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# THE RELATIONSHIP BETWEEN OXYGEN SATURATION AND MUSCLE FATIGUE IN MEN AND WOMEN

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# THE RELATIONSHIP BETWEEN OXYGEN SATURATION AND MUSCLE FATIGUE IN MEN AND WOMEN

A THESIS APPROVED FOR THE
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BY

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## ABSTRACT

Women have been shown to be more fatigue resistant than men during low-intensity submaximal isometric contractions. It has been suggested higher intramuscular pressures, due to the greater muscle mass and absolute strength of men, may lead to greater reductions in skeletal muscle perfusion during exercise and thus lead to an earlier onset of fatigue.. **PURPOSE:** The purpose of this study was to investigate the changes in oxygen saturation that occur during a bout of low-intensity isometric exercise in men and women and determine if muscle fatigue occurs at a common point of oxygen desaturation. **METHODS:** Twenty-four participants (12 male and 12 female) completed four visits consisting of two familiarization visits and two experimental visits. During the familiarization visits, body composition was measured via DEXA and ultrasound, skeletal muscle mitochondrial function was assessed, and participants were familiarized to the isometric exercise protocol. Maximal voluntary contractions (MVC) of the elbow flexors were assessed every visit and for the two experimental visits. An isometric time-to-task failure (TTF) was then performed using a torque equivalent to 20% of MVC using the elbow flexors. During one experimental visit, blood flow occlusion was applied proximal to the elbow flexors during the TTF test and during the other visit blood flow was not occluded—the order these conditions was randomized... MVC was also assessed immediately post exercise and 1-minute post exercise. Oxygen saturation was assessed in the exercising muscles using the deoxyhemoglobin concentration from near-infrared spectroscopy. **RESULTS:** There were no statistical differences in TTF under normal or ischemic conditions for men and women, however if a participant who was almost a statistical outlier was removed, a sex difference would

have been seen. There were no differences in desaturation of hemoglobin between men and women ($p > 0.05$) showing that men and women desaturate to similar amounts at the same relative time points. There were also no differences in mitochondrial function between men and women ($p > 0.05$), however both measures of mitochondrial function were moderately correlated, the time constant ($r= 0.43$) and the slope constant ($r = -0.42$), to TTF. **CONCLUSIONS:** In conclusion, we believe that oxygen availability is partly responsible for differences in fatigue between men and women. Further studies should include a larger sample.

# Chapter I: Introduction

## 1.1 Introduction

Fatigue, often defined as an inability to produce the desired or expected muscular force (Edwards, 1981), is a common symptom associated with many health conditions. In a rccent study 38% of workers reported suffering from fatigue, and two thirds of those with fatigue reported a loss of productive work time due to their fatigue (Ricci, Chee, Lorandeau, & Berger, 2007). This loss of work costs employers an estimated $136.4 billion annually (Ricci et al., 2007). Unexplained fatigue (fatigue with no identifiable physiological or psychology cause) is the primary symptom of certain clinical conditions such as Chronic Fatigue Syndrome (CFS) and Gulf-War Syndrome (GWS) and also a common symptom of chronic diseases such as cancer and cardiovascular disease. As such, a more thorough understanding of the physiological underpinnings of fatigue may lead to more efficacious treatments and limit the indirect and direct healthcare costs associated with fatigue.

Mechanistically, fatigue can be separated into two general categories: 1) central and 2) peripheral. With central fatigue the decline in force production originates from the central nervous system (CNS; e.g. motor cortex, spinal cord, etc.) while peripheral fatigue originates from a failure of the motor axon or more distal structure at the neuromuscular junction or within the muscle (Edwards, 1981). The decline in force during central fatigue is primarily related to reduced motor drive failing to maintain motor-unit recruitment and/or firing rates—collectively termed “muscle activation” (Bigland-Ritchie & Woods, 1984; Enoka & Stuart, 1992) at levels sufficient to maintain the required force. It may be caused by psychological factors such as a decline in

motivation due to a heightened sense of effort, increased core body temperature, depletion of muscle glycogen, a fall in blood glucose, and/or afferent feedback from type III and IV afferent fibers sensing the build-up of metabolites in skeletal muscle (Amann, 2011; Amann et al., 2013; Enoka & Stuart, 1992; Kent-Braun, Fitts, & Christie, 2012). Peripheral fatigue may result from impairments in neuromuscular transmission across the neuromuscular junction, declines in sarcolemma excitability, reduced excitation-contraction coupling resulting in reduced intracellular calcium release, and/or failure of the contractile apparatus (Bigland-Ritchie & Woods, 1984; Kent-Braun et al., 2012). Many of these impairments are often a consequence of insufficient ATP availability resulting in a reduced ability to restore resting membrane potentials, return calcium to the sarcoplasmic reticulum, and perform the cross-bridge cycle (Kent-Braun et al., 2012).

It is well accepted that in comparison to men, women exhibit a greater resistance to fatigue during submaximal, isometric contractions, especially at relatively low percentages MVC (e.g. under 25-30% of MVC) (S. K. Hunter, 2014) across a variety of muscle groups, including the adductor pollicis, elbow flexors, extrinsic finger flexors, and knee extensors (S. K. Hunter & Enoka, 2001). Interestingly, the sex-related differences in fatigue development disappear as the relative intensity of the fatiguing task increases suggesting the amount of muscle mass recruited during the exercise bout may play a moderating role in the observed differences (S. K. Hunter, 2014). Additionally, differences in fatigue development also disappear when men and women are matched for maximal strength (Sandra K. Hunter, Critchlow, Shin, & Enoka, 2004).

This raises the question as to how might muscle mass and maximal strength, and their differences between men and women, play a role in fatigue? When a muscle contracts, intramuscular pressure increases. When this pressure reaches some critical, absolute level it may restrict blood flow to the muscle and limit oxygen delivery. This promotes a greater reliance on anaerobic metabolic pathways which have a limited capacity to generate ATP; leading to fatigue (Bigland-Ritchie & Woods, 1984; S. K. Hunter, 2014). Debate exists regarding the relative or absolute intensity of muscle contractions required to exceed this "critical" threshold and restrict oxygen delivery. Sjogaard et al. (1988) (Sjogaard, Savard, & Juel, 1988) found that normal blood flow was only maintained during contraction levels below 10% of MVC with contractions performed above 10% resulting in progressive reductions in flow for handgrip exercises. Similarly, Jarvholm (1988) (Jarvholm, Styf, Suurkula, & Herberts, 1988) found that contractions of ~15% of MVC were sufficient to reduce muscle blood flow. In contrast to the findings that low force contractions could lead to reduced flow, Barnes (1980) (Barnes, 1980) found that complete blood flow occlusion occurred on average at ~60% of MVC. However when participants were separated into groups based upon their strength (low and high strength), occlusion occurred at ~75% of MVC in the "low" strength group and ~51% MVC in the "high" strength group (Barnes, 1980). Men are generally stronger than women. As such a greater absolute force must be produced at any given relative percentage of their maximal voluntary contraction (MVC) compared to women. Greater force production should result in a larger increase in intramuscular pressure and thus increase the possibility of vascular occlusion and the resulting increased reliance on anaerobic metabolism leading to an earlier onset of

fatigue (Russ & Kent-Braun, 2003). When men and women are matched for strength or when the relative contraction force is high (e.g. >50-75% if MVC) then both men and women generate sufficient force to lead to similar levels of vascular occlusion leading to the findings of similar levels of fatigue in men and women matched for strength and during higher force contractions.

Perfusion is the rate and distribution of blood flow into a tissue (Barrett & Rattigan, 2012). It has been suggested women may have greater muscle perfusion than men due to differences in compression on the feed arteries during low-intensity, sustained isometric contractions (S. K. Hunter & Enoka, 2001). Hunter and Enoka (2001) found that women had a reduced exercise-pressor response (exercise-induced increase in blood pressure) which they attributed to women having greater muscle perfusion in the elbow flexors. They believed that this was a result of women having less muscle mass and a lower target force than men. Evidence also suggests that women have a greater vasodilatory response of the arteries that feed skeletal muscle compared to men during exercise (S. K. Hunter, 2014; Kellawan et al., 2015). During submaximal workloads, the femoral artery dilated to a significantly greater extent in women (~0.5 mm) than in men (~0.1 mm) (Parker et al., 2007). A greater vasodilatory response could result in greater perfusion in women and in turn, less accumulation of metabolites and less loss of oxygen availability limiting fatigue (S. K. Hunter, 2014).

While perfusion and the vasodilatory response have been compared between men and women, to our knowledge, no study has assessed microvascular circulation and oxygen saturation during fatiguing tasks to determine if differences exist between men and women. If the greater absolute force produced by men results in greater reductions

in blood flow to the exercising muscle, it would be expected that they would experience greater oxygen desaturation and reach task failure sooner. As such, the goal of this study was to assess oxygen levels at the muscle using near-infrared spectroscopy (NIRS) which measures oxygenated hemoglobin, deoxygenated hemoglobin, and total hemoglobin.

## 1.2 Purpose

The purpose of this study was to investigate the relationship between oxygen saturation and muscle fatigue in men and women and to determine if there is a common point of oxygen desaturation that leads to muscle fatigue.

## 1.3 Research Questions

1. Will the time-to-task failure differ between men and women at 20% of their MVC under normal and ischemic conditions?
2. Will task failure occur at a similar level of muscle deoxygenation, between men and women under normal and ischemic conditions?
3. Will NIRS assessed mitochondrial function differ between men and women and will a relationship between mitochondrial function and time-to-task failure exist?

## 1.4 Research Hypotheses

1. Time-to-task failure will be reduced in men compared to women at 20% of their MVC under normal conditions, but not under ischemic conditions.
2. Task failure will occur at different levels of deoxygenation during exercise under normal and ischemic conditions in men compared to women.
3. Mitochondrial function will differ between men and women, but higher function will be associated to increased time-to-task failure.

## 1.5 Null Hypotheses

1. Time-to-task failure will be the same in men compared to women at 20% of their MVC under normal and ischemic conditions.
2. Task failure will not occur at different levels of deoxygenation during exercise at 20% of their MVC under normal and ischemic conditions in men compared to women.
3. Mitochondrial function will not differ between men and women.

## 1.6 Significance

This study will contribute to the literature of understanding the sex differences in fatigability. The results will promote more effective strategies to enhance performance and to offset muscle fatigue in men and women.

## 1.7 Limitations

1. Results of this study only apply to men and women aged 18-35.

2. Results of this study only apply to the elbow flexors muscle group.
3. Results of this study only apply to static, isometric exercise.

## 1.8 Delimitations

1. Healthy males and females ranging from 18-35 years of age.
2. Males and females that were capable of performing a fatiguing exercise.
3. Males and females that were free of musculoskeletal injuries.

## 1.9 Assumptions

1. Participants gave maximal effort during all bouts of exercise.
2. Participants followed all guidelines before and after experimental visits.
3. Participants answered all health-related questionnaires honestly.

## 1.10 Operational Definitions

1. **Fatigue:** An acute impairment of performance that results in the eventual inability to produce force (Enoka & Stuart, 1992).
2. **Near-Infrared Spectroscopy (NIRS):** a tool that noninvasively measures skeletal muscle blood flow and oxygen consumption detected by wave length changes in oxygenated hemoglobin, deoxygenated hemoglobin, and total hemoglobin (Lucero et al., 2018).
3. **Time to Task Failure:** a measurement technique that records the time it takes to reach fatigue during an exercise (S. K. Hunter, Critchlow, & Enoka, 2004).

4. **Pressor Response:** the reflex-mediated increase in mean arterial pressure due to an accumulation of metabolites in the muscle that attempts to rectify the mismatch between perfusion and metabolism during an isometric fatiguing contraction (Hunter, 2004).
5. **Perfusion:** the rate and distribution of blood flow into a tissue (Barrett, 2012).

## Chapter II: Review of Literature

As previously stated, the purpose of this study was to investigate sex differences in muscle fatigue and determine if oxygenation is associated with muscle fatigue. This chapter aims to provide an overview of previous literature that discusses sex differences in fatiguing exercises as well as the mechanisms that cause sex differences in muscle fatigue. This literature review is organized into the following sections: (1) Muscle Fatigue, (2) Sex Differences in Fatigue, (3) Near-Infrared Spectroscopy (NIRS) (4) Mechanisms, (5) Summary.

### 2.1 Muscle Fatigue

Fatigue is the failure to maintain the required or expected force or power output (Edwards, 1981). Fatigue can be separated into two different categories: central and peripheral. Central fatigue arises from the central nervous system often through impaired descending drive or reduced motivation. Reduced central drive, motor neuron excitability, and increased negative feedback from types III and IV afferents are all mechanisms of central fatigue (Davis & Walsh, 2010). Central fatigue plays a large role in long duration exercise due to declining motor drive (Bigland-Ritchie & Woods, 1984). It can be demonstrated by an increase in force evoked by electrical stimulation during maximal voluntary effort. If more force is evoked by the stimulation, it shows that some motor units were not recruited or firing fast enough during electrical stimulation (Taylor & Gandevia, 2008). This increase in force is a sign of central fatigue and indicates that central processes proximal to the motor axon are contributing to the loss of force (Taylor & Gandevia, 2008). Central fatigue can also be attributed to

supraspinal mechanisms (Gandevia, Allen, Butler, & Taylor, 1996). Transcranial magnetic stimulation of the motor cortex caused a superimposed twitch in the elbow flexors despite maximal effort from participants. This suggests that motor cortical output was not maximal and was not sufficient to activate all of the motor units in order to produce maximal force. This is a marker of supraspinal fatigue (Taylor & Gandevia, 2008).

Peripheral fatigue arises from the failure of motor neurons or muscles Impaired excitation-contraction coupling, sarcolemma excitability, actomyosin interactions during cross bridge cycling, and reuptake of calcium are all mechanisms of peripheral fatigue (Davis & Walsh, 2010). Crossbridge formation and activation are regulated by interactions among the neuromuscular junction, sarcolemma, sarcoplasmic reticulum, and the contractile proteins actin and myosin (Keyser, 2010). Decreases in muscle ATP do not seem to be enough to negatively impact muscle function on its own, however, increases in ADP and Pi do. A high ADP:Pi ratio, increased $H^+$, and heat may reduce the energy provided by ATP during hydrolysis declining crossbridge function and the force generated by the power stroke (Keyser, 2010). Additionally, increases in $H^+$ inhibit myosin ATPase and thus maximal shortening velocity of fibers. Shortening velocity is limited by the rate of ADP release (Kent-Braun et al., 2012). These increases in $H^+$ as well as Pi tend to reduce the number of crossbridges formed by fast twitch fibers and the force generated in fast and slow twitch fibers (Kent-Braun et al., 2012; Keyser, 2010). Failure in excitation contraction coupling is another place in which peripheral fatigue occurs. T-tubules may fail to signal due to the accumulation of potassium ions that reduce membrane excitability. There also may be failure in calcium

release from the sarcoplasmic reticulum. Increases in intracellular ADP and magnesium inhibit the ryanodine receptor which is responsible for releasing calcium (Kent-Braun et al., 2012). For sustained submaximal exercise, ATP hydrolysis occurs at a faster rate than can be replenished by oxidative phosphorylation and the reliance on glycolysis increases. This is likely related to the maximization of oxygen delivery to the muscles (Keyser, 2010).

