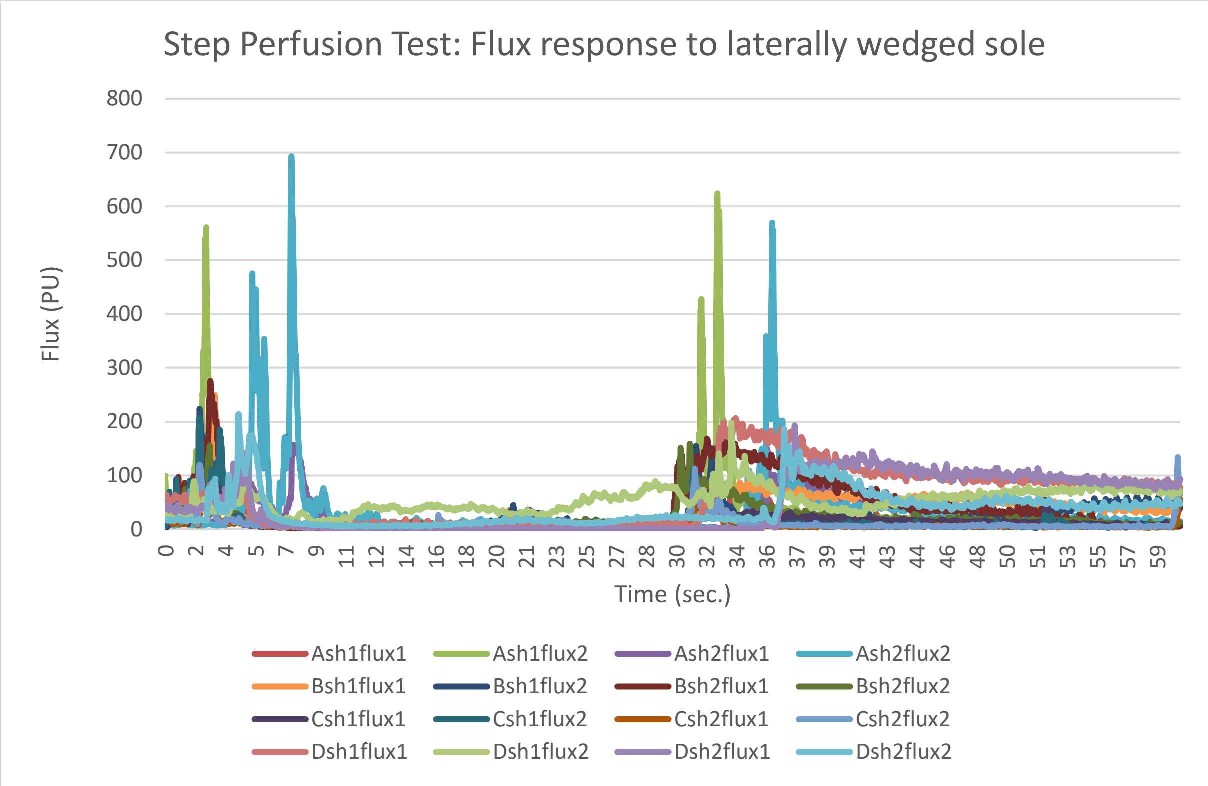

FIGURE 4-7 STEP PERFUSION TEST: LATERALLY WEDGED SOLE

The graphs above indicate movement artefact during the first approximate 10 seconds of the step action from the command “STEP” is given at timestamp 0, and movement artefact within the ten first seconds after the command “REST” at 30 seconds into the measurements.

4.2.1 THE STEP PHASE

When the first 10 seconds of the step phase are cut, the remaining 20 seconds reveal a stable low signal without change trend, in large part between 2-10PU. The most notable spikes were eliminated, where their duration and amplitude point to movement artefact as the cause. The spikes removed were the three marked ones from the flat soled stance of candidate A visible in figure 4-5: trial one on lateral side at approximately 29 seconds in (Ash1flux2), and trial 2 on both sides at approximately 23 seconds in (Ash2flux1 and Ash2flux2). The remaining signals are not guaranteed to be free from movement influence, but they will in that case influence the average to a lesser degree.

When now evaluating the averages over the last 20 seconds of step phase, the clustered column chart in figure 4-8 shows the flux levels in each wedge condition for all candidates, test runs and sides of measurement on the forefoot (medial or lateral). The chart reveals an outlier during the stance on the laterally wedged sole in candidate D during first trial measurement on the lateral side (Dsh1flux2). This is as expected, since looking at figure 4-7 reveals a single high flux measurement above the rest that does not behave in a way to be clearly dismissed in the spike removal step as movement artefact. The identical second trial on subject D (Dsh2flux2) does however not show a similar reading, nor do the trials on subjects A, B or C in the same footwear. The reading could be due to a slight pressure shift to the left foot during this right foot measurement, or due to a pressure shift in the right foot itself towards the medial side, which would cause a higher reading on the lateral side of the foot. The medial reading of the same trial (in lateral wedge of Dsh2flux1) does however not indicate a notably high flux as a consequence of a left foot shift during stance, nor does it read a notably low flux that would result in a medial pressure shift in the right foot during stance. This does not however exclude a possible posterior pressure shift.

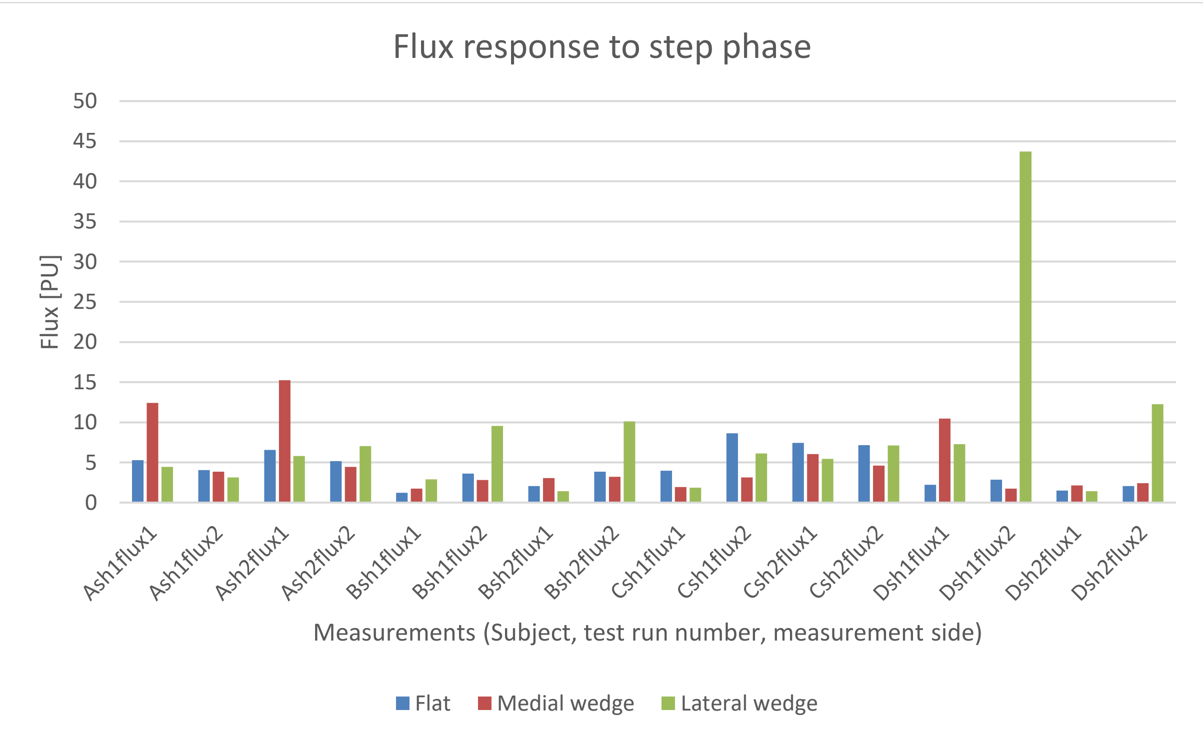

FIGURE 4-8 FLUX RESPONSE TO STEP PHASE

When comparing the flux level in step phase using the flat sole as reference, an interesting pattern emerges, as illustrated in figure 4-9: the flux when using medially wedged shoes gives a greater flux on the medial side, and when using laterally wedged shoes the flux is higher on the lateral side. The readings also reveal that the medial side measurements are highest when using medially wedged shoes, and the lateral side measurements are highest when using laterally wedged shoes. The only exceptions are a low comparative flux level on the lateral side measurement during first test on candidate A (Ash1flux2) in laterally wedged footwear, and a higher flux when using lateral rather than medial shoes on the medial side measurement of candidate B during first test (Bsh1flux1). The top of the column in Dsh1flux2 in figure 4-9 ends at 1534% of flux level in flat sandals and is not visible in the graph. This high reading is due to the outlier during step phase mentioned above.

