Investigating the Impact of External Passive Compression on Central and Peripheral Hemodynamics

by

Jennifer Book

A thesis

presented to the University of Waterloo

in fulfillment of the

thesis requirement for the degree of

Master of Applied Science

in

Mechanical Engineering

Waterloo, Ontario, Canada, 2014

AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

The use of passive compression has been extended from a clinical treatment to an elective tool used by healthy individuals in an attempt to improve exercise performance. The rationale being that graduated compression socks would enhance the capabilities of the muscle pump and therefore increase venous return to the heart, leading to increased cardiac efficiency and better exercise performance. There is currently conflicting evidence regarding the effectiveness of graduated compression socks on improving central and peripheral hemodynamics in a healthy population. These conflicting results are believed to be due to varying test protocols (e.g., type of exercise, duration, and intensity), difference in study populations (e.g., normal participants vs. highly trained athletes), and the variation in the reported strength of the applied pressure (i.e., only reporting the manufacturer's operating pressure). All of these factors make it difficult to draw concrete conclusions on the effect of compression during exercise and recovery.

The goal of this study was to complete a set of controlled experiments to assess the effectiveness of passive compression in healthy subjects and whether they are beneficial for enhancing performance and recovery. The purpose being to compare the results to the discrepancies found in current literature when evaluating external compression in healthy subjects. The scope involved testing 12 healthy individuals who ranged in fitness levels during a simple exercise task while monitoring central and peripheral variables. The experimental protocol involved a three minute baseline period, followed by plantar flexion exercises for five minutes at a rate of 20 raises per minute, and finished with a five minute recovery time. The protocol was repeated twice to investigate the physiological response with and without graduated compression socks. Subjects completed testing on two days, with at least 48 hours between tests, to determine the repeatability of the results. Specific central variables investigated included heart rate, systolic blood pressure, diastolic blood pressure, and cardiac output. Peripherally, popliteal arterial blood velocity, popliteal arterial blood flow, popliteal artery diameter, muscle activity, muscle oxygenation, and the change in pressure from the ankle to knee due to the compression sock were measured.

The results indicated that there were no changes in the central hemodynamics with the addition of the socks. At the peripheral level, there were no significant changes in popliteal artery diameter, mean popliteal arterial blood velocity, or mean popliteal arterial blood flow during any of the testing conditions. During exercise, there was an indication that the subjects who experienced an increase in mean popliteal arterial blood velocity or mean popliteal arterial blood flow with the graduated compression socks behaved more consistently than those who experienced a decrease, as implied by lower standard deviation values. The exercise task did not cause any lasting effects on vasculature as there was no significant difference between the popliteal artery diameter values for baseline and recovery and the subjects experienced the same response (i.e., increase or decrease) with the socks during both baseline and recovery. For muscle oxygenation, results indicated a decrease in blood volume in the leg with the graduated compression socks, and a trend towards increased muscle oxygenation and oxygen extraction during exercise. For recovery, there was a trend towards a lower blood volume in the leg with the graduated compression socks implying

that even post exercise the socks were working to prevent pooling in the leg. For muscle activity, the same muscle activation was required with and without the socks to complete the test. The height at which the plantar flexion task was completed was tied to lifestyle, those subjects reporting irregular exercise, completed the calf raise exercise at lower heights than those who reported frequent exercise. Furthermore, the locally applied pressure was found to vary dynamically during exercise and then return to baseline values during recovery. Moreover, the strength of the pressure change on the leg from ankle to knee was not correlated to the response of the subject for any of the investigated variables. Finally, no significant differences were found in the immediate hemodynamic recovery time with the addition of the sock.

The results found in this study were comparable to other studies investigating the effect of graduated compression socks on hemodynamics. It is not surprising that there were no changes in central hemodynamics, as the external pressure was applied in such a small, localized region. It is also not unexpected that a healthy study population did not lead to significant changes in vascular diameter or blood velocity since the subjects do not suffer from venous deficiencies. The key findings of this study are that the graduated compression socks were beneficial in decreasing blood volume in the leg, as expected with their prescribed function, and have the potential to increase oxygen extraction in a healthy population. Furthermore, the discovery that the local applied pressure varied during exercise should be taken into consideration when utilizing compression socks for various exercise tasks. Finally, this study highlights the importance of control and reporting all aspects of the experimental protocol and data analysis in order to obtain high fidelity results that can be entered, with confidence, into the debate of the effectiveness of graduated compression socks on athletic performance.

Acknowledgements

There are several people without whom the completion of this thesis would not have been possible. To all those who have helped with my research or have helped keep me sane I cannot thank you enough for your support throughout the last two years.

Professor Sean Peterson, thank you for giving me the oppourtunity to pursue my Master's degree and providing the funding to make it possible. Your patience, guidance, and knowledge have made me stronger academically. You've always pushed me to perform to my highest potential both in academia and in my personal life, showing me that I can achieve things I never thought I was capable of (since now I can run 10 km).

Professor Rich Hughson, thank you for your continuous help with the physiology aspects of my research and for allowing me to use your lab and equipment to complete my research.

Professor Duane Cronin, thank you for taking the time to read and review my thesis.

Keyma Prince, thank you for your mentoring throughout my Master's. Without your guidance, advice, and celebrity gossip I wouldn't have made it through.

Rodrigo Villar, thank you for your help throughout data collection and always making me laugh. You have taught me so much about physiology and life, and I am grateful to have had the opportunity to work with you.

Ivan Beentjes, thank you for developing the pressure system and for always offering your time when things went wrong.

To my parents, Lynn and Glenn, and my sister, Allison, thank you for your continuing support whether it involved helping to build test structures, sending care packages, editing, being a voice of reason, or a welcomed escape from the research world. I love you so much and could not have accomplished what I have without your help.

To my grandparents, thank you for your love and support throughout my university career. Without your generosity and encouragement I could have never achieved what I have to this day.

To my boyfriend, Stephen, thank you for being patient throughout my many stages of stress. You have always known what is best for me, even when I am too stressed to see it. Your encouragement and confidence in me are what helped me accomplish what I have. I love you and look forward to what's next.

To my best friend and roommate, Mandy, thank you for putting up with me and always being the person I could come home and laugh with, cry to, or vent to. I can't express how much I appreciate your advice and encouraging words and how much they have helped me make it through the past two years.

To Bentley, I couldn't have made it through my first year without knowing that I would get to see you every few months, I love and miss you so much.

Finally, to all who participated in this study, thank you for your time and patience.

Table of Contents

List of Figures

List of Tables

List of Abbreviations

GCS	Graduated Compression Socks
MRI	Magnetic Resonance Imaging
FEA	Finite Element Analysis
CO	Cardiac Output
HR	Heart Rate
SV	Stroke Volume
ATP	Adrenaline Triphosphate
NGCS	No Graduated Compression Socks
EMG	Electromyography
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
PAR-Q	Physical Activity Readiness Questionnaire
MVC	Maximum Voluntary Contraction
NIRS	Near-Infrared Spectroscopy
BL	Baseline
EX	Exercise
REC	Recovery
ECG	Electrocardiogram
O_2Hb	Oxyhemoglobin
HHb	Deoxyhemoglobin
tHb	Total Hemoglobin (total blood volume)
TSI	Oxygenated Hemoglobin Percentage
MAP	Muscle Action Potential
PAD	Popliteal Artery Diameter
PBV	Popliteal Artery Blood Velocity
PBF	Flow Rate of Blood in the Popliteal Artery
MAP	Mean Arterial Pressure
TPR	Total Peripheral Resistance
MPP	Muscle Perfusion Pressure
DHC	Distance from the Heart to Calf Muscle
GMH	Gastrocnemius Medial Head
GLH	Gastrocnemius Lateral Head
S	Soleus Muscle
COV	Coefficient of Variation
ICC	Intraclass Correlation
SD	Standard deviation
BP	Blood Pressure

List of Symbols

F	Volumetric flow rate of blood
PG	Driving pressure gradient
R	Frictional resistance in a vessel
l	Vessel Length
η	Blood Viscosity
r	Vessel radius
d	Distance between the ankle and knee pressure bladders
ΔP	Change in pressure from the GCS between d
f_d	Doppler frequency
f_t	Transmitted frequency
f_r	Received frequency
v	Velocity
c	Speed of sound
θ	Angle of insonation
OD (λ)	Optical density of tissue
$\varepsilon(\lambda)$	Absorption coefficient
C	Concentration of the chromophore
L	Distance between light entry and exit point
λ	Wavelength
DPF	Dimensionless pathlength factor
$\Delta OD\ (\lambda)_r$	Oxygen independent losses due to scattering in the tissues
$\Delta OD\ (\lambda)$	Change in optical density
ΔC	Change in concentration
v_{raw}	Raw popliteal artery velocity data
$v_{corrected}$	Corrected popliteal artery velocity data
PBV_{mean}	Mean of corrected popliteal artery blood velocity
PBF_{mean}	Mean flow rate in the popliteal artery
t	t-value
$\bar{X}$	Mean
σ_{diff}	Standard error measurement
n	Number of subjects
p	p-value
Δ	Change in a variable
P	Applied Pressure
ρ	Density of the fluid
g	Gravitational acceleration
h	Depth of the pressure sensor with respect to the surface of the fluid

Chapter 1

Introduction

In recent years, the use of graduated compression socks (GCS) has been extended from their traditional use as a clinical tool into the sports market, where athletes are now using compression while running, biking, or performing other endurance sports with the belief that they will increase their performance and/or decrease recovery time [1, 2]. The traditional use of GCS is to prevent pooling of blood in the legs, typically for patients suffering from edema, via passive compression [3-5]. While the clinical use of passive compression has been proven effective, further research is required into its use by healthy active populations. Recent research presents conflicting results as to whether the use of passive compression is beneficial for a healthy population. The human muscle pump works effectively to aid in the return of blood back to the heart from the lower limbs and increase cardiac efficiency and it is the aim of this research project to investigate if this effect could be amplified with the addition of externally applied compression to work in conjunction with the muscle pump, potentially providing a basis for improvement in athletic performance. This chapter will provide background on the cardiovascular system and muscle pump as well as the theory behind passive compression and a discussion of the literature testing compression both in clinical and exercise applications.

1.1 Background

1.1.1 Overview of the Cardiovascular System

The human cardiovascular system is a complex parallel flow network that circulates blood throughout the body (Figure 1.1). It can be thought of in terms of a closed system containing a series of tubes (blood vessels) divided into two circulation pathways that are connected to a pump (the heart). The first circulation pathway is the pulmonary circulation, where blood is carried from the heart to the lungs and back to the heart [6]. The second circulation pathway, the systemic circulation, delivers blood to the organs and tissues, excluding the lungs, and returns blood to the heart. The cardiac cycle consists of two phases, systole and diastole. During systole the cardiac muscle contracts and blood is forced out of the heart and into the pulmonary and systemic circulation systems. During diastole, the heart muscle is relaxed and the heart fills with blood. The heart contains four chambers, the right atrium, the left atrium, the right ventricle, and the left ventricle. The right atrium receives deoxygenated blood returning to the heart from the systemic circulation (venous return). This blood is then drawn into the right ventricle where it is pumped into the lungs (pulmonary circulation) to become oxygenated. Oxygenated blood returns to the heart through the left atrium, where it is subsequently drawn into the left ventricle and pumped back into the systemic circulation to deliver oxygen and nutrients to the body's cells while it simultaneously removes cellular waste for excretion [6].

Blood circulates throughout the body through a series of vessels; arteries are the blood vessels that carry blood away from the heart, while the veins return the blood to the heart. As blood moves through the

body, valves in the heart and veins help ensure that blood flows in one direction [7]. When blood leaves the heart via the main artery, the aorta, it is dispersed through a network of arterial vessels that branch and decrease in diameter with increasing distance from the heart [7]. The pulsatile character of the flow, induced by contraction of the heart, is dampened as the blood travels to smaller arteries, arterioles (smallest vessel in the arterial circulation), and eventually reaches the smallest vessels in the body, the capillaries, where the exchange of oxygen, carbon dioxide, water, and other nutrients and cellular waste occurs [6, 7]. The capillaries, located within the organs and tissues, collect into the venules (smallest vessel in the venous circulation) and then into successively larger veins that increase in diameter as the distance to the heart decreases [6, 7].

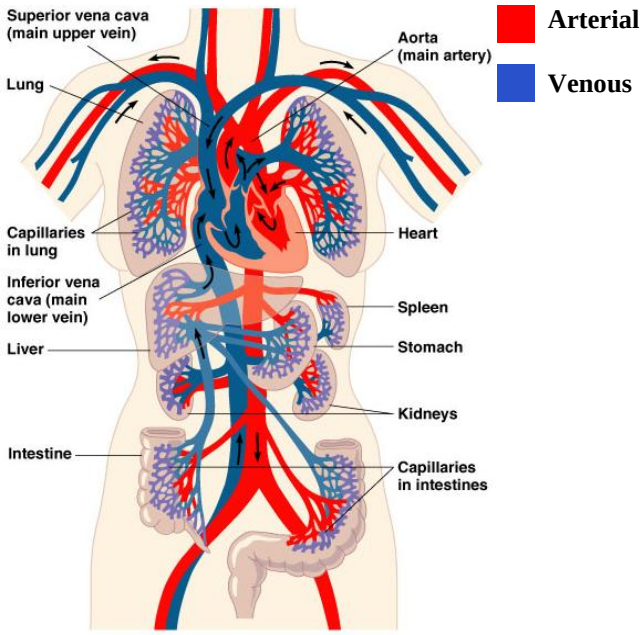


Figure 1.1: An illustration of the human circulatory system (adapted from idHumanBody [8])

The rate at which blood circulates through the vessels (volumetric flow rate of blood) is extremely important, as it is essential in maintaining the health of the body. As previously mentioned, the exchange of oxygen, nutrients, and waste occurs at the capillaries. With good blood circulation this exchange will occur continuously and meet the body's oxygen and nutrient demands to maintain homeostasis. Poor blood circulation decreases the frequency of the exchange and slows the delivery of oxygen and nutrients to organs and tissues, increasing the risk for serious health issues. The volumetric flow rate of blood (F) is related to the driving pressure gradient (PG) and frictional resistance (R) in a vessel, as

$$F = \frac{\mathrm{PG}}{R} \qquad \textbf{Equation 1.1}$$

The pressure gradient term, seen in Equation 1.1, will normally be maintained within a small range due to compensatory mechanisms of the cardiovascular system that work to regulate blood pressure, as it provides the driving force for organ perfusion [7]. The body regulates blood pressure through negative feedback systems, which incorporate pressure sensors called baroreceptors [9]. Baroreceptors respond to stretching of the vessel walls that are generated by increases in arterial pressure [9]. Each baroreceptor has its own threshold and sensitivity to changes in pressure, and as pressure increases additional receptors are recruited [9]. Therefore, if blood pressure starts to rise, activation of the baroreceptors will cause heart rate to decrease, which will in turn cause blood pressure to decrease. If blood pressure starts to decrease below a certain threshold, the opposite effect will occur and heart rate will increase, which will lead to an increase in blood pressure. These changes in blood pressure due to the activation of baroreceptors are mediated by the parasympathetic and sympathetic nervous systems [9].

Due to the regulation of blood pressure, the flow rate becomes mainly dependent on vessel resistance. The resistance within a vessel is related to the vessel length (L), blood viscosity (η), and radius of the vessel (r) as shown in Equation 1.2 [7]. Blood viscosity is related to friction generated by the interactions within the fluid as the blood is flowing (i.e. between fluid molecules in the plasma and red blood cells [7]). The resistance of a given vessel is most sensitive to the vessel radius, being inversely proportional to the fourth power. Thus, as the radius of the vessel decreases, the resistance will significantly increase. Furthermore, the circulatory system continuously branches into a highly parallel system. This continuous branching, as well as the reduction in diameters of vessels as the distance from the heart is increased, leads to dramatically reduced flow rates in smaller vessels compared to larger ones, indicating that the small arteries and arterioles have the highest flow resistance. This reduction in flow rate for smaller vessels is beneficial for the exchange of oxygen to the tissues and organs.

$$R \propto \frac{\eta L}{r^4} \qquad \textbf{Equation 1.2}$$

Equation 1.2 illustrates that the resistance is mainly dependent on vessel radius, which is controlled by local changes in tissue metabolite concentration or the sympathetic and parasympathetic systems [7]. Blood vessels can constrict or dilate in order to regulate blood pressure, alter blood flow within organs, and distribute blood volume in the body [7]. For example, if a muscle is activated due to exercise, it will have a higher metabolic demand and release vasoactive metabolites; therefore, the blood vessels will dilate to increase blood flow into the region. In order for this increase in blood flow to occur, the arterial pressure must be maintained. This is achieved during exercise by increasing cardiac output, the amount of blood ejected per minute, and by constricting the blood vessels going to other organs or muscles that do not require an increase in blood flow [7]. A similar concept occurs when a person stands up and experiences the effects of gravity that draws the blood into the legs. When a person stands, heart rate increases and blood vessels constrict to maintain a normal blood pressure and to prevent pooling of blood in the legs [7].

Figure 1.2 shows the mean pressure in the various constituents of the circulatory system, ranging from the aorta to the vena cava (the largest vein, which feeds the right atrium) and illustrates the flow of blood throughout the body. Blood pressure is highest in the aorta and decreases as the blood moves further away from the heart [7]. The pressure decreases in the aorta and arteries primarily due to simple viscous losses [7]. As blood flows into the smaller arteries and the arterioles it experiences the largest pressure drop (approximately 50 to 70%) due to the increased resistance from the decrease in vessel diameter, as well as increased compliance (capacitance) of the smaller vessels [7]. The pressure continues to decrease as the blood moves into the capillaries, and then onto the venules and veins. However, this decrease is not nearly as great, as shown in Figure 1.2, due to the low resistance of the veins [7].

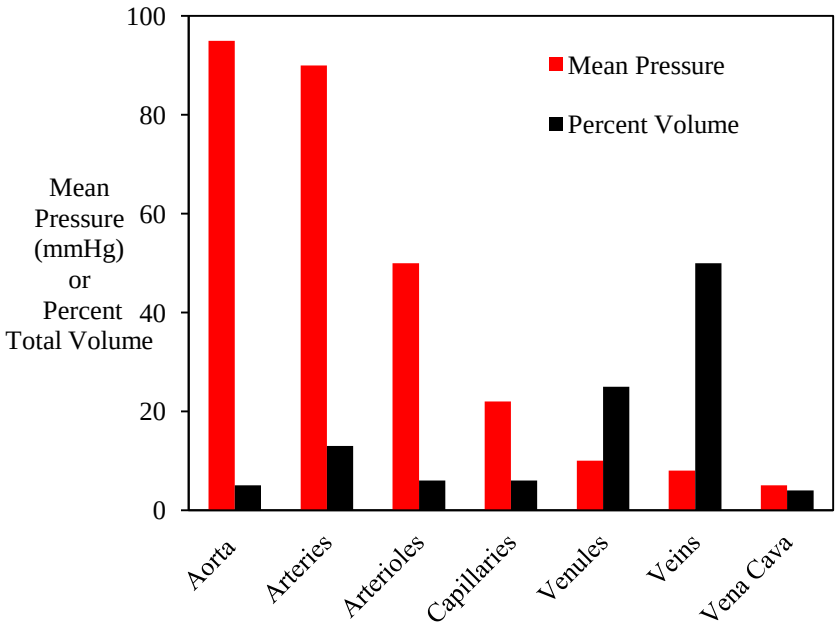


Figure 1.2: Graph depicting the distribution of pressures and volumes in the systemic circulation (data obtained from Klabunde [7])

Figure 1.2 also illustrates the percentage of the blood volume stored in each stage of the circulatory system. The walls of the veins are extremely compliant when compared to the more rigid walls of arteries, and therefore are able to expand and store larger volumes of blood. This compliance leads to the veins acting as capacitors, storing roughly 60 to 80% of the total blood volume. The larger veins have less compliance and therefore will store smaller volumes of blood hence the dramatic decrease in blood storage for the vena cava. This figure shows that the rigid arteries are subject to large pressures, but store very little of the total blood volume (low compliance). In contrast, the veins have a large capacitive effect, with volume changing drastically given a relatively small pressure.

1.1.2 Anatomy of the Lower Leg

The specific lower leg anatomy, including the number and location of the various blood vessels, varies from person to person; however, there are several main vessels present in virtually all people. The main arteries of the calf are shown in Figure 1.3A and include the anterior tibial, posterior tibial, and peroneal (fibular) artery. These three arteries branch off of the popliteal artery, which is the main trunk supplying the calf.

There are three categories of veins within the lower leg: the superficial veins, which are near the surface, the deep veins residing near the bone, and perforating veins, which connect the other two. The role of superficial veins is to act as a conduit, delivering blood collected from the capillaries and venules to the deep vein system through junctions and perforating veins [10]. The main superficial veins of the lower leg are the small saphenous vein and the great saphenous vein (Figure 1.3B). The purpose of the deep veins is to transport blood to the vena cava, which connects back to the heart. The three major vessels of the deep venous system that empty into the popliteal vein include the anterior tibial vein, the posterior tibial vein, and the peroneal (fibular) vein (Figure 1.3B). The main deep veins run parallel to the main arteries. Finally, perforating veins link the superficial and deep vein systems and act as a "check-valve" between the two systems [11]. Perforating veins are activated by the muscle pump (to be described in the following section) and help maintain even and efficient ejection of blood from the leg [11]. Each perforating vein contains at least two valves in order to prevent backflow from the deep system into the superficial system [11].

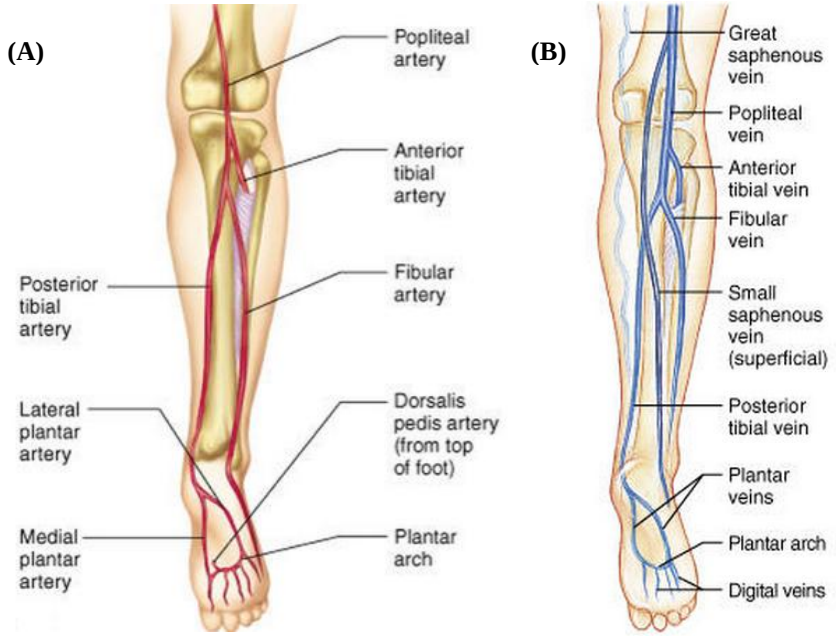


Figure 1.3: A posterior illustration of the main arteries (A) and veins (B) of the lower leg (adapted from Anatomy and Physiology Note Summaries [12])

1.1.3 Muscle pump

In order to expel the volume of blood stored in the deep and superficial veins as seen in Figure 1.2, the body has a physiological mechanism, known as the calf muscle pump, which aids in the return of blood to the heart. The main muscles of the calf are the gastrocnemius and soleus muscles. As shown in Figure 1.4, these muscles surround the deep veins and compress them during muscle contraction to aid in venous return. The muscle pump acts to compress and release the deep veins and therefore creates pressure gradients that encourage the return of blood to the heart, see Figure 1.5 [13]. The veins are divided into sections due to the presence of valves. When the muscle contracts, the pressure within the vein segment increases, causing the upstream valves to close and downstream valves to open, see Figure 1.6A [7]. When the muscle relaxes, a pressure gradient exists that draws blood from the superficial system and opens the upstream valves allowing the vein segment to fill with blood, as illustrated in Figure 1.6B [7]. During contraction, the pressure in the deep veins is very high (roughly 200 mmHg), while the pressure in the superficial veins is low (approximately 30 mmHg) [14]. The deep veins can sustain such high pressures during contraction because the pressure from the muscle does not allow the vein to dilate. During relaxation, the pressure in the deep veins is between 0 and 10 mmHg, and the pressure in the superficial system is around 90 mmHg resulting in filling of the deep veins from the superficial vein network [14].

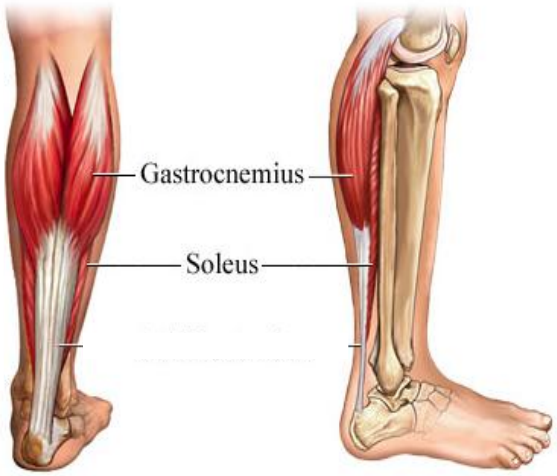


Figure 1.4: An illustration of the main muscles of the calf (adapted from Floota [15])

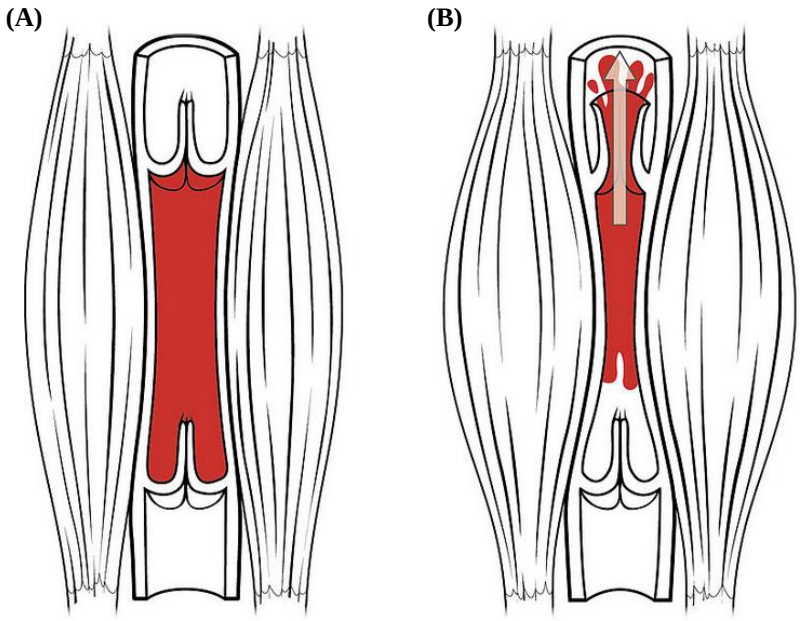


Figure 1.5: An illustration of the mechanisms of the muscle pump showing the muscles relaxed and valves closed (A) and the muscles contracted with the valves opened (B) (adapted from CNX Anatomy and Physiology [16])

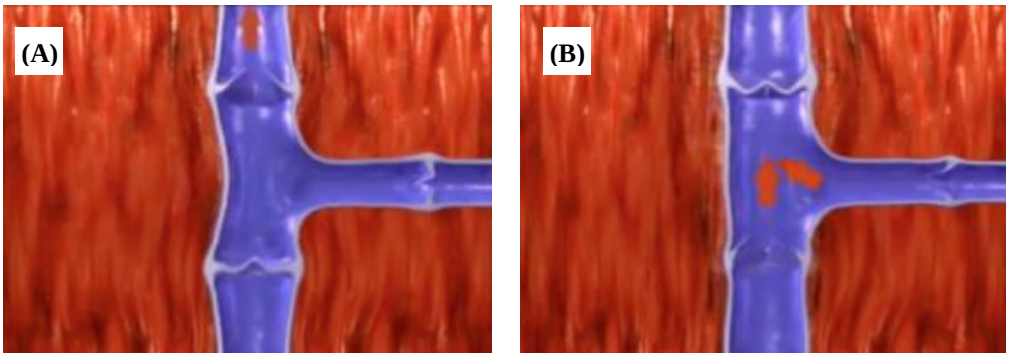


Figure 1.6: An illustration of the direction of blood flow during contraction (A) and relaxation (B) of the muscle (adapted from YouTube [17])

1.1.4 Passive Compression

1.1.4.1 Background of Passive Compression

Passive compression is used to treat venous insufficiencies that reduce the effectiveness of the muscle pump, mainly varicose veins, deep vein thrombosis, and chronic venous insufficiency [18]. These conditions are typically found in older populations, pregnant women, or persons who sit for extended periods of time. In each of these populations there is a higher risk of blood pooling in the legs. Varicose

veins occur when the veins become twisted and enlarged and fail to function properly leading to blood collecting in the legs, which can lead to blood clots or ulcers in the body [19]. Deep vein thrombosis is a condition whereby blood clots form in the deep veins, which can lead to a pulmonary embolism should the thrombosis dislodge and be carried through the circulatory system [20]. Lastly, chronic venous insufficiency is a condition where the valves located in the veins do not function properly, therefore allowing blood to pool and collect in the veins [21]. Compression helps reduce the effects of these conditions and move blood more efficiently by preventing swelling of the leg and reducing the chance that blood will pool and clot [19, 20].

Passive compression is generally applied to the leg in the form of a sock or stocking that can go to the knee or thigh depending on the degree of compression required. These socks have a compression pattern that provides pressure decreasing from distal to proximal (i.e. high pressure at the ankle, lower pressure at the knee or thigh). This compression pattern is referred to as graduated compression and acts to enhance the pressure gradient that exists in the veins to increase venous return. An illustration of the change in applied pressure from the garment is shown in Figure 1.7. The exact mechanisms by which passive compression works are not fully understood, however two methods are generally accepted. The first suggests that compression reduces and helps prevent swelling by increasing the pressure in tissues under the skin, reducing excess fluid leakage from the capillaries, and increasing absorption of tissue fluid by the capillaries and lymphatic vessels [18]. The second method suggests that compression helps control the diameter of the superficial veins, which decreases the risk of pooling and facilitates the return of blood to the heart [18].

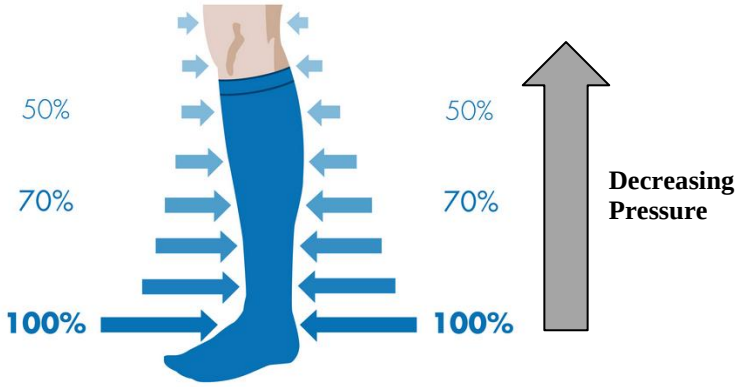


Figure 1.7: An illustration of the applied pressure to the leg from the GCS (adapted from VenaCureEVLT [22])

The strength of the compression garments varies based on the intended use, and can range from values of 8 mmHg to 50 mmHg or higher. For compression higher than approximately 25 mmHg, a prescription from a physician is required. The lower pressure range (8 to 30 mmHg) is utilized for minor to moderate varicose veins and swelling, during pregnancy, after surgery, or in exercise applications [18]. Higher

pressure (above 30 mmHg) is used for chronic venous insufficiency, deep vein thrombosis, severe swelling or varicose veins, and other serious medical issues [18].

Precise measurements of the patient's leg dimensions (ankle, calf, and thigh circumference and calf and leg length) are required in order to ensure the proper sock fit. The proper fit is extremely important, as the applied pressure from the socks can vary when the socks are not fitted or worn properly [23]. Blood flow can be significantly restricted by even a slight increase in the pressure exerted by the sock [23]. An increase in applied pressure above the recommended level could cause occlusion of the superficial or deep veins, making the socks ineffective for treating venous diseases.

Passive compression has been proven effective qualitatively in preventing and minimizing the severity of venous insufficiencies [23-25], however there are limited results in terms of quantitative data. Contradictory results exist on the effect of compression on the structural and functional parts of the vein. A detailed literature survey of the impact of compression on physiological performance metrics, including blood flow velocity and vessel diameters, indicates that there is currently disagreement amongst researchers employing different measurement and analysis techniques. Magnetic Resonance Imaging (MRI) studies [3, 4, 26, 27] in conjunction with Finite Element Analysis (FEA) [28-33] have suggested that while pressure decreases with depth in the leg due to external compression, the superficial vein diameters remain constant and the deep vein diameters decrease. Since both types of veins have nominally the same material properties, these two statements appear to be in contradiction. Ultrasound studies [5, 34, 35] suggest that, in fact, the deep veins compress less due to the attenuation of the compressive stress with depth, which is more palatable. The vast majority of these papers do not, however, clearly indicate relevant factors, such as leg position with respect to the heart, leg muscle activation, or changes in body position. Each of these factors can significantly affect the behavior of the vasculature and hence diameters and blood flow. Therefore, it is extremely important to know them in order to make a fair comparison between the results of the MRI, FEA, and ultrasound studies.

1.1.4.2 Extension to Exercise

The use of passive compression has been extended from a clinical treatment to an elective tool used by healthy individuals in an attempt to improve exercise performance. The rationale being that GCS will enhance the muscle pump, increase venous return, and decrease pooling in the legs, leading to increased cardiac efficiency and therefore stronger performance [36]. During exercise the heart works to maintain cardiac output in order to supply the muscles with a sufficient amount of oxygen rich blood. Cardiac output (CO) is calculated, as shown in Equation 1.3, from the product of heart rate (HR) and stroke volume (SV), the latter of which is the amount of blood pumped out of the heart during each contraction.

$$CO\left(\frac{L}{\min}\right) = HR\left(\frac{beat}{min}\right) * SV\left(\frac{mL}{beat}\right) * 0.001\left(\frac{L}{mL}\right) \qquad \textbf{Equation 1.3}$$

With an increase in the amount of blood returning to the heart, heart rate could potentially decrease as stroke volume increases, while still maintaining cardiac output. There is also the potential for cardiac output to rise due to an increase in stroke volume while maintaining a constant heart rate. Higher cardiac output would mean that more blood can be supplied to the exercising muscles and therefore increase the amount of oxygen the muscle receives. Muscles use oxygen to break down glucose and create fuel in the form of adenosine triphosphate (ATP) [37]. During exercise, the oxygen that reaches the working muscle is immediately converting glucose into energy [37]. When the body cannot maintain the oxygen demand, the muscles begin to convert glucose into lactic acid as a rapid, but inefficient mechanism to produce ATP [37]. The body can only sustain higher intensities of anaerobic exercise for a short time period before the metabolites accumulate and fatigue sets in [37]. During recovery, the muscles require oxygen to replenish pre-exercise ATP levels in the muscle and help the liver break down lactic acid [37]. An increase in oxygen delivery therefore has the potential to enhance muscle performance and aid in faster recovery time [36].

There is however, conflicting evidence for the effectiveness of compression on improving central and localized hemodynamics in a healthy population [1, 2]. When investigating the effects on running, the findings are inconclusive as to whether compression is beneficial. Inconsistency in the findings is reported for various types of exercise (i.e. sprinting, jumping, biking, or long distance running). One study tested 12 endurance-trained athletes and performed a time limit test with the athletes running at 105% of a recent 10 km race pace. It was found that time to exhaustion increased (337 vs. 387 seconds) and peak oxygen uptake was lowered (approximately 62 vs. 53 ml/kgmin) when wearing GCS[38]. Another study looking at 21 moderately trained runners found that time under load (35.03 vs. 36.44 min) and total work (399 vs. 422 KJ) was increased with GCS and that running performance was improved at different metabolic thresholds [39]. Testing compression during normal daily activity in 21 healthy females found that GCS aided in preserving lower leg venous calibre and tone through the veins and lowered calf circumference by 5.2± 7.0 mm [40]. Other studies however find no changes in physiological variables with the addition of compression [1, 5, 36, 41]. For example the effect of compression on the popliteal vein was investigated in 25 healthy males at rest and during ankle exercise and the results found no changes in popliteal vein blood velocity, diameter, or volumetric blood flow [5].

