THE MEASUREMENT OF TOE ARTERIAL BLOOD PRESSURE DURING REST, CYCLING, AND WALKING

by

Joshua Andrew James Goreham

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ABSTRACT

The Portapres® is thought to be a device that can provide accurate toe blood pressure measurements. The first aim of the study was to validate the Portapres® for use on the toe during rest and exercise. The second aim was to determine the effect of cycling exercise on mean arterial pressure in the toe (MAP_T). The Portapres® was able to provide accurate MAP_T values during rest and exercise. It was hypothesized that MAP_T would increase as cadence and power output increased. An increasing cadence was shown to increase MAP_T when comparing cadences of 50 rpm (76.9±36.6 mmHg) and 90 rpm (80.2±37.4 mmHg) while maintaining the same power output (71.9±38.2 W). An increasing power output was shown to increase MAP_T (high power=89.9±36.6 mmHg; low power=76.9±36.6 mmHg) when cadence was kept constant. The results from the study show that increased limb movement and power output increases arterial blood pressure in the toe.

LIST OF ABBREVIATIONS AND SYMBOLS USED

A – longitudinal acceleration

BP –arterial blood pressure

bpm – beats per minute

CC – central command

CI – confidence intervals

df – degrees of freedom

ECG – electrocardiography

EMG – electromyography

HR – heart rate

HR_{max} – maximum heart rate

Hz – Hertz

kg - kilogram

km/hr – kilometers per hour

LD – Laser Doppler

MAP – mean arterial pressure

MAP_B – brachial mean arterial pressure

MAP_T – toe mean arterial pressure

mmHg – millimeters of mercury

PAD – peripheral arterial disease

PAR-Q – Physical Activity Readiness Questionnaire

PPG – photoplethysmography

Q – cardiac output

rpm – revolutions per minute

SD – standard deviation

SV – stroke volume

TBP – toe arterial blood pressure

TPR – total peripheral resistance

VO_2 – oxygen consumption

W – Watts

α = alpha

ω = angular velocity

Δ = change

Π = pi

μ = blood viscosity

ρ = blood density

δ = group III afferents

° = degree

• = multiply

* = statistical significance

a′ = y-intercept

b′ = slope

± = plus minus

% = treadmill grade

↑ – increase

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CHAPTER 1: INTRODUCTION

1.1 Significance

Blood travels from the heart to the rest of the body for many different purposes; but ultimately it is to allow for proper physiological function and to maintain homeostasis. Blood flows through inter-connected blood vessels that are part of the circulatory system. These vessels are not always linear like fluid pipes; instead, they bend, twist, and proliferate by splitting to conform to the body's physiological requirements[1]. Systemic vessels can either deliver oxygen-rich blood throughout the body via the arteries, or can return de-oxygenated blood back to the lungs, through the veins. The arterial system contains arteries, which are broken down into smaller vessels called arterioles, and eventually into microscopic capillaries[2]. After the blood flows through the capillaries, it is then transferred back via the venous system through venules to larger veins, and eventually to the lungs. This venous system includes valves that prevent pooling of the blood due to the effect of gravity, which is one of the main differences between the arterial system and the venous system. For the purpose of this thesis arterial blood pressure (BP) will be investigated.

Pressure is produced when fluid travels through any cylindrical column. Blood that travels through cylindrical blood vessels therefore produces BP, which is the measure of the force of the blood on vascular walls[2]. Although BP can be quantified in pressure units (i.e., mmHg, Pa), the fluid acts much differently in blood vessels than in rigid water pipes. Due to the different types of blood flow found in vessels, it is sometimes difficult to predict BP in many parts of the body. For example, laminar flow can be found in large linear vessels, whereas turbulent flow is seen in irregular-shaped blood vessels.

Furthermore, because the human body is almost always moving, the fluid experiences external forces, and results in changes to the flow. Laminar flow requires a very consistent environment to maintain its uniformity, whereas turbulent flow is more unpredictable[1]. The type of flow is essential in determining the amount of BP that is produced. This concept will be addressed in the literature review section of this thesis.

Blood pressure is essential in determining cardiovascular health. Wilkins et al[3] found that one in five Canadians between 20 and 79 years of age have high blood pressure. Causes of high BP are well documented in the literature[4]; however, not all causes of high BP are controllable. As we age, vessels increase their stiffness and can eventually cause high BP[5]. The lack of vessel distensibility requires large volumes of blood to flow through vessels with rigid walls, which eventually leads to high pressures. A healthy blood vessel is able to dilate or constrict depending on the amount of blood it is transporting. A larger vessel diameter allows for more blood to flow without causing increased pressure force on the vessel walls, which could eventually lead to injury (e.g. thrombosis). Poor lifestyle choices, like diet, sleep, smoking and exposure to stress are detrimental to vascular health, and accelerate the chances that a person will develop cardiovascular disease[4].

Cardiovascular disease is one of the leading causes of death in Canada, and Statistics Canada[6] reported that the cost of treating patients with cardiovascular disease is expected to rise. New therapeutic modalities (i.e., medication, surgery, exercise therapy, etc.) have been developed, but many health problems related to cardiovascular disease remain unanswered. Peripheral artery disease (PAD) is a type of cardiovascular disease in which patients experience pain during daily activities, as well as a decreased quality of life even with new treatment developments[7]. Exercise therapy plays a large role in PAD

rehabilitation due to its ability to increase perfusion pressure to active muscles[8]. The main goal of exercise therapy is to increase arterial blood pressure and flow in the lower limbs to allow for necessary blood perfusion via arteriogenesis[8-9]. Walking is considered to be the best mode of exercise therapy for PAD patients, even though its efficacy is relatively small[10]. Furthermore, a study by Askew et al[11] found that PAD patients were able to cycle longer than they could walk due to experiencing less pain in the affected limb(s). Since the patients could exercise longer, it was expected that more blood could be transported to the active limb(s), and therefore help offset the amount of pain the patients encountered during activity. Unfortunately the mechanisms for the difference in exercise time between the two modes of exercise were, and still are, poorly understood. As such, it is important to develop new exercise therapy strategies using a mechanistic approach. More information on PAD and exercise can be found in Appendix A of this thesis.

Well-known mechanical factors such as systolic and orthostatic forces, cause increases in arterial BP within a body limb segment during human movement[12]. However, Sheriff et al[13] showed that limb motion also causes an increase in limb arterial BP; and studies simulating arterial BP by attaching plastic fluid filled tubes to participants lower limbs while walking[14] and cycling[15] have shown that limb motion has the potential to increase simulated arterial BP. Therefore, comparing various biomechanical factors associated with exercise could provide more information on how BP reacts due to motion.

The purpose of this study was to compare the effect of cycling and walking exercise on toe arterial blood pressure (TBP) of non-disabled individuals. The project is a step towards developing novel exercise modalities for the treatment of PAD, and could eventually improve treatment for those who suffer from PAD. Based on previous work using water-filled tubes and pressure sensors[13-15] and the fact PAD patients were able to

cycle longer than they could walk[11], it was hypothesized that cycle ergometer exercise would generate a higher increase in TBP in comparison to treadmill-walking exercise in a non-disabled population.

Another purpose of this study was to determine if the Portapres® BP device is a valid and reliable tool for the measurement of TBP. Although there are multiple ways to measure TBP, very little research has investigated the use of the Portapres® on the toe[16-17]. Therefore, in order to be confident in the TBP results obtained during cycling, an attempt to validate the Portapres® was necessary by collecting multiple TBP measurements during rest and exercise. Construct validity, concurrent validity, inter-day reliability, and the feasibility of using the device on the toe were assessed in addition to measuring TBP during walking and cycling. Overall, the research project included four research questions, which will be described later.

CHAPTER 2: LITERATURE REVIEW

2.2 Blood Pressure

Blood pressure (BP) can be modulated by three mechanical factors: systolic force, orthostatic force, and force due to movement[12]. Systolic force is derived from the heart contracting (i.e., beating) and results in increases in BP. The second mechanical force is the orthostatic force (i.e., gravitational), which can either increase or decrease BP depending on the location of the measurement in relation to the heart[13]. The third mechanical force is due to movement (e.g., external forces). The effect of movement on BP is lesser known, but is presumably just as important as systolic and orthostatic forces when the body is not at rest. External forces cause reactions within the internal environment and result in changes in BP and flow[13].

2.2 Systolic Force

It is well known that when the heart contracts an increase in BP occurs in the blood vessels due to the systolic pulse[2]. The systolic pulse causes more blood to flow through the vessel, which in turn causes an increase in BP. Blood pressure can be determined using the equation:

Equation 1. $$\Delta P = Q \times R$$

where ΔP is the difference in pressure, Q is the flow, and R is the resistance to flow[18]. The equation can be used to determine flow for any fluid, including blood. When solving for blood flow, the above variables can be re-titled to: mean arterial pressure (MAP),

cardiac output (Q), and total peripheral resistance (TPR). These characteristics will be discussed in detail later.

Flow can be described using Hagen-Poiseuille's Law, and is derived by the formula:

Equation 2. $$Q = \frac{\pi r^4}{8\mu L}$$

where μ is the dynamic viscosity of the fluid, L is the length of the vessel, Q is the flow rate, and r is the radius of the vessel[18]. The radius of the vessel is multiplied to the 4th power, meaning that the radius plays more of a role in determining the resultant flow compared to other variables like viscosity and length. The body is capable of constricting and dilating vessels through autonomic control to meet situational or external demands, which in turn allow for quick blood flow and BP regulation. Vessel elasticity also plays an important role in modulating blood flow and BP. Elastic vascular walls help propel blood through the vessel using a recoil effect, also known as the Windkessel function[18-19]. This causes greater pressures in the smaller peripheral vessels compared to bigger vessels, like the aorta[18]. A palpable BP pulse is created by the systolic force, which is caused by the contraction of the left ventricle and the elastic properties in the vessels.

2.3 Orthostatic Force

Gravity plays a large role in blood circulation while sitting, standing, and resting supine[13, 17]. The effect on BP due to gravity is known as the orthostatic force. Lower body

BP is much larger than upper body BP in an upright posture, and can be explained by the equation:

Equation 3. $$P = \rho g h$$

where *P* is blood pressure, ρ is blood density, g is the gravitational acceleration constant, and h is the change in height between the heart and measurement location. The orthostatic force can cause great variations in BP, and is controlled by routinely constricting the lower limb blood vessels when standing in an upright position[20]. Constriction of lower limb blood vessels prevents pooling and allows blood to be re-circulated via the lungs and heart. However, it is common for people of all ages to be unable to constrict their blood vessels during upright stance, which is known as orthostatic intolerance. Orthostatic intolerance is common among astronauts who have returned to Earth due to becoming accustomed to space where there is zero gravity[20]. Watenpaugh et al[20] published an upright stance model using Equation 3 above to predict mean arterial BP at various heights above and below the heart (Figure 1).

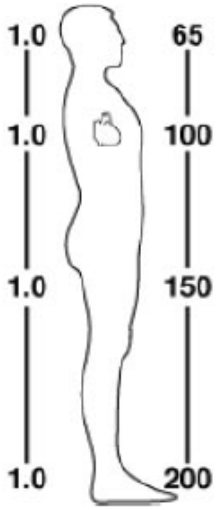

Figure 1. The effect of gravity on arterial blood pressure[20]. Gravity effect (left) and calculated mean arterial pressure (right - millimeters of mercury) at different body parts of a 1.85 m tall person.

A study by Levick et al[21] measured mean arterial BP in the hand and the foot at and below heart level in two subjects. Their findings support the idea that mean arterial BP increases proportionally to the heart height above the pressure measurement site. The published pressure values compare well to a line with a slope of 1 on a capillary pressure (y-axis) vs. height of heart above capillary (x-axis) graph (Figure 2). This means that for every 1 cm increase in height from the heart, the capillary pressure increased by about 1 cm H_2O as well. Their study results provide further evidence that gravity has an effect on BP, and could have an effect on TBP during exercise.

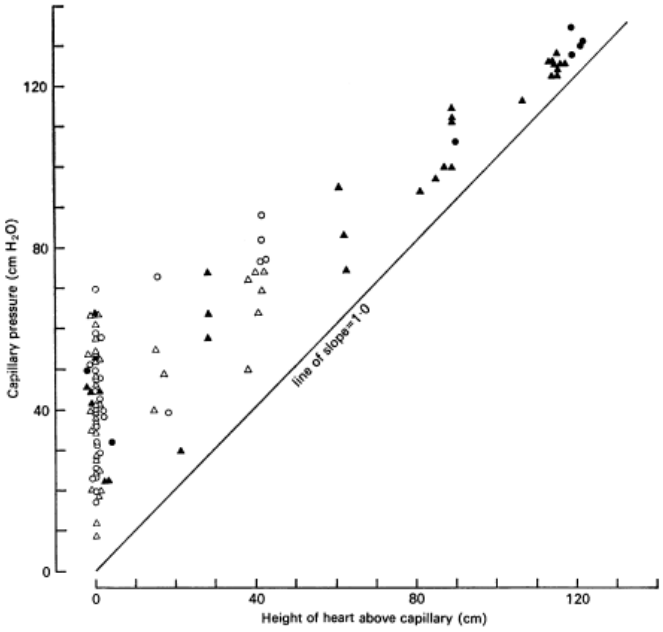

Figure 2. The relationship between single capillary pressures and the height of the measurement below the heart[21]. Hollow markers depict the finger pressures for two participants. Solid markers depict the toe pressures for two participants.

2.4 Movement Force

The third mechanical force that affects BP is movement. Movement is beginning to be studied more often in the attempt to quantify changes in BP. Sheriff et al[13] first showed the importance of understanding the biomechanical and physiological mechanisms that cause increased arterial BP in moving limbs. They found that simple horizontal arm abduction and adduction exercises at 0.75 Hz generate angular motion-related forces that increase liquid and BP in the active upper limb. The increases in liquid pressure were measured by placing a pressure transducer at the endpoint of a plastic water-filled tube, whereas the increases in finger arterial BP were measured by using a Finapres® device. The Finapres® device was used to measure BP in the active and non-active limbs in separate trials (Figure 3).

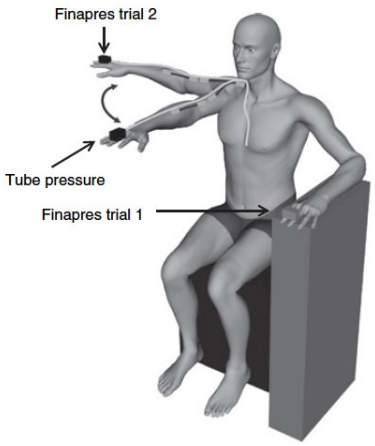

Figure 3. Sheriff et al[13] experimental setup for Trials 1 and 2. Arrows show location of measurement devices for each trial.

Sheriff et al[13 (p 396)] stated the reasoning behind using a water-filled tubes for their experiment:

> 'the static fluid in the tubing would be exposed to the same forces as the column of blood in the arteries within the arm (but not in veins owing to the venous valves). Thus, the pressure developed at the distal end of the tube (at the site of the pressure transducer) would faithfully mimic the pressure developed within the arteries, minus the pressure developed by the heart.'

They found a significant difference ($P < 0.05$) in the water tube's mean pressure change as it increased by 11±2 mmHg during exercise, along with a rise in finger mean arterial pressure in the active arm (18±3 mmHg) compared to the non-active arm (8±2 mmHg). The increase in arterial blood pressure related to motion is approximately 10 mmHg (active arm pressure increase – resting arm pressure increase: 18±3 mmHg – 8±2 mmHg). This value is similar to the liquid pressure increase in the tube (11±2 mmHg). Since the systolic force was present in both the active and non-active arms, the difference between the two arms can be solely related to movement. This similarity displayed the appropriateness of using the water-filled tube as a model for the evaluation of the effect

of movement on arterial BP, even when the systolic forces were not present in the tubing attached to the active limb. The results of the Sheriff et al[13] study show that simple movements can significantly increase liquid and BP in moving limbs.

2.5 Modulations to Blood Pressure During Exercise

2.5.1 Neural Mechanisms

As previously mentioned, arterial blood pressure can fluctuate depending on various internal or external stimuli[12]. There are three known neural reflexes in the autonomic nervous system that regulate BP during exercise. They include central command, the exercise pressor reflex, and arterial baroreflex resetting[22-23] (Figure 4).

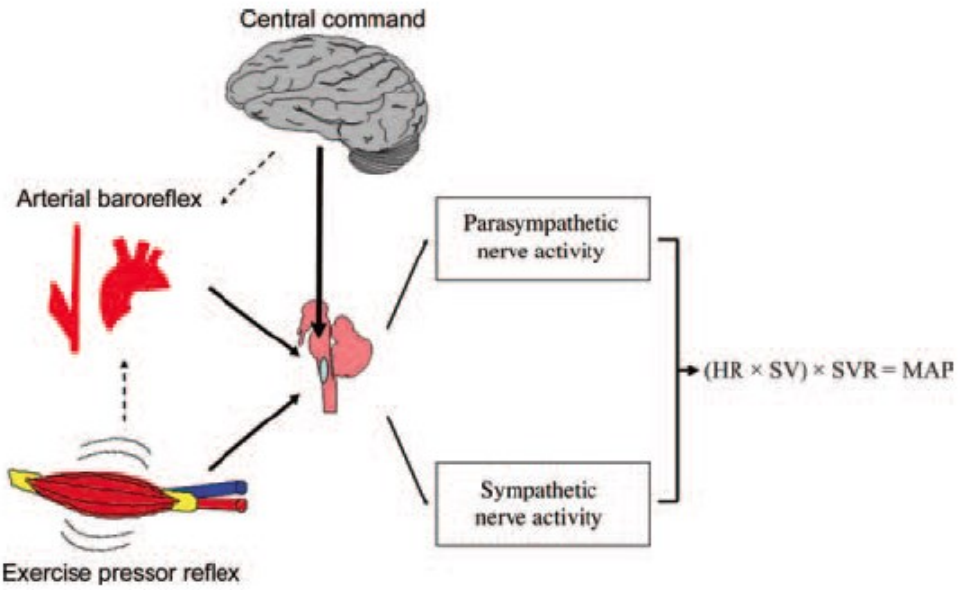

Figure 4. A diagram that illustrates the neural mechanisms responsible for the regulation of cardiovascular control during exercise[22]. HR, heart rate; SV, stroke volume; SVR, systemic vascular resistance; MAP, mean arterial pressure.

All three neural mechanisms are typically discussed by their effect on mean arterial pressure (MAP)[24]. MAP is the average BP in an artery, and is quantified by the equation:

Equation 4. $$MAP = \text{Diastolic BP} + [\tfrac{1}{3} (\text{Systolic BP} - \text{Diastolic BP})]$$

MAP is dependent on three hemodynamic characteristics related to autonomic function [e.g., heart rate (HR), stroke volume (SV), and total peripheral resistance (TPR)] and can be determined by the equation:

Equation 5. $$MAP = (HR \times SV) \times TPR$$

HR can be defined as the amount of times the heart beats in one minute, SV is the amount of blood ejected from the heart in one heart beat, and TPR is the amount of resistance present in systemic circulation (i.e., due to plaque, constriction) and is also known as systemic vascular resistance. Cardiac output (Q), is defined as the volume of blood ejected from the heart in one minute (i.e., the product of HR × SV). Q and the distribution of blood to active versus less active regions of the body both play an important role in the modulation of MAP during exercise[24]. Changes in cardiovascular control during dynamic exercise are due to vagal withdrawal and increased sympathetic neural activity. For example, central command (CC) increases HR and Q at the onset of exercise. This is initially accomplished by a rapid withdrawal of vagal innervation to the sinoatrial node of the heart. As exercise continues, further increases in Q are accompanied by elevated sympathetic innervation to the sinoatrial node (↑HR) and left ventricle (↑SV). In addition

the sympathetic-mediated rise in cardiac output, MAP is further elevated during exercise by increased sympathetic activity to resistance arterioles (↑TPR) in both active and inactive tissue beds[24]. Central command plays an important role in adjusting the arterial baroreflex operating point, which will be discussed later. The exercise pressor reflex also plays a role in altering MAP by responding to increases in mechanical and metabolic stimuli in an active muscle. The exercise pressor reflex changes MAP by also acting on the arterial baroreflex by transmitting signals through group III and IV afferents to the cardiovascular control centre of the medulla[24]. All three neural mechanisms directly affect the components of MAP (i.e., Q and TPR), and will be discussed in more detail below[25-27].

2.5.2 Central Command

Central command is one of three known neural mechanisms responsible for MAP control[24]. Central command is a feed-forward neural mechanism that originates in higher brain centres. From there, the cardiovascular control centre of the medulla is innervated (i.e., nucleus tractus solitarius), and it functions by controlling cardiovascular responses to exercise[23, 28]. Williamson et al[22 (p 52)] writes that CC has been 'classically defined as a feed-forward mechanism involving parallel activation of motor and cardiovascular centres'.

Williamson et al[28] later raises the point that CC may be both a feed-forward and feedback control mechanism as there has been research showing that perception of effort can also alter cardiovascular control[29]. The Williamson et al[28] definition provides evidence that motion is not needed to elicit an increase in cardiovascular function; however, Nobrega et al[30] did report that CC determines the HR response to dynamic

exercise, in this case cycling. With these definitions in mind, and the type of exercise being dynamic and voluntary, the definition of CC for this thesis will be the Williamson et al[22] definition, where parallel activations of motor and cardiovascular centres are used.

2.5.3 Exercise Pressor Reflex

Another neural mechanism responsible for cardiovascular regulation during exercise is the exercise pressor reflex. The exercise pressor reflex originates in skeletal muscle and can be activated via receptors that are sensitive to both mechanical (e.g., stretch, pressure, vibration) and chemical (e.g., metabolites) stimuli. The receptors send afferent information back to the cardiovascular control centre of the medulla[23] (Figure 5). Group III afferent neurons are excited quickly and send mechanical information to regulate cardiovascular function during movement that detects a stretch, vibration, or pressure change to the un-encapsulated nerve endings of Pacinian corpuscles. These changes are detected by receptors in the muscle known as mechanoreceptors (e.g., muscle spindles, Golgi tendon organs), and can show increases in HR and SV within seconds[31]. Group IV afferent neurons have been shown to detect metabolite accumulation in a recently active muscle[24]. These afferents are typically slower to reach excitation, as they travel through un-myelinated C fibers and an accumulation of metabolites must occur[24]. Common metabolites produced by skeletal muscle contraction are lactate, potassium, and phosphate[24]. Although groups III and IV sensory neurons have different primary functions, both are capable of detecting metabolite and mechanical changes in skeletal muscle[24].

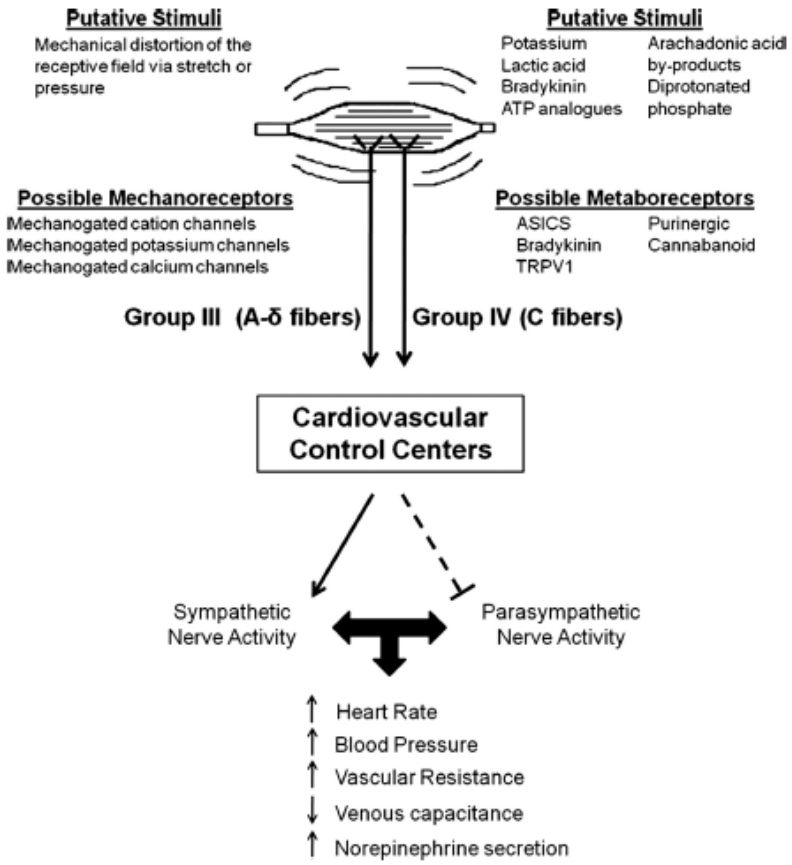

Figure 5. The exercise pressor reflex arc[23]. Figure shows mechanical properties and metabolites responsible for the increase in heart rate, blood pressure, vascular resistance, norepinephrine secretion, and decrease in venous capacitance. Group III (A-δ fibers) are sensitive to mechanical stimuli; whereas Group IV (C fibers) are sensitive to metabolite stimuli in the active muscle. Solid arrows depict direction of afferent signals to cardiovascular control centers, and an increase in sympathetic nerve activity. Dashed line depicts the withdrawal of parasympathetic nerve activity. ATP, adenosine triphosphate; ASICS, acid-sensing ion channels; TRPV1, transient potential vanilloid receptor 1.

2.5.4. Arterial Baroreflex Resetting

The final known neural mechanism that effects MAP is the arterial baroreflex. The main duty of the arterial baroreflex is to maintain adequate perfusion pressure during exercise by resetting its operating point continuously (Figure 6). A review by Potts et al[32] states that the exact locations involved in resetting the arterial baroreflex are not

completely understood; but highlights many studies that support the notion that the nucleus tractus solitarius, and the caudal and rostral ventrolateral medulla are involved.

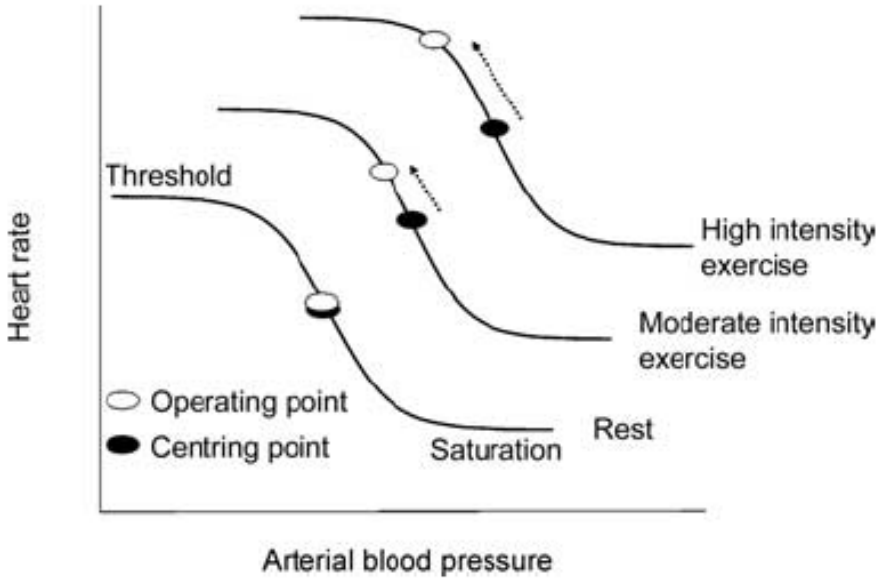

Figure 6. Diagram illustrating the baroreflex stimulus-response curve[22]. Dotted arrows depict the direction the operating point moves in relation to the centering point during different intensities of exercise.

The "operating point" (OP) of the arterial baroreflex is the point at which MAP is controlled at, and is continuously reset during exercise by neurologically elicited changes from either descending (i.e., CC) or ascending (i.e., exercise pressor reflex) stimuli[32]. The resetting of the arterial baroreflex regulates BP and cardiovascular activity during aging, physical deconditioning, and physical training[33]. Williamson et al[22] defined the OP as the pre-stimulus blood pressure (i.e., the BP prior to the onset of exercise). The reason for resetting the OP is to give the arterial baroreflex better control of cardiovascular activity during varying exercise intensities and durations[23-24].

Another point of interest within the arterial baroreflex stimulus-response curve is

the "centering point" (CP). The CP is the point of maximal sensitivity and does not change from rest to heavy exercise intensities[34]. Williamson et al[22 (p 54)] stated that the CP is known as the 'point at which there is equal depressor and pressor response to a given change in blood pressure'. At rest, the OP is equal to the CP, but as discussed above, the OP is reset during exercise to higher blood pressures toward the threshold of the baroreflex stimulus-response curve (Figure 6). The threshold is the blood pressure level when HR stops increasing even though BP is continuing to decrease, whereas the saturation is the blood pressure when HR stops decreasing even though BP is continuing to increase. The importance of these two positions on the baroreflex stimulus-response curve is that they are points in which another physiological variable is required, in addition to HR, to bring BP back to a normal level (i.e., TPR)[22]. As exercise intensity increases, HR and arterial BP increase, causing a gap between the OP and the CP (Figure 6). The opposite occurs as the person returns back to a resting state and ultimately leads to the OP matching the CP.

As mentioned, three neural mechanisms (CC, exercise pressor reflex, and the arterial baroreflex) are needed for the proper control of BP during exercise. However, Kaufman et al[35] reported that autonomic function is dependent on the type of exercise being performed. They found that static exercise (e.g., weight lifting) elicits greater increases in MAP (i.e., due to a large increase in TPR) compared to a dynamic exercise (e.g., running), which causes less increases in MAP (i.e., due to a decrease in TPR). Differences between exercise types are linked to the systemic metabolic vasodilation that is present in dynamic exercise, but to a lesser degree in static exercise[35]. The large decrease in TPR is due to shear stress on the endothelial layer of the vessel (i.e., due to increased blood flow), which causes nitric oxide to be released, and a subsequent

vasodilation effect occurs[36-37]. The decrease in TPR also counteracts the increase in Q during dynamic exercise, and therefore MAP does not increase as much as during static exercise.

Additionally, an increase in intramuscular pressure (i.e., due to increased muscle activity) is another difference that persists in the TPR response between the two modes of exercise (i.e., static and dynamic exercise). A contracted muscle increases intramuscular pressure, which in turn compresses the blood vessel and increases TPR, which then increases MAP. This response is seen in static exercise where isometric contractions are common (i.e., resistance training). It is also important to look at differences in active muscle mass between two modes of exercise, as differences in muscle activity could have large implications on neural mechanisms like CC and the exercise pressor reflex. In relation to this thesis, walking and cycling both require different amounts of muscle to perform the intended actions[38]. Cycling uses only concentric muscle contractions to perform pedal revolutions no matter what the power output or cadence; whereas walking/running require both concentric and eccentric muscle contractions depending on the grade of the walking surface[38]. Running has been shown to require a greater amount of metabolic power compared to cycling when increasing external mechanical power by the same amount[38]. A study by Bijker et al[38] also showed that more electromyography (i.e., muscle activity) was recorded during walking compared to cycling at similar external mechanical power outputs. The difference in electromyography could mean there are more stretch and vibrations in a more active muscle; therefore, an increase in mechanical stimuli from the muscle would cause differences in the exercise pressor reflex response. The reasons above highlight that fact that it is important to understand how different neural mechanisms react when comparing different modes of exercise. Despite

varying amounts of muscle activity between two types of exercise, it is important to explore other ways to maintain cardiovascular control between two different types of exercise. One way standardize cardiovascular demands during exercise is to match the exercise intensity. Even though different muscles are active, the neural effects on the cardiovascular system can be assumed to be similar if exercise intensity is matched.

Overall, there are three main neural mechanisms that contribute to alterations in MAP during exercise. The exercise pressor reflex, central command, and arterial baroreflex all attempt to maintain homeostasis within the body at increased levels of physical exertion. When comparing BP response between two modes of dynamic exercise in a research setting, and by understanding the role of each neural mechanism it becomes critical to maintain similar intensities between the two exercises (i.e., % of age-predicted maximal heart rate) and mechanical workloads between each type of exercise in attempt to elicit a similar cardiovascular response from each neural mechanism.

2.6 Methods of Blood Pressure Measurement

There are multiple techniques to measure arterial BP, including the intra-arterial method, the auscultatory method, the oscillometric method, and the non-continuous (beat-to-beat) method[2]. BP is often measured using the auscultatory method. This method requires a sphygmomanometer and a stethoscope, and is commonly used in clinical settings. Automated BP monitors are now used in clinical and non-clinical settings as well. Automated and manual BP monitors are used to calculate one BP value, which is measured from the brachial artery at one point in time. The technique determines BP by

listening to Korotkoff sounds and is useful as it gives immediate feedback on one's cardiovascular health.

Other forms of BP measurement include non-invasive continuous measurements. An example of a non-invasive type of BP device is the Finapres® BP monitor. The Finapres® uses the volume-clamp method, developed by J. Penaz[39], to measure continuous arterial BP in the finger (i.e., common volar digital artery). The device uses an inflatable cuff on the finger that is equipped with a photocell and a lamp to adjust the cuff pressure according to the amount of blood volume that is measured[39] (Figure 7). The lamp shines through the artery, and the light detector measures the amount of light that was not absorbed by red blood cells. When there are more red blood cells in the artery (systole) the volume is increased, a lesser amount of light is detected, and a higher pressure is reported. The opposite is true during diastole when there are fewer red blood cells in the artery, a greater amount of light is detected, and a lower pressure is reported. The cuff maintains vascular volume by using a feedback loop to unload the vascular wall[39-40], and was developed by Wesseling[40] and his group in 1982. By unloading the vascular wall, the cuff can be readjusted automatically to match the arterial BP, and collect continuously for long periods of time.