## 2.2 Task Failure

Similar to the mechanisms contributing to fatigue, the mechanisms responsible for task failure depend on the task being performed (Gandevia, 2001). Subtle differences in task can be associated with differences in the time to task failure (S. K. Hunter, Duchateau, & Enoka, 2004). Task failure from continuous isometric contractions at lower intensities (<30% of MVC) is thought by some to be mostly due to impaired motor drive (central fatigue) while from continues isometric contractions at greater intensities is believed to be due with mostly impaired muscle contractility (peripheral fatigue) (Place, Bruton, & Westerblad, 2009).

Kent-Braun (1999) tested 5 males and 4 females to estimate the contributions of central and peripheral factors to the development of muscle fatigue (Kent-Braun, 1999). The participants sustained an MVC of the ankle dorsiflexors for 4 minutes. Central activation and peripheral activation was measured, as well as measures of intramuscular metabolism. They found that ~20% of the fatigue developed was due to central factors, measured from CAR and differences between tetanic and voluntary fatigue. A significant reduction in iEMG, but no decline in CMAP indicate the absence of failure

of peripheral activation. Therefore the remainder ~80% was due to intramuscular sources, specifically, increases in $H^+$ (Kent-Braun, 1999). There was little change in Pi or $H_2PO_4^-$, but the fall in pH was strongly correlated with decreases in force.

Another study examined if central neural mechanisms limit the duration of a sustained, low intensity isometric contraction of the knee extensors. Fourteen males performed a sustained isometric contraction at 20% of MVC until failure immediately followed by an electrical stimulation for 1 min at the same target force (Neyroud, Maffiuletti, Kayser, & Place, 2012). After the electrical stimulation, they were asked to resume the voluntary contraction for as long as possible. All subjects were able to develop the 20% of MVC force when electrically stimulated at task failure, suggesting that the lack of force generating capacity from peripheral impairment had not limited the length of the task (Neyroud et al., 2012). Voluntary activation was slightly decreased and MVC decreased after the entire protocol. They concluded that task failure is mainly affected by central factors, whereas MVC force decline is mainly related to peripheral fatigue (Neyroud et al., 2012).

Hunter et al. (2002) tested 8 men and 8 women to compare the effect of task on neural activity and endurance time of a submaximal fatiguing contraction with the elbow flexors (S. K. Hunter, Ryan, Ortega, & Enoka, 2002). They performed sustained isometric contractions at 15% of MVC until failure either by maintaining a constant force while pushing against a force transducer (force task) or by supporting an equivalent inertial load while maintain a constant elbow angle (position task). Despite having a similar reduction in load torque at exhaustion, they found that the endurance time for the force task was twice as long as that for the position task. The rates of

increase in MAP and heart rate, RPE, and fluctuations in force and acceleration were greater for the position task suggesting a greater rate of increase in descending drive to the spinal motor neurons (S. K. Hunter et al., 2002). EMG activity showed identical rates of change for the two tasks suggesting that the output of the motor neuron pool from the spinal cord was similar for the two tasks. They concluded that due to the greater rate of increase in central neural activity during the position task, the briefer time to task failure for the position time was due to differential inputs received by the motor neuron pool. (S. K. Hunter et al., 2002).

Motor unit activity can also affect time to task failure. During a submaximal isometric contraction to failure, there is an increase in motor unity activity including changes in the number of active motor units and modulation in discharge rate (Fallentin, Jorgensen, & Simonsen, 1993). Seven men and seven women performed sustained isometric contractions of the elbow flexors at 20% of MVC three times to compare patterns of muscle activation and endurance time (S. K. Hunter & Enoka, 2003). They found that overall, the endurance time in the third session was longer than the first and second session. Five men and four women increased their endurance time between session 1 and 3 by 60 ± 28%, whereas two men and three women had a -3 ± 11% change between sessions 1 and 3. These two groups were classified as responders and nonresponders, respectively. They suggested that the responders increased their endurance time by altering the level and pattern of muscle activation despite experiencing similar amounts of fatigue between groups as shown by similar reductions in MVC after the fatiguing contractions.

## 2.3 Sex Differences in Fatigue

In general, women are less fatigable than men at isometric fatiguing contractions of similar intensity. However, the differences are task specific and muscle group specific. The muscle group used, the type, the speed, and the intensity of the contraction can all affect fatigability (S. K. Hunter, 2014).

Maughan et al. conducted a study comparing the ability to perform an isometric contraction at different force levels in 25 untrained men and 25 untrained women. They performed sustained contractions of the knee-extensor muscles on their dominant leg until fatigue at 20%, 50%, and 80% of their maximal voluntary contraction (MVC). The men were stronger than the women, however the women showed a greater endurance capacity at the lower force level. At 20% MVC, women lasted longer than the men did (252 ± 5 s vs 180 ± 51 s). However, at 50% and 80% MVC, there was no difference between men and women. The authors report that the differences may be caused by differences in muscle fiber types, contractile properties, or blood perfusion, however they also report that the exact factor(s) responsible cannot be identified yet (Maughan, Harmon, Leiper, Sale, & Delman, 1986).

A similar study was done using the elbow-flexor muscles and developed similar results. 9 young adult men and 9 young adult women completed sustained isometric contractions of the elbow-flexor muscles at 20% and 80% of their MVC. Like the study discussed previously, the women had a longer time to task failure than the men at 20% MVC (17.0 ± 8.7 min vs 10.6 ± 2.0 min), but at 80% MVC were similar to the men (24.3 ± 6.6 s vs 25.0 ± 6.5 s). These authors report that their differences in fatigability could be due to differences in muscle perfusion and women experiencing less peripheral

fatigue at low-force (Yoon, Schlinder Delap, Griffith, & Hunter, 2007). These results are consistent with other studies (S. K. Hunter, A. Critchlow, et al., 2004; S. K. Hunter & Enoka, 2001). However, in another study by Hunter et al., they found no sex difference in fatigability when the men and women were matched for strength (Sandra K. Hunter et al., 2004)

## 2.4 Near-Infrared Spectroscopy (NIRS)

Near-Infrared Spectroscopy (NIRS) is a noninvasive tool that uses the differential absorption properties of hemoglobin to evaluate skeletal muscle oxygenation. Both oxygenated and deoxygenated hemoglobin absorb light at 800 nm, but at 760 nm absorption is primarily by deoxygenated hemoglobin. These assessments of absorption are made at the level of small blood vessels, capillaries, and intracellular sites of oxygen uptake (Mancini et al., 1994). The average depth sensitivity of most NIRS tools is about 1.5 cm which can be a limitation if studying a muscle group surrounded by a thick adipose layer or a person with excess adipose tissue. Another limitation caused by the depth sensitivity is that measurements are restricted to superficial muscles (Ferrari, Muthalib, & Quaresima, 2011).

NIRS can also be used to assess mitochondrial function. In skeletal muscle, mitochondria are responsible for generating fuel needed for contractile activity and physical functioning. Magnetic resonance spectroscopy (MRS) is a common tool used to evaluate mitochondrial function by looking at changes in phosphorus (P) metabolites. More specifically, the recovery of phosphocreatine (PCr) following exercise is assessed due to it being a function of mitochondrial ATP production (Ryan, Southern, Reynolds,

& McCully, 2013). Studies have compared the recovery of oxygenated hemoglobin after exercise with the recovery of PCr, but found inconclusive results (Hanada et al., 2000; McCully et al., 1994). This led to a development using NIRS in combination with a rapid cuff inflation system to measure changes in muscle oxygen consumption without measuring oxygen delivery after submaximal exercise. The recovery of oxygen consumption after exercise should be a function of mitochondrial ATP production and therefore can be used as a measure of muscle oxidative capacity (Ryan et al., 2013). The protocol for this measurement starts with a cuff placed around the limb and inflated 10s after exercise, and every 20s up to 180s and every 30s up to 600s. The duration of the cuff occlusion was 6 s. This protocol is repeated twice, with the second time being offset by 10s from the first to get twice as many measures of oxygen consumption. These time constants were then compared with the time constants for PCr recovery as measured in P-MRS. The time constant for muscle oxygen consumption recovery was significantly correlated to the muscle oxidative capacity and therefore can be used as an index for evaluating muscle oxidative capacity (Nagasawa et al., 2003). A study by Ryan et al. (2013) also cross-validated NIRS measurements of muscle oxidative capacity with P-MRS measurements of muscle oxidative capacity in young healthy adults and found good agreement between them. This agreement suggests that NIRS is a valid method for assessing mitochondrial function.

## 2.5 Blood Flow and Perfusion

Reduced blood flow to a muscle results in a reduction of oxygen delivery to a muscle which is associated with the onset of fatigue (Russ & Kent-Braun, 2003). There

is some evidence that proposes women may have an oxidative advantage compared to men (Kent-Braun, Ng, Doyle, & Towse, 2002). Russ and Kent-Braun (2003) completed a study where they tested fatigue in free-flow circulation conditions and ischemic conditions to see if the sex differences in fatigued were dependent on oxygen utilization. 8 men and 8 women participated in the study where they tested the fatigability of their ankle dorsiflexors. The subjects underwent two fatiguing protocols that were the exact same other than one being performed under free flow circulation conditions and the other being performed under ischemic conditions. As expected, women fatigued less than men during the free flow circulation condition, but there was no difference in fatigability during the ischemic condition. These results suggest that these differences in fatigue are dependent upon blood flow, more specifically delivery of oxygen.

Women also may have a greater muscle perfusion in some muscle groups (S. K. Hunter & Enoka, 2001). Hunter and Enoka (2001) performed a study that targeted to determine the relationship between force and endurance time in a submaximal isometric contraction. 7 men and 7 women went through the protocol consisting of holding an isometric contraction with the elbow-flexor muscles at 20% MVC until they fatigued. Once again, women held their fatiguing contractions longer than the men (1,806 ± 239 s vs 829 ± 94 s). Heart rate and mean arterial pressure (MAP) were also measured and both found to be lower in women during the sustained contraction. These smaller measurements may be related to smaller muscle mass. Force and strength are related to muscle size, so the stronger subjects with larger muscles may experience compression

of the arties perfusing the muscle which leads to a buildup of metabolites that increase MAP (S. K. Hunter & Enoka, 2001).

These ideas are also seen in a study by Barnes (1980). Barnes tested 20 males to study the relationship between maximum isometric strength and the maximum tension needed to produce total occlusion of that muscle. He tested the men at different percentages of their MVC and divided the subjects into high and low strength groups. The contractions began at 10% MVC and increased by 10% until occlusion was reached. The low strength group was found to occlude at 75.5% of MVC and the high strength group occluded at 51.5% MVC. The results also showed that during the lower force contractions, the muscles weren't fully occluded yet, but still saw a restriction of blood flow. Because men are usually stronger than women, it can be restricted for them at similar contraction intensities due to the higher intramuscular pressure the men are exerting (Barnes, 1980).

## 2.6 Fiber Type and Skeletal Muscle Metabolism

Type II muscle fibers generate greater force, but also are more fatigable than type I fibers (Schiaffino & Reggiani, 2011). While everyone has a combination of type I, type IIa, and type IIx, there is evidence that women have a greater proportion of type I fibers, which are slower and less fatigable, than men do in some muscle groups. Specifically, in the vastus lateralis, men and women showed approximately the same amount of fibers, but the type IIa fibers in the men were the greatest in number and the type I fibers in the women were the greatest in number (Staron et al., 2000). These

differences in fiber types may explain the sex difference in fatigability, however more studies are needed.

Metabolic activity within a muscle could also be an explanation for these sex differences. As stated previously, women have a greater proportion of type I fibers; type I muscle fibers have a higher oxidative capacity and are more fatigue resistant than type II fibers. Women have greater type I fibers, therefore they have the ability to utilize oxidative metabolism more than glycolytic pathways like men do (Russ & Kent-Braun, 2003). In a cycle sprint exercise, blood lactate concentrations post exercise were smaller in women than men as well as a smaller reduction of ATP and less of its byproducts. These differences can also be related to the differences in fiber type between men and women and how those fibers' metabolic activity (Esbjornsson-Liljedahl, Sundberg, Norman, & Jansson, 1999).

## 2.8 Menstrual Cycle and Reproductive Hormone Fluctuations

Studies have been contradictory on if there are differences in fatigability and minimal differences in strength over the course of the menstrual cycle (Ansdell et al., 2019; Janse de Jonge, 2003). A study that tested 19 healthy women that were not taking any oral contraception or hormone supplements participated in a protocol that measured strength, fatigability, and contractile properties during difference phases of the menstrual cycle. They were tested during menstruation when estrogen and progesterone are low, during the late follicular phase when estrogen is high and progesterone is low, and during the luteal phase when both estrogen and progesterone are high. Isometric strength and electrically stimulated fatigue of the quadriceps and isokinetic strength and

voluntary fatigue of the knee flexors and extensors were measured. There were no significant changes of strength or fatigability throughout the course of the menstrual cycle. These results suggest that female reproductive hormones do not affect fatigability or strength (Janse de Jonge, Boot, Thom, Ruell, & Thompson, 2001) and therefore cannot be used to explain sex differences in fatigue. However, a more recent study in 2019 tested menstrual cycle-associated modulations in neuromuscular function and fatigability of the knee extensors in eumenorrheic women (Ansdell et al., 2019). They tested 30 women, 15 taking monophasic oral contraceptives and 15 eumenorrheic, and examined them before and after an intermittent isometric fatiguing task at 60% of MVC until failure. They found that time to task failure was longer on day 21 than on days 2 and 14 of the menstrual cycle, suggesting that fatigability of the knee extensors vary across the menstrual cycle and may influence performance (Ansdell et al., 2019). Oral contraception may alter substrate utilization in exercise, however, these changes are very small (Tarnopolsky, 2008).