The majority of studies use individual perception to quantify the degree of muscle soreness as an indicator of the effect of compression on recovery. Several studies have found that participants feel they experience a decrease in muscle soreness with compression [1]. However, in studies where other indicators are used, creatine and lactate levels typically experience no change making it difficult to differentiate if the effect is from the GCS or due to the placebo effect [1]. For example, one study looked at the effect of compression on recovery for 40 competitive runners after a 56 km race and found reduced swelling, lower lactate levels, decrease in muscle damage (lower myoglobin levels in blood), and less perceived pain immediately after exercise and up to 48 hours following running [42]. Another study testing trained runners

for 40 minutes of running found no change in blood lactate and no impact on muscle function or soreness [36].

The existence of conflicting evidence could be in part due to the hypothesis that a healthy population may need an accommodation period to experience the benefits of GCS or due to the various testing regiments [1, 38]. Each study uses different exercise tasks at various intensities and durations. The study populations vary from subjects with normal, moderately active lifestyles to highly trained athletes. The applied pressure from the compression socks varies as well as the locations where the compression is applied (i.e. calf, thigh, full body). Finally, the extent to which the compression is applied during recovery varies from study to study. All of these factors make it difficult to draw concrete conclusions on the effect of compression during exercise and recovery in healthy populations.

1.2 Study Objectives

Although there have been several studies published on the effectiveness of passive compression in healthy populations, there are discrepancies as to whether they are beneficial for enhancing performance and recovery time. Due to the variation in experimental methods in current research protocols, concrete conclusions cannot be accurately drawn. The aim of this study is to complete a set of controlled experiments measuring a variety of physiological factors in an effort to determine the effect of passive compression on a healthy population. Included is the impact of passive compression on peripheral and central hemodynamics at rest and during exercise in a healthy population. For peripheral hemodynamics, the main variables to be investigated include; vessel diameter, blood velocity, muscle activity, oxygen delivery and uptake, and the applied pressure on the lower limb from the GCS. For central hemodynamics, the effect of external compression on heart rate, cardiac output, and blood pressure will be studied. In order to determine the effect of external compression on hemodynamics, the compression study will be compared to a baseline study where no compression is utilized. Investigating the impact of compression during rest, and before and after exercise, will isolate the effect of external compression from the underlying mechanisms of vascular behaviour in the standing position. During exercise, the baseline study will determine the impact of the muscle pump on hemodynamic behaviour, and with the addition of compression, the compound effect of passive compression with muscle pump activity will be resolved.

One key aspect of this study is that the applied pressure on the lower leg due the GCS will be measured and mapped in order to quantify the actual pressure applied to the leg. Previous research studies rarely report on measurements of the compressive force of the passive compression on the legs [1]. This is extremely important as the pressure distribution can vary from the manufacturer reported operational pressure based on leg geometry and sock application. This study will be compared to the conflicting evidence that exists from prior studies on the effectiveness of compression on improving hemodynamics in a healthy population with the hope that additional attention paid to the actual loading from the sock will aid in ending the debate on GCS effectiveness.

It is hypothesized that the addition of the GCS will enhance venous return, and therefore stroke volume, by helping to amplify the affect of the muscle pump. It is also thought that the GCS will decrease blood volume in the leg during the entire protocol since the prescribed clinical function of the GCS is to constrict the calf volume and help prevent blood pooling in the legs. It is believed that investigating plantar flexion exercise in the calf region will lead to no significant changes in central hemodynamics as only a small muscle mass is recruited to complete the task and therefore any local changes in the legs are not anticipated to have an impact on the central system. Furthermore, for muscle activity it is hypothesized that the participants will require less muscle activation on the second day of testing as they become more familiar with the protocol and can complete the task with more fluent motions and potentially less muscle recruitment. Finally, it is believed that the amount of muscle activation required during exercise will be tied to the subject's lifestyle with the rationale being that those subjects that exercise frequently will be able to complete the task more easily and require less muscle recruitment than those who exercise infrequently.

This thesis is organized as follows: the experimental methods are discussed in Chapter 2; the results and discussion are presented in Chapter 3; and the conclusions are made in Chapter 4.

Chapter 2

Experimental Methods

This chapter details the experimental methods, procedures, and equipment used to investigate the effect of external compression on central and peripheral hemodynamics. In addition, this chapter will detail the data reduction and analysis methods employed.

2.1 Overview of the Experimental Procedure

The experimental protocol investigated the effect of external compression on hemodynamics during rest and exercise for two conditions; wearing graduated compression socks (GCS) and not wearing graduated compression socks (NGCS). The testing began with a short rest period, followed by plantar flexion (calf raise) exercises, and finished with a second rest period. Initially, walking was selected as the exercise to investigate since it is an exercise completed by the population on a daily basis. However, walking could not be tested due to the limitations of using ultrasound to obtain muscle blood flow. Electromyography (EMG) tests comparing calf raises to walking illustrated that the total muscle activation of the calf during plantar flexion was similar to that during walking and therefore plantar flexion was considered an appropriate substitute. Results of the EMG study can be found in Appendix A.

Test participants reported to the lab on two occasions with a minimum of 48 hours between testing periods to evaluate repeatability. The order of the experiments was counterbalanced between subjects in order to determine if the order in which they completed the NGCS and GCS tests was relevant. That is, each participant completed the series of tests in the opposite order on the second day of testing (i.e. starting with the GCS condition on the first day of testing and starting with the NGCS condition on the second day, for instance). Furthermore, the experiment was designed so that half of the participants began with the GCS test on the first day of testing, and the other half began with the NGCS test on the first day. The experimental protocol for this study received clearance from the University of Waterloo Research Ethics Committee (ORE #19454).

To investigate the effect of external compression on a global level in the cardiovascular system, HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), and CO were measured. It was hypothesized that the addition of external compression to the lower extremities would enhance venous return to the heart and thus enhance SV. As mentioned in Chapter 1 if there is an increase in SV then there is potential for cardiac output to increase while heart rate is maintained, or there is potential for heart rate to decrease while cardiac output is maintained. It is of interest to see how SBP and DBP respond to changes in other central variables (i.e. HR and CO) due to the negative feedback mechanisms that help to regulate blood pressure. Changes in blood pressure would also provide insight into the resistance of the vessels in the circulatory system and if there is a significant change when the GCS are worn.

To investigate the hypothesis that GCS would enhance venous return at the local level in the lower leg, blood velocity, vessel diameter, muscle activity, muscle oxygenation, and applied pressure were measured. Blood velocity is important to determine the speed at which blood is returning to the heart and if the speed increased with the addition of the sock. Ideally this would be measured in the popliteal vein, as it is the conduit through which blood from the lower legs travels back to the heart. However, due to the low flow of blood in the veins it is difficult to capture using Doppler ultrasound and tends to get filtered out with noise from the system. The experimental uncertainty becomes too high when measuring the velocity of blood in the vein and therefore flow in the popliteal artery was obtained instead. Since the vascular tree is a closed system and this study focuses on a healthy population where blood pooling in the legs is not considered to be an issue, the information obtained from the arterial side should give a direct understanding of what was occurring on the venous side and returning to the heart. Popliteal arterial diameter was measured to determine if the vessel dilated or constricted during the testing protocol, prompting a change in blood flow, when the GCS was applied. Monitoring muscle activity provided details into the amount of muscle activation required to complete the exercise task with and without the GCS. If the muscle activation was similar for the NGCS and GCS cases, then it could be concluded that the participant was completing the same task each time and that the GCS have no effect on muscle activation. Muscle oxygenation was of interest since an increase in SV would imply that more blood is being delivered to the exercising muscles and hence increasing the amount of oxygen the muscle receives. Finally the applied pressure from the GCS was recorded to determine the additional change in pressure aiding venous return to the heart. Continuously measuring these global and local variables provided insight into how the body responds to the addition of the GCS and if the effects were beneficial for a healthy population.

2.2 Participants

Twelve healthy volunteers (7 male, 5 female, age 27.3 ± 6.40 years, body mass 73.0 ± 16.9 kg) participated in the study. All volunteers were instructed to avoid large meals two hours prior to testing, to refrain from heavy exercise 24 hours before testing, and to not consume caffeinated beverages 12 hours prior to testing. Participants received an overview of the protocol from the researchers with the opportunity to raise questions or concerns and were made aware of their right to withdraw from the study at any time. Each volunteer completed consent and health status forms and a physical activity readiness questionnaire (PAR-Q). The health status form included questions about the participant's exercise habits in order to determine their lifestyle. This included asking about the frequency of exercise as well as an explanation of the typical exercise performed. The conclusion from the health status forms was that the volunteers had sedentary to moderate exercise lifestyles. All forms were reviewed before proceeding with testing and any concerns were addressed. The protocol and consent forms are presented in Appendix B.

2.3 Experimental Protocol

Upon arrival to the lab, the participant's height, weight, and calf skinfold (measure of the fat layer below the skin) were measured. These measurements were used as inputs into the data collection devices

described in the next section. Next, the calf region was cleaned with alcohol and electrodes were placed on the leg to attach the EMG to obtain muscle activity information from the gastrocnemius and soleus muscles. A maximum voluntary contraction (MVC) test, which is a measure of the maximum tension the muscle can hold while completing one calf raise, was then performed. The MVC test was completed each day before testing in order to determine the percentage of the MVC that was required to complete the calf raise exercise. This normalization by the MVC values for each day provided insight into the muscle activation required for each participant to perform the test. Following the MVC test, each participant was instructed to complete one calf raise in order to position shoulder blocks to control the calf raise height. This ensured the participants completed the same task during each test. After the placement of the shoulder blocks, the heart rate monitor was connected to the participant and the Finometer® cuff (see Section 2.4) was placed on the middle finger of the left hand. The Finometer® was calibrated and a manual blood pressure measurement was taken to verify the value obtained from the Finometer® after calibration. The manual blood pressure measurement was repeated prior to the second test each day.

Continuing with the experimental set-up, the near-infrared spectroscopy (NIRS) probe (see Section 2.4) was attached to the medial head of the gastrocnemius. Calf circumference was then measured to determine the proper sock size as per the manufacturers recommended sizing method. Commercially available CEP Progressive+ Run Socks were used in this study, which have a manufacturer reported operational pressure range of approximately 15 mmHg to 25 mmHg. Next, a total of four air bladders were applied to the calf using Band-Aids and medical tape to hold them in place to record the applied pressure. Two pressure bladders were placed on both the medial and lateral side of the leg, as shown in Figure 2.1. The bladder locations were based off of anatomical landmarks on the knee and ankle. The distance between the bladders, *d*, differed from person to person due to the varying anatomical landmarks. This variation in *d* meant that the same pressure gradient was not applied to each subject's leg, but instead the change in the GCS pressure between *d* (ΔP) was made equivalent amongst subjects. The ΔP was maintained within 10 ± 3 mmHg by applying additional pressure at the ankle with tensor bandages as necessary. As previously discussed, the pressure applied by the sock varied based on leg geometry and application, the tensor bandages were only utilized if a ΔP of 10 ± 3 mmHg was not achieved independently by the GCS.

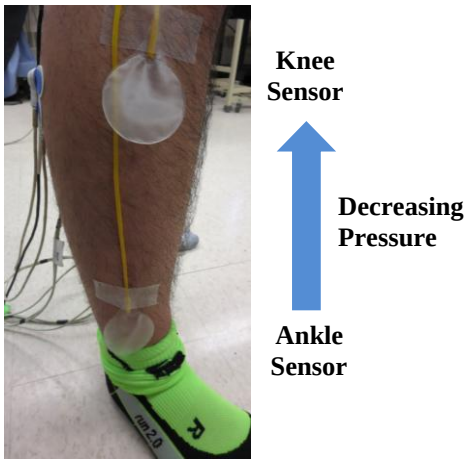


Figure 2.1: Two pressure bladders on both the medial and lateral side of the leg (lateral side shown).

If the GCS test was completed first, then after the compression sock had been properly sized and the desired ΔP was achieved, the popliteal artery in the right leg was located using echo Doppler ultrasound. If the NGCS test was completed first, once the calibration of the Finometer® was completed, the process of locating the artery began immediately and the addition of the pressure bladders and external compression occurred during a break between testing. The location of the popliteal artery was marked for diameter measurements during the testing protocol, as well as for placement of the Doppler ultrasound probe that obtained the velocity signal in the popliteal artery. The Doppler ultrasound probe used for velocity data was adjusted until a clear velocity signal was obtained from the artery with no contamination from the popliteal vein. Finally, a dark cloth was wrapped around the leg, either over the bare calf or on top of the sock to ensure no light affected the NIRS measurement device (see Section 2.4). This wrap applied no additional pressure to the leg and only served as a cover for the NIRS probe, as confirmed by the in situ pressure bladders.

After the experimental set-up was completed, all measurement locations were recorded for future testing and participants sat for 15 minutes with all devices on to allow for stabilization. In between tests, as previously mentioned, there was another break (approximately 15 minutes) while the GCS was removed or added depending on the order of testing. Once the GCS was applied to the leg, a 10 minute accommodation period was used to allow the body to acclimate to the additional pressure [3, 4].

For the testing portion of the protocol, participants initially stood in a natural posture with both feet on the ground for a three minute baseline (BL) to allow their bodies to acclimatize to the standing position. Next, participants completed a five minute exercise period (EX) in which they completed plantar flexion (calf raise) exercises to simulate the activity of the calf muscle during walking. Lastly, participants were again asked to stand in a natural posture for a five minute recovery period (REC). The recovery period was included to allow the body to return to baseline conditions after the completion of exercise. The total

protocol took 13 minutes to complete, see Figure 2.2. The calf raises were performed at a rate of 20 per minute for five minutes to allow the body to come to steady state during exercise. This involved calf raises completed with a period of three seconds, as illustrated in Figure 2.3, where participants were instructed to raise their ankles for one second (Figure 2.3A), lower their ankles for one second (Figure 2.3B), and relax with both feet on the ground for one second (Figure 2.3C). The protocol was then repeated for the opposite condition (i.e., NGCS or GCS depending on the first test completed).

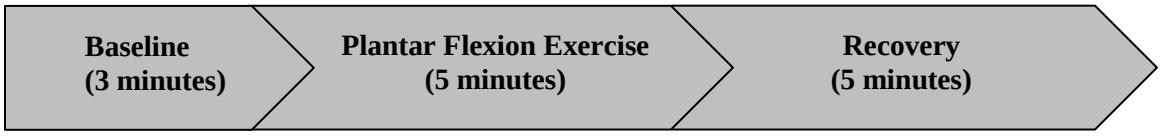


Figure 2.2: Exercise Protocol

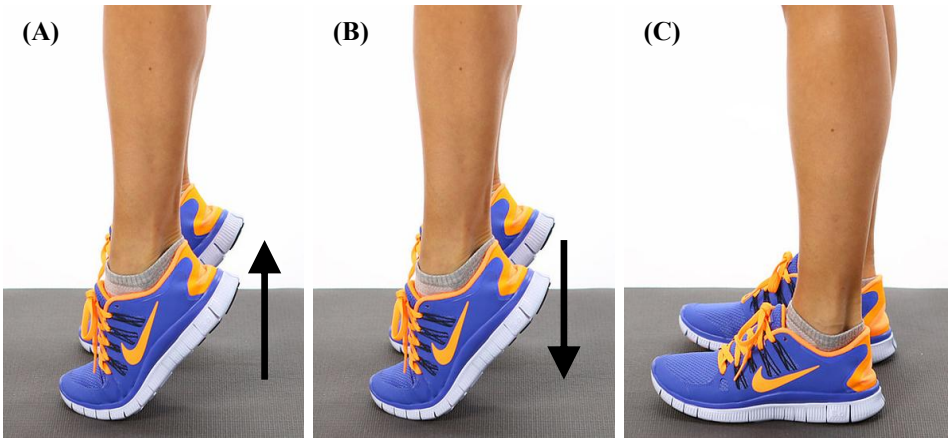


Figure 2.3: Protocol for plantar flexion exercise completed over a period of three seconds. The participant's raised the ankles over a one second duration (A), lowered the ankles over a one second duration (B), and relaxed for one second (C) (adapted from Verge Magazine [43])

All measurements were continuously recorded throughout the testing protocol except for diameter measurements, which were completed during baseline and recovery conditions only. During exercise, with the calf continuously moving it was too difficult to sustain a quality image on the ultrasound, as well as it would require an interruption in the collection of velocity data, as the operator would have had to switch ultrasound systems for a short period of time. More details on data collection are presented in Section 2.4.

2.4 Data Collection

Peripheral and central hemodynamics were monitored using physiological testing equipment, as shown in Figure 2.4 and Figure 2.5. All peripheral measurements were performed on the right leg only. During the experimental protocol, arterial blood pressure was continuously measured by a photoplethysmograph cuff (Finometer, Finapres Medical Systems, Amsterdam, The Netherlands), placed on the middle finger of the left hand (Figure 2.5(A)). This device estimated the cardiac stroke volume from a finger pressure wave and multiplied SV by heart rate to estimate cardiac output, see Section 2.4.1 for

more details. Heart rate was calculated from the R-R interval (beat to beat average) obtained from an electrocardiogram (ECG) (Pilot 9200, Colin Medical Instruments Corp, San Antonio, Texas, USA) (Figure 2.5 (C)) described in detail in Section 2.4.2. Concomitantly, peripheral blood flow was obtained by a 4 MHz Doppler ultrasound probe (Neurovision Doppler Ultrasound, Model 500, Multigon Industries, Elmsford, New York, USA) to determine beat-by-beat blood flow velocity in the popliteal artery, the main feed artery to the calf muscles (Figure 2.5 (B)), see Section 2.4.3. Vessel diameter was measured using an 8-12 MHz linear array ultrasound transducer (L14-6s with M5 system, Mindray Medical International Limited, Shenzhen, China) described in Section 2.4.3. Muscle activity was measured in the gastrocnemius and soleus muscles (calf muscles) using a custom built EMG (Figure 2.5(D)) discussed in Section 2.4.4. The EMG signal was processed using a custom MATLAB program (MATLAB, vR2013a, The Mathworks Inc., Natick, Massachusetts, USA). Blood pressure, heart rate, blood velocity, and muscle activity were sampled at 1000 Hz using a data acquisition system (Powerlab, ADInstruments, Colorado Springs, Colorado, USA) and processed using LabChart analysis software (LabChart, v7.2.5, ADInstruments, Colorado Springs, Colorado, USA). Muscle oxygenation and blood volume were measured on the gastrocnemius medial head using NIRS (PortaLite, Artinis Medical Systems B.V., Elst, The Netherlands) and sampled at a rate of 50 Hz; see Section 2.4.5 for more details on the NIRS system. Finally, the pressure applied to the calf muscles was determined by a custom-built system consisting of a series of bladders placed on the medial and lateral aspect of the calf muscle between the GCS and the skin. The pressure data was acquired at a sampling rate of 10 Hz using LabVIEW software (LabVIEW, National Instruments Corporation, Austin, Texas, USA). The acquisition of dynamic pressure measurements allowed for the applied pressure to be correlated with physiological measurements. More information on the custom pressure system can be found in the Section 2.4.6.

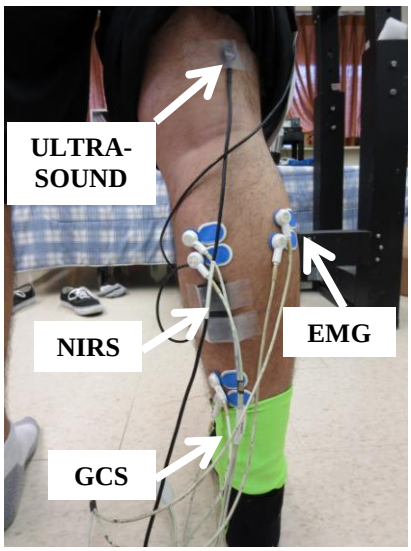


Figure 2.4: Peripheral measurement probes displayed on leg along with the GCS

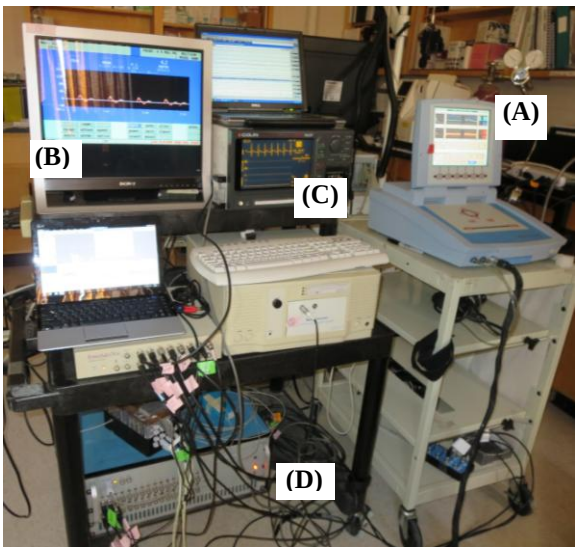


Figure 2.5: Experimental setup including (A) Finometer®, (B) Doppler Ultrasound, (C) Colin Heart Rate Monitor, (D) EMG

2.4.1 Finometer®

The Finometer® utilizes photoplethysmography (a method for measuring changes in volume) to measure blood pressure and heart rate and predict cardiac output. A photoelectric photoplethysmograph cuff is placed on the middle finger of either hand and finger blood pressure is determined using the volume-clamp method [44]. This method measures the volume of the arteries under the finger cuff using a pneumatic servo system and aims to dynamically hold that volume constant by measuring the counter pressure in the finger cuff during the pulsation [44].

The desired blood pressure measurement is the brachial artery blood pressure, which is reconstructed from the finger pressure obtained using an inverse modeling corrector and a height corrector. The inverse modeling corrector is a frequency-dependent transfer function that is used to obtain the brachial pressure waveform model from the measured finger pressure waveform [45]. The height corrector is used to account for the change in hydrostatic pressure due to the location of the brachial artery compared to the finger.

Once the brachial blood pressure is reconstructed, a "Modelflow" algorithm is used to obtain the aortic flow waveform. The "Modelflow" algorithm is a non-linear model of the aortic input impedance consisting of three elements: aortic characteristic impedance, Windkessel arterial compliance, and systemic vascular conductance [44]. The aortic characteristic impedance is the aortic opposition to the pulsatile flow from the left ventricle [45]. The Windkessel arterial compliance is the aortic elastic storing property, and the systemic vascular conductance is a measure of the resistance of all vascular beds [45]. The age, height, and weight of the participants are entered into the system in order to help with the accuracy of predicting the model inputs [44]. Once the aortic flow curve is generated, the area under the curve during systole is proportional to the stroke volume [44]. The stroke volume value is then multiplied by heart rate and an estimate of cardiac output is obtained.

2.4.2 ECG

The ECG non-invasively monitors and records the electrical activity of the heart through three electrodes placed on the chest of the body. Figure 2.6 shows a sample ECG signal for one heartbeat, illustrating the important electrical waveforms. A heartbeat begins with an electrical signal originating in the sinoatrial node located in the right atrium. The signal then moves through the left and right atria (P wave) causing them to contract and move blood to the left and right ventricles. The electrical signal passes through the atrioventricular node when moving into the ventricles, slowing the signal to allow time for the ventricles to fill. Once the signal moves out of the atrioventricular node, it moves quickly across the left and right ventricles causing them to contract and supply blood to the body and lungs, respectively (QRS wave). Finally the ventricles return to their normal state (T wave) and the heart muscle stops contracting, allowing the heart to refill with blood. The process is then repeated anywhere from 60 to 100 times a minute when a person is at rest [46].

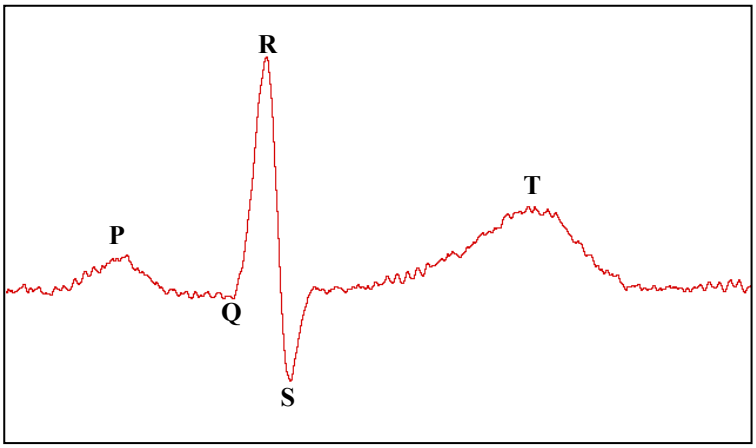


Figure 2.6: Sample ECG signal for one heartbeat illustrating the important waveforms (P wave, QRS wave, and T wave)

2.4.3 Doppler Ultrasound

Ultrasound utilizes high frequency sound waves and their echoes to obtain both structural and functional information. The basic concept of ultrasound is that a transducer converts electrical energy to acoustic signals that generate pulses of ultrasound that are sent through the body. The sound pulses travel into the body and organ boundaries, and complex tissues produce echoes by reflection or scattering, which return back to the transducer. The transducer converts this signal back to an electrical signal. The machine calculates the distance from the probe to the tissue or organ using the speed of sound in tissue and the time delay between transmission and the return of the echo. The machine displays the distances and intensities of the echoes on the screen forming a grey scale image; an example image of the popliteal vein is shown in Figure 2.7 [47].

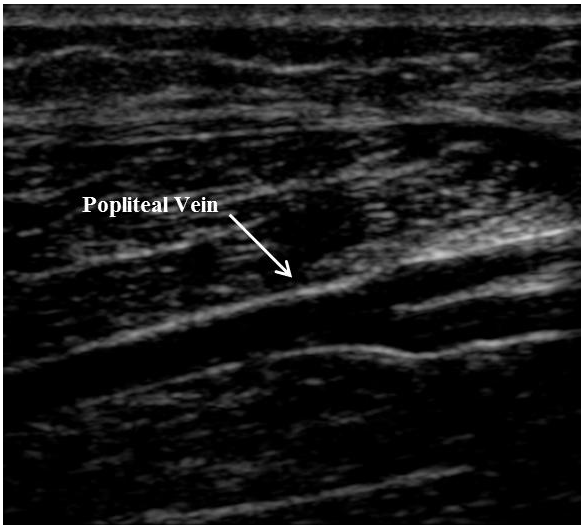


Figure 2.7: Sample ultrasound image of the popliteal vein showing a branch location

Doppler ultrasound is used to determine blood velocity. The sound waves from the transducer bounce off the red blood cells within the vessel and the signal is returned to the transducer with a Doppler shift. The Doppler shift is the change in observed frequency due to the relative motion of the source and the observer [47]. In this case the Doppler shift occurs twice; the first occurs when the transducer is stationary (source) while the blood cells are the moving receivers of the waves (observer), the second is when the ultrasound is back-scattered from the moving red blood cells (source) to the transducer (observer) [47]. The Doppler frequency (f_d) is calculated by subtracting the transmitted frequency (f_t) from the received frequency (f_r) as shown in Equation 2.1 [47].

$$f_d = f_r - f_t$$ **Equation 2.1**

The velocity (v) can then be calculated based off of this shift as shown in Equation 2.2; where c is the speed of sound in tissue (1540 m/s) and θ is the angle of insonation, which is defined as the angle between the flow and ultrasound beam as illustrated in Figure 2.8 [47]. The angle of insonation is extremely important as when the angle is 90° the cosine value is 0 and no Doppler shift will be detected, when the angle is 0°, the cosine value is 1 and the maximum Doppler shift is detected [47]. Therefore it is important to know the angle of insonation in order to determine which component of velocity the transducer is receiving. Finally, the Doppler shift frequencies end up in the audible range (20 Hz to 20 kHz) so the user can hear the signal while using the ultrasound, which helps in operating the system and locating the best velocity signal [47].

$$v = \frac{c f_d}{2 f_t \cos\theta}$$ **Equation 2.2**

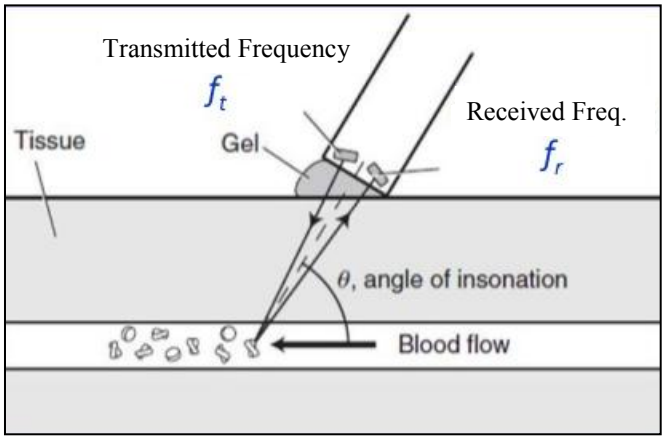


Figure 2.8: Illustration of Doppler ultrasound physics (adapted from Thrush et al. [47])

2.4.4 EMG

EMG measures the electrical voltage generated in the skeletal muscle during contraction, representing neuromuscular activity [48]. The functional unit of a muscle contraction is a motor unit [49]. A motor unit consists of a group of skeletal muscle fibers and the motor neuron that controls them [6]. A motor neuron is a nerve cell that, directly or indirectly, controls the movement of muscles [6]. Skeletal muscle fibers contract when the action potentials (rapid and uniform electrical signals conducted along the membrane of a muscle fiber) of the motor nerve reach a depolarization threshold [6, 49]. The depolarization, which is a decrease in the membrane potential of a cell, spreads through the membrane of the active muscle creating an electromagnetic field where the potential is measured as a voltage [6, 49]. The depolarization is a muscle action potential (MAP) and the motor unit action potential is the sum of the individual MAPs for all of the skeletal muscle fibers in a motor unit [49]. The EMG signal is therefore the summation of the motor unit action potentials in the location where the electrodes are placed on the surface of the skin [49]. Each site where muscle activity is of interest requires two electrodes so that the voltage waveform recorded is the difference in the potential between two electrodes [49]. MAPs occur at random intervals so at any moment the EMG signal can be positive or negative [48]. The electrical signal obtained is amplified and can be processed in several ways (e.g., linear envelope, half-wave rectification, full-wave rectification, root mean square, integrated EMG, or frequency analysis [49]). Figure 2.9 shows an EMG signal obtained from the medial head of the gastrocnemius muscle for two contractions of the calf muscle. Figure 2.9A displays the raw amplified signal obtained from the electrodes, and Figure 2.9B illustrates an example of a signal that has been processed using full-wave rectification (taking the absolute value of the whole signal) and linear envelope (using a low-pass filter on the full-wave rectified signal) [49].

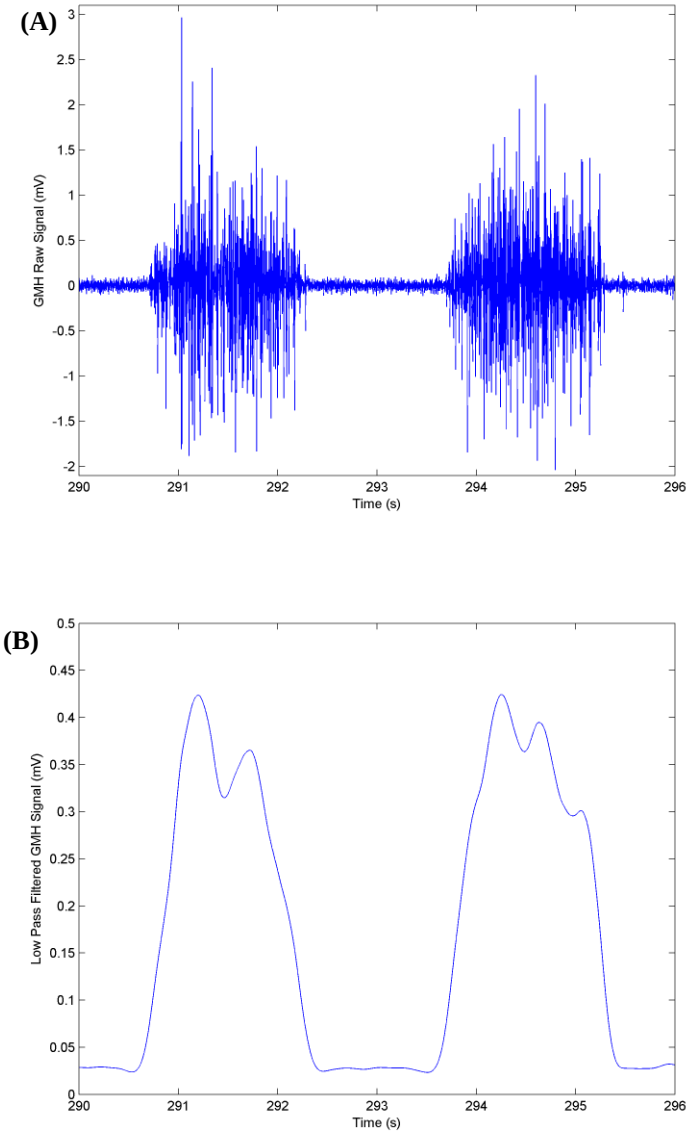


Figure 2.9: A sample EMG signal for two calf contractions showing the raw amplified signal (A) and the processed signal (B) using full-wave rectification and taking the linear envelope.

2.4.5 NIRS

NIRS provides the ability to measure oxygen binding to hemoglobin by studying the interaction of light with tissue in the near infrared spectrum (700-1300 nm) [50]. Tissues have good transparency for light in this spectrum and therefore it is possible to transmit photons through the muscle for monitoring hemoglobin levels [50]. Hemoglobin contains chromophores, which are the portion of molecules that generate colour when they absorb certain wavelengths of light. The main principles of NIRS are therefore that light is emitted from the NIRS source, then absorbed by chromophores in the hemoglobin, and a new wave

emission is generated [51]. The NIRS device captures the new light generated and calculates the optical density for each sample [51]. Lastly, from the optical density values, the changes in oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) are calculated [51].

The concept of NIRS is based on the Lambert-Beer law shown in Equation 2.3; where OD (λ) is the optical density of the tissue, ε(λ) is the absorption coefficient ($mM^{-1}cm^{-1}$), C is the concentration of the chromophore (mM), L is the distance between light entry and exit point and λ is the wavelength used (nm). Equation 2.3 also contains a dimensionless pathlength factor (DPF) to account for an increase in the optical pathlength due to scattering in the tissue. The value of DPF used in this study was 5.84 for an adult calf. Finally, the $OD\ (\lambda)_r$ term represents the oxygen independent losses due to scattering in the tissues. It is assumed that this value remains constant during measurements and therefore a change in optical density (ΔOD (λ)) is converted to a change in concentration (ΔC) as shown in Equation 2.4 [50].

$$OD(\lambda) = \varepsilon(\lambda) * C * L * DPF + OD(\lambda)_r \qquad \textbf{Equation 2.3}$$

$$\Delta C = \frac{\Delta OD(\lambda)}{\varepsilon(\lambda) * L * DPF} \qquad \textbf{Equation 2.4}$$

Equation 2.4 is valid for a medium with one chromophore, however in tissues there are at least two oxygen dependent chromophores present leading to a set of linear equations that is solved by an algorithm in the NIRS software [50]. The Portalite system used in this study uses two wavelengths (760 nm and 850 nm) to obtain information about the two main components of hemoglobin: O_2Hb and HHb. Moreover, NIRS provides information about the total blood volume in the tissue (total hemoglobin, tHb) and the absolute oxygenated hemoglobin percentage (TSI) [50]. Two wavelengths are required due to different absorption spectra for O_2Hb and HHb [50]. Finally, NIRS measurements can only provide relative values for the variables of interest and therefore a baseline condition is required for comparison purposes, for this study the baseline used was the initial three minutes of quiet standing before beginning exercise [51].

