

The Effect of Resistance Training on Vascular Function in Older Adults

by

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ABSTRACT

INTRODUCTION: This study examined the effect of resistance training on exercise induced hyperemia in the brachial and popliteal arteries in order to evaluate this exercise modality as a method to improve endothelial function post-exercise and rest. Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality in developed countries. What is less appreciated, perhaps, is that the great majority of CVD is associated with alterations to the arterial system. The effect of aging on CVD is illustrated simply, but powerfully, by the observation that the risk of CVD increases progressively with age. Given the current and projected increases in the number of older adults in North America, we face the possibility of a ‘new wave’ of CVD in the near future and an associated increase in healthcare burden. Determining how arteries change with respect to age and increased risk of CVD, the mechanisms by which these alterations are mediated, integrated with strategies for the prevention and treatment of arterial aging are, therefore, among our highest biomedical priorities. **METHODS:** Subjects were recruited to participate in a six-week resistance training program, 3x/wk. The conventional resistance training group used a duty cycle of one second concentric, and one second eccentric. The slow eccentric contraction group will use a duty cycle of one second concentric, and five seconds eccentric. Vascular function was evaluated by a series of isometric and isotonic tests, using Laser Doppler ultrasonography. **RESULTS:** Resistance training revealed decreases in resting pulsatility index and systolic peak blood pressure; however, it did not matter which group each participant was assigned, as there was no main effect differences between groups. **CONCLUSION:** Resistance training is proposed as a safe and useful exercise method for muscular hypertrophy and strength gain, but also for increasing peripheral blood flow and vascular conductance as an additional effect. Expanding this research to cover investigation in patient groups is recommended for future consideration.

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List of Symbols, Nomenclature or Abbreviations

±	Plus/Minus
1RM	One Repetition Maximum
6MWT	Six Minute Walk Test
ABI	Ankle Brachial Index
AE	Aerobic Exercise
ATP	Adenosine Triphosphate
BMI	Body Mass Index
CSEP	Canadian Society for Exercise Physiology
CRT	Conventional Resistance Training Group
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
EMG	Electromyography
eNOS	Endothelial Nitric Oxide Synthase
HbA1c	Glycosylated Hemoglobin
HDL	High Density Lipoprotein
K+	Potassium
LDL	Low Density Lipoprotein
MAP	Mean Arterial Pressure
MVC	Maximum Voluntary Contraction
NO	Nitric Oxide
PAR MED-X	Physical Activity Readiness Medical Questionnaire
PAR-Q	Physical Activity Readiness Questionnaire

PI	Pulsatility Index
PT	Post-Training
PVP	Pulse Velocity Profiles
RHR	Resting Heart Rate
RT	Resistance Training
SBP	Systolic Blood Pressure
SEC	Slow Eccentric Contraction Group
VSM	Vascular Smooth Muscle
VC	Vasodilatory Capacity
WIQ	Walking Impairment Questionnaire

Introduction

1.1 Introduction. Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality in developed countries (Lloyd-Jones et al., 2010). What is less appreciated, perhaps, is that the great majority of CVD is associated with alterations to the arterial system (Lloyd-Jones et al., 2010). The effect of aging on CVD is illustrated simply, but powerfully, by the observation that the risk of CVD increases progressively with age (Lloyd-Jones et al., 2010). Given the current and projected increases in the number of older adults in North America, we face the possibility of a ‘new wave’ of CVD in the near future and an associated increase in healthcare burden (Seals, Jablonski, Donato, 2011). As such, establishing a better understanding of the relationship between arterial aging and CVD represents one of our most important clinical challenges. Determining how arteries change with age to increase our risk of CVD, the mechanisms by which these changes are mediated and strategies for the prevention and treatment of arterial aging are, therefore, among our highest biomedical priorities (Seals, Jablonski, Donato, 2011).

Aging is a well-documented cardiovascular risk factor. One of the possible physiological mechanisms through which increasing age may lead to cardiovascular disease is the promotion of endothelial dysfunction (Taddei et al., 2000). The endothelium plays a primary role in the modulation of vascular tone and structure through production of the relaxing factor nitric oxide (NO), which acts by protecting the vessel wall from the development of atherosclerosis and thrombosis. Endothelial dysfunction is characterized by a reduction of the bioavailability of multiple vasodilators, primarily NO. The resulting imbalance leads to an impairment of endothelium-dependent vasodilation, which is the

functional characteristic of endothelial dysfunction (Deanfield et al., 2005). In addition to impaired endothelium-dependent vasodilation, endothelial dysfunction also comprises a specific state of endothelial activation, which is characterized by a proinflammatory, proliferative, and procoagulatory states that favour all stages of atherogenesis (Hadi, Carr, Suwaidi, 2005). The basic mechanisms involved in the establishment of atherosclerosis can significantly reduce the physical size of the arterial lumen which can lead to a further reduction in the synthesis and uptake of NO (Taddei et al., 2000) as well as an increase in blood pressure and a decrease in blood flow (Hadi, Carr, Suwaidi, 2005).

The endothelium is situated between the blood and the tissue of the vascular wall and acts as a protective barrier as it possesses anticoagulatory properties in addition to the regulation of vascular tone and homeostasis (Brandes, Fleming, Busse, 2005). NO is recognized as the primary vasodilatory component of the blood vessels but is also a vital component in a number of other associated factors, most notably its anti-atherosclerotic effects. Endothelial function is usually clinically assessed by determining changes in blood flow or arterial diameter in response to endothelial stimulation, which are estimates of vascular NO bio-availability. Several clinical studies have shown that endothelium-dependent vasodilation progressively declines with age, resulting in an increased arterial stiffness as well as a decrease in blood flow regulation (Singh, Prasad, Singer, MacAllister, 2002).

Endothelial dysfunction represents a common feature and is a strong predictor of cardiovascular disease (Di Francescomarino et al., 2009). Cardiovascular risk factors modify endothelial vasoactive substances such as the prostaglandins and endothelin-1, and activate a number of pro-oxidant processes that reduce the bioavailability of NO (Di

Francescomarino et al., 2009). This leads to a transition from normal endothelial function to endothelial dysfunction. There is a considerable amount of experimental and clinical data indicating that endothelial dysfunction is involved not only in multiple disease states such as atherosclerosis, hypertension, heart failure and diabetes mellitus, but also in the continual physiological process of aging (Franzoni et al., 2004). Aging is one of the most well established risk factors for cardiovascular disease. Even to disregard the implications associated with CVD and aging there is still evidence suggesting that aging is associated with endothelial dysfunction and reduced arterial elasticity. In addition, reduced arterial elasticity parallels changes in impaired endothelium-dependent vasodilation (Hadi, Carr, Suwaidi, 2005). Among aging, other conditions that negatively affect endothelial function include diabetes mellitus, hypertension, hypercholesterolemia, obesity, as well as peripheral arterial disease (Franzoni et al., 2004). Many of these conditions overlap causing a synergistic effect on risk factors associated with CVD (Green et al., 2004).

A build-up of atherosclerotic plaque in the arteries results in decreased blood flow through the effected arteries as well as reducing perfusion of the cerebral, coronary, upper and lower extremities (Knowles et al., 2007). The physical blockage caused by atherosclerotic plaque also results in a reduction in the release and uptake of epithelial NO, decreasing the endothelium-dependent vasodilatory response, increasing systolic and diastolic blood pressure. This increase in blood pressure has a strong and direct association with cardiovascular mortality (Lewington et al., 2002) and is a major risk factor for the development of diseases such as coronary failure, heart failure, and cerebrovascular events (Braith & Stewart, 2006).

Atherosclerosis is the most common underlying etiology affecting endothelial function (National Heart, Lung and Blood Institute, 2011). CVD is easily the leading cause of death globally and is responsible for an estimated 17.3 million deaths in 2008 (World Health Organization, 2013), and is expected to reach 30.3 million globally by 2030 (World Health Organization, 2013). The prevalence of CVD in the general population is 16.9 percent (Diehm et al., 2004). In high risk groups; such as subjects over the age of 50 years, subjects with high blood pressure, or hypercholesterolemia (Shammas, 2007), as well as those with a family history of diabetes or peripheral artery disease (PAD); the risk of developing a CVD related condition is greater than 29 percent (Knowles et al., 2007).

The traditional frontline treatment for CVD is walking based aerobic exercise (AE), which has been prescribed as a form of low intensity physical exercise to reduce symptoms, improve autonomic regulation, build strength, and increase walking endurance. Walking activates the muscles of the lower limb and the muscle contractions stimulate vasodilation (Milani & Lavie, 2007). The increase in blood flow (active hyperemia) results from the complex interaction of local signaling at the vascular smooth muscle (Barclay et. al., 2001). Some of the signaling results from metabolic vasodilation and some results from changes in flow and shear stress within the vessel as the altering contraction/relaxation cycles produce an increase in blood flow (reactive hyperemia). Thus, walking targets the physiologic problem that needs to adapt (specificity), and if performed to the patients' capacity should overload vasodilatory function to stimulate progressive improvement in vasodilatory capacity (VC).

Progressive physiological adaptation is achieved by (1) specific activation of the targeted system or process (specificity principle) and (2) repeated overload of the targeted

system (overload principle) (Pearson et al., 2000). For example, in individuals that have significant vascular resistance measured at the lower limb, this would be the target area. That area would then be overloaded to cause an increase in the muscular activity and muscular response and thus an increase in blood flow to that region. In the case of an individual with diabetes or PAD, conditions which have been shown to demonstrate endothelial dysfunction with resulting reduced blood flow to the lower extremities, physiological adaptation can be achieved by: targeting the gastrocnemius muscles of the lower limb by performing a specific exercise such as calf raise and then overloading that area. This activation of the lower limb near the individuals' maximum capacity would provide an overloading stimulus which would then promote physiologic adaptation of the lower limb.

Until recently, resistance exercise prescription was contraindicated for individuals with cardiovascular diseases, as resistance exercise has been shown to promote high pressures and overload on the heart during high intensity isotonic loading (Braith & Stewart, 2006). Limited research has been conducted on the effects of resistance training (RT), independent of aerobic exercise and the relationship on endothelial function. Ideally, if RT could deliver comparable results to AE, especially with targeted endothelial cell health and lower intensity loading, then this method of RT could be incorporated into regular cardiovascular rehabilitation.

RT is used as an alternative therapy for patients with CVD with the goal of increasing strength or muscle size to combat muscular atrophy caused by disuse. This has been shown to indirectly increase resistance to fatigue (McGuigan et al., 2001; McDermott et al., 2007; McDermott et al., 2008). Theoretically, RT should be able to provide

occlusion/reperfusion stimuli to maximally overload the vasodilatory response in specific muscles of interest. With RT, one can vary the activity to alter both occlusion and reperfusion time in a combination that stimulates sustained hyperemia.

Recent evidence indicates that physical exercise can improve endothelium-dependent vasodilation in healthy humans (Clarkson et al., 1999) and especially in the elderly to improve or reverse some of the age related performance characteristics such as a marked decrease in muscle mass, strength, and power (Quiroz, Kanegusuku, Forjaz, 2009). In addition to muscle alterations, aging also causes alterations in cardiovascular function such as decreased arterial compliance (Chetlin, 2003) which leads to an increase in arterial stiffening, as well as progressive increases in blood pressure (Ferrari, Radaelli, Centola, 2003; Taddei et al., 2000). Thus, this study examines the effect of resistance exercise on reactive hyperemia in the upper and lower limbs in order to evaluate the potential of using this exercise modality to improve peripheral blood flow. The specific hypothesis tested is that RT incorporating the use of moderate concentric and slow eccentric contraction tempo will increase arterial occlusion time, improving resting and post exercise pulsatility index to a greater extent than a conventional RT protocol which utilizes a moderate concentric, moderate eccentric contraction tempo.

Literature Review

2.1 Risk factors associated with CVD. With advancing age, there is increased risk of developing CVD due to a decrease in vascular conductance (especially after reaching 50 years of age) and basal limb blood flow (Tanimoto et al., 2009; Anton et al., 2006).

Atherosclerosis is the number one cause and predictor of CVD. Well defined atherosclerotic risk factors include aging, obesity, tobacco use, diabetes mellitus, hypertension, hypercholesterolemia, as well as a family history of CVD (primarily heart disease and/or stroke) (Milani & Lavie, 2007). An ensuing characteristic of the disease is the affect it has on the structure and function of the aorta and peripheral arteries (Hirsch et al., 2006; Makowsky et. al., 2011).

Although individuals with CVD most noticeably experience conditions related to the arteries supplying the heart and brain, atherosclerosis associated with the disease is not limited to that area. Fat deposits also build up and affect blood flow in the arteries supplying the kidneys, and stomach as well as the peripheral limbs. The history of CVD in Canada indicates that, as a general population, Canadians are at a heightened risk as nine of ten individuals have at least one risk factor for heart disease and stroke (Public Health Authority of Canada, 2009). Among those patients that have died from CVD, 54 percent were due to ischemic heart disease, 20 percent due from cerebrovascular events, and 23 percent due to myocardial infarction (Shammas, 2007).

2.2 Symptoms. Due to the range in various conditions related to CVD, many individuals that are at risk for developing CVD are asymptomatic or have atypical symptoms (Williams et al., 2007). Many individuals do not get diagnosed with CVD until they experience an event such as heart attack, stroke, angina, or heart failure (Braith & Stewart, 2006).

However, some of the most frequent symptoms may include chest pain (angina), shortness of breath, pain numbness, weakness or coldness in the peripheral limbs (especially with poor circulation or narrowed arteries), pain in the neck, jaw, throat, upper abdomen or back (Williams et al., 2007). Poor diet, inactivity, and smoking, as well as a number of other factors pertaining to lifestyle choices, have a major impact on development of CVD (Braith & Stewart, 2006). Symptomology can severely limit the performance of daily physical activities and often impairs the normal personal, social, and occupational functional capacity of these patients, thus representing a disability (Regensteiner & Stewart, 2001; Robbins et al., 2011). This disability can lead to marked and progressive impairment over time, such that many patients become housebound or dependent on others (Milani et al., 2007). Contemporary treatment of CVD is dichotomized into a breakdown of dietary and lifestyle goals, which span from target blood pressure values, lipid profiles, HbA1c (measures the ratio of glycated Hb in relation to total Hb), resting blood glucose, body mass index and waist circumference (Banegas et al., 2011). The parameters of these goals are directed at improving symptoms and consists of AE training, pharmacotherapy, and revascularization through surgical measures. Of these, supervised AE training is currently recommended as first line treatment and is the only one of these interventions that can additionally reduce concomitant cardiovascular risk (Milani & Lavie, 2007).

2.3 Vascular Function and Exercise Hyperemia. At the onset of exercise, blood flow to the active skeletal muscles increases rapidly to meet muscle metabolic demand. The mechanism responsible for matching arterial oxygen delivery to metabolic demand in exercising muscle is not completely understood. Metabolic regulation of vascular tone is achieved through a complex cell signaling system that directly alters vessel caliber

(Barclay et al., 2001). Active hyperemia is the term used to describe the increase in blood flow that occurs with the onset of the muscular activity. In developing force, the muscle utilizes energy and produces metabolic by-products that can influence blood vessel function (Barclay et al., 2001). Also, during contraction, intramuscular pressure increases and this can compress inflow vessels causing reduced or occluded flow (Barclay et al., 2001; Valic et al., 2002). During contraction the muscle compresses the veins within the muscle and expels the venous contents toward the heart. One way flow is ensured through the venous circulation which contains one way valves, and the enhanced arteriovenous pressure gradient results in an increase in arterial inflow to skeletal muscle (Valic et al., 2005).

The ability to sustain high metabolic rates during physical activity depends on a constant supply of energy from oxidative metabolic sources, which requires adequate blood delivery. Thus, it is essential to match the supply of oxygen to the metabolic demand for this key substrate. Over a wide range of metabolic demands, there is a tight linear relationship during steady state conditions between oxygen supply and oxygen utilization (Hughson, 2003).

Muscle metabolic rate is altered by changes in the contraction type (isometric, isotonic), frequency, duration, and amount of force developed. It has been shown that there is a competing negative and positive effect of dynamic muscle contractions and relaxations on muscle perfusion (Lutjemeier et al., 2005). The positive effect is the muscle pump effect, which is a rapid, localized mechanism for increasing blood flow through active skeletal muscle in addition to promoting venous return. The negative effect is that during skeletal muscle contraction, compression of all the vessels impedes tissue perfusion by

increasing resistance to arterial inflow. Several investigators have studied blood flow in contracting muscles in humans while at the same time manipulating venous pressure by positioning a limb above or below the level of the heart (Clifford & Hellsten 2004; Rowell 2004). Results from these studies all favour the hypothesis that there is a muscle pump contribution to the initial enhanced blood flow during muscle work, acting in concert with metabolic vasodilation (Nadland, Walloe, & Toska, 2009).

Once a stimulus occurs, blood flow increases quickly from resting levels (fast phase), passes through a phase whereby it determines the level of blood flow necessary (seeking phase), and finally reaches a steady level (matched phase) during which flow more accurately meets the demands of the skeletal muscle (See Figure 1). The duration and rate of these changes varies with the stimulation characteristics and the type of contraction (Barclay et al., 2001).

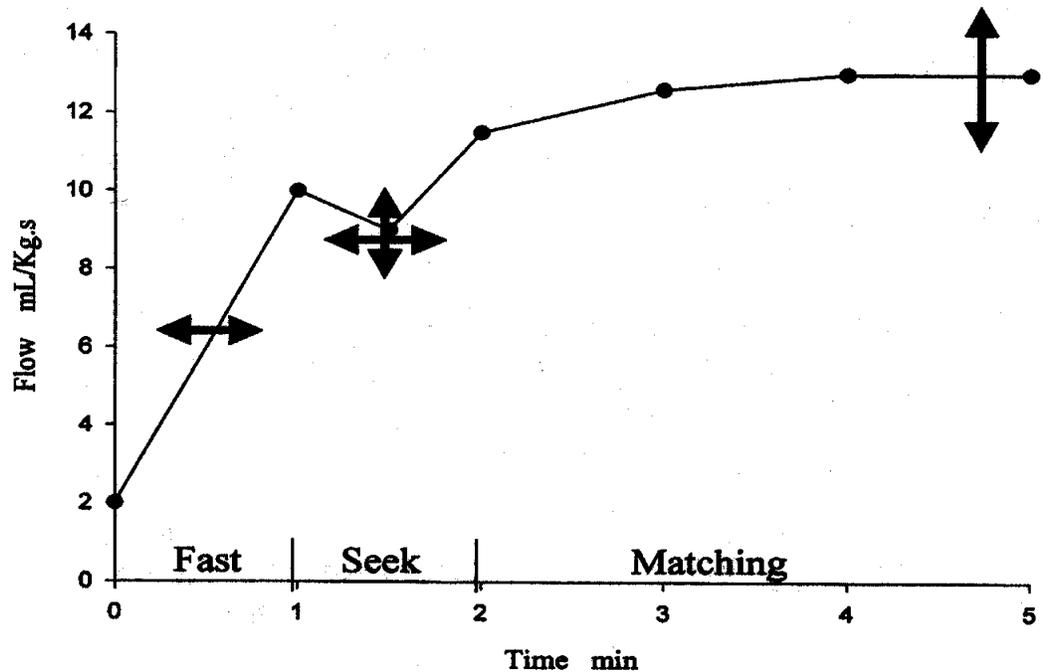


Figure 1 – Pattern of change of blood flow to a skeletal muscle stimulated to contract at time 0. The pattern is normally divided into three components: a fast phase, a seek phase and a steady level flow or matched phase. Arrows indicate components that vary with stimulation conditions (Barclay, Murrant, Woodley, Reading, 2001).

To evaluate the regulatory system involved in exercise hyperemia, the organization of the vascular bed and especially the microvasculature must be considered. For many years, the cross section of the arteriolar wall was viewed functionally as a layer of vascular smooth muscle (VSM) with the number of layers increasing as the vessel radius increases. The functional complexity of the vessel wall increased dramatically with Furchgott and Zawadski's (1980) identification of biological activity associated with the endothelial cell layer. The identification of homocellular gap junctions (between VSM cells and endothelial cells) and heterocellular gap junctions (between VSM cells and endothelial cells) added another dimension to the vascular regulatory potential (Figuroa & Duling, 2009). The presence of these gap junctions suggests that the intima and media of the vessel exist as a

syncytium in which information flows along and/or across the wall (Barclay et al., 2001). In terminal arterioles, local dilation caused by skeletal muscle contraction can be transmitted upstream along the vessel through gap junctions (Murrant, Kim, & Sarelius, 2001). Thus, there is a retrograde, longitudinal component to physiological information transmission through the vascular system. Barclay et al (2001) proposed that a vascular function unit using local and retrograde signaling was responsible for establishing arteriolar radius and the number of perfused capillaries needed to match hyperemia to muscular activity (Barclay et al., 2001). See Figure 2 below for an illustration of potential cell to cell communication that has been observed in a laboratory setting.

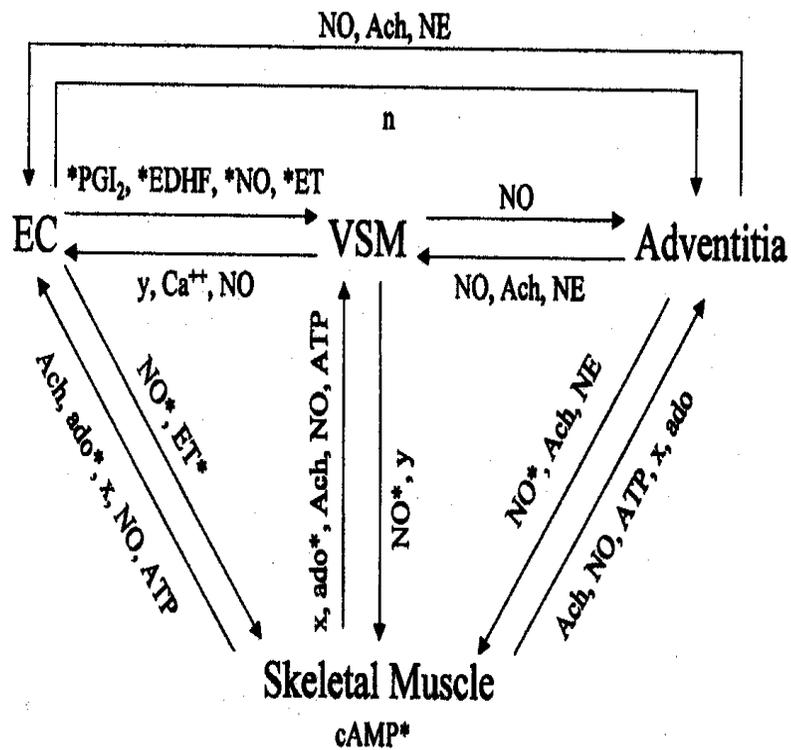


Figure 2 - Potential signals that could interact to regulate the function of the arteriole and skeletal muscle functional unit. Ach = acetylcholine; ado = adenosine; ATP = adenosine triphosphate; EDHF = endothelium-derived hyperpolarizing factor; ET = endothelin-1; NE = norepinephrine; NO = nitric oxide; PGI₂ = prostaglandin I₂ or prostacyclin. The 'x' represents metabolic vasodilators. The 'y' represents unknown products of the vascular smooth muscle. The 'n' represents unknown products of the endothelium. EC indicates endothelial cells and VSM indicates vascular smooth muscle cells (Barclay, Murrant, Woodley, Reading, 2001).