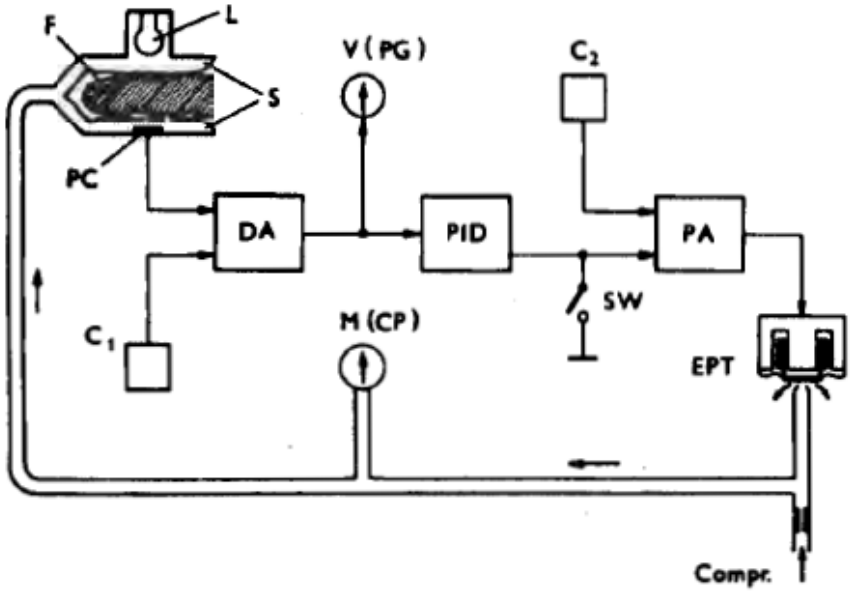

Figure 7. Original block diagram used in Finapres® model founded by J. Penaz[39]. The diagram shows how the various components determine blood volume and calculate arterial pressure. L, lamp; PC, photocell; F, finger; S, segments of transparent pressure cuff; DA, difference amplifier; PID, correcting network; PA, power amplifier; EPT, electro-pneumatic transducer; SW, switch; PG, photoelectric plethysmogram; CP, cuff pressure. C_1, compensation of plethysmogram signal; C_2, external electric signal.

There are multiple uses for the Finapres®, including autonomic nervous system and exercise testing, biomedical research, and basic hemodynamic measurements. Another device, created by Finapres®, is the Portapres®. The Portapres® can produce the same measurements as the Finapres®; however, it is portable which allows the patient to be mobile while the device collects accurate and reliable hemodynamic values.

2.7 Methods of Toe Blood Pressure Measurement

Although many studies have measured finger arterial BP using the Finapres® model, there have only been two known published studies that used the device to measure

TBP. The first study, by Kinsella et al[16], measured TBP in 30 females to determine the effect of pelvic tilt on aortic compression during cephalic singleton pregnancies. Aortic compression was identified when there was a reduction in TBP. The group placed a Finapres® BP cuff on the first toe of the right foot, and an additional Finapres® BP cuff on the middle finger of the right hand. While Kinsella et al[16] recognized that the Finapres® had not been validated for use on the toe, results showed that the TBP values followed changes in finger BP (Figure 8).

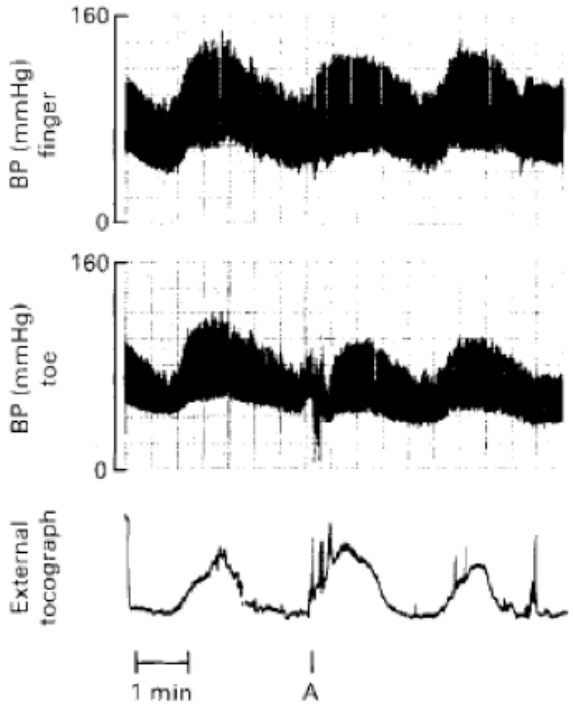

Figure 8. Arterial BP waveform from the right middle finger (top trace) and right first toe (middle trace) during uterine contractions[16].mmHg, millimeters of mercury; min, minute; A, change from sitting to 11° of left pelvic tilt position.

Kinsella et al[16] also stated that there were at times differences in absolute TBP and pulse pressures compared to BP in the finger. This led the researchers to miss aortic compressions, which was the main goal of the study. They stated that this was a minor

problem, and went on to blame it on the fact that the Finapres® was created for the finger and not the toe. They eventually concluded that most compressions were detected from the TBP waveforms, and that the Portapres® was a good device for use on the toe (Figure 9).

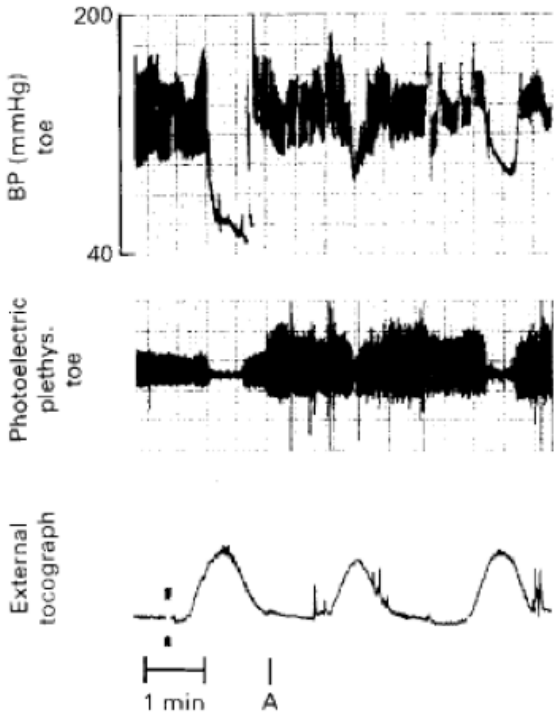

Figure 9. BP tracings during uterine contractions showing aortic compression from the Finapres® on the right first toe (top trace) and photoelectric plethysmography method on the right second toe (middle trace) [16]. mmHg, millimeters of mercury; min, minute; A, gain increased by 2.

Rosales-Velderrain et al[17] measured TBP using a device called the Finometer®, which is another model of the Finapres®. The group measured TBP and blood oxygenation in 10 healthy, young volunteers during rest at six different body tilt angles (-6, 0, 10, 30, 70, and 90 degrees). They stated that the Finometer® could accurately measure TBP at different tilt angles. Participants had a Finometer® TBP cuff attached to

the second toe of their right foot, and TBP was measured for five minutes at each tilt angle. The group compared the collected TBP data to invasive TBP measurements previously collected by Katkov et al[41] and to theoretical TBP values by using the equation:

Equation 6. $$P=\rho gh \bullet \sin\alpha$$

where P = hydrostatic pressure, ρ = blood density, g = gravitational acceleration constant, h = toe-to-heart height, and α = tilt angle. The group applied the measured brachial BP to Equation 6 to calculate theoretical TBP values. They found a correlation of $r = 0.87$ ($P = 0.01$) between the Finometer® and theoretical values (Figure 10). They also found similarities between their TBP measurements and the Katkov[41] data when compared at various tilt angles (Figure 11).

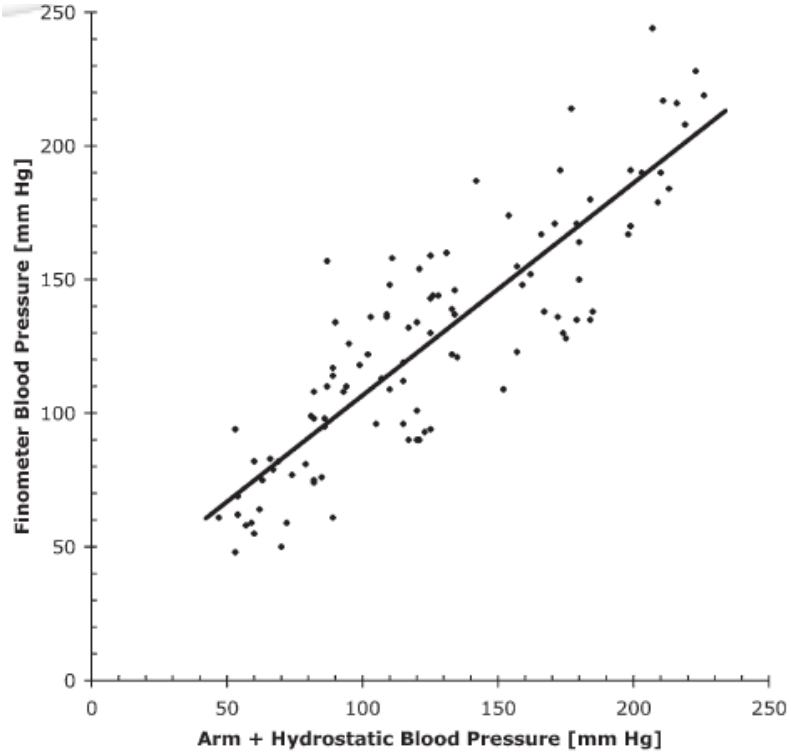

Figure 10. The Finometer® and theoretical TBP values[17]. (r=0.87, P=0.01). mmHg, millimeters of mercury.

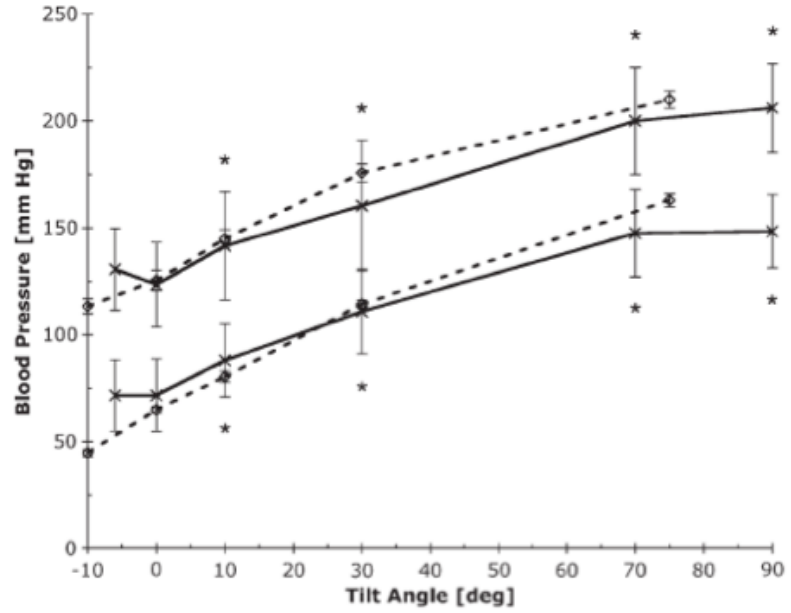

Figure 11. Mean TBP data measured using the Finometer® (solid lines) compared to Katkov et al[41] (1980) data (dashed lines) at different tilt angles[17]. Systolic TBP (top

lines); Diastolic TBP (bottom lines); *, $P<0.05$ TBP data at given angle compared to baseline.

Interestingly, Rosales-Velderrain et al[17] stated that the Finometer® accurately measured TBP when compared to theoretical values ($r=0.87$); however, it has been widely acknowledged that correlation coefficients are not the appropriate statistical analysis to compare two methods of measurement[42]. Correlation coefficients can only detect random error between two methods of measurements, and therefore systematic error goes undetected. Ordinary least products regression analysis and the Bland-Altman method of differences analysis provide more information on the systematic errors of a device (i.e., fixed and proportional biases)[42].

Rosales-Velderrain et al[17] and colleagues experienced several issues while collecting TBP data. First, they were unable to collect TBP data in all participants at 70° and 90°, which they mention may have been due to an increase in BP caused by the contraction of muscles at such large angles and the influence of gravity. Second, the Finometer® was not built to measure such large BP values that are produced by gravity. Third, Rosales-Velderrain et al[17] mentioned constriction of the arteries (i.e., vasoconstriction) hampered TBP collection, and that it may have been related to the toes being too cold at room temperature. To combat vasoconstriction, a heat lamp was used to heat the foot during TBP measurement and reported temperature at the toes was 31±1°C for the participants. Although these temperatures were high, Perez-Martin et al[43] and de Graaff et al[44] both reported no temperature-related problems when measuring TBP via photoplethysmography (PPG) and Laser Doppler (LD) techniques. Both Perez-Martin[43] and de Graaff[44] reported that they collected TBP at room temperatures between 23°C and

25°C in patients with poor vessel health, in whom you would expect a greater potential of vessel resistance. It is interesting that Rosales-Velderrain[17] was still unable to collect TBP since both the de Graaff[44] and Perez-Martin[43] studies reported much lower room temperatures than the Rosales-Velderrain[17] study. Due to this reason it is more likely that there was another reason besides low toe temperatures as to why the participants were unable to provide TBP measurements at large tilt angles. A possible reason could have been due to an increase in lower limb arterial resistance due to increased sympathetic nerve activity to the blood vessels (from the carotid arterial baroreflex) which would also lead to constricted arteries during greater tilt angles (70 and 90 degrees).

TBP has been shown to be an appropriate screening tool for various cardiovascular diseases and has been measured via PPG in healthy[45] and diabetic[46] populations. TBP measurement is often used to determine the severity of diabetes and PAD. An ankle/brachial index of less than 0.9 has been classified as an independent risk factor for cardiovascular disease[47]. Sahli et al[46] measured TBP, ankle BP and brachial BP using PPG in 134 healthy adults, 166 type 1 and 137 type 2 diabetic adults, and determined that TBP measurement was an effective screening tool for PAD. They compared TBP, ankle BP, brachial BP, toe-brachial index, and ankle-brachial index between all condition groups, and found that abnormally low toe-brachial index and TBP were significantly more common than ankle-brachial index and ankle BP in diabetic participants ($P<0.001$). Their findings provide evidence that suggests toe-brachial index should be used more often than ankle-brachial index when determining the incidence of cardiovascular disease in at-risk patients[46].

The Finapres® model is not the only device that has been used to measure TBP. Other studies have investigated various non-invasive devices to measure TBP, among which LD and PPG are the most studied[43,48]. LD non-invasively measures the flow of blood in an artery by using a laser light to highlight red blood cells as they flow through the vessel. The Doppler frequency shift is determined by the reflection of the laser light on the cells, and from this data the red blood cell velocities can be calculated[49]. Using the blood flow and vessel diameter (resistance) that is measured by LD, blood pressures can be calculated using Equation 1. PPG is also a non-invasive form of measuring peripheral BP, and determines BP by measuring the variation in light intensity when the amount of perfusion volume changes in a blood vessel[45]. This is in essence the same technique used in the Finapres® device which was explained in more detail above.

Most research that has investigated TBP measurements has been completed using unhealthy volunteers, typically recruited from hospitals or cardiovascular rehabilitation clinics. Perez-Martin et al[43] and Widmer et al[48] both compared the SysToe (Atys Medical, France) PPG device to LD techniques to validate the use of the PPG system to measure TBP in patients with cardiovascular problems. Participants were included in both studies if they had cardiovascular disease, including claudication, symptomatic or asymptomatic PAD, rest pain, diabetes, or lower limb ischemia. Both studies measured TBP in the patients' big toes or in the second-toe when the big toe had been amputated. The researchers measured patients' systolic TBPs using the device and a pneumatic cuff as described in Perez-Martin et al[43]. An example from the Perez-Martin et al[43] study when systolic TBP reappeared for both LD and PPG devices is shown in Figure 12 below.

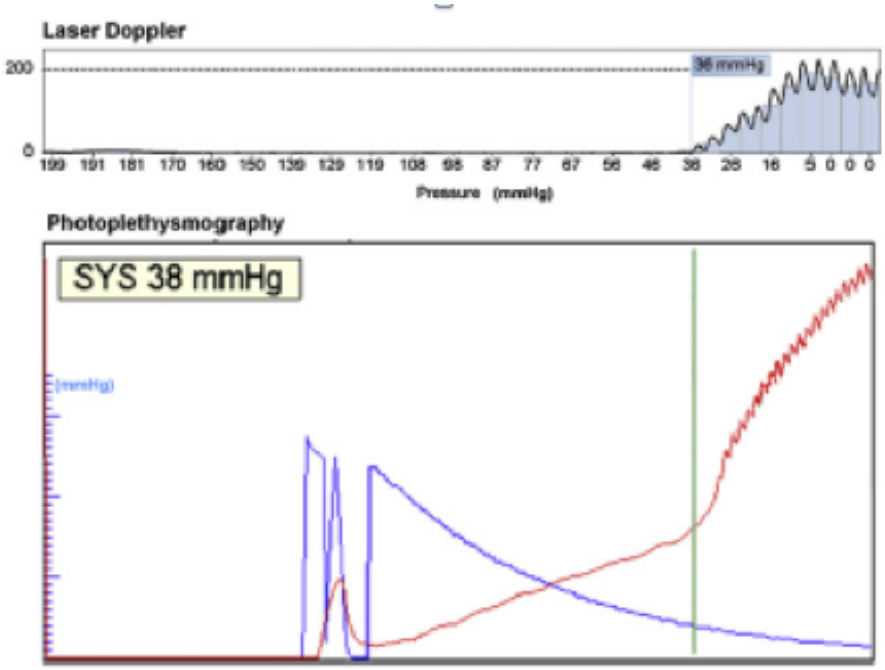

Figure 12. Laser Doppler (LD-top) and photoplethysmography (PPG-bottom) tracings of TBP in one patient with PAD[43]. Top: x-axis, cuff pressure; y-axis, LD signal. Bottom: x-axis, time; y-axis, pressure; blue line, occlusion cuff pressure; red line, PPG signal in % of its maximum amplitude during the measurement; SYS, systolic BP; mmHg, millimeters of mercury.

Perez-Martin et al[43] found that the SysToe PPG device provided reliable TBP measurements when compared to the LD technique. They reported inter-class correlation coefficients for the PPG and LD devices, respectively, of 0.887 and 0.893 on the right leg (n=193), and 0.905 and 0.898 on the left leg. The concordance correlation coefficient was 0.913 on the right leg and 0.915 on the left leg, which indicated concordance between the two devices. A Bland-Altman plot of differences showed their results in a more meaningful way by illustrating how close the differences in PPG and LD were to the average values (Figure 13).

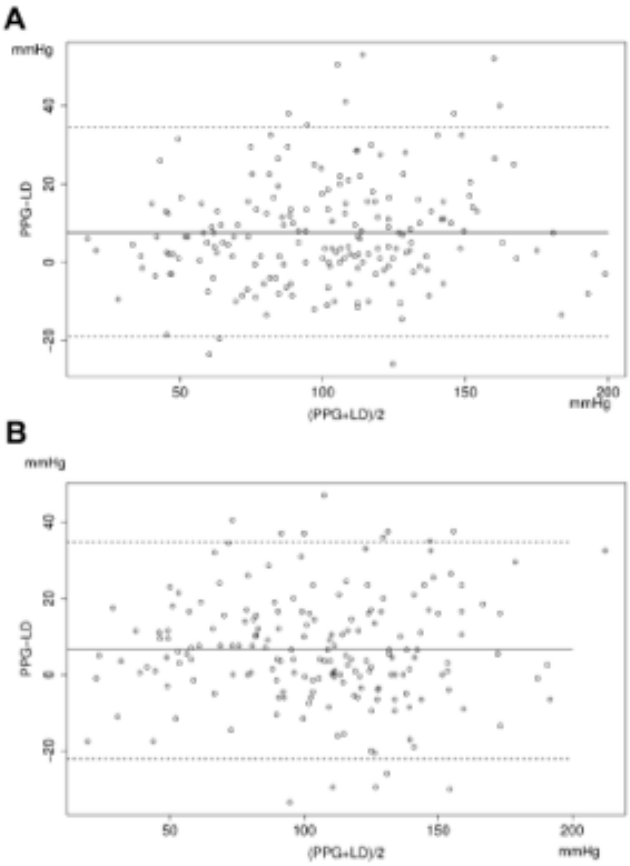

Figure 13. Bland-Altman method of differences plots of Laser Doppler (LD) and photoplethysmography (PPG) data from the right (A) and left (B) legs[43]. Solid line, mean; dashed lines, limits of agreement (i.e., 95% Confidence Intervals). mmHg, millimeters of mercury.

Although Perez-Martin et al[43] presented promising TBP measurement results, Widmer et al[48] presented less-favourable results one-year later. Using a similar collection protocol, Widmer[48] and colleagues found that TBP values varied greatly between the PPG and LD devices. In addition to collecting TBP data with the SysToe PPG (PPG2) device, they also collected PPG data using a Nicolet VasoGuard (Nicolet Vascular Inc., Madison, WI). The group found non-significant mean differences in TBP measurements of 14 mmHg when using the Nicolet device (PPG1) compared to the LD and PPG2 devices. Furthermore, the PPG2 device provided a mean TBP difference of 12 mmHg compared to

the LD device. Although the differences in TBPs between devices were not significant, the values did not fall within the acceptable limit of TBP agreement between devices based on their experience. They stated that acceptable limits of agreement would have to be less than 10 mmHg to be sufficient for use in clinical practice.

Even though the agreement between devices was poor, other reported data supports that both PPG devices had good repeatability. Widmer et al[48] measured two TBP readings per toe on all patients. In doing so, they were able to test the repeatability of the PPG devices. Although the range of differences in TBP values between the first and second measurements were not ideal (0-58 mmHg, and 0-53 mmHg for PPG1 and PPG2 respectively), large differences were not seen often, indicating that both devices have good repeatability (Figure 14). This suggests that the PPG devices can be used to collect TBP data; however, switching devices between measurements is not recommended.

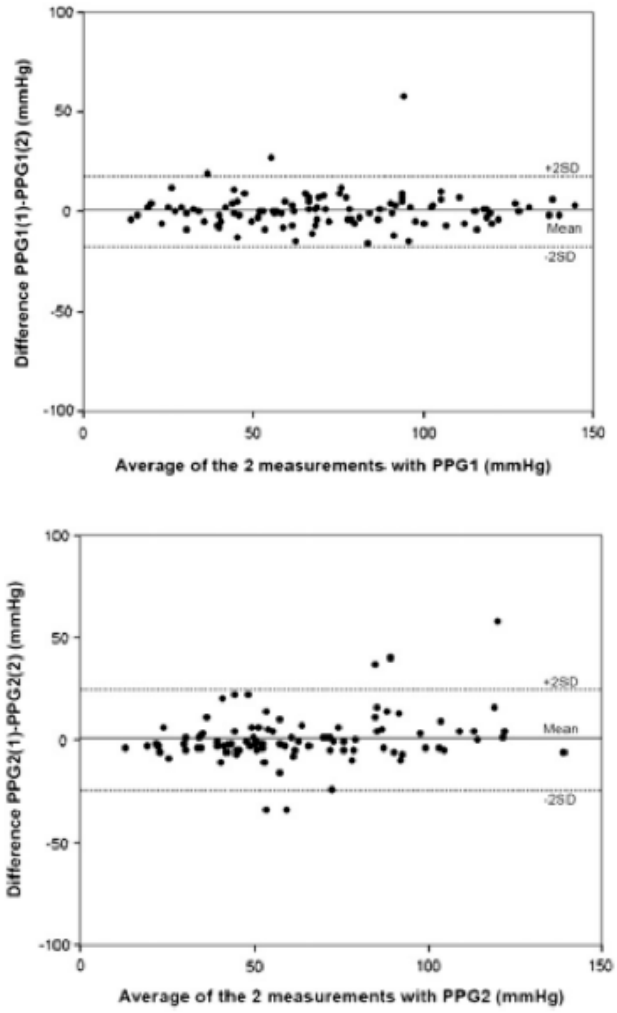

Figure 14. Bland-Altman method of differences plots of PPG1 (top) and PPG2 (bottom) data in the toe on separate days[48]. Solid line, mean; dashed lines, limits of agreement (i.e., 95% Confidence Intervals). PPG1, Nicolet photoplethysmography device; PPG2, SysToe photoplethysmography device; (1), day 1; (2), day 2. mmHg, millimeters of mercury; SD, standard deviation.

Overall, little research on TBP measurements has been conducted, and what has been done has shown contradicting results. Due to this reason, a secondary goal within the thesis was used to further investigate the validity and reliability of the Portapres® device for measurement of BP on the toe.

2.8 Motion and Blood Pressure

As mentioned above, previous literature[13] shows that movement affects arterial BP; therefore, it is important to explore exercise modalities with different movement patterns to understand which exercise mode increases BP the most. Exercise movement patterns can be analyzed using kinematic measurements such as angular velocity and angular acceleration[50-51]. Multiple studies have measured angular velocities and accelerations during movements such as cycling[50] and treadmill walking[51]. Cycling and treadmill walking are complex motions that involve both linear and rotational actions that expose the body to many different mechanical forces[50-51]. Both motions incorporate rotational movements around the internal axes in the lower limb such as at the hip, knee, and ankle joints[50]. Ericson et al[50] reported that the range of motion at the hip, knee, and ankle joints while stationary cycling were equal to the range of motion of the same joints while treadmill walking, although in different positions. They stated that the hip and knee joints are more flexed, while the ankle is more dorsi-flexed during cycling. The range of motion of the joints and the time of the movement allow the angular velocity at each lower limb segment to be determined. Changes in segmental angular velocities can then be used to calculate angular accelerations, which directly translate into greater or smaller changes in liquid pressure due to increases or decreases in centripetal forces[13]. Winter published walking data in his book[51], and showed that maximum positive angular accelerations for lower body segments are 148 rad/s^2 at the foot, 71 rad/s^2 at the leg, and 31 rad/s^2 at the thigh. All maximum positive angular accelerations were within 0.05 seconds of toe off when walking at a velocity of 1.5 m/s. Although cycling and walking motions are studied extensively, very little kinematic data from the cycling motion has

been published. One study by Jorge et al[52] showed that maximum positive angular accelerations during cycling at 80 rpm are much lower than walking at the foot and the leg (30 rad/s^2), but slightly greater at the thigh (35 rad/s^2). It is important to keep in mind that one pedal revolution during cycling at 80 rpm lasts 0.75 second, whereas the walking data reported by Winter[51] was collected from a gait cycle that lasted one second.

Two unpublished studies have looked at how linear and angular motion affect liquid pressure in lower limb segments during cycling and walking. Goreham et al[14] measured liquid pressure changes in water tubes that were attached to the lower limbs during walking. The study aimed to determine the effect of orthostatic and movement-related changes on simulated arterial BP while walking. Simulated arterial BP was measured by attaching two water-filled tubes equipped with pressure transducers from the heart level on the chest to the mid-thigh and mid-shank levels. Participants were required to walk along a five-meter walkway at a self-selected walking speed. The participants walking movements were recorded using 3-D motion capture analysis in order to create a kinematic model that would predict the modulation of the simulated arterial pressure. From their kinematic model, they found that trunk accelerations were the main contributor to movement-related pressure; that orthostatic differences influenced overall liquid pressure more than movement-related components; and that normalized mid-shank pressures (i.e., pressure normalized to participant height) were greater than normalized mid-thigh pressures (mid-shank: 25 to -25 mmHg/m; mid-thigh: 18 to -15 mmHg/m). The large influence of gravity on pressure data were expected due to greater pressures being associated with a greater distance from the measurement site to the heart. The group also found that maximum normalized pressures occurred at 5% and 65% of the gait cycle, and that minimum normalized pressures occurred at 85% of the gait cycle at both the mid-

shank and mid-thigh pressure transducers. Their motion-related pressure models were calculated using the equation:

Equation 7.

$$[A_{\text{HEART}} + (r_{\text{HEART-HIP}} \bullet \omega_{\text{HEART-HIP}}^2)] + [A_{\text{HIP}} + (r_{\text{HIP-KNEE}} \bullet \omega_{\text{HIP-KNEE}}^2)] + [A_{\text{KNEE}} + (r_{\text{KNEE-ANKLE}} \bullet \omega_{\text{KNEE-ANKLE}}^2)] + [A_{\text{ANKLE}} + (r_{\text{ANKLE-TOE}} \bullet \omega_{\text{ANKLE-TOE}}^2)] \bullet \rho$$

$$= \text{Motion-Related Pressure}$$

where A was longitudinal acceleration of the joint, r was length of the segment, ω was the angular velocity of the segment, and ρ was water density (1000 kg/m^3). Orthostatic pressure was calculated by Equation 3 above ($P = \rho g h$), where P was orthostatic pressure, ρ was water density, g was the gravitational acceleration constant, and h was the change in height between the heart and the pressure transducers.

As mentioned, the model created by Goreham et al[14] used longitudinal linear accelerations at the joint and centripetal acceleration ($r\omega^2$) of the segment to calculate longitudinal motion-related pressures (Figure 15). Because of the inertial forces, fluids embedded in the segment had accelerations in the opposite direction of the segment (centrifugal acceleration).

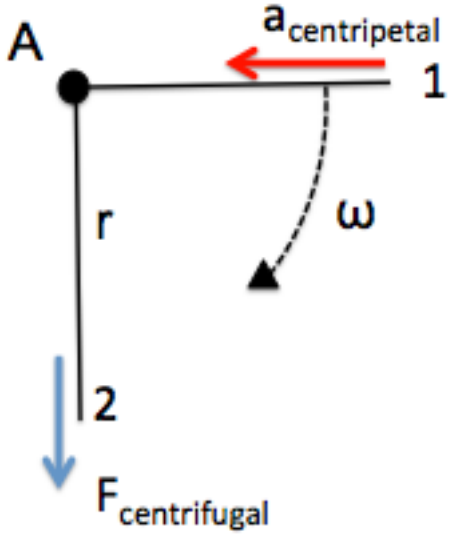

Figure 15. The effects of linear and centripetal accelerations on fluid motion. 1, limb start position; 2, limb finish position; A, linear acceleration of joint; $a_{centripetal}$, centripetal acceleration; ω, angular velocity; $F_{centrifugal}$, centrifugal acceleration acting on fluid; red arrow, direction of centripetal acceleration; blue arrow, direction of fluid; dashed arrow, angular velocity direction; solid line, limb segment; r, length of segment; solid circle, joint center.

Ewig[15] also used two plastic water-filled tubes and pressure transducers at the mid-thigh and mid-shank levels to measure liquid pressure at seven different cycling pedaling cadences: 50, 60, 70, 80, 90, 100, and 110 revolutions per minute (rpm). They found that liquid pressure at the mid-shank level increased as cadence and angular motion increased (50 rpm = 12 mmHg; 110 rpm = 59 mmHg). Results show that significant net positive pressure was generated at pedaling cadences above 80 rpm (i.e., pressures were more positive than negative when cycling at 80 rpm or higher). Similarly, Ewig[15] and Goreham[14] both found that inertial forces of limb segments caused fluid pressure changes. They both concluded that pressure change was the product of linear and angular acceleration happening at each segment of the leg's multilink system. Both studies provide evidence that the complex interaction between different movement components

(i.e. angular accelerations) generate an increase in muscle perfusion pressure during walking. Much like the Sheriff et al[13] study, these findings give further evidence that motion does in fact affect liquid pressure.

One problem with previous literature is the fact that participants were not exercising at similar intensities. That is, participants walked at self-selected speeds in the Goreham[14] study, whereas the participants cycled at different cadences in the Ewig[15] study. Also, Goreham et al[14] reported pressures that were normalized to participant height, which was unlike Ewig[15] who reported absolute fluid pressure values. Therefore, a preliminary model was created using anthropometric body segment lengths derived from Drillis et al[53] for a person with a stature of 1.75 m. The model was created for use in this thesis to compare treadmill walking and cycling motions at the same exercise intensity. The sum of the movement-related angular accelerations was calculated at the foot by using published angular data extracted for walking[51] and cycling[50] over the same duration of time. The preliminary model of the movement-related impulses (angular velocities and accelerations) on arterial blood pressure showed that cycling would have close to twice the effect in comparison to walking (Figure 16).

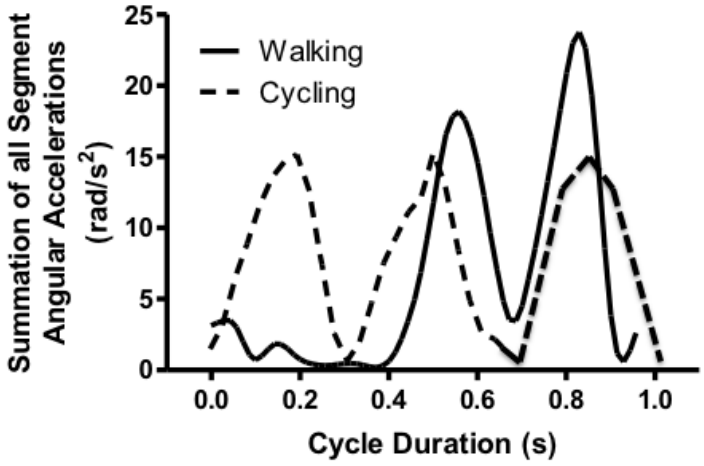

Figure 16. Preliminary model showing the summation of segment angular accelerations for both walking (solid line) and cycling (dashed line). s, seconds; rad, radians.

As mentioned above, measuring liquid pressure in water filled tubes during exercise has been shown to provide similar pressure changes to those measured in an actual finger[13]. Although simulated arterial pressure values are important for predicting TBP, actual arterial BP measurements would be further evidence for different effects on arterial blood pressure between walking and cycling. No published research has used the Portapres® BP monitor to measure TBP during walking or cycling; therefore, possible problems with the equipment were hard to predict.

2.9 Cycling and Walking Mechanics and Movement-Related Changes to TBP

Biomechanical characteristics (e.g., limb angular velocities, angular accelerations, joint range of motion, joint moments, and mechanical power output) can be measured at different speeds and external workloads during cycling and treadmill walking. Sheriff[13] and colleagues state that frequency, angular velocity and accelerations increase blood

flow and BP in active limbs. Therefore, when measuring TBP, it can be expected that necessary changes to TBP would occur based on these factors. One characteristic that is relatively less explored is external mechanical power output (i.e., workload) and its effect on lower limb arterial BP during cycling. That said, there are some seminal papers worth discussing. One study by Haslam et al[54] looked at how brachial arterial BP reacted during single-arm curl, single-leg press, and double-leg press exercises at 20, 40, 60, and 80% of the participant's maximum single lift; and found that MAP increased as workload increased, with the highest pressures being at 80% of their maximum workload. MAP during exercise increased from resting MAP by 16%, 15%, and 20% at 80% of workload in single-arm, single-leg, and double-leg exercises respectively. Although it was unclear if the active arm in single-arm exercise was the same arm where BP was being measured from, an increase in BP was still reported and it can be assumed the active arm's MAP probably increased as well. This data gives confidence that a significant increase in power output during cycling exercise will increase MAP in the lower limbs as well.