2.4.6 Pressure System

A custom system was designed and built to measure the pressure applied to the leg by the GCS. The pressure measuring system consists of four Omega PX309 (0-2 PSI) pressure transducers, 16 PicoPress pressure sensors, and 19 solenoid valves. The pressure sensing elements are a series of air bladders that are placed directly between the skin and the GCS. The system is separated into four sections, as illustrated in Figure 2.10, to allow for the pressure to be measured in four locations simultaneously. Figure 2.10 also shows that each section is separated from the others by a solenoid valve and contains a pressure transducer, four pressure sensors, and four solenoid valves. Figure 2.11 is an image of the system and shows the solenoids and the pressure sensors, which are connected to the transducers via flexible plastic tubing.

Initially, all of the solenoids are opened and a small pressure (< 1 mmHg) is introduced into the system to inflate the pressure sensors. Once all 16 pressure sensors are partially inflated, the three solenoids, which separate the four sections from each other, close. To measure the pressure applied to any sensor, the solenoid valve placed between the pressure sensor and transducer is opened, while the other three solenoids in the section remain closed. This allows the transducer to measure only the pressure applied to the selected sensor. Cycling through the four solenoid valves in a section allows the four sensors to apply their pressure to the transducer in turn. Since continuous monitoring of the applied pressure from the GCS was required for this experiment, only one pressure sensor from each of the four sections was employed. Information regarding the calibration and validation of the pressure system can be found in Appendix C [52].

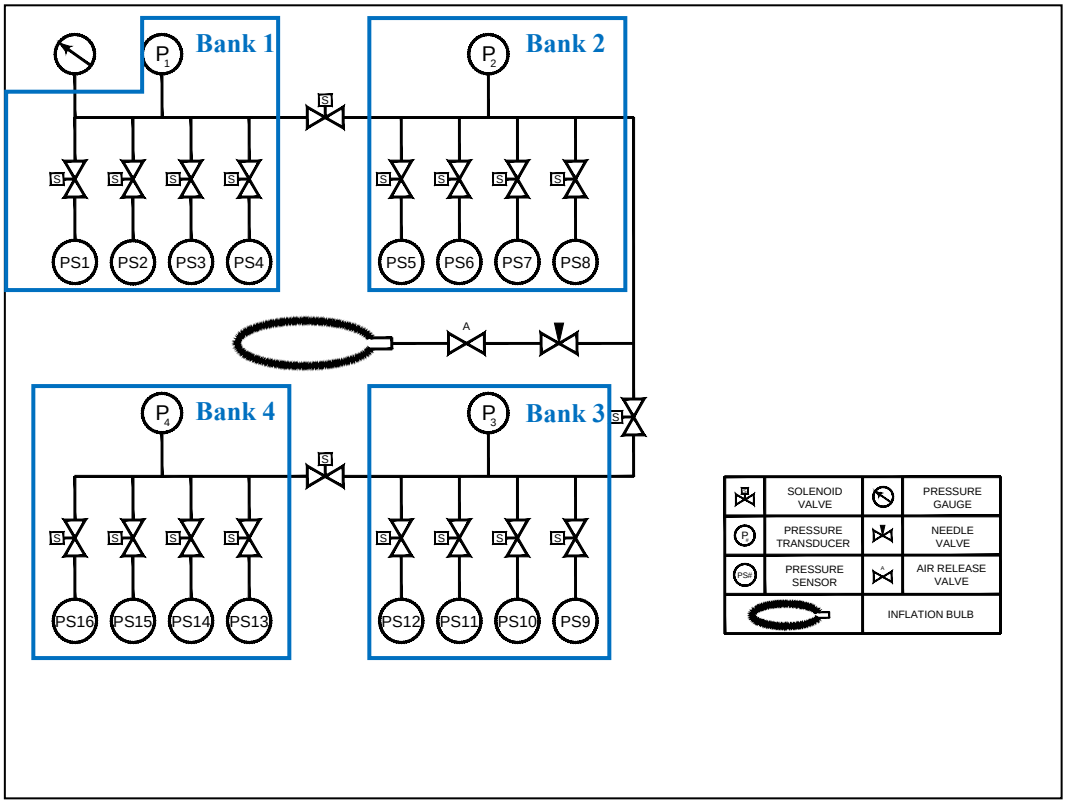


Figure 2.10: Schematic of the pressure sensor system (adapted from Beentjes [52])

Figure 2.11: An image of the pressure sensor system showing the 19 solenoids and the 16 pressure sensors (adapted from Beentjes [52])

2.5 Data Analysis

For central variables, the averages over the entire BL, EX, and REC conditions were computed. Before averages were calculated, the raw data for cardiac output and blood pressure were shifted by one second to account for the delay in the analog signal from the Finometer® to the data acquisition system [44]. Also, the beat-to-beat average for heart rate was calculated from the R-R intervals obtained from the ECG signal. A shorter averaging time of 180 seconds was used for one subject due to noise in the heart rate signal thought to be caused by the placement of the electrodes that led to interruption in the signal due to movement of the chest from breathing. This occurred for only one of the two testing days. Figure 2.12 shows an example of the signal corrupted by the presumed ECG motion compared to a normal heart rate signal. A second subject had noise in the blood pressure and cardiac output signals due to issues with the Finometer® during one of the days of testing. The issues are thought to be due to the machine not being able to maintain a continuous signal for finger pressure due to cold hands of the subject; therefore, a shorter period of 112 seconds was used for computing the average values for that subject. Shorter averaging times were also required for one subject during recovery for both days (108 seconds for day 1 and 248 seconds for day 2) again due to the same issue with the Finometer®. Figure 2.13 illustrates an example of the Finometer® issues by showing a comparison between the interrupted blood pressure waveform (Figure 2.13A) and a typical blood pressure waveform (Figure 2.13B), which only has an interruption in the signal when the calibration occurs.

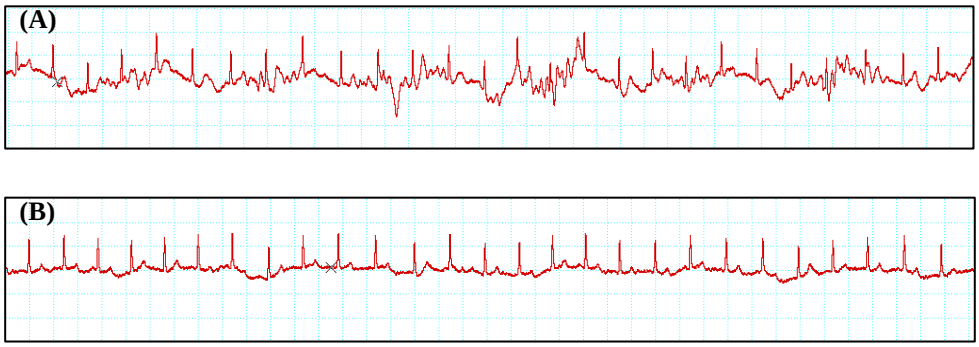


Figure 2.12: Illustration of issues with the heart rate signal for one subject showing a comparison between the interrupted heart rate signal (A) due to the placement of electrodes, and a typical ECG signal (B)

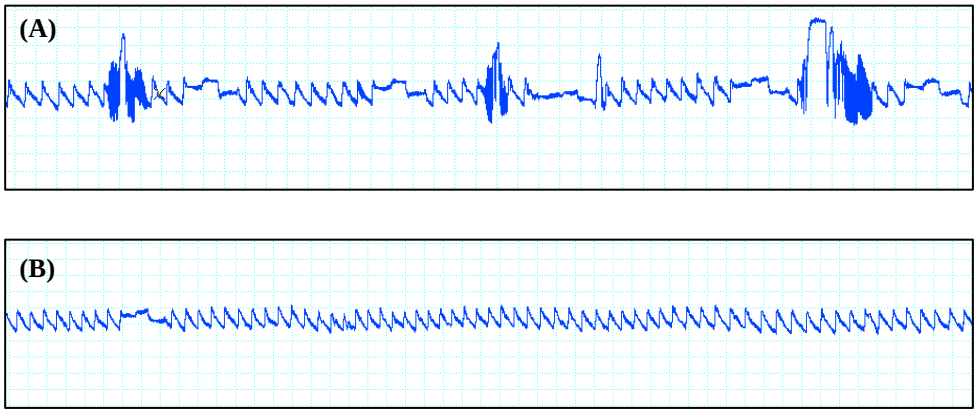


Figure 2.13: Illustration of issues with Finometer® for one subject showing a comparison between the interrupted blood pressure waveform (A) thought to be due to the cold hands of the subject, and a typical blood pressure waveform (B), which only has an interruption in the signal when calibration occurs

For the blood velocity (v) data obtained from the Doppler ultrasound, a low pass digital filter of 10 Hz was applied to the signal as demonstrated in Figure 2.14. The jagged nature of Figure 2.14A illustrates that the data acquisition system had a higher sampling rate than the Doppler ultrasound, leading to the sampling and holding pattern in the signal. The data acquisition system sampled at a rate of 1000 Hz compared to the Doppler ultrasound which had a sampling rate within the range of 140 Hz to 160 Hz. The low pass filter of 10Hz, as illustrated in Figure 2.14B, was selected as it removed noise from the signal and only allowed the frequencies of the physiological signal of interest to pass through. Furthermore, the data was adjusted to account for the typical insonation angle (see Section 2.4.3) of the popliteal artery of 60° as shown in Equation 2.5. This angle of insonation was used for the entire study population after verifying that all subject's popliteal artery was positioned at an angle of approximately 60°. The mean of the corrected velocity (PBV_{mean}) signal was used in further analysis.

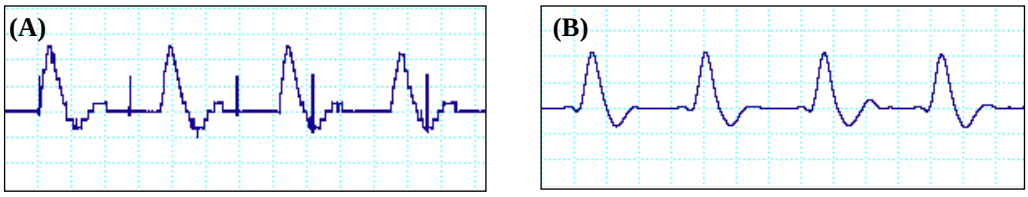


Figure 2.14: Comparison of the raw velocity signal obtained from the popliteal artery (A) and the processed signal when a low pass filter is used with a cut off frequency of 10 Hz (B)

$$v_{corrected} = \frac{v_{raw}}{\cos 60} \qquad \textbf{Equation 2.5}$$

Due to the fact that the ultrasound probe had to be manually held against the subject's leg throughout the entire protocol, it was difficult to obtain a clear signal over the entire testing period. Therefore, the averages for one minute during BL, steady state EX, and REC were used to determine the effect of external compression. The criteria for selecting the minute where the average was taken for each condition involved ensuring there was no obvious contamination in the velocity signal from the popliteal vein or due to operator movements as illustrated in Figure 2.15. It can be seen in Figure 2.15A that when the popliteal vein is also insonated there is a stronger negative velocity, which would affect the average compared to Figure 2.15B where only signal from the popliteal artery is recorded. In some situations it was not possible to obtain a clean signal for one minute for all participants. For the baseline condition, four subjects had time average durations that ranged from 40 to 48 seconds for one day of testing, as these were the longest spans of unadulterated signal. For exercise, one subject required that all test averages be shortened (between 38 and 45 seconds) and two other subjects had averages of 36 seconds and 45 seconds for one day during one test. Finally, for recovery, one subject required a 37 second average on one day for one test.

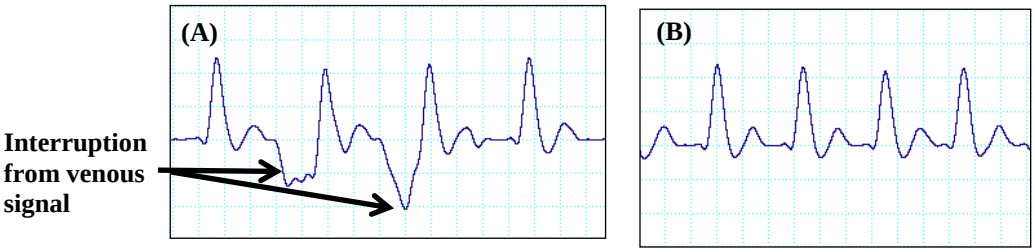
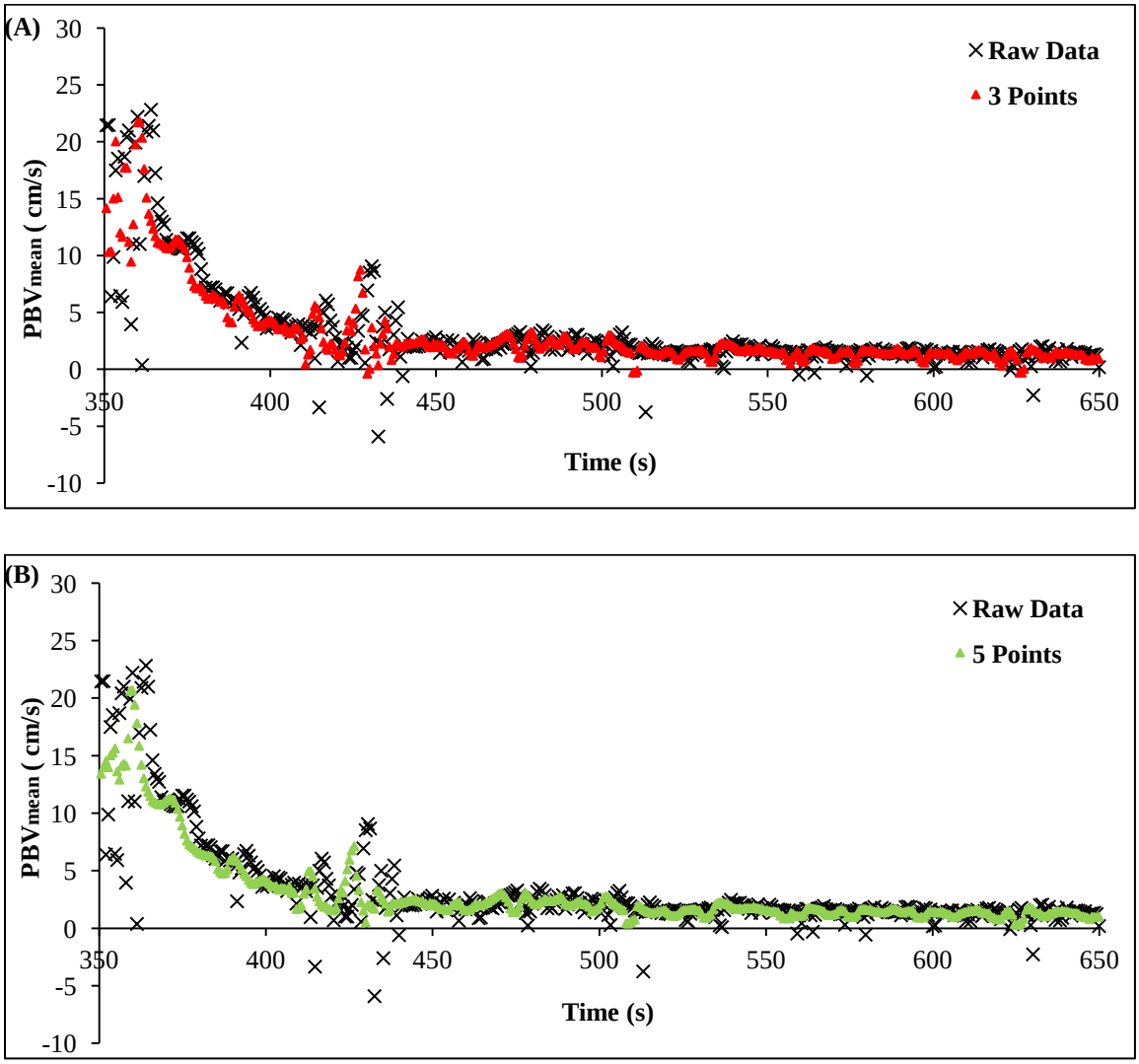


Figure 2.15: Comparison of velocity waveforms during baseline condition showing a waveform disrupted due to venous activity (A) and a clean waveform (B)

The time required for each subject to return to a PBV_{mean} value of 50 % above their average baseline velocity was analyzed to determine the time to recovery for the NGCS and GCS. This time was investigated to determine if the GCS could aid in a faster hemodynamic recovery following exercise. A beat-to-beat average of PBV_{mean} was used and the data was smoothed using a moving average to minimize

variation between heartbeats. Moving averages of various degrees were tested, as illustrated in Figure 2.17 for one subject. A moving average consisting of seven data points was used as it was determined, qualitatively, to smooth the data best without significantly changing the values. The moving average of seven points had fewer outliers when compared to the averages involving fewer points and a more consistent trend. Visual comparisons between moving averages of seven and 10 points were not deemed significant and therefore seven points was selected as the ideal value. The time to recovery was selected when subjects steadily maintained a value of 50% above the average BL velocity or below.



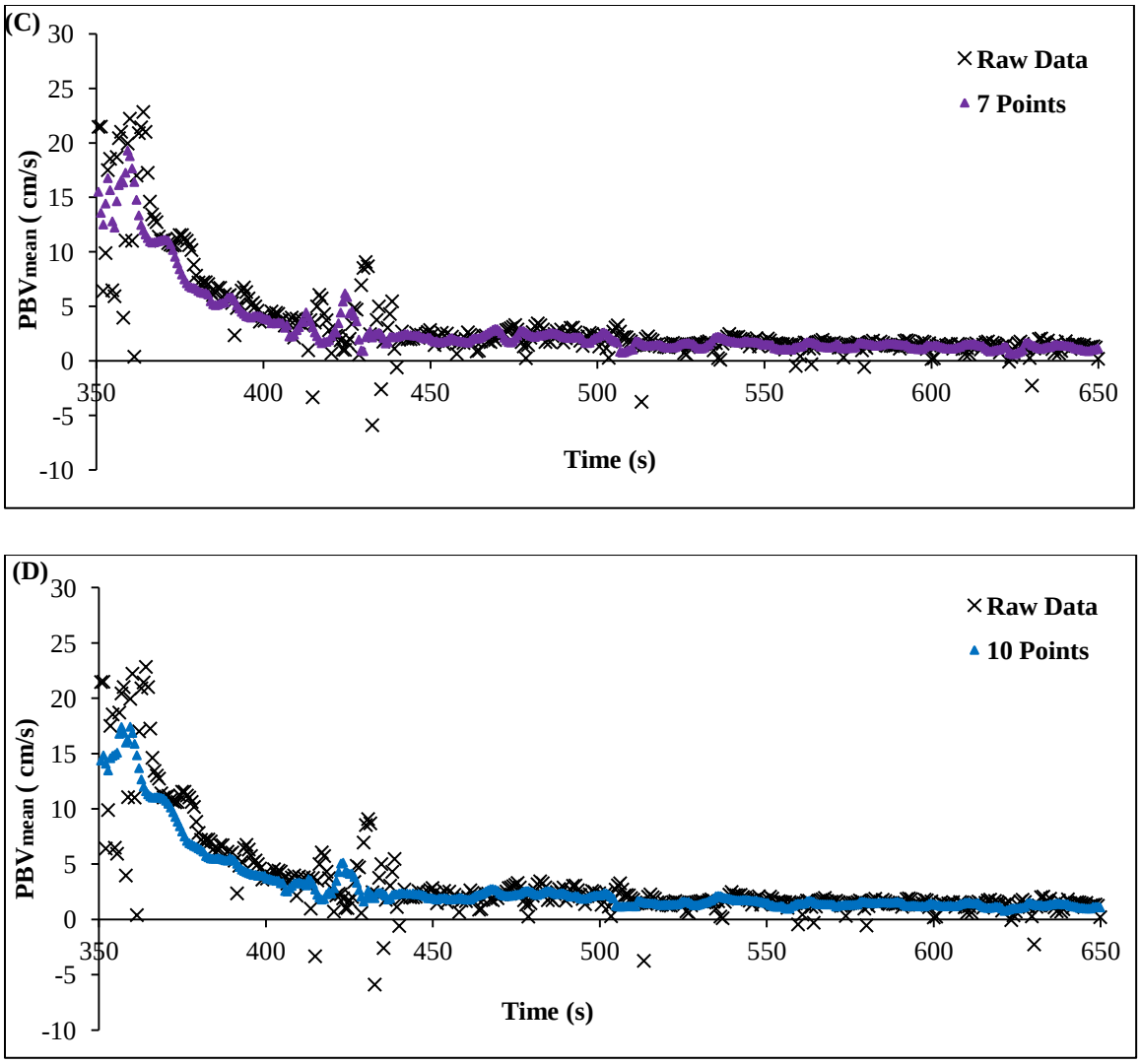


Figure 2.16: Comparison of raw data to moving averages involving varying data points (A: 3 points, B: 5 points, C: 7 points, D: 10 points)

Popliteal artery diameter (PAD) was computed from the diastolic diameter, as this portion of the cardiac cycle has been proven to provide the most stable diameter image for analysis [53]. The average of three measurements was taken. Mean flow rate in the popliteal artery (PBF_{mean}) was calculated using Equation 2.6 [54]. Since the diameter was only measured during baseline and recovery conditions, the diameter obtained during the baseline condition was used to calculate PBF_{mean} for the exercise condition. Mean arterial pressure (MAP), an estimation of the average blood pressure of an individual, was calculated based on SBP and DBP as shown in Equation 2.7 [7].

$$PBF_{mean}\left(\frac{mL}{min}\right) = PBV_{mean}\left(\frac{cm}{s}\right) * \pi * \left(\frac{PAD(cm)}{2}\right)^2 * 60\left(\frac{s}{min}\right) \quad \textbf{Equation 2.6}$$

$$MAP(mmHg) = \left(\frac{1}{3}\right) * SBP(mmHg) + \left(\frac{2}{3}\right) * DBP(mmHg) \qquad \textbf{Equation 2.7}$$

Stroke volume was computed using Equation 2.8 [55]. Total peripheral resistance (TPR), a measure of the overall resistance of the peripheral circulation blood flow, was calculated from Equation 2.9 [55]. Lastly, muscle perfusion pressure (MPP) was estimated using Equation 2.10 [54], which utilizes the distance from the heart to the calf muscle (DHC) to predict the pressure of blood being delivered to the calf muscle.

$$SV\left(\frac{ml}{beat}\right) = \frac{CO\left(\frac{L}{min}\right)}{HR\ (bpm)} * 1000\left(\frac{ml}{L}\right) \qquad \textbf{Equation 2.8}$$

$$TPR\left(\frac{mmHg}{L/min}\right) = \frac{MAP\ (mmHg)}{CO\ \left(\frac{L}{min}\right)} \qquad \textbf{Equation 2.9}$$

$$MPP(mmHg) = MAP(mmHg) + \frac{DHC\ (cm)}{1.36\left(\frac{cm}{mmHg}\right)} \qquad \textbf{Equation 2.10}$$

For NIRS data, tHb, O_2Hb, and HHb were analyzed. In order to determine the effects of external compression on muscle oxygenation during exercise, the difference from the baseline condition must be determined. Therefore the mean of the last 30 seconds of baseline for each variable was subtracted from the values obtained during exercise. To determine the effect of compression during recovery, the difference from the exercise condition was investigated. The averages of the last minute of exercise and recovery were analyzed as the majority of participants had reached steady state by these times. The overall average of each variable for all participants was analyzed for both days of testing. Figure 2.17 shows an example of the raw data obtained for the tHb variable and the locations where the averages were calculated for each condition.

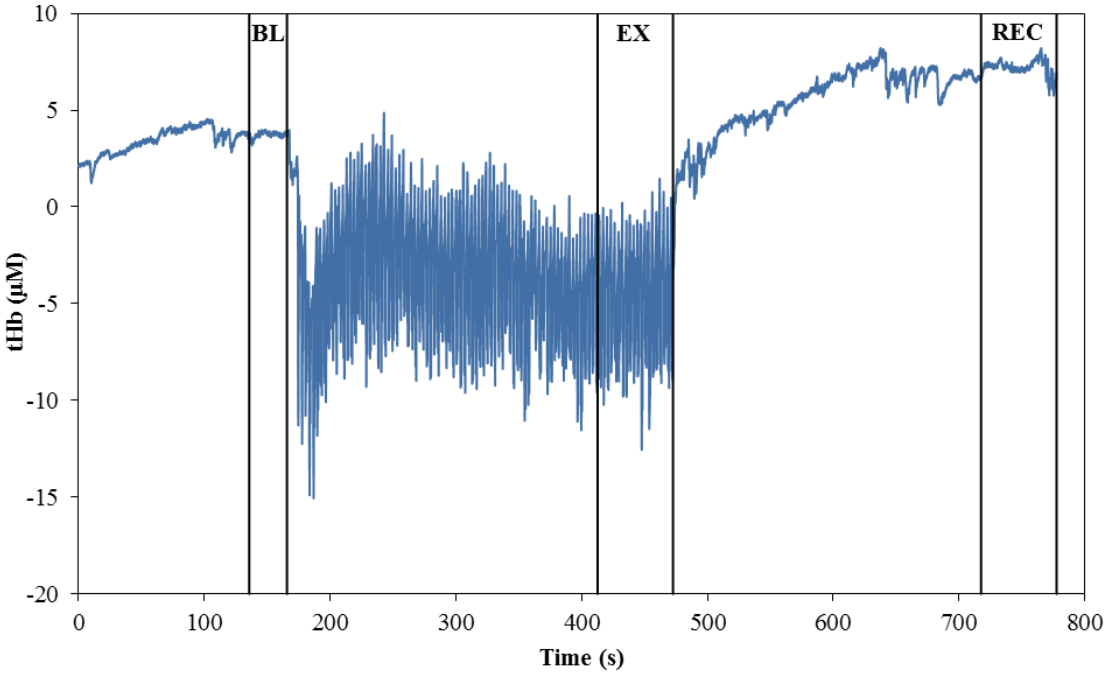


Figure 2.17: Illustration of the time spans over which average values were calculated for NIRS analysis during BL, EX, and REC

The EMG signal was processed using full wave rectification and a linear envelope [53, 56, 57]. The process is illustrated in Figure 2.18. First, the raw data was imported into MATLAB (Figure 2.18A). Next, full wave rectification was completed by obtaining the absolute value of the EMG signal (Figure 2.18B). Finally, the linear envelope was generated by using a low pass second order Butterworth filter with a cut off frequency of 5 Hz, based off of values obtained in literature (Figure 2.18C) [53]. Once the EMG signals were processed, the maximum value of muscle activation during each contraction was calculated. Figure 2.19 shows the EMG signal associated with a contraction cycle. The average of the maximum muscle activity from the gastrocnemius medial (GMH) and lateral heads (GLH) and the soleus muscle (S) during exercise were then added to obtain the total muscle activity for each day of testing. The total muscle activity was then normalized by the total muscle activity from the MVC test for that day (an average of two MVC tests was used). MVC tests were completed on both days due to the possibility for muscle activation to vary between days and also to account for the variation in the locations of the electrodes, though every effort was made to place the electrodes at the same location across both testing days.

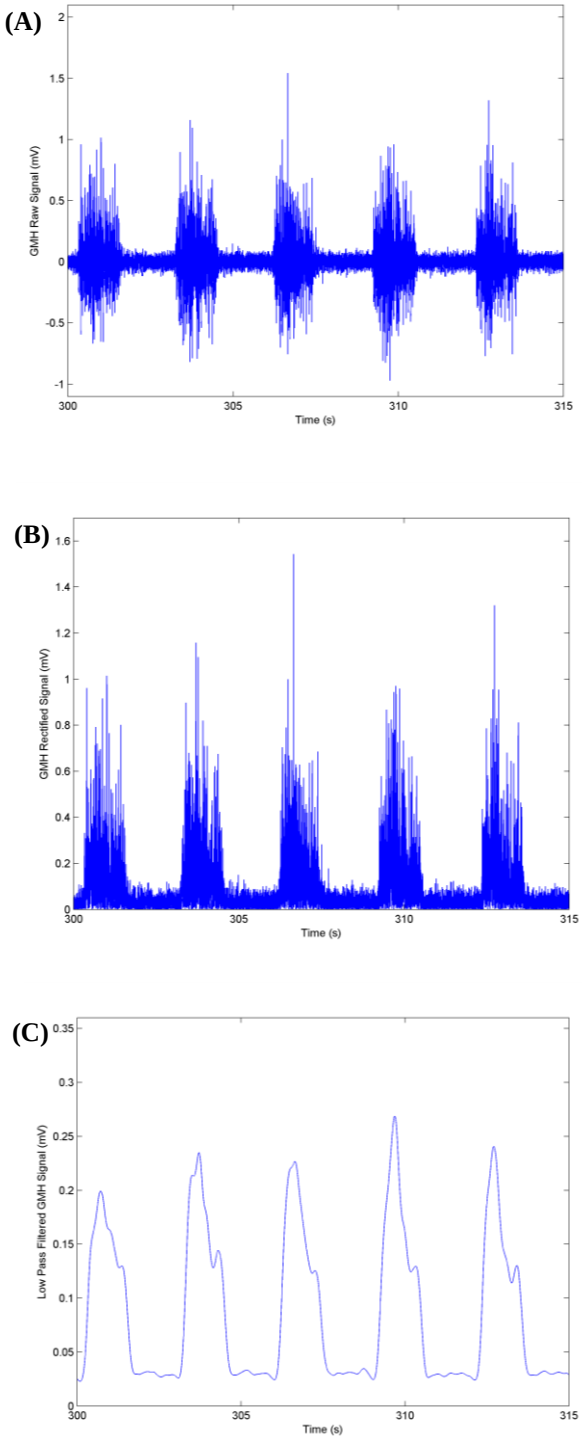


Figure 2.18: GMH muscle activity over a 15 second time period illustrating the raw EMG signal (A), the rectified signal (B), and the processed signal using a low pass second order Butterworth filter with a cut off frequency of 5 Hz (C)

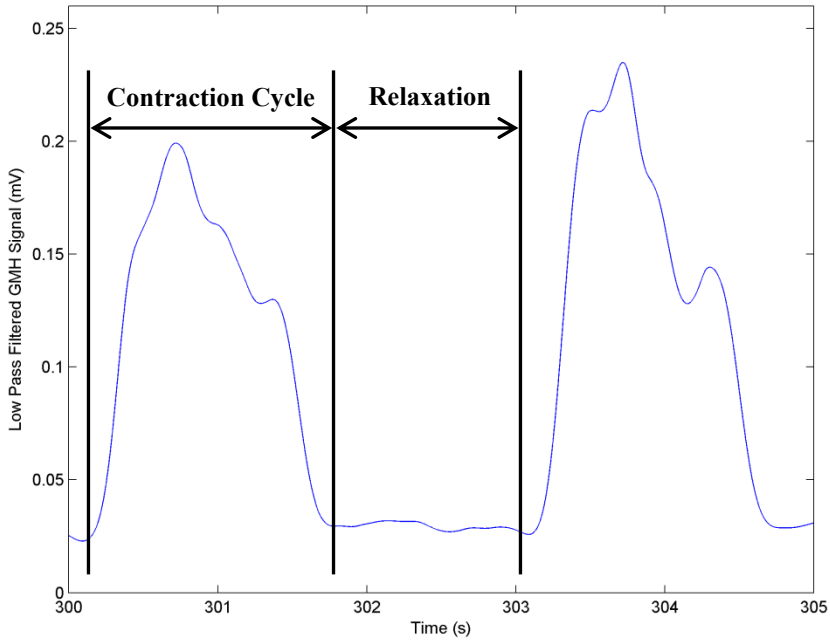


Figure 2.19: Illustration of two contraction cycles (calf raises) where the maximum muscle activity value was obtained

Finally for the applied pressure data, the pressure bladders were attached to the leg with Band-Aids to ensure their position was maintained when the GCS was applied. The pressure from the Band-Aid applied to the bladder was measured and subtracted from the recorded pressure to obtain the applied pressure on the leg due to the GCS. The applied ΔP during baseline, exercise, and recovery conditions are discussed in Chapter 3.

2.6 Statistical Analysis

Repeatability of the GCS tests between days and the control tests with no compression (NGCS) between days was determined using four methods. These methods were also used to prove that the order of testing had no effect on the results. A two-tailed t-test analysis was used to identify statistically significant differences between the tests for both days. The t-value (t) was obtained from Equation 2.11, where the difference in the means ($\bar{X}$) from the two days of testing were divided by the standard error measurement (σ_{diff}) [58]. The standard error was calculated, as shown in Equation 2.12, using the standard deviation (SD) of the differences between days and the number of subjects (n) [58]. Once the t-value was known, the p-value (p) could be found from the t-distribution table [58]. Statistical significance occurred if a p-value of less than or equal to 0.05 was obtained. The coefficient of variation (COV) was calculated to show variability between the tests for the two days using Equation 2.13; the average COV for all subjects is reported in Chapter 3 [59]. Bland-Altman plots were used to show agreement between the two days. The Bland-Altman method calculated the mean difference between the two days of testing, as well as the 95% limits of agreement ($\bar{X}$ ±1.96 SD) [60]. The graphical presentation of the data with the mean and limits of agreements allowed for

visual interpretation of how well the measurements from the two days of testing agreed [60]. Finally, the intraclass correlation (ICC) was used to measure consistency in the data and was calculated using MATLAB [61]. Table 2.1 indicates the levels of consistency for the ICC values obtained [61]. In order to compare the GCS and NGCS tests to determine the effect of compression on physiological variables a two-tailed paired t-test was used with statistical significance occurring for a p-value equal or less than 0.05.

$$t = \frac{\bar{X}_1 - \bar{X}_2}{\sigma_{diff}} \qquad \textbf{Equation 2.11}$$

$$\sigma_{diff} = \frac{SD}{\sqrt{n}} \qquad \textbf{Equation 2.12}$$

$$COV = \frac{SD}{\bar{X}} * 100 \qquad \textbf{Equation 2.13}$$

Table 2.1: ICC levels of consistency

ICC Value	Agreement Level
0 – 0.2	Poor
0.2 – 0.4	Fair
0.4 – 0.6	Moderate
0.6 – 0.8	Strong
> 0.8	Almost perfect

Chapter 3

Results and Discussion

Presented in this chapter are the results of the experimental study on the impact of graduated compression socks on athletic performance. The results from a repeatability analysis completed on the central and peripheral variables for the two days of testing are presented in Section 3.1. The global influence of the GCS on the cardiovascular system is presented in Section 3.2. Finally, the localized influence of the GCS on the legs is then discussed in Section 3.3.

3.1 Repeatability of the effect of GCS on Hemodynamics

In order to ensure that data collected from the testing protocol was repeatable from one day to the next, the testing procedure was performed over a two day span, with a minimum of 48 hours in between tests, as outlined in the experimental protocol in Section 2.2. The results are presented for the central hemodynamics in Section 3.1.1 and for peripheral hemodynamics in Section 3.1.2. The repeatability analysis completed on each variable involved calculating the p-value, the coefficient of variation, the intraclass correlation, and generating Bland-Altman plots, as discussed in Section 2.6.

3.1.1 Repeatability of the Central Hemodynamic Measurements

To determine if the effects of the GCS on central hemodynamics were reproducible, repeatability analysis was completed on the four central variables measured, namely HR, SBP, DBP, and CO. The values obtained from days 1 and 2 were compared for the NGCS and GCS tests for the BL, EX, and REC conditions using the p-test procedure outlined in Section 2.6. As shown in Table 3.1, the p-values for all variables were significantly larger than 0.05, indicating that there was no statistical difference between data collected on different days.