NO is the primary vasodilator substance released by the endothelium. It is a labile, lipid-soluble gas, synthesized from L-arginine through the action of the enzyme eNOS following stimulation by either shear stress/increased flow through the vessel lumen (with consequent NO-mediated vasodilation tending to normalize shear stress) or endothelial agonists such as bradykinin or acetylcholine (Budell, Bartlett, Segel, 2003). Physical exercise augments blood flow and shear stress, resulting in increased NO production and upregulation of constitutive eNOS activity (Di Francesco et al., 2009). Shear stress is a potent physiological stimulus for NO release, playing a role in vasodilation as well as

other molecular mechanisms such as superoxide production (Di Fransecomarino et al., 2009). Repeated episodes of increased blood flow with exercise may elicit an improvement in endothelial function and lead to the long-term benefits of regular exercise. An improvement of vasodilatory function would reduce the complications of atherosclerotic vascular disease. The mechanism is likely to involve chronic increases in NO production mediated by an increase in the expression of eNOS.

There are several other vasoactive compounds and numerous cellular sources of these compounds in skeletal muscle tissue: skeletal muscle cells form NO, prostaglandins, adenosine, lactate, and K^+ ; endothelial cells release NO, adenosine, K^+ , ATP, eicosatrienoic acids, and prostaglandins; and red blood cells can release ATP and NO. In addition, vasodilators may be released from nerve terminals, (e.g., ACh, ATP). All of the above-mentioned vasodilators, except for eicosatrienoic acids, are known to increase in the extracellular fluid of the skeletal muscle cells in response to muscle contraction. Because these compounds are potent vasodilators, they can potentially exert some effect on vascular smooth muscle cells. It is noteworthy that there are multiple cellular sources for most of these vasodilator compounds and that they may act via more than one mechanism to influence exercise hyperemia (Clifford & Hellsten, 2004).

The numerous inhibitor studies performed to date reveal that none of the studied compounds appears to be essential for exercise hyperemia, as the effect of one vasodilator can generally be blocked without a change in blood flow. Nevertheless, these observations do not exclude the possibility that the lack of effect could be due to a compensatory effect of another vasodilator. Such redundancy between vasoactive compounds has been observed in vivo as well as in vitro. It is likely that the importance of specific vasodilator

compounds varies over different phases of blood flow, such as in the case of an onset of exercise to steady state (Clifford & Hellsten, 2004).

2.4 Use of Aerobic Exercise to Improve Vascular Function in CVD Patients. As previously mentioned, supervised AE training is currently recommended as first line treatment for individuals with CVD. A typical intervention program for CVD patients consists of three exercise sessions per week for 12 weeks (Spronk et al., 2009; McDermott et al., 2009). Each participant starts with a five minute of warm up period, followed by 50 minutes of intermittent AE and a five minute cool down. The treadmill starts at zero percent incline and a speed of 3.2 km/hr. The severity of CVD risk can be calculated using a 10-year risk analysis tool taking into account tobacco use, age, gender, HDL-cholesterol, total cholesterol, and blood glucose status. Results are based on percentages, where a one percent risk is associated with ‘low risk’; a three to five percent risk is associated with ‘moderate risk’; and a five percent is associated with a ‘high risk’; upwards of 15 percent is associated with ‘severe or very high risk’ (Perk et al., 2012). During each session, patients are instructed to walk unless they are feeling any sort of chest pain or discomfort, and then rest by sitting on a chair. Once the pain subsides, walking then commences again, with repeated bouts of AE and rest, ideally for a total of 50 minutes. When the participant can walk for ten minutes with no chest pain or discomfort, the treadmill incline is increased by 0.5 percent in the subsequent session. When the incline had been increased to a maximum of 5 percent, the speed is then increased 0.5 km/hr each time to progressively increase exercise intensity. The aim of this progressive procedure is to continuously overload the cardiovascular system and the muscles that are active in during walking

(Wang et al., 2009). Both the level of pain/discomfort score, pain free walking distance and maximum walking distance are recorded. (Sakamoto et al., 2009; Wang et al., 2009).

There is strong evidence to support a central role for AE training to improve the walking ability of patients with chest pain/discomfort (Gardner et al., 2001). In particular, supervised, hospital based AE training is considered effective and is recommended as the initial treatment strategy for patients with CVD associated symptoms such as chest pain/discomfort. The degree of improvement in walking ability after supervised AE training was shown to be significantly better than that of home based training such as “go home and take walks” (McDermott et al., 2004). Regular AE or improved physical activity is associated with increased pain free walking time (Wang et al., 2009), improved blood pressure (Wang et al., 2006), serum lipid profile (Brendle et al., 2001), glycemic control (Izquierdo-Porrera et al., 2000), and reduced central adiposity (Terjung et al., 2002).

A meta-analysis of 22 randomized and non-randomized trials of supervised AE training revealed that pain free walking time improved an average of 180 percent and maximal walking time increased by 120 percent (Watson, Ellis & Leng, 2009). A separate meta-analysis from the Cochrane Collaboration evaluating only randomized, controlled trials concluded that AE improved maximal walking ability by an average of 150 percent (Leng, Fowler & Ernst 2000; Milani & Lavie, 2007). AE induced improvements in walking ability have also been shown to translate into increases in routine daily activity (Gardner et al., 2001). This study also reported that 6 months of AE training improved treadmill walking ability, accompanied by a 31 percent increase in routine daily activity as measured by accelerometry. Moreover, self-reported physical activity improved by 62 percent,

suggesting that patients themselves appreciated this functional improvement (Garg et al., 2006; Sakamoto et al., 2009).

In a study conducted by Brendle et al., (2001) Results of a 6-month AE rehabilitation program improved endothelial function, as indicated by an increase in flow mediated vasodilation of the brachial artery in symptomatic CVD patients with and without PAD. Exercise rehabilitation training increased the time to onset and to maximal claudication pain. These results are in agreement with previous studies that have shown an increase in time to onset and maximal claudication pain. Meta-analyses reported positive effects of AE rehabilitation programs on walking distance in patients with intermittent claudication (IC) in both randomized and nonrandomized studies. Various clinical trials have documented the beneficial effects of low to moderate AE training programs on improving functional capacity in patients with PAD. Consequently, such patients can improve claudication symptoms after only a couple of months of rehabilitation, and are likely to experience continual improvement thereafter. In addition to improving endothelial function and exercise tolerance, 6 months of AE rehabilitation improved calf blood flow after an ischemic response (Brendle et al., 2001)

2.5 Use of Resistance Training Exercise for Improving Vascular Function in CVD Patients.

Previous research suggests that it is chronic ischemia resulting from CVD, rather than disuse, which is the major factor causing fiber atrophy (McGuigan et al., 2001). Fiber area is reduced in patients with symptomatic CVD compared to healthy age matched controls. RT in patients with CVD provides a unique model of how skeletal muscle responds to chronic ischemia. Findings of decreased muscle strength and size of the plantar flexor muscles in patients with CVD could potentially allow for RT as an intervention that may

translate into positive benefits for walking and strength. However, the efficacy of long term (i.e., six months) RT programs has not been determined in patients with symptomatic CVD. As skeletal muscle abnormalities are an important limitation to AE tolerance in patients with CVD, and muscular strength affects their ability to perform daily tasks (McGuigan et al., 2001; McDermott et al., 2007; McDermott et al., 2008). A number of research projects that involve physical activity (both RT and AE) as a treatment option for patients with CVD have targeted the overall health of the individual. Although, there has been promising results in studies regarding improving vascular health, there is still limited research regarding the vascular adaptation to RT in patients with established CVD or individuals with reduced vascular function (McDermott et al., 2007; McDermott et al., 2008).

As a consequence of CVD, many patients become inactive causing atrophy of the calf muscle area and reduced leg strength. This aggravates their condition causing an even greater loss of lower extremity muscle mass, strength and endurance (Ryan, Katzel, Gardner, 2000; McDermott et al., 2007; McDermott et al., 2008). Peak oxygen consumption in patients with claudication is generally half of age matched normal individuals, indicating a level of impairment similar to patients with New York Heart association class III heart failure (Hiatt et al., 2001; American Diabetes Association, 2003). In CVD patients, reduced leg strength and atrophy in lower extremities has been associated with disease severity and functional performance. The mechanisms behind the impaired muscle strength have not been fully elucidated, but a muscle fiber denervation and a decreased type II fiber cross sectional area has been shown (McDermott et al., 2004). The benefits of endurance training in CVD patients are recognized. However, whereas many studies have investigated endurance training, clinical trials of lower extremity RT in

persons with CVD have been small; have yielded mixed results; and have excluded CVD participants without expressing classic symptomology (McDermott et al., 2009).

In addition to improved strength, strength training has been reported to improve endurance performance by improved walking economy (Osteras, Helgerud, Hoff, 2002; Hoff et al., 2007). Walking economy, defined as the oxygen cost at a sub maximal walking workload is one of three factors determining an aerobic endurance performance, the other two being lactate threshold and maximal oxygen consumption. Walking economy is reduced in patients with claudication in that walking patterns change to favour stability over speed. Following a program of strength training, walking economy has been shown to improve by 5-20 percent in CVD patients and in patients with other chronic diseases, as evidenced by a decrease in oxygen consumption at sub-maximal workloads (Wang et. al., 2009). Supporting this concept are reports utilizing alternative exercise programs including RT and moderate intensity interval training (Wang et. al., 2009, Adams et. al., 2006), each yielding as good or greater improvements in walking endurance and walking economy than standard aerobic based exercise programs. The observation that patients with CVD have muscle weakness provides a strong rationale for strength training of lower extremity muscle groups, in order to improve walking ability, as decreased muscular strength in the lower extremities is correlated with an increased prevalence of CVD (McGuigan et. al., 2001; Wang et al., 2009).

A study by Wang and colleagues (2009) examined eight-week strength training duration in CVD patients. Their strength training protocol consisted four sets of five repetitions of a dynamic leg press with emphasis on maximal mobilization of force in the concentric action and a progressive adjusted intensity corresponding to 85-90 percent of

each participant's 1RM. The study demonstrated a 31 percent increase in 1RM, a 103 percent increase in dynamic rate of force development. The increased strength in CVD patients in the study led to an improved endurance performance and thus walking ability, by improving the patients' walking economy. The strength training program resulted in a 9.7 percent increase in walking economy during continuous walking on a horizontal treadmill. The increased 1RM strength induced by the strength training program also correlated positively with rate of force development and with the improved walking economy. Furthermore, the improved walking economy correlated positively with the observed a 13.6 percent improvement in time to exhaustion. Despite documented findings in healthy subjects, but there is limited evidence for effects from strength training on walking time to exhaustion in CVD patients.

The effect of RT on muscle function has been studied in detail, especially pertaining to the direct benefits of CVD and even more specifically, vasodilatory function. RT, through the frequent induced ischemia effectively stimulates adaptive responses in endothelial vasodilation which would be especially useful pertaining to populations demonstrating vascular disease (Adams et al., 2006). Periodic exposure to repeat episodes of exercise induced hyperemia should increase blood flow and augment a vascular response of nitric oxide (NO) and prostacyclin, thereby promoting vasodilation. Research has shown that RT improves hemorheology, thereby facilitating oxygen delivery to ischemic skeletal muscle (Adams et. al., 2006). Although coronary patients demonstrate significant improvements in blood viscosity and tissue oxygen extraction following formal RT, these benefits may be even more applicable for patients with CVD and related conditions (Wang et al., 2009).

2.6 How Resistance Training Could Improve Vascular Function. The vascular endothelium plays an important role in the modulation of vascular tone and function by synthesizing and releasing NO (Tanaka et al., 2006). Physical exercise augments blood flow and shear stress, which results in an increase in NO production and upregulation of constitutive endothelial nitric oxide synthase (eNOS) activity. Shear stress is a potent physiological stimulus for NO release, interfering not only in vasodilation but also in other molecular mechanisms such as superoxide production. Repeated cyclic episodes of occlusion followed by increased blood flow either mechanically through the use of an external cuff (Heffeman et al., 2007) or through the natural occlusion that occurs with RT. Regular continued episodes may elicit an improvement in endothelial function and lead to the long term benefits of regular exercise that ultimately would reduce the complications of atherosclerotic vascular disease. The mechanism is likely to involve chronic increases in NO production mediated by an increase in the expression of eNOS (Di Francescomarino et al., 2009).

In rhythmical AE, such as running, cycling, etc., blood flow to the contracting skeletal muscles can also become limited or occluded during the contraction period due to an augmented intramuscular pressure, and consequently the majority of the blood flow occurs during the relaxation period between contractions (Su et al., 2009). Lutjemeier et al. (2005) reported that although the muscle pump had a net positive effect on muscle blood flow at the lightest work rate, and might provide sufficient perfusion to working muscle; at heavier work rates any enhancement to flow during relaxation was insufficient to fully compensate for the contraction induced impedance to muscle perfusion. Compression of the veins during repeated cycles of muscle contraction relaxation aids venous return to the

heart and has been postulated to increase skeletal muscle perfusion by reducing the downstream venous pressure during relaxation via the muscle pump effect (Lutjemeier et al., 2005; Clifford & Jasperse 2007).

During static muscle activity, blood occlusion occurs due to mechanical compression of the blood vessels that occurs from tension developed by muscular contraction. This also increases intramuscular pressure and decreases blood flow to the region. Consequently, the blood flow to the exercising muscle decreases, or even ceases, if the force developed is high enough (50-80 percent MVC) to overwhelm the increased perfusion pressure. This temporary blood occlusion causes an increase in metabolites as well as a stronger level of shear stress which has been shown to increase up to five times the resting value (Kagaya & Homma, 1997). RT would allow manipulation of occlusion and reperfusion time by varying the duty cycle of RT exercise. Pilot work conducted in the UNB Exercise Physiology Lab suggested that varying the duty cycle to longer occlusion and short reperfusion episodes significantly enhanced post exercise hyperemia when compared to short occlusion-reperfusion cycles that closely mimic running (See Appendix – section one).

A study conducted at the National Institute of Health and Nutrition in Tokyo, Japan examined low intensity resistance training with slow movement and tonic force generation (LST) versus a high intensity resistance training (HN) group with normal speed contractions. The outcome measured was basal limb blood flow. The LST exercise movement was performed to achieve continuous force generation throughout the resistance exercise movement, which is based on the presumption that continuous force generation at >40 percent maximum voluntary contraction has been shown to suppress both blood inflow

to and outflow from the muscle due to an increase in intramuscular pressure. The results indicate that RT even in LST, which used a relatively low mechanical load, is effective for increasing basal femoral blood flow. There was an 18 percent increase in basal femoral blood flow with only a three percent increase in leg muscular size. Moreover, increases in the relative blood flow to leg muscle mass in the two training groups were quantitatively the same as increases in whole leg blood flow. LST promotes muscular hypertrophy and strength gain comparable to those in HN without high mechanical load. LST is proposed as a safe and useful resistance exercise method not only for muscular hypertrophy and strength gain, but also for increasing peripheral blood flow and vascular conductance as an additional effect (Tanimoto et al., 2009).

High intensity RT has been shown to reduce arterial compliance and increase arterial stiffness (Miyachi et al. 2004; Cortez-Cooper et al. 2005; Okamoto et al. 2006). In contrast, habitual moderate intensity RT does not reduce central arterial compliance in middle aged and older adults (Cortez-Cooper et al. 2008). It has been suggested that low intensity RT with an emphasis on ‘slow’ lifting and lowering technique exerts a beneficial effect on vascular function (Okamoto et al. 2008). High intensity RT has been shown to increase arterial stiffness (Miyachi et al. 2004; Cortez-Cooper et al. 2005), which is not commonly recommended for the majority of the population. Acute intermittent elevation of blood pressure during high intensity resistance exercise may induce arterial stiffening, which is an important determinant of chronic arterial stiffness. Regulation of arterial pressure is associated with elevated baseline sympathetic nerve activity and the effects of elevated noradrenalin on VSM tone (Okamoto, Masuhara, Ikuta, 2011).

2.7 Purpose: With this knowledge in mind, the study design tested a RT program that attempted to simulate this principle of a prolonged isometric contraction. The goal was to induce a training response in the vascular system, characterized by an increase in VC. The purpose of this work was to develop evidence based guidelines for using RT to improve the VC of specific muscle groups (i.e. the plantar flexors of the lower limb).

A goal of this study was to determine the most beneficial method of RT that targeted a training effect in the vascular system. This study attempted to increase the blood flow to the working areas of the body as well as increase the VC at rest through RT. Accordingly, the purpose of this study was to determine if elderly individuals participating in a RT program with an emphasis on slow eccentric contraction would experience increased VC relating to endothelial function.

2.8 Alternative Hypothesis Statement: In older male participants, resistance training performed using a slow eccentric contraction phase (one second contraction; five seconds eccentric) compared to resistance training using a short occlusion time (one second concentric; one second eccentric) will:

- i)* improve resting and post exercise pulsatility index in the brachial and popliteal arteries.
- ii)* improve resting and post exercise systolic peak in the brachial and popliteal arteries.
- iii)* improve resting and post exercise mean blood velocity in the brachial and popliteal arteries
- iv)* improve physical exercise variables, specifically musculoskeletal strength and walking endurance

v) decrease variables pertaining to cardiovascular disease, specifically resting heart rate, systolic, diastolic, and mean arterial blood pressure

vi) decrease anthropometric data, specifically waist circumference and body mass index

2.9 Null Hypothesis: Each of the above hypothesis statements will be examined as a null hypothesis.

Methodology

3.1 Participants. Subjects (n = 14) were recruited from the general population in the Greater Fredericton Area using an online poster, electronic newsletter and word of mouth. Inclusion criterion included male gender, age of 50 years or greater, ability to commit to two pre-training testing dates as well as the six-week RT program. Exclusion criterion entailed the following: major amputation, major surgery or a myocardial infarction within the past 3 months, as well as current participation in other exercise related clinical trials. All participants provided written, informed consent (appendices, section two) before engaging in any study related procedures. Participants were required to complete a PAR-Q & YOU form (appendices, section three) before they were eligible to engage in any type of exercise related to the study. Those participants who respond “yes” to any of the items on the “PAR-Q and YOU” form were required to have a “PAR MED-X” form completed by their physician to obtain medical clearance for their involvement in the program (appendices, section four). All testing procedures took place in the Exercise Physiology Lab in the Faculty of Kinesiology at the University of New Brunswick. All weekly supervised RT sessions were conducted in the west gymnasium located in the Lady Beaverbrook gymnasium. This study design and methodology was reviewed and approved by the UNB research ethics board (REB#2012-038). Please see appendices, section five for a complete submission and resubmission of the research and ethics document.

3.2 Experimental Design. This was a quasi-experimental pre-test post-test research design. The 10-week study assessed change in indices of vascular functioning, resting heart rate (RHR), systolic (SBP) and diastolic blood pressure (DBP), aerobic endurance, muscular strength and anthropometric measurements before and after completion of the six-week RT

program that used long or short concentric and eccentric contraction times to alter vascular occlusion time per repetition. Baseline measurements were made at one and four-weeks before beginning resistance training. This baseline assessment period served as a measure of stability in the indices of interest. During baseline testing the participants received education on the principles of RT and familiarized with the strength training equipment and exercises that were going to be used throughout the six-week RT phase. Following baseline assessment, participants were placed into either the slow eccentric contraction (SEC) group or the conventional resistance training (CRT) group. The SEC group were allocated to the morning RT sessions and the CRT group were allocated to the afternoon RT sessions. Participants were allocated to either group based on their availability. If they were available to both sessions they were randomly assigned to either a morning or afternoon group. A T-test was used to assess differences between groups following pre-testing (age, fitness level (6MWT), musculoskeletal strength (table 1), pulsatility index, systolic peak, mean blood velocity for the one to one ratio test (table 3), and the five to one ratio test (table 5). No significant differences were found between the groups prior to the intervention protocol.

Strength testing was measured at the beginning of the six-week RT program and upon completion of the RT program. For safety reasons and participant RT experience, participants completed a 10-repetition maximum test, instead of performing a one repetition maximum test to measure strength. This was evaluated using the Brzycki equation for estimating one repetition maximum: $\text{one repetition maximum} = \text{weight lifted} / (1.0278 - (.0278 * \text{Reps}))$ (Brzycki, 1993).

The intervention consisted of a six-week supervised RT program three times per week. Each session was scheduled for one hour, for a total of three hours per week. This study consisted of two training groups; a CRT group (n=7) and a SEC group (n=7). The exercise protocol for each session consisted of a 10 minute warm up period of low intensity walking to properly initiate a safe increase in blood pressure heart rate. This led into approximately 45 minutes of moderate intensity RT which was followed by a five minute cool down period of low intensity stretching and to return heart rate back to pre-workout levels. Each group performed three sets with one minute rest between each set. The CRT group completed 12 repetitions per set while the SEC group performed five repetitions per set. The CRT group aimed for a work to rest ratio of one second concentric contraction, one second eccentric contraction, and one second rest at the end of each eccentric contraction (three seconds per repetition x 12 repetitions = 36 seconds). The SEC training group aimed for a work to rest ratio of one second concentric contraction, five seconds eccentric contraction, and one second rest (seven seconds per repetition x five repetitions = 35 seconds). The training load for each group was determined by the 10-repetition maximum values from the strength testing and then adjusted to the appropriate repetition maximum percentage (86 percent for the five repetition maximum and 70 percent for the 12 repetition maximum). It is recommended that training load be increased by 2-10% when the individual can perform the current load for one to two repetitions over the desired number (American College of Sports Medicine, 2009). The whole body training program required two days to complete. Training day one consisted of exercises that targeted the chest, back, and arms (CBA). Training day two consisted of exercises that consisted of exercises targeting the legs, shoulders, and core (LSC). The CBA session consisted of

bench press, chest fly, lat-pull down, seated row, bent-over row, bicep curl, triceps extension. The LSC session consisted of squats, leg press, walking lunges, dumbbell shoulder press, lateral raises, as well as various core exercises. Each training session was separated by a minimum of 48 hours (see Figure 3).