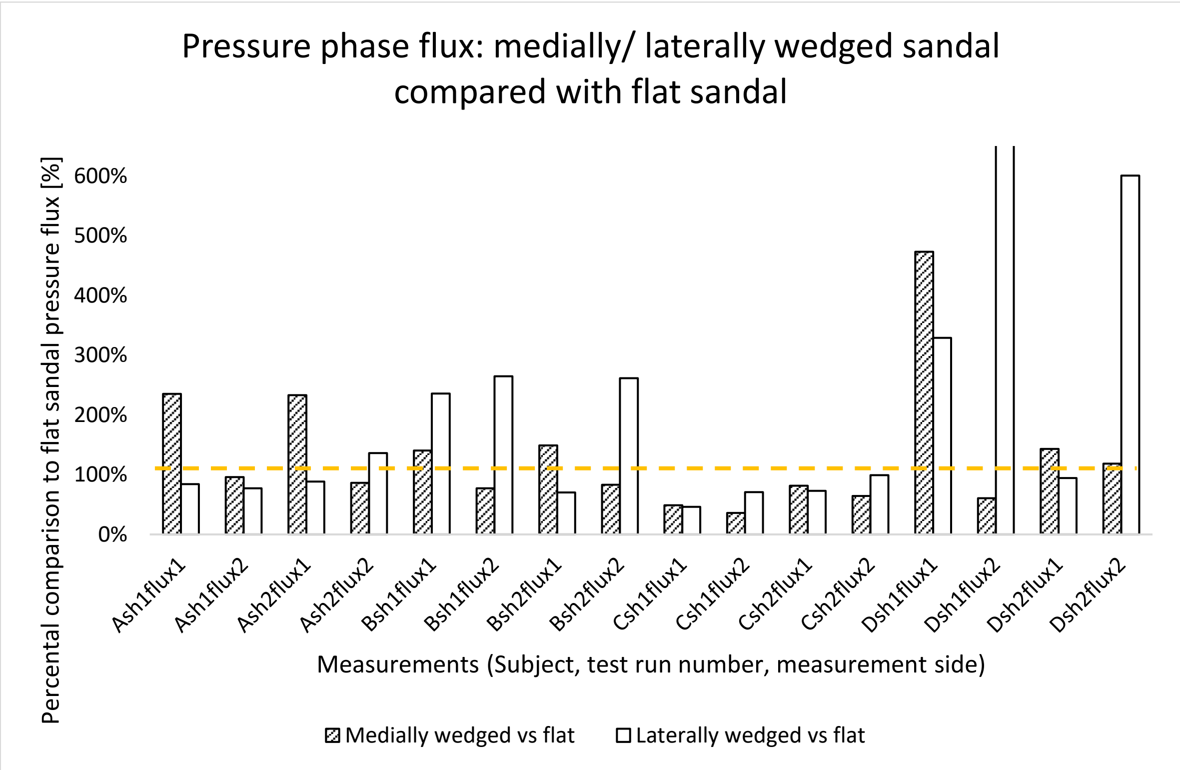

FIGURE 4-9 PRESSURE PHASE FLUX COMPARED TO FLAT SANDAL

When comparing flux level itself during stance on flat sandals, depicted by a yellow line at 100% in figure 4-9, to the flux during stance on wedged sandals, the generally higher flux measurement on medial or lateral side according to footwear as described above surpasses the flux level in flat soles, and the lower flux level does not reach it. This is however not a strict rule, as for example all measurements of candidate C undershoots the flat flux measurements. The average levels compared to flat soles are shown in table 4-4. The forementioned outlier of candidate D is not included in the table.

TABLE 4-5 FLUX LEVELS COMPARED TO FLAT SANDAL FLUX

	Mean		SD	
	Medial measurement	Lateral measurement	Medial measurement	Lateral measurement
Medially wedged vs. flat	188 %	78 %	132 %	25%
Laterally wedged vs. flat	128 %	216 %	100%	188%

Another notable find during step phase is the low dispersion of the data. When looking away from the mentioned outlier in measurement Dsh1flux2, (also identified by *Isolation Forest* anomaly detection algorithm in *Orange Data Mining software* with applying contamination limit of 5 %), the mean and standard deviations across candidates and trials in the same footwear and measurement site shown in table 4-5 reveal a low level and low dispersion of flux in step phase. The boxplots are plotted as shown in figure 4-10 visualizing the quartile percentiles. The flux level during pressure phase across footwears shows a low correlation to the wedge size by a Pearson correlation coefficient of only -0.157 (Calculated in Orange Data

Mining software).

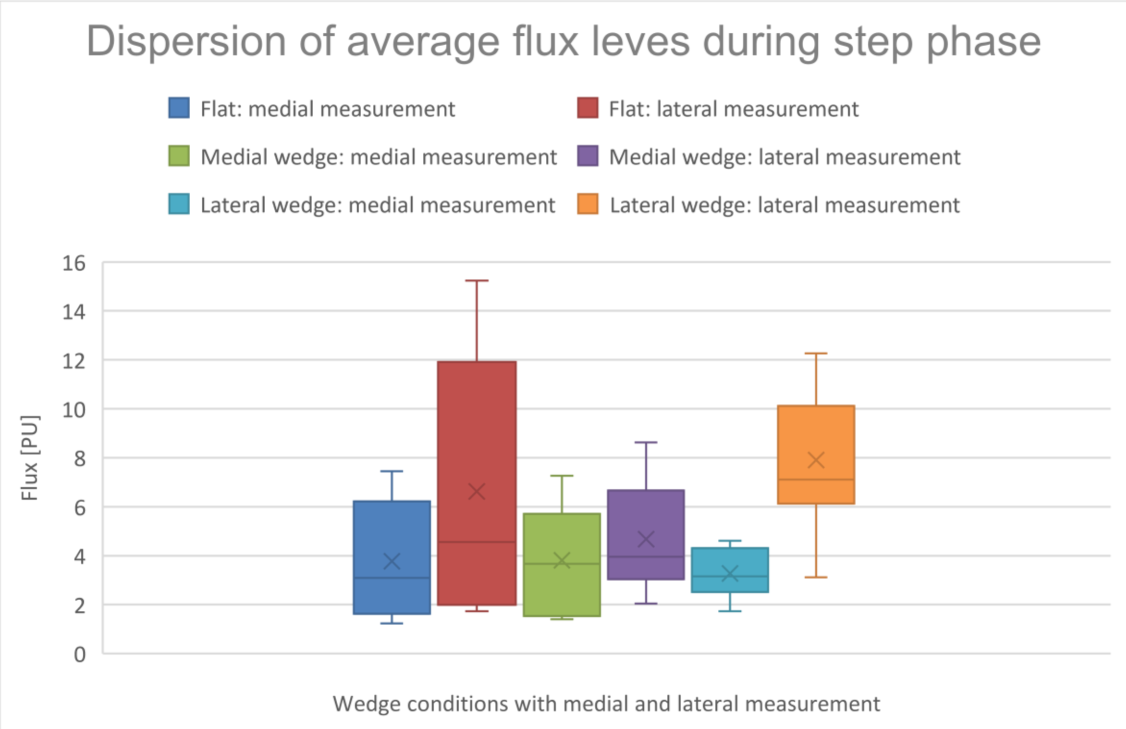

FIGURE 4-10 DISPERSION OF AVERAGE FLUX LEVELS DURING STEP PHASE. SPIKES AND MENTIONED OUTLIER ARE EXCLUDED. MEAN IS MARKED WITH X, AND 50TH PERCENTILE (MEDIAN) IS MARKED WITH MIDDLE LINE.