Table 3.1: P-values for central variables comparing data collected on two different days to demonstrate test repeatability (values in red indicate statistical significance)

	Condition					
	BL		EX		REC	
Variable	**NGCS**	**GCS**	**NGCS**	**GCS**	**NGCS**	**GCS**
HR	0.37	0.46	0.43	0.62	0.33	0.60
SBP	0.31	0.80	0.50	0.83	0.86	0.72
DBP	0.82	0.87	0.77	0.82	0.58	0.79
CO	0.88	0.77	0.59	0.47	0.89	0.69

The COV and ICC for the baseline, exercise, and recovery conditions with and without GCS are shown in Table 3.2. The COV values were close to zero indicating that the values obtained on the two days for each subject did not vary significantly from the mean and therefore had low variability. The ICC values demonstrated consistency between the data for each subject on both days. HR and SBP showed fair to moderate agreement, while CO and DBP showed strong to almost perfect agreement. Finally the Bland-Altman plots indicated good agreement between the two days of testing. Figure 3.1 shows an example plot for the heart rate variable for all conditions for both NGCS and GCS. Figure 3.1 demonstrates good agreement as the mean difference, or bias, is close to zero. The majority of the data falls within the 95% confidence limits, where the large spacing between the upper and lower limits is acceptable given the variation in heart rate between subjects. The remaining Bland-Altman plots for the central variables are shown in Appendix D. These results indicated that even with the day to day human variability, the central variables were still repeatable and showed no statistical differences, low variability, consistency, and good agreement.

Table 3.2: Coefficient of variation (COV) and intraclass correlation coefficient (ICC) for central variables measured over two different days

		Condition					
		BL		EX		REC	
Variable		**NGCS**	**GCS**	**NGCS**	**GCS**	**NGCS**	**GCS**
HR	**COV (%)**	7.14	7.72	6.60	6.79	8.25	7.40
	ICC	0.28	0.40	0.43	0.60	0.24	0.52
SBP	**COV (%)**	4.48	6.37	4.50	4.30	3.65	6.54
	ICC	0.69	0.49	0.62	0.69	0.67	0.24
DBP	**COV (%)**	5.10	5.22	4.88	4.33	6.17	6.11
	ICC	0.75	0.72	0.70	0.82	0.70	0.66
CO	**COV (%)**	13.55	8.99	12.99	11.67	11.08	8.09
	ICC	0.70	0.86	0.76	0.81	0.84	0.90

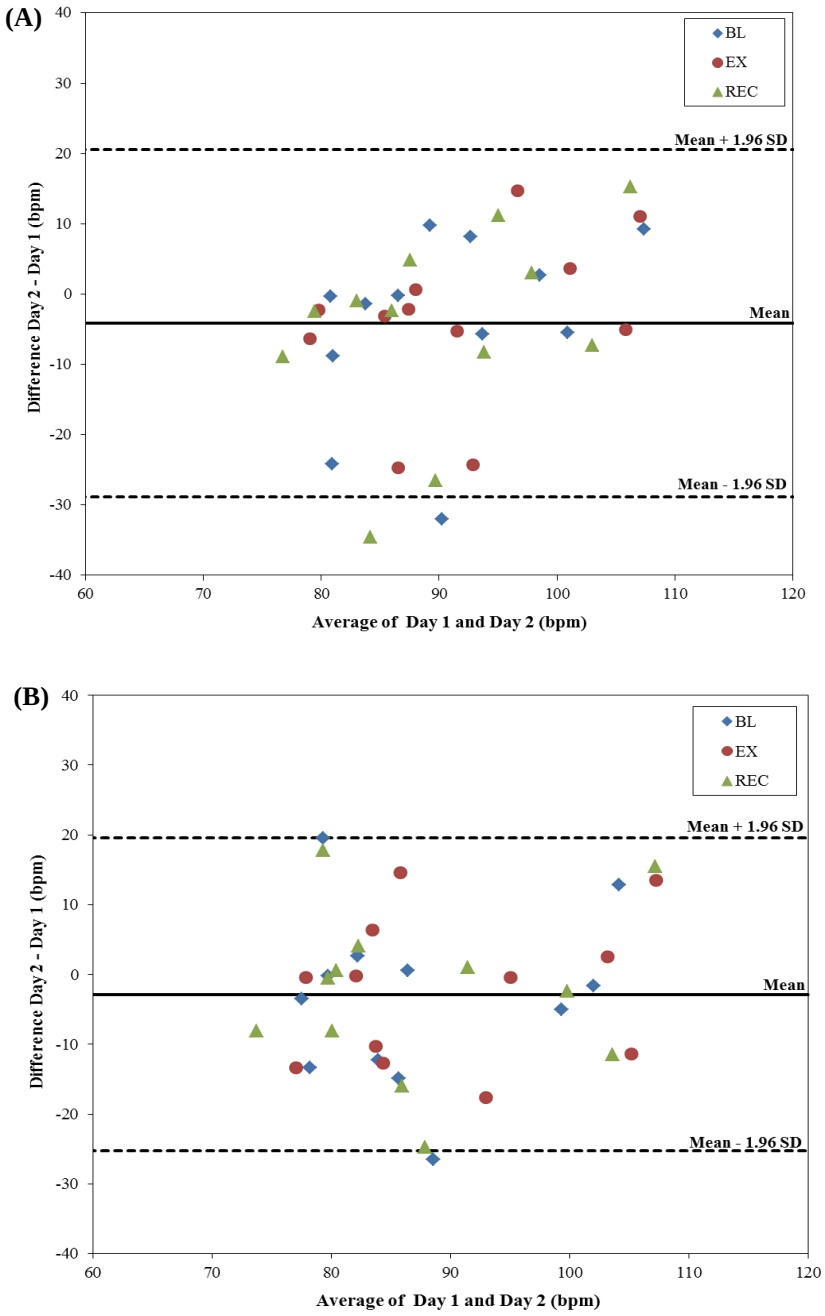


Figure 3.1: Bland-Altman plots comparing heart rate (HR) values for two days of testing for the baseline (BL), exercise (EX) and recovery (REC) conditions for (A) NGCS, and (B) GCS cases. The solid horizontal line indicates the mean of the data and the dashed horizontal lines represent the 95% confidence limits. The upper and lower limits are calculated from the mean ± 1.96 of the standard deviation (SD)

3.1.2 Repeatability of the Peripheral Hemodynamic Measurements

Repeatability analysis was completed on the peripheral measurements for PBV_{mean}, ΔP, and PAD to determine if the localized effects due to the GCS were reproducible. The values obtained from days 1 and 2 were compared for the NGCS and GCS tests for all experimental conditions. Repeatability was only analyzed for ΔP during the BL condition, as during this time the applied pressure difference was equivalent to that generated by the researchers with the GCS and tensor bandages. After this point, during EX and REC, the researchers were unable to control the pressure difference. The medial, lateral, and average ΔP during BL were analyzed. There was no statistical difference between days for any variable with or without GCS as illustrated in Table 3.3, which presents the p-values comparing the measured data for both days of testing, with and without the GCS.

Table 3.3: P-values for peripheral variables comparing data collected on two different days to demonstrate test repeatability (values in red indicate statistical significance)

		Condition					
		BL		EX		REC	
Variable		**NGCS**	**GCS**	**NGCS**	**GCS**	**NGCS**	**GCS**
PBV_{mean}		0.65	0.67	0.83	0.99	0.64	0.60
	Lateral	-	0.12	-	-	-	-
ΔP	**Medial**	-	0.06	-	-	-	-
	Average	-	0.89	-	-	-	-
PAD		0.81	0.79	-	-	0.66	0.90

The COV and ICC for the peripheral variables for baseline, exercise, and recovery for the NGCS and GCS conditions are shown in Table 3.4. For PBV_{mean}, the COV values indicated moderate to low variability. The ICC values showed almost perfect agreement for the baseline and exercise conditions. For the recovery condition there was moderate agreement for the NGCS test, and poor for the GCS case. These results showed that there was consistency in the data for the baseline, exercise, and recovery NGCS tests, while for the recovery GCS the results were not consistent. Evaluating the Bland-Altman plot, as seen in Figure 3.2, the data had a bias close to zero, the majority of the data points fell within the 95% confidence limits, and the interval between the limits of agreement was relatively small for each condition. These results demonstrate agreement within the data between the two days of testing. For ΔP, the COV values indicated moderate variability, and the ICC values indicated inconsistency in the data. For PAD the values for COV were very close to zero and the ICC values were quite high, indicating that the values obtained over both days of testing were consistent and had low variability. The Bland-Altman plots for ΔP and PAD indicated good agreement and can be found in Appendix E.

Some variability in the PBV_{mean} values was expected due do human variability from day to day, and as well as due to the likelihood that the ultrasound probe was not placed in the exact same location on each day, despite every effort to do so. The variability in the recovery period during the GCS condition is believed to be due to variations in the applied pressure therefore leading to varying responses in PBV_{mean}. This variation was only thought to be seen in the recovery portion because the ΔP had changed by varying degrees of magnitude depending on the subject due to movement of the sock during the exercise task. The low ICC values in the ΔP data could be due to the fact that it was difficult to obtain the same pressure difference on the medial and lateral portions of the leg for both days. When the compression sock was placed on the subject's leg it was extremely difficult to make the local pressure at the ankle and knee the same values for the medial and lateral sides. Even when the GCS fibers were aligned properly, the geometry changes on either side of the ankle and knee led to varying localized pressure and hence varying ΔP values.

Table 3.4: Coefficient of variation (COV) and intraclass correlation coefficient (ICC) for peripheral variables measured over two different days

			Condition					
			BL		EX		REC	
Variable			**NGCS**	**GCS**	**NGCS**	**GCS**	**NGCS**	**GCS**
PBV_{mean}		**COV (%)**	30.66	15.75	7.61	15.81	26.78	28.45
		ICC	0.81	0.93	0.98	0.84	0.58	0.16
ΔP	**Lateral**	**COV (%)**	-	20.11	-	-	-	-
		ICC	-	0.01	-	-	-	-
	Medial	**COV (%)**	-	22.68	-	-	-	-
		ICC	-	0.01	-	-	-	-
	Average	**COV (%)**	-	12.65	-	-	-	-
		ICC	-	0.14	-	-	-	-
PAD		**COV (%)**	1.51	1.96	-	-	2.01	1.97
		ICC	0.97	0.96	-	-	0.93	0.97

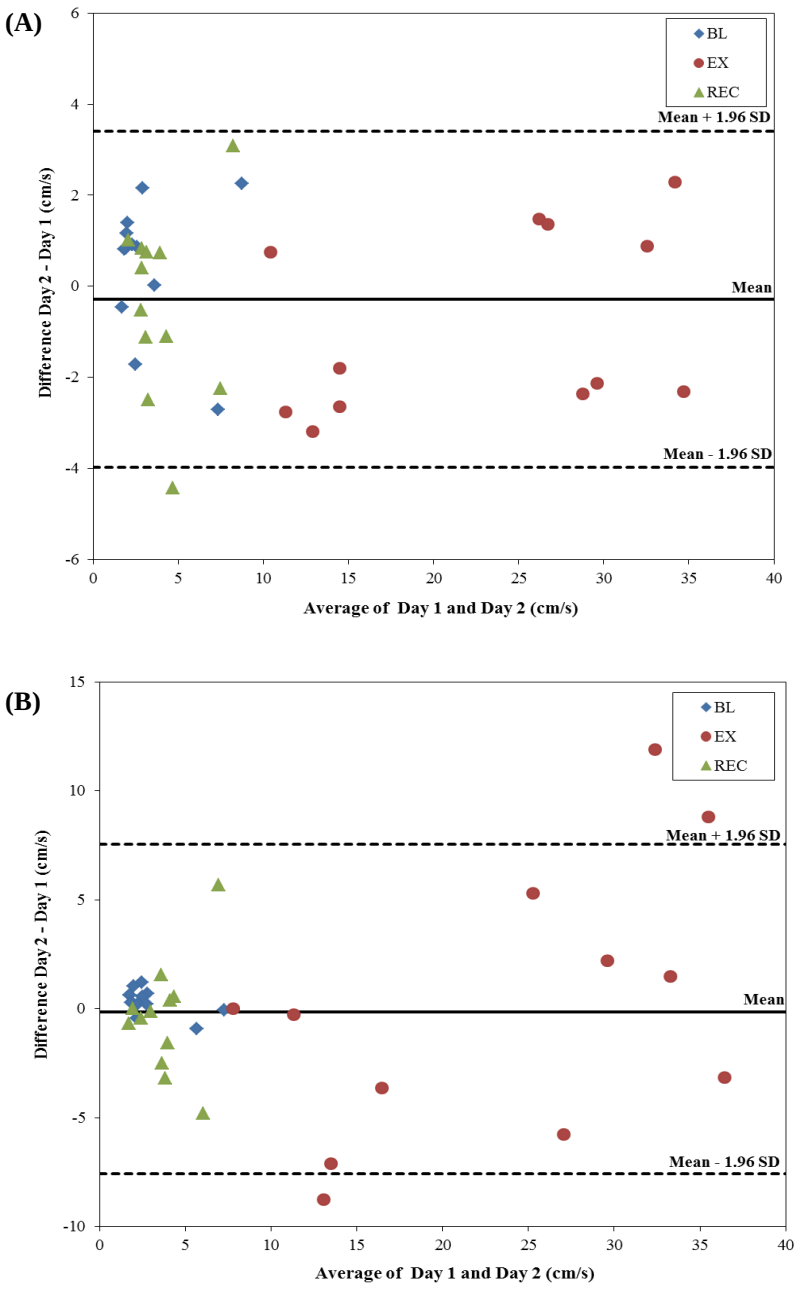


Figure 3.2: Bland-Altman plots comparing mean popliteal blood velocity (PBV_{mean}) values for two days of testing for the baseline (BL), exercise (EX) and recovery (REC) conditions for (A) NGCS, and (B) GCS cases. The solid horizontal line indicates the mean of the data and the dashed horizontal lines represent the 95% confidence limits. The upper and lower limits are calculated from the mean ± 1.96 of the standard deviation (SD)

3.1.3 Discussion of Repeatability of the effects of GCS

The repeatability analysis for both days of testing indicated that the protocol and results were repeatable. All efforts were taken to ensure that the protocol was controlled and that the physiological

measurement locations for all variables were the same. Although locations for the measurement devices were recorded based off of anatomical landmarks, there was still potential for not placing the probes in the exact same locations from one day to the next. Analysis of the repeatability results indicated that the central variables had good consistency, stronger agreement, and lower variability than the majority of the peripheral variables. Peripherally, PAD measurements also showed very strong agreement and low variability, whereas PBV_{mean} results indicated poor to moderate consistency, good agreement, and moderate to low variability. Moreover, ΔP values showed inconsistencies, moderate variability, and good agreement. No statistical differences were found for any of the tested variables. The results of the repeatability analysis were not surprising; strong repeatability was seen in all variables that were not directly related to the pressure or region where pressure was applied (PAD and central variables). The variation in the repeatability results for PBV_{mean} and ΔP could be due to human variability from day to day, human error of the placement of the pressure bladders and ultrasound probe, as well as the application of the GCS.

It was important to determine if the results from both days are repeatable to draw confident conclusions on the benefits of GCS for a healthy population. The results for the central and peripheral hemodynamics during both days of testing are presented in Sections 3.2 and 3.3.

3.2 Influence of GCS on Central Hemodynamics

As discussed in Chapter 1, the central hemodynamics is defined as the variables related to the heart that affect the entire response of the cardiovascular system. The impact of GCS on the central hemodynamics was assessed through bulk cardiac measures, including heart rate, systolic blood pressure, diastolic blood pressure, and cardiac output, as described in Section 2.4. The results for the baseline, exercise, and recovery conditions are presented in Section 3.2.1 and further discussed in Section 3.2.2.

3.2.1 Effect of GCS on Heart Rate, Blood Pressure, and Cardiac Output

Plots comparing HR, SBP, DBP, and CO with and without graduated compression socks for the exercise phase of tests run on day 1 are shown in Figure 3.3 to Figure 3.6. The graphs illustrate the change from the NGCS to GCS condition; red indicates an increase in the variable with the sock and black indicates a decrease in the variable when the sock was worn. Plots for the central variables for the baseline and recovery conditions for day 1, as well as all conditions for day 2 can be found in Appendix F. The p-values obtained for the central variables comparing the NGCS condition to the GCS condition on both days are shown in Table 3.5.

There were no significant changes in HR, DBP, or CO for all phases of the experimental protocol between the NGCS and GCS conditions for either day of testing. For SBP, there was no significant difference during the BL and REC conditions on day 1, or any condition on day 2. However, during the EX condition on day 1 there was a statistical difference between the NGCS and GCS cases ($p=0.04$). This difference is not considered to be due to the addition of the sock, however, since the result was not repeated on the second day of testing and blood pressure can vary significantly in general from day to day.

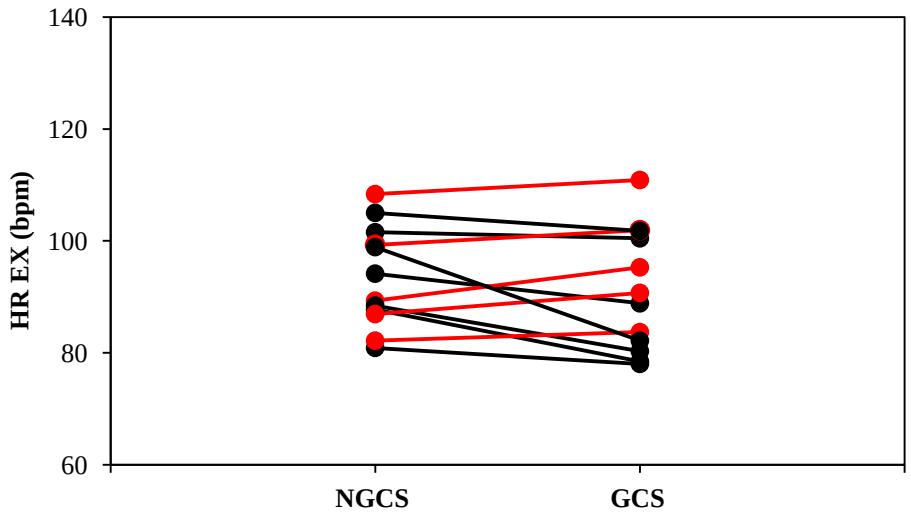


Figure 3.3: Comparison of HR with and without GCS during exercise for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

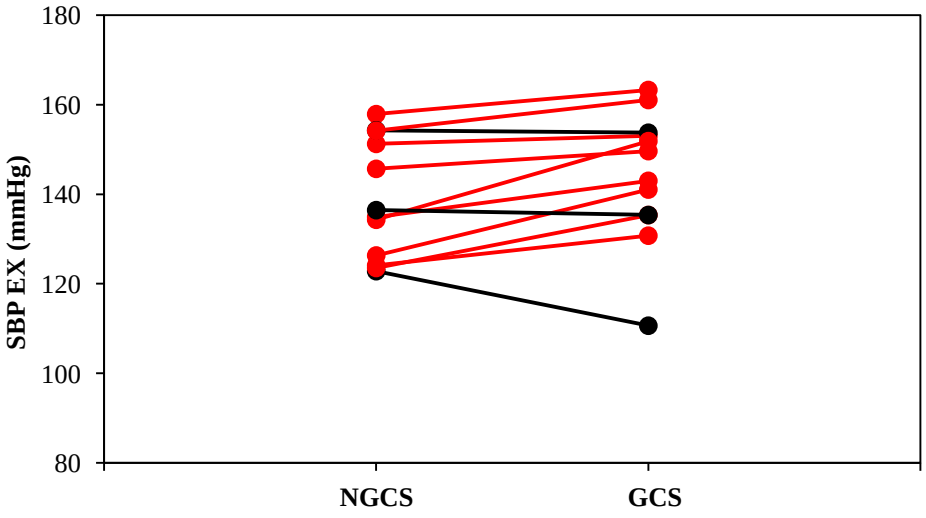


Figure 3.4: Comparison of SBP with and without GCS during exercise for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition

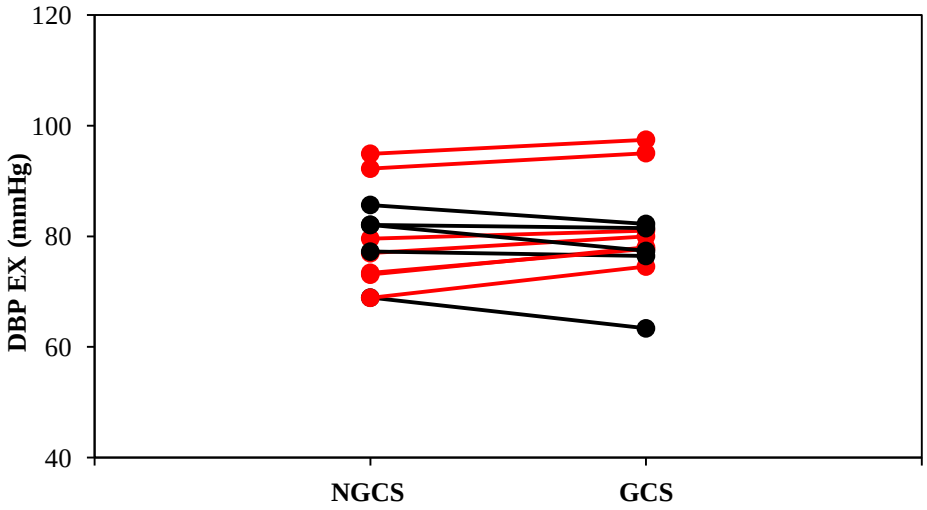


Figure 3.5: Comparison of DBP with and without GCS during exercise for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

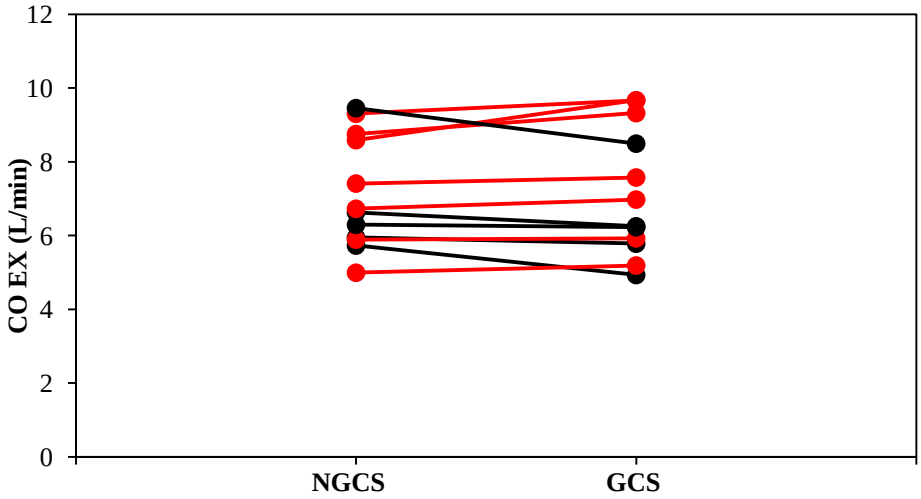


Figure 3.6: Comparison of CO with and without GCS during exercise for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

Table 3.5: P-values for central variables comparing data collected for two conditions, with and without GCS, for two days of testing (values in red indicate statistical significance)

	Condition					
	BL		EX		REC	
Variable	**Day 1**	**Day 2**	**Day 1**	**Day 2**	**Day 1**	**Day 2**
HR	0.09	0.16	0.21	0.42	0.13	0.42
SBP	0.60	0.32	0.04	0.44	0.32	0.88
DBP	0.98	0.35	0.48	0.34	0.94	0.28
CO	0.73	0.41	0.89	0.43	0.74	0.48

The effect of gender was also analyzed to determine if there was a pattern to the manner in which each subject behaved when the sock was worn. Figure 3.7 shows a sample of the gender difference analysis for HR for day 1 during exercise comparing the values with and without the GCS for all subjects. The x symbol represents the male participants and the circles represent the female participants. As demonstrated in Figure 3.7, no gender differences were observed for any variable during all conditions.

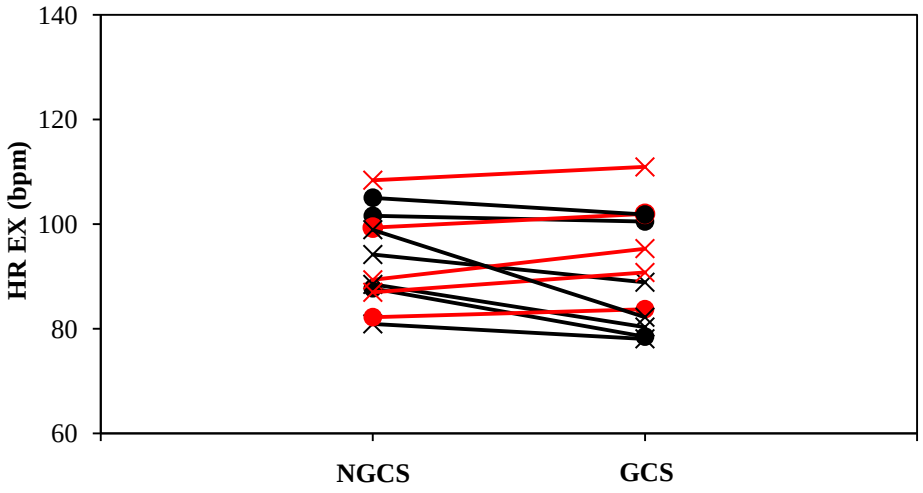


Figure 3.7: Comparison of HR with and without GCS during exercise and the effects of gender for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition, x: male, o: female)

The remaining central variables investigated included MAP, MPP, SV, and TPR. Since these variables are calculated based on the four measured central variables, HR, SBP, DBP, and CO (see Chapter 2), there were no significant differences between the NGCS and GCS conditions. The average values and standard deviations for the study population with and without the GCS for each variable are shown in Table 3.2 for day 1. The information for day 2 can be found in Appendix F.

Table 3.6: Calculated mean and SD values for the study population on day 1 for MAP, MPP, SV, and TPR

		Condition					
		BL		EX		REC	
Variable		**NGCS**	**GCS**	**NGCS**	**GCS**	**NGCS**	**GCS**
MAP	**Mean**	93.59	94.17	99.32	101.61	97.35	98.47
	SD	10.00	9.89	9.67	10.43	9.92	11.58
MPP	**Mean**	161.66	162.24	167.40	169.69	165.43	166.54
	SD	13.27	12.43	12.95	13.85	12.97	13.85
SV	**Mean**	62.47	64.32	76.60	79.02	63.83	66.91
	SD	12.60	16.55	16.00	18.20	16.51	17.63
TPR	**Mean**	16.74	17.50	14.40	14.90	17.69	18.05
	SD	3.13	4.72	2.96	3.76	5.66	6.56

3.2.2 Discussion of the Effect of GCS on Central Hemodynamics

As illustrated in Section 3.2.1, the comparison of the NGCS and GCS tests for the central variables resulted in no significant differences. The outcome that there was no significant change in the central variables due to the addition of the GCS was anticipated with such a localized exercise task and applied pressure region, only involving the small muscle mass of the calf. It was hypothesized that since the investigated region was small, any local physiological changes would not have a substantial effect on central variables. The central hemodynamic response was also investigated for trends that may occur with the addition of the GCS after no statistically significant differences were found. The trends examined included determining if gender played a role in the central response or if the strength of the ΔP affected the response of HR, SBP, DBP, or CO. No trends in the data were identified. The result that GCS had no significant effect on the central response is similar to those found in literature where the central response was either not investigated or no changes were found [1]. Therefore any beneficial effects from the GCS were anticipated to occur at the peripheral level and the results are presented in Section 3.3.

3.3 Influence of GCS on Peripheral Hemodynamics

As described in Chapter 1, the peripheral hemodynamics refers to those variables affected in the local calf region where the external pressure was applied. The variables of interest included vessel diameter, arterial popliteal blood velocity and blood flow, muscle oxygenation, muscle activity, and the applied pressure. The measurement techniques and analysis completed on all variables are described in

Section 2.4 and Section 2.5, respectively. This section is divided into subsections for the three components of the experimental protocol (baseline, exercise, and recovery). The results for the variables investigated are presented and discussed for each condition in the following sections beginning with baseline in Section 3.3.1.

3.3.1 Effect of GCS during Baseline

3.3.1.1 Effect of GCS during Baseline on PAD, PBV, and PBF

There were no significant differences in the PAD values during baseline for either day with the addition of the sock (day 1: $p = 0.95$, day 2: $p = 0.82$). There were also no significant changes in PBV_{mean} or PBF_{mean} between the GCS and NGCS conditions (day 1: PBV_{mean}- $p = 0.39$, PBF_{mean}- $p = 0.23$; day 2: PBV_{mean}- $p = 0.17$, PBF_{mean}- $p = 0.19$). The results of PBV_{mean} and PBF_{mean} with and without the GCS for the baseline condition are shown in Figure 3.8 and Figure 3.9 for day 1, respectively; the results for day 2 can be found in Appendix G. These figures demonstrate that there were also no overall trends in the data. As illustrated in Figure 3.8, six subjects experienced an increase in PBV_{mean} with the addition of the sock (red lines) and six subjects experienced a decrease in PBV_{mean} (black lines). For day two, for the same variable, four subjects experienced an increase, and eight experienced a decrease. These results indicate that there were no notable changes in vasculature with the addition of the GCS. It was hypothesized that there would be less pooling in the leg during BL when the sock was worn, however this was not the case. No change in blood volume was likely due to the fact that all subjects investigated were healthy and did not have any known venous deficiencies, implying that their vasculature performed efficiently in returning blood back to the heart. The baseline period was limited to three minutes to allow the body to stabilize; this time may not have been sufficient for blood to pool in the legs of the healthy participants. Furthermore, a couple of subjects complained of dizziness during the baseline period and therefore were instructed to make slight movements with their legs to avoid fainting. These slight movements, which helped enhance venous return, may have affected any conclusions to be made about pooling while standing still in a natural posture. As previously presented, no significant change in vessel diameter (PAD) with the GCS was therefore related to no significant changes in PBF_{mean}. The vessel investigated was not located in the region where the external compression was applied and therefore no concrete conclusions can be drawn on whether or not the pressure from the sock directly affected the diameters of the superficial and deep veins of the lower leg.

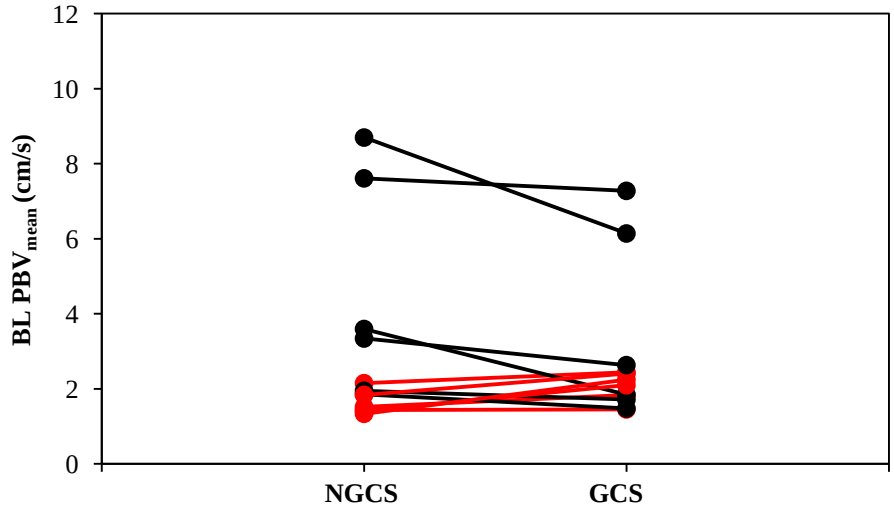


Figure 3.8: Comparison of PBV_{mean} with and without GCS during baseline for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

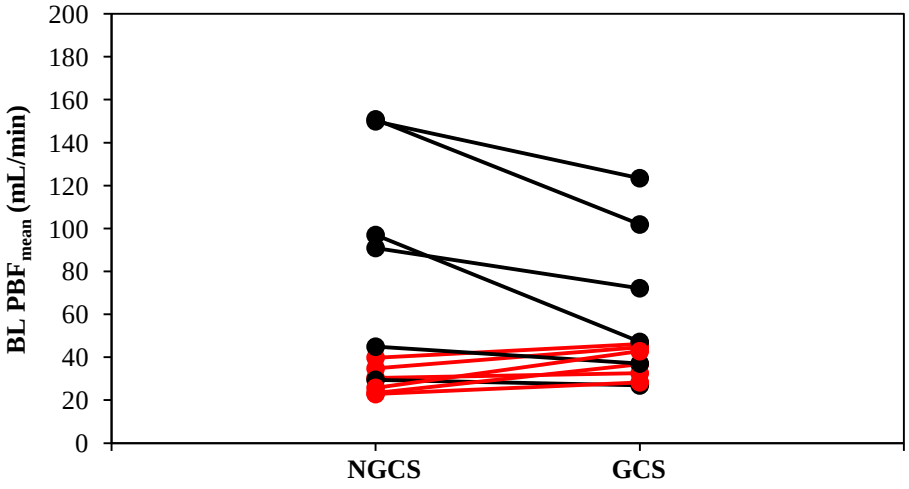


Figure 3.9: Comparison of PBF_{mean} with and without GCS during baseline for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

3.3.1.2 Effect of GCS during Baseline on the Applied Pressure Difference

The ΔP was attempted to be maintained to 10 ± 3 mmHg, as discussed in Chapter 2. For day 1, the average pressure difference applied to the leg was 13.31 ± 2.43 mmHg and for day 2 the average was 13.47 ± 2.97 mmHg during the baseline condition. The overall pressure differences were extremely similar;

however, the individual differences on the lateral and medial sides varied per day due to the difficulty of applying the sock and tensor bandages in the same orientation. For day 1 the ΔP on the medial and lateral sides of the legs were 10.57 ± 1.97 mmHg and 16.05 ± 3.59 mmHg, respectively, whereas for day 2 the ΔP for the medial and lateral sides were 13.34 ± 4.21 mmHg and 13.61 ± 3.34 mmHg, respectively.

3.3.2 Discussion of the Effect of GCS during Baseline

For the peripheral variables during the BL condition there were no significant differences or trends found. No change during BL with and without the GCS indicated that the GCS had no effect on the vasculature of the lower leg. This result was limited to the conclusions that could be drawn from the variables and locations investigated. Theoretically, when the GCS is applied to the leg, the blood volume in the leg should decrease due to a reduction in the diameters of the veins. The lack of impact of the GCS during the BL condition could be due to a few factors. The first reason could be that the ΔP was not sufficient to cause a change in vasculature in a healthy population with no venous deficiencies. The second factor could be the length of the BL condition. The three minute duration may not have been enough time to allow a change in vasculature to occur in the healthy study population. The duration of the BL however was limited to this time due to some participants experiencing symptoms of syncope (increasing HR with decreasing BP). Due to the risk of fainting, all subjects were monitored closely for the initial signs of syncope and were asked to make slight movements with their legs to help blood return to the heart. This led to a shorter baseline period for those subjects who showed high risk of fainting. Unfortunately, due to this unanticipated effect of maintaining the natural posture for a short time there was no way to investigate an extended BL due to the risk of fainting and the necessity to have some movement of the legs. In the literature review, a limited number of papers studied a BL condition. Similar results were obtained by Stein et al. who completed a study on healthy subjects and found no change in popliteal vein blood velocity or diameter during rest while supine or seated when wearing GCS [5]. Following the analysis of the baseline condition, the effect of GCS during steady-state exercise was investigated and is presented in Section 3.3.3.