Typical Training Regiment

Week	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
1	Rest	CBA	Rest	LSC	Rest	CBA	Rest
2	Rest	LSC	Rest	CBA	Rest	LSC	Rest

Figure 3: Two of six weeks of a typical training cycle (CBA: Chest, Back, Arms LSC: Legs, Shoulders, Core)

Participant Health Characterizations

3.3. Demographics A self-reported participant medical history questionnaire (Appendices, section six) was given to collect participant age and information regarding past injuries or medical conditions.

3.4. Anthropometric Data. Body weight and height were measured using a physician’s scale and stadiometer (Seca 763, Hamburg, Germany) to the nearest 0.1 kg and 0.1 cm, respectively. Body mass index (BMI) was calculated using the participants body mass in kilograms divided by their height in meters squared (kg/m^2). Waist circumference was measured to the nearest 0.1 cm using a standard plastic tape measure using the revised CSEP protocol (McGuire & Ross, 2008).

3.5 Ankle Brachial Index. Once the participant had been lying down at rest for 10 minutes, a standard size (10 cm) sphygmomanometer was placed around the participant’s ankle,

between the malleolus and the gastrocnemius and inflated. A laser Doppler ultrasound and pencil probe (5MHz) was used to detect the reappearance of blood flow past the cuff as the pressure in the sphygmomanometer is released. The reappearance of blood flow represents the systolic blood pressure. Systolic blood pressures were taken twice at the posterior dorsalis pedis artery at the left and right leg. Brachial systolic blood pressure was obtained from both arms at the brachial artery. ABI was calculated as the highest ankle systolic blood pressure value divided by the highest brachial blood pressure value (McDermott et al., 2000).

3.6 Blood Analysis. A blood sample was obtained after a two-hr fast. Plasma blood glucose and a lipid profile (LDL, HDL, triglycerides, total cholesterol) were tested. The blood collection procedure was conducted by the project supervisor. The participant's finger was sterilized with an alcohol swab. The finger was then punctured with a lancet (BD Microtainer Contact Activated Lancet, Becton Dickinson Company, New Jersey, USA) and blood was collected in a plastic micro collection container (BD Microtainer Blood Collection Tubes, Becton Dickinson Company, New Jersey, USA). The participants' finger was then wiped and held for 30-90 seconds with a sterile gauze (Stensvold, 2010). The sample was analyzed using a clinical chemistry analyzer (Reflovet Plus, Roche, Basel, Switzerland). For this, a sample of blood was pipetted onto the reagent test strip (Reflotron Test Strips, Roche, Basel, Switzerland) and then placed into the measuring chamber.

3.7 Quality of Life. The Walking Impairment Questionnaire (WIQ) is a common assessment tool for conditions associated with vascular disease and endothelial dysfunction (McDermott et al., 1998). This survey (appendices, section seven) was completed prior to beginning the RT intervention and once the intervention was completed at week 10.

Cardiovascular Function Evaluation

3.8 Heart Rate and Blood Pressure. Resting heart rate (RHR) was recorded using a polar watch heart rate monitor and was verified by wrist palpitation for 15 seconds and calculated to determine the heart rate for one minute. Systolic (SBP) and diastolic (DBP) resting blood pressure was taken using a manual sphygmomanometer (Riester, Jungingen, Germany) after the participant was seated at rest for a 10 minute period. Mean arterial pressure (MAP) was calculated from the equation: $MAP = DBP + 0.33(SBP - DBP)$ (Gauer, 1960).

3.9 Exercise Hyperemia. For the upper limb, a hand grip apparatus was set up to a force transducer (Interface Advanced Force Measurement, 9820-000-1, Arizona USA) to measure the amount of force being generated. The participant was seated in a chair with both arms comfortably resting on a platform above waist level. The participant's left arm was strapped into the hand grip apparatus holding onto a mounted bar with their second and third phalanges holding the hand grip (Figure 14, Appendix – section eight). For the lower limb, an ankle flexion apparatus was mounted to the wall and set up to a force transducer (Premium Transducers Limited, PT 4000-500lb, New South Wales, Australia) to measure the amount of force generated. The participant lay comfortably face down with their left leg strapped into the apparatus (See Figure 15, Appendix – section eight).

For both upper and lower limb devices, each participant completed a maximum voluntary contraction (MVC) to determine the load required for the subsequent tests. In the upper limb, participants were instructed to squeeze the hand grip apparatus with the second and third phalanges to create the greatest amount of force. The MVC for the lower limb required the participant to perform a plantar flexion of the ankle to create the greatest

amount of force. Subjects then completed two tests at each testing site over the same amount of time (180sec) with different work to rest ratios. During static forearm exercise at lower intensities of up to 20-30% MVC forearm blood flow, measured by venous occlusion plethysmography, increased, whereas at higher intensities of 50-80% MVC, it decreased towards or below the resting level (Kagaya & Homma, 1997). During pilot work in the EPL conducted at UNB we found that the 50% MVC value was quite difficult for the sustained contraction test. Participants used 40% of their MVC value of each test. The first test consisted of a five to one work to rest ratio. Each participant completed 18 sets of a five second contraction with a one second rest between each repetition. The second test was an equal work to rest ratio. Each participant completed 90 sets of one second contractions with one second of rest between each repetition. At the end of the intervention, participants were then re-tested on their MVC and conducted the same series of tests. Upon completion of each test, Laser Doppler ultrasonography (Huntleigh Rheo Dopplex II, Cardiff, United Kingdom) and pencil probe (5MHz) was used to collect exercise hyperemic response for 10 minutes after each of the tests to measure the recovery time to return to baseline values. Participants completed these series of tests on three occasions, week one, week four; before the commencement of the six-week RT program and upon completion of the study. As mentioned above, participants were given a visual marker to identify their personal 40 percent MVC value for each test and then instructed to aim for that target. Rate of force was calculated during each test to determine accuracy of attaining the 40 percent target as well as to measure the amount of fatigue that was occurring during both the 1:1 and 5:1 functional tests. For the 1:1 test, the rate of force of the first six contractions was calculated and compared to the last six contractions. This duration of time

for six contractions is a total of twelve seconds. For the 5:1 test, the rate of force of the first two contractions was calculated and compared to the last six contractions. This duration of time for two contractions is equal to twelve seconds as well. The force transducers were calibrated using a pulley system loaded with weighted plates, up to the maximum limit of the force transducer. The force transducers and laser Doppler transmitted their signals to a control panel (National Instruments, BNC-2090, Texas, USA) which was then transmitted to a computer (Dell Incorporated, GX280, Texas, USA). The software program LabVIEW 7.1 (National Instruments, Texas, USA) was used to display the amount of force being generated over time during the functional tests (1:1, 5:1). Upon completion of the tests, the Doppler system, which was also set up to the control panel mentioned above, and connected to another computer that was used to display cardiac cycles over time on the computer monitor during the 10 minute recovery period.

3.10 Six Minute Walk Test. This functional test measures the distance that a patient can walk on a flat, hard surface in a period of six minutes (6MWT, Appendices, section seven). Subjects were instructed to walk as quickly as possible without running, covering as much distance as possible during the allotted six minutes. The gymnasium located in the Lady Beaverbrook gym on University of New Brunswick campus was used. The course in the gymnasium was a 30 meter by 20 meter rectangular shape. Participants were allowed to rest if they developed muscular cramping, excessive breathing or heartbeat, or any other reason that may cause them to stop. Participants were encouraged to continue walking once they were comfortable in doing so. The distance covered with no muscular cramping (Pain Free Walking Time) and total distance covered (timed using a standard stop watch) were recorded for analysis. Participants completed this test at the beginning of week four, before

the commencement of the six-week RT program and again upon completion of the intervention phase. A preliminary trial was completed to allow participant familiarization with the test and also to reduce the learning effect associated with the test. This test has been validated as a valid test for older adults (Jones & Rikli, 1998).

3.11 Musculoskeletal Strength. Before the commencement of the six-week RT program, each participant was assessed on their strength of four foundation exercises (bench press, squat, latissimus pull-down, and dumbbell shoulder press). The SEC group completed sets aiming for five repetitions, while the CRT group aimed for 12 repetitions. Musculoskeletal strength was observed on a daily basis throughout training program. When participant's achieved the number of desired repetitions the weight was increased by 2 – 10% as recommended (Collier et al., 2008; American College of Sports Medicine, 2009).

3.12 Statistical Analysis. All statistical analysis was conducted using the IBM Statistical Package for the Social Sciences (SPSS) v22.0. The primary variables examined were pulsatility index (PI), systolic peak blood pressure (SP), and mean blood velocity (MV). Two-way repeated measures analysis of variance (ANOVA) with Bonferroni's correction was used to examine differences at rest and during the 10 minute recovery period following the two functional exercise tests (1:1, 5:1) at each interval; baseline one and baseline two, baseline one and post-training, baseline two and post-training, as well as between groups. Values will only be considered significantly different if both baseline values are significantly different to the post training (PT) values. Secondary variables included muscular strength (bench press, squat, latissimus pull-down, and dumbbell shoulder press), muscular endurance (6MWT), as well as weight, RHR, SBP, DBP, MAP, BMI, and WC. Two-way repeated measures ANOVA with Bonferroni's correction was also used to

examine differences in pre-test and post-test measurements of secondary variables. Descriptive statistics were calculated for all variables collected at both baseline and post intervention. For all statistical tests, $P < 0.05$ was considered significant. All values are expressed as mean \pm standard deviation.

Results

4.1 Participants. Fourteen ($n = 14$) of the initial sixteen male participants (59.4 ± 5.4 years) completed both baseline measurements, separated by a four-week period and the six-week training program, three times weekly. In regards to training session attendance of the 14 participants that completed both baseline and six-week RT requirements; perfect attendance was recorded for twelve of the fourteen participants. Two participants had 89 percent attendance. In addition, there were two participants that provided baseline measurements at week one and week four but were unable to participate in the 6-week RT program. Reasons for dropping out included: inability to commit to the full 10-week program ($n=1$), and an unrelated aggravation of a previous psychological issue ($n=1$). Previous injuries that were reported included back, rotator cuff, knee, arm and head. All participants reported that these previous injuries do not affect their regular activities of daily living. Medical conditions included diabetes, post-traumatic stress disorder, depression and arthritis. Reported medications included crestor, avodart, tamsulosin, spasmhalt-ASA-8, lyrica, Prozac, Effexor, nortryptiline, Seroquel, prazison, tecta, lorazepam.

Table 1

Participant Anthropometric Data, Heart Rate and Blood Pressure. Reported as mean ± standard deviation.

	SEC		CRT	
	Pre Training	Post-Training	Pre Training	Post-Training
<u>Anthropometric Data:</u>				
WC, cm	93.0 ± 5.40	92.3 ± 4.30*	92.2 ± 5.60	91.7 ± 5.10*
BMI, kg/m ²	29.7 ± 2.30	29.3 ± 2.20	28.4 ± 3.00	28.2 ± 2.80
Height, cm	173.6 ± 9.10	173.6 ± 8.90	175.8 ± 4.90	175.7 ± 5.10
Weight, kg	86.6 ± 11.4	87.7 ± 10.1	85.4 ± 10.5	87.1 ± 9.60
<u>Cardiovascular Data:</u>				
SBP, mmHg	133.4 ± 10.7	130.3 ± 9.10*	130.6 ± 11.5	129.9 ± 9.10*
DBP, mmHg	85.6 ± 9.70	84.9 ± 8.60	87.7 ± 7.30	86.7 ± 6.10
MAP, mmHg	100.7 ± 9.70	99.0 ± 8.40*	101.0 ± 8.40	100.1 ± 6.80*
RHR, bpm	72.7 ± 6.10	72.0 ± 4.70	74.0 ± 5.30	73.6 ± 4.10

Note: * indicates differences between groups at p<0.05. See Table 6 in Appendices Section Ten for statistical p values.

4.2 Quality of Life. The walking impairment questionnaire (WIQ) was completed by each participant, despite none of the participants being clinically diagnosed with a known endothelial dysfunction such as diabetes or PAD. Each participant reported zero degree of difficulty in any of the three segments of the survey (walking distance, walking speed or stair climbing) throughout the pre-test and post-test survey. The primary use of the WIQ is to determine if individuals experience symptoms associated with endothelial dysfunction,

such as intermittent claudication while walking. This information is useful as it determines that no participants in this study experienced severe endothelial dysfunction.

4.3 Cardiovascular Test Assessments. Each participant performed a MVC for the upper and lower limb at the beginning of each testing day; baseline one (B1), baseline two (B2), post-training. Forty percent of each individual's MVC value was used for the exercise hyperemic tests. The MVC values for the upper and lower limb tests for both the SEC group and the CRT group are displayed below in table 2. There were no significant differences between groups (SEC vs CRT) or within each group, comparing each baseline (B1, B2) value to the PT results.

It was determined that the various training conditions were not significantly different in comparison when regarding the resting values before the equal work to rest ratio test (1:1) and the five to one work to rest ratio test (5:1) for both the upper and lower limb. RT did show decreases in pulsatility index and systolic peak at rest, however; it did not matter to which group each participant was assigned, as there was no main effect differences relating to any of the above mentioned variables between groups or over time as well as no interaction effect of group and time.

Table 2

Maximum voluntary contraction values for the hand-grip apparatus and the ankle flexion apparatus at baseline one, baseline two, and post-training for SEC and CRT groups. Reported as mean \pm standard deviation.

	SEC (n = 7)			CRT (n = 7)		
MVC	Baseline 1	Baseline 2	Post-Training	Baseline 1	Baseline 2	Post-Training
Upper (N)	396.3 \pm 76.9	391.1 \pm 71.2	404.2 \pm 76.7	345.0 \pm 94.3	349.4 \pm 92.6	353.2 \pm 90.6
Lower (N)	277.0 \pm 42.5	282.8 \pm 45.5	288.3 \pm 51.3	315.6 \pm 82.1	320.2 \pm 87.6	312.3 \pm 89.6

Note: * indicates differences between groups at $p < 0.05$, α indicates significant within group differences from pre to post testing at $p < 0.05$. See appendices – section ten, table 7 for statistical p values.

4.4 One to One (1:1) Work to Rest Ratio - Upper Limb

Resting Pulsatility Index: The SEC and CRT groups saw significant changes from the PT values compared to baseline values (B1, B2). The SEC experienced a significant reduction in resting PI from the initial baseline values by 0.13 ± 0.69 to 0.19 ± 0.68 data points. The initial baseline resting PI reduced by 0.12 ± 0.52 and 0.13 ± 0.58 data points for the CRT group. Although resting mean blood velocity decreased, the primary decrease in resting pulsatility index was due to a drop in peak systolic blood pressure.

Resting Systolic Peak Blood Pressure: The SEC and CRT groups experienced significant changes from PT values when compared to both B1 and B2 values for the 1:1 work to rest ratio test. The negative decrease from PT values ranged from 3.66 ± 10.49 to 4.70 ± 8.53 $\text{cm} \cdot \text{sec}^{-1}$. As mentioned above this is the most substantial reduction in the equation for pulsatility index. The CRT group displayed a negative change in PT when compared to either B1 or B2 values in SP by 1.41 ± 8.46 to 2.16 ± 7.75 $\text{cm} \cdot \text{sec}^{-1}$. There was no

significant change between B1 and B2 in either the SEC or CRT group. There was also no significant difference between groups.

Resting Mean Blood Velocity: The SEC group experienced a significant change for the 1:1 work to rest ratio tests between PT and baseline values, however; only when comparing PT values to the B1 values, observing a change by $0.97 \pm 2.73 \text{ cm} \cdot \text{sec}^{-1}$. However; values will only be considered significantly different if both baseline values are significantly different to the PT values. The PT and B2 values were not significant for the SEC group so it will be deemed insignificant, given that there was no significant difference between baseline values. The CRT group saw no significant change comparing both B1 and B2 to the PT values.

4.5 One to One (1:1) Work to Rest Ratio – Lower Limb

Resting Pulsatility Index: The SEC and CRT groups saw significant decreases in PT values compared with B1 and B2 for the 1:1 test (0.49 ± 2.49 and 0.52 ± 2.47 data points for the SEC and 0.36 ± 2.20 and 0.10 ± 2.29 data points for the CRT group, respectively).

There were no significant changes in resting systolic peak or resting mean velocity in the lower limb for either the SEC or CRT group.

Table 3

Resting upper 1:1 test results for systolic peak (SP), mean blood velocity (MV), pulsatility index (PI) at B1, B2 and PT for the SEC and CRT groups. Reported as mean ± standard deviation.

1:1 Ratio Test	SEC (n = 7)			CRT (n = 7)		
	B1	B2	PT	B1	B2	PT
Resting Upper						
SP	39.9 ±10.5	38.9 ±8.53	35.3 ±6.11*	39.3 ±8.46	38.6 ±7.75	37.2 ±6.78*
MV	13.9 ±2.73	12.8 ±2.94	12.9 ±2.57	12.0 ±2.66	11.5 ±2.33	11.8 ±2.47
PI	2.81 ±0.69	2.87 ±0.66	2.68 ±0.66*	3.16 ±0.52	3.17 ±0.58	3.04 ±0.53*
Resting Lower						
SP	25.5 ±4.54	25.1 ±4.41	27.1 ±4.70	27.2 ±2.72	26.0 ±3.14	27.3 ±3.28
MV	6.15 ±2.24	5.83 ±2.12	6.25 ±2.06	5.65 ±2.10	5.22 ±1.73	5.33 ±1.71
PI	5.80 ±2.49	5.83 ±2.47	5.31 ±2.14*	6.77 ±2.20	6.67 ±2.29	6.41 ±2.22*

Note: Significance was set at a value of 0.05 between baseline and post training values and is identified by the asterisk (*). See Table 8 in the appendices – section ten for statistical p values.

4.6 Five to One (5:1) Work to Rest Ratio - Upper Limb

Resting Pulsatility Index: The SEC and CRT groups both displayed significant changes at PT compared to B1 and B2 measurements for the 5:1 test condition. The SEC experienced a reduction in baseline resting PI between 0.15 ± 0.73 and 0.20 ± 0.72 data points. The CRT experienced a 0.17 ± 0.50 to 0.19 ± 0.54 drop in resting PI after the PT intervention. Resting mean blood velocity decreased, with the primary decrease in resting pulsatility index due primarily to a drop in the peak systolic blood pressure.

Resting Systolic Peak Blood Pressure: The SEC and CRT groups both experienced a significant change in PT values when compared to both B1 and B2 values for the 5:1 work to rest ratio test. The largest change was observed in this variable with a drop by $3.94 \pm$

9.10 to $6.29 \pm 9.78 \text{ cm} \cdot \text{sec}^{-1}$ in the SEC group. The CRT group saw significant changes in PT values compared to both B1 and B2 values for the 5:1 work to rest ratio test as well with a decrease from 2.72 ± 8.68 to $3.86 \pm 8.94 \text{ cm} \cdot \text{sec}^{-1}$. There was no significant change between B1 and B2 in either SEC or CRT group as well as no significant changes between groups to report.

Resting Mean Blood Velocity: The SEC group experienced a significant change for the 5:1 work to rest ratio condition between PT values and baseline values, however; only for B1, a change of $1.23 \pm 3.24 \text{ cm} \cdot \text{sec}^{-1}$. The B2 values were not significant, which decreased by $0.44 \pm 3.28 \text{ cm} \cdot \text{sec}^{-1}$. The CRT group did not show a significant difference at the 5:1 work to rest ratio test for either of the baseline phases.

4.7 Five to One (5:1) Work to Rest Ratio - Lower Limb

Resting Pulsatility Index: The SEC group displayed significant changes from PT values compared to both baseline (B1,B2) measurements for the 5:1 test condition with a drop between the range of 0.42 ± 2.44 and 0.45 ± 2.36 data points for the SEC. The CRT group displayed a significant change from the initial baseline measurement with a decrease of 0.31 ± 2.18 data points. The second baseline measurement did not show a significant difference with a decrease of 0.29 ± 2.33 data points.

Resting Systolic Peak/Mean Velocity: There were no significant changes in resting systolic peak or resting mean velocity at the lower limb for either the SEC or CRT group.

Table 4

Resting upper 5:1 test results for systolic peak (SP), mean blood velocity (MV), and pulsatility index (PI) for B1, B2 and PT for the SEC and CRT groups. Reported as mean ± standard deviation.

5:1 Ratio Test	SEC (n = 7)			CRT (n = 7)		
Resting Upper	B1	B2	PT	B1	B2	PT
SP	40.9 ±9.78	38.6 ±9.10	34.7 ±7.27*	40.8 ±8.94	39.7 ±8.68	37.0 ±6.89*
MV	14.0 ±3.24	13.2 ±3.28	12.7 ±2.93	12.5 ±2.47	11.6 ±2.53	11.6 ±2.27
PI	2.78 ±0.73	2.83 ±0.72	2.63 ±0.70*	3.14 ±0.50	3.16 ±0.54	2.97 ±0.51*
Resting Lower	B1	B2	PT	B1	B2	PT
SP	25.8 ±4.84	25.8 ±5.04	26.7 ±3.57	26.4 ±2.40	25.3 ±2.50	26.6 ±3.66
MV	6.27 ±2.34	6.10 ±2.20	6.10 ±1.90	5.49 ±1.80	5.16 ±1.50	5.33 ±1.63
PI	5.80 ±2.36	5.77 ±2.44	5.35 ±2.15*	6.70 ±2.18	6.68 ±2.33	6.39 ±2.17*

Note: Significance was set at a value of 0.05 between baseline and post training values and is indicated by the asterisk (*). See Table 9 in the appendices – section ten for statistical p values.