## 2.9 Summary

In summary, there are many different mechanisms that could be responsible for sex differences in fatigue. These differences are muscle group and task specific therefore different mechanisms may be responsible for different tasks and muscle groups. Taking into account the current literature, there are still gaps that need to be filled. The lack of studies that test females in fatigability and exercise training is partly responsible for this (S. K. Hunter, 2014). This study attempted to clear the gap of measuring oxygenation during a fatiguing exercise by using NIRS.

# Chapter III: Methodology

## 3.1 Introduction

Research has shown women are more fatigue resistant than men are during submaximal isometric contractions (S. K. Hunter, A. Critchlow, et al., 2004; S. K. Hunter & Enoka, 2001; Russ & Kent-Braun, 2003; Yoon et al., 2007), especially at low contraction intensities. Evidence suggests the greater muscle mass and greater absolute strength of men, may reduce skeletal muscle perfusion to a greater extent during low-intensity submaximal contractions due to occlusion due to higher intramuscular pressures from higher force contractions (Russ & Kent-Braun, 2003). To date no studies have examined microvascular circulation and oxygen saturation during fatiguing exercise in men and women. This chapter will discuss the methods that were used to measure levels of oxygenated and deoxygenated hemoglobin in men and women during a fatiguing exercise as well as a mitochondrial function test.

## 3.2 Participants

Thirty people were recruited to participate in this study, but only twenty-six completed the study (13 men and 13 women). However, one man and one women were excluded for analysis therefore 12 men and 12 women are included in the analysis below. A power analysis showed 26 participants provided sufficient power to detect an effect of 0.50 SD using a 2 x 2 mixed model ANOVA. The alpha level was set at $p < 0.05$.

Participants were aged 18-35 years. Participants were sedentary and active individuals. Prior to familiarization with data collection procedures, each participant

provided written, informed consent, completed a physical activity readiness questionnaire (PAR-Q), and a 7-day recall of physical activity questionnaire (IPAQ). Participants were excluded from this study if they had existing health conditions that contraindicate strenuous exercise, had any musculoskeletal injuries that would contraindicate exercise with the elbow flexors, or if they answered 'yes' to any questions on the PAR-Q. Participants were asked to refrain from physical activity prior on testing the duration of the study and advised to eat at least three hours before they participate. They were also asked to refrain from eating for 2 hours prior to each visit to and not consume caffeine within 6 hours of each testing visit. Participants were recruited through a convenience sample at the University of Oklahoma. Participants were informed about the study through word of mouth, announcements made in classes, emails, and fliers around the different departments at the University of Oklahoma. This study was approved by the University of Oklahoma Institutional Review Board.

### 3.3 Inclusion criteria

1. Participants within the ages of 18-35 years.
2. Males and females

### 3.4 Exclusion criteria

1. Participants who were outside of the specified age range
2. Participants with musculoskeletal injuries
3. Participants who answered "yes" to any questions on the PAR-Q and/or have any known cardiovascular, pulmonary, or metabolic diseases

4. Female participants who had not had a regular menstrual cycle over the previous 6 months
5. Participants on whom a usable NIRS and EMG signal cannot be collected
6. Female participants who were pregnant

## 3.5 Experimental Overview

There were a total of four visits for all participants for this experiment with an optional fifth visit for women. Two familiarization visits were followed by two (or 3 if chosen) experimental testing visits. The experimental visits were performed using a randomized, cross-over design. During the two experimental visits each participants' maximal voluntary isometric contraction (MVC) of the non-dominant elbow flexors (i.e. biceps) was determined followed by the performance of a submaximal isometric contraction performed at 20% of MVC until task failure under: 1) normal blood flow conditions and 2) ischemic conditions. Electromyography (performed on the long head) and near-infrared spectroscopy (NIRS; performed on the short head) were measured from the biceps brachii during the contractions held to task failure.

*Visit 1 – Familiarization* Written and verbal descriptions of the experiment and all procedures were given and any questions will be answered. Informed consent was completed. A physical activity readiness questionnaire (PAR-Q), menstrual history questionnaire, health status questionnaire, International Physical Activity Questionnaire (IPAQ), and Health Insurance Portability and Accountability Act (HIPPA) form were completed.

Height, weight, and muscle thickness of the biceps brachii via ultrasound were

measured. A dual-energy x-ray absorptiometry (DXA) scan was also performed on the first visit to assess body composition. Female participants complete a pregnancy text before the DXA scan to confirm they were not pregnant and urine specific gravity was measured in all participants to establish hydration status. Once all the measurements have been taken, the participants will begin being familiarized with the exercise protocols.

Participants then had the NIRS probe placed over the belly of the short head of biceps brachii and electromyography electrodes were placed over the long head of the biceps brachii. Then they were seated upright in a KinCom isokinetic dynamometer with their elbow joint on their non-dominant arm flexed to 90° so that their forearm was horizontal to the ground and the force at the wrist was directed upward during voluntary contractions. All positioning was personalized and recorded for each participant. Straps were placed around each shoulder and over the thighs to minimize movement during exercise. The participants then performed three MVC's of the elbow flexors with two minutes of rest between each trial. The two highest efforts that differ by <5% were averaged and considered the participant's MVC for that session. The participants practiced the voluntary isometric contraction at 20% of their MVC for two minut.The placement of the NIRS probe and EMG electrodes were marked with indelible ink to insure similar placement during future testing. EMG and NIRS signals were assessed to ensure that data of sufficient quality to be analyzed could be collected from the participant in future sessions.

*Visit 2 – Familiarization and Mitochondrial Function* The participants' mitochondrial

function was assessed. They assumed a resting supine position for 15 minutes and then blood pressure was taken in their dominant arm. The NIRS probe was then be placed on the belly of the non-dominant biceps brachii and a blood pressure cuff was placed around their upper arm, proximal to the NIRS probe. After a 5-minute rest period, the cuff was inflated to 250mmHg for 60 seconds. After the 60 seconds, it was released and followed by a 5-minute rest period. The cuff was again inflated to 250mmHg for 60 seconds followed by another 5 -minute rest period. After this rest period, the participant performed a 20 second isometric elbow flexion protocol to raise the metabolic rate in the biceps. Immediately following the exercise protocol, the blood pressure cuff around the upper arm was inflated to 250mmHg for 10 seconds and then deflated for 10 seconds. A series of 10 second inflations and 10 second deflations continued for 5 minutes for a total of 15 periods of inflation. Following the final deflation, a 3-minute rest period was provided. Following a further 10 minutes of rest, the assessment of mitochondrial function was performed again. The participants were then seated in the KinCom and repeated the familiarization protocol of the MVCs and holding a voluntary isometric contraction.

*Visit 3 & 4 – Voluntary Isometric Exercise until Task Failure* These two visits were separated by a minimum of 72 hours and were performed in a randomized, counter-balanced manner. Females were tested during the luteal phase of their menstrual cycle estimated from the menstrual cycle questionnaire filled out during the first visit.

Blood pressure was first taken. Then the NIRS probe and EMG electrodes were placed on the belly of the biceps brachii. The participants performed three MVCs. The

participants then held a voluntary isometric contraction at 20% of their MVC until failure. Biofeedback was provided to each participant by displaying a threshold marker on a computer screen that indicated the amount of force they needed to maintain. This marker was preset for each participant using the Biopac data acquisition software. Participants were verbally encouraged to give strong effort during these tasks. The experimenter terminated the exercise once the participants' force dropped by 10% for 3-5 seconds. Participants performed another MVC immediately following task failure and 1-minute post failure. During the fatiguing exercise, blood pressure on the contralateral (dominant) arm and ratings of perceived exertion (RPE) were taken every minute.

The condition in which the fatiguing exercise was performed under was randomized. The participants either performed the fatiguing exercise under normal blood flow conditions or under ischemic conditions. Under ischemic conditions the exercising limb was occluded by inflating a blood pressure cuff over the proximal portion of the arm at a pressure of 100 mmHg above resting systolic blood pressure. *Visit 5 – Optional Visit* Females had an optional fifth testing day during menstruation when estrogen and progesterone are low. During this testing day, they repeated the experimental protocol as performed previously, but only under normal, non-ischemic conditions.

## 3.6 Experimental Procedures

### Ultrasound Assessments of Muscle Thickness

Muscle thickness for the biceps brachii was determined using ultrasound equipment (FF sonic UF-750XT, FukudaeDenshi, Tokyo, JPN). The same researcher performed all

thickness measurements and analyses. The probe was placed perpendicular to the specific limb and the given image was frozen for further analysis. To prevent any compression of muscle or fat, at least 5mm of ultrasound gel will be visible on the display screen. Muscle thickness was measured at maximal girth following the midline of the anterior surface of the upper arm (Bemben, 2002) . Measurements were taken using the software within the ultrasound by drawing a direct line between the composition boundaries and recorded in mm.

**DXA Scan**

Body composition was determined with a whole body DXA scan (Lunar Prodigy Advance; GE-Medical Systems, Madison, WI) and corresponding analysis software (enCore 2011, version 13.60, GE-Healthcare, Madison, WI) according to the manufacturer's instructions. The same researcher performed and analyzed all the scans in accordance to the standard laboratory protocol. Custom regions of interest (ROI) boxes were draw for the four specific sites. The ROI area for the bicep was measured from the armpit to the antecubital fossa. Participants lay in a supine position with their arms resting against the sides of the body. DXA equipment was calibrated on a daily basis following the protocol provided by the manufacturer.

**Maximal Voluntary Contraction (MVC)**

MVCs were measured in the biceps brachii during elbow flexion. The participants performed three MVCs with two minutes of rest separating each contraction. Biceps brachii flexion force WAS recorded using a force transducer and a KinCom

dynamometer connected to a Biopac data collection module. The system displayed the applied force on an LCD screen through the use of Biopac data Acquisition software. The two highest efforts that differ by <5% were averaged and considered the participant's MVC for that session.

**Voluntary Isometric Exercise**

The voluntary isometric exercise task was carried out at 20% until task failure — defined as a decrease in force by 10% for 3 to 5 seconds despite strong verbal encouragement. This exercise was either be performed under normal conditions or under ischemic conditions. The exercising arm under ischemic conditions was occluded at a pressure of 100mmHg above systolic blood pressure. Biofeedback was provided to each participant by displaying a threshold marker on a computer screen that indicated the amount of force they needed to maintain. This marker was preset for each participant using the Biopac data acquisition software. Participants were verbally encouraged to give maximal effort during these tasks.

**Near Infrared Spectroscopy (NIRS)**

NIRS readings were taken throughout the entirety of the voluntary isometric exercise protocol using an Oxiplex TS system (ISS, Champaign, IL, USA). This NIRS device of a single detector and 8 light emitting diodes at wavelengths of 690 and 830 nm. Dynamic reduced scattering coefficients were used to provide absolute concentrations (μM) for deoxy [Hb + Mb], oxygenated [Hb + Mb], total-[Hb +Mb], and saturation %. The deoxy signal has been shown to be relatively stable despite changes

in blood volume and therefore has been used to reliably estimate fractional oxygen extraction (Broxterman et al., 2015). The NIRS probe was calibrated prior to each test per the recommendations of the manufacturer. The NIRS probe was placed around the belly of the biceps brachii muscle. Placement was determined by the use of anatomical landmarks and palpation.

**NIRS Assessment of Mitochondrial Function**

The participants were seated in the chair as previously described. The blood pressure cuff was placed around their upper arm and the NIRS probe was placed around the belly of the biceps brachii as marked during the first familiarization day. After a 3-5 minute rest period, the cuff was inflated to 250mmHg for 60 seconds. After the 60 seconds, it was released and followed by a 3-5 minute rest period. After this rest period, the participant performed a 20 second elbow flexion protocol to raise the metabolic rate. Immediately following the exercise protocol, the blood pressure cuff around the upper arm was inflated to 250mmHg for 10 seconds and then deflated for 10 seconds. A series of 10 second inflations and 10 second deflations continued for 5 minutes for a total of 15 periods of inflation. Following the final deflation, a 3 minute rest period was provided.

## 3.7 Statistical Analysis

SPSS, Sigma Plot, and Microsoft Excel were used for data analysis. A three-way repeated measure ANOVA was conducted to assess differences in deoxygenated hemoglobin measured by near-infrared spectroscopy (NIRS) to sex, time, and condition. Bonferonni post hoc was run when necessary. A two by two mixed model ANOVA was

performed to examined differences in time-to-task failure between sex and the blood flow condition. Independent t-tests were run to assess sex differences in body composition, mitochondrial function, and MVCs. Pearson's Correlation Coefficient test was run to compare MVC and task failure time. The alpha level was set at $p < 0.05$.

# Chapter IV: Results & Discussion

## 4.1 Participant Characteristics

Twelve females (age = 23.9 ± 3.6 yrs, height = 165.6 ± 7.5 cm, and weight = 64.3.1 ± 7.4 kg) and twelve males (age = 24.8 ± 3.3 yrs, height = 181.3 ± 7.0 cm, and weight = 84.7 ± 20.6 kg; values are mean ± SD) were included in the analysis. Table 1 contains data for body composition assessed from DEXA and ultrasound. The DEXA measurements contain total body measurements and a region of interest (ROI) that was measured from the armpit to the antecubital fossa. Independent t-tests showed women had significantly greater total body % fat ($p < 0.001$) and ROI % fat ($p < 0.001$) compared to men. Independent t-tests also showed that men had significantly higher total body lean mass ($p < 0.001$) and ROI lean mass ($p < 0.001$) compared to women. There was no significant difference between sexes for total body fat mass ($p = 0.22$) or ROI fat mass ($p = 0.050$). Women also had significantly greater fat thickness assessed by ultrasound ($p = 0.005$) compared to men while men had significantly greater total muscle thickness ($p < 0.001$) and bicep thickness ($p < 0.001$). There was no significant difference between sexes for brachialis thickness ($p = 0.13$).

**Table 1.** Body Composition Measurements

| | Males | Females |
|---|---|---|
| **DEXA** | | |
| TBFM (g) | 15699.6 ± 9328.0 | 19609 ± 5484.6 |
| ROI FM (g) | 288.6 ± 140.3 | 384.6 ± 78.4 |
| % Fat | 18.1 ± 8.1* | 31.7 ± 7.3* |
| ROI % Fat | 18.9 ± 6.6* | 37.6 ± 5.7* |
| TBLM (g) | 65875.8 ± 12853.5* | 42031.3 ± 5986.3* |
| ROI LM (g) | 1189.3 ± 251* | 637.3 ± 87.2* |
| **Ultrasound** | | |
| Fat Thickness (mm) | 0.23 ± 0.11* | 0.40 ± 0.20* |
| Total Muscle Thickness (mm) | 3.90 ± 0.42* | 2.80 ± 0.30* |
| Bicep Thickness (mm) | 2.89 ± 0.32* | 2.0 ± 0.10* |
| Brachialis Thickness (mm) | 0.91 ± 0.24 | 0.70 ± 0.30 |

Values are mean ± SD

* indicates a significant difference for sex ($p < 0.05$).