3.3.3 Effect of GCS during Steady-State Exercise

3.3.3.1 Effect of GCS during Exercise on PBV and PBF

There were no significant differences between the NGCS and GCS conditions for PBV_{mean} or PBF_{mean} during steady-state exercise (day 1: PBV_{mean}- $p = 0.97$, PBF_{mean}- $p = 0.99$; day 2: PBV_{mean}- $p = 0.49$, PBF_{mean}- $p = 0.45$). The exercise data was analyzed in two ways to determine if there were any beneficial effects from the GCS. The first method involved comparing the PBV_{mean} and PBF_{mean} values during exercise for NGCS and GCS conditions as shown in Figure 3.10 and Figure 3.11 for day 1 (day 2 plots can be found in Appendix G). This method was chosen to determine the effect of the GCS with the muscle pump activated in conjunction with any changes in the vasculature that may have occurred during the baseline condition. The results of the first method revealed a local increase in PBV_{mean} and PBF_{mean} for six subjects for day 1 (11.48 ± 4.56 %) and day 2 (13.22 ± 8.61 %) when the GCS were worn. It is important to note that the subjects that experienced an increase were not all the same for both days; three

subjects experienced an increase on both days. Six subjects experienced a local decrease in PBV_{mean} and PBF_{mean} for day 1 (-15.59 ± 13.81 %) and day 2 (-20.18 ± 15.75 %), with three subjects experiencing the decrease on both days. The second method involved removing the baseline values from the exercise data for each condition to determine whether the change in velocity from baseline was the same with and without the GCS. This method isolated the compound effect of the sock and muscle pump (GCS) when compared to the sole effect of the muscle pump (NGCS) and removed any effects on vasculature experienced during baseline. The results of the second method revealed an increase in PBV_{mean} and PBF_{mean} for seven subjects with the addition of the GCS on day 1 (13.59 ± 5.12 %) and day 2 (14.86 ± 9.06 %) as shown in Figure 3.12 and Figure 3.13 for day 1 (again, plots for day 2 can be found in Appendix G). The second method also indicated a decrease in PBV_{mean} and PBF_{mean} in five subjects on day 1 (-25.86 ± 17.24 %) and day 2 (-29.12 ± 22.53 %). Again, the subjects who experienced the increase and decrease were not all the same for both days, with three subjects having a local increase on both days, and one subject decreasing on both days.

The results of both methods indicated that there are no conclusive trends for PBV_{mean} and PBF_{mean} during steady-state exercise, since the majority of subjects did not experience the same response on both days. Although the average increase in PBV_{mean} with the addition of the GCS was lower than the average decrease in PBV_{mean} without GCS, the standard deviation was considerably lower when the subjects experienced an increase. This difference in the SD demonstrates that those subjects who experienced an increase in the variables had similar responses, where as those subjects that experienced a decrease had very different responses, leading to the large SD values. The fact that the positive or negative effects on PBV_{mean} and PBF_{mean} were not repeatable for all subjects on both days could indicate that the negative effects may be due to the sock application, and therefore the applied pressure changing from the previous testing day.

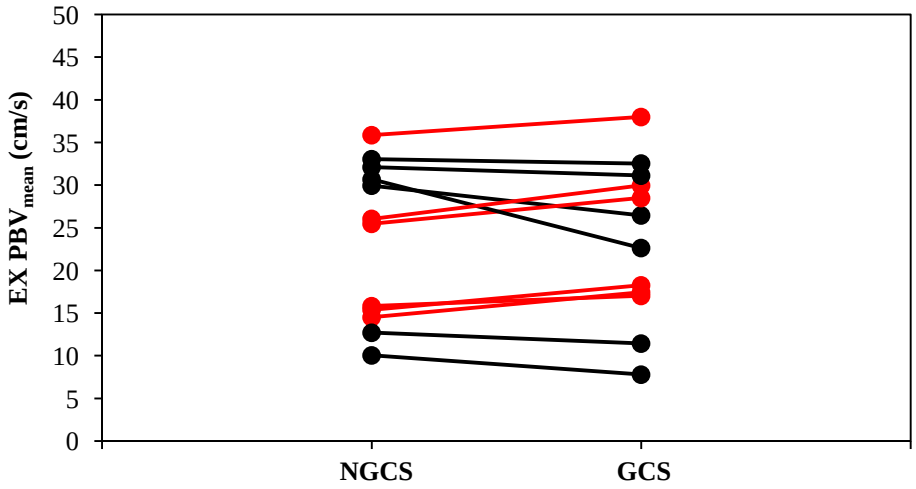


Figure 3.10: Comparison of PBV_{mean} with and without GCS during exercise for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

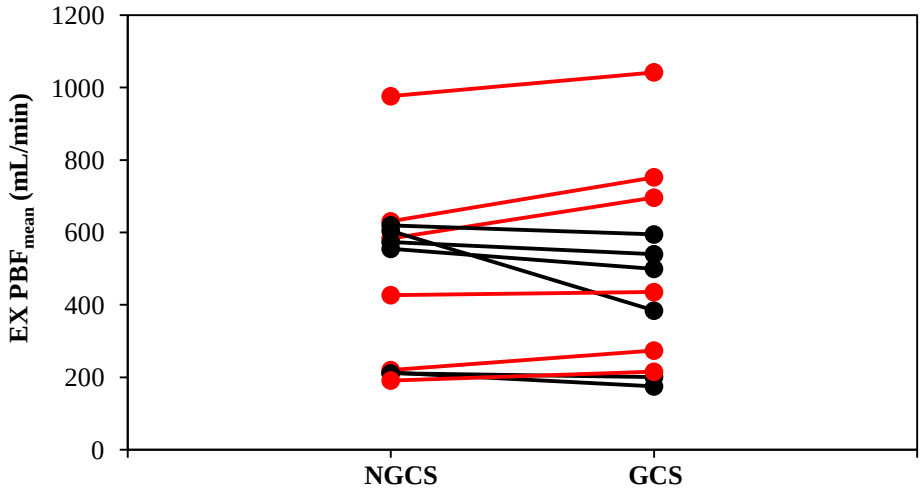


Figure 3.11: Comparison of PBF_{mean} with and without GCS during exercise for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

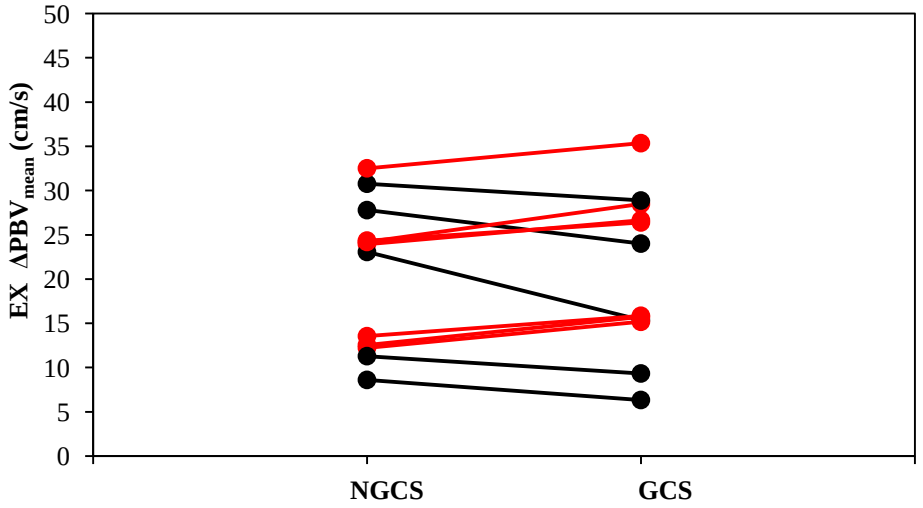


Figure 3.12: Comparison of the change relative to BL values during EX in PBV_{mean} with and without GCS for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

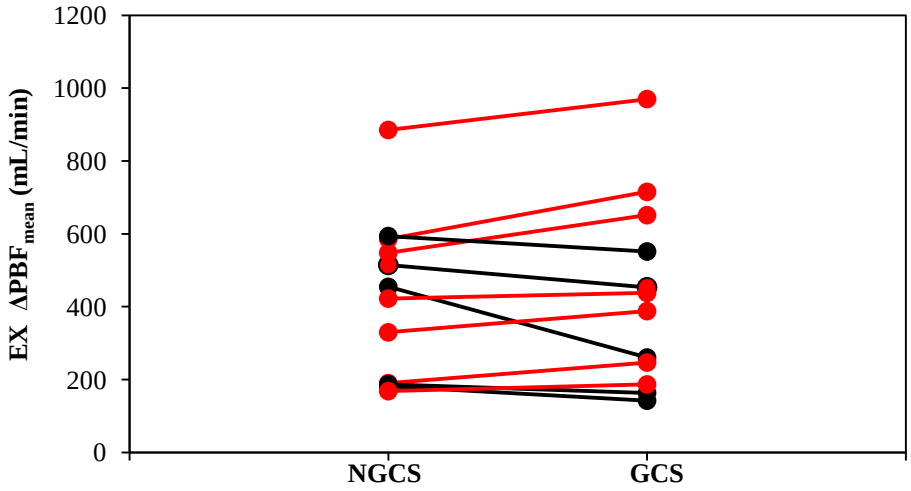


Figure 3.13: Comparison of the change relative to BL values during EX in PBF_{mean} with and without GCS for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

3.3.3.2 Effect of GCS during Exercise on Muscle Oxygenation

For muscle oxygenation there were no significant differences in O_2Hb or HHb for either day of testing. The decreasing trend of HHb on both days when the GCS is worn, as shown in Figure 3.14 and Figure 3.15, however, could indicate an increase in muscle oxygenation with the addition of the sock. HHb has been utilized as a reliable indicator of changes in muscle oxygenation and oxygen extraction [62]. Although this trend is not statistically significant (day 1: $p = 0.10$, day 2: $p = 0.18$), it was repeatable on both days, and shows potential that with higher applied pressures, there is the opportunity to increase oxygen extraction.

For total hemoglobin there was a significant decrease ($p = 0.003$) on day 1 with the GCS indicating a reduction in leg blood volume (Figure 3.14). This result is consistent with the prescribed function of the GCS, which, as discussed in Chapter 1, is to help prevent pooling in the legs for people suffering from venous diseases. There was no significant difference found in tHb with the GCS ($p = 0.71$) for day 2 (Figure 3.15). The significant reduction from day 1 in total hemoglobin in the calf muscle while wearing the GCS implied the external compression was able to overcome the local capacitive behaviour of the venous system in the leg. For day 2, the majority of subjects experienced lower ΔP values, indicating a potential explanation for no significant decrease in tHb. There will also be some variability in the capacitive behaviour of the venous system from day to day due to extrinsic factors such as hydration and nutrition. Overall, the results of the tHb values on day 1 indicated positive evidence that passive compression could impact local blood distribution during exercise.

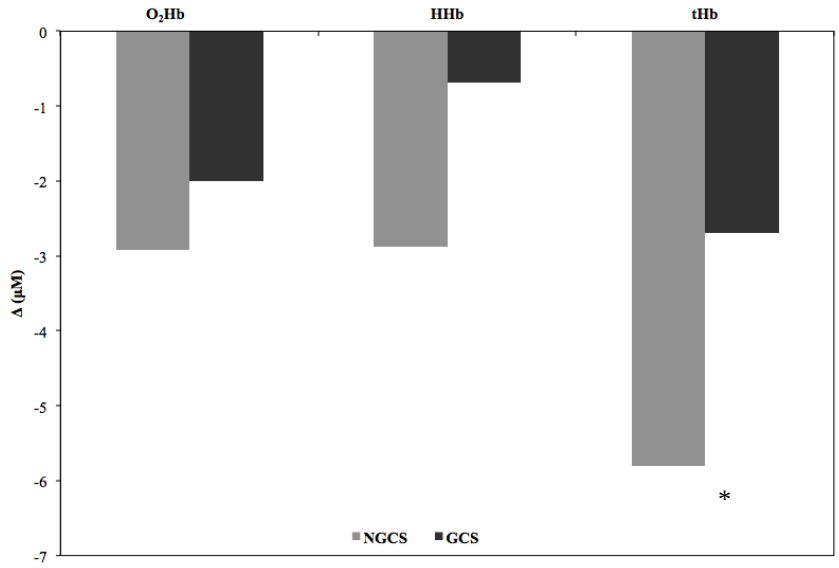


Figure 3.14: Time-averaged muscle oxygenation during EX relative to BL values for plantar flexion exercise for day 1 (O_2Hb: p = 0.40; HHb: p = 0.09; tHb: p = 0.003, with * indicating a statistically significant difference)

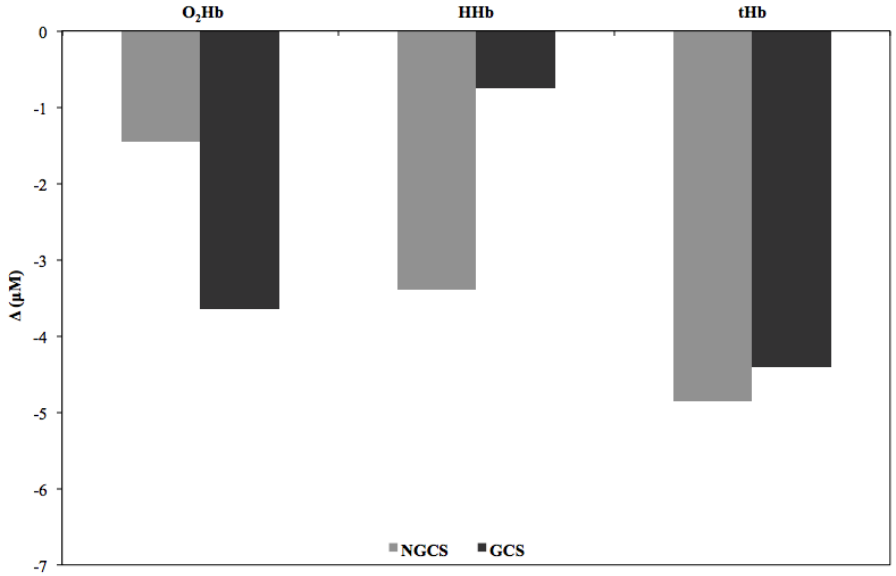


Figure 3.15: Time-averaged muscle oxygenation during EX relative to BL values for plantar flexion exercise for day 2 (O_2Hb: p = 0.12; HHb: p = 0.18; tHb: p = 0.71)

3.3.3.3 Effect of GCS during Exercise on Muscle Activity

There was no significant change in muscle activity with the addition of the GCS, indicating that the same muscle recruitment occurred during both experimental conditions (day 1: p=0.31, day 2: p = 0.68). The plantar flexion exercise required 52.56 ± 24.81% and 55.73 ± 26.80% of the subjects' MVC for

the NGCS and GCS conditions, respectively on day 1, while on day 2 similar values of 47.42 ± 21.06% and 48.97 ± 20.01% were recorded. On day 2, there was an error with one subjects EMG signal and therefore there was no value available for the GCS test, and only information for the final 40 seconds of exercise for the NGCS test. The averages and p-values reported for day 2 therefore include only 11 subjects. The results obtained showed a large standard deviation, which is due to the variation in the calf raise height amongst the subjects, as well as the variation in their MVC values.

Table 3.7 presents the individual results for each subject including the calf raise height, the exercise frequency declared by the subject (R: regular, IR: irregular), and the percentage of the subjects MVC for each test.

Table 3.7: Percentage of MVC required to complete the exercise task for each subject

			Day 1		Day 2	
Subject	**Calf Raise Height (cm)**	**Exercise Frequency**	**NGCS**	**GCS**	**NGCS**	**GCS**
1	5	R	62.95	54.83	60.19	71.86
2	6.5	R	66.86	69.21	62.76	64.01
3	6	R	41.79	37.98	66.00	47.78
4	5.5	R	21.45	27.14	34.82	30.45
5	2.5	IR	32.37	41.69	18.61	-
6	5	R	17.63	18.34	18.47	16.93
7	4.9	R	32.71	31.99	21.19	17.67
8	3.3	IR	63.69	57.99	84.11	76.45
9	3.3	R	74.05	78.70	45.68	52.09
10	4	R	49.02	48.81	45.65	47.14
11	4.5	IR	64.59	79.93	47.79	56.40
12	3.5	IR	103.67	108.07	63.75	57.89

As stated in Section 1.2, there were two hypotheses: The first hypothesis was that the subject would require less muscle recruitment the second time they returned to the lab because they had become familiar with the test protocol; the premise being that after completing the task once the muscle would have some training and the subject would also be more comfortable completing the task, which could potentially generate more fluent motion that requires less muscle activation. This hypothesis was supported by data

from 7 subjects for the GCS condition, and 8 subjects for the NGCS condition. The second hypothesis was that the amount of muscle activation required to complete the exercise task is tied to the subject's lifestyle. The percentage of MVC required to complete the exercise protocol was not related to the subject's frequency of exercise. There was, however, a pattern that those participants that stated they exercised irregularly had lower calf raise heights when compared to those who declared they exercised regularly (average of 3.45 cm for IR vs. 5.03 cm for R). The fact that the majority of participants that declared irregular exercise completed lower calf raise heights than those with regular exercise could obscure the potential result that the percentage of the MVC required is tied to lifestyle. In order to fully evaluate this hypothesis, the calf raise height would have to be maintained at the same value for all subjects.

3.3.3.4 Effect of GCS during Exercise on the Applied Pressure Difference

The ΔP during steady-state exercise varied with the plantar flexion exercise, as shown in Figure 3.16 for one participant. The acquisition of the dynamic pressure measurements allowed for the applied pressure to be referenced to the physiological measurements. The blue line represents the pressure applied at the ankle, the purple line represents the pressure applied at the knee, and the red line represents the PBV_{mean}. Figure 3.16 illustrates two plantar flexion cycles, totaling six seconds. It can be seen that the pressure increased while the subject was raising their ankle (UP) due to the movement of the muscles that stretch the sock and increase the calf circumference. The velocity decreased during this upward motion as the muscle applied more pressure on the arteries, decreasing blood flow. When the subject lowered the ankle (DN) the applied pressure decreased as the muscles and GCS returned to their original locations. The velocity increased as the increased muscle pressure was removed from the artery when the muscle returned to its resting location. During relaxation (RL), the pressure returned to a steady value that was comparable to the initial baseline value and velocity returned to the normal pattern seen when a person is standing in a natural posture. The result that pressure varied during exercise is important to note for applications of the GCS, as the local applied pressure can significantly increase depending on the task completed. If this increase in pressure is significant enough it could begin to affect the vasculature in the leg. Although the local pressure increased during the plantar flexion, the ΔP, and therefore the driving pressure, did not change as the pressure at the ankle and knee increased by relatively the same quantity.

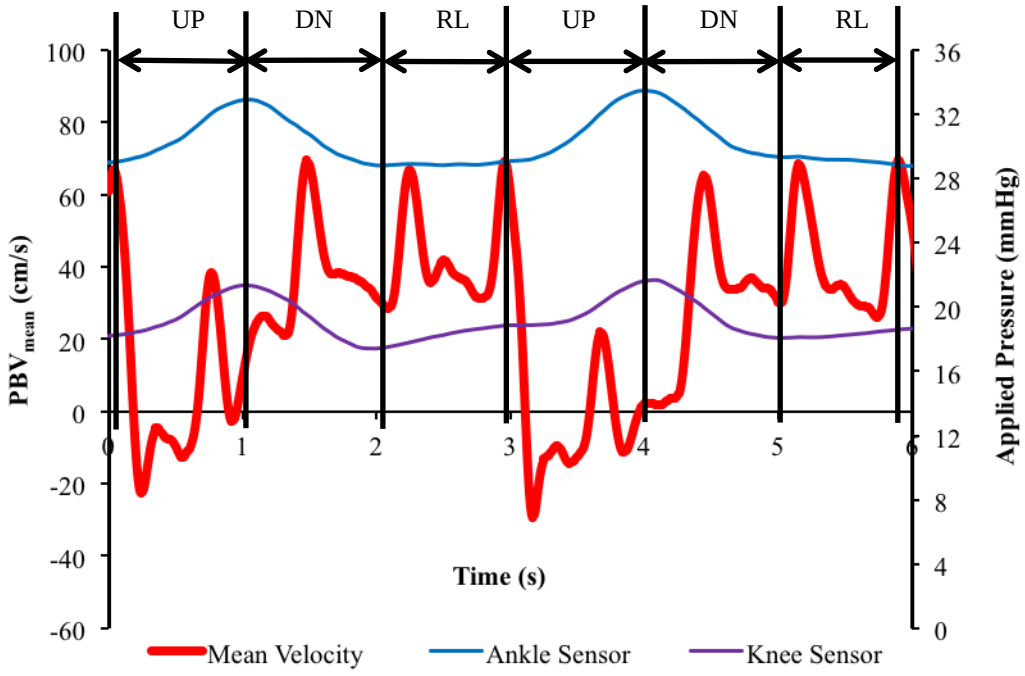


Figure 3.16: PBV$_{mean}$ (left ordinate) and applied pressure (right ordinate) during plantar flexion exercise (UP: ankle rising, DN: ankle lowering, RL: 1 second relaxation)

3.3.4 Discussion of the Effect of GCS during Steady-State Exercise

Analysis of the peripheral variables during steady-state exercise indicated no significant changes in PBV$_{mean}$ or PBF$_{mean}$ when the GCS were worn. Although there were also no trends in the data, the standard deviation on both days for the subjects that increased were much lower than those that experienced a decrease. As previously discussed, this difference demonstrated a uniform response in those subjects that experienced a positive effect from the GCS and indicated that those subjects who experienced a decrease had varying responses. The variation in the decrease in PBV$_{mean}$ or PBF$_{mean}$ values with the GCS were thought to be due to the sock application since the subjects who experienced a positive or negative effect were not repeatable for both days. Even though there were no significant differences in the data, the variation in the results from day to day for each subject illustrated the importance of the application of the GCS. Similar results were found by Stein et al. who studied the effect of ankle exercise (dorsiflexion) on healthy subjects in the supine and seated postures [5]. The researchers found no significant differences in the mean popliteal vein velocity, popliteal vein diameter, or mean popliteal vein volumetric flow rate [5]. Although Stein et al. investigated the effect of compression in different postures than this study, when standing the pressure in the veins that must be overcome to move blood back to the heart increases significantly and therefore if no effect was found in the supine or seated postures, it would not be anticipated to see any effect in the standing posture.

The analysis of the muscle oxygenation indicated positive trends with the addition of the GCS. For the first day of testing there was a significant decrease in tHb, indicating a reduction in the leg blood volume; on day 2 no statistical significance occurred. The reduction in tHb while wearing the GCS on day 1 implied the external compression was able to overcome the local capacitive behaviour of the venous system in the leg and perform the prescribed task of the GCS. There was also a decreasing trend in HHb on both days, which indicated an increase in muscle oxygenation with the GCS. This reduction in HHb demonstrated the potential to increase oxygen extraction by applying stronger external compression to the calf. The results obtained in this study are consistent with those found by Agu et al. who tested 10 subjects with chronic venous insufficiency and investigated muscle oxygenation while completing 10 tip toe exercises with and without compression [25]. The study involved three levels of compression with average pressure differences from ankle to knee of 5.60 mmHg (Class I), 9.50 mmHg (Class II), and 15.12 mmHg (Class III). The results found significant reduction in HHb for the Class II and III compression levels and a reduction in tHb with increasing compression, with a significant reduction found for Class III [25]. The result that a higher pressure difference led to significant differences in HHb and tHb demonstrated the importance of the ΔP. The ΔP used in this study was similar to the ΔP for Class III in the Agu et al. study. Since Class II or Class III compression was required to show significance during exercise for patients with venous deficiencies, it can be deduced that for healthy subjects an even stronger ΔP is required to show statistically significant changes with the addition of the GCS.

There were no significant changes in muscle activity between the NGCS and GCS conditions, indicating that the task was repeatable on both days. The trends in the data suggested that less muscle recruitment was required to complete the task on the second day as subjects had become familiar with the protocol. Another trend indicated that those subjects who reported irregular exercise calf raised to lower heights than those subjects who exercise frequently. Signs of fatigue were not present in the EMG data for any subjects and therefore the plantar flexion exercise task may not have been strenuous enough to assess the capabilities of GCS to help reduce fatigue.

The applied pressure was found to vary during steady-state exercise with the plantar flexion. The pressure increased when the ankle was raised and decreased back to baseline values when the ankle was lowered. The change was thought to be due to movement of the muscle affecting the circumference of the leg. The literature review completed did not encounter many studies where the applied pressure was dynamically measured throughout an exercise task on human subjects. Kumar and Alagirusamy studied bandage pressure *in vitro* using a mannequin leg and an air bladder to simulate expansion and contraction of the calf muscle [13]. Their findings showed that the applied pressure increased when the degree of expansion or contraction increased or when the bandage was wrapped tighter [13]. Moreover, McLaren et al. developed a system to measure dynamic pressure during exercise and completed initial validation testing so the device could be used in further field studies [63]. The variation in the applied pressure during exercise is

important for applications of the GCS. Although no significant change in ΔP was found, the local pressure changes indicate that there is potential to affect the vasculature in localized regions.

The typical use for the GCS in the healthy population is during exercise and recovery conditions. As discussed in this section the GCS showed trends towards beneficial effects with a localized exercise task, the results for the recovery condition are discussed in Section 3.3.5.

3.3.5 Effect of GCS during Recovery

3.3.5.1 Effect of GCS during Recovery on PAD, PBV, and PBF

There were no significant differences in PAD during recovery for either day when comparing the NGCS and GCS conditions (day 1: $p = 0.13$, day 2: $p = 0.75$). Additionally, there were no significant differences between the baseline and recovery diameters for the NGCS and GCS conditions on day 1 (NGCS: $p = 0.21$, GCS: $p = 0.99$) or day 2 (NGCS: $p = 0.98$, GCS: $p = 0.49$). This indicated that the exercise task did not result in any lasting effects in the vasculature at the popliteal level. Furthermore, there were also no significant differences in PBV_{mean} and PBF_{mean} with the addition of GCS during recovery (day 1: PBV_{mean}- $p = 0.67$, PBF_{mean}- $p = 0.66$; day 2: PBV_{mean}- $p = 0.40$, PBF_{mean}- $p = 0.48$) as illustrated in Figure 3.17 and Figure 3.18 for all subjects (plots for day 2 can be found in Appendix G). One notable trend occurred when comparing the effect of the GCS during BL and REC conditions. During REC for PBV_{mean} on day 1, 10 out of the 12 subjects experienced the same response with the GCS as during the BL condition (i.e. if a subject experienced an increase in PBV_{mean} during BL, they also experienced an increase during REC). This trend holds true on day 2 for PBV_{mean}, where 9 out of 12 subjects behaved the same, as well as for PBF_{mean} on both days (day 1: 10/12 subjects, day 2: 8/12 subjects). This trend indicated that no carry over effects from exercise occurred during the recovery time and the body was able to experience the same effects from the GCS as during the baseline conditions.

The REC values for PBV_{mean} and PBF_{mean} were compared to the BL values to determine if the overall averages were similar for both resting conditions. The REC values for both variables were higher than the BL values for the majority of subjects for both NGCS and GCS conditions (day 1: 11/12 subjects, day 2: 8/12 subjects). This result was expected as following exercise it will take the body time to return to homeostasis conditions. The five minute recovery period may not have been enough for all subjects to return to baseline conditions depending on the amount of energy the body required to complete the exercise task. The difference between the REC and BL values for the NGCS and GCS conditions were then compared to determine if the values when the GCS was worn were closer to BL, potentially indicating a faster recovery time. For day 1 for PBV_{mean}, the difference from REC to BL was higher for six subjects with the GCS on day 1, and seven on day 2. For PBF_{mean}, the difference was higher with the GCS for 5 subjects on day 1, and seven on day 2. The results are generally split between subjects who had REC values closer to BL with and without the GCS, indicating that there are no trends to show that the sock had any effect on immediate recovery (see further analysis in Section 3.3.5.4).

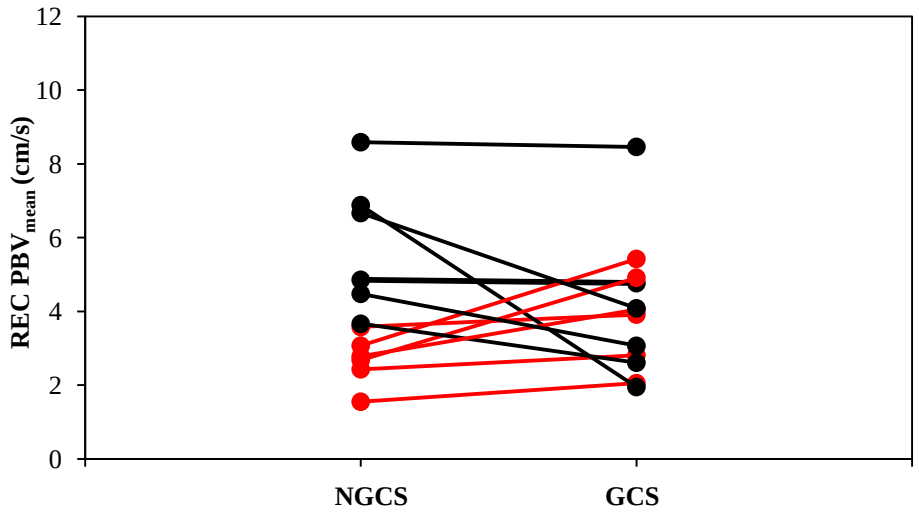


Figure 3.17: Comparison of PBV_{mean} with and without GCS during recovery for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

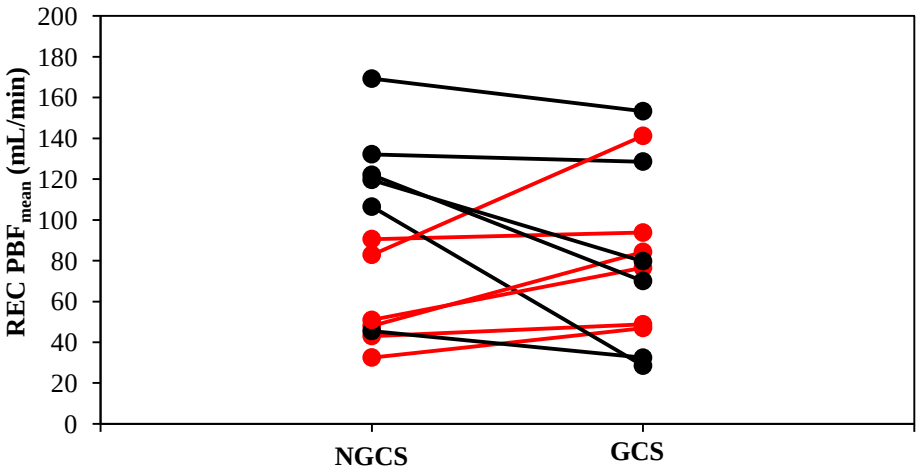


Figure 3.18: Comparison of PBF_{mean} with and without GCS during recovery for all subjects on day 1 (red: increase during the GCS condition, black: decrease during the GCS condition)

3.3.5.2 Effect of GCS during Recovery on Muscle Oxygenation

For muscle oxygenation there were no significant differences for either day of testing when comparing the difference between REC and EX for the NGCS and GCS conditions, as seen in Figure 3.19 and Figure 3.20. There were no repeatable trends in the O_2Hb or HHb data; however, the reduction in tHb in Figure 3.19 indicated that the difference between REC and EX for tHb on day 1 was smaller when the GCS was worn. This signified that the GCS was still maintaining a lower blood volume in the leg during REC, when compared to the NGCS case. On day 2, the values for the change in tHb were almost equivalent

(Figure 3.20). As previously seen in Figure 3.15, the reduction in tHb was not as significant during EX for day 2. Even though the reduction was smaller, the fact that the values are similar for the difference between REC and EX showed that the NGCS and GCS values vary from their respective EX values by similar amounts. Since the EX values showed a small decrease in tHb it was therefore implied that there was a trend towards a lower blood volume with the GCS during REC. This result would be beneficial because it would imply that post exercise the GCS was helping to prevent pooling in the leg and maintain the movement of blood to replenish the working muscle's oxygen supply and remove waste.

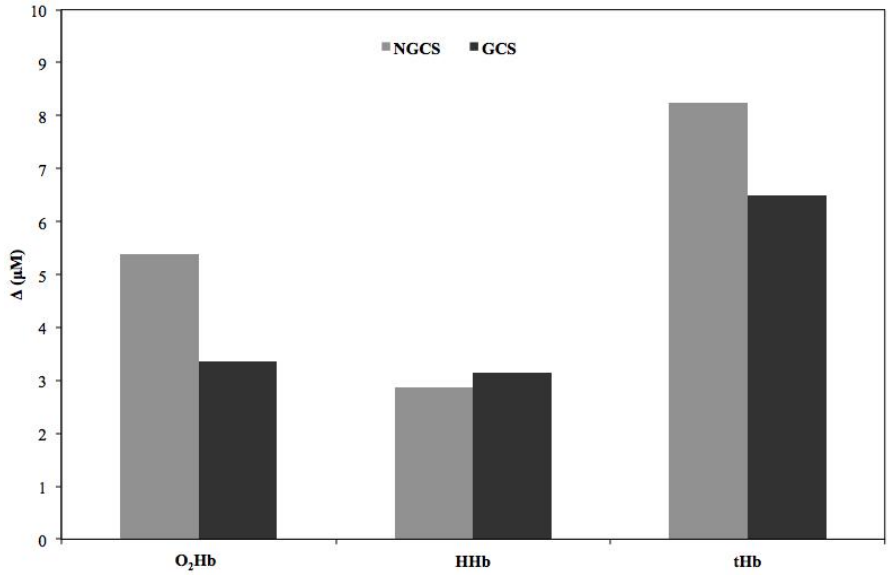


Figure 3.19: Time-averaged muscle oxygenation for recovery compared to the respective exercise values for day 1 (O_2Hb: p = 0.14; HHb: p = 0.85; tHb: p = 0.07)

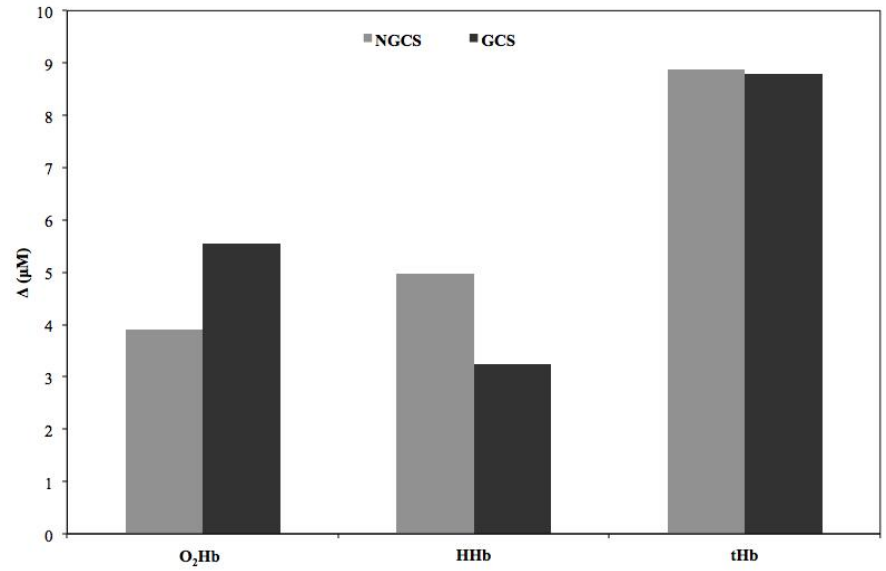


Figure 3.20: Time-averaged muscle oxygenation for recovery compared to the respective exercise values for day 2 (O_2Hb: p = 0.06; HHb: p = 0.16; tHb: p = 0.95)

3.3.5.3 Effect of GCS during Recovery on the Applied Pressure Difference

The ΔP was analyzed immediately following exercise to determine if the pressure difference returned to BL values. Due to issues with a slow leak for the pressure sensor at the medial knee location for several subjects, only the lateral pressure difference was analyzed. Table 3.8 shows the average lateral ΔP and the standard deviation for the 12 subjects for both days for the BL and REC conditions. The change in ΔP between conditions fell within the error associated with the pressure system of ±3 mmHg. The SD values were higher during the REC conditions as the GCS slipped as the subjects were exercising; the degree to which it moved and affected the pressure varied depending on the subject, hence the higher SD values.