It was determined that the various training conditions were not significantly different in comparison when regarding the resting values before the equal work to rest ratio test (5:1) for both the upper and lower limb. In the upper limb there is a significant difference between one of the baseline measurements (B1) and mean velocity, however, if both of the baseline values were not significant it is not considered significant.

4.8 Rate of Force. As mentioned, the rate of force during each test was recorded. Please see the figures below (Figures 4 to 7).

Rate of Force: Upper during 1:1 Ratio Test

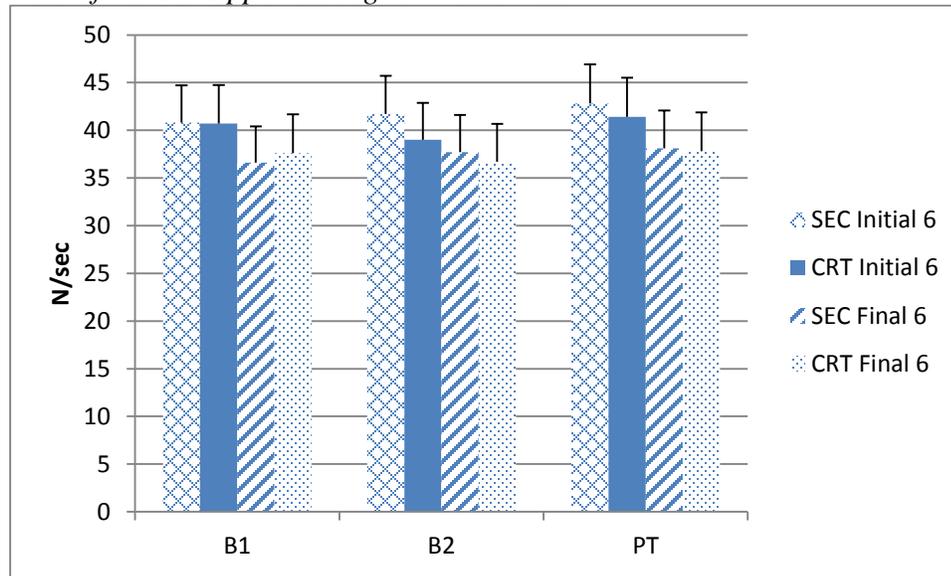


Figure 4 – Initial 6 contractions compared to the final 6 contractions during the 1:1 work to rest ratio vascular test of the upper limb. Reported as mean + standard deviation.

The rate of force comparing the initial six contractions to the final six contractions in the SEC group as well as the CRT group there was an increase in the level of fatigue (Figure 4).

Rate of Force: Lower during 1:1 Ratio Test

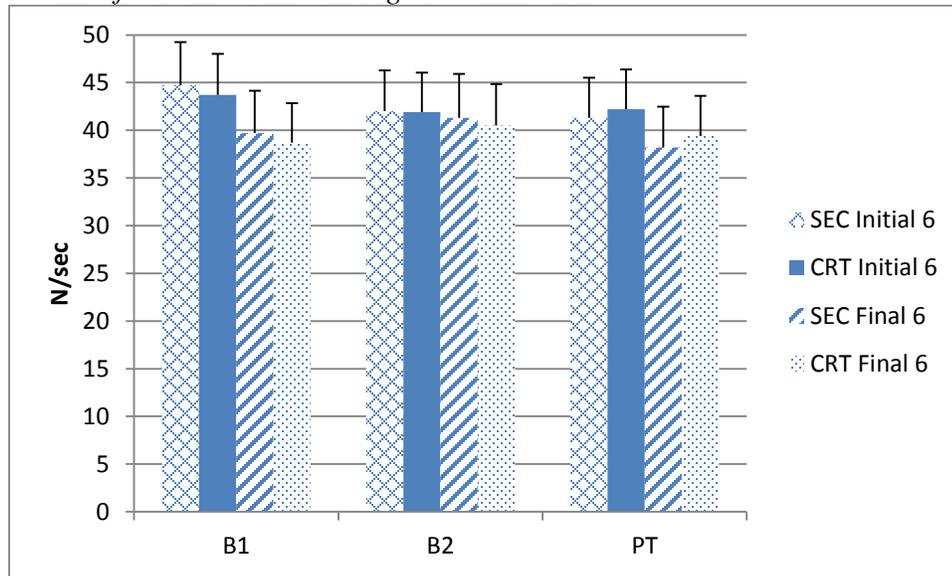


Figure 5 – Initial 6 contractions compared to the final 6 contractions during the 1:1 work to rest ratio vascular test of the lower limb. Reported as mean + standard deviation.

In figure 5, the level of force was above the 40 percent target for each group during the initial six contractions. During the post training testing session participants were more accurate with the control of the ankle flexion apparatus.

Rate of Force: Upper during 5:1 Ratio Test

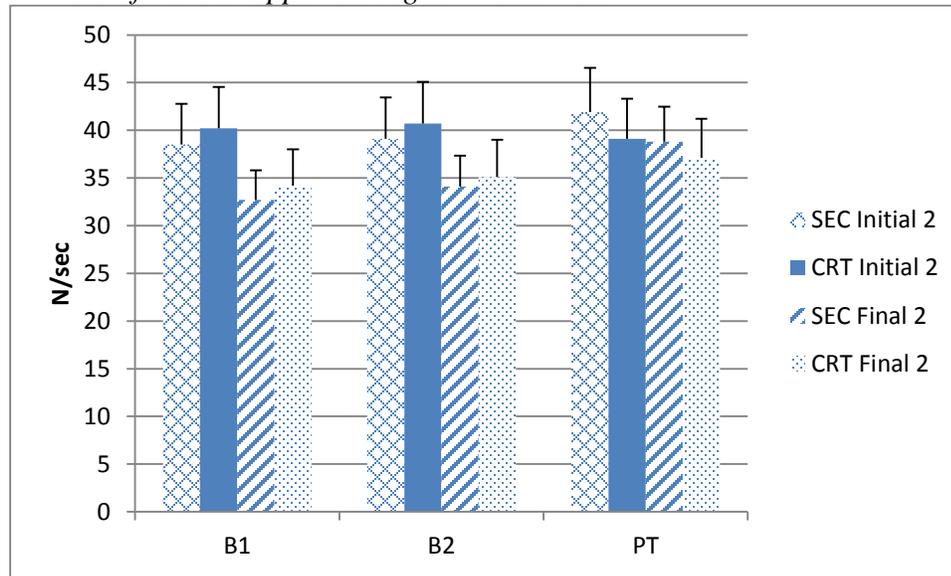


Figure 6 – Initial 2 contractions compared to the final 6 contractions during the 5:1 work to rest ratio vascular test of the upper limb. Reported as mean + standard deviation.

Figure 6 shows a large drop in fatigue from the initial six contractions to the final six contractions in both groups. This does not seem as prevalent in the post training testing session. Figure 7 shows a similar increase in the level of fatigue in the post training testing session in both the SEC and CRT groups.

Rate of Force: Lower during 5:1 Ratio Test

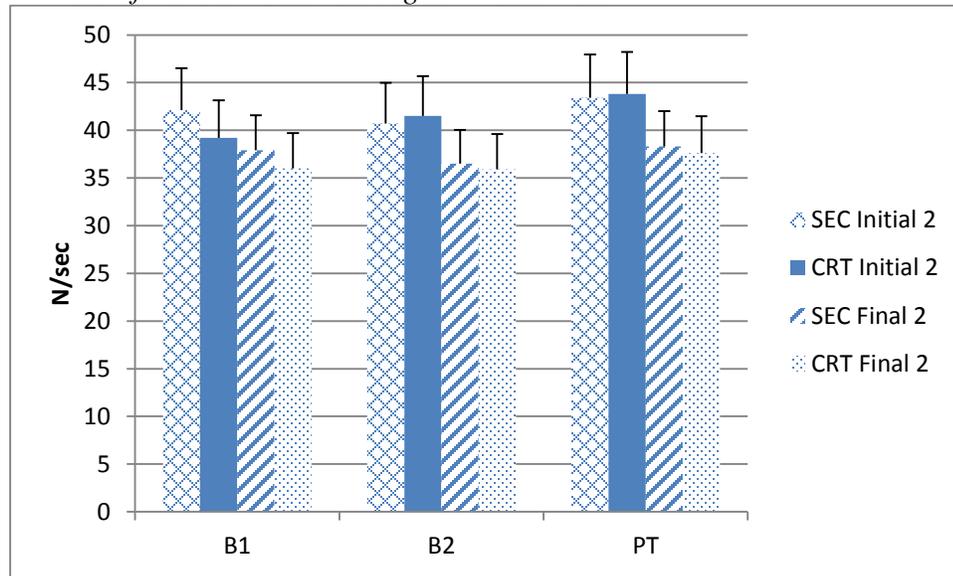


Figure 7 – Initial 2 contractions compared to the final 6 contractions during the 5:1 work to rest ratio vascular test of the lower limb. Reported as mean + standard deviation.

4.9 Post Exercise Hyperemia – (Figures 8 - 13). Despite the level of significance in the baseline and post training resting values of SP, MV, and PI values, there were only a small number of variables that proved to be significant in the post exercise measurements in the SEC and CRT group. There were additional significant differences between baseline and post-training; however, as indicated earlier, if both baseline values were not significantly different that value was not indicated as significant.

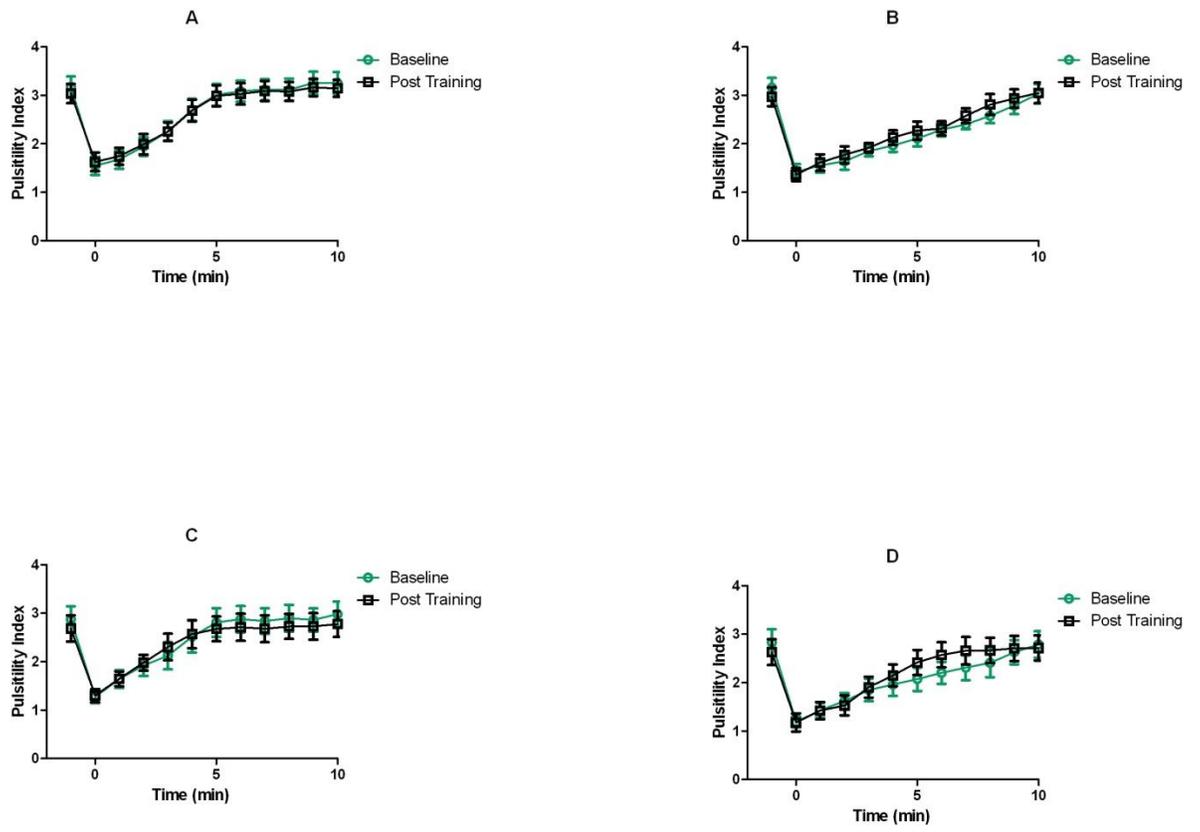


Figure 8 – Upper Body Pulsatility Index Baseline versus Post Test (A = CRT 1:1 Test, B = CRT 5:1 Test, C = SEC 1:1 Test, D = SEC 5:1 Test). Reported as mean \pm standard deviation.

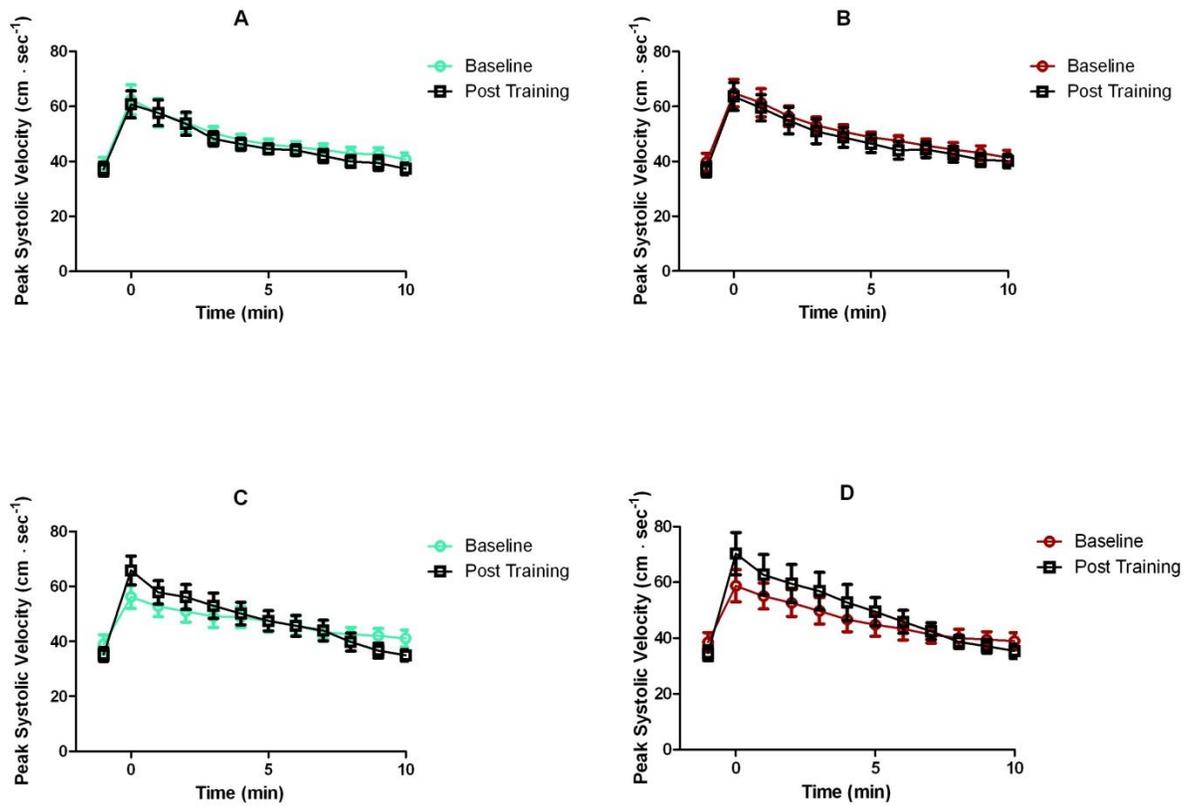


Figure 9 – Upper Body Systolic Peak Baseline versus Post Test (A = CRT 1:1 Test, B = CRT 5:1 Test, C = SEC 1:1 Test, D = SEC 5:1 Test). Reported as mean \pm standard deviation.

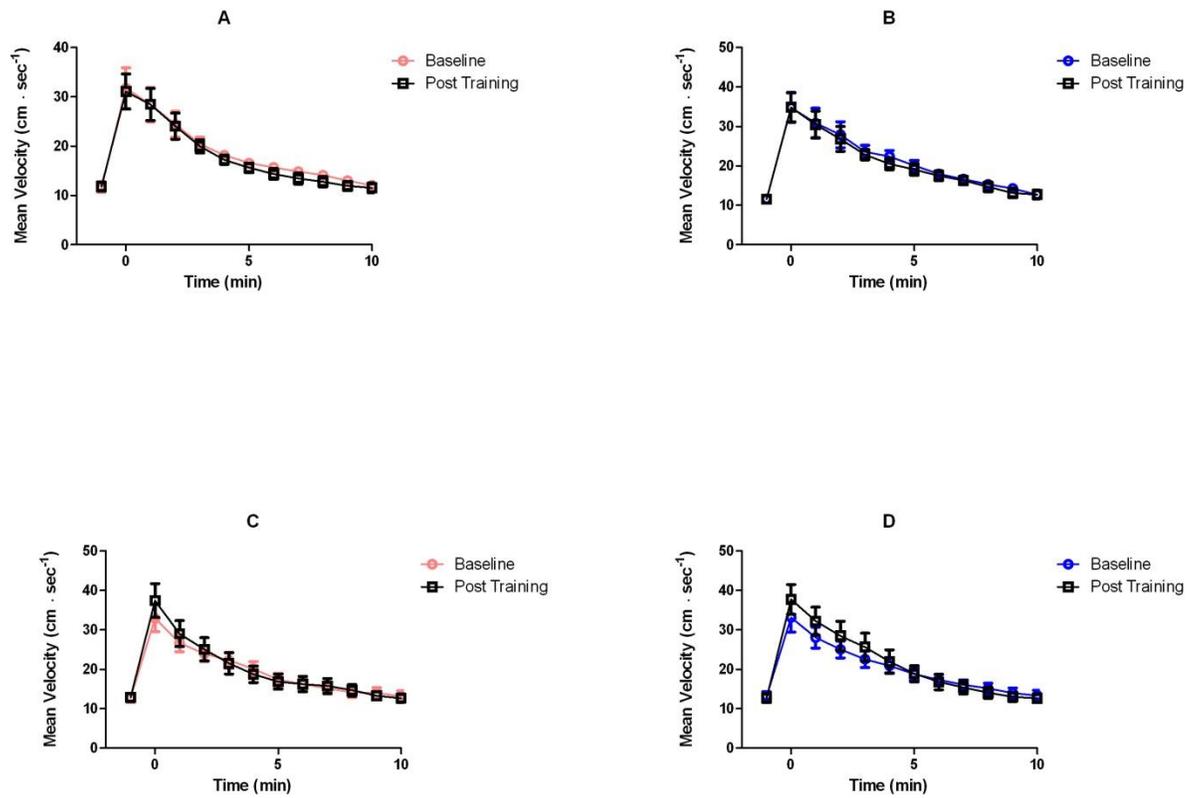


Figure 10 – Upper Body Mean Blood Velocity Baseline versus Post Test (A = CRT 1:1 Test, B = CRT 5:1 Test, C = SEC 1:1 Test, D = SEC 5:1 Test). Reported as mean ± standard deviation.

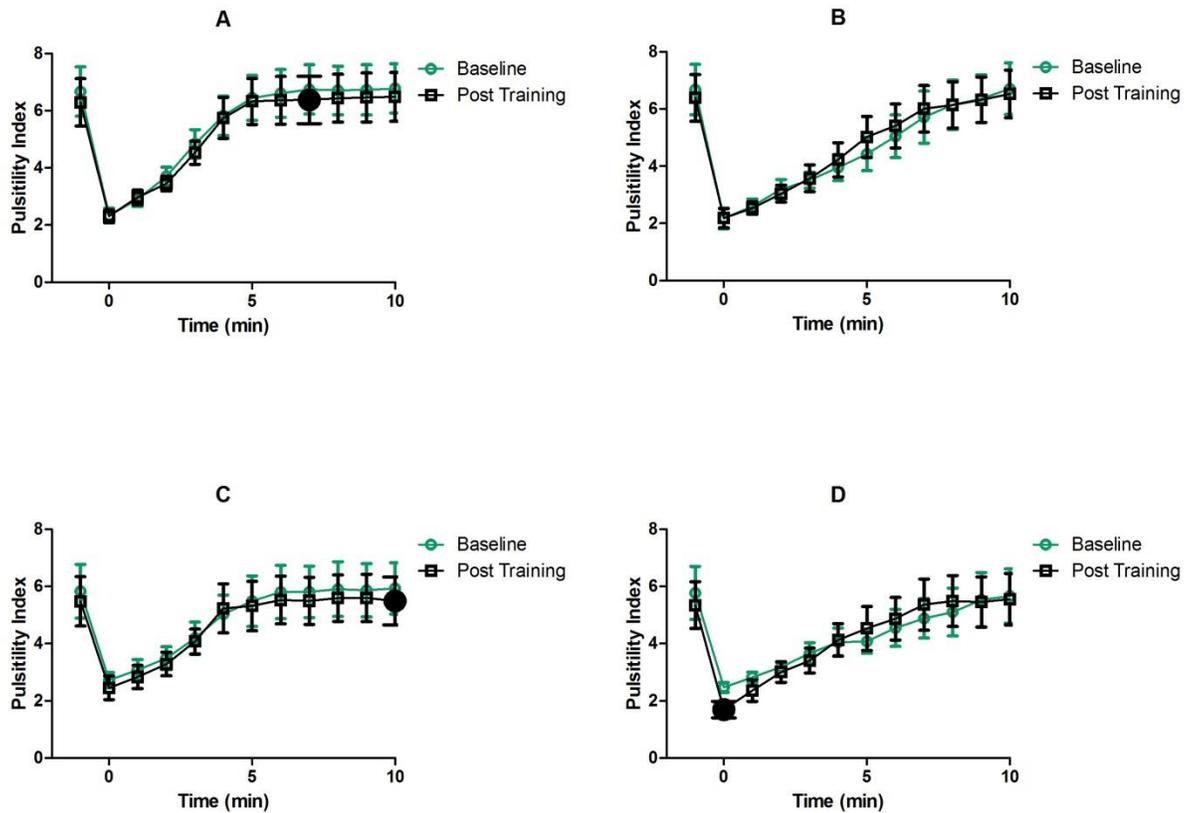


Figure 11 – Lower Body Pulsatility Index Baseline versus Post Test (A = CRT 1:1 Test, B = CRT 5:1 Test, C = SEC 1:1 Test, D = SEC 5:1 Test). Reported as mean \pm standard deviation.