TABLE 4-6 MEAN AND STANDARD DEVIATION OF FLUX AVERAGES AT PRESSURE PHASE. SPIKES AND MENTIONED OUTLIER ARE EXCLUDED.

	Mean	**SD**
Flat: medial measurement	3.77	2.41
Flat: lateral measurement	6.63	5.36
Medial wedge: medial measurement	3.82	2.24
Medial wedge: lateral measurement	4.67	2.22
Lateral wedge: medial measurement	3.28	0.99
Lateral wedge: lateral measurement	7.91	3.00

4.2.2 THE REST PHASE

Looking at the rest phase where the foot is elevated onto a low platform, the flux levels increase notably from a level of approximately 2-10 PU to a level of approximately 100 PU, before slowly decreasing to a level of approximately 20-50 PU. The first few seconds of this reperfusion are, like the pressure phase, also characterized by a noisy signal during the first 10 seconds of transition after the command “REST” is given. When first analyzing the ten first seconds of data succeeding this transition period, (40-50 seconds in on figures 4-5, 4-6 and 4-7) the data reveals the flux levels shown in figure 4-11, and its flux increase from pressure phase in figure 4-12.

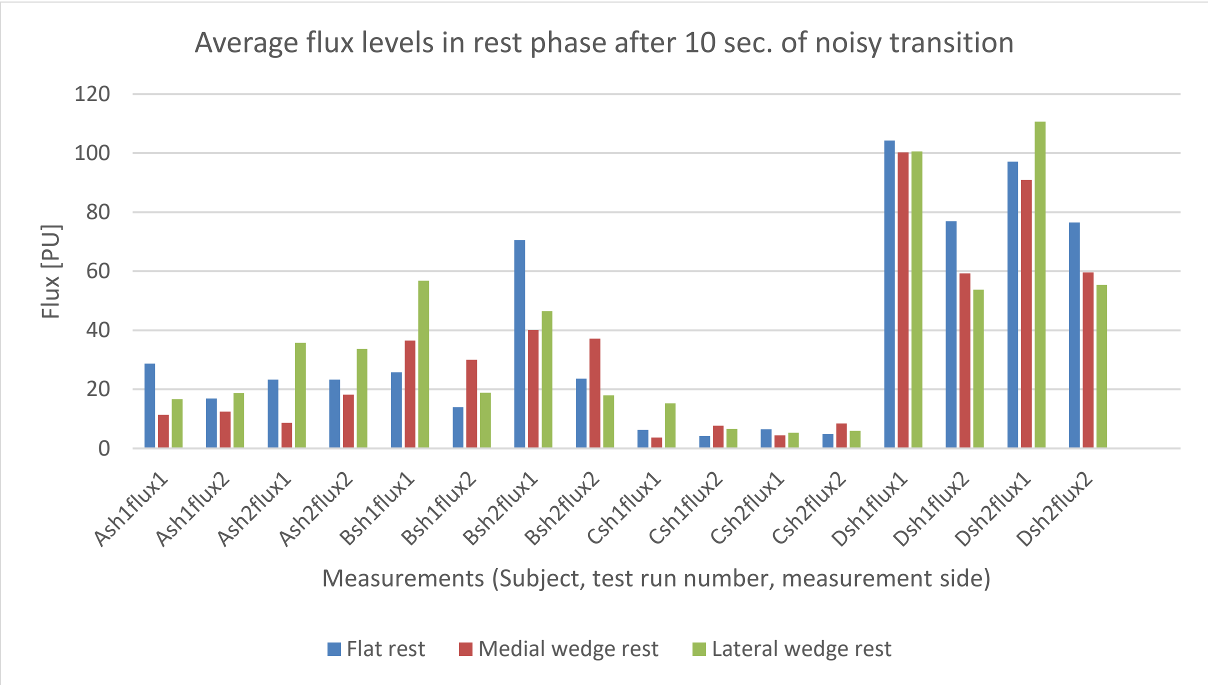

FIGURE 4-11 FLUX IN REST PHASE (40-50 SEC. INTO STEP AND REST-PERIOD)

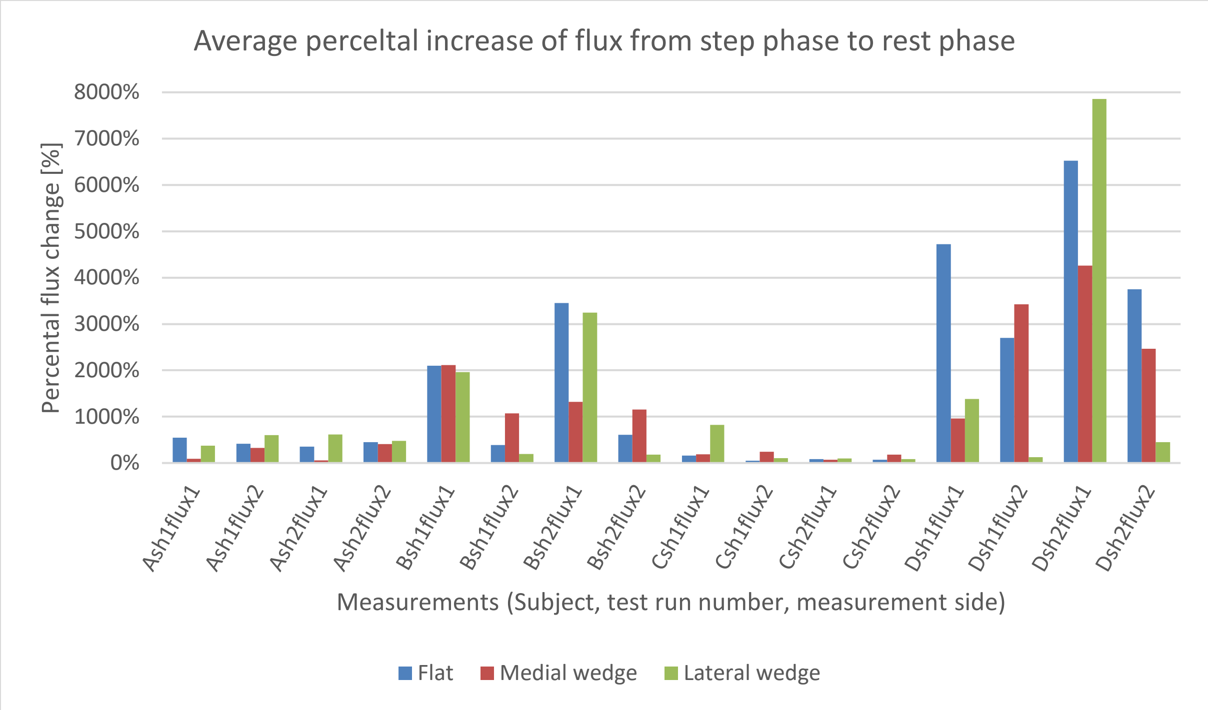

FIGURE 4-12 FLUX INCREASE FROM PRESSURE PHASE TO REST PHASE (REST AT 40-50 SEC. INTO STEP AND REST-PHASE)

A few interesting notes can be made here. First, that the data dispersion is much larger than in step phase, with a standard deviation of 20-40 PU (see table 4-7) between trials in the same footwear and measurement side of the foot, which confirms the indication from figure 4-11 of a high dispersion between candidates, and a better ground of comparison of the wedges within measurements on each candidate. This could be due to a constant sensor placement in all measurements on the same candidate, and a variation the color and texture of the skin and the sensor placement between candidates. Since the pattern is also in the relative changes from pressure phase to rest it can also be explained by variation of forces applied on the heel from candidate to candidate, as the flux increase and flux levels at rest are inversely correlated with the sheer forces applied according to the simplified model presented in table 4-4, in subject order: C-A-B-D which was also the order of the needed of correction from highest to lowest. This is illustrated in figure 4-20. The flux level in rest phase across footwears shows a Pearson correlation coefficient of to the wedge size of -0.887, and the flux change from stance to rest phase shows a Pearson correlation coefficient of -0.732 (calculated using Orange Data Mining software).