## 4.2 Assessment of Maximal Voluntary Contraction

Figure 1 shows MVCs pre exercise averaged across both days (ICC = 0.95). For normal conditions, elbow flexor MVC pre exercise was 335 ± 107 N on average for men and 192.7 ± 47.4 N on average for women. Immediately post exercise MVC was 172.2 ± 42.8 N for men and 129 ± 44.8 for women. 1-minute post exercise MVC was 218.1 ± 73.0 for men and 138.5 ± 51.7 for women. Independent t-tests showed a significant sex difference for pre MVC ($p < 0.001$), immediately post MVC ($p = 0.024$), 1-minute post MVC ($p = 0.005$) with men consistently being stronger than women. For

the blood flow occluded condition, elbow flexor MVC pre exercise was 342 ± 93.8 N on average for men and 182.8 ± 32.9 N on average for women. Immediately post exercise MVC was 149.8 ± 48.9 N for men and 93.7 ± 29.5 for women. 1-minute post exercise MVC was 264.2 ± 54.1 for men and 159.7 ± 32.5 for women. Independent t-tests showed a significant sex difference for pre exercise MVC ($p < 0.001$), immediately post MVC ($p = 0.003$), and 1-minute post MVC ($p < 0.001$). Figure 2 shows the correlation between average pre exercise MVC and upper arm lean mass from the DXA. MVC and upper arm lean mass were highly correlated ($r = 0.913$, $p < 0.001$)

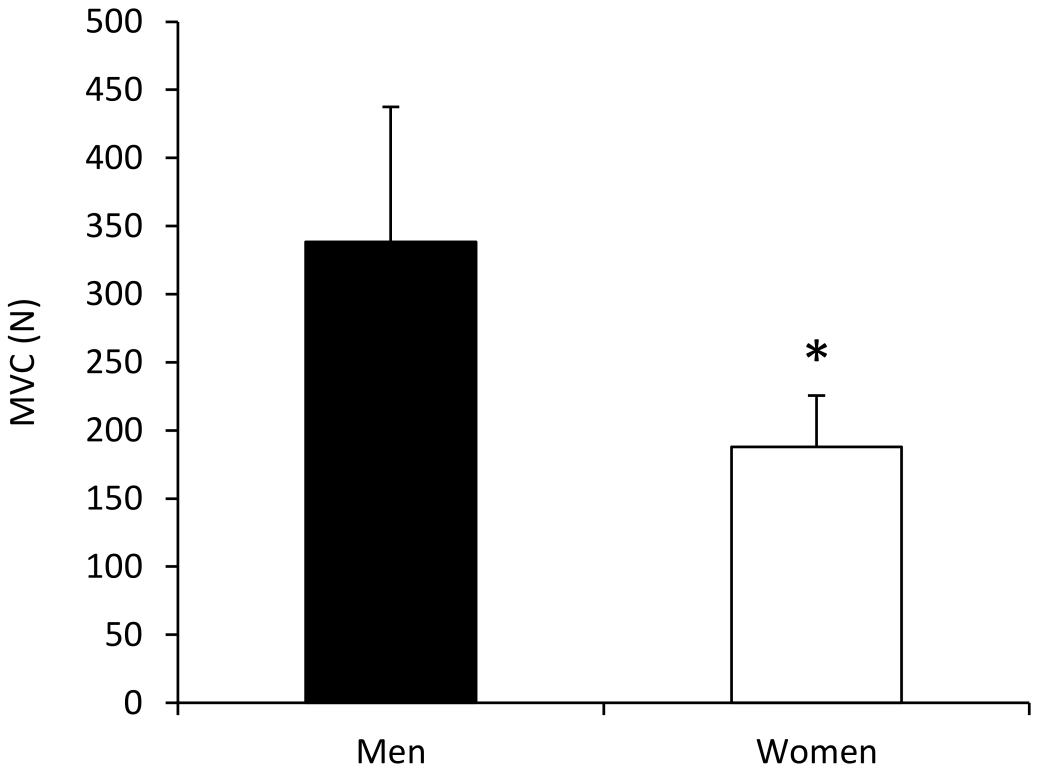


**Figure 1 :** Average MVCs across days before exercise * indicates a significant sex difference ($p < 0.05$). Values are mean ± SD.

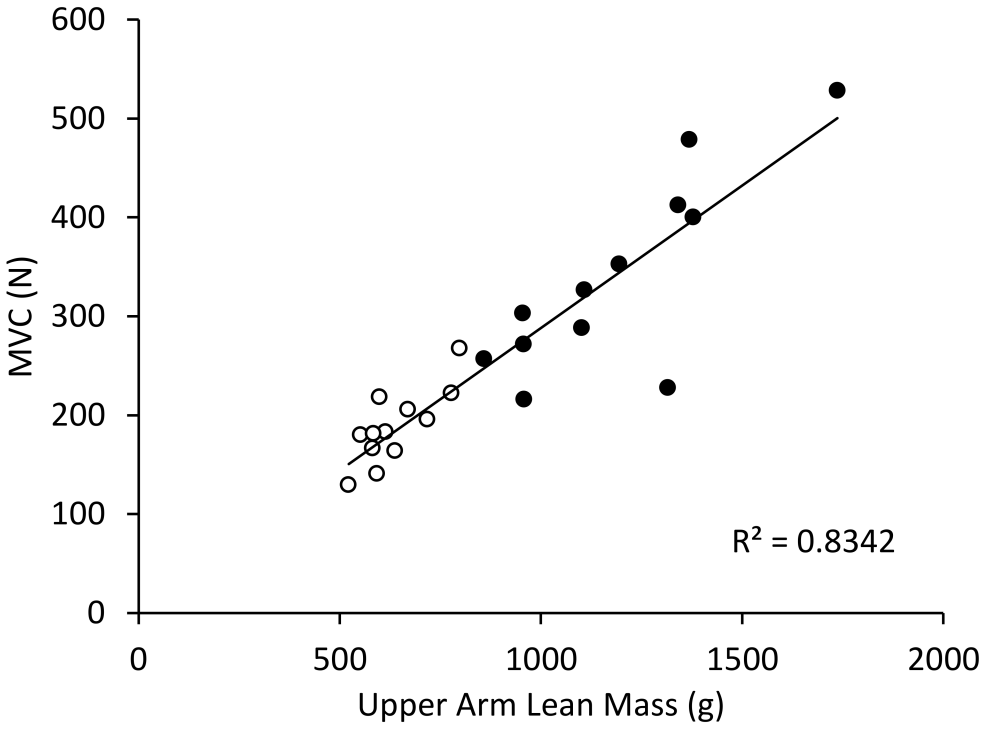


**Figure 2 :** Correlation between MVC pre exercise and upper arm lean mass.

Percent change from pre exercise to immediately post exercise, and % change from immediately post exercise to 1-minute post exercise under normal blood flow conditions and the occluded condition are shown in Figure 3. From pre exercise to immediately post exercise MVC decreased 46.1% ± 13.1% for men and 33.3% ± 13.7% for women. MVC increased from immediately post exercise to 1-minute post exercise by 28.7% ± 40.6% for men and 9.8% ± 33.2% for women ($p = 0.029$). There was not a significant sex difference for % change from immediately post MVC to 1-minute post MVC ($p = 0.225$). In the occluded condition from pre exercise to immediately post exercise MVC decreased 55.8% ± 16.6% for men and 49.3% ± 10.7% for women. MVC

increased from immediately post exercise to 1-minute post exercise by 98.5% ± 87.8% for men and 79.4% ± 40.1% for women. There was not a significant sex difference for % change of MVC from pre to immediately post exercise ($p = 0.275$) and % change from immediately post MVC to 1-minute post MVC ($p = 0.505$).

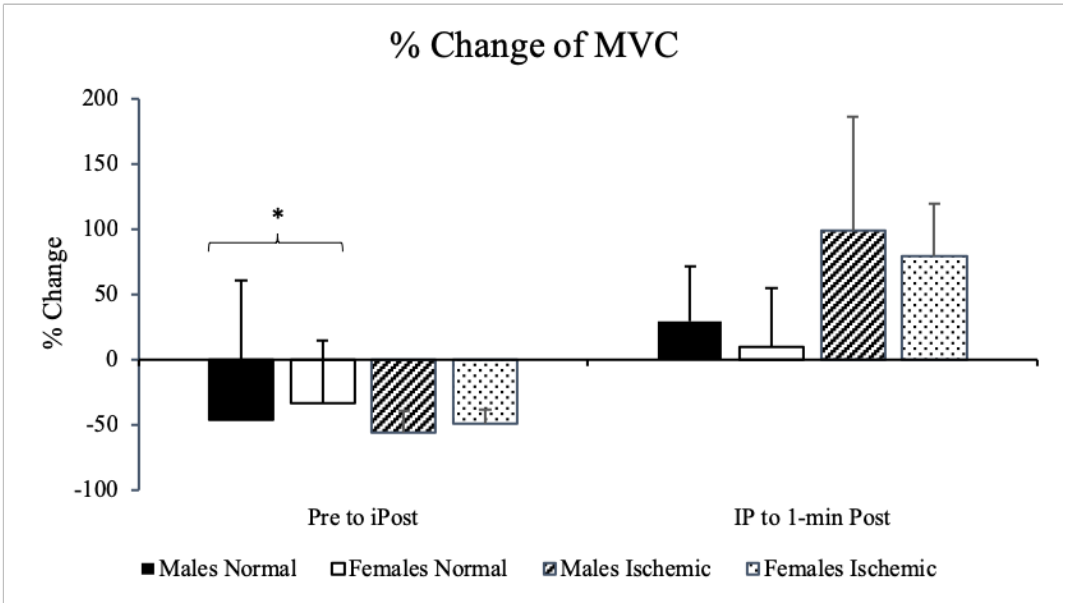


**Figure 3 :** % change of MVC from pre to immediately post exercise and immediately post exercise to 1-minute post exercise under normal and ischemic conditions. * indicates a significant sex difference ($p < 0.05$). Values are mean ± SD.

## 4.3 Assessment of Time-to-Task Failure

Figure 4 shows differences in time-to-task failure under normal and ischemic conditions. Under normal conditions, men performed this task for an average of 631.1 ± 475.5 sec and women performed this task for an average of 905.7 ± 553.2 sec. Under ischemic conditions, men performed this task for an average of 224.7 ± 47.1 sec and women performed this task for an average of 207.5 ± 28.3 sec. The interaction of the 2

x 2 ANOVA was not significant ($p = 0.17$) nor was there a main effect for sex ($p = 0.25$). There was a significant main effect for ischemic condition with TTF being reduced in the occluded, compared to normal flow condition ($p < 0.001$). Despite the lack of an interaction or main effect for sex, a moderate effect favoring women (e.g. women had a larger TTF than men) was observed (Cohen's $d = 0.53$). Additionally, one male participant exhibited a TTF that was 2.70 SD above the mean value for men (1919 sec) shown in Figure 5. Removal of this participant as a potential outlier, makes the interaction term significant ($p = 0.036$) and the post-hoc test between men and women under normal blood flow conditions significant ($p = 0.04$) and nearly doubles the effect size to $d = 0.96$ SD. TTF under normal and ischemic conditions did not significantly correlate to any body composition measurements ($p > 0.05$)

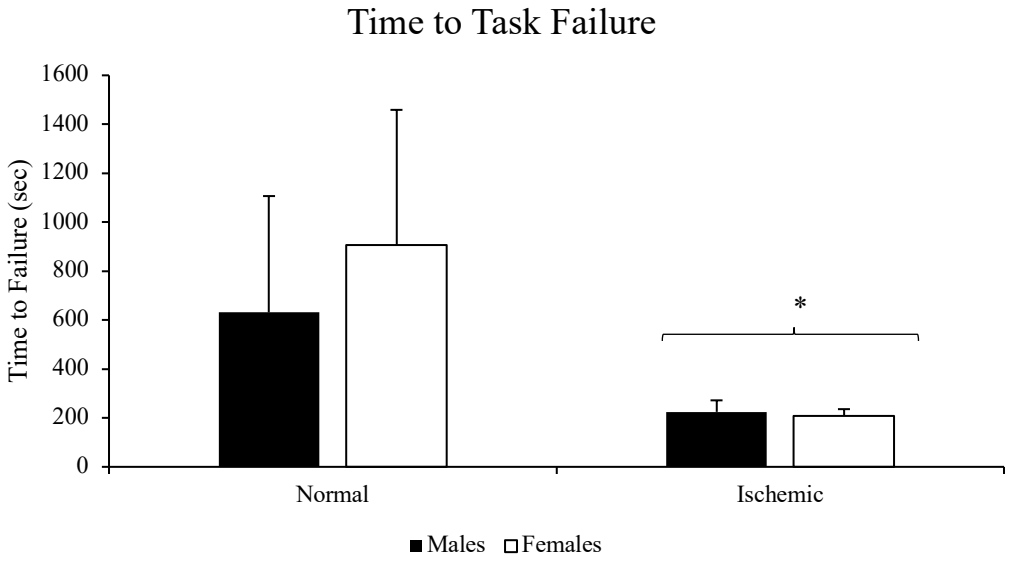


**Figure 4:** Time to task failure under normal and ischemic conditions. No significant differences between men and women. * indicates a significant difference between

conditions ($p < 0.001$). No sex differences observed ($p = 0.17$, Cohen's $D = 0.53$). Values are mean ± SD.