Table 3.8: Comparison of the lateral pressure difference measurements for BL and REC conditions for both days of testing

	Day 1		Day 2	
	BL	**REC**	**BL**	**REC**
Mean	16.05	14.04	13.61	14.28
SD	3.59	6.99	3.39	5.19

3.3.5.4 Effect of GCS on Hemodynamic Recovery Time

The time for each subject to recover to 50% above their average baseline PBV_{mean} was analyzed as described in Section 2.5; the results for each subject's recovery time with and without GCS for both days of testing can be seen in Table 3.9. For day 1, half of the subjects had longer recovery times with the GCS, while the other half had longer recovery times during the NGCS condition. For day 2, ten subjects experienced longer recovery periods with the GCS, while two subjects experienced longer recovery periods without the GCS. For the subjects who required longer recovery times with the GCS, the response was repeatable for both days. For the subjects who required longer recovery times during the NGCS test, two subjects had repeatable responses for both days. For the remaining four subjects on day 2, three had very similar times for the GCS and NGCS recovery periods (Table 3.9, Subjects 2, 4, and 9). The remaining subject had a completely opposite effect on day 2, as shown in in Table 3.9 for Subject 1. The order of testing had no effect on the recovery responses of the subjects. Finally, no statistically significant differences were found between recovery times on either day between the NGCS and GCS cases (day 1: $p = 0.62$, day 2: $p = 0.08$). Since the response of the subjects was split between conditions, no conclusive result could be obtained on whether the addition of the GCS was beneficial for hemodynamic recovery time.

Table 3.9: Time required for subjects to return to 50% above their baseline PBV_{mean} values (time in seconds, red: increase during the GCS condition, black: decrease during the GCS condition)

	Day 1		Day 2	
Subject	**NGCS**	**GCS**	**NGCS**	**GCS**
1	144.04	75.56	63.15	153.3
2	> 300	293.47	296.90	297.04
3	26.23	41.11	26.28	78.25
4	89.26	57.25	42.68	49.69
5	179.72	87.09	280.31	214.42
6	77.57	245.51	156.6	216.09
7	129.92	> 300	52.5	120.63
8	129.75	292.47	52.6	87.38
9	295.18	141.99	46.23	56.46
10	138.45	286.59	248.03	278.59
11	41.64	31.69	291.8	267.47
12	158.13	202.86	146.3	166.52

3.3.6 Discussion of the Effect of GCS during Recovery

There were no significant differences in PAD, PBV_{mean}, or PBF_{mean} during recovery with the addition of the GCS. The only notable trend was that the majority of subjects experienced the same response with the GCS during baseline and recovery. This indicated that there was no carry over effects from the plantar flexion exercise into the recovery period. As previously discussed in Section 3.3.2, Stein et al. also found similar results[3]. For muscle oxygenation there were no significant differences between the NGCS and GCS conditions. There was however, a trend towards lower tHb values indicating that the GCS was still maintaining a lower blood volume in the calf post exercise. Bringard et al. investigated muscle oxygenation in the calf while standing at rest with the addition of external compression and found that there was a decrease in blood volume when the sock was worn, as well as a decrease in the HHb values [62]. Similarly, Agu et al. (previously discussed in Section 3.3.4) studied muscle oxygenation during quiet standing and found significant reductions in HHb and a trend toward lower tHb value with the addition of external compression [25]. These studies did not investigate muscle oxygenation post exercise, which could account for the differences seen in the HHb values.

The ΔP immediately post exercise was comparable to the baseline values with the difference falling within the error associated with the pressure sensor system. The variation in the average ΔP increased during recovery compared to baseline was due to slipping of the sock during the exercise task. Finally for recovery time there was no conclusive result on whether or not recovery occurs faster with the GCS. For half of the subjects the time reach 50% of the BL PBV_{mean} value was longer on both days with the GCS, implying that there was a higher PBV value in the leg and therefore a higher PBF value since there was no change in PAD. The increase in PBF during recovery suggested that PBF during EX was not sufficient and hence created an oxygen deficit in the calf muscles. The body works to replenish this deficit by maintaining higher blood flow during recovery until the oxygen debt has been repaid. If this was the case for these subjects it is believed that there would have been significant changes between the NGCS and GCS conditions during EX and REC in the peripheral variables, however, this did not occur except for lower blood volume in the leg with the GCS. Since the response of the PBV_{mean} with the GCS remained the same between BL and REC, the GCS was not believed to have had significant carry over effects into the recovery period. Since no other variables suggested that there would be a longer recovery period with or without the GCS, and the results were not statistically significant, this study implied that the GCS have no noteworthy effect on recovery time. The literature review completed found no studies that looked at PBV immediately following exercise for comparison purposes as the majority of studies investigate the effect of GCS on recovery based on personal opinion of muscle soreness several hours post exercise [1].

Chapter 4

Conclusions and Recommendations

This chapter provides a summary of the results and highlights the key findings of the experimental study completed on investigating the impact of GCS on a healthy population. Chapter 4 also presents recommendations for future experiments for testing the benefits of GCS during exercise and rest conditions.

4.1 Conclusions

The goal of this study was to complete a set of controlled experiments to assess the effectiveness of passive compression on athletic performance in healthy subjects. The impact of passive compression on peripheral and central hemodynamics was investigated at rest, during exercise, and during recovery by measuring global and local variables in the cardiovascular system. Centrally, no changes were found in HR, CO, SBP, or DBP indicating that the external pressure applied to the legs had no effect on central hemodynamics. Peripherally, there were no significant changes in PAD, PBV_{mean}, or PBF_{mean} during any of the testing conditions. During exercise, there was an indication that the subjects who experienced an increase in PBV_{mean} or PBF_{mean} with the GCS behaved more consistently than those who experienced a decrease, as implied by lower standard deviation values. Moreover, during recovery, there was also no significant difference between the PAD values for BL and REC, indicating that the exercise task did not result in any lasting effects on the vasculature at the popliteal level. The result that there were no carry over effects from EX was also confirmed with a trend in PBV_{mean} and PBF_{mean}, where subjects experienced the same response with the GCS during both BL and REC. For muscle oxygenation, results indicated a decrease in blood volume in the leg with the GCS, and a trend towards increased muscle oxygenation and oxygen extraction during EX. For recovery, there is a trend towards a lower blood volume in the leg with the GCS, implying that post-exercise the socks are working to prevent pooling in the leg. For muscle activity, there were no significant differences between the NGCS and GCS conditions illustrating that the same muscle recruitment was required for both conditions. Furthermore, the locally applied pressure was found to vary dynamically during exercise and then return to baseline values during recovery. Moreover, the strength of the ΔP was not correlated to the response of the subject with the addition of the GCS. Finally, no significant differences were found in the recovery time of PBV_{mean} with the addition of the sock.

Overall the results found in this study were comparable to other studies investigating the effect of GCS on hemodynamics. It is not surprising that there were no changes in central hemodynamics as the external pressure was applied in such a small, localized region. It was also not unexpected that a healthy study population did not lead to significant changes in vasculature diameter or blood velocity since the subjects do not suffer from venous deficiencies and have normally operating cardiovascular systems. This study illustrated that the GCS are beneficial in decreasing blood volume in the leg, as expected with their prescribed function, and have the potential to increase oxygen extraction in a healthy population.

Furthermore, it was discovered that the local applied pressure varied during exercise and this variation should be taken into consideration when utilizing GCS for various exercise tasks. Moreover, this study was completed with a high level of control in an attempt to address previous issues found in current research and to aid in the development of concrete conclusions on the effect of compression on healthy subjects. The findings prove that the applied pressure is extremely important and since this is a variable that is often not monitored in current research, it could be a contributing factor as to why there is such variation in the reported results. Also, as discussed in Section 1.1.4.2, the majority of studies use individual perception to quantify the effect of compression during recovery. The current study presents the effect on hemodynamics both before and after exercise to allow for a complete picture of how the GCS affects hemodynamics. This study highlights the importance of control and reporting all aspects of the experiment in order to obtain high fidelity results that can be entered, with confidence, into the debate of the effectiveness of GCS on athletic performance.

4.2 Recommendations

For future work involving the investigation of the effect of external passive compression on hemodynamics, the following changes to the current study's experimental protocol are recommended:

1. Increase the ΔP of the external compression. It is believed that the pressure applied to the leg in this study was not substantial enough to generate significant differences in the peripheral variables, specifically PAD, PBV_{mean}, PBF_{mean}, or muscle oxygenation. Agu et al. only began to show significant differences in muscle oxygenation for subjects with venous deficiencies at ΔP levels of 9.5 mmHg to 15.12 mmHg [25].

2. Control the calf raise height to the same level for all subjects. There was a trend indicating that those subjects that reported irregular exercise completed calf raises at lower heights than those who exercised frequently. Maintaining a calf raise height slightly above the average value for those who reported irregular exercise (i.e. 4 cm) would ensure that all participants could complete the task, as the value is low enough to account for the variation in stature and foot size. By controlling the calf raise height, the percentage of the subjects' MVC required to complete the exercise task could be compared and indications of fatigue or the effect of exercise frequency could be derived.

3. Increase the duration of plantar flexion exercise to determine the effect of the GCS during fatigue. The results of this study indicated no significant carry over effects from the EX condition into the REC period. By increasing the duration of the exercise task, subjects could be pushed to their fatiguing levels and the effect of the GCS during fatigue could be investigated to determine if the sock has beneficial effects in enhancing performance.

4. Employ a more demanding exercise task in the experimental protocol. Utilizing a more demanding exercise task that requires larger muscle recruitment (e.g., running) where higher blood flow demands are placed on the body may elicit more significant and measurable changes in the central variables.

5. Map the pressure distribution of the GCS on the calf. Currently only four sensors are placed at the knee and ankle of the medial and lateral sides of the leg to provide insight into the ΔP driving changes in hemodynamics. Since no significant changes were observed in central or peripheral hemodynamics in this study it is believed that gaining a better understanding of the pressure over the entire calf could aid in the explanation of the hemodynamic response in future studies.

References

[1] B.A. MacRae, J.D. Cotter, R.M. Laing, "Compression garments and exercise: Garment considerations, physiology, and performance," *Sports Med*, **41**(10) pp. 815-843 (2011).

[2] D.P. Born, B. Sperlich, H.C. Holmberg, "Bringing light into the dark: Effects of compression clothing on performance and recovery," *International Journal of Sports Physiology and Performance*, **8**, pp. 4-18 (2013).

[3] S.P. Downie, D.N. Firmin, N.B. Wood, S.A. Thom, A.D. Hughes, J.N. Wolfe, and X.Y. Xu, "Role of MRI in investigating the effects of elastic compression stockings on the deformation of the superficial and deep veins in the lower leg," *Journal of Magnetic Resonance Imaging*, **26**, pp. 80-85 (2007).

[4] G. Mosti, "Compression and venous surgery for venous leg ulcers," *Clinics in Plastic Surgery*, **39**(3), pp. 269-280 (2012).

[5] P.D. Stein, F. Matta, A.Y. Yaekoub, S.T. Ahsan, A. Badshah, F. Younas, J.E. Denier, "Effect of compression stockings on venous blood velocity and blood flow," *Thrombosis and Haemostasis*, **103**(1), pp. 138-144 (2010).

[6] D.G. Silverhorn, *Cardiovascular Physiology,* Fourth Edition, San Francisco: Pearson Education Inc., 2007.

[7] Klabunde, R.E, *Cardiovascular Physiology Concepts*, 2nd Edition, Wolters Kluwer, Ch.5.

[8] "Function of the Cardiovascular System", id Human Body, 2014. [Online]. http://idhumanbody.com/function-of-the-cardiovascular-system.html. [Accessed August 20, 2014].

[9] L.B. Rowell, "Reflex Control during Orthostasis" in Human Cardiovascular Control, New York: Oxford Press, 1993.

[10] "Ch.1 Venous Anatomy and Pathophysiology", American College of Phlebology, 2013. [Online]. http://www.phlebology.org/pdfs/Ch1_pp1-4.pdf . [Accessed February 10, 2013].

[11] "Communicating (Perforator) Veins", *ProSono Professional Ultrasound Services*, pp. 13-18, 2006.

[12] "Circulatory System Anatomy", Anatomy and Physiology II, 2013. [Online]. http://legacy.owensboro.kctcs.edu/gcaplan/anat2/notes/APIINotes5%20Circulatory%20Anatomy.htm [Accessed February 1, 2013].

[13] B. Kumar, A. Das, and R. Alagirusamy, "Analysis of sub-bandage pressure of compression bandages during exercise", *Journal of Tissue Viability*, **21**, pp. 115-124 (2012).

[14] H. Orsted, L. Radke, and R. Gorst, "The Impact of Musculoskeletal Changes on the Dynamics of the Calf Muscle Pump", *Ostomy/Wound Management*, **47**(10), pp. 18-24 (2001).

[15] "Calf Muscles", Floota, 2013. [Online]. http://www.floota.com/muscles_of_the_calf.html. [Accessed February 20, 2013].

[16] "Anatomy & Physiology", OpenStax CNX, 2014. [Online]. http://cnx.org/content/col11496/1.6/. [Accessed June 10, 2014].

[17] "Vein Muscle Pump". YouTube, 2009 [Online]. http://www.youtube.com/watch?v=O2HEwdnF4o4. Accessed: February 15, 2013.

[18] "Leg Health", Jobst,2013. [Online]. http://www.jobst-usa.com/. [Accessed February 9, 2013].

[19] "Varicose Veins", Mayo Clinic, 2013. [Online]. http://www.mayoclinic.com/health/varicose-veins/DS00256 . [Accessed February 9, 2013].

[20] "Deep Vein Thrombosis (DVT)", Mayo Clinic, 2013. [Online]. http://www.mayoclinic.com/health/deep-vein-thrombosis/DS01005 .[Accessed February 9, 2013].

[21] "Chronic Venous Insufficiency (CVI)", Cleveland Clinic, 2009. [Online]. http://my.clevelandclinic.org/disorders/venous_insufficiency/hvi_chronic_venous_insufficiency.aspx . [Accessed February 9, 2013].

[22] "Compression Stockings", VenacureEVLT, 2009. [Online]. http://venacure-evlt.com/varicose-veins/treatments/compression-stocking/. [Accessed August 20, 2014].

[23] B. Byrne, "Deep vein thrombosis prophylaxis: The effectiveness and implications of using below knee or thigh-length graduated compression stockings", *Heart Lung*, **30**, pp. 277-284 (2001).

[24] M. Hirai, H. Iwata, and N. Hayakawa, "Effect of elastic compression stockings in patients with varicose veins and healthy controls measured by strain gauge plethysmography", *Skin and Research Technology*, **8**, pp. 236-239 (2002).

[25] O. Agu, D. Baker, A.M. Seifalian, "Effect of graduated compression stockings on limb oxygenation and venous function during exercise in patients with venous insufficiency," *Vascular*, **12**(1), pp. 69-76 (2004).

[26] F. Lurie, V. Scott, H.C. Yoon, and R.L. Kistner, "On the mechanism of action of pneumatic compression devices: Combined magnetic resonance imaging and duplex ultrasound investigation," *Journal of Vascular Surgery*, **48**, pp. 1000-1006 (2008).

[27] H. Partsch, G. Mosti, and F. Mosti, "Narrowing of leg veins under compression demonstrated by magnetic resonance imaging (MRI)," *International Journal of Angiology*, **29**, pp. 408-410 (2010).

[28] S. Avril, L. Bouten, L. Dubuis, S. Drapier, and J.F. Pouget, "Mixed experimental and numerical approach for characterizing the biomechanical response of the human leg under elastic compression," *Journal of Biomechanical Engineering*, **138**, pp. 1-8 (2010).

[29] S. Avril, P. Badel, L. Dubuis, P.Y. Rohan, J. Debayle, S. Couzan, and J.F. Pouget, "Patient-specific modeling of leg compression in the treatment of venous deficiency," *Studies in Mechanobiology, Tissue Engineering and Biomaterials*, **9**, pp. 217-238 (2012).

[30] X.Q. Dai, R. Liu, Y. Li, M. Zhang, and Y.L. Kwok, "Numerical simulation of skin pressure distribution applied by graduated compression stockings," *Studies in Computational Intelligence*, **55**, pp. 301-309 (2007).

[31] L. Dubuis, S. Avril, J. Debayle, and P. Badel, "Identification of the material parameters of soft tissues in the compressed leg," *Computer Methods in Biomechanics and Biomedical Engineering*, **15**(1), pp. 3-11 (2012).

[32] Y. Lin, K.F. Choi, A. Luximon, L. Yao, J.Y. Hu, and Y. Li, "Finite element modeling of male leg and sportswear: contact pressure and clothing deformation," *Textile Research Journal*, **81**(14), pp. 1470-1476 (2011).

[33] R. Liu, Y.L. Kwok, Y. Li, T.-T. Lao, X. Zhang, and X. Dai, "A three dimensional biomechanical model for numerical solution of dynamic pressure functional performances of graduated compression stockings (GCS)," *Fibers and Polymers*, **7**(4), pp. 389-397 (2006).

[34] R.S.A Lord and D. Hamilton, "Graduation compression stockings (20-30mmHg) do not compress leg veins in the standing position," *Journal of Surgery*, **74**, pp. 581-585 (2004).

[35] B. Partsch and H. Partsch, "Calf compression pressure required to achieve venous closure from supine to standing positions," *Journal of Vascular Surgery*, **42**(4), pp. 734-738 (2005).

[36] A. Ali, R.H. Creasy, and J.A. Edge, "Physiological effects of wearing graduated compression stockings during running", *Eur J Appl Physiol*, **109**, pp. 1017-1025 (2010).

[37] A.C. Guyton and J.E. Hall, "Sports Physiology" in Textbook of Medical Physiology, Eleventh Edition, Philadelphia: Elsevier Saunders, 2006.

[38] A. Varela-Sanz et al, "Effects of Gradual-Elastic Compression Stocking on Running Economy, Kinematics, and performance in Runners", *Journal of Strength and Conditioning Research*, **25** (10), pp. 2902-2910 (2011).

[39] W. Kemmlar et al., "Effect of Compression Stockings on Running Performance in Men Runners", *Journal of Strength and Conditioning Research*, **23** (1), pp. 101-105 (2009).

[40] C.L.Buhs et al.,"The effect of graded compression elastic stockings on the lower leg venous system during daily activity", *J Vasc Surg*, **30**, pp. 830-835 (1999).

[41] A. Ali, M.P. Caine, and B.G. Snow, "Graduated compression stockings: Physiological and perceptual responses during and after exercise", *Journal of Sports Sciences*, **25**(4), pp. 413-419 (2007).

[42] K.E. Welman, "The value of graduated compression socks as a post-exercise recovery modality in long distance models," Ph.D. dissertation, Dept. of Sport Science, University of Stellenbosch, 2011.

[43] "Stay Fit at Work", Verge Magazing, 2014. [Online]. http://www.vergemagazine.co.uk/girls/2014/06/stay-fit-work/. [Accessed September 24, 2014].

[44] "FinometerTM user's guide", FMS, Finapres Medical Systems BV, 2002.

[45] N. Gagné, "Developing a non-invasive method to monitor cardiovascular control during orthostatic challenge considering the limitation of the FinometerTM", Master's Thesis for University of Waterloo, pp. 12 – 17, 2009.

[46] "Understanding the Heart's Electrical System and EKG Results", National Heart, Lung, and Blood Institute, 2012. [Online]. http://www.nhlbi.nih.gov/health/health-topics/topics/hb/understanding.html. [Accessed October 27, 2014].

[47] A. Thrush and T. Hartshorne, *Peripheral Vascular Ultrasound: How, Why and When*, Second Edition. London: Elsevier Churchill Livingstone, 2005.

[48] M.B.I. Reaz, M.S. Hussain, F. Mohd-Yasin, "Techniques of EMG signal analysis: Detection, processing, classification and applications", *Biology Procedures*, **8**(1), pp.11-35 (2006).

[49] G.S.Rash, "Electromyography fundamentals". [Online]. http://faculty.educ.ubc.ca/sanderson/courses/HKIN563/pdf/EMGfundamentals.pdf. [Accessed October 20, 2014].

[50] M. Dat, "Introduction to near infrared spectroscopy", Artinis Medical Systems, 2013.

[51] T. Beltrame, "SEMINAR – KIN 670: Utilization of near-infrared spectroscopy (NIRS) during exercise testing", University of Waterloo, 2013.

[52] I. Beentjes, "Pressure Sensing System", Work Report for University of Waterloo, 2013.

[53] R. Villar and R.L. Hughson, "Effect of altered arterial perfusion pressure on vascular conductance and muscle blood flow dynamic response during exercise in humans," *Journal of Applied Physiology*, **114**(5), pp. 620-627 (2013).

[54] R.Villar, "Effect of arterial blood perfusion pressure on vascular conductance and muscle blood flow at rest and exercise", PhD Thesis for University of Waterloo, pp. 22-23, 2012.

[55] K. Fraser, "Postural effects on brain blood flow and cognition in heart failure", Master's Thesis for University of Waterloo, pp. 31, 2014.

[56] A. Schmitz et al., "Differences in lower-extremity muscular activation during walking between healthy older and young adults", *Journal of Electromyography and Kinesiology*, **19**, pp. 1085-1091 (2009).

[57] D.A.Winter and H.J. Yack, "EMG profiles during normal human walking: Stride-to-stride and inter-subject variability", *Electroencephalography and Clinical Neurophysiology*, **67**, pp. 402-411 (1987).

[58] "t Distribution", Six Sigma Material. [Online]. http://www.six-sigma-material.com/t-distribution.html. [Accessed October 1, 2014].

[59] "FAQ: What is the coefficient of variation?", IDRE UCLA. [Online]. http://www.ats.ucla.edu/stat/mult_pkg/faq/general/coefficient_of_variation.htm. [Accessed November 19, 2014].

[60] P.S. Myles and J.Cui, " Using the Bland–Altman method to measure agreement with repeated measures", *Br. J. Anaesth*, **99**(3), pp. 309-311 (2007).

[61] "Intraclass Correlation Coefficient Explained", Stats To Do. [Online]. https://www.statstodo.com/ICC_Exp.php. [Accessed November 19, 2014].

[62] A.Bringard et. al, "Effects of compression tights on calf muscle oxygenation and venous pooling during quiet resting in supine and standing positions", *The Journal of Sports Medicine and Physical Fitness*, **46**, pp. 548-554(2006).

[63] J. McLaren et. al, "Preliminary development of a wearable device for dynamic pressure measurement in garments", *Procedia Engineering 2* , pp. 3041-3046 (2010).

Appendix A: EMG Comparison of Walking and Plantar Flexion

A small study was completed on two subjects to determine the difference in muscle activity during walking and plantar flexion. The subjects were instructed to walk on a treadmill for five minutes at a speed that they felt was similar to their normal walking pace (Subject 1: 2.6 mph, Subject 2: 3.5 mph). On a separate day, the muscle activity during five minutes of plantar flexion was investigated. The total muscle activity in the gastrocnemius muscle was compared for both cases. The soleus muscle was later added to the GCS study to investigate the entire activation of the calf and therefore it was not investigated in this study. The results are illustrated in Table A.1 and indicate that for Subject 1 the plantar flexion task required approximately 19 % more than walking at normal pace, and for Subject 2 the plantar flexion task required 41 % less than normal walking pace. The variation between the two subjects is due to gender, height, weight, and therefore normal walking pace. There is also the potential for error as the treadmill and calf raise task were completed on two separate days therefore some human variability will exist as well as the potential that the EMG electrodes were not placed in the exact same locations on both days. This study indicates that the muscle activation for the plantar flexion task is similar to walking and would correspond well to subjects walking at slower speeds where less muscle activation is required.

Table A.1: Comparison of the total muscle activation in the gastrocnemius for plantar flexion and walking

Subject	Plantar Flexion (mV)	Walking (mV)
1	0.88	0.71
2	0.38	0.64

Appendix B: Participant Protocol and Health Forms

The following forms were provided to the participants upon arrival to the lab for testing. Small changes were made to the protocol described in the Information Letter as discussed in Chapter 2. These changes were made clear to the subjects before consenting to the experiment. The health forms were assessed before beginning the protocol to ensure that the experiment was safe for each subject.

UNIVERSITY OF Waterloo

INFORMATION LETTER

Cardiorespiratory &Vascular Dynamics Lab
University of Waterloo

You have been invited to take part in a research study. This letter will outline the purpose of the project, describe the procedures that are required, tell you about potential risks and benefits to yourself, and discuss your rights and confidentiality issues. If you wish to participate, you will be asked to sign a consent form at the time of the study. Feel free to ask any questions you might have at any time.

Study Title:

Can cardiac function be improved by increasing venous return via external compression of the lower legs?

Researchers and Contact Information:

Sean Peterson, PhD phone: 519-888-4567 ext 38722 e-mail: peterson@uwaterloo.ca

Richard Hughson, PhD phone: 519-888-4567 ext 32516 e-mail: hughson@uwaterloo.ca

Department of Mechanical and Mechatronics Engineering, Centre for Bioengineering and Biotechnology, University of Waterloo, Waterloo, ON, N2L 3G1

Department of Kinesiology, Faculty of Applied Health Sciences, University of Waterloo, Waterloo, ON, N2L 3G1

Student investigator

Jennifer Book phone: 519-888-4567 ext 38722 e-mail: jlbook@uwaterloo.ca

Collaborators

Rodrigo Villar, PhD phone: 519-888-4567 ext 38073 e-mail: rvillar@uwaterloo.ca

Chekema Prince, Msc phone: 519-888-4567 ext 38722 e-mail: cprince@engmail.uwaterloo.ca

What is the purpose of this study?

This research is designed to determine the effect on cardiac function by increasing venous return via external compression of the lower leg. The understanding of the effect of compression on venous return can bring new insights about improvement of cardiac function with workload reduction on the heart and cardiac system in different populations, such as; cardiovascular disease, peripheral vascular disease, workers with regular and sustained periods of exercise and athletes. Such information can be used to create new tools and strategies to improve cardiovascular responses to challenges of daily living activities as well as recreational and sports activities having a direct impact on the quality of life. The study data will be used for Jennifer Book Master's thesis.

What will I be asked to do? How much time will it take?

Participants will be asked to attend two laboratory sessions. In the first session, participants will be asked to complete the consent form, health status form and par-Q questionnaire that will be reviewed by researchers Rodrigo Villar, PhD and Jennifer Book (student investigator). The participant's height and weight will then be measured and a familiarization of the procedures will be completed, including data collection and protocols that will be used in this study. Next the arteries and veins of the lower legs will be identified using Doppler ultrasound. The participant may ask as many questions as they want to clarify the information presented. In the second session, the participant will be asked to stand-up and hold a custom designed frame to provide support while standing on one leg. Their body weight will be supported by the left leg on a wood platform and their right leg will be free with no support with the ankle kept at a 90º angle. Next, the participant will be asked to wear a graduated compression sock on the right leg and stand-up again using the frame for support to perform plantar flexion (calf raises) exercise for 6 minutes. Heart rate, blood pressure, cardiac output, artery and vein diameters and velocities and muscle activity will be continuously measured during the tests. The total time commitment will be 6 hours (2-3 hours per day of testing). All of these measurements used are non-invasive and all procedures will be taken by trained researchers.

Am I eligible?

This study focuses on 18-40 years old healthy men and women. You will be asked to complete a Health Status Form that determines eligibility for the study. This one-page form will ask important information about your health, including past and current medical conditions and current medications. Smokers and those with any current medical problem related to cardiovascular disease, kidney disease, chronic inflammatory disease, diabetes, neurological disorders or skin sensitivity (i.e., psoriasis) will be excluded from participation in this study.

What are the procedures? Will there be any risk involved?

On arrival at the laboratory, your height and weight will be measured and you will fill out the Physical Activity Readiness Questionnaire (PAR-Q) and the medical screening form. We will ask you to stand-up and hold the custom designed frame, which will be adjusted to provide optimal comfort for you. Your right foot will be free with no support while your left leg will step on a support. Then, heart rate, blood pressure, cardiac output, blood velocity, blood vessel diameter, blood flow and muscle activity will be measured at baseline. After baseline measurements are taken you will be asked to wear a graduated compression sock on your right leg and repeat the standing test as previously described. Following, you will be asked to place both feet on the ground to perform 6 minutes of exercise (calf raises). Heart rate, blood pressure, cardiac output, blood velocity, blood vessel diameter, blood flow and muscle activity will be measured during standing and exercise phases. All of these measurements used are non-invasive and all procedures will be taken by trained researchers. The non-disposable equipment will be sanitized between uses by alcohol wipes.

Heart Rate measurements

Heart rate will be continuously monitored beat by beat by an electrocardiogram (ECG) through 3 spot electrodes on the skin surface. The disposable electrodes are normally placed in the upper and lower portions of the chest (two on the left side and one on the right side). The ECG electrodes will be placed by a researcher of the same sex. **In a very small group of individuals, a skin rash might occur due to the adhesive on the electrodes.** There is no way of knowing this ahead of time. The rash, if it develops, will resolve itself within a day or so. Avoid scratching the rash and keep the area clean.

Blood Pressure measurements

Arterial blood pressure will be measured by a small cuff placed on the middle finger and from a cuff placed around your upper arm. This device applies light pressure around the finger in order to determine the

pressure in these arteries. Any discomfort should be minimal with this measurement system. **In case of discomfort, please notify the researcher immediately.**

Cardiac output measurements ($\dot{Q}$)

Cardiac output ($\dot{Q}$) will be estimated from the finger arterial pulse wave by a small cuff placed on the middle finger. From a cuff placed around your upper arm the brachial arterial wave will be reconstructed based on the finger arterial wave through a modelflow algorithm method to represent the shape of the aortic waveform. This model includes age, sex, height, and weight as factors to estimate stroke volume. Cardiac output values will be calculated as a product of heart rate and stroke volume measurements.

Ultrasound Measurements of blood flow velocity and blood vessel diameters

Ultrasound is a non-invasive technique used to measure the velocity of red blood cells moving through the arteries and to image the blood vessels. The blood flow velocity will be measured in the popliteal artery in the back of the leg (popliteal fossa located in the back of the knee) by Doppler ultrasound. A probe will be placed over the skin with the ultrasound directed toward the blood vessel and this probe will be held by the researcher. The probe will be adjusted to the minimum power level necessary to obtain a clear signal. At this level you should not notice any sensation. This method is widely used. **However, in the unlikely event that you should feel a sharp pain or burning, please inform the experimenter immediately.** In the very unlikely case that a skin burn should occur, it should be treated as any other burn by application of cold compress, first aid cream and sterile covering. The procedure involves the use of water soluble ultrasound gel. It can be removed simply by applying water and wiping the skin and/or hair with a paper towel or a cloth. The arteries and veins will be imaged by the use of echo Doppler ultrasound. This technique is entirely non-invasive. The probe will be held against the skin in the back and front of the lower leg to image the diameter of the arteries and veins as well as obtain blood velocity tracings. Ultrasound monitoring requires the use of water-soluble, hypoallergenic gel between the probe and the surface of the skin. Ultrasound procedures will be conducted by a researcher delegated to do so by a physician under the Delegation of a Controlled Act.

Muscle activity measurements

Muscle activity will be measured by electromyography (EMG) through 7 skin surface electrodes. The disposable electrodes are placed on the lower leg on the right and left gastrocnemius, specifically in the biggest portion of the muscle (maximum circumference) and soleus muscles placed beside the gastrocnemius tendon. Before the electrodes are placed, the area will be sterilized with alcohol and cleaned with cotton balls. The hairs will be shaved by a disposable razor to allow better signal during data collection. This procedure is safe. **In a very small group of individuals, a skin rash might occur due to the adhesive on the electrodes.** There is no way of knowing this ahead of time. The rash, if it develops, will resolve itself within a day or so. Avoid scratching the rash and keep clean.

Are there any special instructions I should follow?

We will request that you refrain from consuming alcohol, caffeinated beverages, and from engaging in vigorous exercise (that is, exercise where you are breathing so hard that you would be unable to carry on a conversation) **24 hours** prior to testing. We also request that you do not eat a large meal **within 2 hours** of testing. You should wear comfortable exercise clothing such as shorts, t-shirt, socks and -sneakers.

Will I benefit from this study?

There are no direct benefits to participation in the study. You will gain more knowledge about the effects of passive and active compression on cardiovascular hemodynamic responses, the research process, and

appreciate the types of changes that can happen during these procedures. It is important to understand if compression can affect cardiovascular hemodynamics by improving the return of blood back to your heart through the veins and therefore decreasing the heart workload. This study may have implications for different populations such as increasing performance by athletes, decreasing fatigue for workers that spend a lot of time standing or walking (soldiers, firefighters, police officers, delivery workers) and improving circulation for older people, people with cardiovascular diseases or peripheral vascular disease. **If requested, you will be provided a feedback letter concerning the responses of all participants as soon as possible following the completion of the study.**

Will I be rewarded for volunteering my time?

There will be no remuneration for this study.

Can I withdraw from the study?

Your participation in this study will be voluntary. **You may withdraw from the study without penalty or any consequences** by making the researchers aware of your decision.

How confidential and secure is my personal information?

Each participant will be identified by a special identification code known by the main investigator and the research assistants. After all of the identifying information has been removed, the data will be kept for 25-years in an encrypted format in a password-protected secure location, locked in the Cardiorespiratory and Vascular Dynamics Laboratory in Burt Mathews Hall 2421 at the University of Waterloo. The results will be used for publications in conferences, papers, and reports. The participant's name or any type of identification information will be not included to maintain confidentiality.

Has this study received ethics clearance?

This project has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee (ORE# 19454). You may contact the Director at the University, Maureen Nummelin, PhD, by phone at 519-888-4567, ext 36005, or by email at maureen.nummelin@uwaterloo.ca with any comments or concerns about your participation in this study.

We would like to remind you that if you have questions, you can contact us at any time. Our contact info is on the first page of this letter. Thank you for considering our study.

CONSENT OF PARTICIPANT

Cardiorespiratory &Vascular Dynamics Lab
University of Waterloo

Study Title:

Can cardiac function be improved by increasing venous return via external compression of the lower legs?

Researchers and Contact Information:

[1]**Sean Peterson, PhD** phone: 519-888-4567 ext 38722 e-mail: peterson@uwaterloo.ca

[2]**Richard Hughson, PhD** phone: 519-888-4567 ext 32516 e-mail: hughson@uwaterloo.ca

Student investigator

[1]**Jennifer Book** phone: 519-888-4567 ext 38722 e-mail: jlbook@uwaterloo.ca

Collaborators

[1]**Chekema Prince, Msc** phone: 519-888-4567 ext 38722 e-mail: cprince@engmail.uwaterloo.ca

[2]**Rodrigo Villar, PhD** phone: 519-888-4567 ext 38073 e-mail: rvillar@uwaterloo.ca

[1]Department of Mechanical and Mechatronics Engineering, Centre for Bioengineering and Biotechnology, University of Waterloo, Waterloo, ON, N2L 3G1

[2]Department of Kinesiology, Faculty of Applied Health Sciences, University of Waterloo, Waterloo, ON, N2L 3G1

I have read the information presented in the information letter about the procedures and risks involved in this study. I have had the opportunity to ask any questions related to the study and have received satisfactory answers. I am aware that I may withdraw from the study without penalty at anytime by making the researchers aware of this decision. If I have any further questions about participation in this study I know that I may contact Richard Hughson, PhD, by phone at 519-888-4567, ext. 32516, or by e-mail at hughson@uwaterloo.ca.

This project has been reviewed and received ethics clearance through a University of Waterloo Research Ethics Committee (ORE# 19454). I was informed that I may contact the Director, Maureen Nummelin, PhD, at 519-888-4567, ext. 36005, or by e-mail at maureen.nummelin@uwaterloo.ca with any comments or concerns about my participation in this study.

With full knowledge I agree, on my own free will, to be a participant in the research project identified above. I am aware that by signing the consent form, I am not waiving my legal rights or releasing the investigator(s) or involved institution(s) from their legal and professional responsibilities.