TABLE 4-7 MEAN AND STANDARD DEVIATION OF FLUX AVERAGES AT REST PHASE (AFTER 10 SEC. TRANSITION).

Footwear	Mean [PU]	SD
Flat: medial measurement	45.31	39.61
Flat: lateral measurement	30.05	29.73
Medial wedge: medial measurement	37.00	29.73
Medial wedge: lateral measurement	29.12	21.35
Lateral wedge: medial measurement	48.47	32.03
Lateral wedge: lateral measurement	26.37	19.41

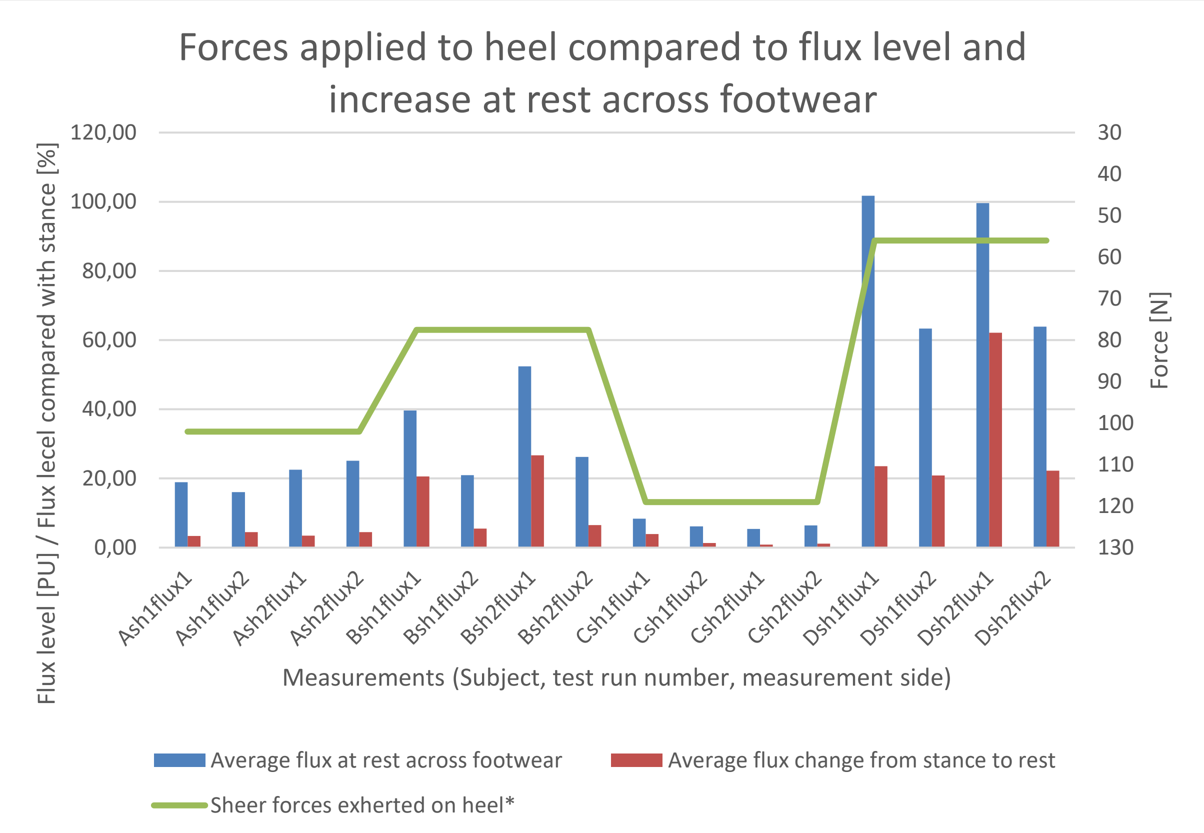

FIGURE 4-13 SHEER FORCES APPLIED TO FOOT COMPARED TO FLUX INCREASE AND LEVEL AT REST. SHEER FORCES ARE FROM A SIMPLIFIED CALCULATION.

It is also noteworthy that the increase of flux from step to rest phase is almost consistently lower on the lateral side of the forefoot when using lateral footwear (47% of the change on medial side) and flat footwear (14% of the change on the medial side) and is higher on the lateral side of the forefoot using the medially wedged footwear (102% of the change on the medial side).

When further comparing the measurements within candidates by again using the flat sandaled flux as a ground of comparison, the pattern shows a complementing pattern to that discovered in the pressure phase. Here the flux level relative to the flat sandaled flux level tends to be higher when using medially wedged shoes on the lateral side of the foot, and higher when using laterally wedged shoes on the medial side of the foot, as shown in figure 4-14. The lateral side measurements of candidate A (Ash1flux2 and Ash2flux2) are exceptions.

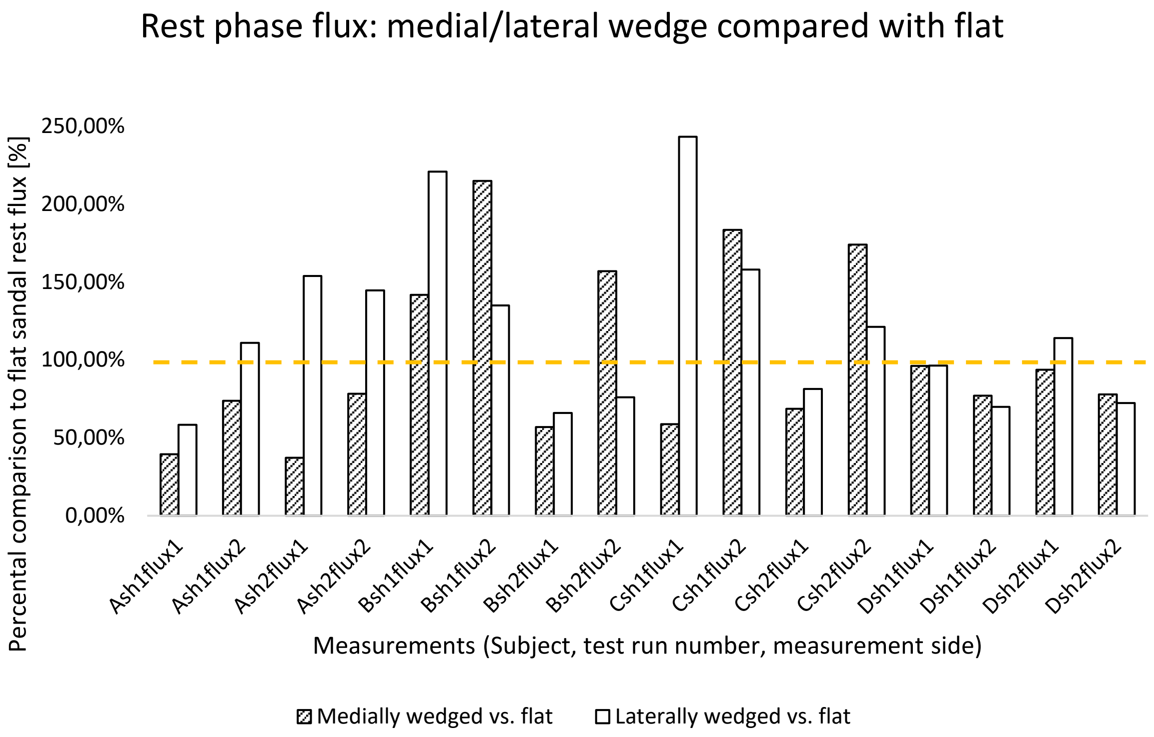

FIGURE 4-14 REST PHASE FLUX: MEDIAL/ LATERAL WEDGE COMPARED TO FLAT SANDAL

When looking at the flux level itself compared to flat sandaled rest flux, the levels (see table 4-8) show on average a slightly higher flux level compared with the flat sandaled flux, except medial measurement after stance on medially wedged shoes.