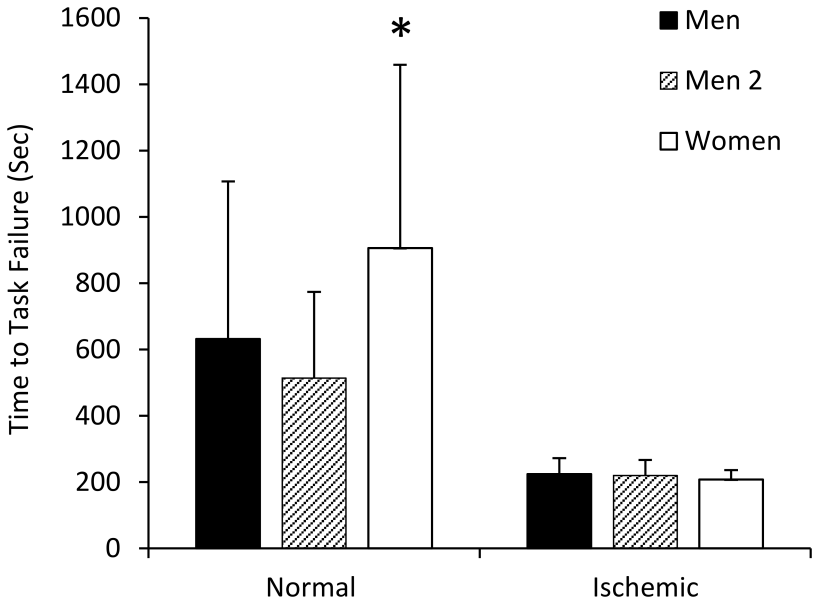


**Figure 5:** Time to task failure under normal and ischemic conditions excluding potential male outlier. *indicates a significant sex differences ($p = 0.04$, Cohen's $D = 0.96$). Values are mean ± SD.

## 4.4 Assessment of NIRS during Time-to-Task Failure

A 3 second average was taken at 20%, 40%, 60%, 80% and 100% of time elapsed during the time to task failure test. The percent change of deoxygenated hemoglobin from start of exercise was then calculated and reported in Figure 6. A three-way repeated measures ANOVA showed a significant condition main effect ($p = 0.02$) with deoxygenated hemoglobin being elevated to a greater extent in the occluded

condition. The ANOVA also showed a significant time main effect ($p < 0.001$). A Bonferonni post hoc analysis confirmed that deoxygenated hemoglobin was significantly greater at all time points compared to start of exercise ($p < 0.001$). There were no significant differences between the other time points ($p > 0.05$). There was not a significant main effect for sex ($p = 0.476$) as seen in figures 6. There was a significant 2-way interaction for condition x time ($p = 0.018$) as seen in figure 8. Post-hoc tests found no differences in the percent change in deoxygenated Hb at 20% ($p = 0.051$) and 60% ($p = 0.06$) of TTF, but elevated [Hb] at 40% ($p = 0.01$). 80% ($p = 0.01$), and 100% ($p = 0.02$) of TTF. There was not a significant interaction for condition x sex, time x sex, or condition x time x sex ($p > 0.05$).

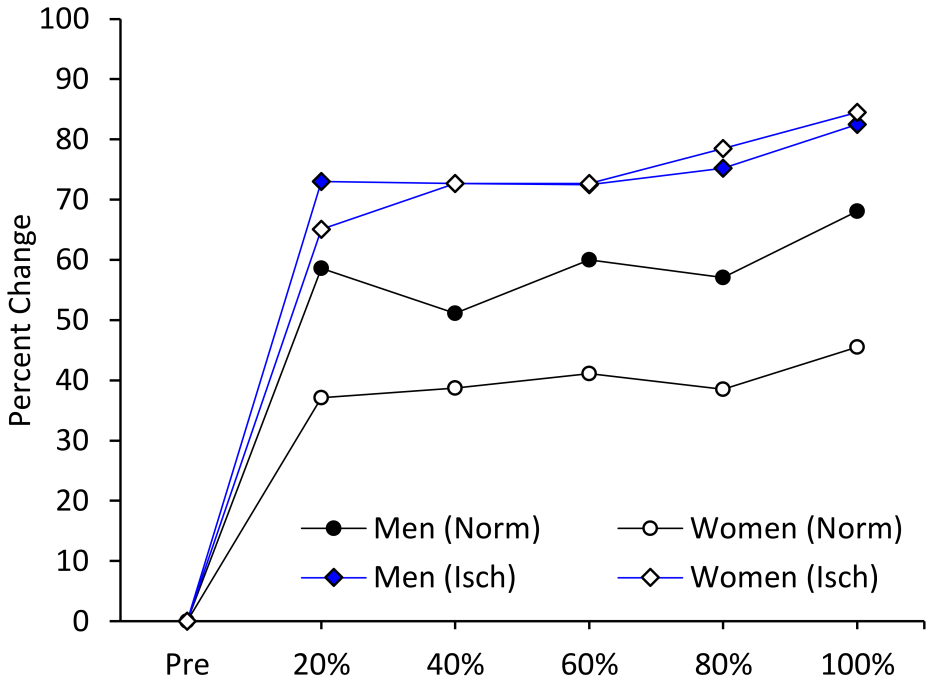


**Figure 6:** % change of deoxygenated hemoglobin under normal and ischemic conditions between sexes displayed as a percentage of time elapsed during TTF. No significant sex x condition effect. Values are mean ± SD.

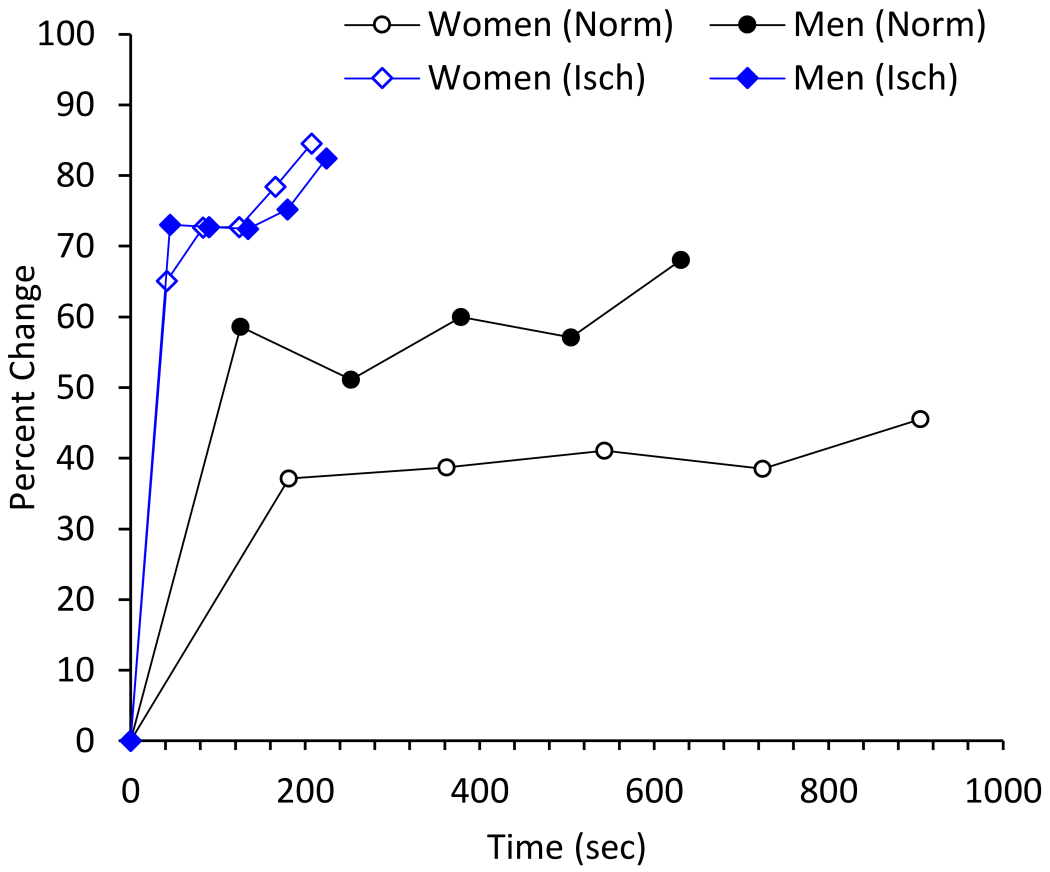


**Figure 7:** % change of deoxygenated hemoglobin under normal and ischemic conditions between sexes displayed as average time elapsed in seconds during TTF. No significant sex x condition effect. Values are mean ± SD.

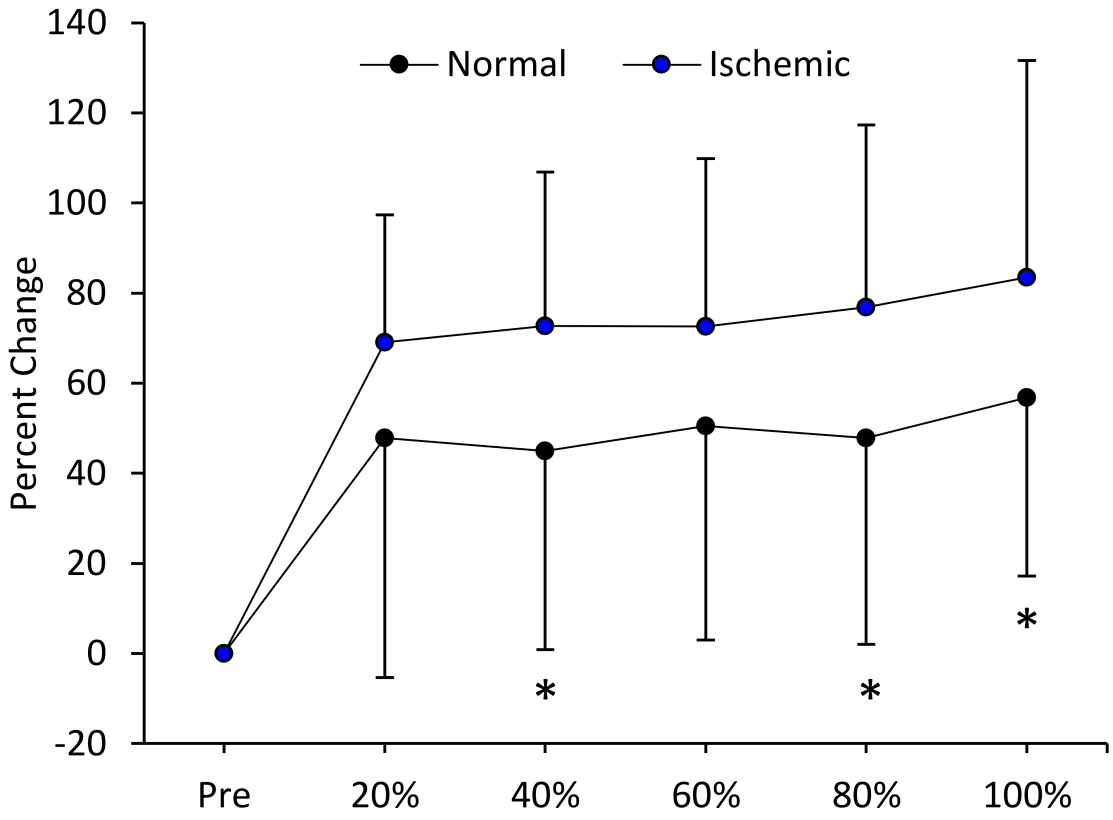


**Figure 8:** % change of deoxygenated hemoglobin under normal and ischemic conditions displayed as a percentage of time elapsed during TTF. A significant condition x time effect was seen at 40% ($p = 0.01$). 80% ($p = 0.01$), and 100% ($p = 0.02$) of TTF. Values are mean ± SD.

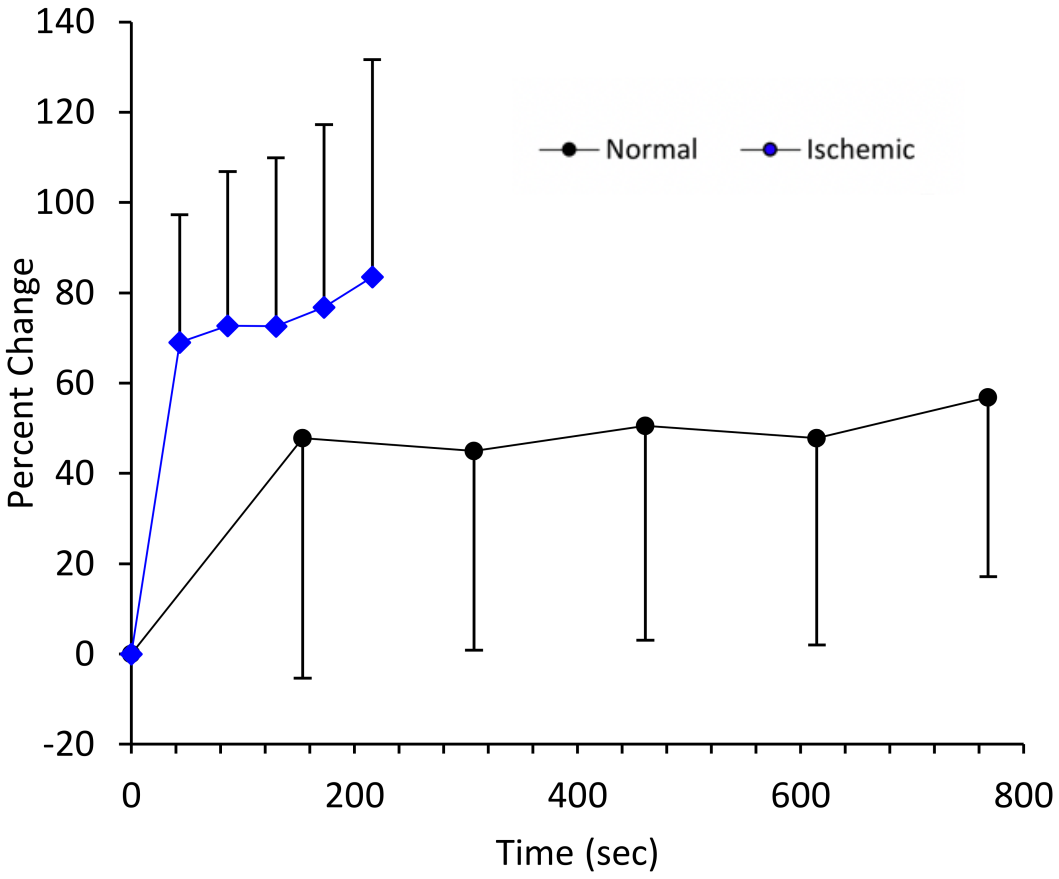


**Figure 9:** % change of deoxygenated hemoglobin under normal and ischemic conditions displayed as the average time elapsed in seconds during TTF.

## 4.5 NIRS Assessment of Mitochondrial Function

Mean time constants from the mitochondrial function test are shown in figure 6 with the mean slope constants (k) shown in figure 7. An independent t-test showed no significant sex difference for the time constant ($p = 0.22$, Cohen's $d = -0.53$) nor the slope constants ($p = 0.40$, Cohen's $d = 0.36$).