_____ _____

Participant (print name) Participant (signature)

_____ _____

Witness (print name) Witness (signature)

_____ _____

Date Location

HEALTH STATUS FORM

Study: Can cardiac function be improved by increasing venous return via external compression of the lower legs? ID#: _____

SELF REPORT CHECK LIST

Health Problems

Rheumatic Fever	( )	Bleeding disorders	( )
Diabetes	( )	Kidney and liver disease	( )
Heart Murmur	( )	Anemia	( )
High Blood Pressure	( )	Epilepsy	( )
High Cholesterol	( )	Varicose Veins	( )
Congenital Heart Disease	( )	Disease of Arteries	( )
Heart Attack	( )	Emphysema, Pneumonia	( )
Heart Operation	( )		
Heartburn	( )	Back Injuries	( )
Raynaud's disease	( )	Arthritis	( )
Bleeding from Intestinal Tract	( )	Peripheral vascular disease	( )
Enteritis/colitis/diverticulitis	( )		

Drug reactions, food allergies and allergies and sensitivities to gels or adhesives (specify):_____
_____
_____

List medications or vitamin supplements taken in last 3 months:
1._____3._____
2._____4._____

For females: Pregnant ____ Nursing ___

List of symptoms

Irregular Heart Beat	( )	Fatigue	( )
Chest Pain	( )	Cough Up Blood	( )
Short of Breath	( )	Back Pain/Injury	( )
Persistent Cough	( )	Leg Pain-Injury	( )
Dizziness	( )		

Habits: Smoking: Never ( ) Ex-smoker ( ) Regular ( ) Average # cigarettes/day ( )
Exercise: Never ( ) Irregular ( ) Regular ( ) Specify:

Researchers name: Rodrigo Villar, PhD and/or Jennifer Book
Signature of Researcher:_____
Date:_____

The current study has been identified as requiring medical clearance: Yes ( ) No **(X)**

Smokers and those with any current medical problem related to cardiovascular disease, kidney disease, chronic inflammatory disease, diabetes, neurological disorders or skin sensitivity (i.e., psoriasis), peripheral vascular disease and Raynaud's disease will be excluded from participation in this study.

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

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.

Appendix C: Validation of the Pressure Sensor System

The pressure sensor system was calibrated using a series of hydrostatic tests. Each of the 16 bladders were submerged in water to a known depth. The applied pressure (P) is a function of depth as shown in Equation C.1, where ρ is the density of the fluid, g is the gravitational acceleration, and h is the depth of the pressure sensor with respect to the surface of the fluid.

$$P = \rho g h \qquad \textbf{Equation C.1}$$

The applied pressure obtained from the pressure sensor system was compared to the expected pressure, calculated from Equation C.1. The results are shown in Figure C.1 where the reading from the transducer is compared to the calculated pressure. The experimental pressures obtained match closely to the calculated expected pressures. The greatest disparity between the calculated pressure and the measured pressure is approximately 8% over the entire pressure transducer's range [52]. This maximum difference correlated to a value of approximately 3 mmHg and this value was used as the measurement error in the pressure system. Taking into consideration the possible errors that could be introduced into the calculated pressure including human error, the surface tension of the water affecting a precise h measurement, and the deformation of the sensor while submerged in the fluid, the pressure values showed good correlation.

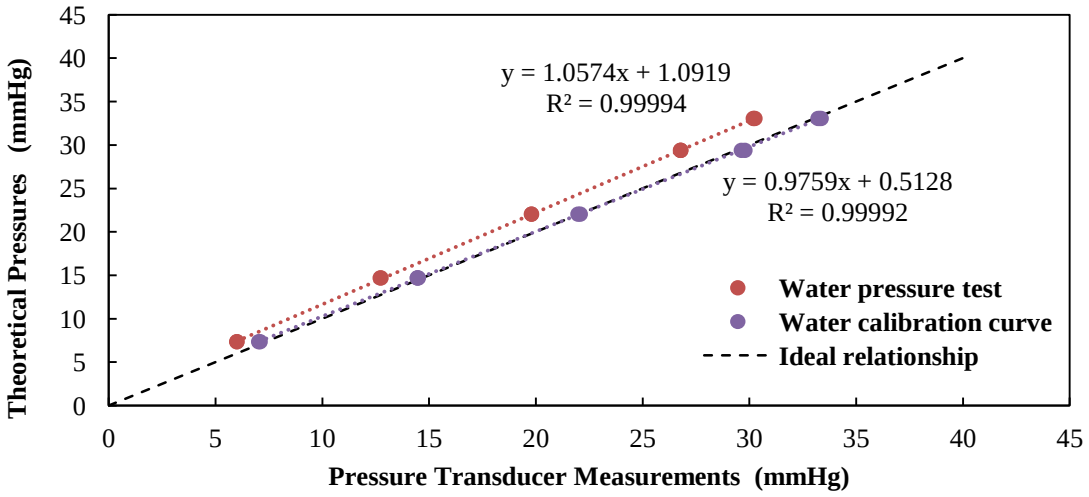


Figure C.1: Pressure measurements from the NIST calibrated pressure sensor graphed vs. the theoretical pressure [52]

A second series of hydrostatic tests were completed on a mannequin leg to mimic the test protocol. Two banks of sensors (eight sensors in total) were tested three times and plotted against the expected pressure as seen in Figure C.2 and Figure C.3. Since these two banks of sensors demonstrated good correlation and the previous individual hydrostatic tests led to the same conclusion, the remaining two

banks were not tested. After the completion of the hydrostatic tests, the pressure system was validated and it was established that the pressure sensor system was measuring the actual applied pressure to the sensor.

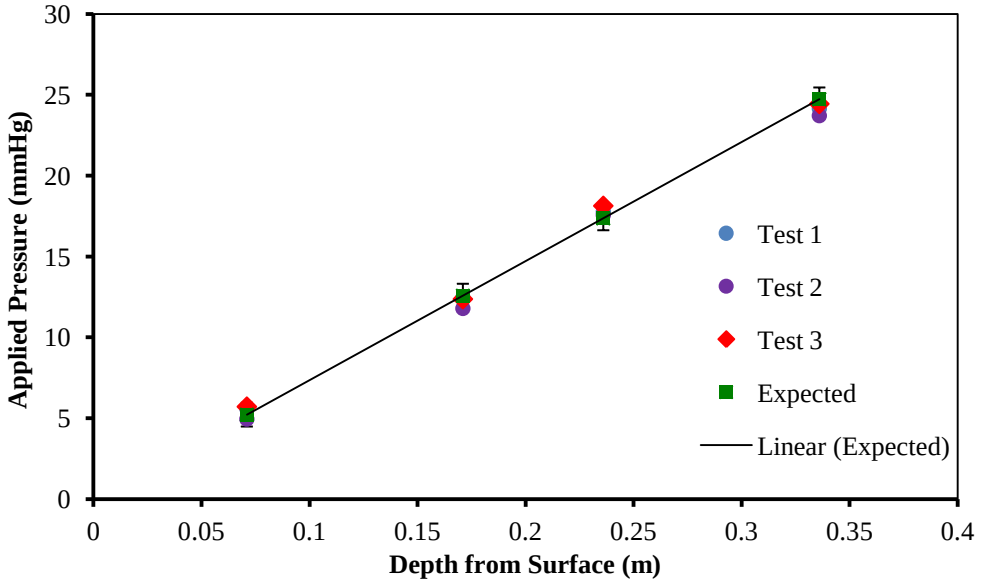


Figure C.2: Comparison of the hydrostatic test results for three tests completed on pressure sensor 9 to 12 compared to the expected pressure

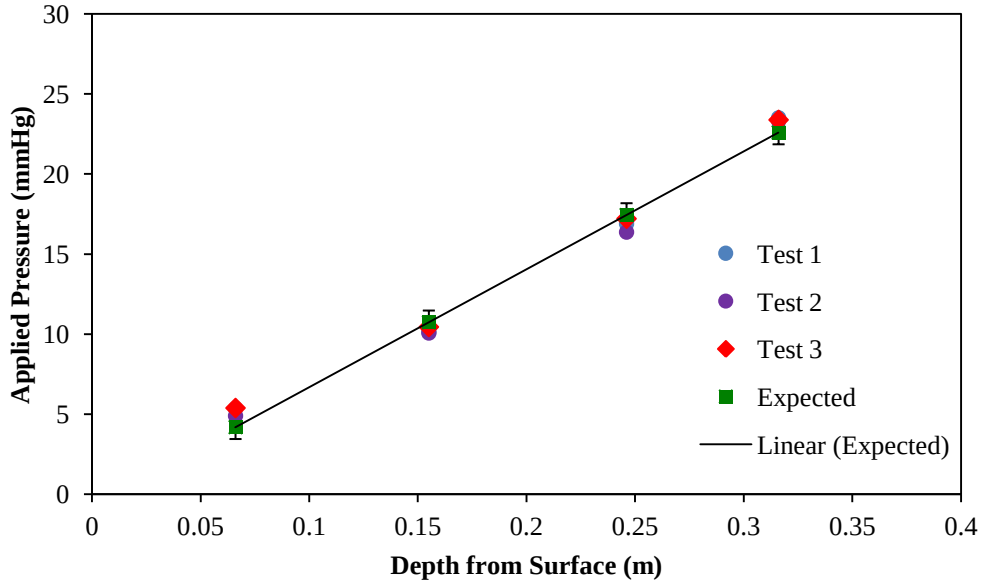


Figure C.3: Comparison of the hydrostatic test results for three tests completed on pressure sensor 13 to 16 compared to the expected pressure

Appendix D: Bland-Altman Plots for Central Variables

The following figures show the Bland-Altman plots for the remaining central variables. As stated in Chapter 3, the plots show good agreement within the 95% confidence levels contributing to the conclusion that the results were repeatable between days.

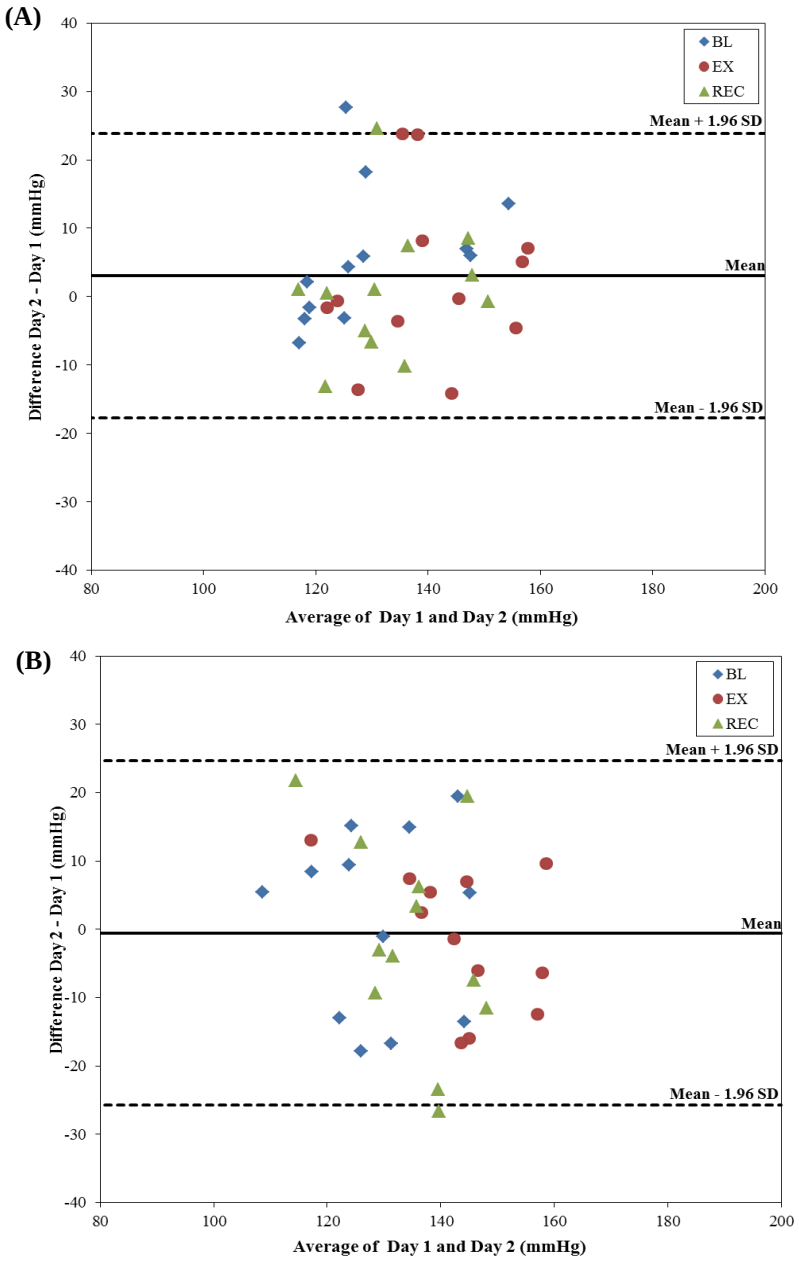


Figure D.1: Bland-Altman plots comparing SBP values for two days of testing for the BL, EX and REC conditions for (A) NGCS, and (B) GCS. The solid horizontal line indicates the mean of the data and the dashed horizontal lines represent the 95% confidence limits. The upper and lower limits are calculated from the mean ± 1.96 of the SD.

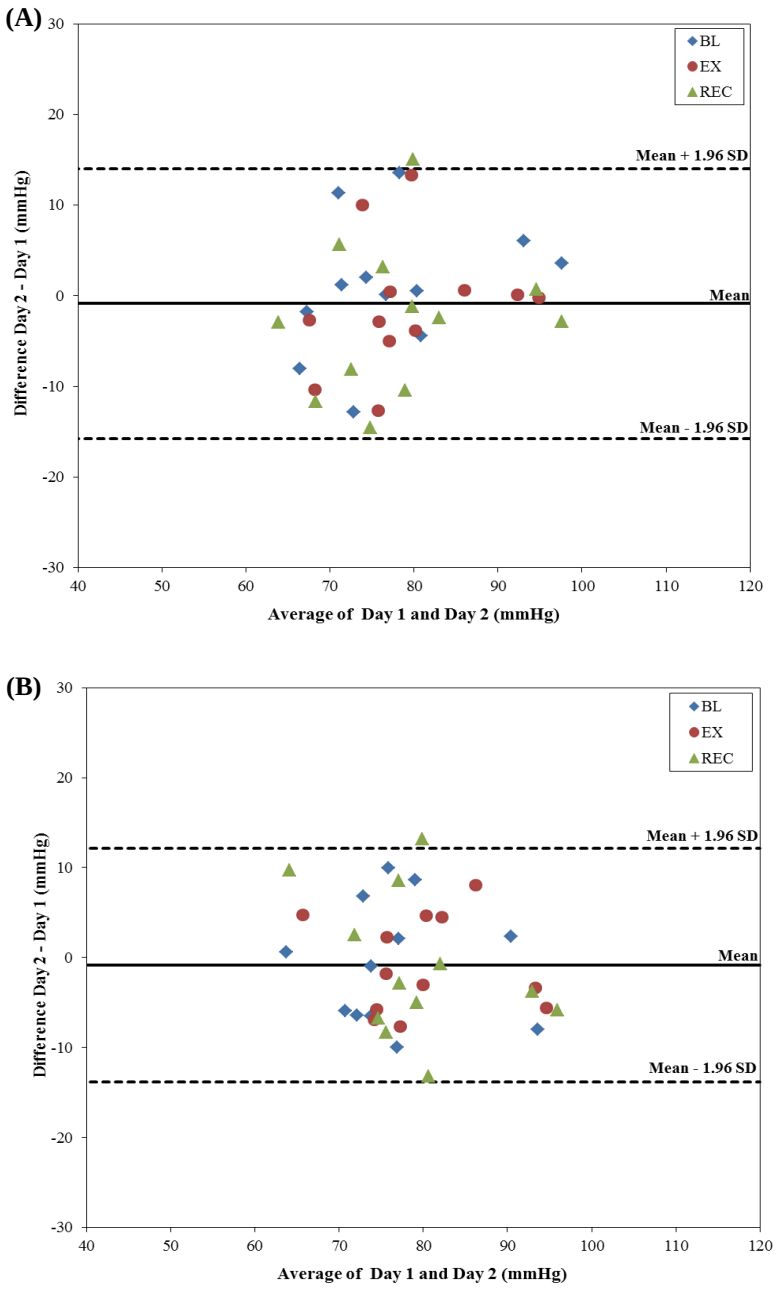


Figure D.2: Bland-Altman plots comparing DBP values for two days of testing for the BL, EX and REC conditions for (A) NGCS, and (B) GCS cases. The solid horizontal line indicates the mean of the data and the dashed horizontal lines represent the 95% confidence limits. The upper and lower limits are calculated from the mean ± 1.96 of the SD.

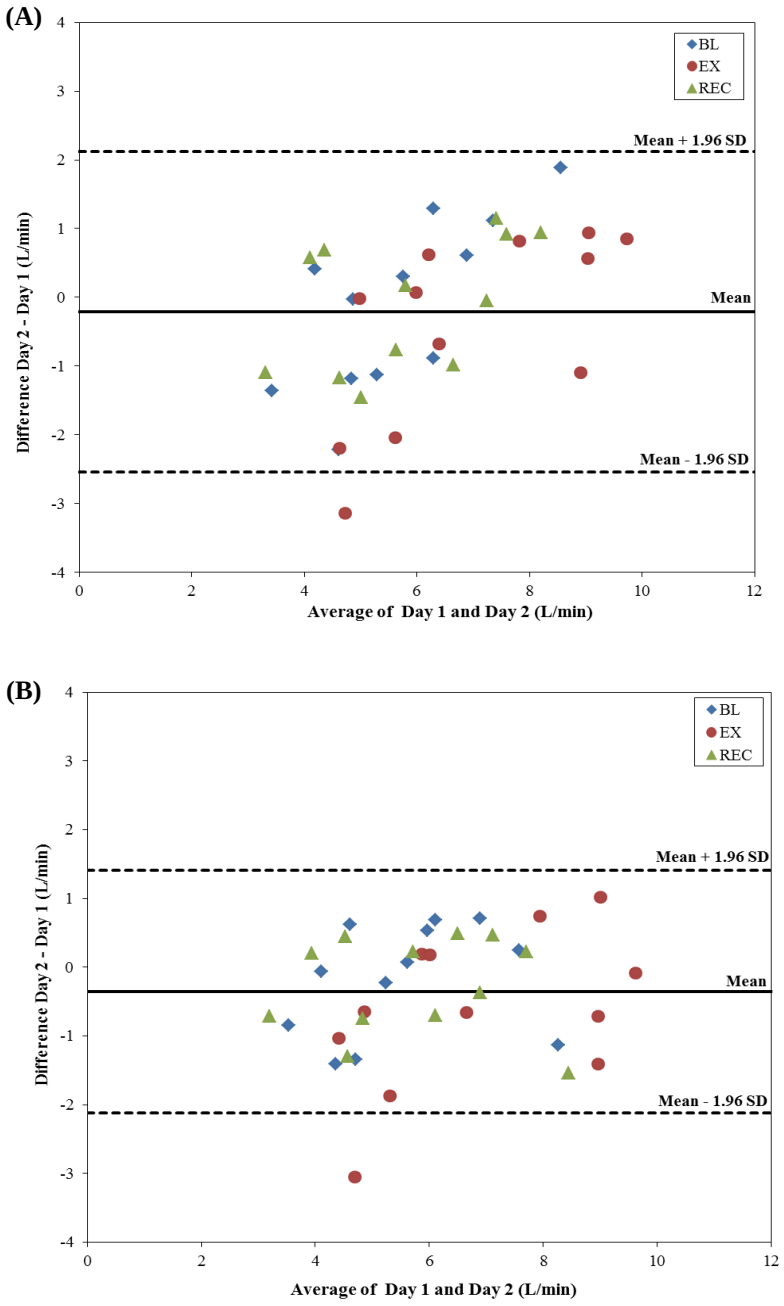


Figure D.3: Bland-Altman plots comparing CO values for two days of testing for the BL, EX and REC conditions for (A) NGCS, and (B) GCS cases. The solid horizontal line indicates the mean of the data and the dashed horizontal lines represent the 95% confidence limits. The upper and lower limits are calculated from the mean ± 1.96 of the SD.

Appendix E: Bland-Altman Plots for Peripheral Variables

The following figures show the Bland-Altman plots for the applied pressure and diameter measurements. As discussed in Chapter 3, the plots show good agreement within the 95% confidence levels leading to the conclusion that the results had good agreement between days.

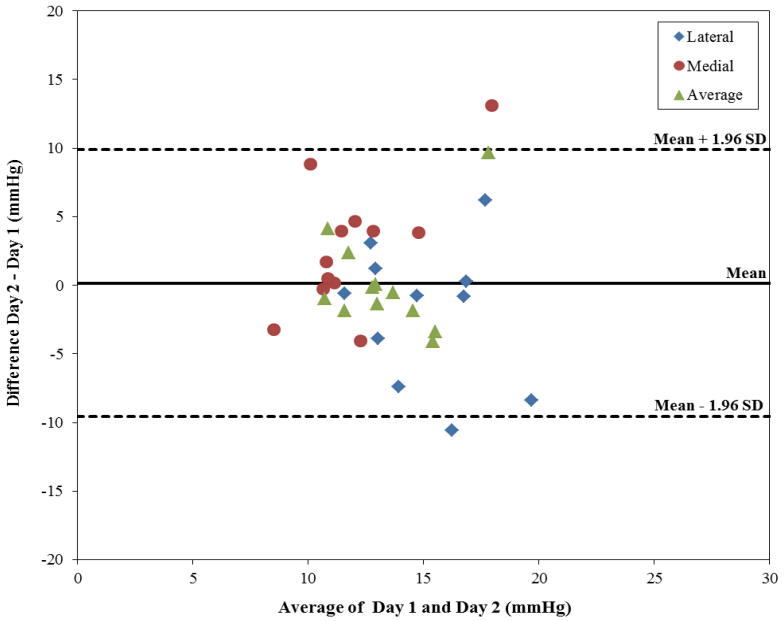


Figure E.1: Bland-Altman plot comparing the pressure difference, ΔP, for the two days of testing on the lateral and medial sides of the leg as well as the overall average pressure difference. The solid horizontal line indicates the mean of the data and the dashed horizontal lines represent the 95% confidence limits. The upper and lower limits are calculated from the mean ± 1.96 of the SD.

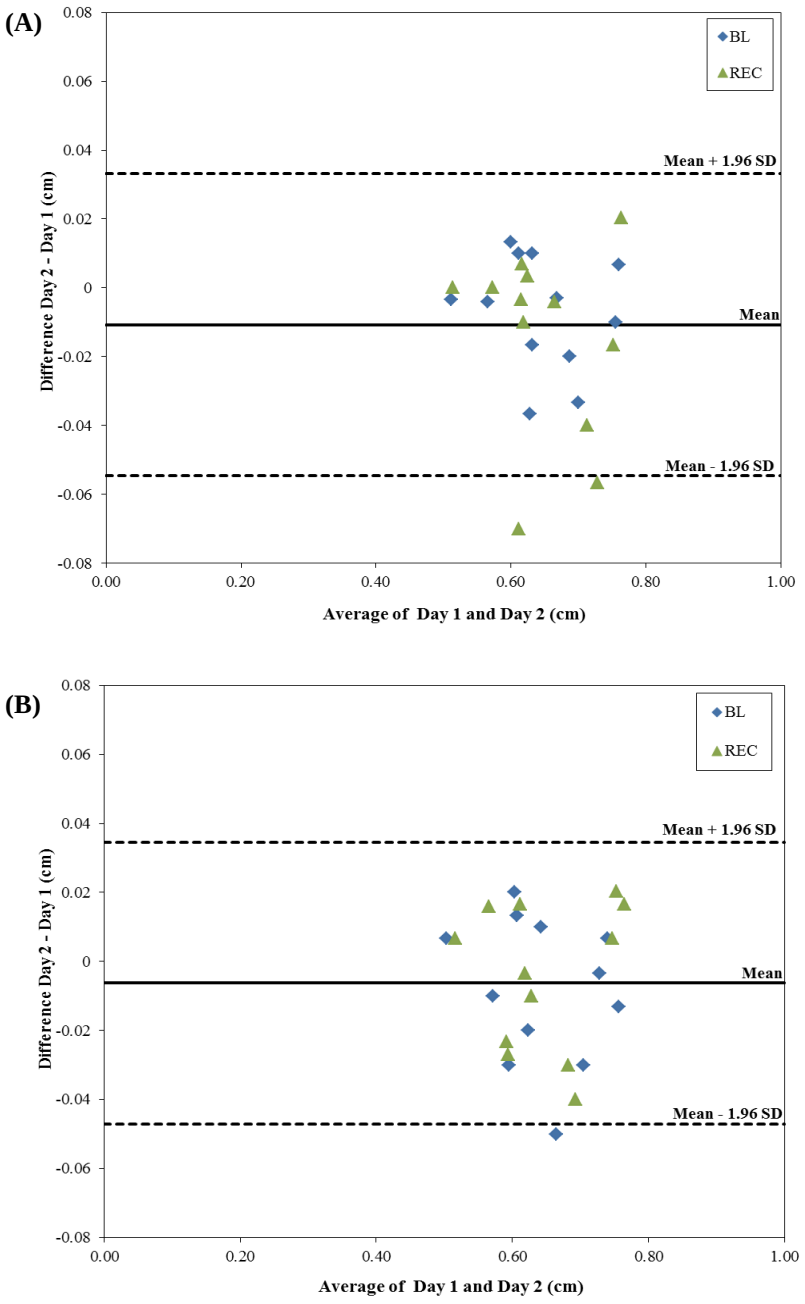


Figure E.2: Bland-Altman plots comparing the popliteal artery diameters (PAD) during BL and REC for two days of testing for (A) NGCS, and (B) GCS conditions. The solid horizontal line indicates the mean of the data and the dashed horizontal lines represent the 95% confidence limits. The upper and lower limits are calculated from the mean ± 1.96 of the SD.

Appendix F: Central Variables NGCS and GCS Comparison Graphs

The following figures illustrate the comparison of the values obtained during the NGCS and GCS tests for HR, SBP, DBP, and CO. Figures D.1 to D.8 show the comparisons for the baseline and recovery conditions for day 1, while Figures D.9 to D.20 show the results for all conditions for day 2. For all graphs, red indicates an increase in the variable during the GCS condition, and black indicates a decrease in the variable when the sock is worn. Table D.1 shows the obtained values for MAP, MPP, SV, and TPR for day 2 of testing. As discussed in Chapter 3, no significant differences were found between conditions for the central variables.

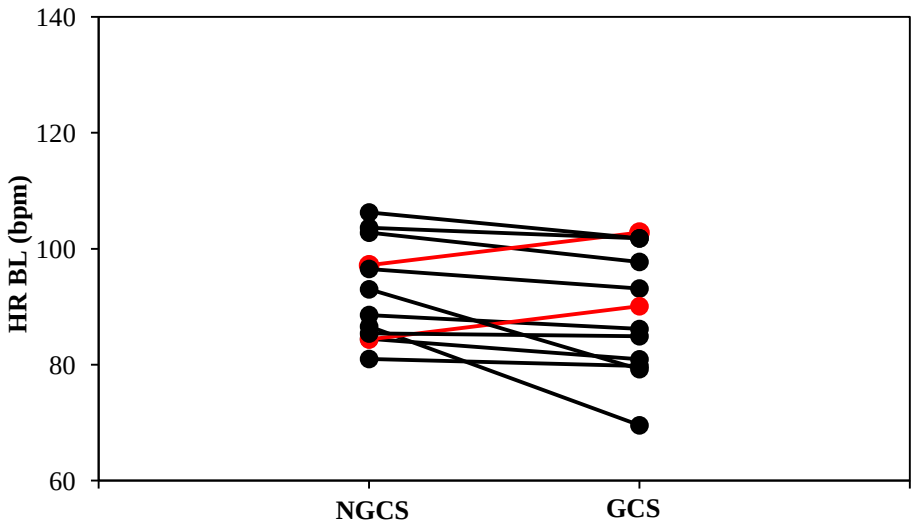


Figure F.1: Comparison of HR with and without GCS during baseline for all subjects on day 1(red: increase during the GCS condition, black: decrease during the GCS condition)

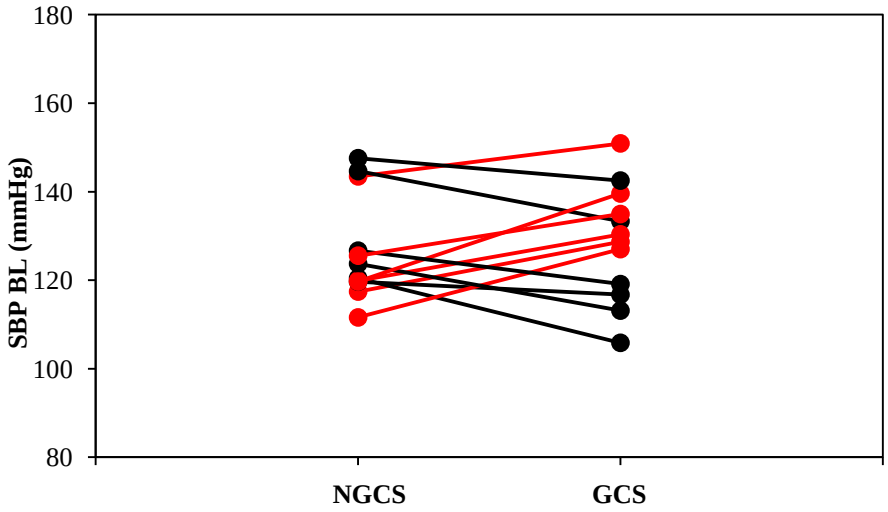


Figure F.2: Comparison of SBP with and without GCS during baseline for all subjects on day 1(red: increase during the GCS condition, black: decrease during the GCS condition)

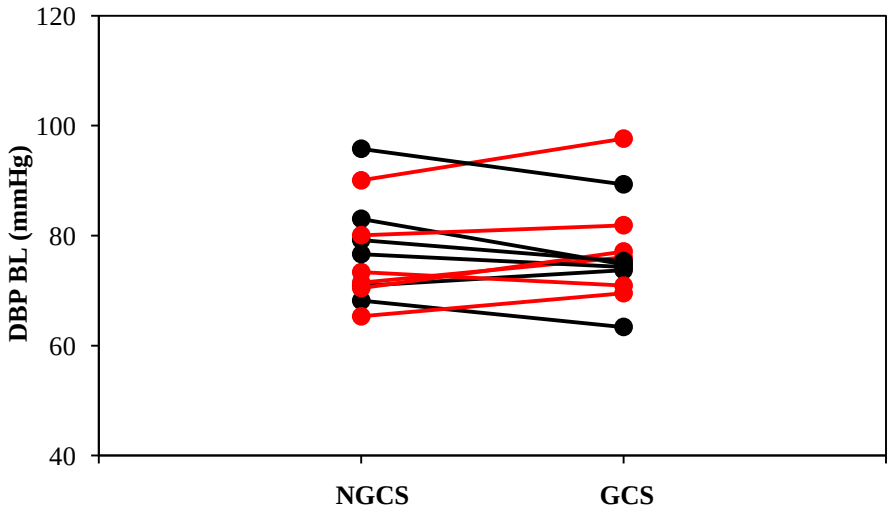


Figure F.3: Comparison of DBP with and without GCS during baseline for all subjects on day 1(red: increase during the GCS condition, black: decrease during the GCS condition)

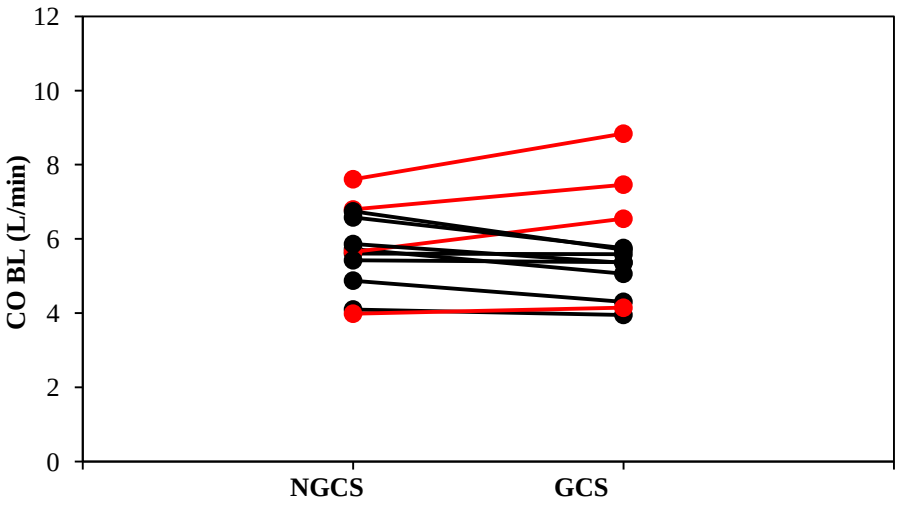


Figure F.4: Comparison of CO with and without GCS during baseline for all subjects on day 1(red: increase during the GCS condition, black: decrease during the GCS condition)

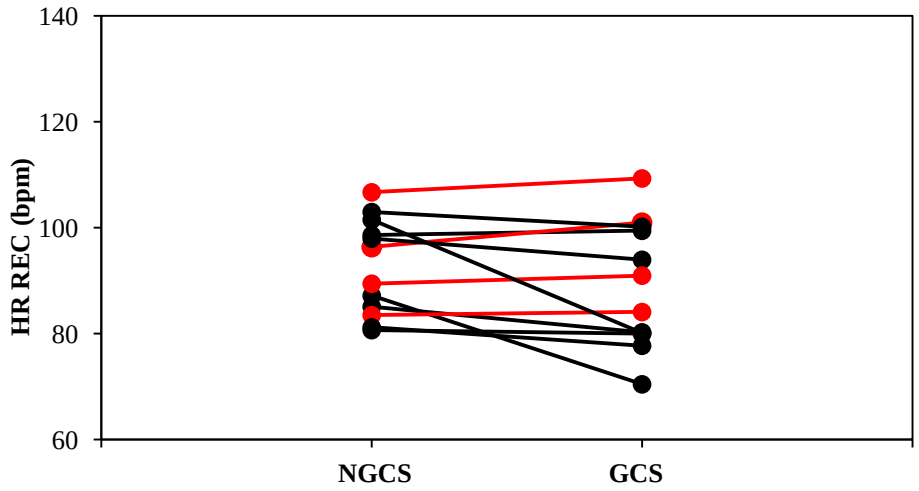


Figure F.5: Comparison of HR with and without GCS during recovery for all subjects on day 1(red: increase during the GCS condition, black: decrease during the GCS condition)

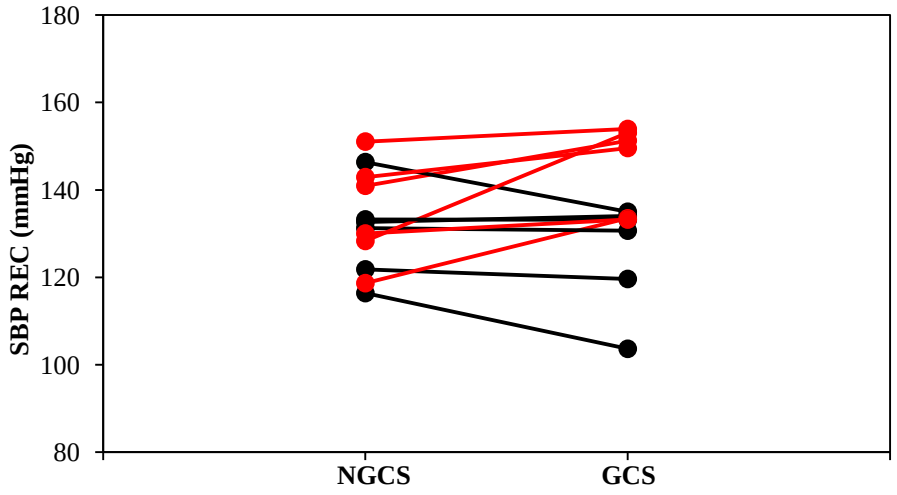


Figure F.6: Comparison of SBP with and without GCS during recovery for all subjects on day 1(red: increase during the GCS condition, black: decrease during the GCS condition)