TABLE 4-8 AVERAGE FLUX LEVELS AT REST IN MEDIALLY/ LATERALLY WEDGED SANDALS COMPARED TO FLAT SANDALS

	Mean		SD	
	Medial measurement	Lateral measurement	Medial measurement	Lateral measurement
Medially wedged vs. flat	74 %	130 %	35 %	59 %
Laterally wedged vs. flat	129 %	111 %	70 %	35 %

4.3 FINDINGS FROM THE STATIC POSTAMBULATORY PERFUSION TEST

The Static Postambulatory Perfusion Test is presented and analyzed using the trend analysis of the moorVMS software. Using the trend analysis software reduces the noise from movement artefacts by dividing the data into periods of 10 seconds and selecting the minima of each period. These minima values are presented here as a moving average over 60 seconds. This is a method that eliminates signal spikes, including most cable movement artefacts, and high frequency signatures such as cardiac and respiratory flux changes. Despite some information loss in this form of analysis and a slightly artificially lower flux level, it illustrates the long-term trends of the signal well. The trend analyses are plotted in figures 4-15 to 4-18 in segments 30 second duration. Candidate C reported coughing from middle of the start measurement, and this is likely the cause of the middle peak in subject C in figure 4-18. Candidate D lost sensor contact on the medial side during start, and the measurement is therefore throughout this measurement in the same figure.