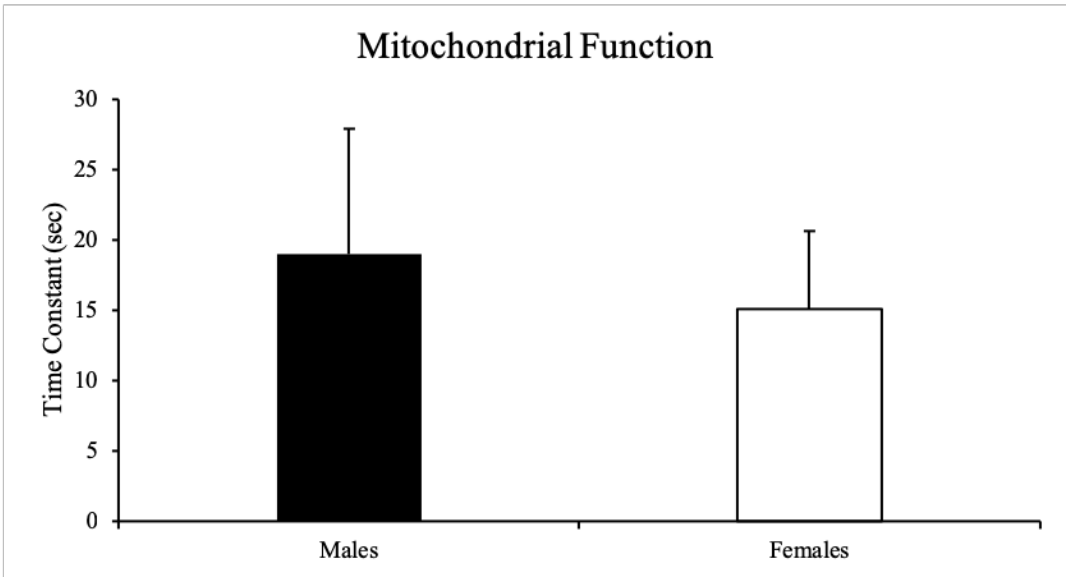


**Figure 10:** Time constants from the mitochondria function test. Values are mean ± SD.

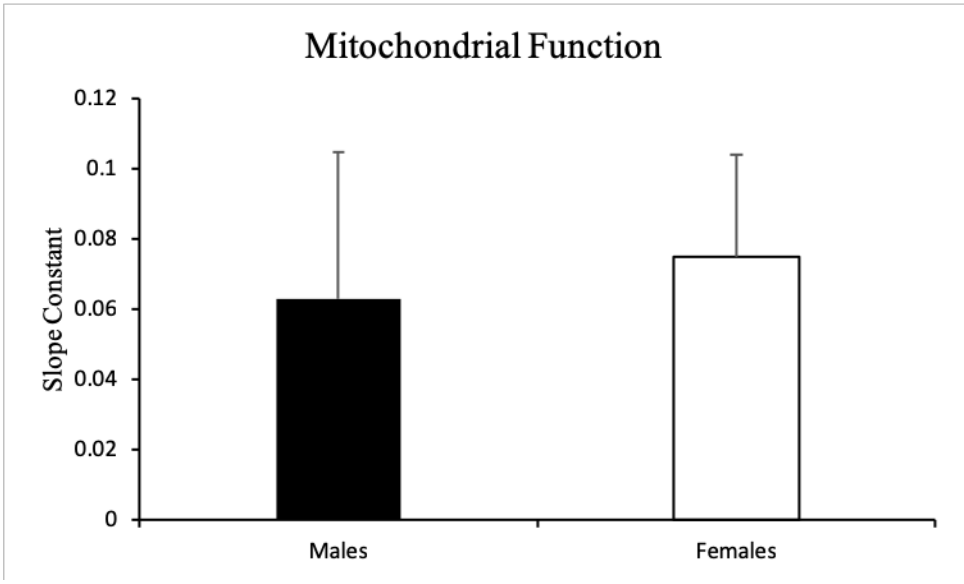


**Figure 11:** Slope constants from the mitochondria function test. Values are mean ± SD.

## 4.6 Relationships between MVC and Mitochondrial Function and TTF

MVC did not correlate with TTF under normal blood flow conditions ($p > 0.05$; $p = -0.263$) and can be seen in Figure 8. However, both measures of mitochondrial function were found to moderately correlate with TTF with $r = 0.43$ ($p = 0.038$; Figure 9) for the slope constant and $r = -0.42$ ($p = 0.048$; Figure 10) for the time constant.

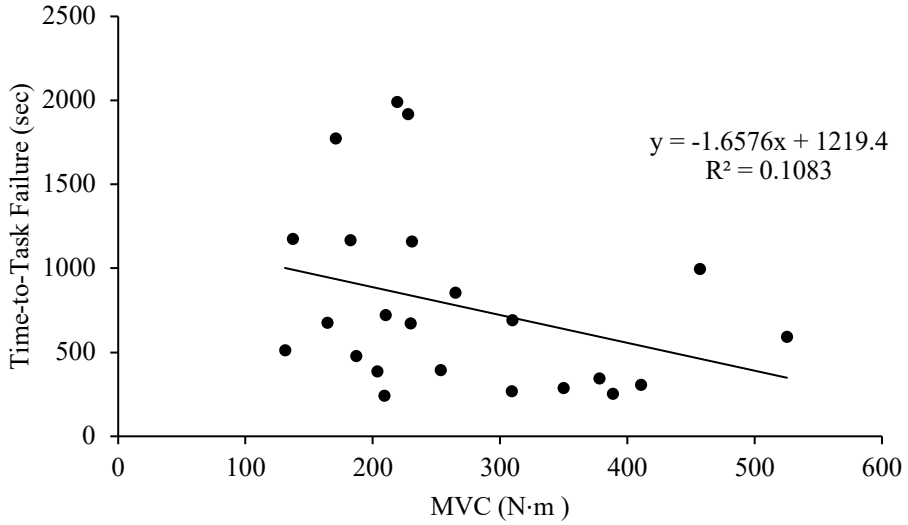


**Figure 12** – Relationship between maximal isometric strength of the elbow flexors and time-to-task failure under normal blood flow conditions.

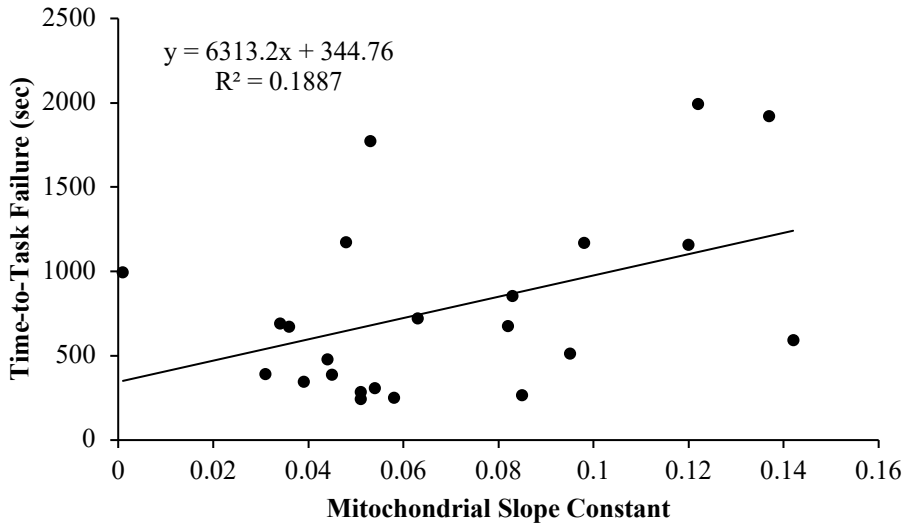


**Figure 13** – Relationship between mitochondrial slope constant (larger equates to better mitochondrial function) of the elbow flexors and time-to-task failure under normal blood flow conditions.

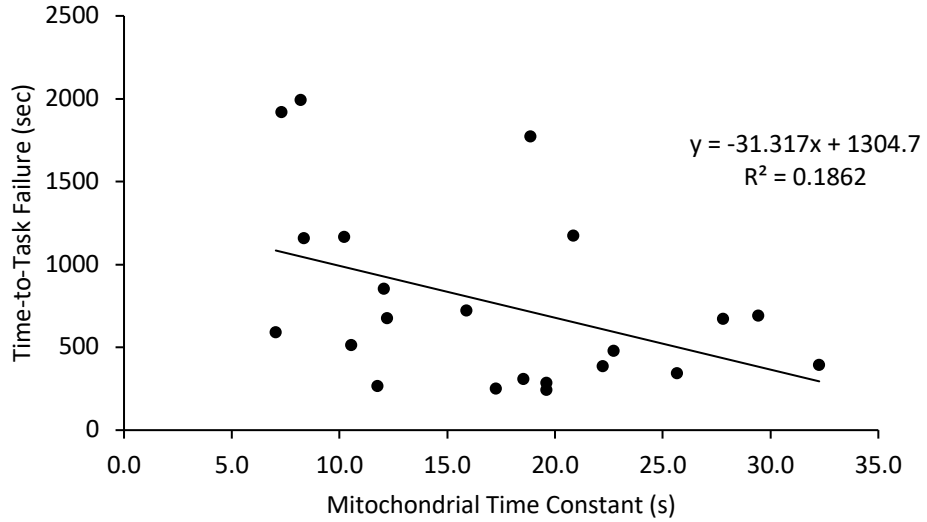


**Figure 14** – Relationship between mitochondrial time constant (shorter equates to better mitochondrial function) of the elbow flexors and time-to-task failure under normal blood flow conditions.

## 4.7 Assessment of RPE

RPE was taken every minute during the time to task failure test. The value given at the relative mid point and end point for every participant was analyzed. No sex differences were observed under normal conditions for the midpoint ($p = 0.205$) and the endpoint ($p = 0.583$) or under ischemic conditions for the midpoint ($p = 0.528$) and the endpoint ($p = 0.169$). Table 2 shows RPE averages for men and women.

**Table 2.** Rate of Perceived Exertion (RPE) averages

| | | Males | Females |
|---|---|---|---|
| **Normal** | | | |
| | Midpoint | 16 ± 1.8 | 17.1 ± 2.2 |
| | Endpoint | 19.4 ± 0.8 | 19.6 ± 0.7 |
| **Ischemic** | | | |
| | Midpoint | 15.7 ± 1.4 | 16.1 ± 1.8 |
| | Endpoint | 19.7 ± 0.5 | 19.2 ± 1.1 |

RPE is on a scale from 6 to 20 with 6 being no exertion to 20 being the most exertion able to be performed. Values are mean ± SD

## Discussion

The purpose of this study was to investigate the relationship between oxygen saturation and muscle fatigue in men and women and to determine if there is a common point of oxygen desaturation that leads to muscle fatigue. Our primary findings were: 1) as expected, men were stronger had greater lean mass than women, 2) no significant sex differences were observed in time-to-task failure, 3) no mitochondrial function differences were found between men and women, and 4) task failure occurred at similar percent changes in the deoxygenation of hemoglobin between men and women.

### 4.8 Body Composition and Maximal Strength

As expected, men were found to have greater lean tissue mass, greater bicep thickness, and greater muscle thickness in their upper arms compared to women. Additionally, men had reduced percent fat and fat thickness when compared to women in their upper arm. Men were also significantly stronger in their elbow flexors, as expected, than women based on their MVCs. Hunter and Enoka (2001) examined sex differences and fatigue in the elbow flexors of 7 men and 7 women. The average MVC for their men was 393 N compared to 335 N in the present study and for women was 177 N compared to 192 N in the present study (S. K. Hunter & Enoka, 2001). While it is difficult to make a direct comparison between studies, the fact that our men were weaker and women were stronger than a previous report could have an influenced our findings-as will be discussed further below. Men and women exhibited a decline in MVC after the fatigue test in the present study. This finding is similar to what has been reported previously (S. K. Hunter & Enoka, 2001) and provides an indication that a

similar, maximal effort was provided during the TTF test.

## 4.9 Time-to-Task Failure

We found that there was not a significant difference in time-to-task failure between men and women under normal blood flow conditions as well as under ischemic conditions with occlusion. Previous literature has clearly established that women are able to hold their time to failure longer than men during low intensity isometric tasks when they are not matched on maximal strength—making our results unexpected (Clark, Collier, Manini, & Ploutz-Snyder, 2005; S. K. Hunter & Enoka, 2001; Russ & Kent-Braun, 2003; B. C. Thompson, Fadia, Pincivero, & Scheuermann, 2007; West, Hicks, Clements, & Dowling, 1995; Yoon et al., 2007). Hunter and Enoka (2001) conducted a study where they tested TTF in the elbow flexors of 14 people (7 men and 7 women). They reported that the TTF in their women was 1,806 seconds—double the duration of our women at 905 seconds. TTF in their men was 829 seconds—198 seconds longer than our men (S. K. Hunter & Enoka, 2001). In spite of these differences in TTF, our MVCs were fairly similar. MVCs for their men compared to ours was 393 N and 335 N respectively and for women was 177 N and 192 N (S. K. Hunter & Enoka, 2001). Decline in MVC after TTF was also relatively similar with our men having a slightly larger reduction in force. The percent decline in MVCs for their men compared to ours was 39% and 46% respectively and for women was 34% and 33% (S. K. Hunter & Enoka, 2001). These data suggest that we should have seen similar results in TTF since our numbers and patterns are similar, so why we did not remains unclear. Yoon et al (2007) also conducted a study looking at TTF in the elbow flexors between men and

women (Yoon et al., 2007). They reported that the TTF in their women was 1,020 seconds. This is closer to our results at 905 seconds, but still longer by an average of about 2 minutes. Unlike the previous study by Hunter and Enoka (2001), the results of their men (636 seconds) compared to our men (631 seconds) were very similar. Avin et al. (2001) had participants comlete a sustained contraction at 50% of MVC until failure and found that women were once again more fatigue resistant than men at the elbow (Avin et al., 2010). Because of the differences in intensity between their study and the present study, it is difficult to compare time to failure, however their overall trend is different than ours.