In Figure 11 - panel A, there is a significant change between baseline ($B1 = 6.77 \pm 2.13$, $B2 = 6.74 \pm 2.30$) measurements and the post training value ($PT = 6.45 \pm 2.25$) at minute seven. In panel C, there is a significant difference at minute ten ($B1 = 6.05 \pm 2.36$, $B2 = 6.04 \pm 2.38$, $PT = 5.97 \pm 2.21$) as well as a significant difference at minute zero in panel D ($B1 = 2.45 \pm 0.53$, $B2 = 2.47 \pm 0.44$, $PT = 1.69 \pm 0.76$). These significant points are denoted by a large black circle in place of the black square.

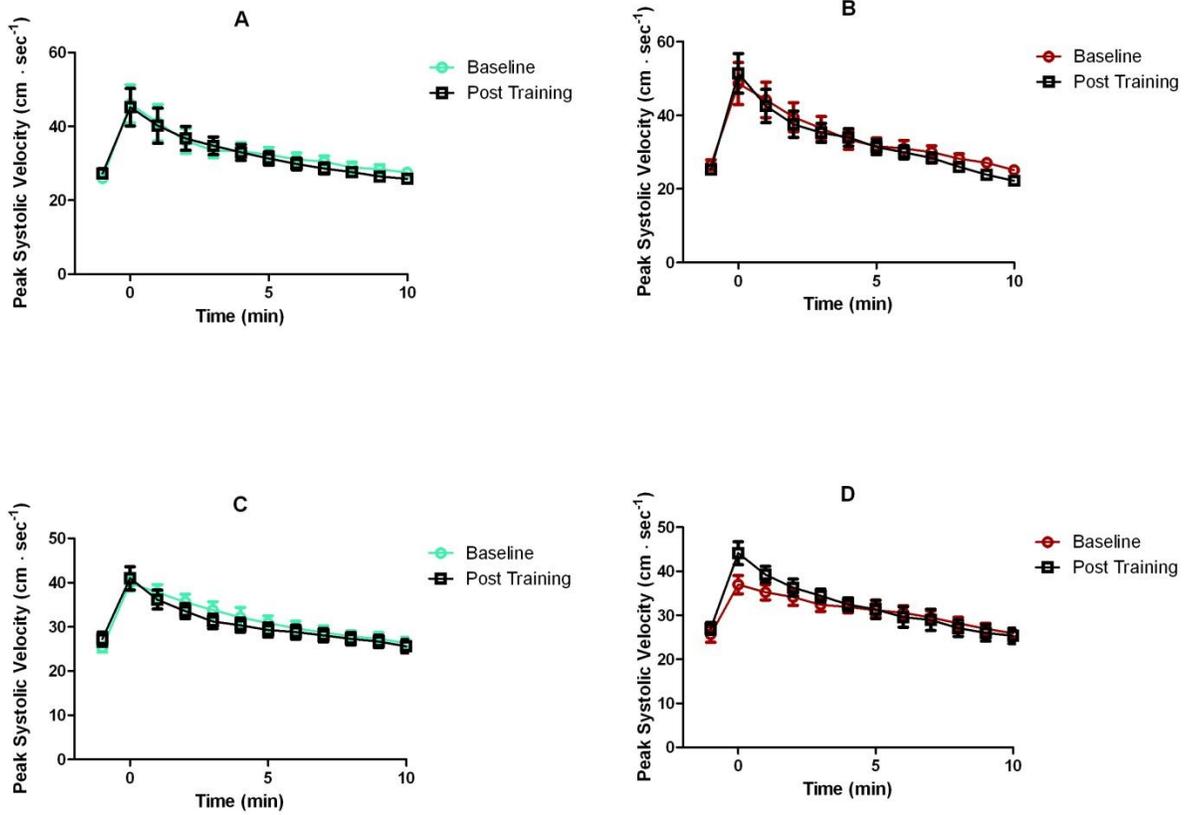


Figure 12 – Lower Body Systolic Peak Baseline versus Post Test (A = CRT 1:1 Test, B = CRT 5:1 Test, C = SEC 1:1 Test, D = SEC 5:1 Test). Reported as mean \pm standard deviation.

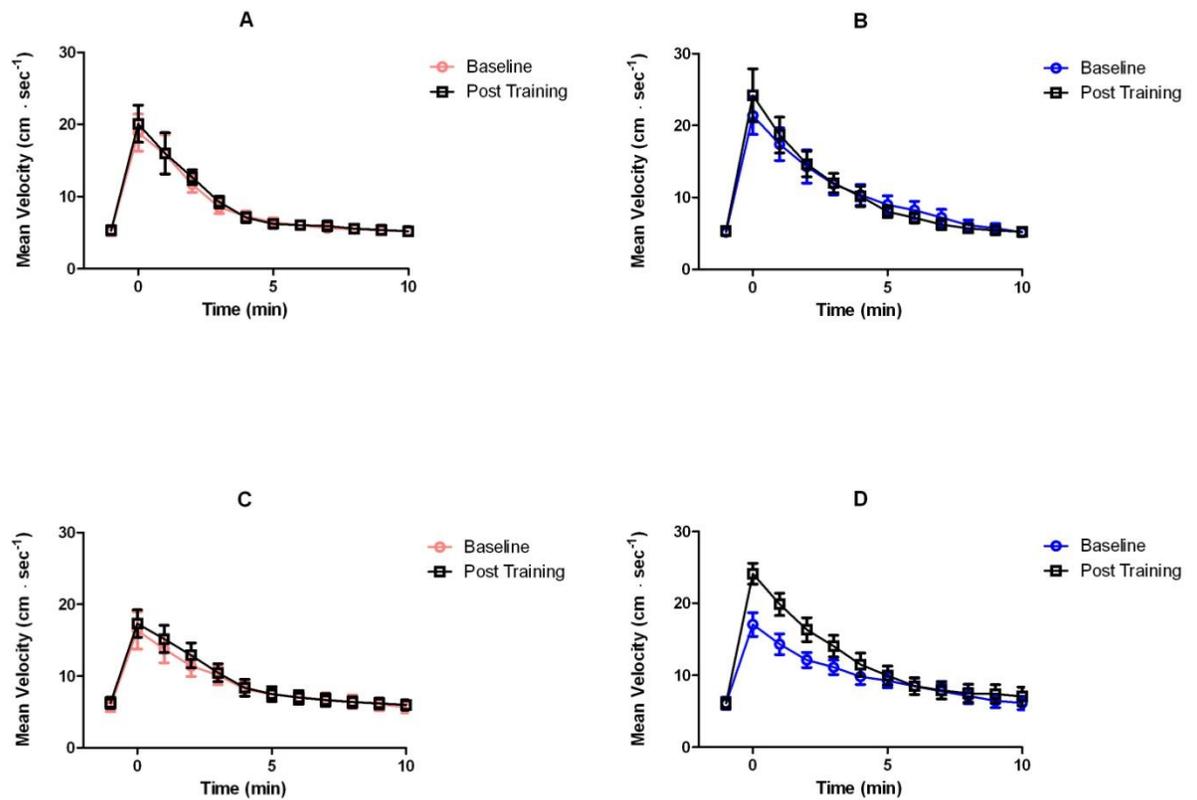


Figure 13 – Lower Body Mean Blood Velocity Baseline versus Post Test (A = CRT 1:1 Test, B = CRT 5:1 Test, C = SEC 1:1 Test, D = SEC 5:1 Test). Reported as mean \pm standard deviation.

4.10 Six Minute Walk Test. Baseline average 6MWT values for the SEC group were 527.9 ± 28.4 meters. Post intervention average 6MWT scores were 556.4 ± 36.5 meters. The pre-post values for the CRT group were 555.1 ± 27.6 meters and 571.4 ± 24.4 meters. No participant required a rest or stoppage during either the baseline or post-test. Both groups displayed a significant change between the pre and post values. There was no significance between groups. See Appendix – section ten, table ten.

4.11 Musculoskeletal Strength. Each participant increased their musculoskeletal strength. In the four foundation exercises (bench press, latissimus pull-down, shoulder press, squat)

the average absolute increase for the SEC group for each of these exercises was 4.49 ± 5.05 , 9.60 ± 6.41 , 3.09 ± 1.50 , and 14.6 ± 11.3 kgs. In comparison the change for the CRT group was 4.17 ± 4.14 , 8.80 ± 10.6 , 3.59 ± 2.5 , and 13.0 ± 11.6 kgs. These increases resulted in a significant change for each foundational exercise. There was a significant change between groups for the shoulder press and squat exercises. See Appendix – section ten, table ten.

Table 5

Exercise Parameters for the 6MWT and compound muscle activities (reported as mean \pm standard deviation)

	SEC		CRT	
	Pre-Training	Post-Training	Pre-Training	Post-Training
6MWT (m)	527.9 \pm 28.4	556.4 \pm 36.5*	555.1 \pm 27.6	571.4 \pm 24.4*
Bench Press (kg)	5.91 \pm 5.00	10.4 \pm 5.05*	6.23 \pm 3.50	10.4 \pm 4.14*
Latissimus Pull-Down (kg)	30.7 \pm 7.95	40.3 \pm 6.41*	33.8 \pm 7.91	42.6 \pm 10.6*
Shoulder Press (kg)	4.00 \pm 1.23	7.09 \pm 1.50* α	3.82 \pm 1.55	7.41 \pm 2.50* α
Squat (kg)	15.9 \pm 6.32	30.5 \pm 11.3* α	13.0 \pm 7.45	26.0 \pm 11.6* α

Note: * indicates a significance of < 0.05 between baseline and post training values. α indicates a significance of < 0.05 between SEC group and CRT group. See Table 10 in the appendices – section ten for statistical p values.

General Participant Health Data

4.12 Ankle Brachial Index. The average ankle brachial index was 1.03 ± 0.07 . Nine participants were in the ‘normal’ category (1.0-1.2) Four participants were in the ‘acceptable’ category (0.9 – 1.0), while one participant was in the ‘some arterial disease’ category.

4.13 Blood Analysis. A blood sample was taken prior to the start of the RT program. No PT sample was taken as this was a pilot study conducted over a six-week intervention. The

profiles measured can take up to three months to recognize a change in the typical population. Average triglyceride samples were 1.72 ± 0.40 mmol/L. Six participants were above the normal range of 1.70 mmol/L. Two of these participants were in the higher risk category (2.26 - 5.65). Average glucose was 5.36 ± 0.93 mmol/L. All fourteen participants were in the normal range for a two-hour fasting blood glucose test. Average cholesterol was reported at 4.39 ± 0.83 mmol/L. Eleven participants were in the normal range with three participants in the 'borderline high' category. Average hemoglobin was 15.79 ± 0.92 g/dL. All fourteen participants were in the normal range for this sample.

Discussion

5.1 Discussion. There is limited, although a growing body of evidence outlining the relationship between physical activity and endothelial function. This study explores the potential of developing a RT protocol with that targets endothelial health as the primary training response. This type of RT would be most beneficial for older individuals among others that may be susceptible to decreased endothelial function.

The most significant finding from this study is that every participant involved in the study, regardless of resistance tempo experienced a decrease in resting pulsatility index at both the upper (brachial) artery and the lower (popliteal) artery. This would suggest that their endothelial function improved, as a higher pulsatility index is indicative of greater resistance which could be associated with atherosclerotic as well as other inflammatory processes causing a narrowing in the lumen of the blood vessel. When these conditions occur, there is an increase in vessel resistance that can lead to a reduction in distal perfusion pressure and blood flow.

Another finding in this study was a change in resting systolic peak at the upper (brachial) artery that was demonstrated in both groups. This indicates that a regular, scheduled RT program, regardless of resistance tempo decreased resting systolic peak. A direct effect of this is a decrease on the demand of endothelial cells to recognize and respond to increased levels of shear stress and cyclic strain, which include triggering a variety of cellular responses that involve alterations in cell morphology, cell function, and gene expression (Ando & Yadamoto, 2011).

These findings extend our current understanding of the relation between RT and basal limb blood flow. This study acknowledges that through RT, both slow eccentric

contraction and conventional RT may improve resting arterial resistance measured through pulsatility index score in an older male population. Individuals in both the SEC and CRT group used 70 percent of their 1RM to attain the five and 12 repetition target. These numbers are based on the repetition maximum estimation equation by Bryzicki (see methodology pg. 23). These findings suggest that moderate intensity RT, regardless of contraction velocity, may be an effective strategy for increasing basal limb perfusion without the reduction in arterial compliance (Okamoto, Masuhara, Ikuta, 2011) and increase in arterial stiffness that has been associated with high intensity RT in healthy males (Miyachi et al., 2004; Cortez-Cooper et al., 2005). Further testing should be conducted to ensure RT is safe and applicable to CVD populations.

The primary goal of this study was to determine if RT can result in an improvement in resting hyperemia and post exercise hyperemia, comparing a slow eccentric RT group to individuals in a conventional RT group. Secondary variables included comparing differences in musculoskeletal strength, walking endurance, functional ability (walking impairment), body mass index, waist circumference and blood pressure between the SEC and CRT groups. Resting hyperemia did improve in all participants; however, there was no evidence to support any real improvement in post exercise hyperemia in either the SEC or CRT group. Both groups displayed significant improvements in strength, walking endurance, systolic blood pressure, mean arterial pressure, and waist circumference. There were no improvements with regard to the WIQ. This may be due to the fact that this group of participants have an active lifestyle and reported zero degree of difficulty with walking on the WIQ.

In a study conducted by Cohen et al (2007), endothelial function was examined following a 14-month resistance exercise training program in twenty-nine adults (60.5 ± 7.6 years of age) with type-2 diabetes. Endothelial function was measured using a laser Doppler flow technique which assessed the circulation in the forearm in response to vasoactive compounds. Measurements were performed at baseline, two months following the introductory training program, and at 14 months, at the conclusion of the study. After the two month introductory training program, participants were split into either a home based training program or a training center facility based program. The results demonstrated that a strength training program in adults with type-2 diabetes is associated with an improvement in endothelial dependent vasodilation at 14 months but not at a two month interval. At the end of the two month period, every endothelial dependent vasodilation testing parameter showed no change or a negative change. At the conclusion of the study, there were improvements in endothelial dependent vasodilation, suggesting that improvement in vascular response may not be purely due to improvement in endothelial function, but in addition to an enhancement of smooth muscle responsiveness to vasodilators such as nitric oxide. Despite a lower exercise compliance, limited exercise equipment, and no supervision, the home-based subjects experienced improvement in endothelial function at the conclusion of the study. Although intensity is a crucial component of RT, for long term health, the above results suggests that the duration of an exercise program may also be an important element to consider when designing a program for improvements associated with endothelial function and vascular health.

Another study examined the effect of combined resistance and aerobic training on reactive hyperemia in 39 healthy men 19 to 38 years old (Kawano, Fujimoto, Higuchi,

Miyachi, 2009). Subjects were randomly assigned into a high intensity resistance training group (HIR), a moderate intensity resistance training group (MIR) or a combination of high intensity resistance training and moderate intensity aerobic training (COMBO). Forearm blood flow was measured by using a mercury filled silastic strain-gauge plethysmograph. Measurements were taken following a reactive hyperemic procedure at three intervals, baseline, two-month interval, and upon completion of the study at four months. The results show no significant change in brachial blood pressure, resting heart rate and forearm blood flow in all groups after the initial two-month exercise intervention. After four months of training, forearm blood flow following the reactive hyperemic procedure increased significantly in the MIR and COMBO groups. Moderate intensity training increased forearm blood flow response to reactive hyperemia; however, in this case; the high intensity resistance training did not. Although the duration of repetition tempo is not stated in the article, the authors do indicate that the exercise volume of the HIR were lower than the MIR. The total time that tonic force was applied to the muscular function in the MIR group was longer compared with the HIR group. This suggests that resistance exercise completed over a longer duration (four months) with a higher volume may induce improvement of endothelial function in the microvasculature of the forearm.

Tanimoto and colleagues (2008) examined low-intensity resistance exercise with slow movement and tonic force generation versus traditional high-intensity resistance training at normal speed. Thirty-six healthy male individuals (19.0 ± 0.2 years of age) participated in the study two times per week for 13 weeks. Participants were divided among the two training groups and a control group. The training program consisted of a whole-body training session, twice weekly for 13 weeks. The slow movement training program

utilized a three second concentric phase and a three second eccentric phase. The traditional training group utilized a one second concentric phase and a one second eccentric phase. Vessel diameter and pulse wave blood velocity of the femoral artery and carotid artery were measured using a laser Doppler. Ankle brachial index was measured with a semi-automated device over the brachial and dorsalis pedis arteries. Echocardiography was used to measure left ventricular function. This study revealed that of the eleven variables tested among the three groups, the only significant ($p < 0.05$) change was mean blood velocity in the femoral artery observed in the two training groups. The findings of the Tanimoto study indicate that the slow eccentric training group experienced muscular hypertrophy and strength gain and increases in peripheral blood flow and vascular conductance comparable to the high intensity training group. This was achieved without high mechanical load which is associated with increased levels of shear stress which could be problematic for individuals with vulnerable endothelial function.

The above mentioned studies discuss various results relating to RT and endothelial health. A key trend within the available body of research, including this research thesis, is the lack of significant changes in endothelial function at or less than two months duration. This is indicative that program duration is an important factor. In addition, all studies utilized various combinations, resistance tempo and training modalities to attempt to improve endothelial function. These studies demonstrate that RT, regardless of tempo, does warrant further investigation of maintenance and improvement of endothelial health in both healthy and disease populations over the long term duration.

5.2 Limitations. As there were few significant differences found in either the SEC or CRT group in relation to post exercise hyperemia, this particular approach to improving

endothelial function in a healthy population can be eliminated from future research. Further research should include populations with greater room for improvement due to a vascular function issue to completely discredit this method of experimentation. There is substantial literature that supports slow eccentric RT as a method to enhance endothelial function through direct stimulation of the vascular system (Anton et al., 2006; Tanimoto et al., 2006). Previous studies have demonstrated that low-intensity RT with slow movement and the generation of tonic force on muscular function induces hypertrophy through the hypoxic intramuscular environment, (Tanimoto et al., 2006) and this may lead to the activation of angiogenesis. That being said, it appears the primary limitation of this study is the duration of the training program. Participants trained three times each week over a six week period. As discussed in the articles above, each study did not see significant changes after a 2-3 month training intervention. Two of these articles later showed significant results after intervals of four and 14 months (Kawano, Fujimoto, Higuchi, Miyachi, 2009; Cohen et al., 2007). Several studies (Cohen et al., 2009, Kawano, Fujimoto, Higuchi, Miyachi, 2009) provide a training program introduction that extends over a number of weeks. This is useful to familiarize participants to the type of exercises as well as correcting for breathing, technique, and tempo of the training program. In addition, this helps to decrease the initial rapid increases in strength that are experienced with new or returning exercisers that is the result of neuromuscular adaptations. The training program in combination with training experience of the participants was a major limitation. Due to varying degrees of RT experience, the program had to be tailored to the individuals with the least amount of experience; however, this could be avoided with an introductory

training program to ensure each participant is on a similar level or with individualized training.

A few challenges that may have played a factor is the health status of the participants. Although the average age of the participants was 59.4, the overall health status was above average compared to the general population in that age range. This is shown by the diagnostic tools that were used to gauge vascular health (6MWT, ABI, Blood Analysis, WIQ), as well as the self-reported healthy active lifestyle. The average ABI was 1.03 ± 0.07 . Nine participants were in the ‘normal’ category (1.0-1.2). Four participants were in the ‘acceptable’ category (0.9 – 1.0), while one participant was in the ‘some arterial disease’ category. There is no action required for the normal and acceptable categories (Aboyans et al, 2012). The recommended action for the category of ‘some arterial disease’ is the management of risk factors. Continuation of a structured physical fitness program is a major component in managing these risk factors. No participants were in the category of moderate or severe arterial disease, both of which are recommended to see a vascular specialist (Aboyans et al., 2012). As reported in the results section, no participants reported difficulty or impairment in the WIQ and displayed that in the 6MWT with above average test results for the age group. The blood analysis results also displayed normal levels for two-hr resting BG, cholesterol, and Hb with the triglyceride level being the sole variable slightly above normal.

In addition, there are two factors that may have limited the success of the project, the first being the recruitment process. The primary source of public exposure was through the UNB e-newsletter. The population that has access to this newsletter is primarily faculty, ex-faculty, alumni and current students, which may not be representative of the general

population of the greater Fredericton area. The second factor is that the study was entirely voluntary, and although perhaps not so much of a limitation as a reality of research, this may have led to a non-representative sample of older male adults. In addition, many participants communicated leading an active lifestyle and displayed an interest in the study as an alternate source of exercise throughout the winter months. These participants were self-motivated and enthusiastic about the program and were not referred by a doctor or health professional to seek a more active lifestyle. In contrast, within a population such as individuals with severe diabetes or PAD there is a greater degree of endothelial dysfunction and thus, room for more absolute, recognizable improvement.

5.3 Potential improvements of experiments and treatments. As mentioned above, the duration of the program is one of the most important components leading to an improvement in endothelial health. Individuals need to engage in a regular structured resistance exercise program three times per week for a minimum of four months. As indicated by the research, no studies examining endothelial health were able to demonstrate significant changes in less than the suggested duration. In particular, new individuals to exercise or those who have taken extended time off from exercise need an extended program to instil lifestyle changes that may help to reverse years of inactivity.

Some of the diagnostic tools that were used for this study were not representative of the population that was recruited. Tailoring the tools to the participants or more preferably tailoring the individuals to the desired assessment tools would allow these tools to be utilized to their true nature. The 6MWT and WIQ were not ideal for the participants in this study. However, these tools could be beneficial in a study involving individuals with a walking impairment as a result of endothelial dysfunction or symptoms of IC or

diagnosed PAD. This could be improved by adjusting the recruitment process to target the desired population and possibly through alternative methods of recruitment such as a doctor/hospital recommendation.