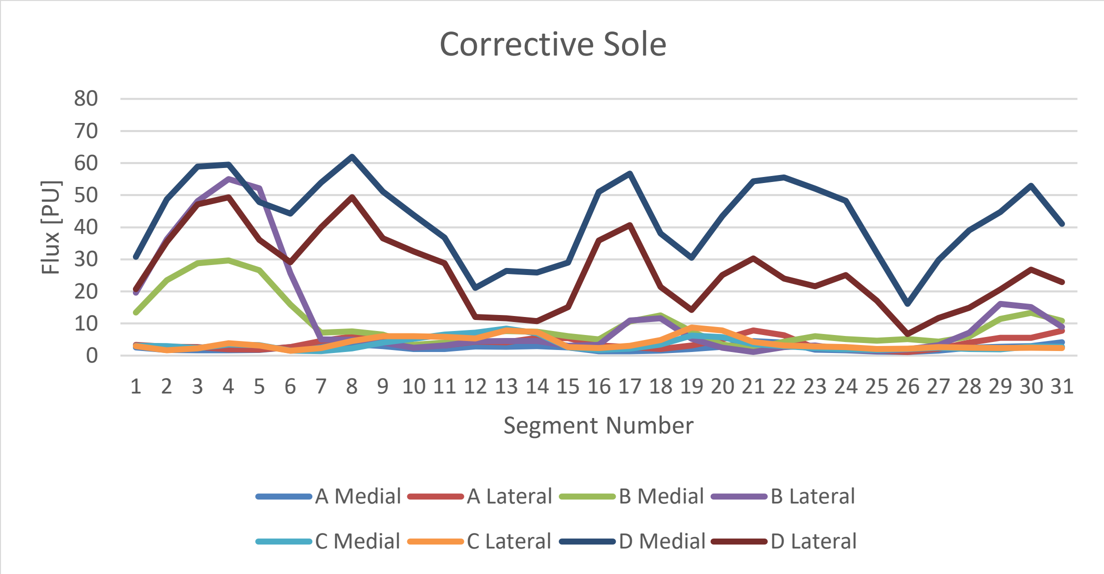

FIGURE 4-15: POSTAMBULATORY TEST: TREND OF FLUX AFTER WALKING WITH MEDIALLY WEDGED SANDALS

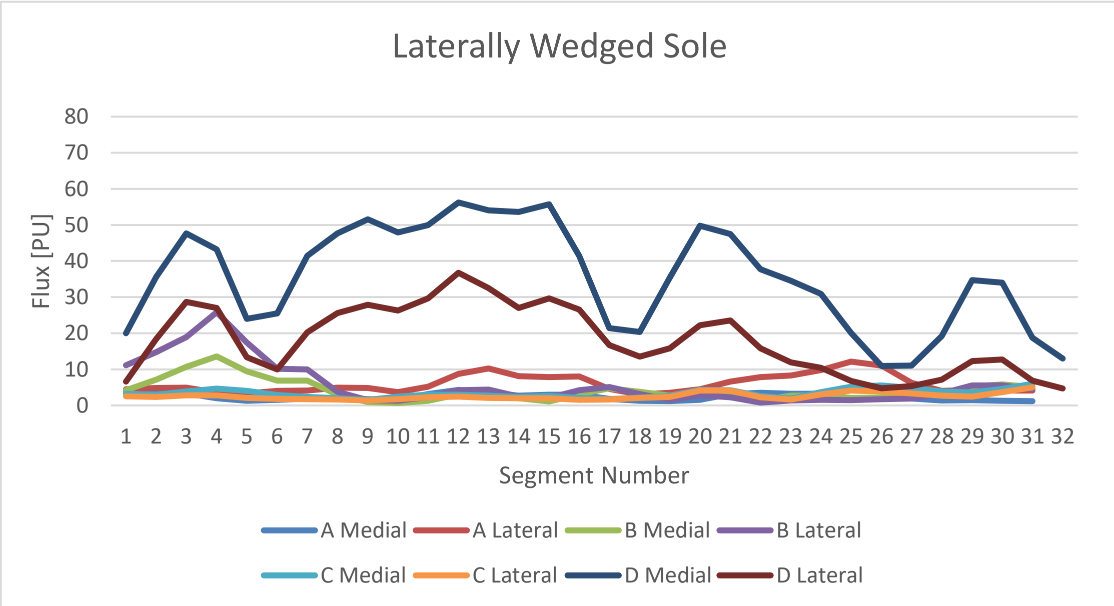

FIGURE 4-16 POSTAMBULATORY TEST: TREND OF FLUX AFTER WALKING WITH LATERALLY WEDGED SANDALS

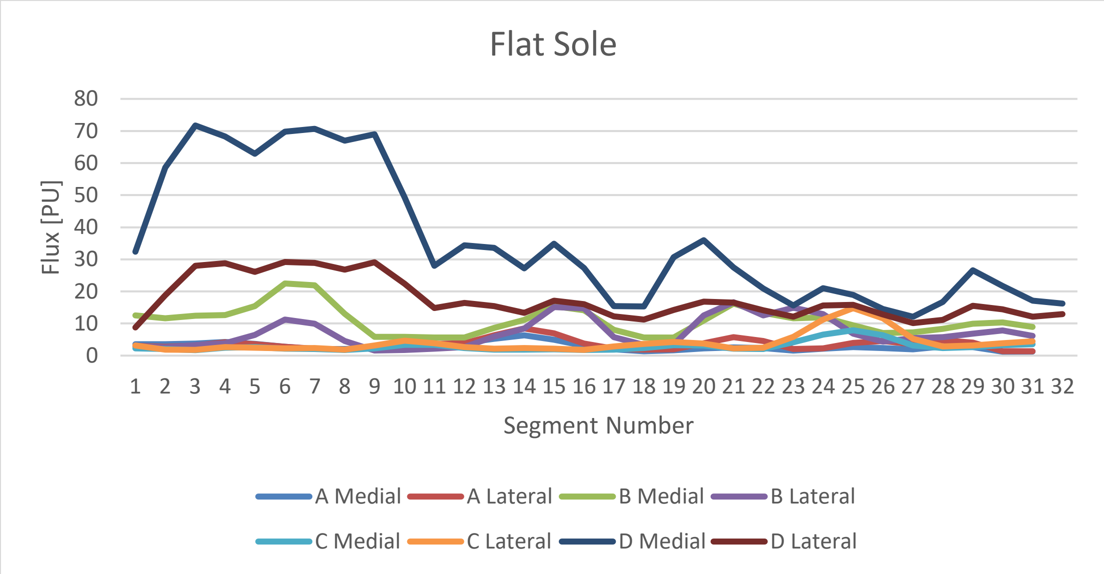

FIGURE 4-17 POSTAMBULATORY TEST: FLUX TREND AFTER WALKING WITH FLAT SANDALS

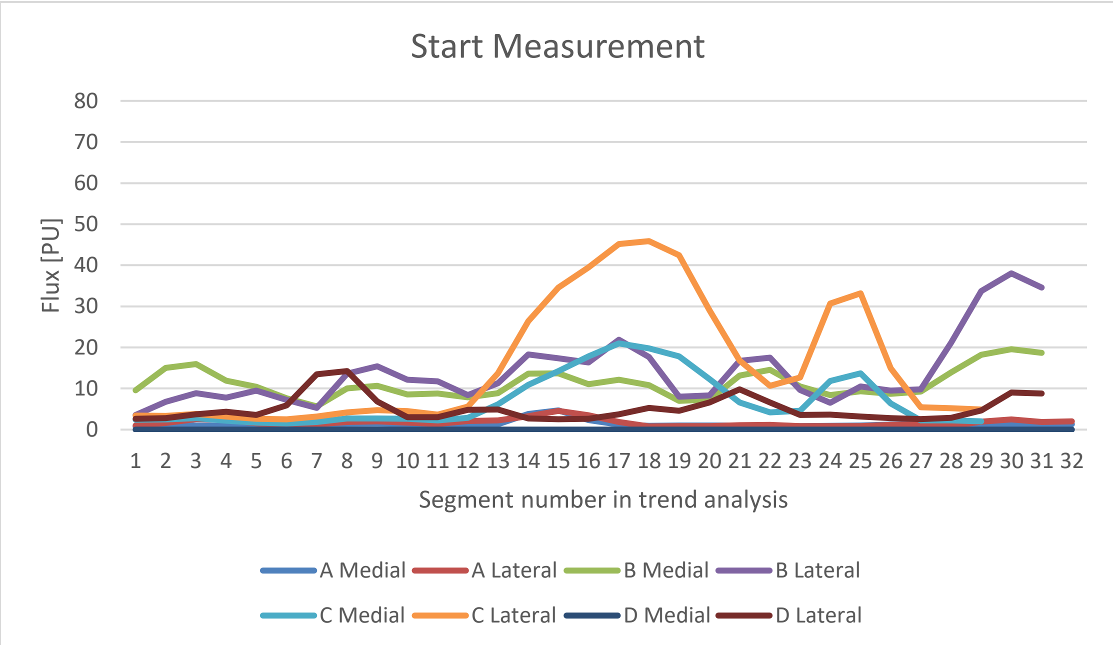

FIGURE 4-18 POSTAMBULATORY TEST: FLUX TREND AFTER INITIAL MEASUREMENT

In this Postambulatory test, the sensor is not attached throughout stimuli and rest measurement since the stimuli in this case is a walking exercise for the duration of 10 min. There is therefore a transition time of approximately 15 seconds until subject is in supine position and sensors are attached onto pre-marked areas. On the other hand, the stimulus in this test is longer than the thirty second stance of the Step Perfusion Test. Unlike the Step

Perfusion Test, the long-term response to the Static Postambulatory Perfusion Test does not generate a reproducible perfusion signal peak. The flux levels show a variation between subjects that s likely due to inter-individual physiological differences in anatomy and physiology, such as skin thickness and baseline foot perfusion. The relative flux response after walking with medially and laterally wedged shoes do not present any trends of interest to the research questions, when compared to the flat sandal flux response or initial measurement.

The first flux peak that occurs around 90 seconds into the measurement was compared across trials. The flux change from flat soled measurement to the medial wedged measurements was in all trials greater on the lateral side of the forefoot than on the medial side. there was no such pattern when the same lateral foot signals were compared to initial lateral foot measurements. A pattern also appeared when comparing the flux level after walking with flat sandals to the initial measurements which revealed a higher flux level on the medial side of the forefoot. Further comparisons between measurement sides, footwear and correlations to wedge corrections needed in each subject did not show any significant patterns. When analyzing the data for binary patterns one must keep in mind that the chance of random data generating a consistent pattern across four trials, is 12.5%. Similar problems are encountered in non-binary analysis. One might have drawn conclusions based on several coinciding patterns, e.g. if the medial to lateral signal ratio were high across all trials with a medial wedge, and low across all trials with a lateral wedge, in addition to similar patterns when comparing trials to initial rest conditions. But no such coinciding trends were found. The postambulatory results are therefore inconclusive.