Another study by MacDougall et al[55] explored how brachial systolic and diastolic BP was modulated during upper and lower limb exercises. The group studied the BP response in five male bodybuilders (aged 22 to 28 years) as they completed single-arm curls, overhead presses, and both double- and single-leg presses. They measured BP using a catheter in the left brachial artery, which was attached to a pressure transducer. Unfortunately the participants only exercised the non-catheterized arm and both legs; therefore BP data from the moving limb were not reported. The exercises were completed at 80, 90, 95, and 100% of the participant's one repetition maximum; however little data between the workloads (i.e, 80% one repetition maximum) was reported. The researchers found that there was a large initial increase in both systolic and diastolic BP when the

weight was lifted for all exercises. As the weight was lowered the systolic and diastolic BP decreased towards pre-exercise levels only to increase to even greater levels during the next repetition. The trend of increasing BP continued until the last repetition where BP was found to be the greatest and then drastically decreased for up to 10 seconds after the completion of the exercise (Figure 17). The group attributed the rapid decrease in BP to the sudden perfusion of a previously occluded and vasodilated muscle.

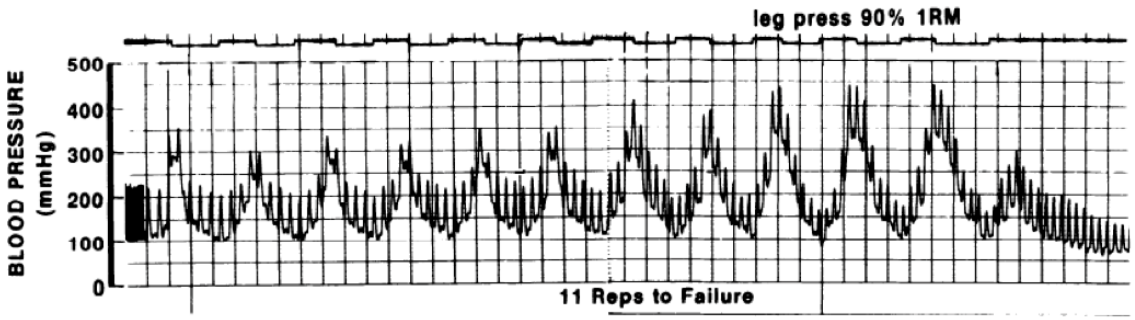

Figure 17. Trace of the blood pressure response for one participant performing double leg press exercise at 90% of one repetition maximum[55]. mmHg, millimeters of mercury; x-axis grid, one square is one second.

The researchers also reported that BP was greater for exercises that used more muscle mass (i.e., double leg press versus single leg press), and that an exercise workload of 95% one repetition maximum provided greater peak systolic and diastolic BP compared to 100% repetition maximum workloads (Figure 18).

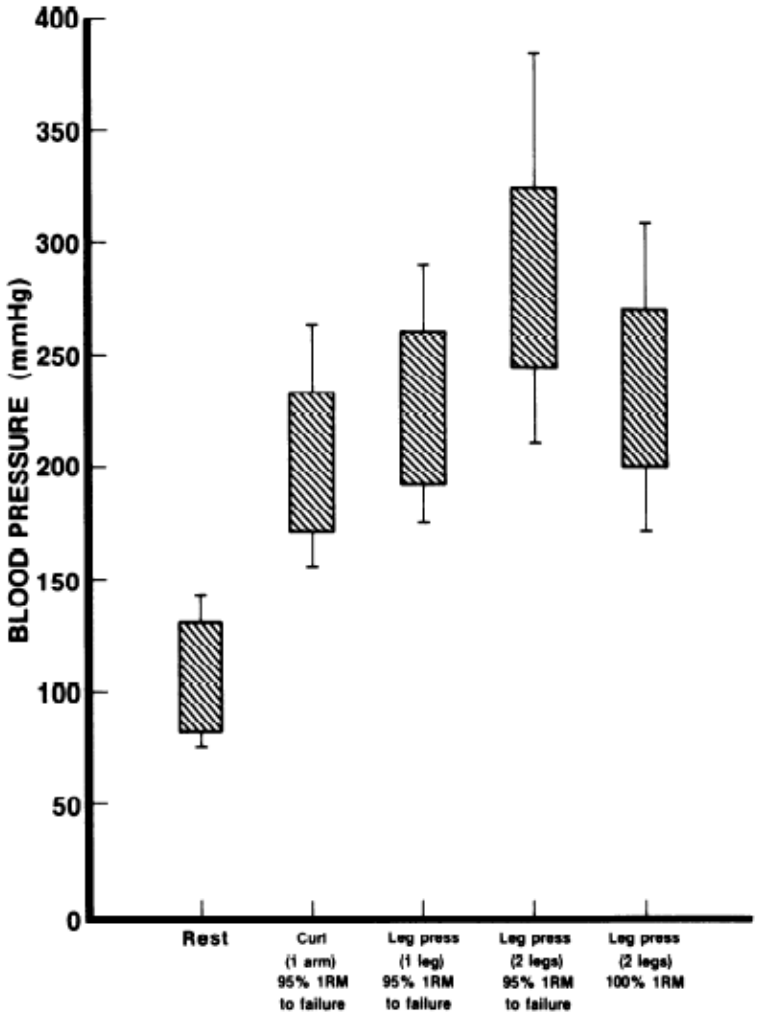

Figure 18. The peak systolic and diastolic brachial BP for all exercises (shown in mean ± standard deviation five participants)[55]. mmHg, millimeters of mercury; 1RM, one repetition maximum; error bars, standard deviation.

Their reasoning behind both of these findings was that the increase in muscle mass activation caused more compression on the vasculature, which increased BP. They acknowledged that if an increase in muscle mass was the only reason for an increase in BP then the BP response during double-leg press exercise should be double that of the BP response during single-leg press exercise. They blame an increase in accessory muscle activation during single-leg presses for why the difference in BP is not exactly half of that during double-leg press exercise. Overall, this research shows that muscle mass and

exercise intensity plays a large role in the BP response during dynamic exercise that uses large amounts of muscle mass.

The research above shows that in a complex research study that investigates physiological (i.e. BP) and biomechanical (i.e. cadence, mechanical power output) parameters it is important to control for as many external variables as possible. One issue when comparing cycle cadences is that external mechanical power outputs can differ depending on the intended angular velocity of the pedal crank and amount of resistance present[50]. Unfortunately, HR vs. cadence has been shown to represent a parabolic relationship when power output and cadence are kept constant. A study by Coast et al[56] was designed to determine the optimal cadence at five different mechanical power outputs in five trained cyclists. The participants each completed five maximal cycling tests where workload increased every three minutes until exhaustion. Each test was completed at a different cadence (40, 60, 80, 100, or 120 rpm), and power output increased by 50 watts every three minutes. Maximum HR was recorded for each power output and cadence at the end of each completed three-minute interval. The researchers found that a parabolic relationship developed at each power output when a comparison of HR vs. cadence was made (Figure 19). The lowest point on each parabolic curve was deemed as the optimal cadence for each power output.

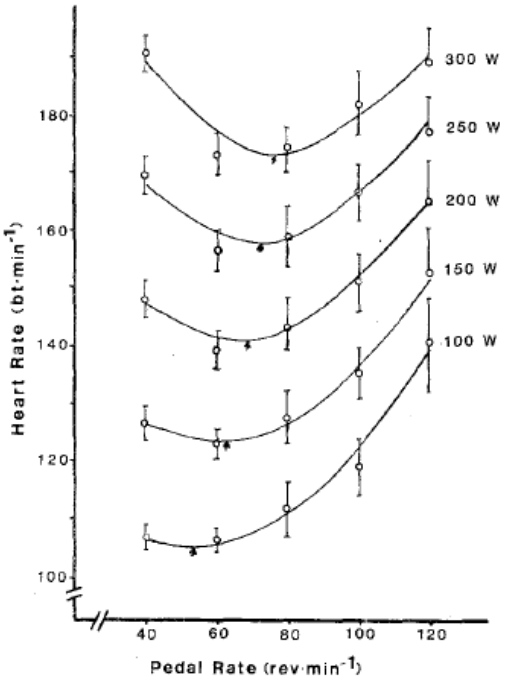

Figure 19. Heart rate (bt•min^{-1}) vs. pedal rate (i.e., cadence in rev•min^{-1}) at different power outputs (W)[56]. Each line represents a different power output. Heart rates were significantly different between cadences (*P=0.05*). Mean ± standard error (error bars) shown for 5 subjects during each condition. Arrows denote optimal cadence at each power output. bt•min^{-1}, beats per minute; rev•min^{-1}, revolutions per minute; W, watts.

Coast et al[56] then compared optimal cadence and power output (Figure 20), which showed a linear relationship, that is, when power output increased the optimal cadence followed. However, the study also showed evidence that a linear relationship is not present when comparing HR and cadences when power output is held constant. Their findings state that when comparing conditions the same mechanical power output, and heart rate cannot be equal between two groups when also comparing different cadences. Due to these findings, the present study required three cycling conditions in order to control for heart rate, cadence, and mechanical power output. In other words, when comparing the effect of cadence on MAP (a high cadence vs. a low cadence) there had to be either a difference in power output or heart rate, but not both.

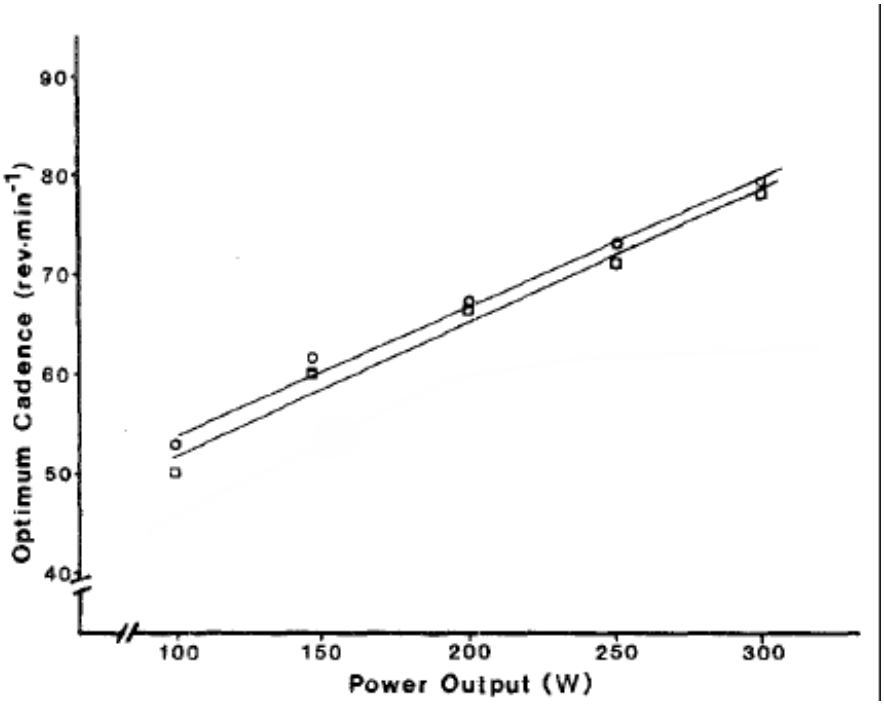

Figure 20. Optimum cadence (rpm) vs. power output (W)[56]. Circles denote optimal cadence from heart rate data. Squares denote optimal cadence from maximal oxygen consumption (VO_2) data. rev•min^{-1}, revolutions per minute; W, watts.

Overall, the literature above illustrates the fact the combining biomechanical and physiological characteristics in a single study can become complex. The body reacts to different stimuli in a variety of ways, and therefore it should be apparent that the results of the study could result in many different conclusions.

2.10 Research Questions

1. Is the Portapres® blood pressures monitor a valid and reliable tool for measuring TBP?
2. Does a greater cycling cadence affect TBP differently than a lower cycling cadence?
3. Does a greater mechanical power output affect TBP differently than a lower mechanical power output?
4. Does cycle ergometer exercise increase TBP more than treadmill-walking exercise in the same non-disabled individuals at similar exercise intensities?

2.11 Purpose and Hypothesis

As mentioned, exercise therapy is often used for the rehabilitation of various types cardiovascular disease. It is important to enhance our knowledge of exercise therapy using a mechanistic approach to understand exactly what exercise is doing to the affected areas of the body. BP is an important factor when rehabilitating cardiovascular disease. Therefore, understanding how BP reacts in the lower limbs is important to prescribing exercise therapy to affected patients. It is also important to use valid and reliable research tools to answer the research questions relating to exercise therapy and disease prevention. Very little research has been conducted on the use of the Portapres® BP monitor on the toe. Therefore, it is expected that this study will broaden the knowledge regarding whether or not researchers and clinicians should use the Portapres® on the toe.

The current study had two purposes. The first purpose was to determine the concurrent and construct validity, the inter-day reliability, and the feasibility of the Portapres® BP monitor on the toe during rest and locomotion. The second purpose was to determine if cycle ergometer exercise increased TBP more than treadmill-walking exercise in the same non-disabled individuals at similar exercise intensities. The results of this study may aid in understanding the effect of movement on arterial BP modulation. The hypothesis of the first research question was that Portapres® is a valid and reliable tool for measuring TBP. Although there are mixed results on the use of other devices on the toe, it is evident that the Portapres® has successfully collected TBP in the past in both the Kinsella[16] and Rosales-Velderrain[17] research studies.

Based on the results from the Sheriff[13], Ewig[15], and Goreham[14] studies that showed increases in angular motion and increasing cadence which subsequently caused increases in fluid pressure, it was hypothesized that a greater cycling cadence would provide greater TBP compared to a lower cycling cadence. Based on the results from the Haslam[54] and MacDougall[55] studies, which both found increases in brachial MAP caused by increasing workloads in upper- and lower-body exercise; it was expected that a greater mechanical power output would result in greater TBP compared to a lower mechanical power output.

Finally, the walking and cycling preliminary model (Figure 16) constructed from published walking[51] and cycling[50] data showed that cycling would have close to twice the effect on TBP in comparison to walking due to the movement-related impulse effect on arterial BP. From these results, it was hypothesized that cycling at 50 and 90 rpm would provide greater increases in TBP compared to walking at a speed that elicited a heart rate of 60% of HR maximum.

CHAPTER 3: METHODS

3.1 Study Design

The research project was designed to answer four primary research questions. Concurrent validity, construct validity and inter-day reliability was determined by using a single subject repeated measures design comparing TBP with brachial BP before and after exercise, TBP during slow cycling at different toe heights, and TBP measurements between two testing days. TBP was measured using a single subject design during cycling at different mechanical power outputs and cadences on a cycle ergometer. The study design allowed the researcher to compare the increase in TBP between cycling conditions for each participant. Exercise intensity was controlled at 60% of age-predicted heart rate maximum (HR_{max}) in two of the cycling conditions in order to minimize the chemically mediated component of exercised-induced increases in arterial blood pressure (BP)[57].

3.2 Study Location

All testing for the study was conducted in the Biomechanics, Ergonomics, and Neuroscience Laboratory located in room 217 of the Dalhousie University Dalplex facility.

3.3 Participants

Participants were not eligible for this study if they (a) were under the age of 18 or older than 64 years, (b) answered "Yes" to any question on the Physical Activity Readiness Questionnaire (PAR-Q), (c) had a body mass index (BMI) greater than 30 kg/m^2, (d) were a current or recent smoker, (e) had been diagnosed with a cardiovascular, respiratory, or metabolic illness, (f) had been prescribed high blood pressure or any other

heart medications, (g) had a resting blood pressure greater than 140/90 mmHg[58], (h) had Raynaud's disease, (i) had a history of fainting, (j) were pregnant, or (k) had been instructed by their family doctor to not engage in strenuous physical activity. Evidence has shown that there is an increase of collagenous fibers in aging arteries, which reduces vessel elasticity, an increase in atherosclerosis[5] in persons older than 65, and an impairment of endothelium-dependent vasodilation[59]. Due to this evidence, an upper-limit age range was introduced for this study. Recruitment flyers were placed throughout Dalhousie University's Dalplex facility (Appendix B). An additional exclusion criterion for participants was whether the participant could provide reliable TBP data using the Portapres® device during Day 1 of testing. If reliable TBP data during rest or exercise could not be attained, the participant was not required to attend the laboratory on Day 2. The study protocol was approved by the Dalhousie Research Ethics Board (REB# 2012-2839).

3.4 Sample Size

To determine an appropriate sample size, published mean values and standard deviations of similar research projects were considered[13]. The increase in mean finger arterial pressure during horizontal flexion exercise of a swinging arm and a resting arm was measured. Based on the rise in mean arterial pressure of the swinging arm (18 ± 9 mmHg) versus the resting limb (8 ± 6 mmHg), an effect size of 0.55 was calculated (http://www.uccs.edu/~faculty/lbecker/). This value was entered into a power calculator (G Power v3.1.3) using a two factor (exercise mode by time) repeated measures ANOVA with a power (beta) of 95%, and an alpha value of 0.05 resulted in an estimated sample

size of 14. The aim was to recruit a maximum of 20 participants to account for potential difficulties obtaining suitable TBP recordings and attrition.

3.5 Experimental Protocol

The study included two days of testing for each individual participant. Each test day consisted of approximately two hours of lab time equalling a total of four hours per participant. Upon initial contact via email or phone, all interested participants received a copy of the study's Informed Consent form (Appendix C) and a Physical Activity Readiness Questionnaire (PAR-Q) (Appendix D). Interested participants were encouraged to read all forms to ensure that they were still willing and eligible to participate in the study. Interested participants were not required to visit the lab on Day 1 if they found that they were no longer interested or eligible for the study due to the study's exclusion criteria.

Day 1 consisted of eligibility screening and resting HR, BP, and TBP values were recorded. The exercise workloads that participants cycled and walked on Day 2 were also determined during Day 1. Any screening that was not completed upon initial contact with the participant was completed as soon as possible on Day 1 (i.e., reliable TBP values, BP, etc.). Day 2 consisted of exercising at workloads that were established on Day 1, followed by a post-exercise recovery period in which HR, TBP and brachial BP were measured. The protocol was followed once for each exercise mode. The detailed study protocol is described below.

One day prior to experimental days, participants were asked to refrain from consuming alcohol, caffeine, nicotine or performing strenuous bout(s) of physical activity. Pescatello et al[60] showed that systolic BP remained 5 ± 1 mmHg higher for 12.7

hours after 30 minutes of stationary cycling in normotensive participants. The study's findings provide evidence that arterial BP should not be considered to be in a normal state within 12.7 hours of a bout of cycling at 70% of the participant's maximum oxygen consumption[60]. Participants were asked to rest (6-8 hours of sleep) the night before both testing days, consume their last meal three hours prior to each testing session and be well hydrated (i.e., one cup of water per hour leading up to testing). The participants were asked to attend the lab at approximately the same time of day for both experimental sessions. This recommendation allowed for physiological characteristics to be similar on both testing days (i.e., same amount of physical activity, fatigability, diet, etc.).

The time commitment for the first experimental day was between 60 to 120 minutes depending on the fitness level of the participant and equipment function. For example, less fit participants typically spent less time on the graded protocol tests than the more fit participants because they tended to reach their goal HR quicker. Duration of Day 1 testing was also dependent on equipment function (i.e., Portapres® not measuring TBP immediately, etc.). Participants signed an Informed Consent form and completed a PAR-Q immediately after arriving at the laboratory on Day 1. If participants answered "yes" to any questions on the PAR-Q, or met any exclusion criteria, they were excluded from the study. Because participants were provided with an Informed Consent Form and PAR-Q prior to attending Day 1 in the lab, participants were often deemed eligible to participate prior to attending, making this a quick process. The PAR-Q form is a screening method used by health professionals to ensure the client or participant is deemed physically ready to exercise[61].

When the participant was deemed eligible to participate in the study, the testing equipment, protocols, risks, and rationale for the study were then re-explained to them.

The participants were encouraged to ask questions, and informed that they may remove themselves from the study at any time. Participants were then asked to change into proper exercise clothing (e.g., shorts and t-shirt) using private changing rooms for further screening and to perform two non-fatigable exercise tests. Participants were equipped with a Polar FT1 HR monitor (Tempe Oy, Finland) on both days of testing. The HR monitor was used for real-time HR values to ensure participants were exercising at the appropriate intensity, but were not used in data analysis for this study.

Participants had their height (cm) and weight (kg) measured immediately after changing into their exercise attire. Resting HR and brachial BP were measured using an HR monitor and an automated BP cuff (General Electric Healthcare Model V100, Mississauga, ON) from participants' right brachial artery as they rested supine on a hospital style bed. A HR, systolic and diastolic BP measurement was recorded once per minute for five minutes for each participant. The HR and BP measurements were averaged and recorded as participants' resting HR and BP. As participants' rested for five minutes, their TBP was measured using a Portapres® BP monitoring device. A continuous TBP waveform was collected for five minutes during the resting period from the second-toe of the right foot (i.e., plantar digital artery). Participants' average HR and BP were used to determine if participants were in a resting state following each exercise condition. If a participant was within ± 5 bpm and ± 5 mmHg of their HR and BP, the participant was deemed eligible to commence the next exercise protocol. The systolic and diastolic TBP measurements were derived from the TBP measurements at the four-minute mark of the rest period, and were used to calculate the MAP of the toe (MAP_T).

A participant's age was used to determine their age predicted HR_{max} (in beats per minute, bpm) by the Fox and Haskell equation below. A participant's HR_{max} was then

used to determine the exercise workload during Day 2 testing. Participants exercised at a workload that elicited 60% of their HR_{max}. The Fox and Haskell equation has been shown to provide standard deviations of 7-11 beats per minute when testing the formula to true HR_{max} values; however, the equation was deemed sufficient to use for the purpose of this research in young, healthy individuals[62].

Equation 8. $220 - \text{Age} = \text{Age-predicted } HR_{max}$

$60\% \times \text{Age-predicted } HR_{max} = 60\% \ HR_{max}$

Following the five-minute resting period, participants were asked to sit on a bike with a seat at 100% right greater trochanter height[63]. The seat height was based on greater trochanter height to keep limb segment angles similar between participants. With the Portapres® BP cuff still attached to the participants' toe, they cycled at 6 rpm for one minute. This exercise was titled the "Slow Orthostatic" trial, and was completed to determine if TBP changed due to changes in toe height. Participants started with their foot at the top of the pedal crank, and sixty seconds was spoken aloud by the researcher. At ten-second intervals, participants' feet would return to the top of the pedal crank. It was hypothesized that participants' TBP would change by the same amount as the change in toe height depending on where their foot was located along the pedal crank (i.e., 34 mmHg for 34 cm change in toe height). Exploratory testing in the laboratory using kinematic motion analysis showed that toe height changed by 34 cm from the top to the bottom of the pedal crank in six participants during slow cycling. The hypothesis was based on Equation 3, which was discussed previously in the literature review section of this thesis.

As mentioned previously, one of the primary goals for Day 1 testing was to determine the exercise intensity of participants for Day 2. To achieve this goal, all participants completed two incremental cycling tests and an incremental walking test. For each cycling test, participants maintained a constant cadence (50- or 90-rpm) until they reached 60% HR_{max}, at which time the protocol ended. Participants' fitness levels determined how long the protocol would last, as more-fit participants cycled longer at higher mechanical power outputs than less-fit participants. The sequence of protocols for each participant on Day 1 (i.e., 50-rpm or 90-rpm) and Day 2 (i.e., high power-low cadence, low power-high cadence, or low power-low cadence) were determined randomly by flipping a coin. Each test on Day 2 required two coin flips (e.g., low or high power, low or high cadence). No blinding was used for data collection and analysis due to one primary investigator.

Following the Slow Orthostatic trial, participants cycled at 90-rpm for three minutes to ensure the Portapres® successfully collected TBP data while cycling at higher cadences. If TBP data were collected with no disruptions in the TBP waveform, a participant was deemed eligible to continue with the cycling portion of the study. Participants then completed a short walking test to ensure they could walk on a treadmill at a sufficient speed and grade to reach 60% HR_{max} with the Portapres® still maintaining a reliable TBP measurement. Pilot data showed that the Portapres® could not provide appropriate TBP data from the second toe when walking barefoot or with sandal-type shoes. Due to this issue, participants wore a DARCO OrthoWedge® forefoot shoe (DARCO International Inc., Huntington, WV) on their right foot during the walking test (Figure 21).

Figure 21. Picture of DARCO OrthoWedge® shoe which was used during the study's walking protocol[64].

The DARCO wedge shoe was expected to reduce ground reaction forces (GRF) acting on the forefoot of the participant during walking. The primary use for the wedge shoe is to avoid pressure and maintain mobility for patients that have had foot surgery, diabetes, bunions or other foot pain. After properly re-attaching the Portapres® BP cuff to the toe and securing the wedge shoe, participants began walking on the treadmill at 2 km/hr and a 0% grade. As participants became comfortable walking with the wedge shoe, the speed was increased by 0.3 km/hr every minute. During exploratory testing, the Portapres® would often stop working due to increases in GRF at higher speeds or problems finding the arterial pulse. If this happened during the protocol, the treadmill grade was increased to reallocate the participants' body weight to the posterior portion of the body and foot. Participants were deemed eligible to continue the treadmill walking portion of the study if they were able walk without interrupting the Portapres® waveform, while maintaining 60% HR_{max} for a minimum of ten-minutes. The Portapres® BP cuff was then removed from participants' toes.

Each participant then completed two cycling tests with incrementing mechanical power at a constant cadence (50 or 90-rpm) and one walking test with incrementing speed

and treadmill grade, all separated by ten-minutes of rest. All incremental tests were dependent on if a participant could cycle and walk while maintaining proper Portapres® function. For example, if a participant could cycle but not walk while maintaining a TBP waveform then they would not be required to complete the incremental walking test on Day 1 or any walking tests for the remainder of the study (i.e., Day 2). The main goal of the incremental exercise tests was to determine the mechanical power output, and the speed and grade of the treadmill that elicited 60% of $HR_{max,}$ so participants could exercise at the given intensity on Day 2. Participants' HR was monitored with a Polar HR monitor during incremental testing on Day 1. Participants' starting workloads depended on how participants perceived their fitness level (i.e., "active" or "non-active"). For cycling tests, "non-active" participants began cycling at a mechanical power output of 20 W, whereas "active" participants began cycling at 40 W. Mechanical power output increased continuously at a rate of 20 W every three minutes until termination. The test was terminated when participants' HR reached 60% HR_{max}. All cycling tests were completed on a VELOtron Dynafit PRO, Racer Mate® Inc. (Seattle, WA) cycle ergometer (Figure 22). A small sponge-like cushion (0.1 m by 0.2 m) was attached to the cycle ergometer's right pedal with medical tape to keep participants' toes away from the pedal and to increase comfort at high mechanical power outputs and cadences. Examples of the incremental cycling protocols are shown in Table 1 and Table 2 below.

Figure 22. VELOtron Dynafit PRO, Racer Mate® Inc. cycle ergometer used for the study's cycle ergometer protocol[65].

Table 1. The incremental cycling protocol used for active participants.

Time (min)	Power Output (W)
0.0	40
3.0	60
6.0	80
9.0	100
12.0	120
15.0	140
18.0	160
21.0	180
24.0	200

min, minutes; W, watts.

Table 2. The incremental cycling protocol used for non-active participants.

Time (min)	Power Output (W)
0.0	20
3.0	40
6.0	60
9.0	80
12.0	100
15.0	120
18.0	140

min, minutes; W, watts.

Participants' 60% HR_{max} value was recorded and the corresponding cadence and mechanical power output were used during the cycling exercise protocol on Day 2. A ten-minute rest period followed the first graded cycling protocol to allow physiological characteristics to return to resting levels. BP and HR were measured once every two minutes while participants rested supine. Once resting BP and HR levels had been reached, participants began a second cycle ergometer test using the same protocol as the first. After participants completed the second graded exercise test at the remaining cadence (50- or 90-rpm), they rested supine and another resting data collection procedure ensued. HR and BP were measured until they returned to resting levels. Participants then completed the incremental walking test, given they could walk with the Portapres® and obtain reliable TBP waveforms.

The incremental walking test used a Modified Bruce Treadmill protocol (Table 3)

to determine the speed and grade participants would walk at on Day 2. Again, participants' perceived fitness levels determined their initial workload. "Non-active" participants began walking on the treadmill at a speed of 2.7 km/hr and a 0% grade for three minutes (Stage 1). "Active" participants began walking at a speed of 2.7 km/hr and a 10% grade for three minutes (Stage 3). Each stage was three-minutes in duration. If participants' HR were below 60% HR_{max} at the end of each three-minute stage, the speed and grade were changed in accordance with Table 3. All walking tests were completed on a Trackmaster® 1-metre 425CP Treadmill (Newton, KS).

Table 3. The modified Bruce Treadmill testing protocol used for both active and non-active participants.

Stage	Speed (km/hr)	Grade (%)
1	2.7	0
2	2.7	5
3	2.7	10
4	4.0	12
5	5.5	14
6	6.8	16
7	8.0	18
8	8.9	20
9	9.7	22
10	10.5	24
11	11.3	26

km/hr, kilometers per hour; %, treadmill grade.

When participants' HR reached a steady state of 60% HR_{max} during the last two minutes of a stage, the test was terminated. A steady state HR was defined as a HR that did not change by more than five beats per minute (bpm) within the final two minutes of a stage. The 60% HR_{max} was recorded and the corresponding treadmill speed and grade

were used during the treadmill walking exercise protocol on Day 2. A ten-minute rest period followed the treadmill testing to allow physiological characteristics to return to resting levels. During the resting period, BP and HR were measured once every two minutes while participants rested supine. Once BP and HR levels had returned to resting levels, participants were allowed to leave the laboratory. Resting times were dependent on participants' fitness level and the rate at which their HR and BP returned to resting values. Figure 23 illustrates a visual representation of the methods used for Day 1 of the study.

Day 1	TIME (minutes)							
	Preparation	Rest	Exercise 1	Rest	Exercise 2	Rest	Exercise 3	Rest
	0:00-0:10	0:10-0:20	0:20-0:35	0:35-0:50	0:50-1:05	1:05-1:20	1:20-1:35	1:35-2:00
Informed Consent, PAR-Q								
HR								
BP								
TBP								

Figure 23. Day 1 illustration of the study's methods. HR, heart rate; BP, brachial blood pressure; TBP, toe arterial blood pressure; PAR-Q, Physical Activity Readiness Questionnaire; Exercise, cycle (50 rpm), cycle (90 rpm), walking; shaded cells, data being collected.

The second experimental day occurred at least 24 hours following Day 1. Day 2 testing consisted of three separate fifteen-minute cycle ergometer exercise protocols, and one walking protocol each followed by a ten-minute post-exercise recovery period. The three cycling conditions were as follows: (1) 90 rpm, low mechanical power output (90L), (2) 50 rpm, low mechanical power output (50L), and (3) 50 rpm, high mechanical power output (50H). Each fifteen-minute exercise condition included a five-minute warm-up, and a ten-minute data collection period.

On Day 2, participants returned to the laboratory following the same nutrition and physical guidelines as Day 1. Participants changed into the exercise attire, and were equipped with electrocardiography (ECG) and electromyography (EMG) electrodes, kinematic motion tracking markers, and the Portapres® BP measuring device on the second toe of the right foot. One ECG electrode was attached to participants' left clavicle, and the other electrode was attached to the level of their seventh rib on the left side of their body. The electrical signal measured between the two ECG electrodes produced a raw QRS complex signal and was used to determine the timing of heartbeats. EMG electrodes were attached to four different muscle sites and one bony landmark of the participants' right leg. Muscles and the bony landmark of interest were the tibialis anterior (TA), soleus (SOL), rectus femoris (RF), biceps femoris (BF), and the medial epicondyle of the humerus. The EMG signals were used to determine when a muscle of interest was active or relaxed. kinematic motion tracking markers were attached to the acromion, greater trochanter, lateral epicondyle of the femur, lateral malleolus, calcaneus, and fifth metatarsal of participants' right legs. Kinematic data were used to measure toe height during the Slow Orthostatic cycling trial, and was used to determine linear and

angular motions during exercise. The Portapres® BP cuff was attached to participants' second toe on their right foot.

After participants were equipped with all the testing equipment, they rested supine on a hospital bed and resting HR, BP, and TBP measurements were collected. All measurements were collected simultaneously for five minutes and averaged. The averaged HR, BP, and TBP values were used to determine if participants were in a resting state following resting conditions during Day 2 testing. The Day 2 resting protocol was identical to the Day 1 resting protocol, which was outlined above.

Following the initial resting condition, participants completed another Slow Orthostatic trial for one-minute. Immediately following the Slow Orthostatic trial, participants began one of the three cycling conditions or the walking condition if they were able to provide reliable TBP data. Participants began the first cycling protocol at a low mechanical power output (20 W) to prepare for exercise. The mechanical power output increased for the first five minutes and then reached the predetermined value from Day 1 testing. For example, if a participant reached 60% HR_{max} on Day 1 at a cadence of 90 rpm, and a mechanical power output of 50 W, then the Day 2 protocol would begin at 20 W and increase to 50 W by the five-minute mark of the protocol. After cycling for five minutes at the given cycling cadence, participants would usually be at 60% of their HR_{max}. If by chance a participant was ±5 bpm from the target HR, the mechanical power output was adjusted accordingly to elicit the desired HR effect. After the initial five-minute warm-up, the mechanical power output and cycling cadence remained constant for the remaining ten-minutes of the fifteen-minute protocol. Participants' HR, TBP, EMG, and kinematic data were collected continuously during the final ten-minutes of each cycling protocol. If during the cycling test the participants' HR changed by ±5 bpm from

their 60% HR_{max} value, then mechanical power output was adjusted until their HR returned to within 3 bpm of 60% HR_{max}. The selected protocols were created to ensure participants cycled at the same exercise intensity during both the 50H and 90L cycling conditions. Immediately following the first cycling condition, participants rested supine and their HR, BP, and TBP were measured for ten minutes or until physiological conditions returned to resting values. When HR, BP, and TBP returned to resting values participants began the second cycling condition.

The second cycling test condition was one of the two remaining cycling conditions (50H, 50L, or 90L). The protocol was repeated for the second cycling condition as outlined above with only minor changes. For example, a participant would cycle at either 50 or 90-rpm and a high or low mechanical power output. Immediately following the second fifteen-minute exercise period, the participant dismounted from the cycle ergometer and again rested supine for ten-minutes or until physiological values returned to a resting state.