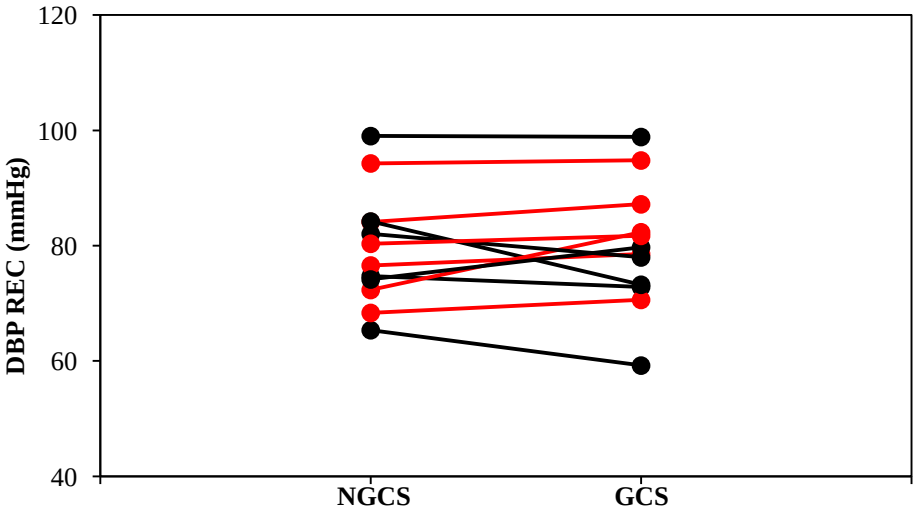


Figure F.7: Comparison of DBP with and without GCS during recovery for all subjects on day 1(red: increase during the GCS condition, black: decrease during the GCS condition)

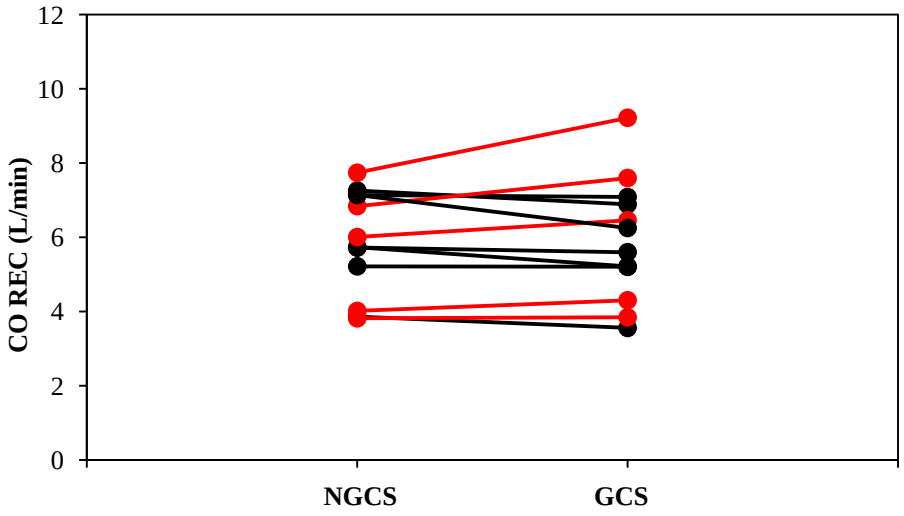


Figure F.8: Comparison of CO with and without GCS during recovery for all subjects on day 1(red: increase during the GCS condition, black: decrease during the GCS condition)

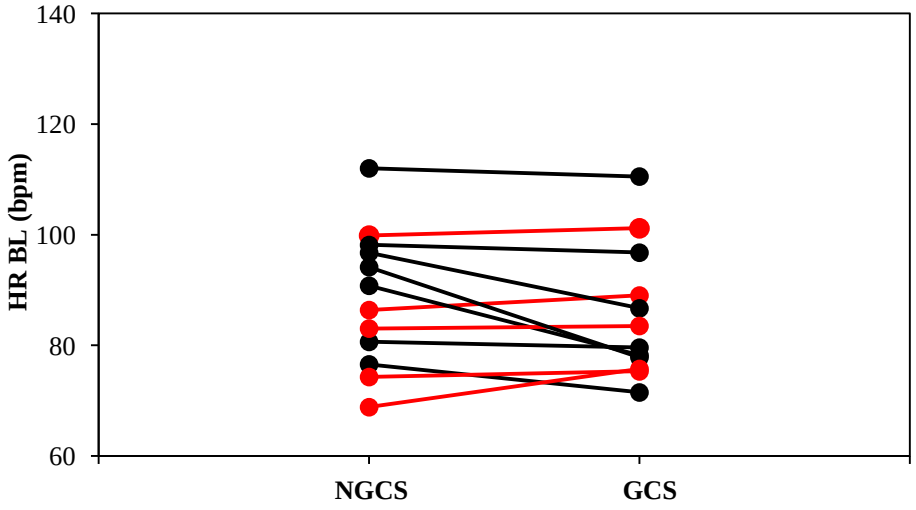


Figure F.9: Comparison of HR with and without GCS during baseline for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

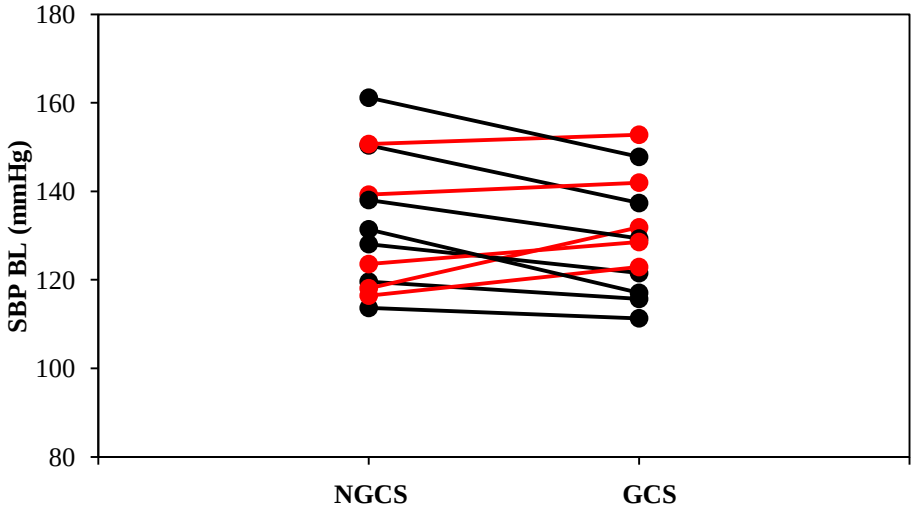


Figure F.10: Comparison of SBP with and without GCS during baseline for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

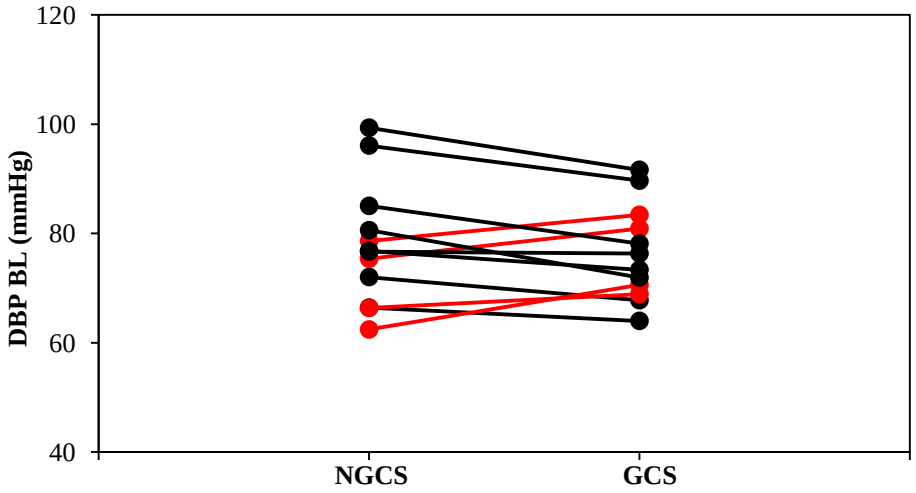


Figure F.11: Comparison of DBP with and without GCS during baseline for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

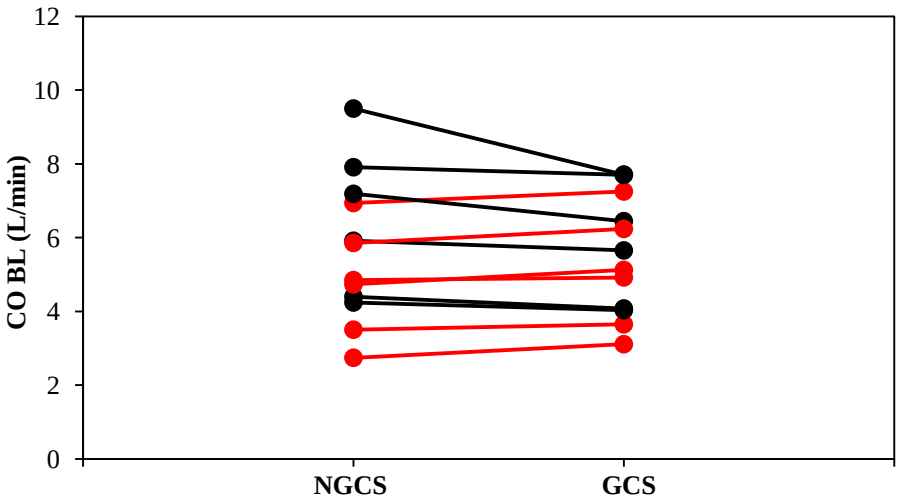


Figure F.12: Comparison of CO with and without GCS during baseline for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

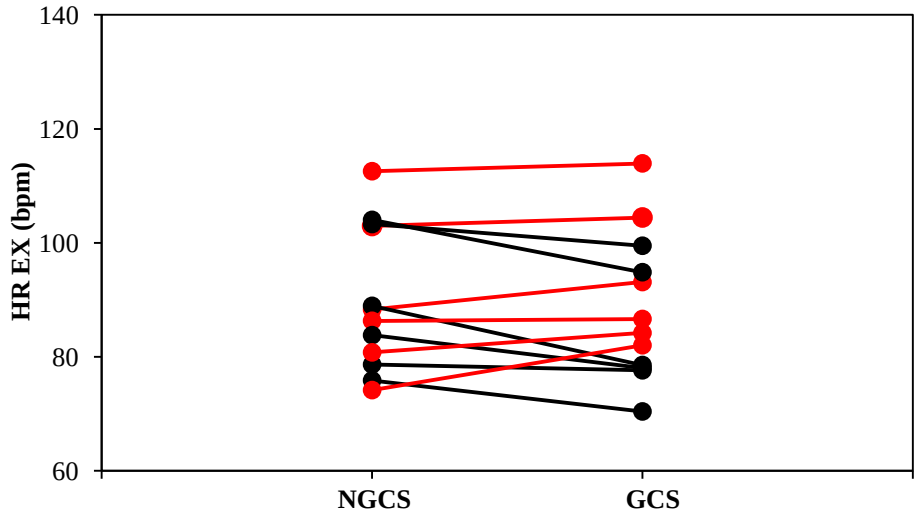


Figure F.13: Comparison of HR with and without GCS during exercise for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

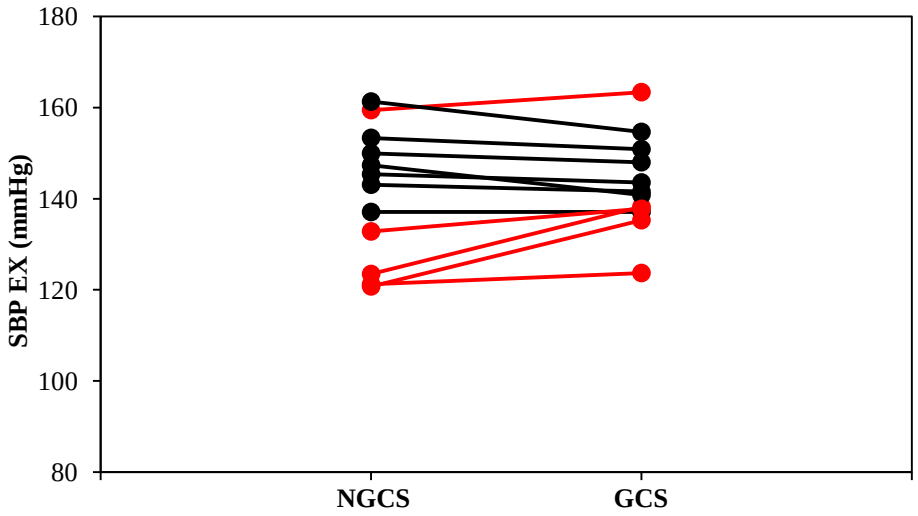


Figure F.14: Comparison of SBP with and without GCS during exercise for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

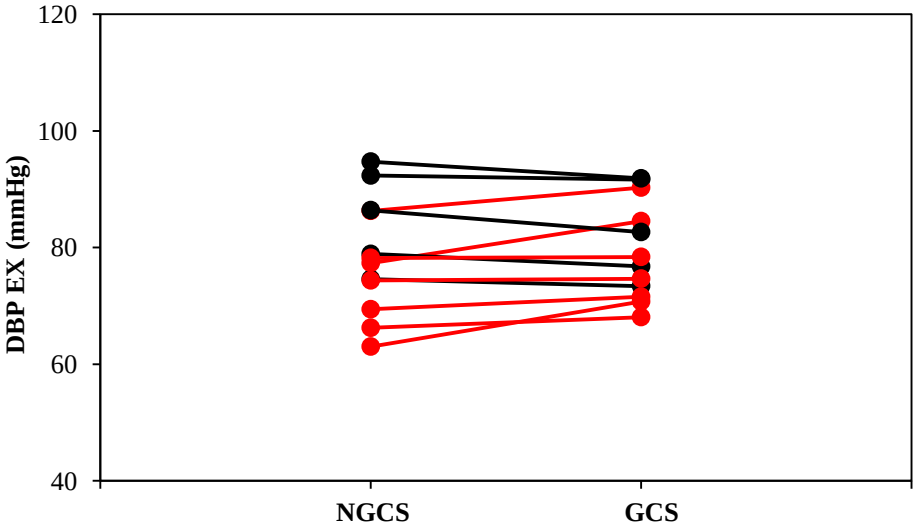


Figure F.15: Comparison of DBP with and without GCS during exercise for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

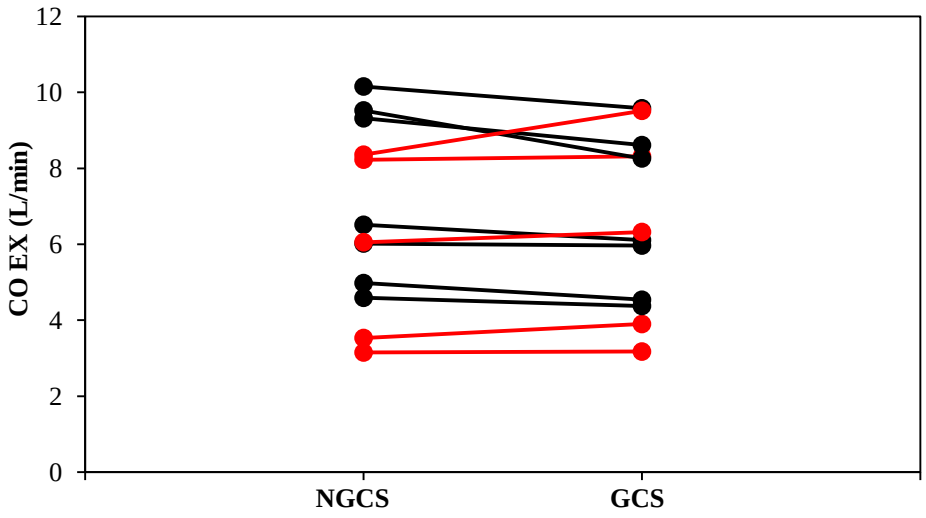


Figure F.16: Comparison of CO with and without GCS during exercise for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

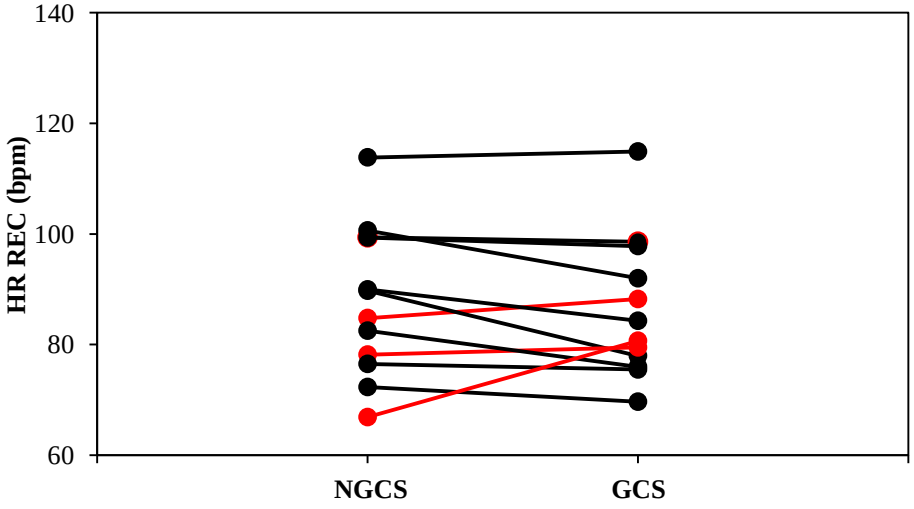


Figure F.17: Comparison of HR with and without GCS during recovery for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

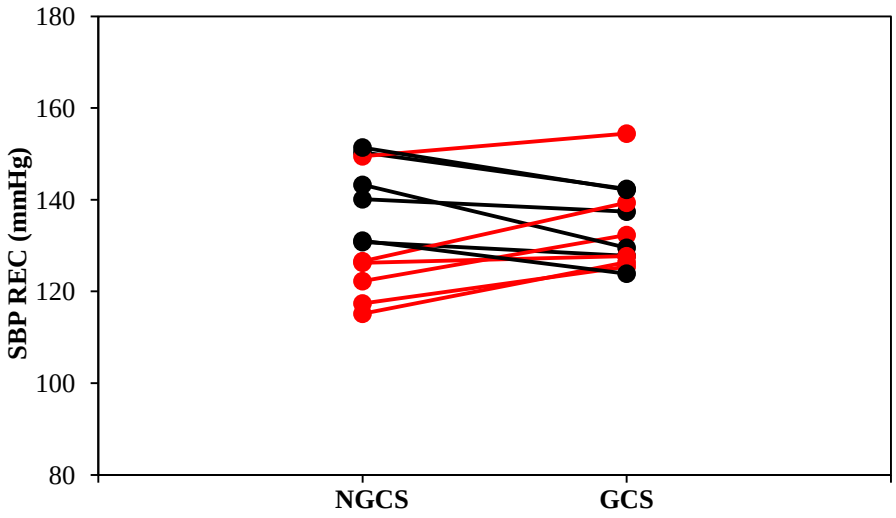


Figure F.18: Comparison of SBP with and without GCS during recovery for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

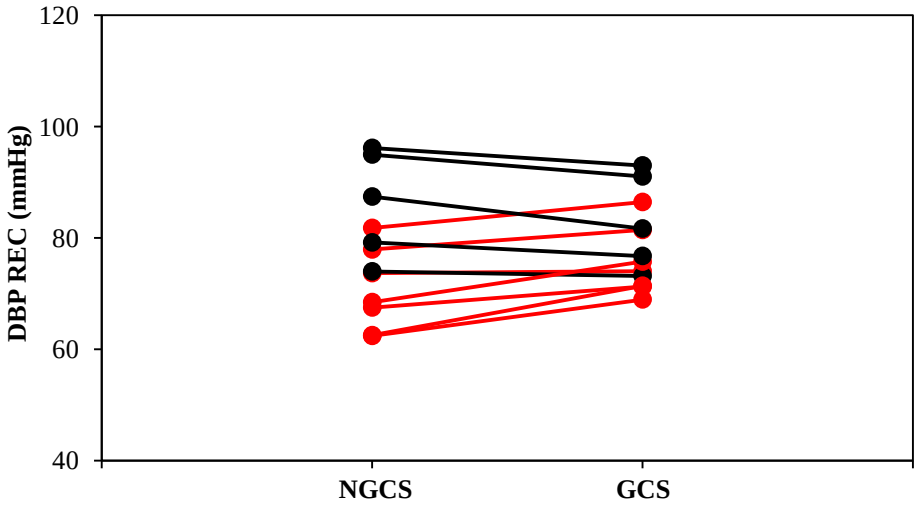


Figure F.19: Comparison of DBP with and without GCS during recovery for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

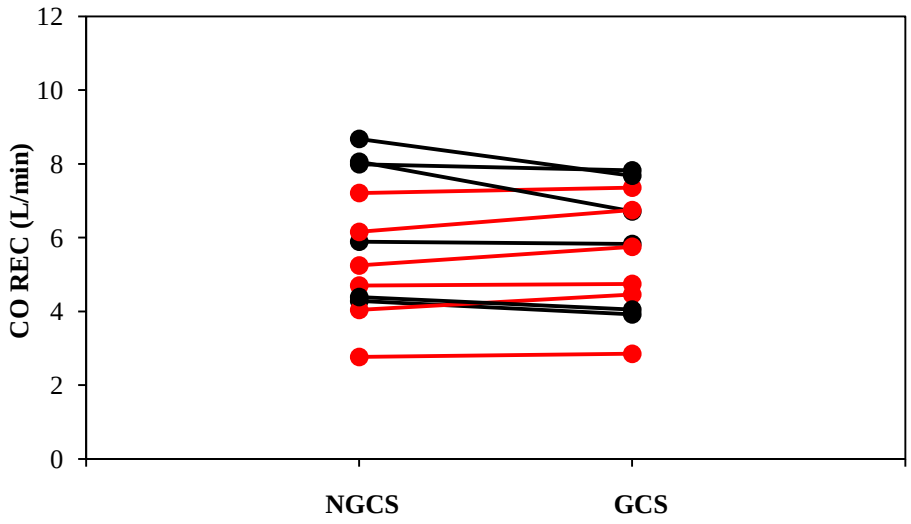


Figure F.20: Comparison of CO with and without GCS during recovery for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

Table F.1: Calculated mean and SD values for the study population on day 2 for MAP, MPP, SV, and TPR

		Condition					
		BL		EX		REC	
Variable		**NGCS**	**GCS**	**NGCS**	**GCS**	**NGCS**	**GCS**
MAP	**Mean**	96.16	94.20	99.42	100.67	95.99	97.17
	SD	12.26	9.69	11.01	8.69	11.58	7.64
MPP	**Mean**	164.24	162.28	167.49	168.74	164.06	165.25
	SD	15.81	13.35	14.86	12.73	14.67	11.17
SV	**Mean**	64.47	65.49	75.57	75.59	67.11	66.93
	SD	21.41	20.55	27.97	28.36	22.77	21.00
TPR	**Mean**	18.71	18.30	16.82	17.19	18.31	18.63
	SD	6.03	4.62	7.06	6.35	6.63	5.84

Appendix G: Day 2 Graphs for PBV_{mean} and PBF_{mean}

The following figures illustrate the comparison of the PBV_{mean} and PBF_{mean} values obtained during the NGCS and GCS tests for BL, EX, and REC conditions for day 2 of testing. For all graphs, red indicates an increase in the variable during the GCS condition, and black indicates a decrease in the variable when the sock is worn. As discussed in Chapter 3, no significant differences were found between conditions for either variable.

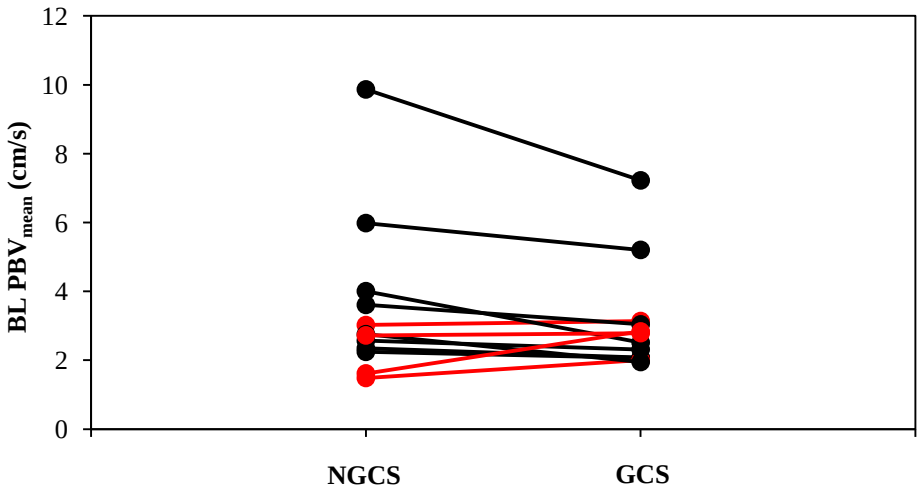


Figure G.1: Comparison of PBV_{mean} with and without GCS during baseline for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

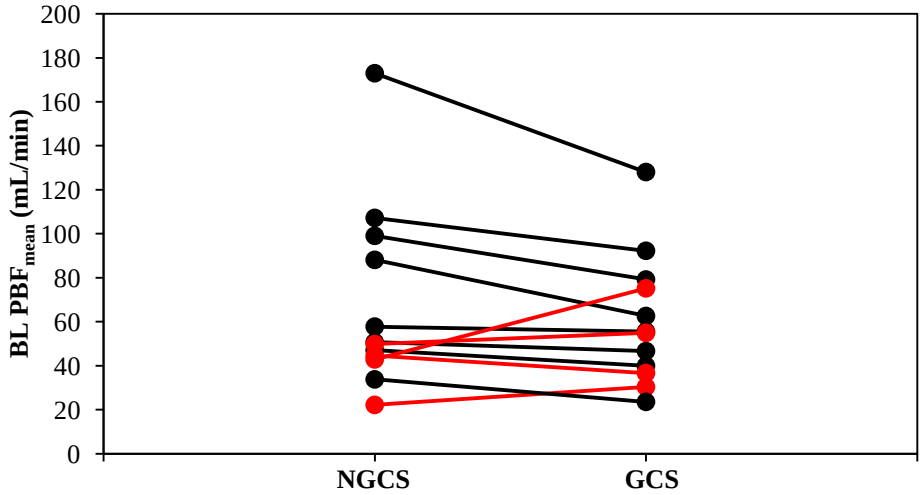


Figure G.2: Comparison of PBF_{mean} with and without GCS during baseline for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

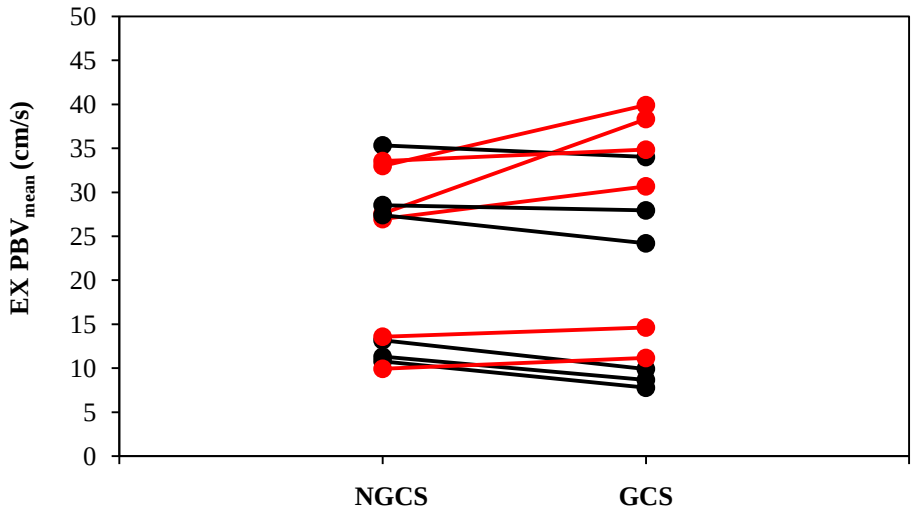


Figure G.3: Comparison of PBV_{mean} with and without GCS during exercise for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

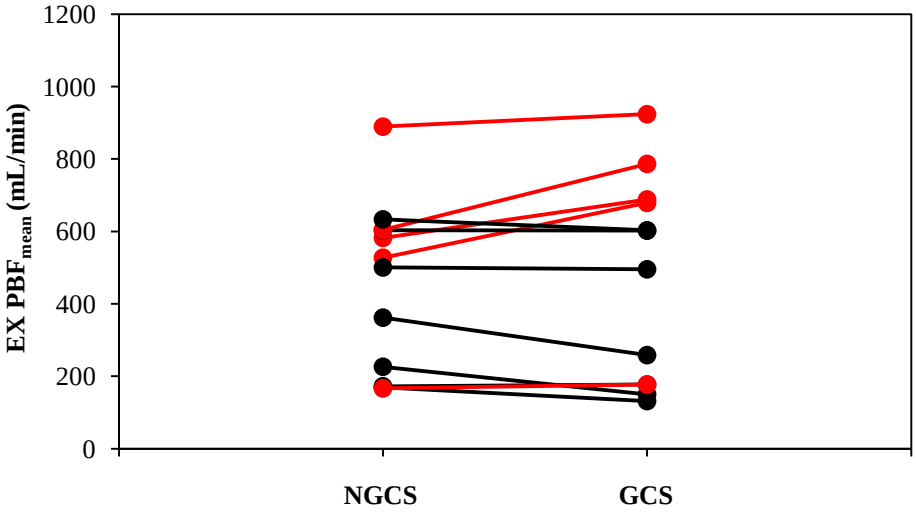


Figure G.4: Comparison of PBF_{mean} with and without GCS during exercise for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

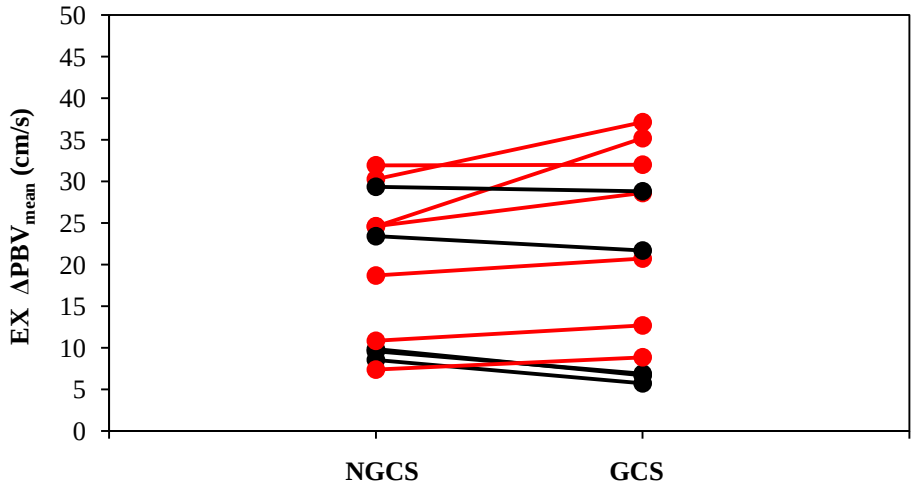


Figure G.5: Comparison of the change relative to BL values during EX in PBV_{mean} with and without GCS for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

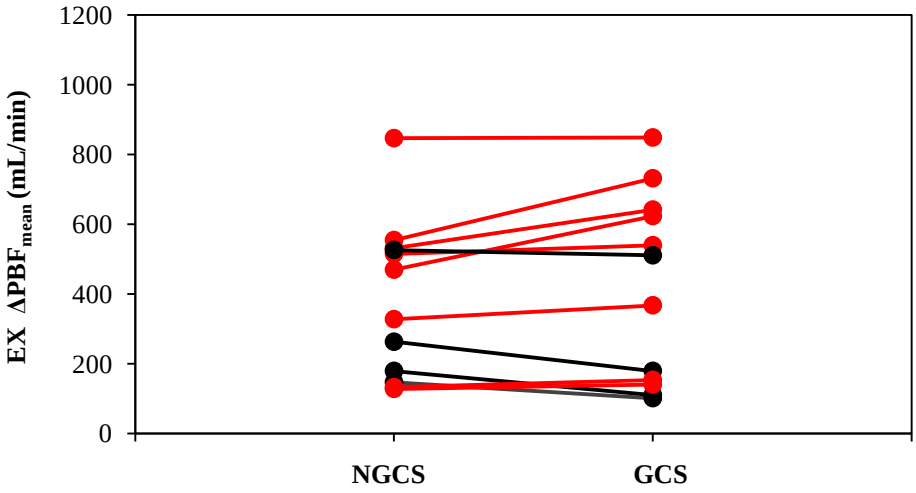


Figure G.6: Comparison of the change relative to BL values during EX in PBF_{mean} with and without GCS for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

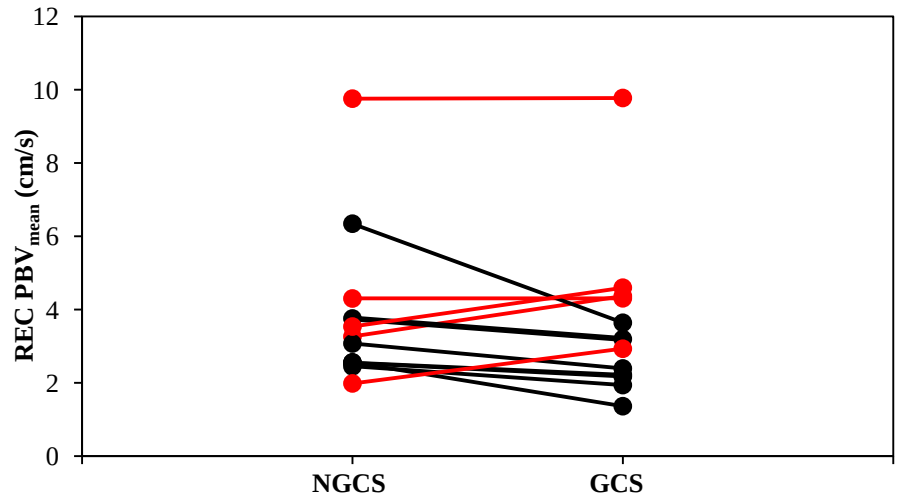


Figure G.7: Comparison of PBV_{mean} with and without GCS during recovery for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)

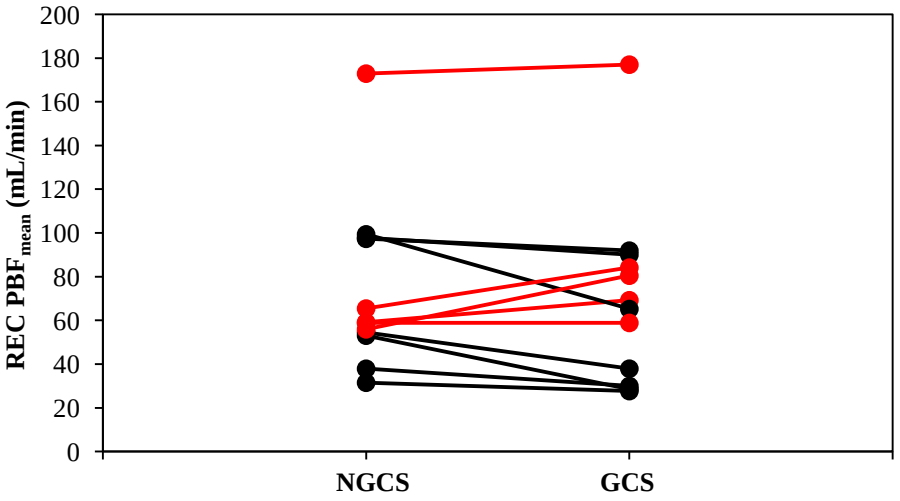


Figure G.8: Comparison of PBF_{mean} with and without GCS during recovery for all subjects on day 2 (red: increase during the GCS condition, black: decrease during the GCS condition)