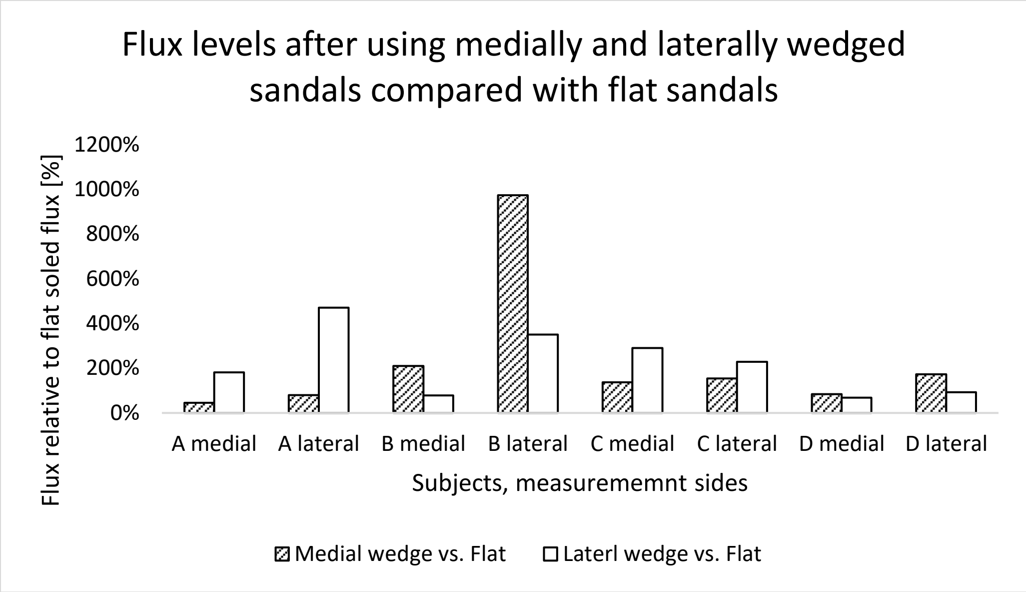

FIGURE 4-19 FLUX LEVELS COMPARED TO FLAT SANDAL FLUX IN FIRST PEAK OF POSTAMBULATORY TEST

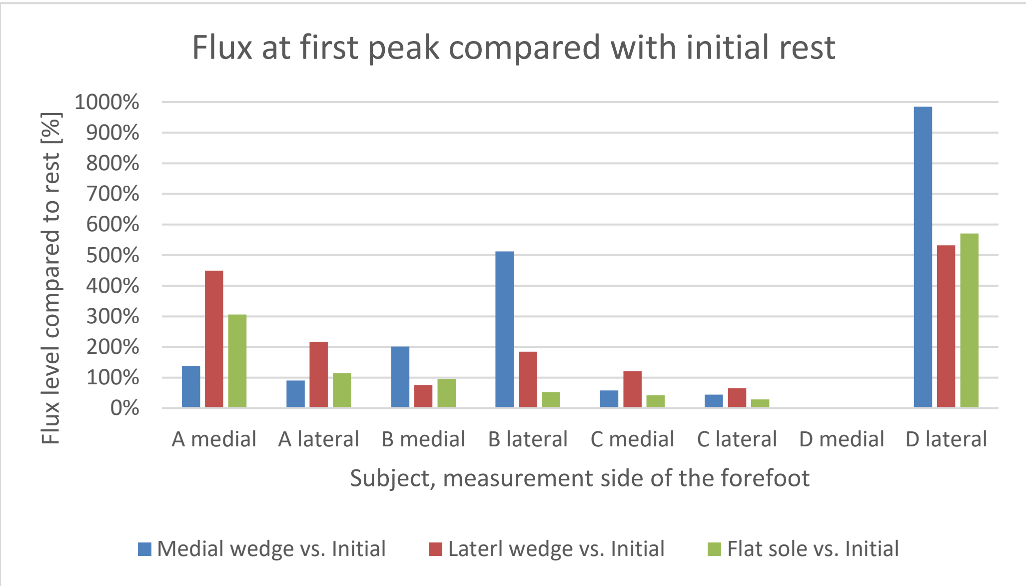

FIGURE 4-20 FLUX LEVELS COMPARED TO REST PERIOD DURING THE FIRST PEAK OF THE POSTAMBULATORY TEST

5 DISCUSSION OF THE RESULTS

In this section the results from the previous chapter will be discussed in light of the hypothesis made in section 1.4 and how they address the research questions posed there. The findings will also be compared with the literature that was reviewed in section 2 and the models there that explain the circulation in the feet. The chapter ends with an evaluation of the research, its significance and application, and recommendations for future study.

5.1 ADDRESSING THE RESEARCH QUESTIONS, HYPOTHESIS AND LITERATURE

Research Question 1:

> ***"Is the forefoot flux greater while standing on corrective soles compared to standing on flat or laterally wedged soles?"***

This first research question is answered by the Step Perfusion Test during step phase. Its results reveal that there are coinciding patterns in the comparisons between the medial and lateral flux levels across footwear. The flux level relative to flat sandaled flux was higher on the medial side during stance on medial wedges (188 %, SD = 132 %) than on the lateral side (78 %, SD = 25 %), and higher on the lateral side during stance on lateral wedges (216 %, SD = 188 %) than on the medial side (128 %, SD = 100 %).

This was the opposite result from of the expectation in the hypothesis, which was that the wedged side would show a lower perfusion level due to a vasoconstriction in the peripheral skin on the side that is under wedge pressure. The results indicate that the heel wedge successfully shifts the pressure onto the opposite side of the foot. The degree of pronation seems to present a pressure-dependent vascular constriction during stance. The results also also suggest that the medial sole has a positive effect in the offloading of the first metatarsal head (and reducing the ulceration risk there), albeit at the expense of the flux on the lateral side of the forefoot. The comparisons of the average flux levels compared to flat sandaled flux show some inconsistency however, as the flat soled flux was not a consistent middle position between the two opposite wedge conditions. As a result, the laterally wedged sandals displayed a higher perfusion than the flat sandal on both sides of the forefoot.

The low level and dispersion of the data during step could be caused by a the naturally limited range of flux levels above zero that could result from the pressure of a weightbearing stance. The coinciding patterns found in the step perfusion test showed a high standard deviation in the relative flux levels. The influence of an outlier like the one found in one of the measurements at rest in candidate D proved unacceptably large in such a small pool of samples. This indicates a low significance of the results.

Research Question 2:

> ***"Is the forefoot flux response at rest greater after having stood on corrective soles compared to having stood on flat or laterally wedged soles?"***

The increase of flux is as expected, with an increased flux at the beginning of each rest phase as blood returns to microtissue that has been temporarily blanched as the supply to the smaller blood vessels in the skin that were blocked by applied surface pressure. The question is whether the reperfusion levels can reveal only a pressure dependent reperfusion pattern, or if they also show a perfusion pattern determined by the degree of pronation correction in each subject as a result of a changed contact area or vascular constriction due to wringing effect during pronated gait. Examples of such mechanical distortions that reduce blood flow are illustrated below.

FIGURE 5-1 MECHANICAL DISTORTIONS THAT CAN REDUCE BLOOD FLOW

The flux measurements in the rest phase of the Step Perfusion Test showed the opposite and complementing pattern to the relative flux in pressure phase. Here, the flux level compared with the flux level after stance in flat sandal is higher in the measurement on the opposite side of the wedge side, giving a higher flux level on the medial side after stance in laterally wedges shoes and vice versa. This was again contrary to the hypothesis, which was that the expected low perfusion on the wedged side of the foot during pressure phase would cause a high flux level once the foot is elevated during rest. The results are however in line with the findings during pressure phase – the foot side with the lowest perfusion during step is the side with the highest perfusion during rest, with a lateral side measurement after medially wedged stance of 130 %, SD = 59 %, and a medial side measurement after laterally wedged stance of 129 %, SD = 35 %. The increased flux on the opposite side from step phase indicates a reperfusion of an area that was unperfused during stance, and functions as an indirect measurement of the flux at stance, which is the relevant measure when assessing reduced ulceration risk. The results do not point to a global reduction of the forefoot flux, but rather a mediolateral change in accordance with the wedge applied.

Research Question 3:

> ***"Is the forefoot flux response at rest greater after having walked with corrective shoes for 10 minutes, compared to having walked on flat or oppositely wedged woot wear?"***

This question is addressed in the Static Postambulatory Perfusion Test. The long-term and short-term results of this protocol showed to few coinciding patterns between the footwear, measurement sides of the forefoot and wedge correction to be conclusive. This could mean that the flux response to the introduced stimuli is of low duration and is not captured by the postambulatory measurement in supine position because of the transition time between activity and measurement. When looking at the response duration of the Step Perfusion Test as a comparison, a clear stabilization of the flux signal occurs after the 30-second rest period. This is demonstrated when looking at the transition between the last period of rest with elevated foot together with its continuous transition into final rest period. The flux has reached an average slope of 0.01 PU per second using linear regression in the 30 second period of final rest. The average slopes over ten second intervals can be seen in figure 4-15. The first interval starts one second in around peak, and the measurements of FR that were interrupted before their conclusion were not included. This stabilization indicates that the length of the flux response to stance is approximately 30 seconds in the Step Perfusion Test, and despite the longer stimulus exposure in the Static Postambulatory Perfusion Test, the response peak in the postambulatory perfusion test is likely lost in the 15 second transition time between walk and supine measurement with attached probes.