Finally, following the resting period after the second condition, participants completed the third and final fifteen-minute cycling condition. The cadence and mechanical power output for the final condition was the only possible remaining condition (50H, 50L, or 90L). After the final condition, participants' rested supine until physiological characteristics returned to a rested state. All equipment were removed from the participants, and they were allowed to leave the laboratory unless they were able to walk with the Portapres®, in which case they would complete a 15-minute walking test at the pre-determined treadmill speed and grade. The total duration for Day 2 was approximately two to two and half-hours depending on how long it took the participant to

return to a rested state. Figure 24 below shows a visual representation of the Day 2 methods for the research study.

Day 2	TIME (minutes)									
	Preparation	Rest	Exercise 1	Rest	Exercise 2	Rest	Exercise 3	Rest	Exercise 4	Rest
	0:00-0:30	0:30-0:35	0:35-0:50	0:50-1:00	1:00-1:15	1:15-1:25	1:25-1:40	1:40-1:50	1:50-2:05	2:05-2:15
HR										
BP										
TBP										
KINE										
EMG										

Figure 24. Day 2 illustration of the study's methods. HR, heart rate; BP, brachial blood pressure; TBP, toe arterial blood pressure; KINE, kinematics; EMG, electromyography; Exercise, cycle (50 rpm, high power output), cycle (50 rpm, low power output), cycle (90 rpm), walking; shaded cells, data being collected.

Participant safety was a top priority of this study. Participants' HR were monitored at all times to ensure they did not over-exert themselves. Participants were only exercising at 60% of their $HR_{max,}$ so over-exertion was not an issue in any case. The researcher was trained at the undergraduate level (minimum) on using necessary testing equipment. There was always a researcher present that was trained in First Aid and CPR,

and a telephone was on site for emergency use; however, a First Aid response was never needed in this study. During the treadmill walking protocol, participants were equipped with a magnetic quick release safety cord attached to their shirt to stop the treadmill in case they lost their balance and began to fall. This safety feature was not needed for this study.

3.6 Data Collection

A Polar HR monitor was used to collect continuous HR values during Day 1 data collection. ECG was used to monitor continuous beat-to-beat HR during Day 2 data collection. Two ECG electrodes were positioned on the left clavicle and seventh rib, and were sampled at a frequency of 2000 Hz. To minimize lead placement errors, a trained investigator (JG) performed the ECG setup for all data collection sessions. HR was required in order to measure when participants were exercising at 60% of their HR_{max}. HR was also required to ensure participants were exercising at an appropriate intensity and to monitor their safety during the protocols.

Beat-to-beat TBP was measured non-invasively using an automated BP device (Portapres® Model-2, Finapres® Medical Systems, Amsterdam, The Netherlands), and was used to show differences in TBP between cycling and treadmill walking, and during rest. The Portapres® was attached to the second toe on the participants' right foot. The Portapres® front end unit was attached just proximal and anterior to the participants' ankle. The Portapres® system includes three sizes of blood pressure cuffs. A small cuff was used on toes with a middle phalanx circumference of 45-55 mm, a medium cuff was

used on 55-65 mm toes, and a large cuff on 65 to 75 mm toes. Only the small and medium sized cuffs were used in this study.

All kinematic data were measured using an Optotrak Certus® camera system from Northern Digital Inc. (Waterloo, ON). The Certus® system consisted of infrared emitters attached to bony landmarks and a column of three infrared cameras which were stationed approximately 5 m from the cycle ergometer and treadmill. The system allowed for the measurement of three-dimensional positions with an accuracy of 0.1 mm and a resolution of 0.01 mm. The motion of the right leg was recorded by placing kinematic markers on the base of the fifth metatarsal, calcaneus, lateral malleolus, lateral femoral condyle, greater trochanter and acromion. The three-dimensional position of each bony landmark was sampled at a frequency of 200 Hz and analyzed using NDI First Principles™ and MATLAB software.

Muscle activity was measured using electromyography (EMG). Participants' right legs were shaved at four locations (three × three centimeter squares) and rubbing alcohol wipes were used to reduce input impedance between the electrodes and their skin. The electrode placement locations were determined using Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM) guidelines[66]. The four muscles of interest were the tibialis anterior, soleus, rectus femoris, and biceps femoris. A ground electrode was placed on the medial epicondyle of the humerus. The EMG signals were amplified using a Bortec AMT-8 system (gain: 100 - 15000; band-pass filter: 10 – 1000 Hz). EMG data were acquired using Northern Digital Inc. software at a frequency of 2000 Hz. Northern Digital Inc. is a scientific data acquisition computer program that is used in physiological testing, and was also used to collect KINE data for this study.

Kinematic and EMG data from the 50H, 50L, and 90L cycling conditions were

not analyzed for this project. See "Future Direction" section for information on how these data will be used.

3.7 Data Analysis

Three datasets were analyzed to determine if the Portapres® BP monitor was a valid tool for TBP measurements during rest and locomotion. Inter-day reliability was determined by comparing TBP values that were collected during the initial rest periods on Days 1 and 2. TBP data used in the analysis were collected during the initial 5-minute rest condition. TBP and BP values were compared between the initial resting condition and immediately after the 50H cycling condition to determine concurrent validity. The Slow Orthostatic trial determined the Portapres® construct validity by comparing TBP during cycling at 6 rpm and theoretical TBP values based on change in toe height.

3.7.1 Construct Validity

TBP and kinematic data collected during the Slow Orthostatic cycling test were imported into the MATLAB workspace (Natick, MA). Using MATLAB code, the TBP data were filtered at 0.3 Hz using a 4^{th} order low pass Butterworth filter. The data were filtered to minimize the effect of the systolic pressure on TBP. The "findpeaks" function returned the maximum TBP values during the six revolutions, and a "forloop" returned the minimum TBP values. The differences between maximum and minimum TBP values were calculated by subtracting the two maximum and minimum values. The resultant matrix returned six TBP values, which were the measured TBP values from the six revolutions of the Slow Orthostatic cycling test.

Changes in toe height during the Slow Orthostatic cycling test were used to determine the theoretical TBP values. Vertical toe position data (y) were extracted from the kinematic data set, and were imported with the TBP data. The toe position data were low pass Butterworth filtered at 1 Hz to smooth the data for precise height detection. The "findpeaks" function was used to find the maximum toe position in the y-direction and a "forloop" was used to return the minimum toe positions. The toe heights for each of the six revolutions were calculated by subtracting the minimum toe position from the maximum toe position. The kinematic analysis was completed for each participant with acceptable kinematic data. Finally, the changes in toe heights from all participants were then converted from millimetres to metres, and then averaged. The average change in toe height equaled 0.34m. This height was applied to Equation 1 ($P=\rho gh$) to determine the theoretical TBP value. A one-sample t-test was used to compare each change in TBP during slow cycling (six rpm) for all participants to a theoretical value of 34 mmHg. The one-sample t-test and descriptive statistics were calculated using GraphPad Software (La Jolla, CA).

3.7.2 Concurrent Validity

MAP_T and brachial mean arterial pressure (MAP_B) measurements from the initial rest period on Day 2 and immediately following the 50H cycling condition were analyzed to determine concurrent validity. MATLAB software was used to create code to complete the calculations for data analysis. The raw TBP data from the initial rest period on Day 2 was imported into the MATLAB workspace. A Fast-Fourier Transformation determined the frequency components of the TBP waveform. All noise was eliminated from the signal by using a low-pass Butterworth filter at a frequency just above the TBP waveform

frequency. The cut-off frequency was 200 Hz for all participants. The filtered data were then re-filtered using the "filtfilt" function in MATLAB. The "filtfilt" function is a zero-phase digital filter, which ensures the data does not experience distortion by running the data through the filter in both forward and reverse directions. All TBP values within 30 seconds of the 4th BP measurement during the resting period were extracted from the filtered TBP data. The TBP data were extracted at fifteen seconds before and fifteen seconds after the 4th BP measurement. For example, if the brachial BP measurement were at 3:55 of the rest period, then TBP data were extracted between 3:40 and 4:10. Systolic and diastolic TBP's were determined by using the "findpeaks" function in MATLAB. The findpeaks function found the maximum TBP measurement within a certain time frame. For example, if there were 30 heartbeats in 30 seconds, the "findpeaks" function would return 30 maximum TBP values. The "forloop" function then determined the minimum TBP between all maximum TBP values. Maximum TBP values were classified as systolic TBP, and minimum TBP values were classified as diastolic TBP values. Systolic and diastolic brachial measurements had already been recorded; therefore, no analysis was needed for their calculation. MAP_T and MAP_B were then calculated using systolic and diastolic TBP values using the Equation 4 from the literature review (i.e., MAP = Diastolic + [⅓ (Systolic – Diastolic)]. Resting MAP_T values were then statistically analyzed. The same code and protocol were used for after exercise TBP data analysis. The time when the first BP measurement after the 50H cycling condition was recorded was titled the "elapsed time after exercise". The elapsed time after exercise determined what time was used for TBP data analysis. Thirty seconds of TBP data were also used for this analysis (i.e., same as before exercise analysis). For example, if the first brachial BP measurement was 45 seconds after a participant's 50H cycling condition,

then TBP data were analyzed between 30 seconds and one minute, which is 30 seconds surrounding the time of the brachial artery BP measurement.

TBP and brachial BP measurements before exercise were tested for Concurrent Validity of the Portapres®. The measurements included MAP, systolic, and diastolic measurements. Three statistical methods were used in concurrent validity analysis. First, a Model II ordinary least products (OLP) regression analysis was performed on Day 2 "Before Exercise" data. The OLP regression analysis assessed the fixed and proportional bias between both measurement sites. The OLP method was chosen because it accounts for random error within both sets of measurements on both X and Y-axes, unlike the ordinary least squares (OLS) method, which only accounts for error in the Y-axis[42]. The OLP analysis requires the y-intercept (a′) and the slope (b′) of the OLP regression line. Fixed bias was defined as "one method giving values that are higher (or lower) than those from the other by a constant amount" [42]. Fixed bias was determined by calculating the 95% confidence intervals (CI) for a′ and determining whether it included "0". If the 95% CI band did not include "0", the data were classified as having a fixed bias. Proportional bias was defined as "one method that gives values that are higher (or lower) than those from the other by an amount that is proportional to the level of the measured variable"[42]. Proportional bias was determined by calculating the 95% CI of b′ for each data point, and was deemed to have proportional bias if it did not include a value of "1".

The second statistical test used to determine the Portapres® concurrent validity was the method of differences by Bland and Altman[67]. The differences of the two measurement sites were plotted on the Y-axis, and the average of the two BP measures was plotted on the X-axis. Proportional bias was determined by applying the OLS

analysis method to the Bland-Altman method of differences data. A one-sample t-test comparing "0" to the slope of the method of difference data (OLS regression line) was used to detect proportional bias. A one-sample t-test detected fixed bias by comparing the mean difference data to "0". Statistical significance determination was set at $P<0.05$.

The third statistical test included another OLP regression analysis on the change in MAP_B versus the change in MAP_T from before exercise compared to after exercise (i.e., $\Delta MAP_B = MAP_B$ after – before exercise; $\Delta MAP_T = MAP_T$ after – before exercise). The OLP analysis was intended to show proportional and fixed bias' between MAP_B and MAP_T after exercise in comparison to before exercise. All data were analyzed and all figures were prepared using GraphPad Software, Inc.

3.7.3 Inter-Day Reliability

MAP_T and MAP_B measurements from initial resting periods on Day 1 and Day 2 were analyzed to determine inter-day reliability. Using MATLAB software, a code calculated and analyzed the data. The raw TBP data from the initial rest period on Day 1 was imported into the MATLAB workspace. A Fast-Fourier Transformation (FFT) determined the frequency components of the TBP waveform. All noise were eliminated from the signal by using a low-pass Butterworth filter at a frequency just above the TBP waveform frequency. The cut-off frequency was 200 Hz for all participants. The filtered data were then re-filtered using the "filtfilt" function in MATLAB. The "filtfilt" function is a zero-phase digital filter, which ensures the data does not experience distortion by running the data through the filter in both the forward and reverse directions. All TBP

values within 30 seconds of the 4th BP measurement during the resting condition were extracted from the filtered TBP data. The TBP data were extracted between fifteen seconds before, and fifteen seconds after the 4th brachial BP measurement. Systolic and diastolic TBP's were determined by using the "findpeaks" function in MATLAB. The "findpeaks" function found the maximum TBP measurement within a certain time frame. A "forloop" code then determined the minimum TBP between all maximum TBP values. Systolic and diastolic brachial BP measurements had been recorded; and therefore, did not have to be calculated. MAP_T and MAP_B were then calculated using systolic and diastolic TBP and brachial BP values from Equation 4. The same code and protocol was then used to analyze Day 2 data.

All quantitative MAP, systolic, and diastolic measurements from the toe and brachial arteries were tested for inter-day reliability using OLP and Bland-Altman analysis. First, a Model II OLP regression analysis was performed on Day 1 and Day 2 TBP and brachial BP data using a method similar to that used for concurrent validity analysis. The second statistical test included a Bland-Altman method of differences analysis to determine inter-day reliability of the Portapres®. The differences of Day 1 and Day 2 TBP measurements were plotted on the Y-axis, and the average of the two measurements was plotted on the X-axis. Proportional and fixed biases were determined using a method similar to that used for concurrent validity analysis. Statistical comparisons was set at $P<0.05$.

3.7.4 Toe Blood Pressure during Cycling Conditions

Toe blood pressure was analyzed between three cycling conditions: 50H, 50L, and 90L. HR analysis was required to determine when each participant was exercising within five bpm of their age-predicted 60% HR_{max}. Plus or minus five bpm was considered to be steady-state exercise in this study. HR values were determined by analyzing ECG data for each condition. The collected ECG data provided real-time beat-to-beat analysis of the participants' HR during exercise. Using MATLAB code, heartbeats were counted over 30-second intervals for the entire cycling condition. For example, HR at the 30-second time point of exercise was calculated by adding all heart beats between 15- and 45-second time points and multiplying the number by two. This calculation was used to convert the calculated value into bpm. This calculation continued every second for the full five-minute duration[13]. By averaging the HR data, it determined what the participants' HR was throughout all cycling conditions. One-minute of TBP values were extracted from the TBP data set when HR was within five bpm for both the 50H and 90L cycling conditions. This allowed for any effects of HR on TBP to be controlled for during the 50H and 90L cycling conditions. One-minute of TBP data were also extracted from the 50L condition when participants were at steady-state HR.

As previously mentioned, physiological and biomechanical data were collected for ten-minutes for each condition. To make the large amount of data more manageable, the ten-minute files of data were divided into two, five-minute files. All data were analyzed in five-minute intervals. An example of HR data for the three cycling conditions is shown in Figure 25. HR is considered equal for the participant during the 50H and 90L conditions between 30- and 90-seconds (one-minute). One-minute of TBP data were

averaged for each condition, and the value was deemed the MAP_T value for the condition. Each participant provided three MAP_T values using this method of analysis.

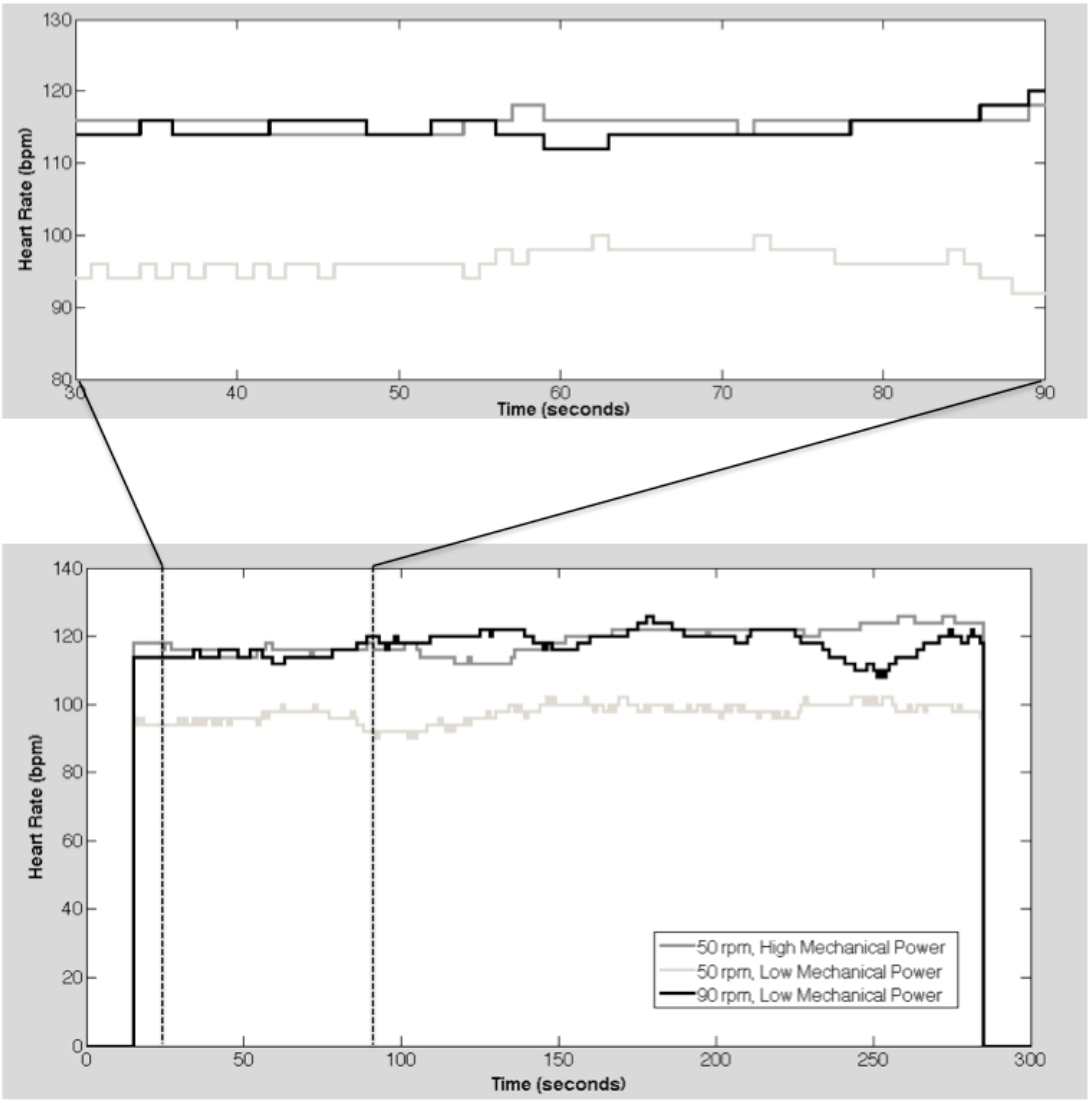

Figure 25. An example of averaged HR data for one participant during the three cycling conditions. The top graph highlights the analyzed portion of HR data. The bottom graph highlights five minutes of HR data for each of the three cycling conditions. bpm, beats per minute; rpm, revolutions per minute; vertical dashed lines, one-minute of analyzed data.

MAP_T, HR, and mechanical power output data during cycling were analyzed using two statistical methods. The first method included three Wilcoxon's non-parametric

matched-pairs signed rank tests while controlling for one of the three independent variables (cadence, power, and HR). The Wilcoxon's matched-pairs signed rank test was used as preliminary analysis to show that the data were not normally distributed. The Wilcoxon test was analyzed using GraphPad Software (La Jolla, CA).

The second statistical method used was a multiple linear regression in SPSS (Chicago, IL). The regression included three independent variables and one dependent variable. The independent variables were cadence, normalized mechanical power, and normalized HR. The dependent variable was normalized MAP_T. HR, mechanical power, and MAP_T were normalized for two reasons. The first reason was to reduce the variability of resting heart rates between participants. More fit participants had lower resting HR compared to less fit participants. The second reason data were normalized was again due to participants having different levels of fitness. Some more fit participants required large mechanical power outputs to reach an exercise intensity of 60% HR_{max}, whereas less fit participants required lower mechanical power outputs to reach 60% HR_{max}. Therefore, by normalizing the low mechanical power by the high mechanical power it reduced the variability between participants. Normalized HR, normalized mechanical power, cadence and MAP_T were used in the multiple linear regression due to their linear relationships at the two different cycling cadences. Normalized HR was calculated by subtracting resting HR from the cycling condition HR (i.e., HR while cycling at a certain condition) and dividing the calculated value from the resting HR subtracted from the age-predicted HR maximum value. Normalized mechanical power was calculated by dividing the low power value (i.e., mechanical power during 90L and 50L conditions) by the high power value (i.e., 50H mechanical power was always 1). Normalized MAP_T was calculated by

dividing the MAP_T produced during the cycling condition by the original resting condition MAP_T. Cadence was not normalized (i.e., either 50 or 90 rpm). The regression model included the "Enter" method and "exclude cases listwise" was used for missing values. Residuals were calculated using the Durbin-Watson method. A p value < 0.05 was used for determining significance.

CHAPTER 4: RESULTS

4.1 Participant Characteristics

The study population included 16 non-disabled, normotensive participants (6 male, 10 female) aged 20-26 years from Dalhousie University. Twenty-one participants originally met the written inclusion criteria; however, not all participants (5) were able to provide sufficient TBP in all conditions, and were therefore excluded. Fifteen out of sixteen participants provided TBP values during the cycling conditions of the study. The physical characteristics of the participants whose data were included in the study are shown in Table 4 below.

Table 4. The descriptive statistics of the study's participants.

Description	Value
Age (years)	21.9 ± 1.9
Height (m)	1.73 ± 0.1
Mass (kg)	70.4 ± 9.3
Male	6
Female	10

m, meters; kg, kilograms; mean ± standard deviation.

4.2 Construct Validity

In total, 15 participants provided 75 acceptable TBP values (Figure 26A), which were included in the construct validity portion of the study. Four participants provided four TBP values, four other participants provided six TBP values, and six participants provided five TBP values. Only one TBP value was excluded from analysis due to being more than 3 SD from the overall mean (75.0 mmHg). There should have been 90 TBP values (15 participants, 6 revolutions); however, 14 revolutions were either absent or were unable to be extracted from the raw data due to participant error (i.e., did not cycle at the appropriate cadence). Variability within participants can be seen in Figure 26B.

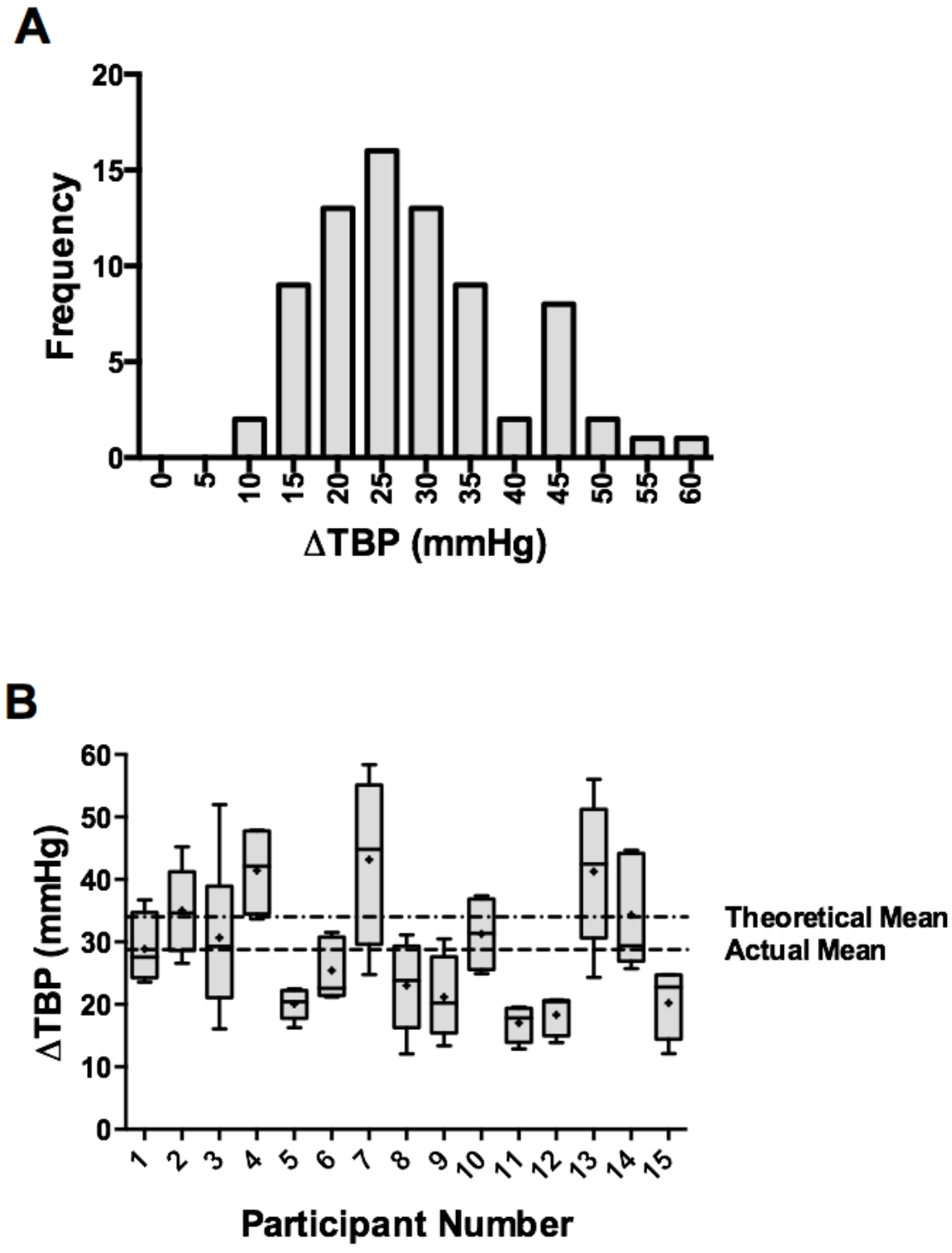

Figure 26. Construct validity data. Panel A. Histogram of all ΔTBP values. B. Individual participant data. mmHg, millimeters of mercury; change in TBP, ΔTBP.

Six participants were able to provide acceptable kinematic data during the Slow Orthostatic trial. Kinematic data were used to show how TBP reacted due to the change in distance from the heart to the toe. The best (Figure 27A, 27C) and worst (Figure 27B, 27D) case of TBP and kinematic data are shown below.

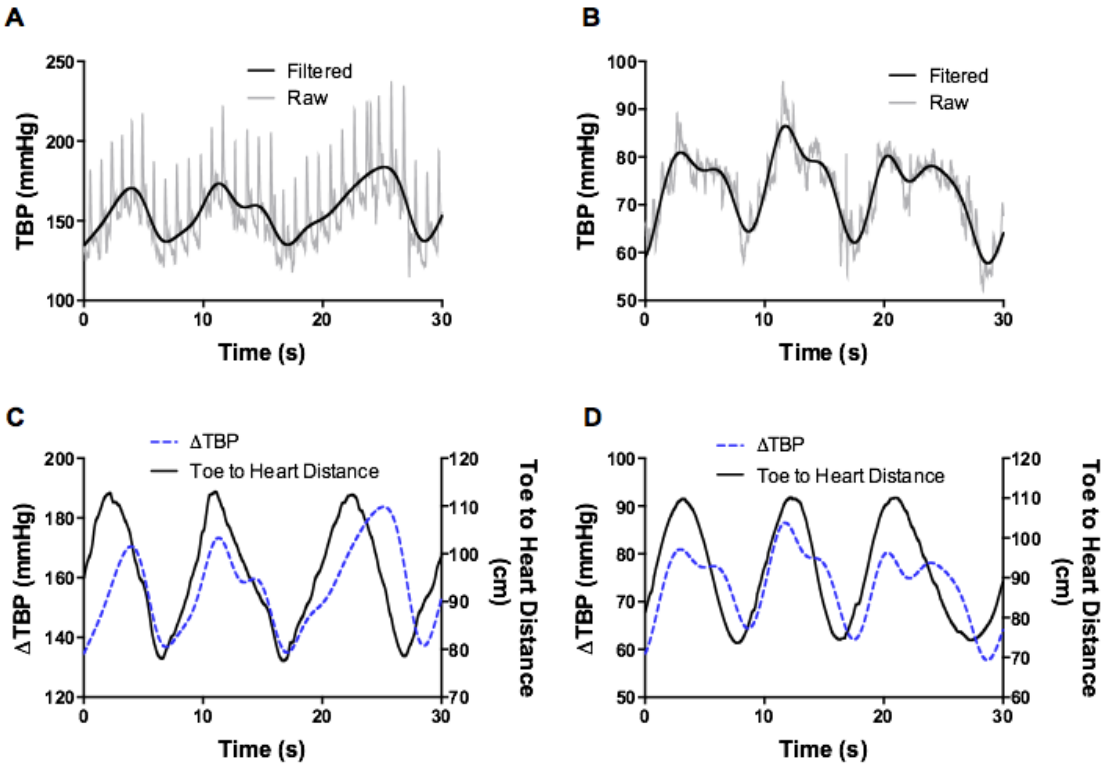

Figure 27. Examples of TBP during Slow Cycling (6 rpm) for two participants. A. Participant 1: Raw and Filtered (Low-Pass Butterworth 0.3 Hz) TBP data B. Participant 2: Raw and Filtered TBP data C. Participant 1: ΔTBP and filtered toe distance from heart (cm; 1 Hz). D. Participant 2: Change in TBP and toe distance from heart (cm). mmHg, millimeters of mercury; cm, centimeters; Δ, change.

The one-sample t-test showed that the actual mean (28.75 mmHg) was significantly different from the theoretical mean of 34 mmHg (P<0.0001; Table 5, Figure 26B).

Table 5. Descriptive statistics of one-sample t-test.

Description	Value
Theoretical mean	34.0
Actual mean	28.8
Discrepancy	5.25
95% CI of Discrepancy	-7.73 to -2.77
t, df	4.22, df =75
P value (two-tailed)	< 0.0001
Significant (α=0.05)?	Yes

t, t-statistic; df, degrees of freedom; α, alpha value.

4.3 Concurrent Validity

Concurrent validity was assessed in 16 participants (6 male, 10 female). The first question asked to determine concurrent validity was whether MAP_B equaled MAP_T at rest before exercising. Raw brachial and TBP data that were collected during rest on Day 2 are presented in Table 6, and an example of a TBP waveform from Day 2 measurements on Participant #8 is shown in Figure 28.

Table 6. Individual participants raw TBP and brachial BP measurements while at rest on Day 2. All values are in mmHg.

Participant	Toe			Brachial		
	MAP_T	$Systolic_T$	$Diastolic_T$	MAP_B	$Systolic_B$	$Diastolic_B$
1	79.2	117.0	60.4	75.7	103	62
2	71.8	113.4	51.0	84.7	130	62
3	62.3	82.6	52.1	87.3	134	64
4	71.8	105.7	54.8	82.7	122	63
5	87.5	134.4	64.0	90.0	120	75
6	98.4	111.3	91.9	83.3	112	69
7	67.2	87.7	57.0	76.0	102	63
8	37.2	63.8	23.9	78.7	122	57
9	73.2	117.6	51.1	84.7	110	72
10	68.4	97.7	53.7	74.0	96	63
11	59.6	77.0	50.9	71.3	102	56
12	76.3	117.8	55.5	77.0	109	61
13	68.7	86.3	59.8	78.3	107	64
14	69.1	98.8	54.2	75.3	110	58
15	59.0	79.3	48.9	75.3	108	59
16	69.5	100.5	54.0	86.3	119	70
mean	69.9	99.4	55.2	80.0	112.9	63.6
SD	13.2	18.9	13.1	5.5	10.7	5.4

mmHg, millimeters of mercury; SD, standard deviation; MAP_T, toe mean arterial pressure; MAP_B, brachial mean arterial pressure; $Systolic_T$, toe systolic blood pressure; $Systolic_B$, brachial systolic blood pressure; $Diastolic_T$, toe diastolic blood pressure; $Diastolic_B$, brachial diastolic blood pressure.

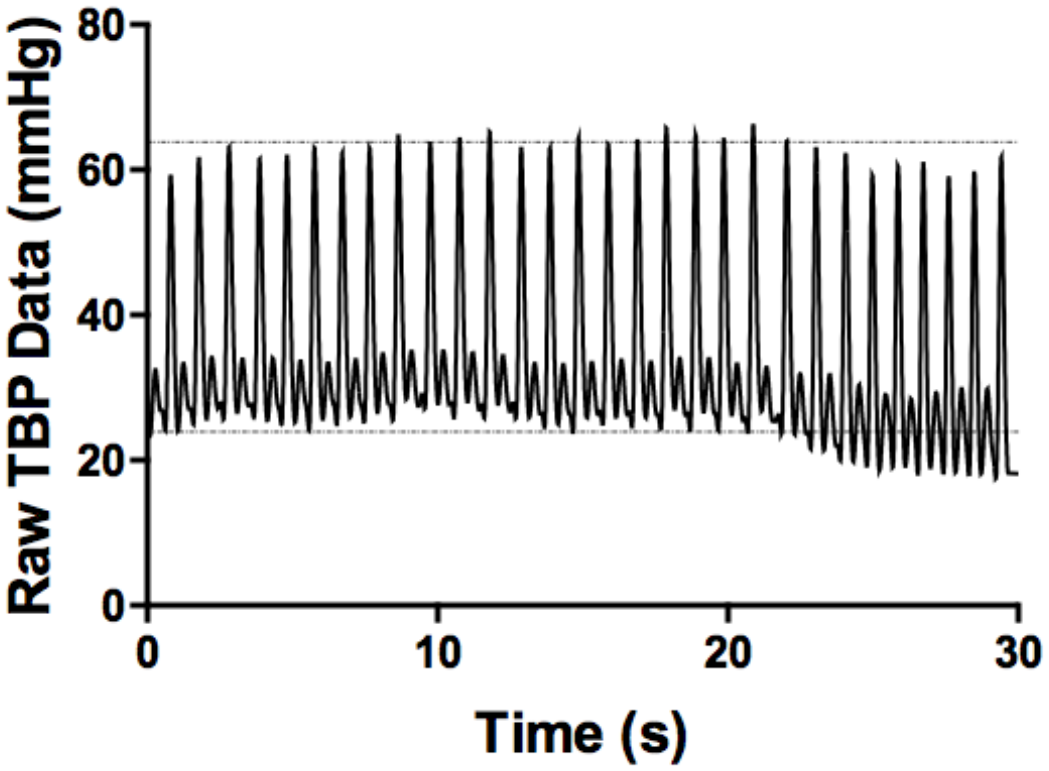

Figure 28. Example of Participant #8's raw TBP waveform during initial rest on Day 2. mmHg, millimeters of mercury; s, seconds; top dotted line, average systolic TBP; bottom dotted line, average diastolic TBP.