We can speculate that the lack of differences between men and women in our study is likely due to the relatively small sample (12 men and 12 women) of the present study, lack of effort from participants, and the presence of a potential outlier in the sample of men. One male participant exhibited a TTF that was 2.70 SD above the mean value for men, with him included (1,919 seconds). While that does not meet the accepted threshold of 3 SD from the mean to be termed a statistical outlier, it needs to be considered. Especially in light of the fact that if this participant was removed from the analysis that the difference between men and women in TTF does reach statistical significance and the size of the observed difference nearly doubles from 0.53 SD to 0.96 SD—much more in line with previous reports. We believe that testing more people would further confirm a sex difference in time to task failure.

The observation that there were no sex differences under ischemic conditions was in line with previous literature. Russ and Kent-Braun (2003) examined sex specific differences in fatigue under free-flow circulation and ischemic in the dorsiflexors of 8

men and 8 women. They reported during intermittent contractions, women and men fatigued equally under ischemic conditions, but that men fatigued quicker under normal blood flow conditions (Russ & Kent-Braun, 2003). They attributed the observation that sex differences in fatigue were eliminated under ischemic conditions to differences in the metabolic pathway utilization during muscle contractions—a shift to more anaerobic metabolism. Similarly, Clark et al. (2005) examined sex specific differences in fatigue under normal blood flow and ischemia of the knee extensors in 11 men and 11 women. They found that under sustained contractions, in the quadriceps, men and women fatigued equally under ischemic conditions (179 sec vs 165 sec respectively), but that men fatigued before women under normal blood flow conditions (169 sec vs 214 sec respectively) (Clark et al., 2005) which they suggested was caused by differences in muscle blood flow and/or muscle metabolism.

## 4.11 NIRS

NIRS was measured in the biceps brachii throughout TTF. As expected, deoxygenated hemoglobin increased from pre exercise relatively early on during the fatigue test, and tended to level off by 20-40% of TTF. Interestingly, there was not a significant difference in the percent change in the deoxygenated hemoglobin concentration between sexes when expressed as a percentage of TTF (e.g. at 20%, 40%, of TTF, etc.) exercise under normal or ischemic conditions. However, ischemic conditions in comparison to normal conditions produced larger concentrations of deoxygenated hemoglobin. There appears to be a common level of desaturation, but it is specific to a flow condition. This finding suggests that it likely took women longer to

reach the same levels of deoxygenation as men, since the majority of the women took longer to reach task failure under normal blood flow conditions.

We originally believed men would experience greater oxygen desaturation due to them having greater reductions in blood flow to the exercising muscle. However, our results suggest that men do not have greater oxygen desaturation when compared to women, the desaturation just occurs more quickly. We did not measure blood flow, however, in 2015, Kellawan et al. tested 23 women and 22 men and found that on average, women had a 23% larger relative forearm blood flow response when compared to men during 5 minutes of exercise at 15% of MVC (Kellawan et al., 2015). Taking those results into consideration with ours, we can assume our women also had a larger relative blood flow response at 20% of MVC and, typically, a longer duration than 5 minutes. Hunter and Enoka (2001) found that the longer endurance times of women of TTF in the elbow flexors was associated with a reduced pressor response in comparison to men (S. K. Hunter & Enoka, 2001). These results would contribute to the explanation of why the men in the present study desaturated more quickly than the women.

## 4.10 Mitochondrial Function

The NIRS assessed slope constant and time constant from the biceps brachii were similar to those reported in previous studies using similar techniques (McCully et al., 1994; Ryan et al., 2013). Using the NIRS to assess mitochondrial function is a somewhat newer technique and has been cross-validated with phosphorus magnetic resonance spectroscopy (P-MRS) to assess oxidative capacity of skeletal muscle (Ryan et al., 2013). We did not find a sex difference in mitochondrial function. Given that

none of our participants reported performing significant amounts of upper body endurance exercise, the lack of a sex difference is unsurprising. To our knowledge, this is the first study examining sex differences utilizing this method of measuring mitochondrial function with NIRS so further research to confirm our results seems warranted. There has also not been a study looking at P-MRS assessment of mitochondrial function and sex differences.

Similarly to our findings, a study by Thompson et al. (2013) found no differences in mitochondrial function, specifically mitochondrial respiration, in the gastrocnemius between men and women. They tested 19 men and 11 women via muscle biopsy and completed four assays measuring activity of electron transport chain complexes I, II, III, and IV (J. R. Thompson et al., 2013). These measurements represent the ability to transport substrates, transfer electrons to the respiratory chain, reduce electron acceptors, and shuttle electrons to oxygen (J. R. Thompson et al., 2013). Although they used a different muscle and a different technique to test mitochondrial function than in our study, we found similar results.

Similarities in mitochondrial function suggest that the moderate (or large based upon whether one male participant is excluded) effect size favoring women in TTF were not due to measureable differences aerobic metabolism in the biceps brachii. However, both measures of mitochondrial function were found to moderately correlate with TTF under normal blood flow conditions—suggesting that while it may not account for sex differences, that mitochondrial function does play a role in TTF. In skeletal muscle, mitochondria are responsible for generating energy for muscle contractions and the function of the mitochondria is related to exercise performance

(Holloszy, 1967). This relationship may explain the moderate correlation with TTF.

## Chapter V: Conclusions

We did not observe a sex difference in time to task failure, however, even with one male participant who was almost a statistical outlier, we still had a moderate effect size (Cohen's d = 0.53). These results led us to answer one of our research questions and fail to reject our null hypothesis as men did not have a lower time-to-task failure compared to women. We also found that there was no noticeable difference in pattern of desaturation of hemoglobin. This led us to fail to reject our second null hypothesis as we did not see a difference in desaturation between men and women. However, we did answer our second research question and find that task failure occurs at relatively similar points of desaturation between men and women. Lastly, we did not find differences in mitochondrial function between men and women which led us to fail to reject our third null hypothesis as we did not see differences in mitochondrial function between men and women. Although, we did answer our last research question by our finding of a moderate correlation between TTF and mitochondrial function. There were some limitations to this study. A larger sample size is needed to reach a larger effect size. We also tested men and women who were trained and untrained. It would be interesting for future studies to test larger muscle groups as well as individuals who are highly endurance trained in those muscle groups.

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# APPENDIX A: IRB APPROVAL LETTER

The UNIVERSITY of OKLAHOMA

**Institutional Review Board for the Protection of Human Subjects**

**Approval of Initial Submission – Expedited Review – AP01**

**Date:** October 24, 2017 **IRB#:** 8598

**Principal Investigator:** Christopher D Black **Approval Date:** 10/24/2017 **Expiration Date:** 09/30/2018

**Study Title:** The Effects of Transcutaneous Electrical Nerve Stimulation and Isometric Exercise on Pain Perception Prior to and Following an Acute Bout of Exercise

**Expedited Category:** 4

**Collection/Use of PHI:** Yes

On behalf of the Institutional Review Board (IRB), I have reviewed and granted expedited approval of the above-referenced research study. To view the documents approved for this submission, open this study from the *My Studies* option, go to *Submission History*, go to *Completed Submissions* tab and then click the *Details* icon.

As principal investigator of this research study, you are responsible to:

- Conduct the research study in a manner consistent with the requirements of the IRB and federal regulations 45 CFR 46.
- Obtain informed consent and research privacy authorization using the currently approved, stamped forms and retain all original, signed forms, if applicable.
- Request approval from the IRB prior to implementing any/all modifications.
- Promptly report to the IRB any harm experienced by a participant that is both unanticipated and related per IRB policy.
- Maintain accurate and complete study records for evaluation by the HRPP Quality Improvement Program and, if applicable, inspection by regulatory agencies and/or the study sponsor.
- Promptly submit continuing review documents to the IRB upon notification approximately 60 days prior to the expiration date indicated above.
- Submit a final closure report at the completion of the project.

If you have questions about this notification or using iRIS, contact the IRB @ 405-325-8110 or irb@ou.edu.

Cordially,

Lara Mayeux

Lara Mayeux, Ph.D.
Chair, Institutional Review Board

## APPENDIX B: INFORMED CONSENT

**Consent Form**
**University of Oklahoma Health Sciences Center (OUHSC)**
**University of Oklahoma – Norman Campus**
**The Relationship between Oxygen Saturation and Muscle Fatigue in Men and Women Principal Investigator: Christopher Black, PhD**
**Sponsor: Health and Exercise Science Department**

This is a research study. Research studies involve only individuals who choose to participate. Please take your time to make your decision. Discuss this with your family and friends.

**Why Have I Been Asked To Participate In This Study?**

You are being asked to take part in this study because you are a healthy adult (18-35).

**Why Is This Study Being Done?**

The purpose of this study is to examine the relationship between oxygen saturation and muscle fatigue.

**How Many People Will Take Part In The Study?**

About 30 people will take part in this study. All visits will take place in the Sensory and Muscle Function Laboratory located in the Health and Exercise Science Department at the University of Oklahoma Norman campus.

**What Is Involved In The Study?**

If you agree to be in this research, you will be asked to visit the Sensory and Muscle Function Laboratory in the Health and Exercise Science Department at the University of Oklahoma Norman campus for 4-5 separate visits.

*Visit 1*

Height, weight, and muscle thickness of the biceps will be measured. Muscle thickness will be measured by ultrasound. A DXA scan, which measures body composition, will also be taken and you will provide a urine sample to check hydration status. Female participants will complete a urine pregnancy test before the DXA scan. Then, you will practice doing isometric elbow flexion exercises using maximal effort (MVC) on your non-dominant arm. Isometric elbow flexion involves pulling up as hard as you can against an immoveable object. You will then practice holding an isometric elbow flexion task at 20% of your maximal voluntary contraction (MVC) for two minutes. The NIRS (Near-Infrared Spectroscopy), measuring how much oxygen is in your blood, and

EMG (electromyography) measuring the electrical activity of your muscle, will be placed on the biceps brachii during the exercising testing.

*Visit 2*

Your blood pressure will first be taken. Then, you will perform a mitochondrial function test. The NIRS will be placed in the same spot it was from your first visit and a blood pressure cuff will be placed around your upper arm. You will rest for 5-minutes, followed by a cuff inflation to 250mmHg for 60 seconds. Then you will rest for another 5-minutes followed by another cuff inflation to 250mmHg for 60 seconds. You will rest for another 5-minutes followed by a 20 second elbow flexion exercise. Immediately after the exercise, the cuff will be inflated for 10 seconds and then deflated for 10 seconds. A series of 10 second inflations and 10 second deflations will continue for 5 minutes for a total of 15 periods of inflation. Following the final deflation, you will rest for an additional 10 minutes and then the test will be performed again. Then you will then practice doing isometric elbow flexion exercises using maximal effort. You will then practice holding a isometric elbow flexion task at 20% of MVC for two minutes.

In order to eliminate testing bias the order of the following testing visits will be randomized—all visits will be performed, but the order will vary.

*Visit 3*

Your blood pressure will first be taken. Then, you will perform three MVCs separated by 2 minutes. The NIRS probe and EMG electrodes will then be placed on your biceps on your non-dominant arm. You will then hold a voluntary isometric contraction at 20% of your MVC until failure under normal conditions. You will perform an MVC immediately following failure and 1 minute post failure. Blood pressure of the opposite arm and RPE (rate of perceived exertion) will be taken every minute during testing.

*Visit 4*

Your blood pressure will first be taken. Then, you will perform three MVCs separated by 2 minutes. The NIRS probe and EMG electrodes will then be placed on your biceps brachii on your non- dominant arm and a blood pressure cuff will be placed around your upper arm. You will then hold a voluntary isometric contraction at 20% of your MVC until failure under ischemic conditions. The ischemic conditions consist of the blood pressure cuff being inflated to 100mmHg above your systolic blood pressure. You will perform an MVC immediately following failure and 1 minute post failure. Blood pressure of the opposite arm and RPE (rate of perceived exertion) will be taken every minute during testing.

*Visit 5 – optional for females*

This visit will be completed during menstruation. Your blood pressure will first be taken. Then, you will perform three MVCs separated by 2 minutes. The NIRS probe

and EMG electrodes will then be placed on your biceps brachii on your non-dominant arm. You will then hold a voluntary isometric contraction at 20% of your MVC until failure under normal conditions. You will perform an MVC immediately following failure and 1-minute post failure. Blood pressure of the opposite arm and RPE (rate of perceived exertion) will be taken every minute during testing.

**How Long Will I Be In The Study?**

We think that you will be in the study for 4-5 visits, each lasting roughly 45-60 minutes.

There may be anticipated circumstances under which your participation may be terminated by the investigator without regard to your consent.

You can stop participating in this study at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first.

**What Are The Risks of The Study?**

If you participate in this research, you will be exposed to radiation from a DXA scan (a type of x- ray). The amount of radiation to which you will be exposed from one DXA scan is approximately less than 1% of the amount of radiation that we are exposed to each year from natural background sources of radiation. The risk of radiation exposure is cumulative over your lifetime.

Performing maximal effort elbow flexions may cause some discomfort and the effort required to produce maximal force will be uncomfortable. You may experience some lightheadedness or nausea. There is also the risk for cardiovascular events when performing elbow flexion. There will also be some discomfort or pain from the occlusion during the mitochondrial function test and one of the time to task failure tests. You will be closely monitored for any issues.

**Are There Benefits to Taking Part in The Study?**

If you agree to take part in this study, there is no direct medical benefit to you. We hope that the information learned from this study will benefit other patients in the future. You will be able to learn your body composition.

**What Other Options Are There?**

You may choose not to participate in the study.

**What about Confidentiality?**

Efforts will be made to keep your personal information confidential. You will not be identifiable by name or description in any reports or publications about this study. We

cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. You will be asked to sign a separate authorization form for use or sharing of your protected health information.

There are organizations outside the OUHSC that may inspect and/or copy your research records for quality assurance and data analysis. These organizations include the US Food & Drug Administration and other regulatory agencies. The OUHSC Human Research Participant Program office, the OUHSC Institutional Review Board, and the OUHSC Office of Compliance may also inspect and/or copy your research records for these purposes.

**What Are the Costs?**

There is no cost to you if you participate in the study.

**Will I Be Paid For Participating in This Study?**

You will receive a $10 gift card after completing the 4 required visits. If you are one of the three men or three women who have the longest exercise time-to-task failure, you will receive an additional $10 gift card. If you are a female and decide to complete the optional 5$^{th}$ visit, you will receive an additional $5 gift card.

**What if I am Injured or Become Ill while Participating in this Study?**

In the case of injury or illness results from this study, emergency medical treatment is available. You or your insurance may be charged for this treatment. Complications arising as a result of the natural progression of an underlying or pre-existing condition will be billed to you or your insurance. Please check with the investigator or with your insurance company if you have questions. No other funds have been set aside by the University of Oklahoma-Norman or the University of Oklahoma Health Sciences Center to compensate you in the event of injury, illness, or for other damages related to your event of injury or illness.