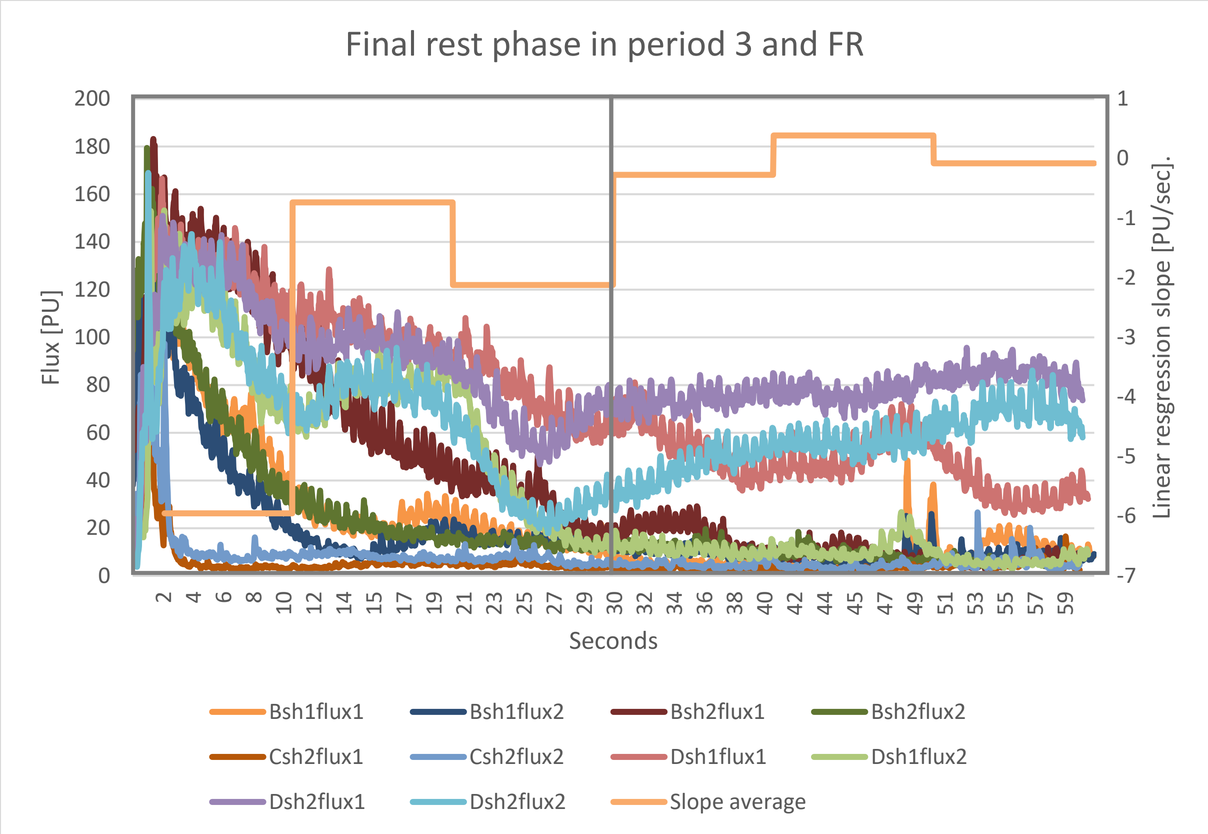

FIGURE 5-2 SLOPE AVERAGES OVER TEN SECOND INTERVALS IN REST AND SUBSEQUENT FR. INTERRUPTED MEASUREMENTS ARE NOT INCLUDED.

The Fast Fourier transform frequency analysis of the postambulatory analysis speaks to the high signal quality provided by the test protocol, since the power spectrum shows a clear Frequency signature in the cardiac frequency band around 1.1 Hz besides the peaks in the myogenic (0.05-0.15 Hz), sympathetic (0.02-0.05 Hz) and endothelial (0.008-0.02 Hz) frequency bands, indicating activity in the smaller blood vessels, autonomic nervous system and the cellular interface between the blood flow and blood vessels respectively. These all play a part in regulating the plantar circulation in the glabrous skin of the feet and ensuring homeostasis. An example of the FFT Power spectrum of the Postambulatory Perfusion Test is illustrated in figure 5-2 below, from the medial and lateral measurements of candidate D when wearing medially wedged sandals.

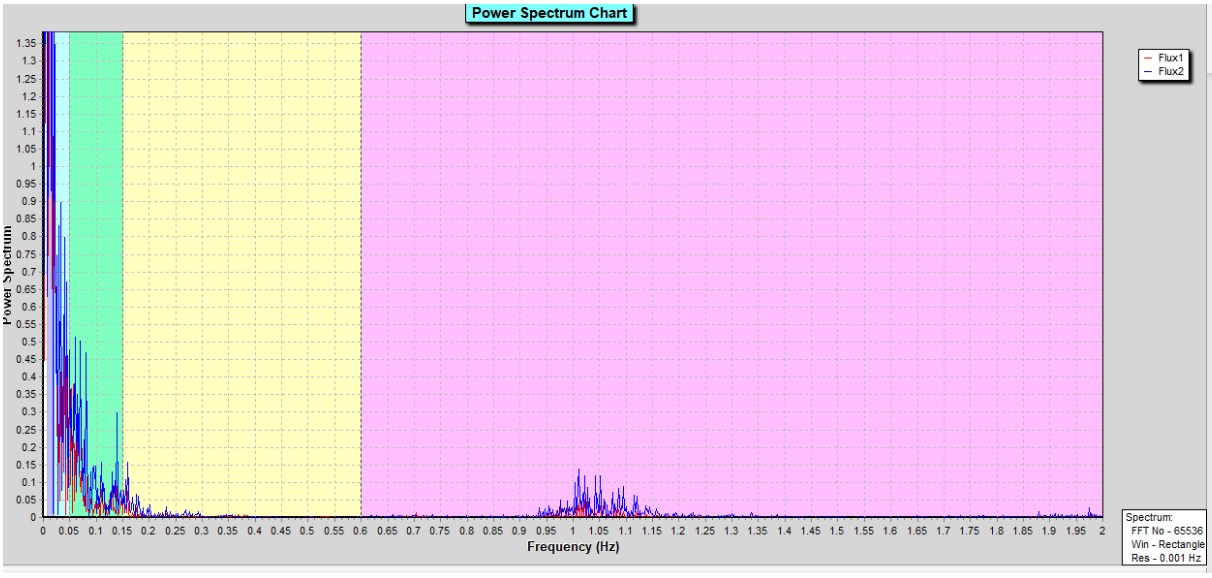

FIGURE 5-3 EXAMPLE OF AN FFT POWER SPECTRUM OF A POSTAMBULATORY PERFUSION MEASUREMENT

Research Question 4:

> ***"Does the flux response across trials correlate with the subject's weight or needed degree of correction?"***

The average increase of the flux from stance to rest phase (and the flux level at rest) was inversely correlated to the degree of pronation assessed in each subject. It indicated that the subjects with a more moderate pronation had a larger percental flux response. This could be a random correlation of a varying flux level between subjects due to physiological variations in skin. The correlation is not explained by a mediolateral pressure shift since the flux level is correlated to the wedge size across both medial and lateral side measurements. Nor does it appear to be the cause of a pressure-independent vascular constriction related to pronating subjects, such as the wringing effect of the Achilles tendon in the *whipping phenomenon* (Wezenbeek, et al., 2017), (Karzis, et al., 2016). That is because the flux level relative to stance is higher in the less pronated subject, and therefore not a reperfusion response to vascular constriction related to pronation. The correlation found in this experimental protocol should be tested on a lager sample scale to uncover if the correlation holds.

5.2 APPLICATION, WARNINGS AND RECCOMENDATIONS

The results indicate that a local corrective heel wedges show a promising offloading pattern on the medial side of the forefoot heel. This could have future application as a preventative care for diabetes patients, but the lateral side must not be put at risk in high-risk patients. Further larger-scale testing is recommended to assess the absolute comparative flux levels between the medially and laterally wedged shoes and the flat sandals used as a ground of comparison. The study showed a clear coinciding pattern of the mediolateral comparison of flux levels in wedged footwear.

6 CONCLUSION

The experimental study revealed that the response to wedged footwear is most notable within the immediate 30 seconds of step stimuli of short duration, and probably peaks within the same time frame after 10 min. walk stimuli. Supine measurements after walk stimuli compared across footwear did not reveal any patterns in a long-term trend analysis of the lower frequency bands. The short-term response showed to few coinciding patterns to be conclusive.

The step perfusion test of 30 seconds stance and 30cevonds subsequent rest with elevated foot revealed that the medially wedged sandal resulted in a higher flux level relative to flat sandal flux on the medial side of the forefoot (188 %, SD=132 %), and that laterally wedged sandals gave a higher relative flux on the lateral side (216 %, SD=188 %) during stance. The relative flux levels during foot elevation after stance show the opposite and complementary trend, coinciding with the first findings. This suggests that the degree of pronation presents a pressure-dependent vascular constriction during stance. It also suggests that the medial sole has a positive effect in the offloading of the first metatarsal head (and reducing the ulceration risk there), albeit at the expense of the flux on the lateral side of the forefoot. The comparisons of the average flux levels compared to flat sandaled flux show some inconsistency however, as the flat soled flux was not a consistent middle position between the two opposite wedge conditions. As a result, the laterally wedged sandals displayed a higher perfusion than the flat sandal on both sides of the forefoot.

The percental flux change from stance to foot elevation is inversely correlated to the pronation degree of the subject (Pearson correlation coefficient of -0.732) but is not explained by vascular constrictions attributed to pronation. Further testing is recommended to confirm correlation here, and to confirm and increase the significance of the findings.

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