Ordinary least products (OLP) analysis provided data stating that there was fixed bias, but no proportional bias in MAP between the two measurement sites (Table 7; Figure 29A). The OLP analysis showed that there was no proportional or fixed bias in systolic BP; but there was proportional and fixed bias in diastolic BP between measurement sites (Table 7, Figure 29B, 29C).

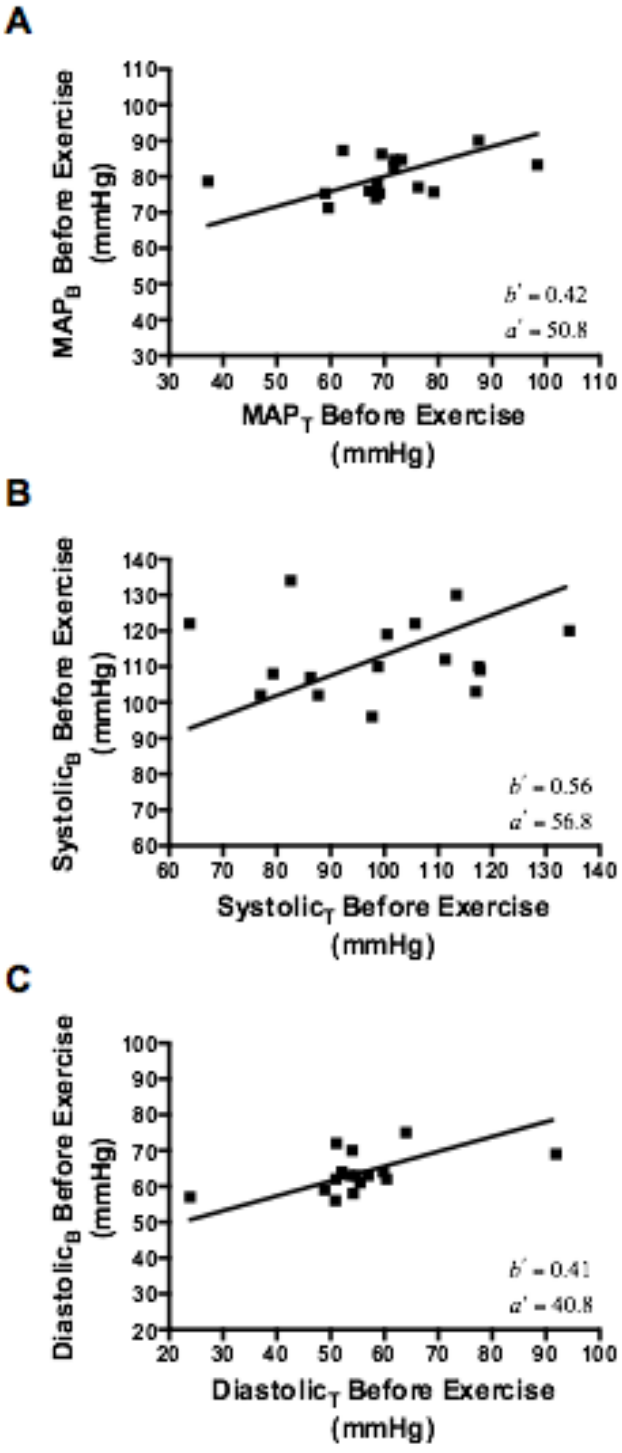

Figure 29. Ordinary least products (OLP) analysis of BP during rest. Panel A. MAP_T vs. MAP_B, B. $Systolic_T$ vs. $Systolic_B$, C. $Diastolic_T$ vs. $Diastolic_B$. mmHg, millimeters of mercury; MAP_T, toe mean arterial pressure; MAP_B, brachial mean arterial pressure; $Systolic_T$, toe systolic blood pressure; $Systolic_B$, brachial systolic blood pressure; $Diastolic_T$, toe diastolic blood pressure; $Diastolic_B$, brachial diastolic blood pressure. a′, y-intercept; b′, slope.

Table 7. Concurrent validity outcomes of different quantifiable measures of BP during rest by ordinary least products (OLP) regression analysis.

Variable	r	a'	95% CI for a'	b'	95% CI for b'	Proportional bias	Fixed bias
MAP	0.36	50.8	6.1, 95.5	0.42	-0.21, 1.05	NO	YES
Systolic	0.05	56.8	-637.7,751.3	0.56	-6.31, 7.43	NO	NO
Diastolic	0.50	40.8	17.5, 64.1	0.41	0.002, 0.83	YES	YES

r, product-moment correlation coefficient; a′, b′, coefficients in ordinary least products regression model (Y)=a′+ b′(X); a′, y-intercept; b′, slope; proportional bias, if 95% CI for b′ does not include 1; fixed bias, if 95% CI for a′ does not include 0.

The Bland-Altman (BA) method of difference analysis shows a presence of fixed bias and proportional bias in MAP, systolic BP, and diastolic BP between both measurement sites during rest (Table 8, Figure 30A, 30B, 30C).

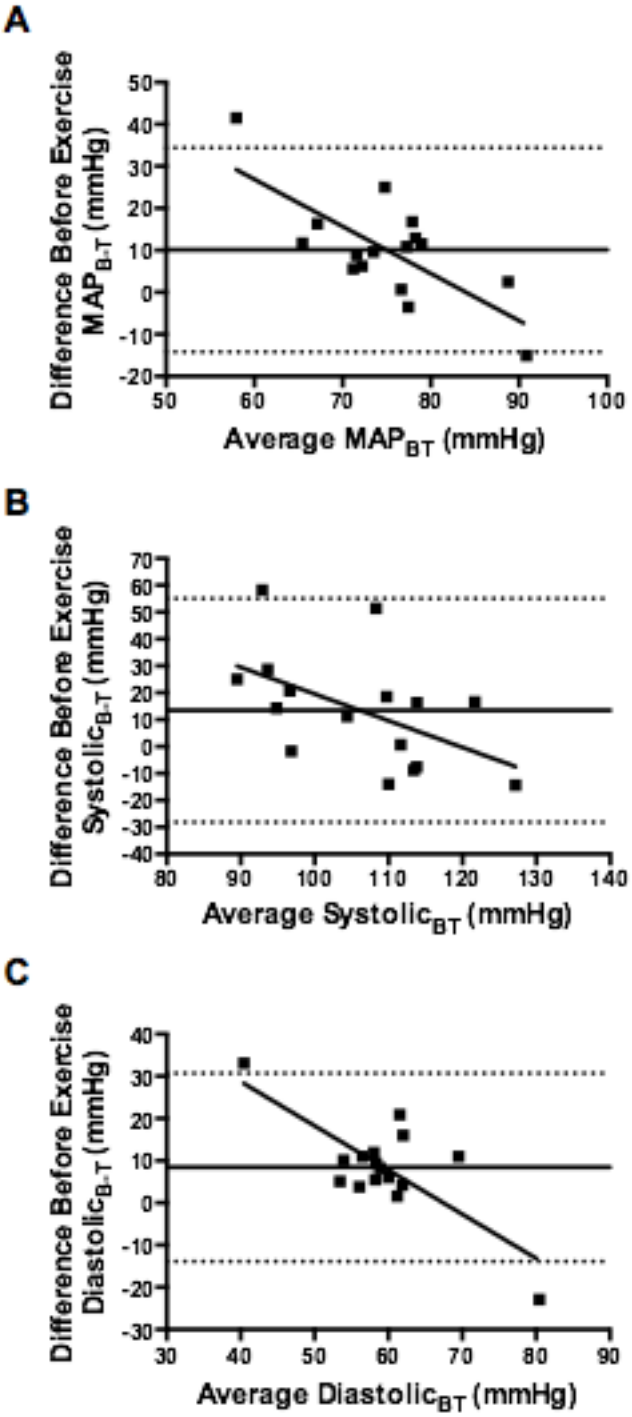

Figure 30. Bland-Altman method of differences analysis of BP during rest. Panel A. Average MAP_{BT} vs. Difference $MAP_{B\text{-}T}$, B. Average $Systolic_{BT}$ vs. Difference $Systolic_{B\text{-}T}$, C. Average $Diastolic_{BT}$ vs. Difference $Diastolic_{B\text{-}T}$. Dashed horizontal lines, 95% CI's; mmHg, millimeters of mercury; $_{B\text{-}T}$, brachial BP minus toe BP; $_{BT}$, average of brachial and toe BP.

Table 8. Concurrent validity outcomes of different quantifiable measures of BP during rest by the Bland-Altman method of differences analysis.

Variable	***r***	***b***	***P*** (OLS)	Proportional bias	Mean difference ± S.E.M	95% CI for mean difference	***P*** (t-test)	Fixed bias
MAP	0.73	-1.12	0.001	YES	10.09±3.1	3.5, 16.7	0.005	YES
Systolic	0.52	-0.99	0.04	YES	13.44±5.3	2.1, 24.8	0.02	YES
Diastolic	0.75	-1.05	0.0007	YES	8.43±2.9	2.4, 14.5	0.01	YES

r*, product-moment correlation coefficient for the Bland-Altman method of differences plots;* b, ordinary least squares (OLS) slope of the Bland-Altman method of differences plots; P (OLS), the P value for the OLS slope (versus 0); CI, confidence interval; P (t-test), the P value for the one sample t-test on the mean differences (versus 0); $P < 0.05$.

The second question of interest to determine the concurrent validity of the Portapres® was if the effect of exercise was the same on MAP_B as it was on MAP_T. MAP_T and MAP_B data were collected and analyzed on 16 participants. The average time it took to obtain resting TBP and BP measurements after exercise was 28.9 ± 13.9 seconds. Raw brachial and TBP data that were collected after exercising on Day 2 is presented in Table 9.

Table 9. Individual participants raw TBP and brachial BP measurements immediately after cycling at 50 rpm and a high mechanical power output on Day 2. All values are in mmHg.

Participant	Toe			Brachial		
	MAP_T	$Systolic_T$	$Diastolic_T$	MAP_B	$Systolic_B$	$Diastolic_B$
1	55.2	81.6	42.0	82.7	132.0	58.0
2	69.5	100.4	54.1	96.3	139.0	75.0
3	57.0	70.4	50.2	100.0	146.0	77.0
4	70.0	83.5	63.2	94.7	152.0	66.0
5	65.5	99.4	48.6	98.7	140.0	78.0
6	69.7	101.2	54.0	95.3	148.0	69.0
7	86.8	123.9	68.3	86.7	118.0	71.0
8	47.3	54.0	43.9	95.0	151.0	67.0
9	47.3	61.6	40.2	89.0	141.0	63.0
10	54.8	74.5	44.9	78.7	120.0	58.0
11	73.8	80.6	70.5	81.3	114.0	65.0
12	50.6	60.2	45.8	86.3	137.0	61.0
13	78.3	84.7	75.1	88.3	135.0	65.0
14	55.7	58.3	54.3	90.0	142.0	64.0
15	49.9	81.9	33.9	84.7	134.0	60.0
16	68.7	106.9	49.6	76.3	115.0	57.0
mean	62.5	82.7	52.4	89.0	135.3	65.9
SD	11.9	19.7	11.6	7.2	12.5	6.7

mmHg, millimeters of mercury; SD, standard deviation; MAP_T, toe mean arterial pressure; MAP_B, brachial mean arterial pressure; $Systolic_T$, toe systolic blood pressure; $Systolic_B$, brachial systolic blood pressure; $Diastolic_T$, toe diastolic blood pressure; $Diastolic_B$, brachial diastolic blood pressure.

An OLP analysis was applied to the change in MAP_T data vs. the change in MAP_B data (Figure 31). A slope (b′) of 0.38 and a y-intercept (a′) of 11.5 were determined. The 95% CI for the b′ was -1.3 to 2.1 meaning there was no proportional bias, and the 95% CI for a′ was -17.1 to 40.0 meaning there was no fixed bias present in the data. MAP_B increased after exercise in 15 of 16 participants. MAP_T increased in 5 participants and decreased in 11 participants after the 50H cycling condition.

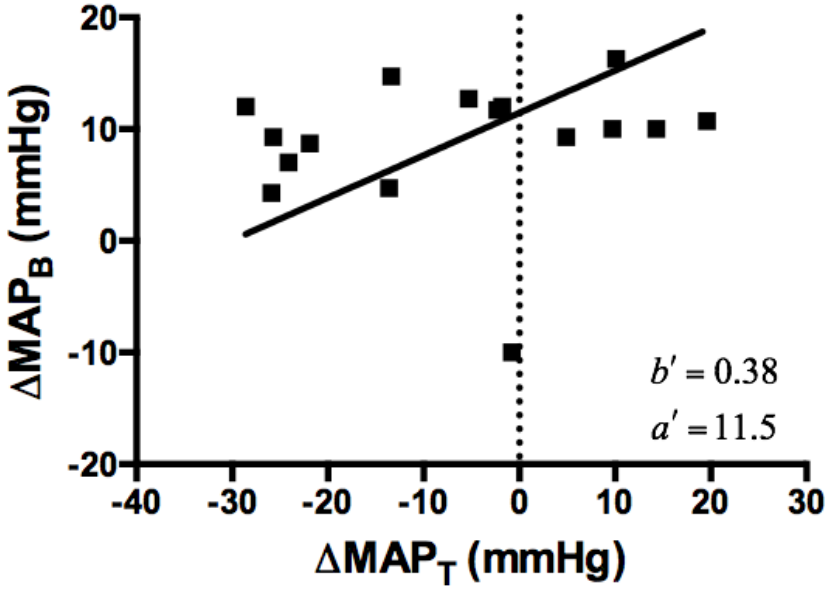

Figure 31. The effect of exercise on MAP in the toe ($_T$) and brachial ($_B$) arteries. Ordinary least products (OLP) analysis of ΔMAP_T and ΔMAP_B before to after exercise. mmHg, millimeters of mercury; a′, y-intercept; b′, slope.

4.4 Inter-day Reliability

Inter-day reliability was tested in 16 participants (6 male, 10 female). TBP and brachial BP values measured on Day 1 and Day 2 are shown in Table 10 and Table 11.

Table 10. TBP values measured on Day 1 and Day 2. All values are in mmHg.

Participant	Day 1			Day 2		
	MAP_T	$Systolic_T$	$Diastolic_T$	MAP_T	$Systolic_T$	$Diastolic_T$
1	57.9	73.9	49.9	79.2	117.0	60.4
2	100.1	121.9	89.2	71.8	113.4	51.0
3	84.0	97.9	77.0	62.3	82.6	52.1
4	74.3	86.5	68.2	71.8	105.7	54.8
5	87.7	131.2	66.0	87.5	134.4	64.0
6	72.0	97.4	59.3	98.4	111.3	91.9
7	112.2	152.4	92.1	67.2	87.7	57.0
8	45.0	70.3	32.3	37.2	63.8	23.9
9	64.8	99.2	47.6	73.2	117.6	51.1
10	58.7	83.7	46.3	68.4	97.7	53.7
11	63.7	79.4	55.9	59.6	77.0	50.9
12	54.9	96.7	34.0	76.3	117.8	55.5
13	104.8	124.4	95.0	68.7	86.3	59.8
14	110.9	143.7	94.4	69.1	98.8	54.2
15	48.8	79.4	33.4	59.0	79.3	48.9
16	56.3	88.3	40.3	69.5	100.5	54.0
mean	74.8	101.6	61.3	69.9	99.4	55.2
SD	22.5	25.4	22.6	13.2	18.9	13.1

Table 11. Brachial BP values measured on Day 1 and Day 2. All values are in mmHg.

Participant	Day 1			Day 2		
	MAP_B	$Systolic_B$	$Diastolic_B$	MAP_B	$Systolic_B$	$Diastolic_B$
1	84.3	115	69	75.7	103	62
2	84.3	129	62	84.7	130	62
3	89.0	141	63	87.3	134	64
4	92.3	125	76	82.7	122	63
5	87.0	117	72	90.0	120	75
6	76.3	103	63	83.3	112	69
7	77.0	111	60	76.0	102	63
8	69.7	105	52	78.7	122	57
9	91.3	134	70	84.7	110	72
10	60.0	92	44	74.0	96	63
11	75.7	109	59	71.3	102	56
12	75.0	109	58	77.0	109	61
13	81.3	114	65	78.3	107	64
14	83.0	117	66	75.3	110	58
15	74.3	107	58	75.3	108	59
16	71.3	100	57	86.3	119	70
mean	79.5	114.3	62.1	80.0	112.9	63.6
SD	8.7	12.9	7.9	5.5	10.7	5.4

An OLP analysis showed that there was no fixed or proportional bias in MAP, Systolic, or Diastolic measurements in the toe or brachial measurement sites between the two testing days. Statistical results from the OLP analysis are shown in Figure 32 and Table 12 below.

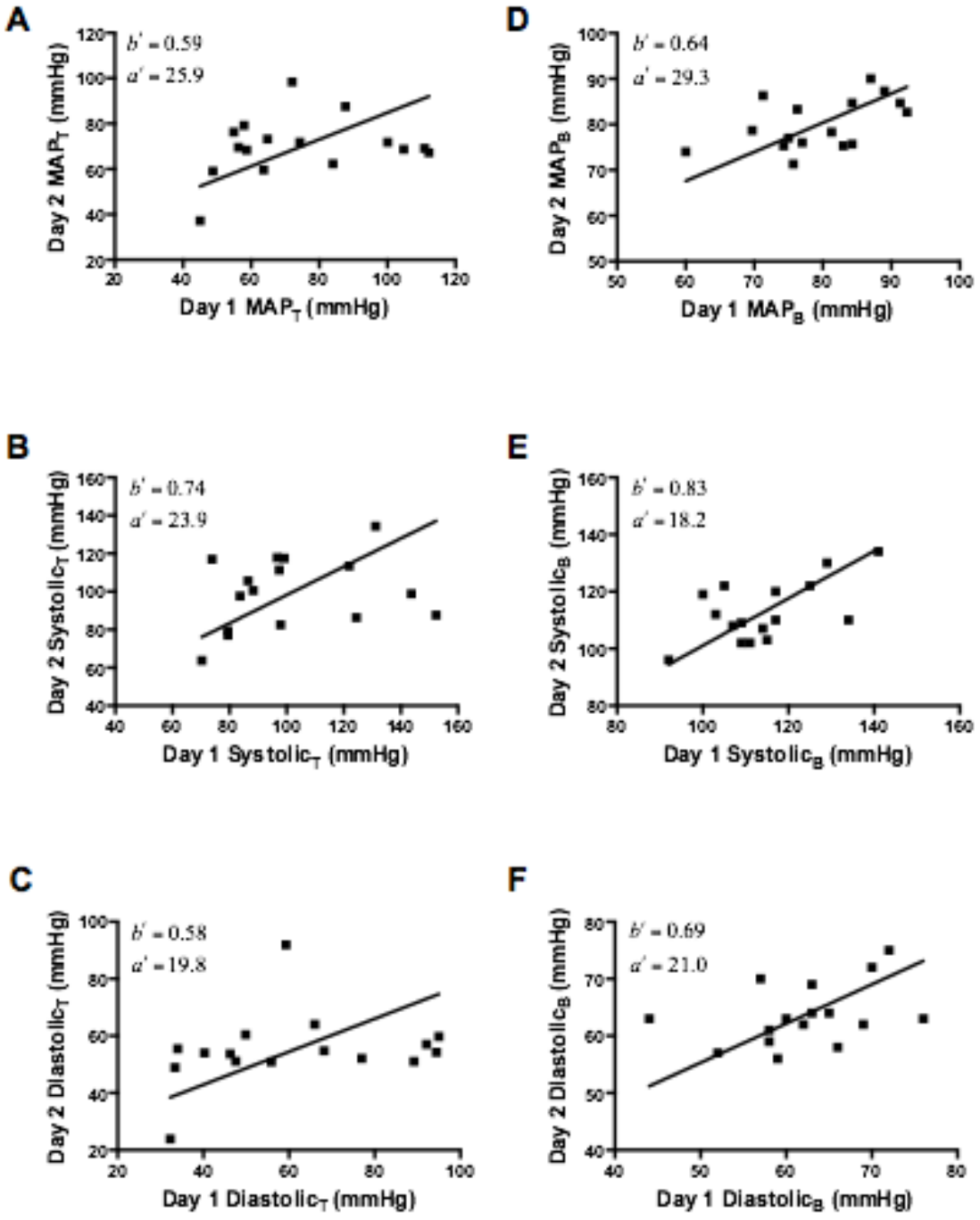

Figure 32. Inter-day Reliability of TBP and BP. Panel A. Ordinary least products (OLP) analysis of MAP_T B. OLP analysis of $Systolic_T$; C. OLP analysis of $Diastolic_T$; D. OLP analysis of MAP_B; E. OLP analysis of $Systolic_B$; F. OLP analysis of $Diastolic_B$. mmHg, millimeters of mercury; a′, b′, coefficients in OLP regression model (Y)=a′+ b′(X); a′, y-intercept; b′, slope; solid line, OLP line of best fit.

Table 12. Reliability outcomes of different quantifiable measures of BP by ordinary least products (OLP) regression analysis.

Variable	r	a'	95% CI for a'	b'	95% CI for b'	Proportional bias	Fixed bias
Toe							
MAP	0.23	25.87	-83.43- 135.2	0.59	-0.814-1.994	NO	NO
Systolic	0.25	23.86	-151.7-199.4	0.74	-0.935-2.422	NO	NO
Diastolic	0.25	19.81	-62.62-102.2	0.58	-0.689-1.844	NO	NO
Brachial							
MAP	0.51	29.34	-20.41-79.09	0.64	0.015-1.260	NO	NO
Systolic	0.59	18.23	-55.32-91.70	0.83	0.189-1.468	NO	NO
Diastolic	0.38	20.99	-38.55-80.54	0.69	-0.265-1.638	NO	NO

r, *product-moment correlation coefficient;* a′, b′, coefficients in ordinary least products regression model (Y)=a′+ b′(X); a′, y-intercept; b′, slope; proportional bias, if 95% CI for b′ does not include 1; fixed bias, if 95% CI for a′ does not include 0.

The Bland-Altman method of differences analysis shows proportional bias in the $Diastolic_T$ measurements between the two testing days. No fixed or proportional bias was present in MAP, systolic BP, or diastolic BP measurements in the brachial artery or MAP and systolic BP measurement at the toe between the two testing days. Statistical results from the Bland-Altman analysis are shown in Figure 33 and Table 13 below.

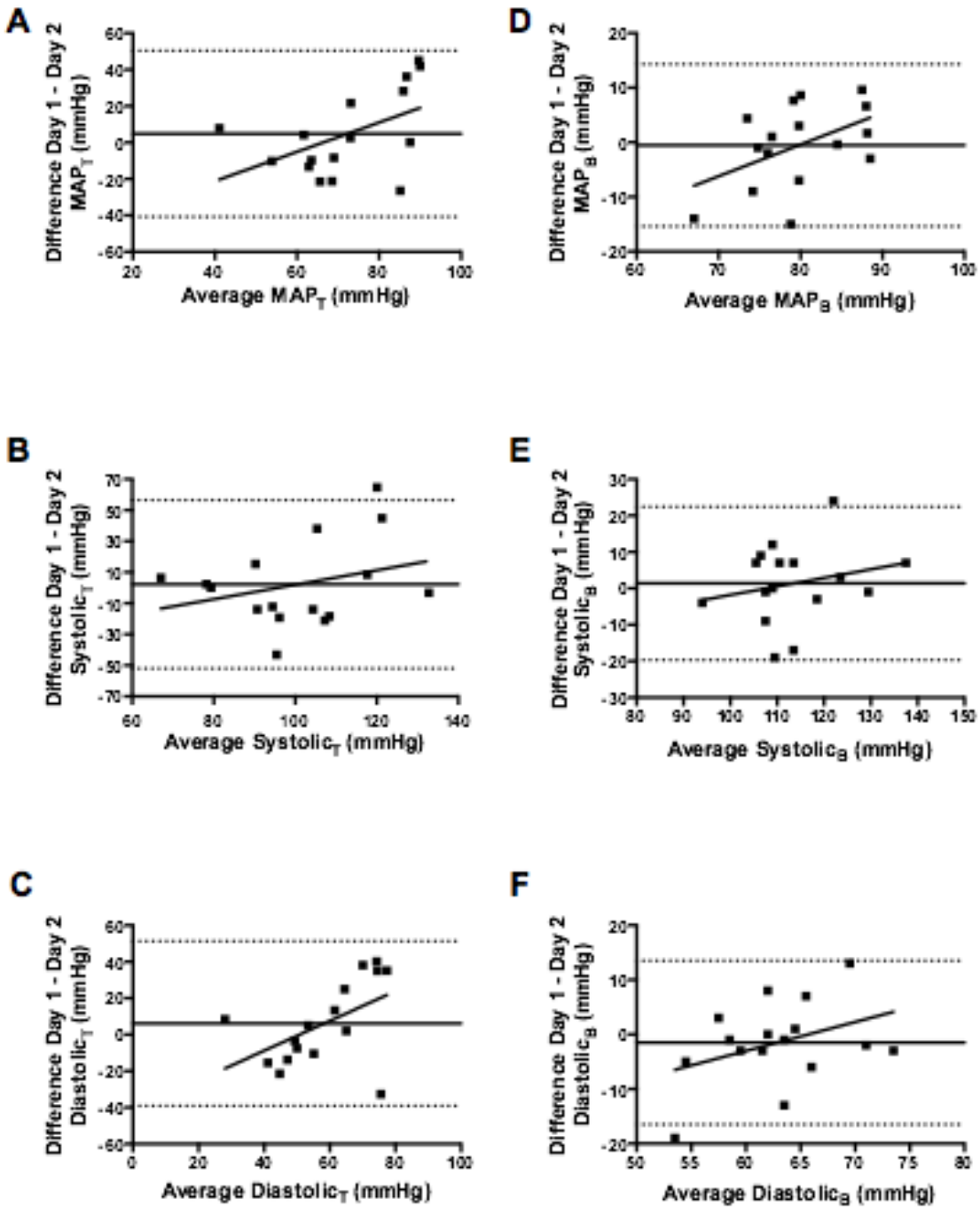

Figure 33. Inter-day Reliability of TBP and BP. Panel A. Bland-Altman method of differences (BA) analysis of MAP_T B. BA analysis of $Systolic_T$; C. BA analysis of $Diastolic_T$; D. BA analysis of MAP_B; E. BA analysis of $Systolic_B$; F. BA analysis of $Diastolic_B$. mmHg, millimeters of mercury; solid-line, mean; dotted-line, mean ± SD.

Table 13. Reliability outcomes of different quantifiable measures of BP by the Bland-Altman method of differences analysis.

Variable	***r***	***b***	***P*** (OLS)	Proportional bias	Mean difference ± S.E.M	95% CI for mean difference	***P*** (t-test)	Fixed bias
Toe								
MAP	0.50	0.80	0.05	NO	4.81±5.8	-7.6, 17.2	0.42	NO
Systolic	0.30	0.47	0.26	NO	2.21±6.9	-12.5, 17.0	0.75	NO
Diastolic	0.51	0.82	0.04	YES	6.11±5.8	-6.2, 18.4	0.31	NO
Brachial								
MAP	0.48	0.58	0.06	NO	-0.55±1.9	-4.6, 3.5	0.77	NO
Systolic	0.22	0.23	0.39	NO	1.38±2.7	-4.4, 7.1	0.62	NO
Diastolic	0.39	0.53	0.14	NO	-1.50±1.9	-5.6, 2.6	0.45	NO

r, product-moment correlation coefficient for the Bland-Altman method of differences plots; b, ordinary least squares (OLS) slope of the Bland-Altman method of differences plots; *P* (OLS), the *P* value for the OLS slope (versus 0); CI, confidence interval; *P* (t-test), the *P* value for the one sample t-test on the mean differences (versus 0); $P < 0.05$.

4.5 Feasibility of Portapres® during Locomotion

Multiple exploratory experiments were used to test the feasibility of the Portapres® during different modes of locomotion. TBP was collected in only two participants during walking (Table 14). No participants were able to reach 60% of their HR_{max} while walking with the Portapres® on their toe during exploratory tests or actual data collection trials. Exploratory walking tests were completed unsuccessfully on one male (26 years, 1.610 m, 80.0 kg) and one female participant (29 years, 1.700 m, 54.7 kg).

Table 14. Explanation on what data were collected for each recruited participant.

Participant	Cycling?	Walking?	Why No Walking?	Amount of walking data collected (minutes)
1	Y	N	Error	0
2	Y	N	Error	0
3	Y	N	Error	0
4	Y	N	Error	0
5	Y	N	Error	0
6	Y	N	Error	0
7	Y	N	Error	0
8	Y	N	Error	0
9	Y	N	Error	0
10	Y	N	Error	0
11	Y	N	Error	0
12	Y	N	Error	0
13	Y	N	Error	0
14	Y	N	Error	0
15	Y	N	Stopped 6 times	4
16	N	N	No Pulse	0
17	N	N	Stopped 4 times	6
18	N	N	Stopped 2 times	2
19	N	N	Low Plethys	0
20	N	N	No Pulse	0
21	N	N	Low Plethys	0

Y, yes; N, no; plethys, plethysmogram.

During testing on the male participant, TBP was collected at very low exercise intensities (<50% HR_{max}) while using arm support (Figures 34 and 35). Arm support was required to reduce the GRF and to lessen Portapres® errors due to large forces interacting with the TBP cuff. The participant's HR while walking at 2.3 km/hr and a 0% grade was 72 bpm (37% HR_{max}), and 86 bpm (44% HRmax) while walking 4.8 km/hr and a 0% grade.

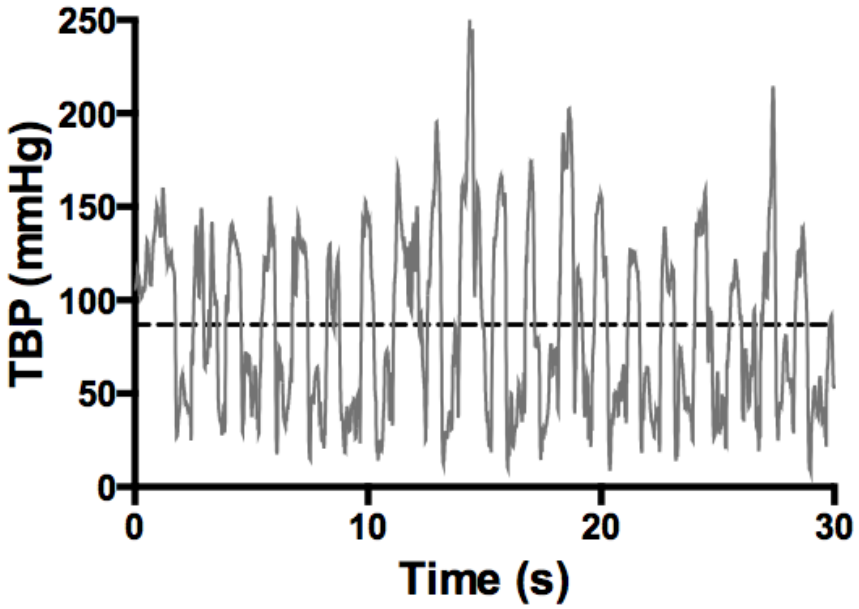

Figure 34. Walking at 2.3 km/hr, 0% grade with arm support. Dashed line depicts MAP_T. mmHg, millimeters of mercury; s, seconds.

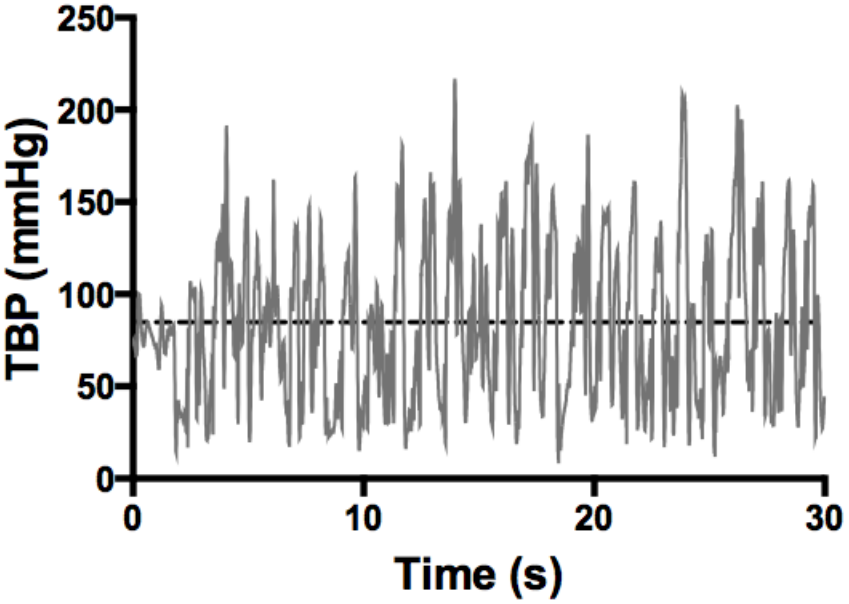

Figure 35. Walking at 4.8 km/hr, 0% grade with arm support. Dashed line depicts MAP_T. mmHg, millimeters of mercury; s, seconds.

The female participant's HR reached 58% HR_{max} while walking at 4.8 km/hr and a 5% grade while using arm support. However, during a six-minute walking trial, the Portapres® failed four times at four different walking speeds (Figure 36).