5.4 How the findings fit with current treatment options for endothelial dysfunction. The primary findings of this thesis show improvements of vascular resistance in resting pulsatility index and resting systolic peak regardless of which training protocol was applied. This decrease was due in large part to a reduced spike in peak systolic blood pressure. Current approaches to treating PAD patients is endurance training three to five times per week for a desired duration of 50 minutes, depending on stoppage time due to claudication pain. Recently, supportive literature has indicated that RT should be included in treatment options for CVD (Hornbuckle et al., 2012; Williams & Stewart, 2009). The idea of RT prescribed to a delicate population could actually trigger a cardiovascular related event such as a heart attack or stroke (Williams et al., 2007); however, recent findings suggest that much of the reasoning behind prescribing RT is relating to the secondary findings, such as increases in musculoskeletal strength and to also combat muscular atrophy. Resistance training has shown promise toward improvements in vascular function in healthy adults; however, further testing is necessary to include research on patients with CVD to determine if the same results would be observed.

5.5 Future Directions. Future experiments would benefit from the inclusion of the standardized non-invasive flow mediated dilation test to assess endothelial function through extended duration of occlusion (2-5min) and measuring the rate of reperfusion. This test uses high resolution ultrasound imaging, under baseline conditions and during hyperemia induced by inflation and deflation of a sphygmomanometer cuff. This is usually

performed around the forearm (brachial artery), distal to the site scanned with ultrasound. The induced shear stress caused by the increased blood flow following transient ischemia induces NO release, which in turn causes local arterial vasodilatation. Endothelial function is estimated as the percentage increase in vessel diameter from baseline conditions to maximum vessel diameter during hyperemia. This test is the gold standard for endothelial function and has been validated in studies involving adults with elevated cardiovascular risk factors such as smoking, PAD, hypercholesterolemia, hypertension, hyperglycemia, and hyperhomocysteinemia (Bots et al., 2004).

Future treatment interventions should include an introductory training program for a minimum of six to eight weeks depending on previous experience to allow participants to develop a basic level of mobility and understanding of the exercises as well as to ensure participants are past the neurological phase before expecting to achieve physiological muscular/vascular adaptation. For general application incorporating an aerobic component in addition to RT should be implemented; however, for research purposes the results from a RT program should be tested against the aerobic gold standard for specific rehabilitation programs. The theory of increased time under tension and slow movement moderate intensity RT are some of the most recent theories in microvascular health relating to preventative medicine. Thus, identifying intensities and duration of activities is essential to determine the most efficient strategy in progressing research forward. Heart rate monitors, calculations pertaining to repetitions, as well as questionnaires to determine perceived exertion may be helpful in this area.

Further research should incorporate patients with a known endothelial dysfunction such as participants with metabolic disorder, diabetes, severe symptoms related to CVD,

or PAD. This would enable researchers to determine if the effects of a similar RT program could improve endothelial function. A longer training period would be beneficial to ensure training experience is equalized, as some individuals progressed at a higher rate which may have impacted the results (trained versus untrained).

Physiological and Clinical Implications

6.1 Physiological and Clinical Implications. While there have been improvements in the detection and treatment of diabetes, and PAD throughout the past decade, increased attention is shifting toward extending and improving the quality of life in patients. Though pharmaceutical type therapy is commonly used to aid improvement in quality of life, they do not adequately address the physical problems encountered such as fatigue, intermittent claudication, muscular atrophy and weight gain (Campbell et al., 2004).

The present findings have potentially important physiological and clinical implications. Conventional RT increases muscle mass and strength (Kosek et al., 2006; Mero et al., 2012). It is widely accepted that such training also facilitates performance of daily tasks, and promotes spontaneous physical activity especially in the elderly and in subjects with low physical capacity (Borst, 2004; Hunter *et al.*, 2004). Several recent studies showed the beneficial influence of high-intensity RT on vascular function, contributing to increases in basal whole leg blood flow (Miyachi et al., 2005; Anton et al., 2006). The present study in older male adults suggested that the RT program, regardless of tempo, resulted in an improvement in resting pulsatility index in the upper and lower limb for both protocols, as well as resting systolic peak in the upper limb for both testing protocols, musculoskeletal strength, and walking endurance. In addition, RT is not associated with reduced central arterial compliance (Miyachi et al., 2005; Cortez-Cooper et al., 2005; Okamoto et al, 2006) as well as increased arterial stiffness, marked elevation of blood pressure thereby increasing shear stress on the vasculature (Tanimoto & Ishii, 2006). Thus, RT may be a safe and effective method of exercise for increasing peripheral blood flow.

In addition to the characteristic reduction in blood flow to the lower limbs, conditions such as diabetes and PAD have been shown to reduce the amount of blood flow to the heart and brain. Both of these conditions are also likely to be a sign of a more widespread accumulation of fatty deposits in the arteries which is attributable to increased risk of cardiovascular disease, stroke and early mortality. This direction of research will provide insight into how different duty cycles used during RT effect the dilatory capacity in patients with a known endothelial dysfunction. This research may help to develop a deeper understanding of the compromised vascular system that occurs as a result of aging. In future developments the efficacy of this treatment option may further be applied to the inclusion of conditions related to the development of CVD.

Conclusion

7.1 Conclusion. Many studies that incorporate training programs designed for individuals with CVD experience improvements in the vascular system indirectly by targeting improvements in hypertrophy and activities of daily living (Adams et al., 2006; McDermott et al., 2009; Okamoto, Masuhara, Ikuta, 2007; Wang et al, 2009). The theory of targeting the endothelial system directly is a novel and innovative approach that, through further research may help develop treatment exercise strategies as a primary approach to further improving rehabilitation and more importantly prevention of CVD.

The results of the present study indicated that RT increased basal blood flow may have improved vascular conductance at rest. RT is proposed as a safe and useful exercise method for muscular hypertrophy and strength gain, but also for increasing peripheral blood flow and vascular conductance as an additional effect. This study investigated preventative effects for healthy individuals, not curative effects for patients with metabolic syndrome, diabetes, PAD, or other diseases relating to CVD. Expanding this research to cover investigation of patient groups is recommended for future consideration.

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Appendix – Section One

PILOT STUDY: Participants performed two tests, each consisting of 80 second contractions. One test was a constant 80 second contraction and the other was a 160 second test with one second contractions paired with one second rest between each repetition. Recovery period was measured for seven minutes upon the completion of each test. Figure 9 shows the seven minute recovery period after each test protocol. The test protocol that consisted of a 1:1 work to rest ratio reaches the baseline value much faster than the test with the constant work rate.

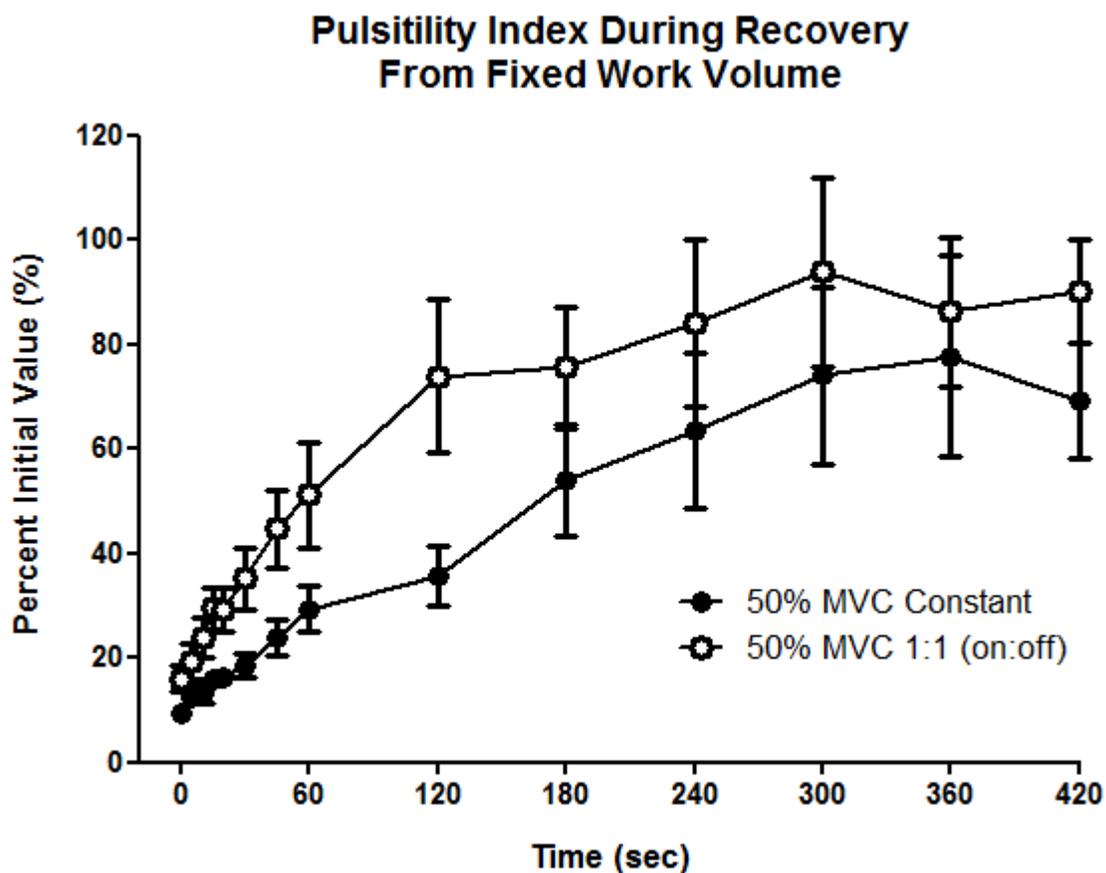


Figure 9: Pulsatility Index trace of a seven minute recovery period after an 80 second constant contraction and 160 second one second work to rest ratio test.

Appendix – Section Two

PROJECT TITLE: The examination of the effect of slow concentric resistance training on vascular function in older adults

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YOU ARE INVITED TO PARTICIPATE IN THE FOLLOWING RESEARCH STUDY BEING CONDUCTED IN THE FACULTY OF KINESIOLOGY AT THE UNIVERSITY OF NEW BRUNSWICK. THIS PROJECT HAS BEEN REVIEWED BY THE RESEARCH ETHICS BOARD OF THE UNIVERSITY OF NEW BRUNSWICK AND IS ON FILE AS REB 2012-038.

BACKGROUND

Aging is a well-documented cardiovascular risk factor because blood vessels can lose their ability to dilate fully as we get older. These arteries become more rigid and narrow preventing blood from reaching and nourishing our tissues; especially during exercise. In extreme cases this results in peripheral artery disease; a condition that causes pain in the lower legs with exertion. The traditional frontline treatment for improving dilator function and peripheral artery disease is walking-based aerobic exercise. The repeated muscle contractions help stimulate the blood vessels to dilate and over time can reduce the pain associated with walking.

Resistance training is also used to help patients with peripheral artery disease. The goal of resistance training is to increase muscle size and strength size to counteract the muscle wasting that often occurs with diminished blood vessel function. Resistance exercise should also restore some lost vasodilator function however; this has not been well studied. In this study, we intend to evaluate how effective resistance training exercise is for improving vasodilator function in older adults.

APPLICATION OF THE STUDY

The purpose of this work is to determine if resistance training with a slow contraction speed will improve the dilatory capacity better than conventional resistance training protocols that use fast contraction speeds. This may result in the development of evidence based guidelines for altering resistance exercise programs to improve vasodilatory capacity in older adults.

EXPERIMENT DESIGN

- This study will involve 6 laboratory evaluation sessions to evaluate vascular function in your lower arm and leg. Two sessions will occur at the four weeks prior to the training program as a baseline measure. Two will occur at the beginning of the program and two will occur at the end of the program. You will need to wear a loose fitting short-sleeve t-shirt and shorts during each of the lab sessions. The lab sessions take place in the Kinesiology Exercise Physiology Lab located in the L.B. Gymnasium.

Each lab session will take approximately one hour (6 laboratory hrs. total).

- Each volunteer will participate in a six week supervised resistance training program **appropriate for your age and capability**. The program is supervised by a Canadian Society for Exercise Physiology Certified Personal Trainer®. The training program consists of three one hour sessions per week for six weeks. Training sessions will run week days (Monday thru Friday) and each session will be separated by a minimum of 24 hours.

Total time commitment for the resistance training program is 18 hrs (3 hrs per week over 6 weeks). In addition, please allocate time for travel and changing clothes before and after each session.

DETAILS OF LABORATORY EVALUATION SESSIONS:

These sessions are designed to measure how well the blood vessels in your arms and legs dilate.

Recording equipment: Non-invasive sensors are placed on your skin over top of the muscle and blood vessels of interest. Muscle activity (electromyography) is measured using small sticky disks with wires attached to recording amplifiers. The sensors record the electrical activity generated **by** your muscles. Near-Infrared Spectroscopy (NIRS) sensors shine infrared light into your skin and record light that is reflected back to the surface. This information is used to measure blood volume changes in your muscle. A small amount of ultrasound gel will be placed in the crook of your elbow and behind your knee and a pen-like Doppler ultrasound probe will be touched to your skin to measure flow flowing through an artery supplying blood to your lower arm and lower leg.

Your Tasks In These Sessions:

1) While seated comfortably, you will squeeze a lever as hard as you can for 5 to 10 seconds. This is called a Maximum Voluntary Contraction (MVC) and is used to set the criteria for the rest of the testing. A similar test will be done for the leg. You will lie face down on a padded table with your foot in a holder. You will flex your ankle as hard as you can for 5 to 10 seconds.

2) To evaluate your vascular function, each participant will perform the following tests for the arm and for the leg:

i) You will squeeze the lever or flex your ankle at 40% of your MVC strength 90 times over 180 seconds. Each contraction is held for 1 second and there is 1 second of rest between contractions. Once the task is finished, the Doppler flow probe will be used to measure the blood flow for 10 minutes while you rest to recover. You receive feedback from a computer screen while doing the tests so that you can keep proper pace and contract at the correct strength.

ii) You will squeeze the lever or flex your ankle at 40% of your MVC strength 18 times over 108 seconds. Each contraction is held for 5 seconds with one second of rest between contractions. Once the task is finished, the Doppler flow probe will be used to measure the blood flow for 10 minutes while you rest to recover. You receive feedback from a computer screen while doing the tests so that you can keep proper pace and contract at the correct strength.

iii) A blood pressure cuff will be placed around the upper arm/thigh and inflated to temporarily stop blood flow to your forearm/calf for 2 minutes. The cuff will then be deflated and blood flow will be restored. The Doppler flow probe will be used to measure the blood flow for 10 minutes while you rest to recover.

Note: Please inform us if you have a deep vein thrombosis or are receiving Warferin or Coumadin (blood thinners).

4) In **one** pre-training and **one** post-training session, we will take **one** small blood sample from a finger tip using a disposable automated lancing device. This is the same type of lancing device that a diabetic patient would use on a daily basis. During the blood sampling procedure you will feel a momentary sting when the lance produces a small cut on the tip of your finger. The painful sensation will subside quickly and there will be no lasting discomfort. The lancing device is very accurate and precise – making the cut as small and painless as possible. The dimensions of the cut are 1.5mm long by 2.0 mm deep resulting in 6 to 10 drops of blood being produced (50 to 100µL). These wounds clot and heal quickly.

DETAILS OF THE RESISTANCE TRAINING PROGRAM:

- All training sessions will be guided by a CSEP Certified Personal Trainer. Participants will receive education on the principles of strength training relating to vascular function and will be familiarized with the strength training equipment and exercises that will be used throughout the program. Attention will be designated to the safety of the participants while performing the resistance training exercises.
- The training program will last for 6 weeks. You are required to attend three 1-hour training sessions each week for 6 weeks. The sessions will be held Monday through Friday in either the morning or evening. You must allow 24hrs of rest between sessions, with a maximum of two consecutive days in a row. Attendance will be recorded and each participant must attend 80% (14 of 18) of the sessions in order for the data to be included in the study.
- The protocol for each session will be:
 - i) 10 minutes of warm-up activities such as walking and stretching.
 - ii) 40 minutes of moderate intensity resistance training using a combination of free weights and resistance machines.
 - iii) 10 minutes of cool activity such as walking and stretching.
- There are two experimental groups in this study. One group will perform the resistance exercise to the tempo of 1 second lift, 1 second hold, 1 second return. The other group will perform the exercises to the tempo of 1 second lift, 1 second hold, 4 seconds return.
- Each resistance training session will involve 8-10 exercises and you will complete 2 to 3 sets of each exercise. A set involves approximately 30 seconds of muscle work with one minute of rest between each set.
- The weights used in this program are set to the individual participant's ability and will represent 60 to 70% of their repetition maximum, making this program a ***moderate intensity program***. During the program you should feel as though you are exerting some effort, you should feel warmer than at rest, you may sweat a bit, your heart rate will increase somewhat and you might breathe a little more quickly. You should not feel as though you are exerting your maximal effort to perform the exercises and each training session should feel tired but not exhausted.
- Those unaccustomed to exercise may be somewhat stiff and sore after the first few training sessions. This is normal and part of the adaptation your muscle undergoes as it becomes more trained. The trainer will show you some stretches that can alleviate some discomfort. The initial soreness should disappear after the first few sessions and is unlikely to appear again during the program.

POTENTIAL RISKS AND DISCOMFORTS

Engaging in resistance training with proper supervision poses little risk. During the resistance training sessions you may feel a “burning sensation” associated with intense muscular effort. You may hold your breath in order to maintain the effort. This may cause your heart rate and blood pressure to increase slightly. All of these responses are normal and associated with muscular effort. Once the muscular effort stops the sensations will rapidly reverse back to normal. You may experience delayed muscle soreness after completion each session. This sensation will feel like tightness in your muscles. Stretching and proper nutrition will help in decreasing this effect. This feeling will begin to decrease throughout the program as your body adapts to the program.

During the laboratory evaluation, when we stop the flow of blood to your forearm with the blood pressure cuff your arm will begin to feel like it has fallen asleep with a “pins and needles” sensation. This sensation will fade and your arm will become numb. Once the blood flow is restored the sensations will reverse and you will feel pins and needles again briefly before returning to normal sensations. **Stopping blood flow to your arm for 2 minutes will not produce any lasting effect or impairment.**

The techniques and equipment used to assess arterial pulse waves and muscle oxygenation pose no identifiable risk to you. Individuals that have known allergies to the adhesive in medical tape or an allergy to ultrasound gel should not participate in this study.

The activities you perform in this study pose minimal risk to you, the participant. ***Participation in this study is strictly voluntary, and thus you are free to withdraw at any time.***

POTENTIAL BENEFITS TO SUBJECTS AND/OR SOCIETY

The minimum physical activity requirements for Health Canada are 150 minutes per week. Participation in this study meets these requirements (180 min/wk). We will provide you with feedback on group results should you wish. The results of this study will enable us to better understand the changes in arterial blood flow that occur before, during and after exercise. This may lead to better strategies that result in early detection and treatment of blood flow abnormalities for the purpose of preventing the development and progression of vascular disease.

CONFIDENTIALITY

Any information that is obtained in connection with this study and that can be identified with you will remain completely confidential and will only be disclosed with your permission. Only the investigators will have access to the data. All data will be stored in a locked environment within the principle investigator’s office at the University of New Brunswick and will remain there for a period of two years, at which point it will be destroyed. A participant ID number in place of your name will be used to code all data and as such you will not be identified. In addition, the results of the study will not include your individual data unless you have given prior consent.

PARTICIPATION AND WITHDRAWAL

You can choose whether to be in this study or not. If you volunteer to be in this study, you may withdraw at any time without consequences of any kind. During the data collection you may exercise the option of removing your data from the study. You may also refuse to answer any questions you don't want to answer and still remain in the study.

QUESTIONS

Should you have any questions regarding this project, feel free to address them to the principal investigator. If you wish to speak to someone not associated with the project, please feel free to contact Dr. Wayne Albert, Dean of the Faculty of Kinesiology (506)453.4576, or Stephen Turner, Chair of the University of New Brunswick's Ethics Review Board (ethics@unb.ca), (506)453.5189.

If you wish to volunteer in this study, please complete the section on the next page. Thank you for your participation.

CONSENT FORM

The purpose of this study has been explained to me by _____ . I have understood the information, including the risks of participation, and agree to participate in the study. I have been given a copy of the Consent form, which I have read and understood. I have been given an opportunity to ask questions about the study and my participation, and I understand that I may ask questions at any time.

By signing this form, I agree to participate in the study with the understanding that I may withdraw from it at any time, without penalty.

_____	_____	_____
Name of Participant (Print)	Signature of Participant	Date
_____	_____	_____
Witness (Print)	Signature of Witness	Date

.....

If you wish to be informed of the research results, please provide contact information.

Name:

Address:

Telephone #:

Email address:

Appendix – Section Three

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	
<input type="checkbox"/>	<input type="checkbox"/>	1. Has your doctor ever said that you have a heart condition <u>and</u> that you should only do physical activity recommended by a doctor?
<input type="checkbox"/>	<input type="checkbox"/>	2. Do you feel pain in your chest when you do physical activity?
<input type="checkbox"/>	<input type="checkbox"/>	3. In the past month, have you had chest pain when you were not doing physical activity?
<input type="checkbox"/>	<input type="checkbox"/>	4. Do you lose your balance because of dizziness or do you ever lose consciousness?
<input type="checkbox"/>	<input type="checkbox"/>	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?
<input type="checkbox"/>	<input type="checkbox"/>	6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?
<input type="checkbox"/>	<input type="checkbox"/>	7. Do you know of <u>any other reason</u> why you should not do physical activity?

If
you
answered

YES to one or more questions

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

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

NO to all questions

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

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

DELAY BECOMING MUCH MORE ACTIVE:

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

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

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

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

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

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

NAME _____

SIGNATURE _____

DATE _____

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

WITNESS _____

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



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Appendix – Section Four

Physical Activity Readiness
Medical Examination
(revised 2002)

PARmed-X

PHYSICAL ACTIVITY READINESS MEDICAL EXAMINATION

The PARmed-X is a physical activity-specific checklist to be used by a physician with patients who have had positive responses to the Physical Activity Readiness Questionnaire (PAR-Q). In addition, the Conveyance/Referral Form in the PARmed-X can be used to convey clearance for physical activity participation, or to make a referral to a medically-supervised exercise program.