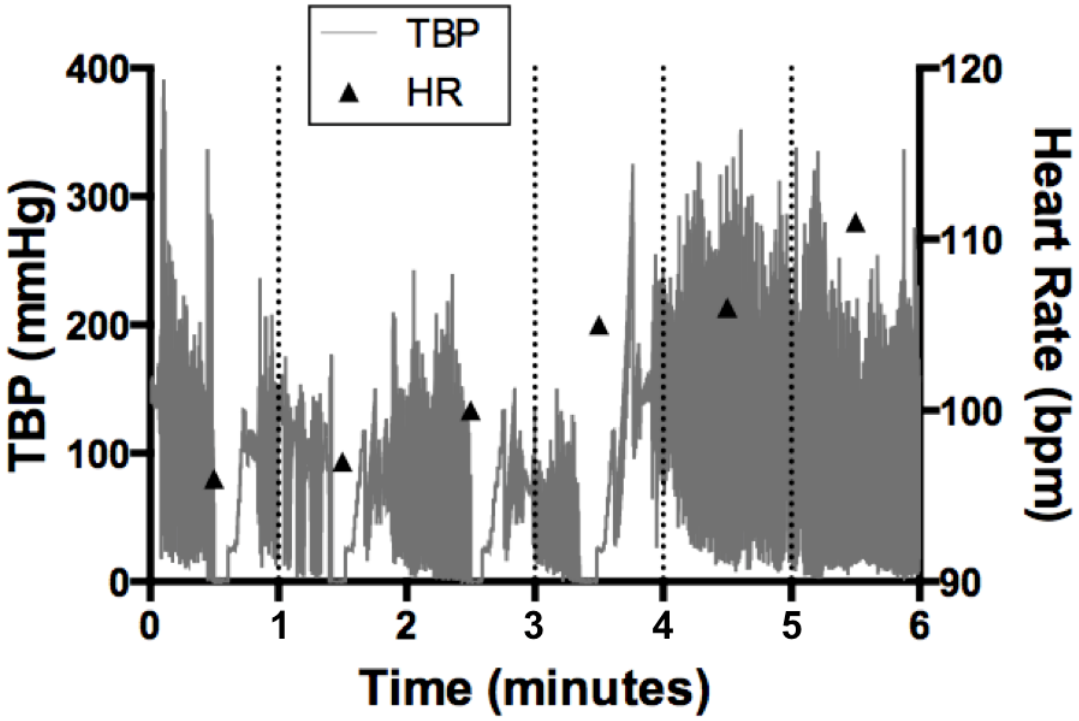

Figure 36. Walking at 2.7 to 4.8 km/hr, 5% grade with arm support. Dotted lines depict changes in treadmill speed. mmHg, millimeters of mercury; HR, heart rate; bpm, beats per minute; s, seconds.

4.6 TBP during Cycling

TBP was collected during cycling in 14 participants (9 Females, 5 Males) for all three cycling conditions (50H, 50L, and 90L). TBP was collected successfully in the 50H and 90L cycling conditions but not in the 50L condition for one additional female participant. Data from participants' 8 and 10 were excluded from any analysis involving the 50L data due to large variability and being much larger than their measurements during the other cycling conditions and during rest. All raw MAP_T, HR, and mechanical power data for each cycling condition is shown in Table 15. An example of TBP, MAP_T, HR, and toe kinematic (y-axis) data are presented for Participant #2 in Figure 37.

Table 15. Participants' mechanical power output (W), HR (bpm), and MAP_T (mmHg) data for cycling conditions.

Participants	50H			90L			50L		
	Power	HR	MAP_T	Power	HR	MAP_T	Power	HR	MAP_T
1	195	119.5	76.7	170	119.3	53.2	170	104.1	49.3
2	130	120.1	58.1	80	117.6	50.1	80	101.4	38.9
3	72	126.0	30.6	36	130.3	24.4	36	113.0	31.3
4	87	113.7	77.2	70	116.4	68.6	70	106.8	43.6
5	105	122.5	167.9	90	122.2	164.3	90	110.3	131.6
6	135	119.0	131.0	120	117.4	95.0	120	110.5	72.4
7	95	112.5	129.6	75	113.7	96.1	75	107.2	123.9
8	63	126.0	76.7	35	126.0	47.0	35	109.0	91.7
9	62	122.2	64.7	45	119.7	94.1	45	112.6	45.4
10	80	120.3	69.9	57	121.2	39.7	57	102.3	130.3
11	60	122.3	86.3	30	122.0	85.0	30	99.8	69.5
12	105	119.2	100.3	57	118.7	100.1	57	98.1	58.1
13	80	128.2	133.0	48	127.3	140.5	48	106.0	123.9
14	117	110.7	53.8	94	106.0	72.4	94	101.3	64.5
15	60	121.1	92.9	33	118.1	72.7	NC	NC	NC
mean	96.4	120.2	89.9	69.3	119.7	80.2	71.9	105.9	76.9
SD	36.9	4.9	36.6	38.2	5.8	37.4	38.2	4.8	36.6

W, watts; bpm, beats per minute; mmHg, millimeters of mercury; NC, not collected.

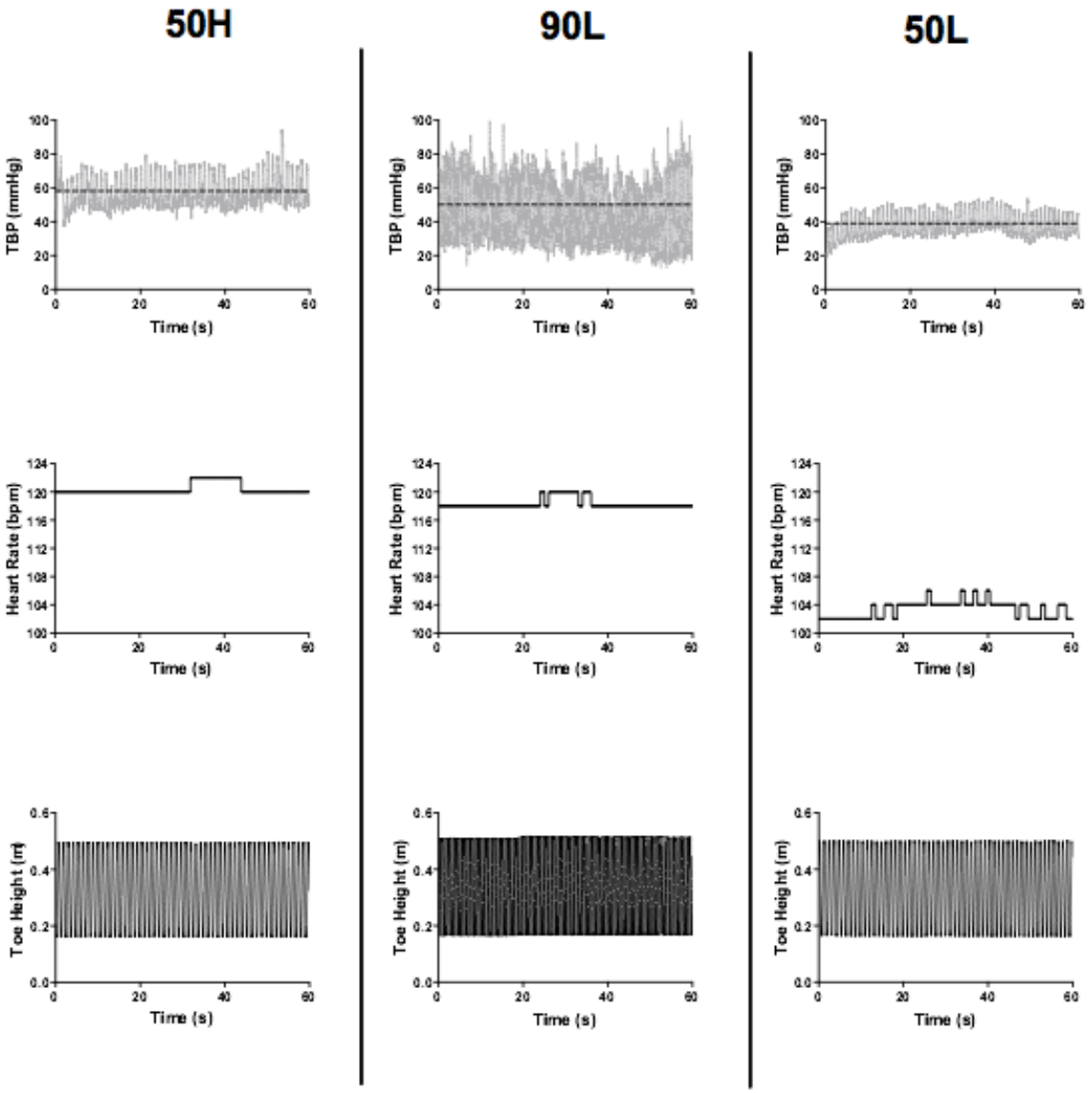

Figure 37. Participant #2 TBP, MAP_T, HR, and toe height for each cycling condition (50H, 90L, and 50L). mmHg, millimeters of mercury; bpm, beats per minute; m, metres; s, seconds; dashed line, MAP_T.

4.6.1 Effect of Cadence

MAP_T during the 90L condition (86.9 ± 38.4 mmHg) was significantly greater than MAP_T for the 50L condition (71.0 ± 35.6 mmHg; $P < 0.027$) in 12 participants (Figure 38, Panel A) at the same mechanical power output (119.7 ± 5 W; Figure 38B) and

a different HR ($P < 0.0001$; Figure 38C). MAP_T was greater in the 50L condition compared to the 90L condition for two out of 12 participants (Figure 38D).

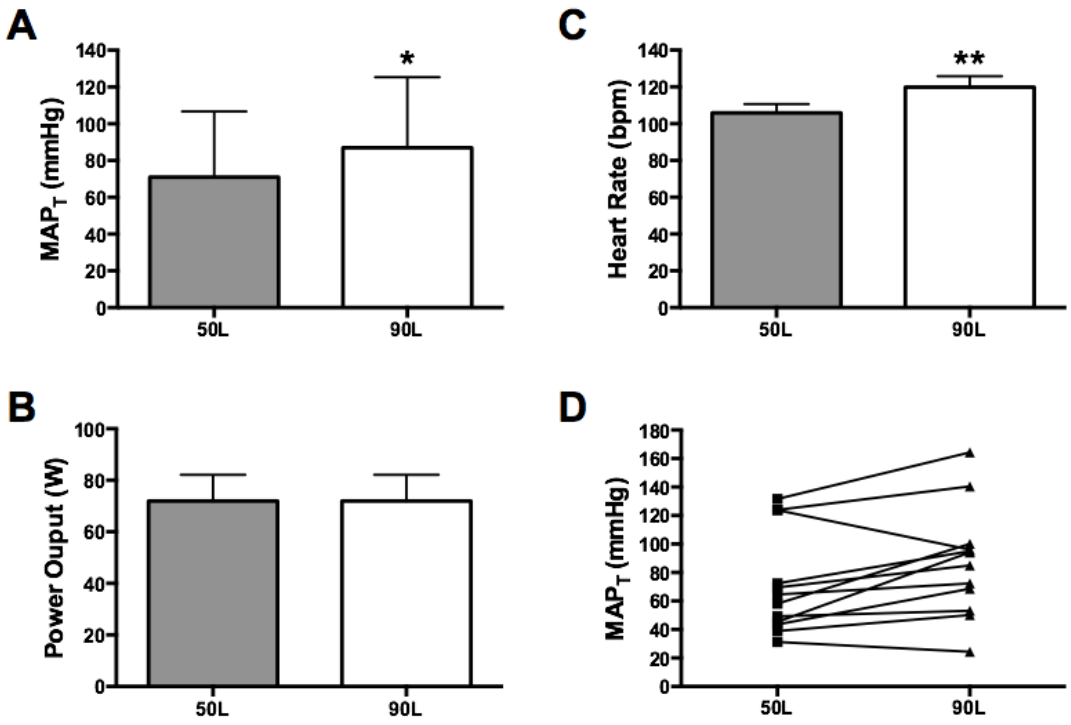

Figure 38. Mechanical Power Output controlled analysis (Panel A). 50L, 50 rpm-Low Mechanical Power Output; 90L, 90 rpm-Low Mechanical Power Output; *, $P < 0.05$. B. Power Output, C. Heart Rate, D. Individual MAP_T by condition; **, $P < 0.0001$.

4.6.2 Effect of Mechanical Power Output

MAP_T during the 50H condition (92.4 ± 40.5 mmHg) was significantly greater than MAP_T for the 50L condition (71.0 ± 35.6 mmHg; $P < 0.0049$) in 12 participants (Figure 39A) at the same cadence (50 rpm), a larger mechanical power output ($P < 0.0001$; Figure 39B), and a higher HR ($P < 0.0001$; Figure 39C). MAP_T was greater in the 50L condition compared to the 50H condition for two out of 12 participants (Figure 39D).

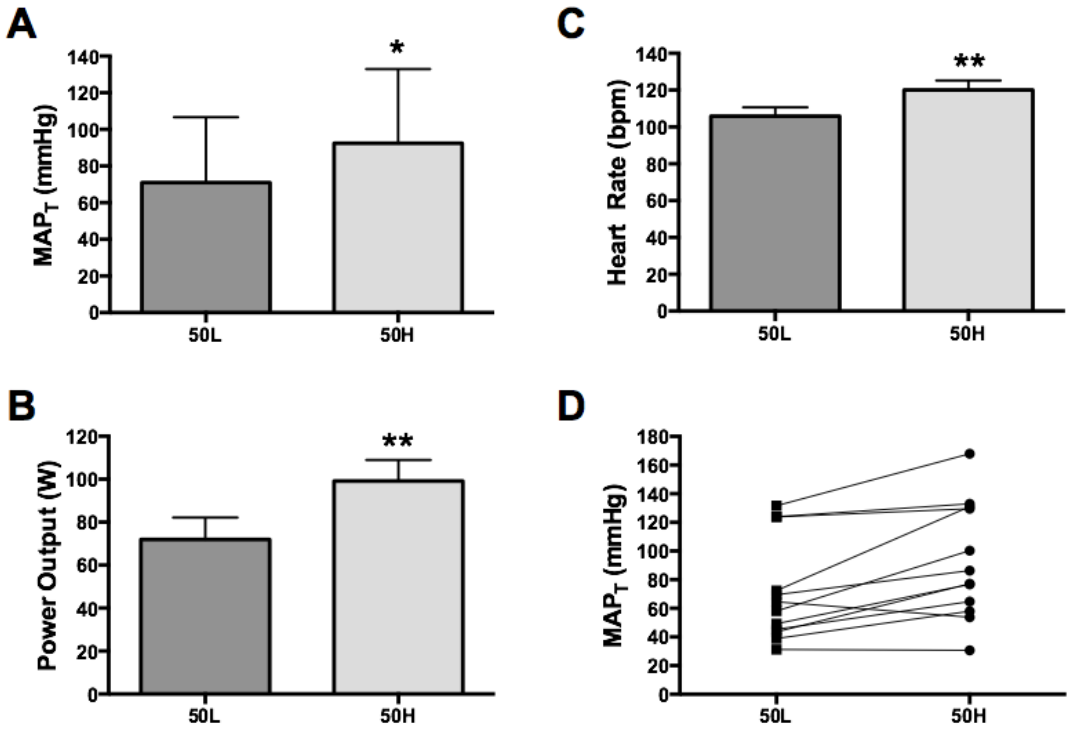

Figure 39. Cadence controlled analysis (Panel A). 50H, 50 rpm-High Mechanical Power Output; 50L, 50 rpm-Low Mechanical Power Output; mmHg, millimeters of mercury; *, $P < 0.01$. B. Power Output; W, watts C. Heart Rate; bpm, beats per minute. D. Individual MAP_T by condition; **, $P < 0.0001$.

4.6.3 Heart Rate Controlled

MAP_T during the 50H condition (89.9 ± 36.6 mmHg) was significantly greater than MAP_T for the 90L condition (80.2 ± 37.4 mmHg; $P < 0.0413$) in 15 participants (Figure 40A) at a different cadence (50 vs. 90 rpm), a larger mechanical power output ($P < 0.0001$; Figure 40B), and the same HR ($P > 0.05$; Figure 40C). MAP_T was greater in the 90L condition compared to the 50H condition for two out of 12 participants (Figure 40D).

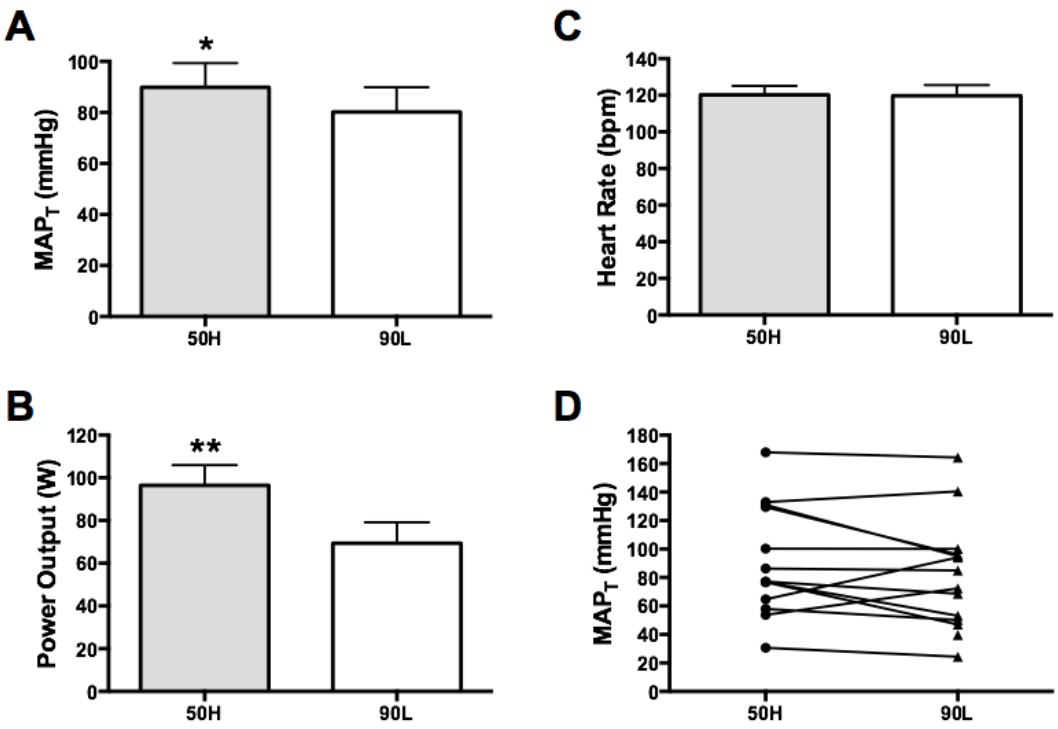

Figure 40. Heart Rate controlled analysis (Panel A). 50H, 50 rpm-High Mechanical Power Output; 90L, 90 rpm-Low Mechanical Power Output; *, $P < 0.05$. B. Power Output, C. Heart Rate, D. Individual MAP_T by condition; **, $P < 0.0001$.

4.6.4 Multiple Linear Regression

The multiple linear regression analysis showed no correlations between the independent variables and MAP_T. An r^2 of 0.076 was calculated, which means only 7.6% of the variance in MAP_T measurements can be explained. Correlations, significance levels, and descriptive statistics are shown in Table 16 below.

Table 16. Correlations, significance levels, and descriptive statistics of independent variables vs. MAP_T.

Variable	r	P	Mean ± SD	N
Cadence	0.043	0.398	63.33 ± 19.1	39
Power	0.193	0.120	0.80 ± 0.2	39
HR	0.031	0.425	0.39 ± 0.1	39
MAP_T	-	-	1.19 ± 0.5	39

r, product-moment correlation coefficient for the Multiple Linear Regression plots; SD, standard deviation; N, number of values analyzed; $P < 0.05$.

CHAPTER 5: DISCUSSION

The thesis had two aims. The first aim was to determine the validity and reliability properties of the Portapres® BP monitor for measuring TBP in non-disabled individuals. The second aim was to examine the changes in TBP occurring during cycling and walking.

Four experiments were completed using a Portapres® BP monitor in attempt to answer the primary research questions. The first aim of the thesis was explored in three ways. First, construct validity was determined by comparing the change in measured TBP to the expected change in TBP during slow cycling. The changes in TBP that occurred were due to the change in the orthostatic component within one revolution during cycling. Second, the concurrent validity of the Portapres® was determined by comparing the measured TBP to the brachial BP at rest and after a bout of cycling exercise. Third, the inter-day reliability of the Portapres® was determined by comparing Day 1 TBP values to Day 2 TBP values. The second aim of the study was explored by measuring TBP during three conditions of cycling exercise. Each condition had different effects on TBP due to their unique biomechanical characteristics (mechanical power output and cadence) and HR. Unfortunately no TBP could be collected during walking due to various problems that occurred with the TBP waveform (i.e., equipment errors, protocol, etc.).

The thesis was unique because of the use of the Portapres® to collect data on the toe. The thesis provided some interesting findings, which adds to the literature as only two other known published studies have used a similar BP recording device on the toe[16-17]. Both of the studies used the Finapres® during rest; therefore, it is believed that this

thesis was the first to collect TBP during lower-body exercise. Based on the results of the study, multiple implications can be made and are discussed below.

5.1 Construct Validity

The changes in TBP due to the change in toe distance from the heart during slow cycling had some variability. A kinematic analysis on six participants showed an average change in toe height from the top of the pedal crank to the bottom of the pedal crank to be 34 cm. A one-sample t-test showed that the actual mean of 28.75 mmHg was significantly different from a theoretical mean of 34 mmHg. The variability found in the results can be expected as human physiology can rely on multiple variables that are not present in controlled environments. The original hypothesis was that TBP would change in accordance with the change in distance from the toe to heart level. In a tube that is completely linear with a fixed diameter (i.e., a plastic tube filled with water) a change in height from heart level to the measurement site changes the internal pressure of the fluid in the tube ($P=\rho gh$). In a previous study, Rosales-Velderrain et al[17] compared the theoretical differences in TBP to the actual measured TBP and reported a correlation value of $r=0.87$. Their measurements were collected under static conditions, and apparent differences in theoretical and actual measurements were found (Figure 10). However, these differences were not quantified.

TBP in this study was expected to oscillate above and below the average toe to heart level distance during slow cycling (i.e., if the average toe to heart distance was 100 cm, then the average ΔTBP should be 100 mmHg). This was not seen in all cases, as

shown in the histogram of TBP values presented in Figure 26A. Panel A illustrates that the majority of TBP values were between 22.5 and 27.5 mmHg, but there were many TBP values above and below the expected value of 34 mmHg.

The variability within the TBP measurements is not completely understood; however, some suggestions can be made. First, the participants were instructed to keep a slow and steady cadence of six rpm during the one-minute Slow Orthostatic trial. At times, participants may have generated too much force on the pedal crank, which could have caused an increase in cuff pressure at the toe. If this happened then larger pressures would be expected. Although pedal force was not measured in this study, the toe position versus time graphs showed very little deviation from the expected toe position curve in six participants (Figure 27). Although kinematic data were not collected in all participants, it was believed that all participants followed the slow cycling instructions as best they could. As mentioned previously, if the researcher noticed the participant was cycling too fast (or too slow) then the corresponding TBP for that revolution was not used in analysis. It was important to exclude these TBP values as had a change in cuff pressure occurred due to a greater or lesser force on the pedal then there may have been more abrupt changes in toe kinematics, which would affect TBP. An example would be the amount of time different participants spent at the top or bottom of the pedal crank compared to their counterparts. Figure 27 (C and D) show the height difference from the toe to the heart over time. Panel C had a slightly steeper peak than Panel D, which may provide evidence that the velocity of the foot affected TBP. Panel C shows a ΔTBP of ~30 mmHg, where Panel D only shows a ΔTBP of ~22 mmHg. Again this was only a possibility as there was only a difference of ~1 second between the participants at the bottom position of the pedal crank.

Second, pulse pressure may have played a role in ΔTBP compared to foot height. Panel A and B of Figure 27 shows the best and worst cases of ΔTBP during the Slow Orthostatic trials for two participants. One noticeable difference in the raw TBP waveform is that the TBP in Panel A has a very large and pronounced pulse pressure, whereas Panel B shows a very small pulse pressure. The pulse pressure is the difference between the systolic (maximum) and diastolic (minimum) blood pressures in one heart contraction. The large pulse pressure difference between participants could be due to the Portapres® BP cuff being misaligned on the toe. The appropriate alignment of the photocell and lamp is essential in measuring BP in an artery (Figure 41).

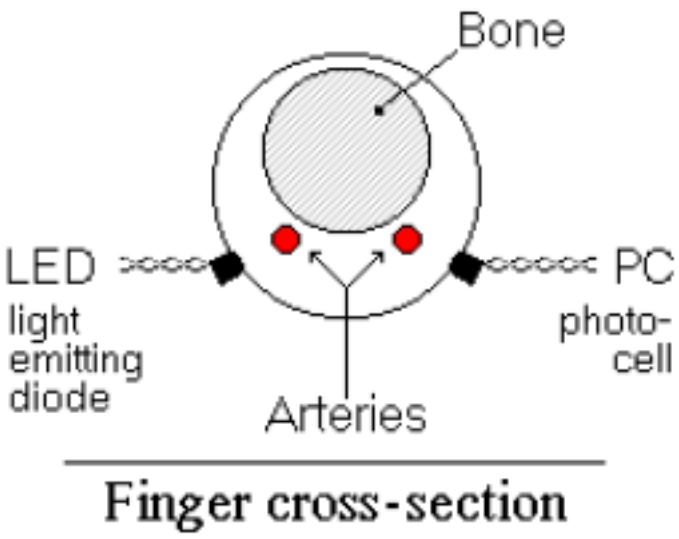

Figure 41. A frontal view of the appropriate cuff position on a finger for reliable BP measurements using the Portapres® device[68].

If the BP cuff was misaligned on the toe during the worst case (Figure 27A) and only a portion of the light travelled through the plantar digital arteries then the BP values would have been underreported. For example, if more light is being detected during systole and diastole due to the fact the light did not travel through the entire artery, then

the absolute BP values would be less because the Portapres® would believe there is less blood volume in the arteries. In the same situation pulse pressure would not be affected, as both systole and diastole would be equally underreported. However, it has been shown that the diameter of peripheral artery's increase during systole and decrease during diastole[69] (Figure 42). Therefore, if the arteries were larger during systole more light would travel through the arteries; whereas less light would travel through the arteries during diastole, which would affect pulse pressure.

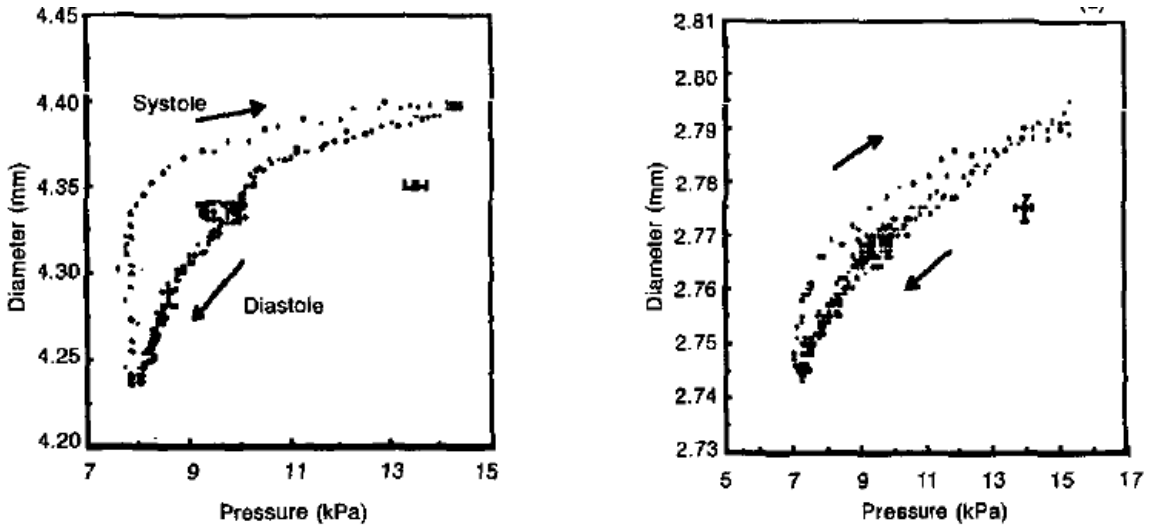

Figure 42. Figures showing how a typical brachial artery (left) and radial artery (right) diameters change during systole and diastole[69]. mm, millimeters; kPa, kilopascal; arrows, direction of systolic and diastolic BP during one cardiac cycle.

Again, the purpose of measuring the change in toe height vs. ΔTBP was to see if the Portapres® showed construct validity. The results of the study show that the Portapres® had some measurement error (~5 mmHg) when measuring TBP using the study's protocol. One of the goals with slow cycling at six rpm was to see any changes in TBP that were due to systolic and orthostatic forces. The systolic force was mostly attenuated from the raw TBP waveform by filtering, and was therefore believed to have

very little effect on the TBP measurements during slow cycling. That said it was hard to predict how much of an effect slow movement (six rpm) had on acquired TBP values. Future studies should look into better ways to control for movement artifact when measuring the effect of the orthostatic force on TBP. Only one other study had looked at how a change in toe height from heart level affected TBP using a Finapres® device. However, a comparison of our data and the data from the study by Rosales-Velderrain (2011) cannot be accurately made, as the researchers used a Pearson-product moment correlation to analyze their data. Correlations are not the appropriate method to compare measurements as mentioned in the literature review section of this thesis.

5.2 Concurrent Validity

One of the primary goals of this research was to determine if the Portapres® could provide valid and reliable BP measurements on the toe. It was important to compare the TBP values collected in this study to TBP values collected by others to determine their normalcy. Sahli et al[46] collected TBP values from the first toe in 134 healthy control participants (49.5 ± 11.7 years) while they rested supine. The group placed a pulse oximeter sensor to measure the pulse signal on the tip of the first toe, and a Criticon™ BP cuff on the proximal portion of the toe. With the use of a sphygmomanometer, the cuff pressure was inflated to occlude blood flow, and then slowly released until the pulse returned. The pressure at which the pulse reappeared was deemed the systolic TBP of the first toe (to the nearest 2 mmHg). The group found the mean systolic TBP to be 121 ± 2 mmHg in the healthy participants, with a mean systolic brachial BP of 131 ± 2 mmHg and diastolic brachial BP of 80 ± 2 mmHg. The mean systolic TBP values at rest recorded

for this thesis was 99.4 ± 18.9 mmHg, or ~20 mmHg less than the TBP in the study by Sahli[46]. The mean brachial systolic and diastolic BP for the current study were 112.9 ± 10.7 and 63.6 ± 5.4 mmHg, or 19 and 17 mmHg less, respectively. The decrease in BP and TBP values between studies could be due to the obvious age difference in participants or that 11.9% of their participants were smokers. Since similarly smaller brachial and TBP values were observed in the present study, compared to the Sahli[46] study, it gives confidence that this thesis' participants TBP values at rest were accurate.

An interesting finding was that diastolic BP at rest had proportional and fixed bias when calculated using both the OLP and Bland-Altman techniques. That said there was no fixed or proportional bias in systolic BP values, and only fixed bias in MAP values when using the OLP technique. The reason MAP had fixed bias can be explained by the fact MAP was calculated using an equation that relied more heavily on diastolic than systolic pressures. MAP was calculated using Equation 4, where it was equal to diastolic pressure plus one-third of pulse pressure. Therefore, there was more of an effect on MAP due to diastolic BP compared to systolic BP, which in turn caused the bias to be transferred to the MAP analysis. Overall, it can be concluded that there was fixed and proportional bias present in the diastolic BP values at rest, but it was important to understand how the data were calculated before relying on statistical analyses.

The second portion of the concurrent validity results showed that brachial BP increased in all but one participant after exercise compared to before exercise (50H condition), whereas TBP increased in 5 participants and decreased in 11 (Figure 31). This finding was interesting because our results were similar to the results of a study by Desvaux et al[70]. The group measured ankle and brachial systolic BP in 15 trained and 15

untrained participants aged 14 to 30 years before and after maximal cycling exercise. Both groups completed an incremental cycle ergometer test until exhaustion (untrained: 260 W, 41.5 ± 4.0 ml $O_2 \bullet kg^{-1} \bullet min^{-1}$; trained: 330 W, 58.4 ± 2.8 ml $O_2 \bullet kg^{-1} \bullet min^{-1}$). Ankle and brachial BP in both legs and both arms were measured once every minute for three minutes prior to cycling, and once per minute for the first ten minutes (i.e., 1st, 2nd, 3rd,…,10th minute after exercise) and once every two minutes until the 30th minute after cycling (i.e., 12th, 14th, …, 30th minute after exercise). The group found that ankle systolic BP decreased in untrained participants from 132.3 ± 23.0 mmHg before exercise to 126.3 ± 22.7 mmHg one minute after exercise. However, trained athletes ankle systolic BPs slightly increased one minute after exercise (148.9 ± 28.7 mmHg) compared to before exercise (143.1 ± 9.0 mmHg). Interestingly, systolic BP also eventually decreased in the trained group two minutes after exercise. The brachial BP data from the Desvaux et al[70] study were similar to the current study, as both of their groups increased their brachial BP from before exercise compared to after exercise (untrained: 123 ± 20.6 to 170.2 ± 23.4; trained: 121.9 ± 14.5 to 186.5 ± 17.0 mmHg).

Although interesting, the training effect found in the Desvaux et al[70] results were not replicated in the current study. The five participants who had an increase in TBP after exercise had an average resting HR of 67bpm whereas the 11 participants who had a decrease in TBP after exercise had an average resting HR of 62bpm. If trained versus untrained status is based on resting HR, this study's results are the opposite of the Desvaux et al[70] study. One limitation to their study was that the group did not report any mechanisms to explain their results besides mentioning that the decreased ankle systolic BP response was probably due to changes in HR and vascular resistance post-exercise.

Another notable finding of the thesis was how the difference in toe and brachial MAP changed after exercise in relation to the sum of the MAP for the same two measurement sites at rest (Figure 43). A trend occurred and showed that the difference in MAP between the brachial and toe sites increased more after exercise in participants who had greater total body resting MAP (i.e., an average of brachial and toe MAP). An OLP analysis was also applied to the data in Figure 43, and a slope (b′) of -1.87 and a y-intercept (a′) of -123.8 were calculated. The 95% CI for the b′ was -0.4 to 3.4 meaning there was proportional bias, and the 95% CI for a′ was -235.5 to -12.0 meaning there was also fixed bias present in the data.

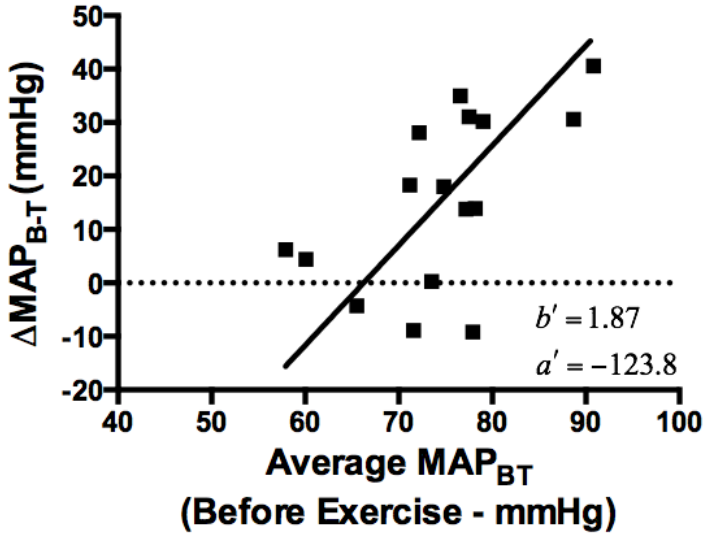

Figure 43. The change in brachial and toe MAP after exercise compared to before exercise (ΔMAP_{B-T}) versus the average resting MAP. (MAP_{BT}). mmHg, millimeters of mercury; Δ, after minus before exercise MAP; $_B$, brachial; $_T$, toe; a′, y-intercept; b′, slope.

Although the mechanisms behind this finding are not understood, it is interesting as it gives preliminary evidence that differences between upper and lower body

measurement sites become larger when there is a greater average resting MAP between the two measurement sites.

5.3 Inter-day Reliability

Although statistical analyses only showed one case of proportional bias within the inter-day TBP data, the limits of agreement in the TBP measurements (Figure 33, Panels A-C) were much larger than the limits of agreement for the brachial BP measurements (Figure 33, Panels D-F). Widmer et al [48] reported that an acceptable limit of agreement in clinical practice for two TBP measurements is 10 mmHg. As mentioned, the limits of agreement in this study were much larger than 10 mmHg (i.e., 50 to -40 mmHg), and can be attributed to multiple reasons. First, the possibility of equipment error is always a concern when testing new equipment, or old equipment for a new purpose. Therefore, there is a chance that some, if not all of the large TBP limits of agreement are due to the Portapres® being used improperly, or not collecting TBP from the intended plantar digital artery.

Unfortunately, no other published studies have investigated reproducibility of TBP measurements in a healthy population. However, a study by de Graaff et al[44] looked at the one-week reproducibility in TBP measured using LD, and PPG techniques in 60 patients that were at-risk for vascular disease. The group filtered LD data using two different methods (LD_3: 3 seconds; $LD_{0.03}$: 0.03 seconds) to detect changes in blood flow (LD_3) and heart beats ($LD_{0.03}$). Their results showed limits of agreement that were well above 10 mmHg as well (LD_3: -27 to 34; $LD_{0.03}$: -24 to 34; and PPG: -29 to 36), and were comparable to results of this thesis. It would be expected that the limits of agreement for

an at-risk population would be much lower than a normal population; given the fact the TBP measurements in their participants were approximately 60 mmHg. Lower limb BP is typically lower in cardiovascular patients compared to healthy controls due to arterial occlusion in the form of atherosclerosis in their vessels. The level of occlusion is typically in the calf area, which is above the level of the TBP measurement[71]. According to Equation 1, less blood flow to the toe would decrease TBP as well, as long as vessel resistance in the toe remained the same. If correct, this concept would mean low TBP values also lead to less room for variability and therefore lower limits of agreement[44, 72]. The limits of agreement found using healthy participants in this thesis seem to be more appropriate compared to the de Graaff et al[44] results when using this evidence. However, this does not mean the Portapres® is ready to be used on a clinical or healthy population.

When comparing the current study to similar studies it is important to keep in mind how many participants were tested in the other studies. For example, the limits of agreement in a Bland-Altman analysis largely depend on the amount of participants that were included in the analysis, as the limits of agreement were calculated by the mean of differences ± 1.96 × standard deviation (SD) of the differences. The standard deviation was calculated by the equation:

Equation 9: $$SD = \sqrt{\frac{\Sigma(x - \bar{x})^2}{n-1}}$$

where x is a TBP value, $\bar{x}$ is the sample mean, and n is the number of participants. According to this equation when n increases the SD decreases, which therefore causes the limits of agreement to decrease. The inter-day reliability portion of this thesis only included 16 participants where another similar study included 60 participants[44]. Future

studies should consider recruiting more participants, as the strategy could give more appropriate results simply due to a larger sample size.

The significance of these findings is that the Portapres® cannot, at this time, be used to measure TBP in a clinical population until it can provide better inter-day reliability (i.e., lower limits of agreement between measurements on separate days). For example, according to the TBP values found using our methods, a group of PAD patients taking part in an exercise intervention study over an extended period of time would have to provide very large changes in TBP (i.e., more than 45 mmHg) to show any sign of benefit form the exercise. The large amount of change in TBP is probably not feasible in a disabled population considering they have very low TBP to begin with. Therefore, it would not be appropriate to expect such large changes in this population due to exercise.

To conclude, a study with a different testing protocol and more participants may provide better results than the current study's methods. Future studies should investigate other measurement protocols to increase inter-day reliability with the Portapres® in attempt to lower the limits of agreement so PAD detection and rehabilitation progress can be measured using the device.

5.4 Feasibility of Portapres® during Locomotion

A major part of this research was to determine whether the Portapres® could measure TBP during rest and locomotion. The two modes of exercise that were to be investigated were walking and cycling. The reason for investigating the selected modes of

exercise was due to their prevalence in rehabilitation of cardiovascular patients. Walking and cycling are common exercises due to their effectiveness in increasing perfusion pressure to the lower limbs in a population affected by PAD[11]. It was originally hypothesized that cycling would elicit greater TBP compared to walking because of the greater lower limb angular accelerations present during the cycling motion. The original goal of the research was to match walking and cycling exercise intensities to compare the TBP values associated with each type of exercise. However, early in the data collection phase of the project it became apparent that acceptable TBP values could not be collected during walking. Many modifications to the footwear were made to enhance the probability of successfully collecting TBP values during a normal gait cycle; however, very little success ensued.

All participants attempted to walk with the Portapres® on their toe and various forms of footwear including the DARCO wedge shoe. Although the DARCO wedge shoe allowed for more TBP collection during walking compared to barefoot or sandal trials, it did not allow for TBP collection at sufficient exercise intensities to include in analysis. For example, in an exploratory walking test on one female participant (Figure 36) the Portapres® encountered errors four times in a six minute trial. The participant walked at speeds of 2.7 to 4.8 km/hr, and at a 5% grade with arm support and only reached ~50% of her HR_{max}. In order to collect continuous TBP data without experiencing errors the participant would have had to exercise at a much lower workload, which would not have been a sufficient intensity to compare to cycling TBP values.

In addition to body weight support by the treadmill arm railings, it was believed that the wedge shoe did reduce reaction forces from the ground onto the toes during

walking, which in turn allowed for small amounts of TBP collection at lower walking speeds. Also, the wedge shoe and an increased walking grade altered gait mechanics compared to flat ground walking; however, this would not be typically replicated in a disabled population. The increased walking grade was required to shift the participant's center of mass towards the posterior of their foot and body, which reduced pressure on the forefoot and toes. This modification showed minimal effectiveness.

No published articles were found on impact affecting Portapres® BP waveform collection. This was probably because the Portapres® was not made for use in situations where impact may occur. One study by Imholz et al[73] tested the feasibility of the Portapres® on the middle and the annular fingers of 8 normotensive and 16 hypertensive participants over a 24 hour time period. The participants were asked to follow a strict regimen in a hospital setting, which included rest, exercise (i.e., cycling at 50 W and 50-60 rpm, walking), and daily living activities to determine how the Portapres® reacted to different, everyday stimuli. The group found that the Portapres® was able to provide continuous, non-invasive ambulatory finger BP waveforms during all conditions with very few interruptions. They reported that only 249 minutes of BP data were lost due to movement, out of a total of 34,556 minutes of collected data. They also reported that two out of six normotensive participants had a marching artifact in their finger BP data while walking. They believe the artifact was due to the oscillation of the hand during the walking motion. Imholz et al[73 (p 65)] also reported that 'avoiding brisk hand movements resulted in fewer waveform artifacts'. They mentioned that there were no artifacts in the BP waveform during cycling, which was probably due to the fact the hand was stationary during the lower-limb movement. Overall, it seemed from the study's findings that the

Portapres® was able to withstand light movement during testing, but again, no impact on the pressure cuffs was described.

Future research using the Portapres® BP monitor on the toe should investigate the possibility of creating a toe BP cuff. A more rigid and protected cuff may be able to withstand more movement and impact compared to the generic finger cuffs. Large impacts could possibly rotate the BP cuff, which could cause the light source in the cuff to miss the intended artery. Again, it is important to reiterate the Portapres® was not created for use on the toe, therefore most problems in TBP data collection can be attributed to using a piece of equipment for something it was not intended to be used for.

Measuring TBP using the Portapres® was much more feasible during cycling in comparison to walking. This can be attributed to the cycle ergometer's adaptability and due to less reaction forces acting on the toes. For example, the cycle ergometer's right pedal was wrapped with a sponge-like cushion to allow the participant to reduce the amount of force being transferred to the foot and the toes. Also, all participants were able to maintain an appropriate cadence with their foot placed anteriorly on the pedal so that the toes were not in contact with the pedal (i.e., midfoot to rearfoot contact).

5.5 TBP during Cycling

The final portion of the thesis investigated how TBP reacted due to cycling at different cadences, mechanical power outputs, and heart rates. Fifteen participants completed the cycling protocol of the study. The protocol included three conditions that elicited different physiological effects, which provided some interesting findings.

Originally it was not known how the Portapres® would react to high velocity limb motion. Therefore, reliability, validity, and feasibility experiments were completed to determine the measurement properties of the Portapres® when measuring TBP. The experiments provided various results that were discussed in detail above. If the possibility of equipment errors is ignored the results from the cycling portion of the thesis can possibly be explained. Before discussing the effect of the cycling conditions on MAP_T it is important to discuss why MAP_T decreased during exercise compared to resting MAP_T values.

It was expected that MAP_T would increase during exercise for all cycling conditions. This expectation was not seen as MAP_T decreased during cycling compared to resting MAP_T. This was interesting because it is well known that cardiac output (Q) increases during exercise, which is one way to increase MAP[74-75]. This concept can be related back to Equation 1, which was explained in the literature review of this thesis. The equation simply states that MAP can only increase due to an increase in Q or an increase in TPR or both. Although Q was not measured in this research; it can be assumed that it increased during exercise from rest due to the increase in HR, which was seen in all participants. Therefore, according to the equation above, the only way for MAP to decrease is for a subsequent larger decrease in TPR, which would be required to outweigh the increase in Q. Past research has shown an increase in arterial compliance[76-77] and vascular conductance[75] after cycling exercise, which would decrease TPR, and could have caused the decrease in MAP_T that was seen in the results.

A decrease in lower limb MAP due to cycling exercise has been observed before, and was discussed in the concurrent validity portion of this discussion[70]. Another study published by Desvaux et al[78] measured ankle and brachial systolic BP in normal subjects

before and one-minute following maximal exercise on a cycle ergometer. The group used a similar exercise protocol as their other study[70] as participants again cycled to exhaustion. Brachial and ankle (postero-tibial) systolic BP measurements were collected using the oscillometric method by four automatic sphygmomanometers on both arms and both legs. The group found brachial systolic BP significantly increased ($P < 0.005$) from 123.0 ± 12.1 mmHg at rest to 149.6 ± 16.5 mmHg one-minute following exercise; whereas ankle systolic BP significantly decreased ($P < 0.05$) from 127.7 ± 11.7 mmHg at rest to 110.4 ± 7.5 mmHg one-minute after exercise. Interestingly, these BP findings occurred when HR was significantly greater ($P < 0.005$) after exercise (112.4 ± 19.6 bpm) compared to before exercise (72.8 ± 12.2 bpm). The results of the Desvaux et al[78] study provide more evidence that the decrease in MAP_T seen during the 50H, 90L, and 50L conditions of this study are accurate.

Due to the lower MAP_T values during cycling, two exploratory tests were completed to learn more about how TBP acted during rest and during various body positions and cycling movements. One female participant (21 years, 1.71 m, 66.3 kg) completed two exploratory cycling tests after previously signing the study's Informed Consent and PAR-Q forms. During the first exploratory cycling test #1 (Figure 44), the participant came to the lab and rested supine for five minutes. The participant was equipped with a Portapres® BP cuff on the second toe of her right foot. She began the test by resting supine on a clinician's bed for an additional 45-seconds, where MAP_T was 71.0 mmHg. She then sat on a cycle ergometer (VELOtron, RacerMate® Inc., Seattle, WA) with the seat at 100% greater trochanter height, and positioned her foot at the bottom of the pedal crank for 30-seconds. The position produced a MAP_T of 135.4 mmHg. The participant then cycled one-half revolution and sat with her foot at the top of the pedal

crank for another 30-seconds, which produced a MAP_T of 118.8 mmHg. She then cycled at 50 rpm for one minute and 30 seconds at a mechanical power output of 50 W. Cycling at that intensity produced a MAP_T of 103.9 mmHg, and a range in TBP of 71.4 to 147.7 mmHg. After cycling, the participant rested on the cycle ergometer for another 45 seconds with her foot at the bottom of the pedal crank. MAP_T during this time was 86.9 mmHg, which was 48.5 mmHg less than the measured MAP_T when the participant was at the same position prior to cycling. Finally the participant rested supine for the remaining one minute of the exploratory test. The resting MAP_T was 45.0 mmHg, and 26 mmHg less than the original rest period. The large peak in TBP at approximately 35 seconds (Figure 45) was due to the GRF from the participant's foot when transferring from the bed to the cycle ergometer.

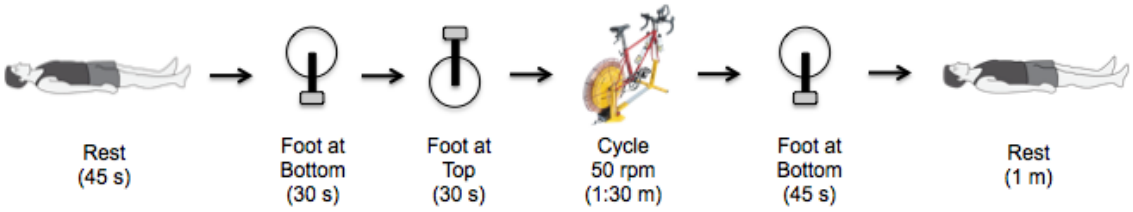

Figure 44. A visual representation of the first exploratory cycling test. s, seconds; m, minute.

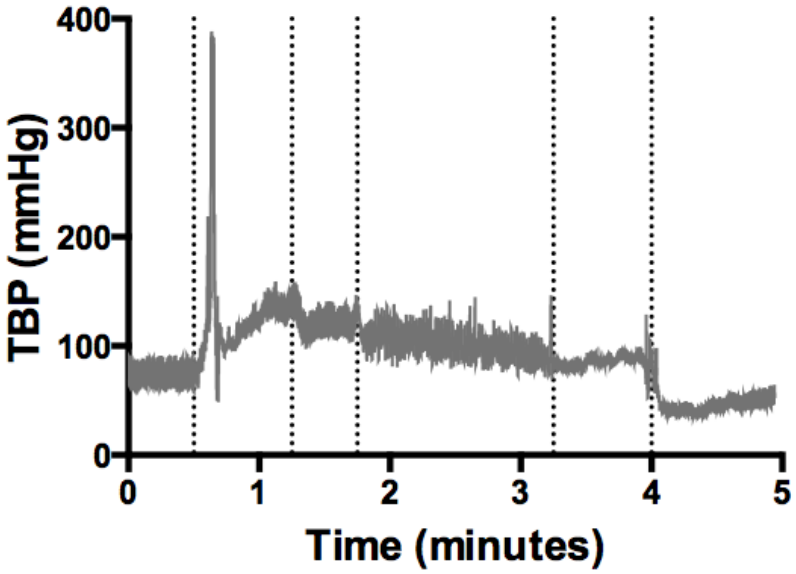

Figure 45. TBP data from cycling test #1 during various body positions and motions (dotted lines). mmHg, millimeters of mercury; rpm, revolutions per minute.

A similar protocol was followed for a second exploratory cycling test (Figure 46). The same female participant rested supine for one minute, and a MAP_T of 87.8 mmHg was recorded. The participant then stood up from the bed and sat on the cycle ergometer with the seat at 100% greater trochanter height. For one minute and 15 seconds the participant sat on the cycle ergometer with her foot at the bottom of the pedal crank. A MAP_T of 139.8 mmHg was produced during this time frame. The participant then cycled one-half revolution and sat with her foot at the top of the pedal crank for another one minute and 15 seconds (MAP_T = 141.3). The participant then cycled at 50 rpm for two minutes and 45 seconds at a mechanical power output of 50 W. The participant's MAP_T was 84.3 mmHg when cycling at 50 rpm. The participant then increased their cadence and cycled at 70 rpm for one minute and 15 seconds at a mechanical power output of 50 W, which produced a MAP_T of 61.4 mmHg. After cycling for 4 minutes the participant rested on the cycle ergometer for two-minutes with her foot at the bottom of the pedal crank

(MAP_T = 74.1 mmHg; minimum: 60.3 mmHg; maximum: 92.1 mmHg). The participant then returned to the clinician's bed and rested for one minute (MAP_T = 41.4 mmHg). The peak in TBP at one minute, 15 seconds and ten minutes, 15 seconds was due to a GRF produced when the participant transferred from the bed to the cycle ergometer and vice versa (Figure 47). The large peak in TBP at four minutes, 30 seconds was due to the reaction force of the pedal onto the foot when beginning to cycle (Figure 47).

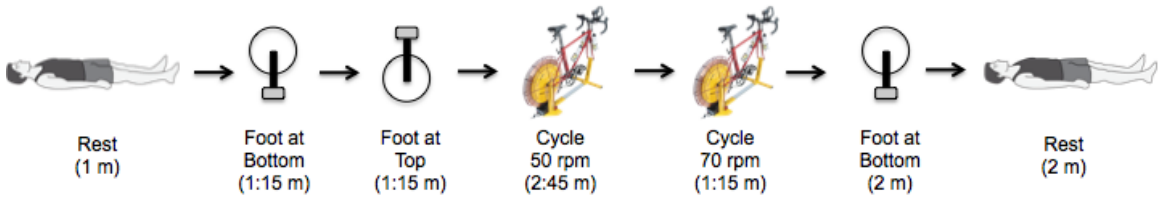

Figure 46. A visual representation of the second exploratory cycling test. m, minutes.

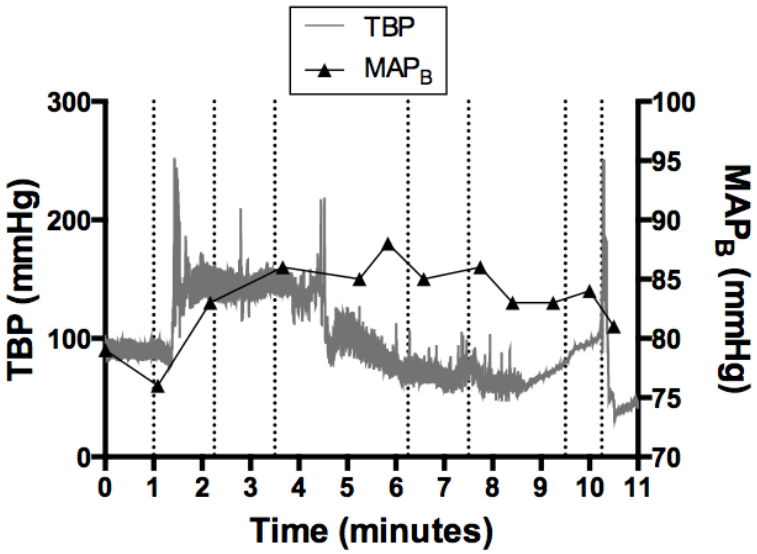

Figure 47. TBP and Brachial mean arterial pressure (MAP_B) data from cycling test #2 during various body positions and motions (dotted lines). Black triangles depict brachial MAP at various time points. Grey lines depict TBP. mmHg, millimeters of mercury; rpm, revolutions per minute; MAP_B, Brachial Mean Arterial Pressure.

The TBP waveforms from the exploratory tests clearly show that MAP_T decreases during cycling. Another interesting finding is that pulse pressure after cycling is much less than pulse pressure prior to cycling. This can be due to Portapres® error, or vessel characteristics caused by exercise.

5.5.1 Effect of Mechanical Power Output

If the TBP values are in fact accurate one of the study's hypotheses can be verified, as TBP was expected to be elevated when the mechanical power output during cycling was greater. Statistical analysis showed that the 50H condition provided significantly greater TBP values compared to the 90L and 50L conditions. It can be argued that HR was greater during the 50H condition compared to the 50L condition as well; however, according to the Desvaux et al[78] study outlined above HR does not always have as great of an effect on MAP. The HR effect was not explained, but could be due to vessel characteristics (i.e., diameter); however more research is needed on this topic.

Furthermore, the external mechanical power output during cycling is measured in Watts, and is defined as the amount of mechanical work (in Joules) over the amount of time (in seconds) it takes to produce the work. The internal mechanical power is defined as the summation of all joint net moments of force multiplied by the joint angular velocities for all articulations involved in the motion[50], and is directly related to metabolic cost (i.e., total energy expenditure)[79]. Gross mechanical efficiency can be calculated by dividing mechanical energy (Joules per minute) by the total energy expenditure, and has been shown to depend on cycling experience in the past[79-80]. A study by Pierre et al[79]

found that gross efficiency was higher (15% versus 11%) while cycling at a low cadence (40 rpm) and a high power output (80 W) compared to a low cadence (40 rpm) and low power output (40 W) in 14 healthy male participants (Figure 48). They also found that gross efficiency was higher (11% versus 6.5%) when cycling at a low cadence (40 rpm) compared to a high cadence (100 rpm) at the same power output (40 W) (Figure 48).

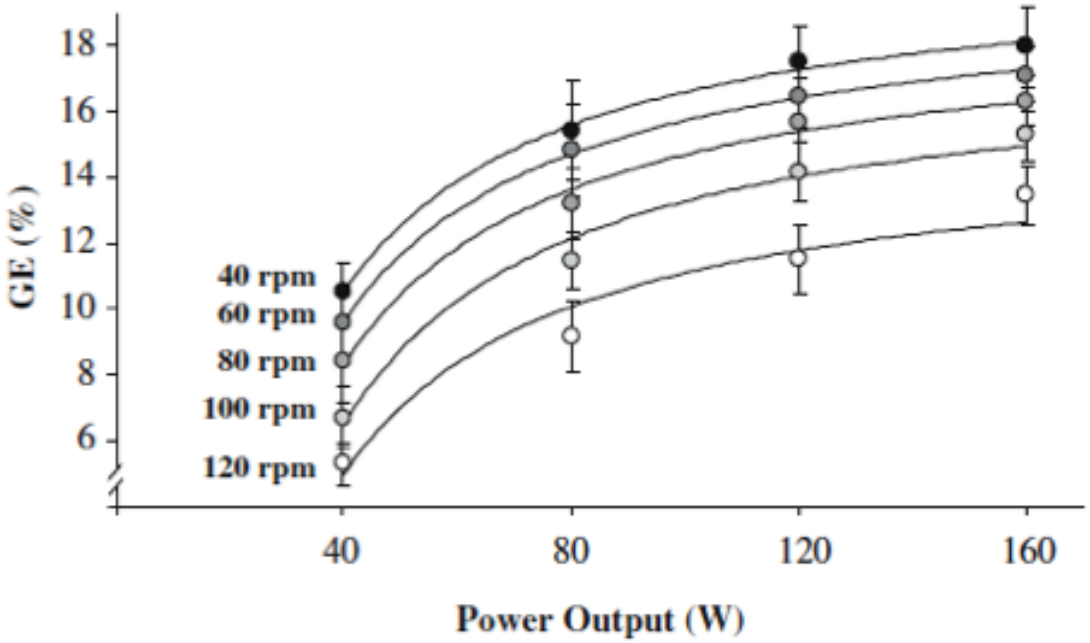

Figure 48. Gross efficiency (GE) versus power output (W) at different cycling cadences. Circles denote mean value at different cadences (different coloured circles) [79]. Error bars, standard deviation; W, watts; rpm, revolutions per minute.

The cadences used by Pierre et al[79] (40 and 100 rpm) are similar to those used in the thesis protocol (50 and 90 rpm) and important inferences from this comparison can be made. The results from the Pierre et al[79] study shows that the 50H condition of this study is the most efficient condition (15%), whereas 90L would be the least efficient condition

(6.5%). That said, the relationship does not explain why HR was higher in the 50H condition compared to the 50L condition, as it would be expected the 50L condition would have the higher HR due to its lower efficiency. The 50H condition produced more power (4800 Joules per minute; J/min) compared to the 50L condition (2400 J/min), but required 50% more energy to do so, therefore an increase in HR was required (Figure 49). The same can be said for why 90L produced a greater HR, as although the 90L and 50L conditions both produced 2400 J/min of power, the 90L required 75% more energy (Figure 49).

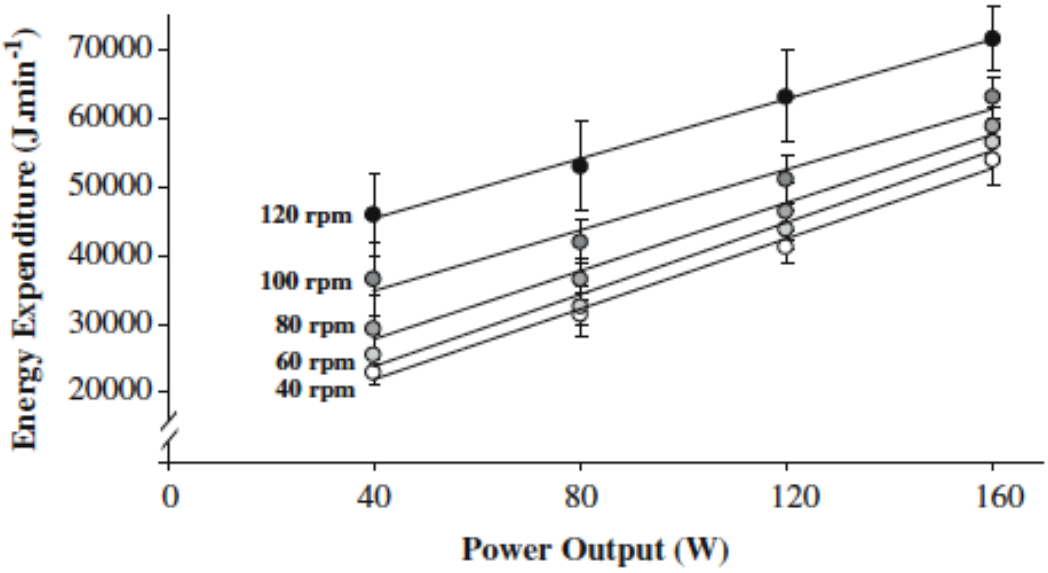

Figure 49. The change in energy expenditure due to increasing power output (W) and cadence (rpm)[79]. Circles denote mean value at different cadences (different coloured circles). Error bars, standard deviation; W, watts; rpm, revolutions per minute; J min^{-1}, Joules per minute.

The results from the Pierre et al[79] study show that there is an increase in energy expenditure when cycling at higher cadences compared to lower cadences while maintaining the same power output. The increase in energy expenditure requires more blood flow to meet the metabolic demand, which would increase MAP as per Equation 1

($\Delta P = Q \times R$)[81]. The equation shows that MAP would increase as long as the decrease in resistance (i.e., vasodilation due to nitric oxide release by the increased shear stress on the vessel endothelium) is less than the increases in blood flow in the active muscles.

5.5.2 Effect of Cadence

One of the main purposes of the study was to determine the effect of cadence on TBP. It was hypothesized that cycling at higher cadences would cause greater increases in TBP due to larger angular accelerations at the higher cadences. Data from the 90L and 50L conditions showed that TBP was significantly greater when cycling at 90 rpm compared to 50 rpm, and a greater TBP at the higher cadence was observed in 12 of 14 participants. HR was significantly greater during the 90L condition compared to the 50L condition even though the mechanical power output was the same. As mentioned, this increase in HR can be attributed to the increase in energy expenditure at the higher cadence, and it could be due to the increase in sympathetic nerve activity triggered by central command from higher brain centres. For example, HR being greater during a higher cadence compared to a lower cadence despite the same mechanical power output could be due to the increase in limb movement frequency. Central command has been found to be responsible for increasing respiratory rate and arterial blood pressure in paralyzed cats simply due to increasing limb movement frequency[82]. The respiratory coupling with limb movement frequency has also been seen in humans and other mammals[83-84] as well. Arterial blood pressure could also be increased due to the increase in mechanical activity within a muscle. Group III muscle afferents are excited when there are increases in pressure, vibration, and stretch within an active muscle, as noted in the

literature review section of this thesis[24]. Therefore, if a limb is moving at an increased frequency there could be an increase in mechanical stimuli within the muscle, which could cause an increase in HR and SV due to the exercise pressor reflex.

A comparison can be made when looking at the difference in TBP between cycling cadences in this study to the results from the Ewig[15] study. Ewig[15] found an increase of approximately 4 mmHg in simulated arterial BP at the shank level when increasing cadence from 50 to 90 rpm. The increase of 4 mmHg at the mid-shank level is completely due to movement and orthostatic related forces, and is about four times less than the increase of 16 mmHg at the toe level between the 50 and 90 rpm cadences in this study. It can be expected that the increase in TBP would be greater than shank pressures due to greater movement related forces at the toe. This can be attributed to the angular accelerations being greater at toe compared to the shank during the cycling motion[15]. Furthermore, systolic and diastolic BP fluctuations were clearly visible in the toe during rest in this study; therefore it can be believed that the systolic force would be present during exercise as well. The systolic force would be nonexistent in a water tube, which was used in the Ewig[15] study. For these reasons it can be believed that the increases in TBP are partially linked to movement related forces.

5.5.3 Multiple Linear Regression

A multiple linear regression was also used as a method of statistical analysis to determine the effect of cadence, mechanical power output, and HR on TBP. Unfortunately, the regression results did not provide any insight into how each of the

independent variables explains TBP during cycling. An r^2 value of 0.076 was calculated, which meant the model could only explain ~8% of the data. Any variability in the TBP data would affect the linear regression results and this can partly be due to the low number of participants in the study. Regression models require a certain amount of data per variable to be reliable[85]. Continuous data, like the data collected in this study, have shown to be reliable when the number of predictors (i.e., cadence, power, HR) is less than the sample size (n) divided by 10 for average data, and 20 (i.e., n/20) for data that is narrowly distributed[85]. The data measured in this thesis could be deemed narrowly distributed, as the age between all participants was 6 years[85]. Using this evidence, this study would have required more than 60 participants to obtain acceptable results from a multiple linear regression analysis.

5.6 Strengths, Limitations, and Assumptions

The study methods were the primary strength of the study, as it allowed multiple outcome measures to be collected during various conditions. The collected data enabled the researchers to explore multiple biomechanical and physiological characteristics that helped answer the study's primary research questions. Measurement tools such as kinematic markers, EMG, ECG, and the Portapres® blood pressure monitor allowed for important physiological data to be collected that smaller scale studies do not measure with similar constructs. Ultimately, the outcome measures allowed the researchers to take a first step in determining what mechanisms are primarily involved in modulating TBP during cycling.

Another strength of the study was that TBP was collected successfully in healthy resting participants with very little problems. Prior to collecting data for this study it was not known if the Portapres® would be capable of collecting acceptable TBP measures. Other studies had issues collecting TBP with the Portapres® due to low toe temperatures. Although toe temperature was not collected, a constant room temperature of 24°C seemed to provide appropriate TBP measurements in most participants. Very few participants required assistance in raising the toe temperature. For example, a space heater was used in three cases to raise toe temperature with very little success. Two females and one male required the space heater, and all three participants were eventually excluded from the study due to constant low plethysmograph readings on the Portapres® controller. Since an increase in toe temperature did not alleviate the problem it was expected that these participants always have low blood flow to their toes compared to the rest of the participants who were able to provide acceptable TBP values. Another attempt to increase blood flow to their toes was having them cycle at 60 rpm for 2-3 minutes. This method was not successful in all three participants.

A limitation of the study was that the results are not generalizable to a population that would require exercise therapy as rehabilitation tool. However, the researchers believed it was important to measure changes in arterial BP during movement in a non-disabled population before testing a clinical sample. The study provided evidence for the possibility of future research on patients with PAD. Another limitation was that although many variables were collected that are known to increase BP, there were other variables that would have been helpful to learn more about the TBP response to exercise. For example, as highlighted in the literature review of this thesis, there are three neural mechanisms that are known to increase MAP during exercise. Central command, the

exercise pressor reflex, and arterial baroreflex resetting can also be assumed to have affected TBP in the study's protocol, but the capacity in which they were present is unknown. Chemical mechanisms like carbon dioxide, adenosine, nitric oxide, magnesium, and potassium are known to affect vasodilation; however, the metabolite concentrations were not collected, and therefore could have had a large effect on the results[77]. Future studies may look into collecting blood samples after each mode of exercise to see if various metabolites played a role in the TBP response.

The study had multiple assumptions as well. First, it was assumed that any changes in TBP were due to differences in linear and angular motion, and not due to other mechanisms that effect BP (i.e., neural, muscle pump, etc.). The analysis used a biomechanical approach to quantify TBP changes due to exercise by examining the effect of cadence and mechanical power output.

The Portapres® was also assumed to be the best way to measure TBP during movement. Very few groups have measured TBP during rest, and no one has collected TBP during movement. Therefore, it was difficult to compare the Portapres® results to other devices used in other studies. Future research is required to determine if other techniques are more appropriate for TBP measurement during movement. Furthermore, the Portapres® was created to measure finger arterial BP in the common volar digital arteries in the finger (Figure 50).

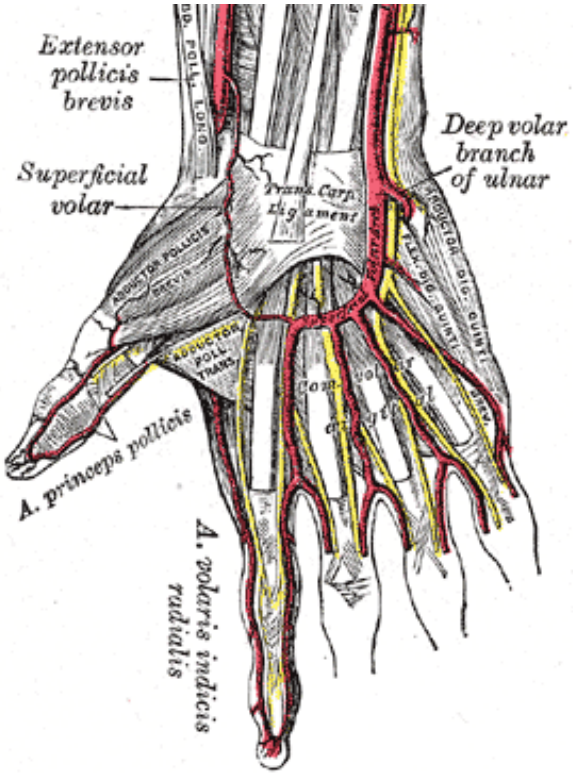

Figure 50. A diagram of the arteries found in the finger. Figure 527 in Gray's Anatomy of the Human Body[86].