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. The PAR-Q by itself provides adequate screening for the majority of people. However, some individuals may require a medical evaluation and specific advice (exercise prescription) due to one or more positive responses to the PAR-Q.

Following the participant's evaluation by a physician, a physical activity plan should be devised in consultation with a physical activity professional (CSEP-Certified Personal Trainer™ or CSEP-Certified Exercise Physiologist™). To assist in this, the following instructions are provided:

PAGE 1: Sections A, B, C, and D should be completed by the participant BEFORE the examination by the physician. The bottom section is to be completed by the examining physician.

PAGES 2 & 3: A checklist of medical conditions requiring special consideration and management.

PAGE 4: Physical Activity & Lifestyle Advice for people who do not require specific instructions or prescribed exercise.

Physical Activity Readiness Conveyance/Referral Form - an optional tear-off tab for the physician to convey clearance for physical activity participation, or to make a referral to a medically-supervised exercise program.

This section to be completed by the participant									
<p>A PERSONAL INFORMATION:</p> <p>NAME _____</p> <p>ADDRESS _____</p> <p>TELEPHONE _____</p> <p>BIRTHDATE _____ GENDER _____</p> <p>MEDICAL No. _____</p>	<p>B PAR-Q: Please indicate the PAR-Q questions to which you answered YES</p> <p><input type="checkbox"/> Q1 Heart condition</p> <p><input type="checkbox"/> Q2 Chest pain during activity</p> <p><input type="checkbox"/> Q3 Chest pain at rest</p> <p><input type="checkbox"/> Q4 Loss of balance, dizziness</p> <p><input type="checkbox"/> Q5 Bone or joint problem</p> <p><input type="checkbox"/> Q6 Blood pressure or heart drugs</p> <p><input type="checkbox"/> Q7 Other reason:</p>								
<p>C RISK FACTORS FOR CARDIOVASCULAR DISEASE: <i>Check all that apply</i></p> <p><input type="checkbox"/> Less than 30 minutes of moderate physical activity most days of the week.</p> <p><input type="checkbox"/> Excessive accumulation of fat around waist.</p> <p><input type="checkbox"/> Currently smoker (tobacco smoking 1 or more times per week).</p> <p><input type="checkbox"/> Family history of heart disease.</p> <p><input type="checkbox"/> High blood pressure reported by physician after repeated measurements.</p> <p><input type="checkbox"/> High cholesterol level reported by physician.</p> <p><i>Please note: Many of these risk factors are modifiable. Please refer to page 4 and discuss with your physician.</i></p>	<p>D PHYSICAL ACTIVITY INTENTIONS:</p> <p>What physical activity do you intend to do?</p> <p>_____</p> <p>_____</p> <p>_____</p>								
This section to be completed by the examining physician									
<p>Physical Exam:</p> <table border="1"> <tr> <td>Ht</td> <td>Wt</td> <td>BP (i)</td> <td>/</td> </tr> <tr> <td></td> <td></td> <td>BP (ii)</td> <td>/</td> </tr> </table> <p>Conditions limiting physical activity:</p> <p><input type="checkbox"/> Cardiovascular <input type="checkbox"/> Respiratory <input type="checkbox"/> Other</p> <p><input type="checkbox"/> Musculoskeletal <input type="checkbox"/> Abdominal</p> <p>Tests required:</p> <p><input type="checkbox"/> ECG <input type="checkbox"/> Exercise Test <input type="checkbox"/> X-Ray</p> <p><input type="checkbox"/> Blood <input type="checkbox"/> Urinalysis <input type="checkbox"/> Other</p>	Ht	Wt	BP (i)	/			BP (ii)	/	<p>Physical Activity Readiness Conveyance/Referral:</p> <p>Based upon a current review of health status, I recommend:</p> <p><input type="checkbox"/> No physical activity</p> <p><input type="checkbox"/> Only a medically-supervised exercise program until further medical clearance</p> <p><input type="checkbox"/> Progressive physical activity:</p> <p><input type="checkbox"/> with avoidance of: _____</p> <p><input type="checkbox"/> with inclusion of: _____</p> <p><input type="checkbox"/> under the supervision of a CSEP-Certified Exercise Physiologist™</p> <p><input type="checkbox"/> Unrestricted physical activity—start slowly and build up gradually</p> <p>Further information:</p> <p><input type="checkbox"/> Attached</p> <p><input type="checkbox"/> To be forwarded</p> <p><input type="checkbox"/> Available on request</p>
Ht	Wt	BP (i)	/						
		BP (ii)	/						



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PARmed-X PHYSICAL ACTIVITY READINESS MEDICAL EXAMINATION

Following is a checklist of medical conditions for which a degree of precaution and/or special advice should be considered for those who answered "YES" to one or more questions on the PAR-Q, and people over the age of 69. Conditions are grouped by system. Three categories of precautions are provided. Comments under Advice are general, since details and alternatives require clinical judgement in each individual instance.

	Absolute Contraindications	Relative Contraindications	Special Prescriptive Conditions	
	Permanent restriction or temporary restriction until condition is treated, stable, and/or post-acute phase.	Highly variable. Value of exercise testing and/or program may exceed risk. Activity may be restricted. Desirable to maximize control of condition. Direct or indirect medical supervision of exercise program may be desirable.	Individualized prescriptive advice generally appropriate: - limitations imposed, and/or - special exercises prescribed. May require medical monitoring and/or initial supervision in exercise program.	
				ADVICE
Cardiovascular	<input type="checkbox"/> aortic aneurysm (dissecting) <input type="checkbox"/> aortic stenosis (severe) <input type="checkbox"/> congestive heart failure <input type="checkbox"/> crescendo angina <input type="checkbox"/> myocardial infarction (acute) <input type="checkbox"/> myocarditis (active or recent) <input type="checkbox"/> pulmonary or systemic embolism—acute <input type="checkbox"/> thrombophlebitis <input type="checkbox"/> ventricular tachycardia and other dangerous dysrhythmias (e.g., multifocal ventricular activity)	<input type="checkbox"/> aortic stenosis (moderate) <input type="checkbox"/> subaortic stenosis (severe) <input type="checkbox"/> marked cardiac enlargement <input type="checkbox"/> supraventricular dysrhythmias (uncontrolled or high rate) <input type="checkbox"/> ventricular ectopic activity (repetitive or frequent) <input type="checkbox"/> ventricular aneurysm <input type="checkbox"/> hypertension—untreated or uncontrolled severe (systemic or pulmonary) <input type="checkbox"/> hypertrophic cardiomyopathy <input type="checkbox"/> compensated congestive heart failure	<input type="checkbox"/> aortic (or pulmonary) stenosis—mild angina pectoris and other manifestations of coronary insufficiency (e.g., post-acute infarct) <input type="checkbox"/> cyanotic heart disease <input type="checkbox"/> shunts (intermittent or fixed) <input type="checkbox"/> conduction disturbances - complete AV block - left BBB - Wolf-Parkinson-White syndrome <input type="checkbox"/> dysrhythmias—controlled <input type="checkbox"/> fixed rate pacemakers <input type="checkbox"/> intermittent claudication <input type="checkbox"/> hypertension: systolic 160-180, diastolic 105+	<ul style="list-style-type: none"> - clinical exercise test may be warranted in selected cases, for specific determination of functional capacity and limitations and precautions (if any). - slow progression of exercise to levels based on test performance and individual tolerance. - consider individual need for initial conditioning program under medical supervision (indirect or direct).
Infections	<input type="checkbox"/> acute infectious disease (regardless of etiology)	<input type="checkbox"/> subacute/chronic/recurrent infectious diseases (e.g., malaria, other)	<input type="checkbox"/> chronic infections <input type="checkbox"/> HIV	variable as to condition
Metabolic		<input type="checkbox"/> uncontrolled metabolic disorders (diabetes mellitus, thyrotoxicosis, myxedema)	<input type="checkbox"/> renal, hepatic & other metabolic insufficiency <input type="checkbox"/> obesity <input type="checkbox"/> single kidney	variable as to status dietary moderation, and initial light exercises with slow progression (walking, swimming, cycling)
Pregnancy		<input type="checkbox"/> complicated pregnancy (e.g., toxemia, hemorrhage, incompetent cervix, etc.)	<input type="checkbox"/> advanced pregnancy (late 3rd trimester)	refer to the "PARmed-X for PREGNANCY"

References:

Arak, G.A., Wigle, D.T., Mac, Y. (1992). Risk Assessment of Physical Activity and Physical Fitness in the Canada Health Survey Follow-Up Study. *J. Clin. Epidemiol.* 45:419-433.

Mottola, M., Wolfe, L.A. (1994). Active Living and Pregnancy. In: A. Quinney, L. Gauvin, T. Wolf (eds.), **Toward Active Living: Proceedings of the International Conference on Physical Activity, Fitness and Health**. Champaign, IL: Human Kinetics.

PAR-Q Validation Report, British Columbia Ministry of Health, 1978.

Thomas, S., Reading, J., Shephard, R.J. (1992). Revision of the Physical Activity Readiness Questionnaire (PAR-Q). *Can. J. Sp. Sci.* 17: 433B-345.

The PAR-Q and PARmed-X were developed by the British Columbia Ministry of Health. They have been revised by an Expert Advisory Committee of the Canadian Society for Exercise Physiology chaired by Dr. N. Gedhill (2002).

No changes permitted. You are encouraged to photocopy the PARmed-X, but only if you use the entire form.

Disponible en français sous le titre
«Évaluation médicale de l'aptitude à l'activité physique (X-AAP)»

Continued on page 3...

Physical Activity Readiness
Medical Examination
(revised 2002)

	Special Prescriptive Conditions	ADVICE
Lung	<input type="checkbox"/> chronic pulmonary disorders	special relaxation and breathing exercises
	<input type="checkbox"/> obstructive lung disease	breath control during endurance exercises to tolerance; avoid polluted air
	<input type="checkbox"/> asthma	
	<input type="checkbox"/> exercise-induced bronchospasm	avoid hyper ventilation during exercise; avoid extremely cold conditions; warm up adequately; utilize appropriate medication.
Musculoskeletal	<input type="checkbox"/> lowback conditions (pathological, functional)	avoid or minimize exercise that precipitates or exacerbates e.g., forced extreme flexion, extension, and violent twisting; correct posture; proper back exercises
	<input type="checkbox"/> arthritis—acute (infective, rheumatoid, gout)	treatment, plus judicious blend of rest, spinning and gentle movement
	<input type="checkbox"/> arthritis—subacute	progressive increase of active exercise therapy
	<input type="checkbox"/> arthritis—chronic (osteoarthritis and other conditions)	maintenance of mobility and strength; non-weightbearing exercises to minimize joint trauma (e.g., cycling, aquatic activity, etc.)
	<input type="checkbox"/> orthopaedic	highly variable and individualized
	<input type="checkbox"/> hernia	minimize straining and isometrics; strengthen abdominal muscles
	<input type="checkbox"/> osteoporosis or low bone density	avoid exercise with high risk for fracture such as push-ups, curl-ups, vertical jump and trunk forward flexion; engage in low-impact weight-bearing activities and resistance training
CNS	<input type="checkbox"/> convulsive disorder not completely controlled by medication	minimize or avoid exercise in hazardous environments and/or exercising alone (e.g., swimming, mountain climbing, etc.)
	<input type="checkbox"/> recent concussion	thorough examination if history of two concussions; review for discontinuation of contact sport if three concussions, depending on duration of unconsciousness, retrograde amnesia, persistent headaches, and other objective evidence of cerebral damage
Blood	<input type="checkbox"/> anemia—severe (< 10 Gm/dl)	control preferred; exercise as tolerated
	<input type="checkbox"/> electrolyte disturbances	
Medications	<input type="checkbox"/> antianginal	NOTE: consider underlying condition. Potential for: exertional syncope, electrolyte imbalance, bradycardia, dysrhythmias, impaired coordination and reaction time, heat intolerance. May alter resting and exercise ECG's and exercise test performance.
	<input type="checkbox"/> antihypertensive	
<input type="checkbox"/> beta-blockers		
<input type="checkbox"/> diuretics		
<input type="checkbox"/> others		
<input type="checkbox"/> antiarrhythmic		
	<input type="checkbox"/> anti-convulsant	
	<input type="checkbox"/> digitalis preparations	
	<input type="checkbox"/> ganglionic blockers	
Other	<input type="checkbox"/> post-exercise syncope	moderate program
	<input type="checkbox"/> heat intolerance	prolong cool-down with light activities; avoid exercise in extreme heat
	<input type="checkbox"/> temporary minor illness	postpone until recovered
	<input type="checkbox"/> cancer	if potential metastases, test by cycle ergometry; consider non-weight bearing exercises; exercise at lower end of prescriptive range (40-65% of heart rate reserve), depending on condition and recent treatment (radiation, chemotherapy); monitor hemoglobin and lymphocyte counts; add dynamic lifting exercise to strengthen muscles, using machines rather than weights.

*Refer to special publications for elaboration as required

The following companion forms are available online: <http://www.csep.ca/bms>

The **Physical Activity Readiness Questionnaire (PAR-Q)** - a questionnaire for people aged 15-69 to complete before becoming much more physically active.

The **Physical Activity Readiness Medical Examination for Pregnancy (PARMed-X for PREGNANCY)** - to be used by physicians with pregnant patients who wish to become more physically active.

For more information, please contact the:

Canadian Society for Exercise Physiology
370-18 Louisa, Ottawa, ON K1R 6Y6
Tel: 1-877-651-3755 • FAX: (613) 234-3565 • Online: www.csep.ca

Note to physical activity professionals...

It is a prudent practice to retain the completed Physical Activity Readiness Conveyance/Referral Form in the participant's file.



© Canadian Society for Exercise Physiology www.csep.ca/bms

Continued on page 4...

Physical Activity Readiness
Medical Examination
(revised 2002)

PARmed-X PHYSICAL ACTIVITY READINESS MEDICAL EXAMINATION



PARmed-X Physical Activity Readiness Conveyance/Referral Form

Based upon a current review of the health status of _____, I recommend:

- No physical activity
- Only a medically-supervised exercise program until further medical clearance
- Progressive physical activity
 - with avoidance of: _____
 - with inclusion of: _____
 - under the supervision of a CSEP-Certified Exercise Physiologist™
- Unrestricted physical activity — start slowly and build up gradually

- Further information:
- Attached
 - To be forwarded
 - Available on request

Physician/clinic stamp:

_____ M.D.
 _____ 20____
 (date)

NOTE: This physical activity clearance is valid for a maximum of six months from the date it is completed and becomes invalid if your medical condition becomes worse.

Appendix – Section Five

FOR REB USE ONLY:

File No.:

Date Complete App'n. Rec'd.:

Approved/Approved with.:

Modification/Rejected.:

Date.: _____

.....

University of New Brunswick Application for Review of Research Involving Humans

Principal Investigator(s): Name(s); Academic Status (Faculty, Undergraduate Student or Graduate Student); Academic Unit, e-mail Address, Office Telephone, Home Telephone:

<p>Jonathan Baillie Faculty of Kinesiology University of New Brunswick Fredericton P.O. Box 4400 Fredericton, NB Canada. E3B 5A3 Office Phone: 506-453-4893 Home Phone: 506-471-8546 Email: baillie.jonathan@unb.ca</p>
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Title of Proposed Research:

<p>The Examination of Slow Eccentric Contraction Training on Vascular Function in Older Adults</p>

Commencement Date: 04/15/2012
31/07/2012

Completion Date:

Co-Investigator(s): Academic Unit, e-mail address, Office Telephone

<p>N/A</p>

Supervisor(s) (if Principal Investigator is a student); Academic Unit, e-mail address, Office Telephone:

<p>Stacey Reading PhD. Assistant Professor</p>

Faculty of Kinesiology
University of New Brunswick Fredericton
P.O. Box 4400
Fredericton, NB
Canada. E3B 5A3
Office Phone: 506-453-4893
Home Phone: 506-206-1735
Email: sreading@unb.ca

The undersigned parties certify that they have read, and undertake to comply fully with, the Tri-Council Policy Statement “Ethical Conduct for Research Involving Humans.”

Principal Investigator(s): _____

Co-Investigator(s): _____

Supervisor(s): _____

The undersigned certifies that the proposed research has been reviewed by, and is acceptable *in all respects* to, the academic unit(s) responsible.

Dean/Director/Chair(s)

Typed Name: **Tim McGarry**

Signature _____

Date submitted to the REB: **March 20, 2012**

1. Summary: Provide here, in approximately 300 words, a summary of the proposed research, indicating clearly the role of the research subjects and any procedures to which they will be subjected.

The proposed study will examine resistance training (RT) exercise on vascular function of the upper and lower limbs in order to evaluate the efficacy of using resistance training to improve vasodilatory reserve. During a normal muscle contraction, intramuscular pressure increases and temporarily reduces or occludes blood flow through the muscle. Upon relaxation, intramuscular pressure decreases and blood flow is restored. This mechanical action on the blood vessels contributes to the total vasodilation that occurs in a muscle in response to contractile activity. Previous work in our lab showed that muscular work performed with short

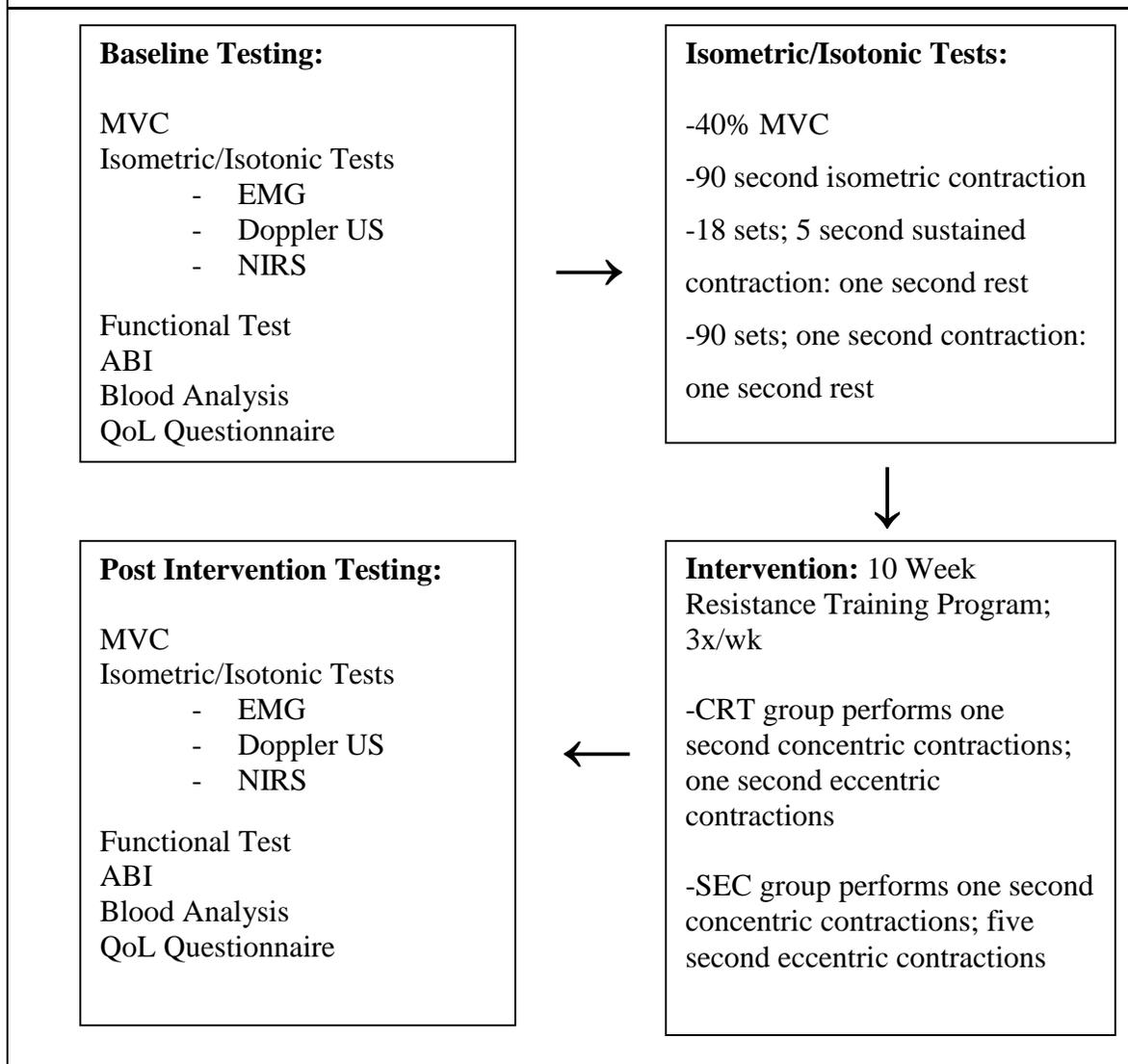
contraction-relaxation cycles produced a smaller and shorter vasodilation when compared to an equivalent amount of work performed using fewer but longer held contractions.

To extend these findings, the proposed study will test the hypothesis that RT exercise performed at a tempo that increases activation time (e.g. slow eccentric phase of a lift) will provide an overload training stimulus to the vasculature such that it will improve vasodilatory capacity of the limb. Male participants over 50 years of age will be recruited from the general population to participate in a 10 week RT program 3 times per week. There will be two groups in this study. The conventional resistance training (CRT) group will use a muscle activation cycle of one second concentric, one second isometric, and one second eccentric (1:1:1). The slow eccentric contraction (SEC) group will use a duty cycle of one second concentric, one second isometric, and five seconds eccentric (1:1:5) to maximize flow restriction.

Pre- and Post-testing of vascular function will be done by having participants attend two testing days, one day for upper body and one day for lower body (4 sessions total). Active and reactive hyperaemia (vascular function) will be evaluated using a hand-held duplex Doppler system and custom made software. Blood velocity will be recorded from the brachial artery (arm) or popliteal artery (leg) while the participant squeezes (forearm) or rotates (ankle extensors) a lever attached to a force transducer. Post-occlusive (reactive hyperaemia) blood velocity will be measured in both vessels after arresting blood flow by application of a tourniquet (Blood pressure cuff) for 2 minutes. Two sets of muscular contraction exercises will be performed for the upper and lower limb. Each set will be matched for total work however; the work will be completed using either short or long contraction-relaxation cycles. Each set requires approximately 2 minutes of muscular work with 10 minutes of post contraction blood velocity monitoring. The muscular contraction strength is set to 40% of the participant's maximum voluntary contraction strength (MVC). Each set will be paced using a metronome. Throughout the tests and recovery periods, near infrared spectroscopy (NIRS) and electromyography (EMG) electrodes will be placed on the muscle belly (gastrocnemius or flexor carpi radialis) to measure blood flow and muscle activity.