This study intended to collect TBP measurements from the plantar digital artery in the toe (Figure 51). It was assumed that the plantar digital arteries were similar in structure and location in the toe as the common volar digital arteries structure and location in the finger. Therefore, it was thought that the Portapres® provided acceptable BP values in the toe compared to those normally collected in the finger.

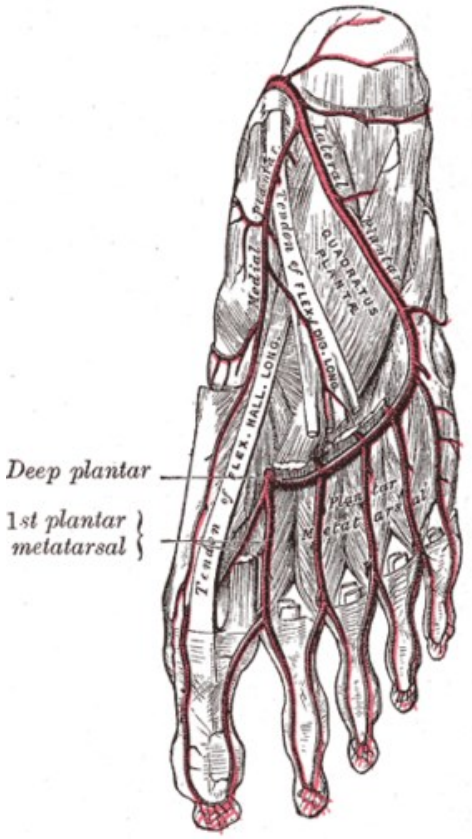

Figure 51. A diagram of the arteries found in the foot. Figure 555 in Gray's Anatomy of the Human Body[86].

It was also assumed that TBP was the best way to measure low limb BP during exercise, as people can argue that TBP is not the most optimal measurement for lower limb BP; however, TBP measurement has become more prevalent in clinical practice. TBP has not only been shown to be an effective screening method for identifying diabetic patients with PAD, but also to be more efficient than ankle BP measurements in diagnosing the disease[46]. A reason for this could be that the toe has the most distal lower limb artery, which therefore must be below the claudication or lesion site in an affected artery[87]. Therefore, an assumption for this study was that TBP offers a representative BP value of the lower limb, and can be used to quantify lower limb BP.

5.7 Future Direction

Multiple studies within the thesis explored TBP during rest and locomotion. Although not all of the research goals were met, important questions were developed in order to further explore other areas of TBP research. More research is needed to determine the most efficient and appropriate way to measure TBP during rest and exercise. The next step in advancing the field of TBP research is to determine the method that provides the best TBP measurements during rest or activity with very little movement. Although TBP collection during exercise is interesting, a more practical use of TBP measurement may be more beneficial for a disabled population at this time. For example, if a device were available and able to provide reliable and valid TBP measurements during rest, patients with PAD could participate in more exercise intervention studies, and more inferences could be made on how the exercise intervention actually influenced their lower limb circulation. Therefore, the main goal at this time should be to create a TBP monitor device that provides accurate results, and can be used in basic research studies.

Future studies could also look at the acute and chronic TBP and ankle BP response to lower limb exercises using similar protocols as used in this thesis. For example, if continuous TBP and ankle BP waveforms are collected simultaneously during exercise more analysis can determine if BP at both sites are reacting in the same manner, which could ultimately allow for more validation of the Portapres® device during exercise. That said it is extremely important to understand how lower limb BP acts in the

minutes following exercise as well for a disabled population, as post-exercise hemodynamics are also important for vascular rehabilitation.

Another direction to determine the effectiveness of the Portapres® during exercise would be to complete an arm-crank ergometer study with the Portapres® BP cuff on the finger. By investigating finger BP during high and low cadences and mechanical power outputs during arm ergometer exercise more information on the arterial response to exercise may be answered. Again, the Portapres® was meant for use on the finger, therefore if similar BP results are obtained using the arm ergometer method as were found in lower limb ergometer exercise (e.g., the exercise performed in this thesis) then some of the study's conclusions may be verified.

Finally, kinematic and electromyography data were collected during the cycling protocols in this study. Future analysis will look at creating a model to predict changes in TBP during cycling at different cadences and mechanical power outputs. The model will hopefully help explain the effect of motion and muscle activity on arterial BP, and be similar to the models developed by Ewig[15] and Goreham[14] that were mentioned above.

5.8 Conclusion

It can be concluded that the Portapres® BP monitor can be used on the toe under certain circumstances. TBP values were obtained during rest and during exercise in a laboratory setting; however, more research studies are needed to answer further questions regarding the effectiveness of using the Portapres® on the toe. Moderate exercise did cause difficulties when trying to obtain acceptable TBP values, especially during walking.

A new protocol is required to determine how TBP reacts to the walking motion. Finally, the Portapres® did provide acceptable TBP values during three different conditions of cycling. A greater cycling cadence was found to be related to an increase in TBP compared to lower cycling cadences. Due to this finding, it can be concluded that angular acceleration does cause an increase in actual TBP values.

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APPENDIX A: PERIPHERAL ARTERIAL DISEASE AND EXERCISE

Peripheral Arterial Disease (PAD) is a serious cardiovascular condition with quality of life implications due to the pain and physical limitations that are associated with the disease[8]. PAD is a common medical disorder[88], affecting approximately 12% of the general adult population and upwards of 20% of people over the age of 75. The disease is associated with increased morbidity and mortality, and when symptomatic, it causes pain in the legs known as intermittent claudication[71]. This pain arises from plaque build-up in the peripheral arteries, and is associated with a reduced blood perfusion generated by the occlusion[88]. Circulation problems arising from PAD can result in other secondary issues such as ulcers, tissue atrophy, or gangrene[71]. Currently, management prescriptions for intermittent claudication include walking, with either a gradual increase in speed or grade (i.e., slope of the treadmill), until maximum pain tolerance is achieved[10, 71, 88-89]. However, walking may not be the most effective exercise treatment to improve circulation while also increasing pain tolerance in the lower leg. In a recent systematic review of rehabilitation treatments for people with intermittent claudication, Frans et al[8] found that no definitive exercise therapy could be decided upon due to differing exercise interventions, but most studies included walking. A study by Hiatt et al[10] found patients with PAD who walked for 12 weeks increased their walking time by 5.1 minutes before having to discontinue because of pain (9.6±5.7 to 14.7±7.3 minutes, $P<0.05$). Other research in this area has shown that a minimum of six months of exercise therapy (i.e., walking) is required to see an increased pain tolerance in PAD patients[90]. The main exercise therapy goal for patients with intermittent claudication is to increase walking distance[8]; however, other modes of physical activity have been tested within the PAD

population, such as resistance training[91-93], circuit training[94-95], and stationary cycling[11, 96-97].

The outcome measures used in cycling research on PAD patients were typically cardiopulmonary characteristics including minute ventilation, respiratory exchange rate, and maximal oxygen uptake[11, 96]. Askew et al[11] measured systolic blood pressure (BP) after both cycling and treadmill walking exercise, but did not find a significant difference in BP between the two modes of exercise. This may be due to their experimental design, as BP was measured two minutes after exercise. Measuring BP during or immediately after exercise may have shown a different result, as the body would have had less time to return to a resting state. One interesting finding of the study was that participants had longer maximal exercise time while cycling in comparison to treadmill walking[11]. (Askew, 2002) This finding is important to note since exercising for a longer period of time causes a greater cumulative blood flow to the active muscles. An increase in the amount of blood being circulated is beneficial for patients with PAD, as more blood will reach their peripheral muscles. (20) An increase in cumulative blood flow is also essential for increasing blood perfusion in skeletal muscle; however, Askew (2002) did not report a mechanism for their findings. Sheriff et al[13] showed that limb motion may be one of the mechanisms that could increase blood perfusion to active muscles. In addition they reported that past literature has shown that this increase in blood perfusion can also be attributed to vascular conductance[98-101], exercise[101-102], and the muscle pump[98-99, 101,103-105.

APPENDIX B: STUDY RECRUITMENT POSTER

DALHOUSIE UNIVERSITY
Inspiring Minds

SCHOOL OF
HEALTH AND HUMAN PERFORMANCE
Critical Thinking Collaborative Learning Meaningful Research

"The effect of cycling versus treadmill exercise on blood flow and perfusion pressure responses in the lower limb"

We are looking for healthy volunteers to participate in a research study who:

- Are between the ages of 18-64
- Do not smoke
- Have a normal resting blood pressure (less than 140/90 mmHg)
- Are able to attend two, two-hour long testing sessions at a research laboratory in Dalhousie University's Dalplex facility
- Are able to engage in light to moderate physical activity (cycling and walking)

For more information about this study, or to volunteer for this study, please contact us at:

902-494-2754
biodynamics.dalhousie@gmail.com

902-494-2754
biodynamics.dalhousie@gmail.com

APPENDIX C: STUDY INFORMED CONSENT FORM

CONSENT FORM

Project Title: The effect of cycling versus treadmill exercise on blood flow and perfusion pressure responses in the lower limb.

We invite you to take part in a research study being conducted in part by Josh Goreham and Ben MacAskill. They are Dalhousie University students in the Department of Kinesiology. Taking part in the research is your decision and you can leave the study at any time. If you are a student at Dalhousie University, your grades or academic standing will not be affected if you decide not to participate in the research study. The information below explains what you will be asked to do and any benefit, risk, or discomfort that you might experience. You should discuss any questions you have about this study with Ben or Josh. Their contact information is listed below.

Who Is Conducting the Research Study

Josh Goreham (Principal Investigator)	School of Health and Human Performance/Kinesiology	(902) 499-0172 josh.goreham@dal.ca
Michel Ladouceur, PhD (Graduate Supervisor)	School of Health and Human Performance/Kinesiology	(902) 494-2754 michel.ladouceur@dal.ca
Ben MacAskill (Co-Investigator)	School of Health and Human Performance/Kinesiology	bn609897@dal.ca
Derek S. Kimmerly, PhD (Honours Supervisor)	School of Health and Human Performance/Kinesiology	(902) 494-2570 dskimmerly@dal.ca

Purpose and Outline of the Research Study

Peripheral arterial disease (PAD) is a common blood vessel disorder. PAD can lead to more serious issues if not managed and treated properly. The symptoms of PAD are aches, cramps, and numbness. PAD presents pain in the lower legs when the patient attempts to exercise. Currently, the exercise prescription includes a supervised treadmill-walking program. This is to increase blood flow to the lower limbs.

Previous research shows the ability of increased circular motion around a joint to increase limb blood flow and blood pressure in the upper body. This study will look to see if the same results will be found in the lower limbs. The study will involve healthy individuals. Treadmill exercise will be compared to stationary bike exercise at the same intensity.

Blood flow, blood pressure, and heart rate will be collected at rest, during, and after exercise. These measures will be analyzed to determine if cycling exercise results in higher blood flow and blood pressure in the lower limbs. Blood pressure and flow that increases and stays higher for longer periods of time is helpful to patients with vascular disorders. This study could provide support for other forms of treatment for patients suffering from vascular disorders. The purpose of this study is to explore the effects of treadmill walking and cycle ergometer exercise on blood pressure and blood flow in the lower limbs.

Who Can Participate in the Research Study

To address the research purposes we need approximately twenty (20) healthy individuals aged 18-64. The participants will have normal blood pressure (systolic pressure $\leq$ 120 mmHg and diastolic pressure $\leq$ 80 mmHg).

You have been invited to participate in this research study because you are a healthy individual between the ages of 18 and 64 with a normal resting blood pressure.

You will not be eligible for this study if you:

(a) are under the age of 18 or older than 64 years
(b) answered "Yes" to any question on the Physical Activity Readiness Questionnaire (PAR-Q)
(c) have a body mass index (BMI) greater than 30 kg/m^2
(d) are a current smoker
(e) have been diagnosed with a cardiovascular (i.e., high blood pressure, etc.), respiratory (e.g., asthma, etc.) or metabolic (e.g., diabetes, etc.) illness
(f) have been prescribed high blood pressure or any other heart medications
(g) have a resting blood pressure of more than 140/90 mmHg
(h) have Raynaud's disease (i.e., a medical condition that restricts blood supply to the fingers, toes, ears and/or the nose)
(i) have a history of fainting
(j) are pregnant
(k) have been instructed by your family doctor to not engage in strenuous physical activity

Eligibility Justification:

(a) The age range of 18 to 64 years old was set to ensure participants are of age to consent. Also, some health organizations have found that people over the age of 64 are more likely to fall. This is due to increased balance and mobility issues while exercising. The selected age range removes these issues from the study.

(b) If you answer, "Yes" to any question on the PAR-Q you are ineligible to participate. PAR-Q guidelines show that you may not be ready for the type of physical activity used in this study if you answer yes to a question.

(c) Body mass index is a tool to categorize body fat based on height and weight. BMI is equal to your weight in kilograms (kg) divided by your height in meters squared (m^2). We will determine your BMI by measuring your weight and height during the screening process. A BMI greater than 30 kg/m^2 is classified as "obese". An obese individual has increased health risks while exercising.

(d) Participants who smoke are at a higher risk of cardiovascular problems while exercising. Also, their cardiovascular health is not as good as one who does not smoke. The study is only accepting participants who are deemed healthy. This is to provide results that are relevant to a healthy population.

(e) Cardiovascular disease, respiratory disease, or metabolic disease classifies a participant as unhealthy. The results of unhealthy participants are not needed for this study.

(f) High blood pressure and heart medications affect blood pressure and blood flow. Participants' results may be affected if they are taking such medications. They cannot participate in the study because their condition may affect the results.

(g) A resting blood pressure of more than 140/90 mmHg increases the risk of health problems due to hypertension, which is a resting blood pressure above 140/90 mmHg. A resting blood pressure at this level is unhealthy. Hypertensive participants should see their doctor as soon as possible as they are at an increased health risk while exercising. Also, elevated blood pressures will introduce error into the study. Therefore, exemption from the study is necessary. Resting blood pressure will be measured for five minutes. One reading per minute will be recorded. After five minutes the readings will be averaged.

(h) Raynaud's disease is a serious medical condition. It restricts blood flow to the hands, feet, nose and ears. Participants with this condition may have different results compared to those who are healthy.

(i) Fainting is considered a serious issue while exercising. Fainting during the study while using heavy exercise equipment can be dangerous to the participant and researchers. Anyone with a history of fainting is ineligible to participate in the study.

(j) Pregnant participants are ineligible to participate. This is due to possible changes in health while pregnant. Also, chances of falling and reduced balance often are seen in pregnant women.

(k) Family doctors make the final decision on participation in the study.

Other screening tools:

You will have to complete the Physical Activity Readiness Questionnaire (PAR-Q). The PAR-Q will determine if you need to see your doctor before becoming more physically active. This form is used to determine whether a participant is eligible to participate in the study.

Blood pressure measurement is also used as a screening tool. Blood pressure will be measured while at rest using an automated blood pressure reader. One blood pressure reading every five minutes will be measured. This will be completed immediately following the Questionnaire screening process. The five readings will be averaged. Blood pressure will be measured from the upper left arm.

What You Will Be Asked to Do

We will ask you to engage in light to moderate physical activity. You will have your heart rate, blood pressure, blood flow and movement measured. This will help us understand the effect of cycling versus treadmill exercise on blood flow and blood pressure responses in the lower limb.

You will be asked to refrain from drinking alcohol or caffeine, using nicotine, or performing brisk physical activity 24 hours before test days. It is suggested that you get 6-8 hours of sleep prior to testing. It is recommended that you eat your last meal three (3) hours before each testing day and be well-hydrated (1 cup of water per hour). You will be asked to attend the lab at the same time of day for the second testing session. A minimum of 24 hours will be required between each testing day. You will be asked to report to room 217 of the Dalhousie Dalplex sports facility. Please make sure that you bring clothes that are comfortable for exercise, preferably shorts to allow for placement of equipment.

<u>Day 1</u>

The anticipated time commitment for the first test day will last 135 minutes. The first 10 minutes will consist of reading and signing this informed consent form. You will then read and sign the physical activity readiness questionnaire. Once deemed eligible, you will then have the testing equipment, protocols, risks, and rationale for the study explained to you. You will be encouraged to ask questions, and be informed that you may drop out of the study at any time. At this time, you will be asked to change into proper clothes to perform exercise tests using a private change room. You will be required to have sticky patches on different locations of body so the researchers can acquire the data for the study. The locations are outlined later in this form. Also, if you require help placing the sticky patches in the right locations you can ask for a researcher of the same sex to help you. We will need to know before you attend the lab for testing on Day 2 if you would like a researcher to help you. You can let us know on Day 1 before you leave the lab.

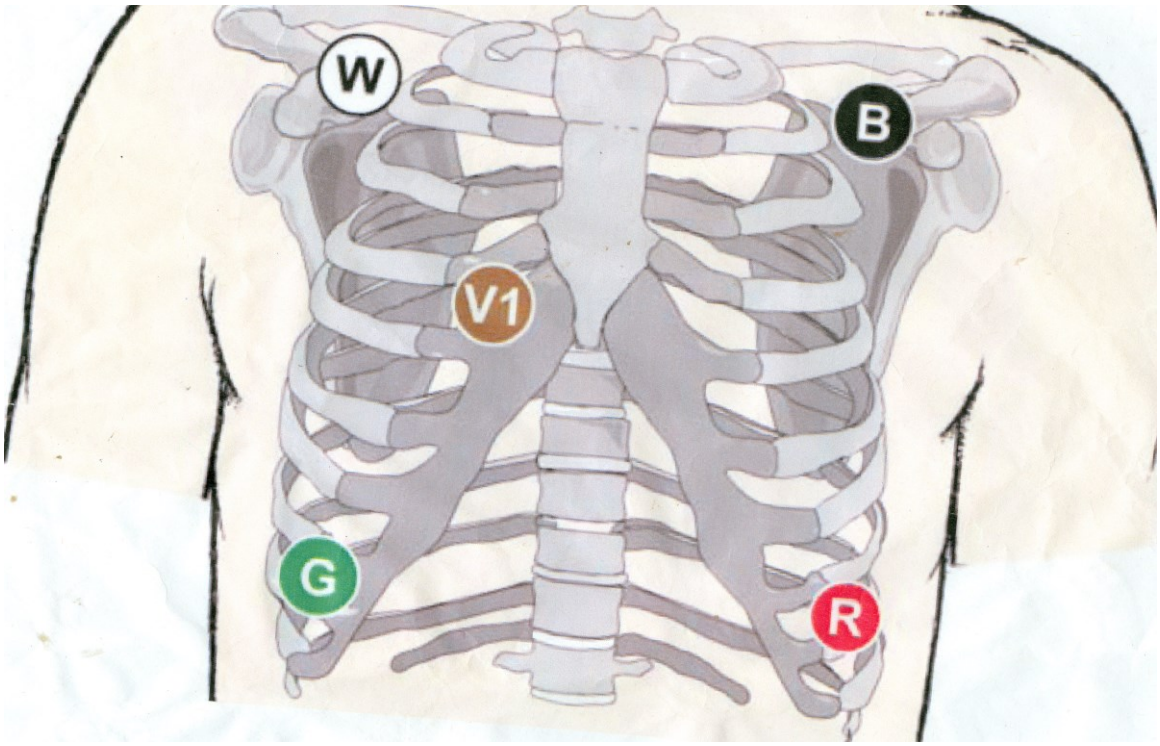
We will also ask you the following questions on Day 1 to find out what exercise level you will start exercising at:

Do you regularly engage in vigorous treadmill walking 2-3 times per week?
Do you regularly engage in vigorous cycling 2-3 times per week?

You do not have to answer these questions if you wish not to. If you do not answer these questions the researchers will ask that you start exercising at level one (beginner exercise level).

The following measurements will be collected during this study:

Heart Rate: A device called an electrocardiogram (ECG) and a Polar™ heart rate monitor will be used to measure heart rate. To use the ECG, five sticky patches will be positioned on your chest and rib cage. A trained investigator or yourself will attach the sticky patches. A diagram of patch placement is seen below.

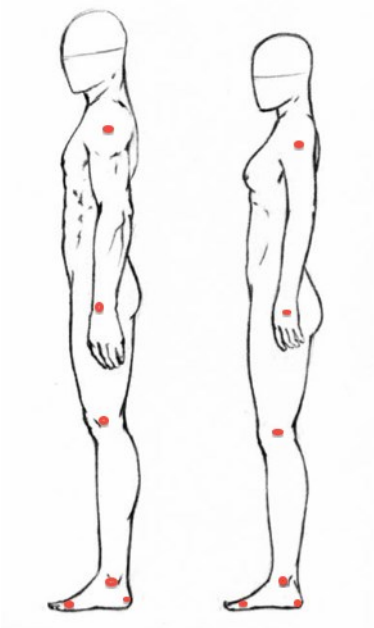


Calf Blood Flow: Measured by inflatable pressure cuffs placed on a thigh and ankle of the same leg, and a rubber band secured around the largest part of the calf. When measuring calf blood flow, the thigh cuff will be inflated and deflated to a relatively low level of pressure (40-75 mmHg) every 15 seconds by an automated rapid cuff inflator. The level of inflation pressure depends on your blood pressure, which will increase after you exercise. The pressure cuff will be inflated to a level that closes the veins in the leg. Some people may have higher pressure in their veins compared to others. This pressure is

typically between 40 and 75 mmHg for a healthy person. The ankle cuff will be inflated to a high pressure designed to temporarily stop blood flow to your foot. This cuff will not be inflated for longer than 2 minutes at a time. Some people find pressure cuffs painful. If you have felt pain from pressure cuffs in the past you may not want to take part in the study.

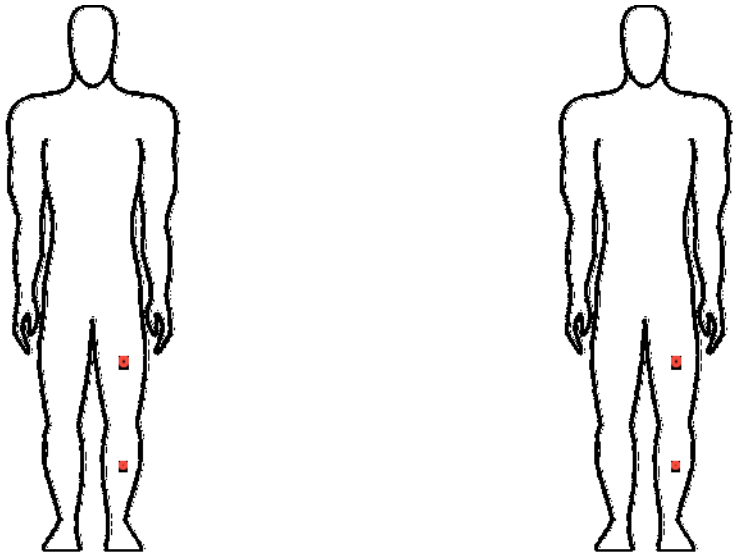
Toe Blood Pressure: Toe blood pressure will be measured by using a valid automated blood pressure device. The toe blood pressure cuff will be placed around your second toe and connected to a control unit secured by a strap around your shin. The toe pressure cuff does not inflate to a very high pressure. Toe blood pressure will only be measured while you are exercising.

Motion Analysis: Movement data will be measured using a camera system. Five markers attached to the shoulder, hip, knee, ankle and foot will capture movement. The camera system only shows positions of bony landmarks. This movement data is used to measure velocity and acceleration of your legs. By signing this document you consent to having your exercise movement measured by a camera system.



Muscle Activity: Muscle activity recordings will be recorded by shaving your legs at five locations. Each location is shaved as an area of 3 centimeters by 3 centimeters. This is to ensure proper room for the sticky patch electrodes. The exact locations shaven are at the front of the lower leg, the calf, the thigh and the hamstrings. A ground patch will be placed on the side of the knee. This allows us to know which muscles are active during exercise. A diagram of patch location is shown below.

Front View: Back View:



Exercise Intensity: You will be exercising at sixty percent of your maximum heart rate. This will be determined using the following math equation: 0.60 × (220 – your age).

Stationary Bike Test: You will be asked to participate in two separate cycling tests. You will be asked to cycle at a pedaling rate of 90 revolutions per minute (rpm) for the first cycling test. You will be asked to cycle at a pedaling rate of 50 rpm for the second cycling test. You will receive visual feedback to help you keep the pace. The cycle tests will start at a low intensity (50 to 100 Watts). This depends on your current level of physical fitness. The intensity will be increased every 3 minutes by 45 or 90 Watts. This also depends on your fitness level. The intensity that increases your heart rate to the 60% maximum value will be the intensity that you will exercise at on Day 2 (see below). You will then undergo a rest period, before the treadmill exercise test begins.

Treadmill Test - The treadmill test begins by walking at a speed of 1.7 miles per hour with a slight incline on the treadmill. The speed and incline will increase every 3 minutes until your heart rate reaches the 60% maximum heart rate value. This will be the treadmill speed and incline that you will exercise at during the second test day.

Day 2

The second test day will occur at least 24 hours after Day 1. It is expected to last 155 minutes. You will arrive to the lab and be asked to lie on your back while you are set up for measurements of heart rate, arm blood pressure, toe blood pressure, and calf blood flow (20 minutes).

Exercise Period: You will then perform a two cycling tests (50 and 90 rpm) and a treadmill test. The order of these tests will be randomly chosen for you. You will have a 5-minute warm-up for each test at your choice of intensity. The intensity will then be increased to the same level that caused the 60% maximum determined on Day 1. You will continue to exercise at this intensity for 10 minutes. If your heart rate increases or

decreases by 5 or more beats per minute away from the 60% values, we will adjust the intensity accordingly to try and change your heart rate back to the target level.

Post-Exercise Recovery Period: The post-exercise passive recovery will begin within one minute following the end of exercise. You will be instructed to lie on your back with one of your lower legs supported slightly above the level of the heart. Blood flow will be measured in 30-second intervals for 2 minutes (4 measurements every 2 minutes). There will then be a 3-minute period when calf blood flow is not measured. This cycle will repeat for the entire 20-minute post-exercise recovery period. Once your heart rate, arm blood pressure and calf blood flow values have returned to resting levels you will begin the second exercise test. Your toe blood pressure will be measured for one minute after each exercise test as well.

Once your heart rate and blood pressure have returned to resting levels you will be finished the experiment.

Possible Benefits, Risks and Discomforts

There are no direct benefits to you by participating in this study. General health information will be provided to the participant upon request. This includes resting blood pressure, heart rate and calf blood flow. Interested participants are to write their contact information on the bottom of the signature page of this informed consent form. All results will be either mailed or e-mailed to the participant.

The following measurement tools will be used to record data for the study:

Heart Rate and Muscle Activity Measurements: Small sticky patches will be placed on your chest, shoulders, ribcage and leg muscles. The patches will record the electrical activity of your heart and skeletal muscles. A small rash may develop on the skin after you remove the patches. This is due to the adhesive but should disappear within 48 hours.

Toe Blood Pressure: A small cuff will be placed around the second toe. This cuff is used to measure your blood pressure. When in use, the cuff will inflate with air and you should feel it gently squeeze your toe. Your toe may turn slightly blue and feel numb or tingly when this cuff is inflated. The symptoms go away once the cuff pressure is reduced. Some people may feel slight pain in this procedure. Pain is not expected to be any worse than what you would feel when a physician takes your blood pressure. If you have felt pain due to blood pressure cuffs in the past you may not want to be a part of this study.

Arm Blood Pressure: A pressure cuff will be placed around your upper left arm. During certain phases of the experiment this cuff will be inflated to levels that will temporarily prevent blood from entering your forearm. This occlusion will last no longer than one minute. During cuff inflation you may feel a “pins and needles” sensation your left arm. Your left forearm and hand may turn slightly blue and feel numb when the cuff is inflated. All of these sensations should quickly disappear when the cuff pressure is reduced. Some people may feel slight pain in this procedure. Pain is not expected to be any worse than what you would feel when a physician takes your blood pressure. If you

have felt pain due to blood pressure cuffs in the past you may not want to be a part of this study.

Calf Blood Flow: This procedure involves the inflation of a low-pressure cuff over a thigh for a period no longer than 15 seconds at a time. There will also be a high-pressure cuff placed around the ankle of the same leg for a period no longer than 2 minutes. Sensations and possible discomforts associated with the high-pressure cuff may include "pins and needles", a bluish or whitish change in the colour of the skin of the foot. These sensations will quickly go away once the pressure in the ankle cuff has been released. There are no known medical risks associated with the stoppage of blood flow to the foot for a 2-minute period of time. Some people may feel slight pain in this procedure. Pain is not expected to be any worse than what you would feel when a physician takes your blood pressure. If you have felt pain due to blood pressure cuffs in the past you may not want to be a part of this study.

The chance that a healthy person with no cardiovascular disease will experience sudden cardiac arrest during brisk activity (such as jogging) is very small (1 in 565 000). The exercise being performed in the study is classified as moderate activity. We suspect the probability of a participant to experience serious harm (such as a heart attack) is even smaller (1 in 565 000+).

Compensation / Reimbursement

There will be no compensation or reimbursement offered for participating in this study.

Privacy and Confidentiality

Information that you provide to us will be kept private. Only the research team at Dalhousie University will have access to this information. We will describe and share our findings in a thesis, class presentations, and Kinesiology conference presentations. We will be very careful to only talk about group results so that no one will be identified. This means that ***you will not be identified in any way in our reports***. The people who work with your information have special training and have an obligation to keep all research information private. Also, we will use a participant number (not your name) in our written and computerized records. This information will not contain your name. Your identifying information will be kept in a separate file. It will be held in a locked cabinet, in a locked room. All electronic records will be kept secure in a password-protected, encrypted file. The file will be on the researcher's personal computer [or on a Dalhousie University secure server].

Confidentiality: All information collected during this study will remain confidential. It will be stored in locked offices and on secured computers. Only the principal investigator and other researchers involved in the study will have access. You should know that the results of this study will be made available to the scientific community. This will happen through publication in a scientific journal. Neither your name nor any reference to you will be used in creating or publishing these results. Also, you will have access to your

own data, as well as the group data when it becomes available and if you are interested. To ensure confidentiality of participant information each participant will be assigned an 8-character identification code. Each code and its files will be labeled and stored in a secured file folder. The folder will be on a computer in Dr. Michel Ladouceur's office in the Dalplex. There will be an encryption coded security system that only PI's, Dr. Michel Ladouceur and Dr. Derek Kimmerly will have access to.

If You Decide to Stop Participating

Participating in this study is completely voluntary. You are free to leave the study at any time. If you decide to stop participating in the study, you can decide whether you want information that you have contributed to be removed. The other option is to allow us to use that information. You may also refuse to answer any questions we ask during the study and still remain a participant except for the eligibility questions found on page 2 of this form. All eligibility screening procedure questions must be answered due to the safety concerns of participating in this study. An example of a question you could refuse to answer would be "Do you regularly engage in vigorous cycling 2-3 times per week?" This question is used so the researchers can further understand your level of cycling fitness. In no way is this question related to your safety, so you do not have to answer it if you wish not to. Investigators reserve the right to withdraw you from the study if they believe that reasons have arisen which warrant doing so.

How to Obtain Results

We will provide you with a short description of group results when the study is finished. Individual results will be provided if requested by the participant. You can obtain these results by including your contact information at the end of the signature page. You can also receive results by contacting us through email at biodynamics.dalhousie@gmail.com. All results will be either mailed or e-mailed to the participant in such case.

Questions

We are happy to talk with you about any questions or concerns you may have about your participation in this research study. If you have any questions about the study, please contact Josh Goreham, Dr. Michel Ladouceur, Dr. Derek Kimmerly, or Ben MacAskill. Their contact information is on the first page of this document. Fred McGinn is an ethics advisor at the Dalhousie School of Health and Human Performance. He is also available at any time for contact at (902) 494-1196. Do not hesistate to contact us with questions, comments, or concerns about the research study. We will tell you if any new information becomes available that could affect your decision to participate.

If you have any ethical concerns about your participation in this research, you may also contact Catherine Connors. Catherine is the Director of Research Ethics, at Dalhousie University. You can contact her at (902) 494-1462, or email: ethics@dal.ca.

Title

The effect of cycling versus treadmill exercise on blood flow and perfusion pressure responses in the lower limb.

Consent:

I HAVE READ AND UNDERSTAND THE ABOVE EXPLANATION OF THE PURPOSE AND PROCEDURES OF THE PROJECT. MY QUESTIONS HAVE BEEN ANSWERED TO MY SATISFACTION. I AGREE TO PARTICIPATE IN THIS STUDY WITH THE UNDERSTANDING THAT I MAY WITHDRAW AT ANY TIME. I HAVE ALSO RECEIVED A SIGNED COPY OF THE CONSENT FORM. I VOLUNTARILY CONSENT TO PARTICIPATE IN THIS STUDY.

Participant's Signature	**DATE**
Print Name of Participant	**DATE**
Witness (Research Assistant)	**DATE**

I confirm that I have explained the nature and purpose of the study to the participant names above. I have answered all questions. In my judgment the participant is voluntarily and knowingly giving informed consent and possesses the legal capacity to give informed consent and participate in this research study

Name of Person Obtaining Consent	**Signature**	**Professional**

Relationship to Participant:

Contact Information (If you wish to receive your individual results they will be either be mailed by post or emailed to you depending on your preference. Please fill in your information on the line you prefer.):

Mailing Address:

Email Address:

APPENDIX D: PHYSICAL ACTIVITY READINESS QUESTIONNAIRE

Physical Activity Readiness Questionnaire - PAR-Q (revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO	
☐	☐	**1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?**
☐	☐	**2. Do you feel pain in your chest when you do physical activity?**
☐	☐	**3. In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	**4. Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	**5. Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?**
☐	☐	**6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	**7. Do you know of any other reason why you should not do physical activity?**

If you answered

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:

- If you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- If you are or may be pregnant – talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME _____

SIGNATURE _____ DATE _____

SIGNATURE OF PARENT or GUARDIAN (for participants under the age of majority) _____ WITNESS _____

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

CSEP | SCPE