The pre/post training evaluation will also include a 6 minute walk test (6MWT) to evaluate functional exercise capacity and pain free walking time. This is performed on a long flat surface. Participants are instructed to cover as much distance as possible over the given period. Two hour post-prandial blood glucose and a blood lipid profile will be measured from a capillary blood sample obtained by finger prick in the Exercise Physiology Biohazard Lab (samples collected by lab supervisor). The ankle/brachial index (ABI) will be measured using standard technique of blood pressure cuff and duplex Doppler. All participants will complete a PAR-Q & YOU form before they are eligible to engage in any type of exercise

related to the study. Those participants who respond “yes” to any of the items on the “PAR-Q and YOU” form will be required to see their physician to complete a “PAR MED-X” form to obtain medical clearance for their involvement in the program. In addition, participants will complete a medical history questionnaire and a walking impairment questionnaire (WIQ). Please see attached forms. See below for a flowchart of the proposed study.



2. Risk: In your opinion, does this research pose more than minimal risk (Tri-Council Policy, Section 1.C1) to participating subjects? *Yes* *No X*

If yes, provide here a statement that describes in detail the aspects of the research procedure that pose a risk to subjects, and provide your assessment of the risk of harm (probability

and severity). Note that not only physical injury but also anxiety or embarrassments are included in the concept of harm. Describe means adopted to minimize risk, and means (such as provision of counseling) to deal with harms, which subjects may experience. Describe as well the potential benefit, which will result from this research, which justifies the above risk of harm.

N/A

3. Deception: Does this research involve deception or partial disclosure? *Yes No X*

If yes, refer to the Tri-Council Policy, Section 2, specifically Article 2.1(c) and subsequent commentary, and provide here an explanation of how you plan to comply with the requirements of that Section for debriefing. Describe as well the potential benefit, which will result from this research, which justifies waiving the normal requirements for full disclosure.

N/A

4. Funding: Has funding been received for this research? *Yes No X*

If yes, *from* what agency and for what period?

N/A

If yes, *from* what agency and for what period?

N/A

5. Research Subjects:

5.1 Number of Subjects: How many subjects will participate in this research? **40**

5.2 Recruitment: How will they be recruited, and from what population?

Newspaper ads, bulletin board ads and community newsletter ads will be used to recruit subjects from the greater Fredericton area and surrounding communities.

6. Informed Consent:

6.1 Informing Subjects: How will the nature of the research be explained to potential subjects, in compliance with Section 2D of the Tri-Council Policy? Attach a copy of any document(s), such as an explanatory letter, to be used for this purpose.

The principal investigator will discuss the nature of the project with each subject prior to the collection of any data. During the discussion details concerning data collection techniques, instrumentation, and the subject's role during the experiment

will be given. The voluntary nature of the subject's participation and their right to withdraw from the experiment at any time will be clearly indicated.

6.2 Consent: If written evidence of informed consent will be obtained, attach a copy of the consent form. (See Requirements for Informed Consent Forms.) **If written evidence of informed consent will not be used, explain here, in detail, how you intend to comply with the requirements of Section 2A of the Tri-Council Policy:** see particularly Article 2.1(b) and subsequent commentary.

Prior to beginning any data collection the subject will read and sign an Informed Consent Form. Please see attached form.

6.3 Children as Research Subjects: If the proposed research involves children as subjects, provide here a statement indicating how compliance with Section 2E, and specifically with Articles 2.5, 2.6 and 2.7 of the Tri-Council Policy, will be achieved.

N/A

6.4 Incompetent Adults as Research Subjects: If the research involves adults of diminished competence as subjects, provide a statement indicating how compliance with Section 2E, and specifically with Articles 2.5, 2.6 and 2.7 of the Tri-Council Policy, will be achieved.

N/A

7. Inducements: Will any inducements (money, grade points, etc.) be offered to encourage participation? *Yes* *No X*
If yes, indicate here how compliance with Section 2B of the Tri-Council Policy (concerning voluntariness) will be achieved. If academic rewards are to be used, give details of alternative means of achieving equivalent rewards.

N/A

8. Private Information: Does the proposed research involve accessing identifiable personal information about subjects by means of surveys, questionnaires, etc.? *Yes X No*

If yes, indicate here, in detail, how you propose to meet the requirements of the Tri-Council Policy, Section 3, specifically Article 3.2. A copy of any questionnaire, survey document or interview schedule to be used should be attached as well.

See attached documents

9. Feedback: Describe the measures, which you propose for providing feedback to research subjects concerning the outcome of the research.

Upon completion of the study a summary of the main findings and their significance will be distributed to interested study participants.

10. Data Security: Describe the measures, which you propose for ensuring the security of any identifiable personal data, which will be retained after completion of the research.

Each subject will be assigned an identifier (i.e. subject 001) that will be used on all data collection sheets and files. A master list connecting the identifier to the subject contact information will be stored in a locked filing cabinet in the faculty supervisor's office. At the completion of the study the master list will be destroyed.

11. Continuing Review: All research requires brief annual reports and a brief report upon completion of the research. Suitable report forms are included at the end of this file. **Research involving more than minimal risk may require additional measures for continuing review.** If your research involves more than minimal risk, describe here the measures you propose for facilitating continuing review of this research, in compliance with Article 1.13 of the Tri-Council Policy.

N/A

12. Additional Information: Please feel free to append any additional information, which you feel may be helpful to the REB in evaluating this application.

Surface recording EMG electrodes will be placed on the active muscles of either the forearm or calf. This will measure the amount of muscle activity occurring throughout each test. NIRS sensors containing an infrared light emitter and detector will be placed on the skin over the belly of the active muscles. This device measures the total blood flow throughout the duration of the test and recovery period. Adhesive disks keep all the sensors and electrodes in place. Each electrode and sensor has a wire that connects it to our recording equipment.

Each participant will perform the following test two times, once for the calf trial and once for the forearm trial.

- total**
- 1) 90 sets of one second contractions with equal rest between each set, for a time of 180 seconds.**
 - 2) 18 sets of five second sustained contractions with one second rest between each set, for a total time of 108 seconds.**

Forearm trials: Participants will sit in a chair with their testing arm extended over a table, strapped into the apparatus. They will be instructed to pull on the handle on the apparatus by contracting the 2nd and 3rd fingers.

Calf trials: Participants will lay face down on a massage table with their feet hanging off the edge. They will extend their foot pushing against an apparatus that is mounted to the wall.

They will receive feedback on how hard and often they need to contract their muscles to maintain the necessary force from a computer screen.

Each participant will conduct a maximum voluntary contraction (MVC) for each apparatus. This is the maximum amount of force that can be generated for one repetition. For each test, the participant will use 40 percent of their MVC.

After completion of each test, a small pen-like ultrasound probe will be held against the skin for a 10 minute period. Ultrasound gel will be placed on the inside of either the arm or the back of the knee, depending on the test. This will record the velocity at which blood flow is travelling through the artery.

At the end of the 10 week training program, participants will be retested on their MVC and will conduct the same series of tests.

In addition, a third test to evaluate reactive hyperemic response will be conducted by placing a blood pressure cuff around the upper portion of either the arm or thigh and inflated so that it occludes blood flow to the forearm/calf for 2 minutes. The cuff will then be deflated and blood flow will be restored. Measurements will be taken to determine the time for blood flow to return to a normal resting level. During the 2 minute occlusion of blood flow there will be a feeling of numbness or tingling develop in the fingers/toes that may be a little uncomfortable. This is normal and will rapidly disappear when the cuff is deflated. Even though blood flow to the forearm/calf has been briefly stopped no damage or injury will result.

In one session, we will take a small blood sample from your finger tip using a disposable automated lancing device. This is the same type of lancing device that a diabetic patient would use on a daily basis. During the blood sampling procedure there will be a momentary sting when the lance produces a small nick in the side of the tip of your finger. This sensation will be momentary and there will be no lasting discomfort. The lancing device is very accurate and precise – making the cut as small and painless as possible. The dimensions of the cut are 1.5 mm long by 2.0 mm deep resulting in 6 to 10 drops of blood being produced (30 to 50 μ L).

University of New Brunswick

Application for Modification of Research Project Involving Humans

REB File Number: 2012-038

Application Date: May 11, 2012

Project Title:

<p>The Examination of Slow Eccentric Contraction Training on Vascular Function in Older Adults</p>

Principal Investigator Name(s): Jonathan Baillie PI Signature(s):

Supervisor Name(s): Dr. Stacey Reading Signature(s):

Summary of Requested Modifications:

Will the risk of harm or deception/partial disclosure change?	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>
---	------------------------------	--

Will the nature or the objectives of the research change?	Yes <input type="checkbox"/>	No <input checked="" type="checkbox"/>
---	------------------------------	--

Will the changes to the research design be	major <input type="checkbox"/>	minor <input checked="" type="checkbox"/>	none <input type="checkbox"/>
--	--------------------------------	---	-------------------------------

Will the changes to the ethics protocol be	major <input type="checkbox"/>	minor <input type="checkbox"/>	none <input checked="" type="checkbox"/>
--	--------------------------------	--------------------------------	--

Which sections of the approved REB application will be affected by the modification(s)?

**List all affected Sections (e.g. Recruitment, Consent, ..., Data Security) below.

Detailed Description of the Requested Modifications:

Outline the planned changes to the research design and/or ethics protocol (status before the changes and after the changes) along with justifications and implications.

Of the original document:

Page 22: The intervention will change from a ten week program to a six week program.

Page 25: Blood Chemistry will now only be taken one time (not twice).

Page 27: There will be six laboratory evaluation sessions instead of the original four. Two sessions will occur at four weeks prior to the training program as a baseline measure. Two will occur at the beginning of the program and two will occur at the end of the program.

Page 49: Page 2 of the Participant Informed Consent Form will change to match the changes of the above mentioned modifications (6 laboratory sessions and 6 weeks).

If more pages are needed, please attach them and check here:

Please append the approval from your ERC with respect to these changes if relevant.

Appendix – Section Six

Self Reported Participant Information

This form is beneficial for use of a screening tool, as well as in the unlikely event that an accident or an incident occurs during a training session. Therefore, it is essential that the principal investigator is aware of any medications and conditions (asthma, etc.). In the case of interpreting data, this may also help to explain any data that may stand out.

Name: _____

DOB (mm/dd/yyyy): _____

Medications/Prescriptions: _____

Previous Injuries: _____

Medical Conditions: _____

Date of Diagnosis (mm/dd/yyyy): _____

This section to be measured by Principle Investigator:

Weight (kg) _____ Height (m) _____

Resting Heart Rate: _____

Resting Blood Pressure – Systolic _____ Diastolic _____

Additional Comments:

--

Appendix – Section Seven

The Peripheral Arterial Disease (PAD) Walking Impairment Questionnaire

Overview: Regensteiner et al developed a questionnaire for evaluating walking impairment in patients with peripheral arterial disease (PAD). This can be used to identify patients with significant impairment and to monitor effectiveness of therapeutic interventions. The authors are from the Universities of Colorado and Rochester.

Parameters :

- (1) difficulty walking a distance during the past month
- (2) difficulty walking at a certain speed during the past month
- (3) symptoms associated with walking impairment

Walking Distance	Degree of Difficulty	Points
walking indoors (around the house)	no	3
	some	2
	much	1
	did not do	0
walking 50 feet	no	3
	some	2
	much	1
	did not do	0
walking 150 feet (0.5 blocks)	no	3
	some	2
	much	1
	did not do	0
walking 300 feet (1.0 blocks)	no	3
	some	2
	much	1
	did not do	0
walking 600 feet (2.0 blocks)	no	3
	some	2
	much	1
	did not do	0

walking 900 feet (3.0 blocks)	no	3
	some	2
	much	1
	did not do	0
walking 1500 feet (5.0 blocks) or more	no	3
	some	2
	much	1
	did not do	0

walking distance score =

= (20 * (points for walking indoors)) + (50 * (points for walking 50 feet)) + (150 * (points for walking 150 feet)) + (300 * (points for walking 300 feet)) + (600 * (points for walking 600 feet)) + (900 * (points for walking 900 feet)) + (1500 * (points for walking 1500 feet))

where: each distance is walked is used as a weighting factor for the points from the degree of difficulty.

fraction of maximal walking distance score = (walking distance score) / 6060

Walking Speed	Degree of Difficulty	Points
walking 1 block slowly? (about 1.5 mph)	no	3
	some	2
	much	1
	did not do	0
walking 1 block at an average speed? (about 2.0 mph)	no	3
	some	2
	much	1
	did not do	0
walking 1 block quickly? (about 3.0 mph)	no	3
	some	2
	much	1
	did not do	0
running or jogging 1 block? (about 5.0 mph)	no	3

shortness of breath?	no	3
	slight	2
	some	1
	much	0
heart palpitations?	no	3
	slight	2
	some	1
	much	0
other problems? (please list)	no	3
	slight	2
	some	1
	much	0

where:

- A total symptom score was not calculated. This was the questions "were not a ranked series."
- The data was presented as "a percentage of the maximal score possible of 4.0."

Interpretation:

- minimum walking distance score: 0
- maximum walking distance score: 34.5
- minimum walking speed score: 0
- maximum walking speed score: 6.60
- The score can be used to compare impairment before and after vascular surgery.

Performance:

- Changes in questionnaire scores correlated with some measurements of treadmill performance.
- Retesting in an untreated control group showed similar scores after 12 weeks.

References:

Regensteiner JG Steiner JF et al. Evaluation of walking impairment by questionnaire in patients with peripheral arterial disease. J Vascular Medicine Biology. 1990; 2: 142-152. (Appendix I pages 150-151).

	some	2
	much	1
	did not do	0

walking speed score = (1.5 * (points for walking slowly)) + (2 * (points for walking at average speed)) + (3 * (points for walking quickly)) + (5 * (points for running or jogging))

where: each speed is walked is used as a weighting factor for the points from the degree of difficulty.

fraction of maximal walking speed score = (walking speed score) / 34.5

Symptoms of Walking Impairment	Degree of Difficulty	Points
pain or aching in your calves?	no	3
	slight	2
	some	1
	much	0
pain or aching in your thighs?	no	3
	slight	2
	some	1
	much	0
pain stiffness or aching in your joints (knees or hips)?	no	3
	slight	2
	some	1
	much	0
pain or discomfort in your chest?	no	3
	slight	2
	some	1
	much	0
weakness in one or both of your legs?	no	3
	slight	2
	some	1
	much	0

Appendix – Section Eight



Figure 14 – A participant engages in forearm muscular contraction during a pilot study. As mentioned in the methodology, the participant can see the 40 percent target (red line) on the left computer screen while the computer on the right measures force.

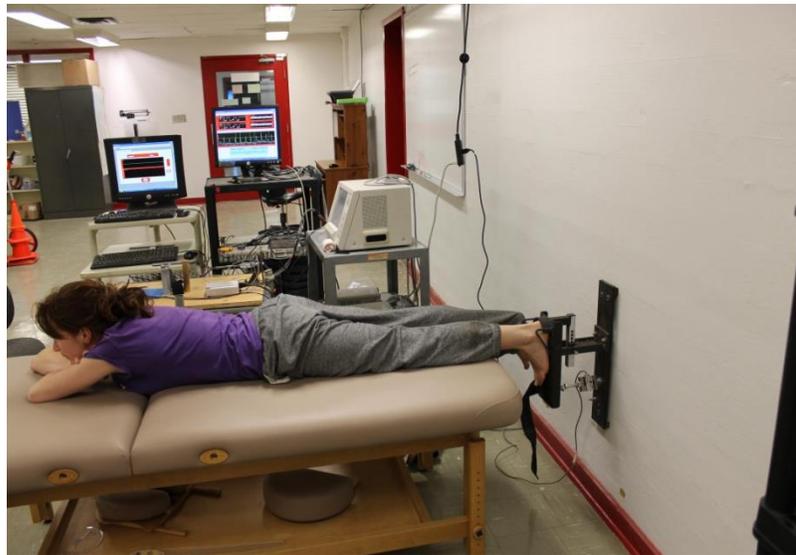


Figure 15 – A participant lies in the prone position while demonstrating the ankle flexion apparatus which is hooked up to the force transducer.

Appendix – Section Nine

6 Minute Walk Test Instructions

General Information:

- individual walks without physical assistance for 6 minutes and the distance is measured
 - start timing when the individual is instructed to "Go"
 - stop timing at 6 minutes
 - assistive devices can be used but should be kept consistent and documented from test to test
 - if physical assistance is required to walk, this should not be performed
 - a measuring wheel is helpful to determine distance walked
- should be performed at the fastest speed possible

Set-up and equipment:

- ensure the hallway free of obstacles
- stopwatch
- measuring wheel recommended to calculate distance

Patient Instructions (derived from references below):

"Cover as much ground as possible over 6 minutes. Walk continuously if possible, but do not be concerned if you need to slow down or stop to rest. The goal is to feel at the end of the test that more ground could not have been covered in the 6 minutes."

6 Minute Walk Test

Name: _____

Assistive Device and/or Bracing Used: _____

Date: _____

Distance ambulated in 6 minutes: _____

References:

Butland RJ, Pang J, Gross ER, Woodcock AA, Geddes DM. Two-, six-, and 12-minute walking tests in respiratory disease. *Br Med J (Clin Res Ed)*. 1982 May 29;284(6329):1607-8.

McGavin CR, Gupta SP, McHardy GJ. Twelve-minute walking test for assessing disability in chronic bronchitis. *Br Med J*. 1976; 3;1(6013):822-3.

Rossier P, Wade DT. Validity and reliability comparison of 4 mobility measures in patients presenting with neurologic impairment. *Arch Phys Med Rehabil*. 2001;82(1):9-13.

Appendix – Section Ten

Table 6 – Statistical p values for pre and post-training measurement of anthropometric and cardiovascular data for SEC, CRT and combined (no main effect difference).

	SEC (Pre – Post)	CRT (Pre – Post)	COMBINED (Pre- Post)
<u>Anthropometric Data:</u>			
WC, cm	.030	.034	.037
BMI, kg/m ²	.201	.632	.810
Height, cm	.766	.356	.677
Weight, kg	.071	.231	.181
<u>Cardiovascular Data:</u>			
SBP, mmHg	.005	.009	.035
DBP, mmHg	.394	.376	.430
MAP, mmHg	.045	.022	.038
RHR, bpm	.376	.573	.688

Table 7 – MVC statistical p values for baseline comparisons (B1 – B2), and baseline – post training comparisons (B1 – PT, B2 – PT) for SEC and CRT groups.

MVC	SEC (n = 7)			CRT (n = 7)		
	B1 – B2	B1 - PT	B2 - PT	B1 – B2	B1 - PT	B2 - PT
Upper (N)	.301	.248	.421	.850	.291	.601
Lower (N)	.323	.408	.388	.376	.320	.208

Table 8 – Statistical p values for systolic peak, mean velocity, and pulsatility index at rest prior to 1:1 Ratio Test for upper and lower body. Baseline comparisons (B1 – B2), and baseline – post-training comparisons (B1 – PT, B2 – PT) for both SEC and CRT groups as well as combined (no main effect difference).

1:1 Ratio Test	SEC (Pre – Post)			CRT (Pre – Post)			Combined (Pre – Post)		
Resting Upper	B1-B2	B1-PT	B2-PT	B1-B2	B1-PT	B2-PT	B1-B2	B1-PT	B2-PT
SP	.355	.042	.043	.128	.046	.012	.310	.010	.029
MV	.723	.086	.123	.106	.698	.385	.237	.270	.738
PI	.187	.017	.011	.875	.044	.003	.326	.016	.035
Resting Lower	B1-B2	B1-PT	B2-PT	B1-B2	B1-PT	B2-PT	B1-B2	B1-PT	B2-PT
SP	.173	.434	.358	.117	.939	.403	.164	.575	.786
MV	.132	.696	.141	.209	.363	.206	.775	.320	.256
PI	.347	.019	.010	.145	.004	.007	.458	.045	.024

Table 9 - Statistical p values for systolic peak, mean velocity, and pulsatility index at rest prior to 1:1 Ratio Test for upper and lower body. Baseline comparisons (B1 – B2), and baseline – post-training comparisons (B1 – PT, B2 – PT) for both SEC and CRT groups as well as combined (no main effect difference).

5:1 Ratio Test	SEC (Pre – Post)			CRT (Pre – Post)			COMBINED (Pre – Post)		
	B1-B2	B1-PT	B2-PT	B1-B2	B1-PT	B2-PT	B1-B2	B1-PT	B2-PT
Resting Upper									
SP	.313	.002	.025	.151	.016	.028	.168	.018	.046
MV	.210	.049	.110	.896	.336	.256	.645	.560	.378
PI	.336	.023	.008	.819	.006	.003	.578	.034	.048
Resting Lower									
SP	.971	.677	.651	.126	.938	.472	.222	.809	.878
MV	.309	.626	.544	.072	.545	.367	.474	.984	.606
PI	.753	.011	.009	.820	.008	.008	.345	.034	.032

Table 10 - Statistical p values for walking endurance test, and strength exercises (bench press, latissimus pull down, shoulder press, and squat) Pre and post-training values were compared for both SEC and CRT groups as well as combined (no main effect difference).

	SEC (Pre – Post)	CRT (Pre – Post)	COMBINED (Pre- Post)
6MWT (m)	.001	.000	.044
Bench Press (kg)	.000	.000	.000
Latissimus Pull-Down (kg)	.000	.000	.000
Shoulder Press (kg)	.001	.002	.000
Squat (kg)	.000	.000	.000

Curriculum Vitae

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Universities attended:

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Conference Presentations:

Atlantic Provinces Exercise Sciences, presentations: *The relationship between exercise and cortisol response after a 6-week exercise intervention in breast cancer survivors (2009), measuring direct versus indirect calorimetry (2010). Examination of slow eccentric contraction on endothelial function in older adults (2012)*

Crossroads Conference – Dalhousie University *The relationship between exercise and cortisol response after a 6-week exercise intervention in breast cancer survivors (2009), Examination of slow eccentric contraction on endothelial function in older adults (2012)*