**What Are My Rights As a Participant?**

Taking part in this study is voluntary. You may choose not to participate. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled.
If you agree to participate and then decide against it, you can withdraw for any reason and leave the study at any time. However, please be sure to discuss leaving the study with the principal investigator or your regular doctor. You may discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled.

We will provide you with any significant new findings developed during the course of the research that may affect your health, welfare, or willingness to continue your participation in this study.

You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study has completely finished. You consent to this temporary restriction.

**Whom Do I Call If I have Questions or Problems?**

If you have questions, concerns, or complaints about the study or have a research-related injury, contact Angelina Curiel at (405) 326-3221 or angelina@ou.edu or Christopher Black, PhD at (706) 255-3750 or cblack@ou.edu.

If you cannot reach the Investigator or wish to speak to someone other than the investigator, contact the OUHSC Director, Office of Human Research Participant Protection, at 405-271-2045.

For questions about your rights as a research participant, contact the OUHSC Director, Office of Human Research Participant Protection at 405-271-2045.

**Signature:**

By signing this form, you are agreeing to participate in this research study under the conditions described. You have not given up any of your legal rights or released any individual or entity from liability for negligence. You have been given an opportunity to ask questions. You will be given a copy of this consent document.

I agree to participate in this study:

| | | |
|---|---|---|
| PARTICIPANT SIGNATURE (age>18)<br>*(Or Legally Authorized Representative)* | Printed Name | Date |
| SIGNATURE OF PERSON OBTAINING CONSENT | Printed Name | Date |

## APPENDIX C: HIPPA

**AUTHORIZATION TO USE or SHARE**
**HEALTH INFORMATION[1] THAT IDENTIFIES YOU FOR RESEARCH** *An Informed Consent Document for Research Participation may also be required. Form 2 must be used for research involving psychotherapy notes.*

Title of Research Project: **The Relationship between Oxygen Saturation and Muscle Fatigue in Men and Women**

Leader of Research Team: **Christopher D. Black, PhD** Address: **1401 Asp Avenue, #110 SFC, Norman, OK, 73019**

Phone Number**: 706-255-3750 (cell); 405-325-7668 (office)**

If you decide to sign this document, University of Oklahoma Health Sciences Center (OUHSC) researchers may use or share information that identifies you (protected health information) for their research. Protected health information will be called PHI in this document.

**PHI To Be Used or Shared**. Federal law requires that researchers get your permission (authorization) to use or share your PHI. If you give permission, the researchers may use or share with the people identified in this Authorization any PHI related to this research from your medical records and from any test results. Information used or shared may include all information relating to any tests, procedures, surveys, or interviews as outlined in the consent form; medical records and charts; name, address, telephone number, date of birth, race, government-issued identification numbers, and nothing else.

**Purposes for Using or Sharing PHI.** If you give permission, the researchers may use your PHI to determine if it is safe for you to participate in the exercise used in this study.

**Other Use and Sharing of PHI**. If you give permission, the researchers may also use your PHI to develop new procedures or commercial products. They may share your PHI with other researchers, the research sponsor and its agents, the OUHSC Institutional Review Board, auditors and inspectors who check the research, and government agencies such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (HHS), and when required by law. The researchers may also share your PHI with with your physician and/or a University of Oklahoma physician in the event of a serious health risk or adverse event that occurs during the study.

**Confidentiality**. Although the researchers may report their findings in scientific journals or meetings, they will not identify you in their reports. The researchers will try

to keep your information confidential, but confidentiality is not guaranteed. The law does not require everyone receiving the information covered by this document to keep it confidential, so they could release it to others, and federal law may no longer protect it.

**YOU UNDERSTAND THAT YOUR PROTECTED HEALTH INFORMATION MAY INCLUDE INFORMATION REGARDING A COMMUNICABLE OR NONCOMMUNICABLE DISEASE.**

**Voluntary Choice**. The choice to give OUHSC researchers permission to use or share your PHI for their research is voluntary. It is completely up to you. No one can force you to give permission. However, you must give permission for OUHSC researchers to use or share your PHI if you want to participate in the research and, if you cancel your authorization, you can no longer participate in this study.

Refusing to give permission will not affect your ability to get routine treatment or health care unrelated to this study from OUHSC.

**Canceling Permission**. If you give the OUHSC researchers permission to use or share your PHI, you have a right to cancel your permission whenever you want. However, canceling your permission will not apply to information that the researchers have already used, relied on, or shared or to information necessary to maintain the reliability or integrity of this research.

**End of Permission.** Unless you cancel it, permission for OUHSC researchers to use or share your PHI for their research will never end.

**Contacting OUHSC**: You may find out if your PHI has been shared, get a copy of your PHI, or cancel your permission at any time by writing to:

Privacy Official or University of Oklahoma Health Sciences Center PO Box 26901
Oklahoma City, OK 73190

If you have questions, call: (405) 271-2511 or

Privacy Board
University of Oklahoma Health Sciences Center PO Box 26901
Oklahoma City, OK 73190

(405) 271-2045.

**Access to Information.** You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study is completely finished. You consent to this temporary restriction.

**Giving Permission**. By signing this form, you give OUHSC and OUHSC's researchers led by the Research Team Leader permission to share your PHI for the research project listed at the top of this form.

**Patient/Participant Name (Print):** _____

_____ _____

Signature of Patient-Participant or Parent if Participant is a minor — Date

*Or*

_____ _____

Signature of Legal Representative** — Date

**If signed by a Legal Representative of the Patient-Participant, provide a description of the relationship to the Patient-Participant and the authority to act as Legal Representative:

_____

OUHSC may ask you to produce evidence of your relationship.

***A signed copy of this form must be given to the Patient-Participant or the Legal Representative at the time this signed form is provided to the researcher or his representative.***

APPENDIX D: INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

# INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (October 2002)

## LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

### FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

***Background on IPAQ***

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

**Using IPAQ**

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

**Translation from English and Cultural Adaptation**

Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

**Further Developments of IPAQ**

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

**More Information**

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

# INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

***PART 1: JOB-RELATED PHYSICAL ACTIVITY***

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

   ☐ Yes

   ☐ No ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ **days per week**

   ☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

   _____ **hours per day**
   _____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

_____ **days per week**

☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

***PART 2: TRANSPORTATION PHYSICAL ACTIVITY***

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

## *PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY*

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

***PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY***

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous**

physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
_____ **hours per day**
_____ **minutes per day**

***PART 5: TIME SPENT SITTING***

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**
_____ **minutes per day**

## This is the end of the questionnaire, thank you for participating.

## APPENDIX E: PHYSICAL ACITVITY READINESS QUESTIONNAIRE

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

# PAR-Q & YOU

**(A Questionnaire for People Aged 15 to 69)**

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

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

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

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

**If you answered**

### YES to one or more questions

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

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

### NO to all questions

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

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

**DELAY BECOMING MUCH MORE ACTIVE:**

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

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

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

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

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

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

NAME _____

SIGNATURE _____ DATE _____

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

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



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# APPENDIX F: MENSTRUAL HISTORY QUESTIONNAIRE

**Department of Health and Exercise Science**

**University of Oklahoma**

**MENSTRUAL HISTORY QUESTIONNAIRE**

Participant ID:_____Date:_____

We are asking you to give us as complete a menstrual history as possible. All information is strictly confidential.

Are you pregnant (circle your response)

YES- Do not complete the rest of this form

NO- Continue to section A.

**SECTION A: CURRENT MENSTRUAL STATUS**

1. Approximately how many menstrual periods have you had during the past 12 months? (please circle what months you have had a period. This means from this time last year to the present month)

**Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec**

2. What is the usual length of your menstrual cycle (first day of your period to the next onset of your period)?

_____days. Today is day _____ of your present menstrual cycle.

3. When was the date of the onset of your last period?

4. When do you expect you next period?

5. What is the average length (number of days) of your menstrual flow?
_____ days

How many of these days do you consider "heavy"?_____days

6. Do you take oral contraceptives or any other medication that includes estrogen and/or progesterone?

   If yes, how long have you been taking this medication?_____

   What is the brand name and dosage of this mediation?_____

Has this medication affected your menstrual cycle (regularity, length and amount of flow)? If yes, indicate changes.

# HEALTH SCREENING QUESTIONNAIRE

## Form 2.2 Health Screening Questionnaire

This questionnaire identifies adults for whom physical activity might be inappropriate or adults who should

consult a physician before beginning a regular physical activity program.

### Section 1 Personal and emergency contact information

Name:_____ Date of birth:_____ Address: _____ Phone: _____ Physician's name: _____
Height: _____ Weight: _____

Person to contact in case of emergency

Name: _____
Phone:_____

### Section 2 general medical History

Please check the following conditions you have experienced.

***Heart History***

_____Heart attack
_____Heart surgery
_____Cardiac catheterization
_____Coronary angioplasty (PTCA)
_____Cardiac pacemaker/implantable cardiac defibrillator

***Symptoms***

_____Cardiac rhythm disturbance _____Heart valve disease _____Heart failure
_____Heart transplantation _____Congenital heart disease

_____You experience chest discomfort with exertion.
_____You experience unreasonable shortness of breath at any time. _____You experience dizziness, fainting, or blackouts.
_____You take heart medications.

***Additional Health Issues***

_____You have diabetes (type 1 or type 2).
_____You have asthma or other lung disease (e.g., emphysema).
_____You have burning or cramping sensations in your lower legs with minimal physical activity. _____You have joint problems (e.g., arthritis) that limit your physical activity.

_____You have concerns about the safety of exercise.
_____You take prescription medications.
_____You are pregnant.

## Section 3 Risk-factor assessment

***Risk Factors for Coronary Heart Disease***

_____You are a man ≥45 yr.

_____You are a woman ≥55 yr.

_____You smoke or you quit smoking within the previous 6 mo.

_____Your blood pressure is ≥140 or ≥90 mmHg.

_____Your total cholesterol is ≥200 mg · $dl^{-1}$, or low-density lipoprotein (LDL-C) is ≥130 mg · $dl^{-1}$, or high- density lipoprotein (HDL-C) is <40 mg · $dl^{-1}$.

_____You have prediabetes.

_____You have a close male blood relative (father or brother) who had a heart attack or heart surgery before the age of 55 or a close female blood relative (mother or sister) who had a heart attack or heart surgery before the age of 65.

_____You are physically inactive (you do not participate in at least 30 min of moderate

intensity (40%- 60% $\dot{V}O_2R$) physical activity at least 3 days · $wk^{-1}$).

_____Your body mass index (BMI) is ≥30 kg · $m^{-2}$ or your waist circumference is >40 in. (102 cm) for men or >35 in. (89 cm) for women.

## Section 4 medications

Are you currently taking any medication? ❍ Yes ❍ No
If yes, please list all of your prescribed medications and how often you take them, whether daily (D) or as

needed (PRN).
_____
_____
_____ Of the medications you have listed, are there any you do not take as prescribed?

## Section 5 Physical activity Patterns and objectives

List the type, frequency, intensity (e.g., light, moderate, vigorous), and duration of your weekly exercise. Note the intensity at which you plan to exercise and list the specific goals for your exercise program.

Please inform the fitness professional immediately of any changes that occur in your health status.

***Patient Information Release Form***

If you have answered *yes* to questions indicating that you have significant cardiac, pulmonary, metabolic, or orthopedic problems that may be exacerbated with exercise, you agree it is permissible for us to con- tact your physician regarding your health status in compliance with the Health Information Portability and Accountability Act of 1996 (HIPAA).

Signature: _____ Date: _____ Fitness staff signature: _____ Date:_____ To be completed by fitness professional (circle one):

AHA and ACSM risk stratification: ❍ Low ❍ Moderate ❍ High

Physician consent: ❍ Yes ❍ No

## APPENDIX H: EMAIL RECRUITMENT SCRIPT

## Email Recruitment

To whom it may concern,

Angelina Curiel and Dr. Chris Black are looking for research participants. We are conducting research regarding the relationship between oxygen saturation and muscle fatigue in men and women. If you are a male or female between the ages of 18-35 we would like to invite you to participate! Females must not be pregnant and must have a regular menstrual cycle over the past 6 months.

There will be 4-5 visits that will each last approximately 45 minutes to 1 hour. Visits 1-2 consist of filling out paperwork, a DXA scan to test your body composition, familiarizing you to the protocol, and a mitochondrial function test. Visits 3-4 and the optional visit 5 (for females only) will consist of a fatiguing exercise under normal and ischemic conditions. You will be compensated for your participation at the conclusion of the study.

If you have any questions or would like to participate in the research, you can contact me at (405) 326-3221 or angelina@ou.edu or Dr. Chris Black at (705) 255-3750 or cblack@ou.edu

Best,

Angelina Curiel

**The University of Oklahoma is an equal opportunity institution**

## APPENDIX I: VERBAL RECRUITMENT

# Verbal Recruiting Script

Hello, my name is Angelina Curiel. I am a graduate student in Dr. Chris Black's Sensory and Muscle Function Lab at The University of Oklahoma in the Health and Exercise Department. We are conducting research regarding the relationship between oxygen saturation and muscle fatigue in men and women. I am inviting you to participate because you are a male or female between the ages of 18-35.

There will be 4-5 visits that will each last approximately 45 minutes to 1 hour. Visits 1-2 consist of filling out paperwork, a DXA scan to test your body composition, familiarizing you to the protocol, and a mitochondrial function test. Visits 3-4 and the optional visit 5 (for females only) will consist of a fatiguing exercise under normal and ischemic conditions. You will be compensated for your participation at the conclusion of the study.

If you have any questions or would like to participate in the research, you can contact me at (405) 326-3221 or angelina@ou.edu or Dr. Chris Black at (705) 255-3750 or cblack@ou.edu

Best,

Angelina Curiel

**The University of Oklahoma is an equal opportunity institution**

**APPENDIX J: RECRUITMENT FLYER**

# Interested in Muscle Fatigue?

## Research Participants Needed

The Sensory and Muscle Function Lab is conducting a study titled:

*The Relationship between Oxygen Saturation and Muscle Fatigue in Men and Women*

**To participate**

- Males and females between 18-35 years of age.
- Healthy participants with no cardiovascular or neurological disorders and free from any musculoskeletal injuries.
- Females: not pregnant.

**4 - 5 visits required**

- Total time commitment is approximately 5 hours.
- Testing will take place in the Sensory and Neuromuscular Functions lab at the University of Oklahoma Norman Campus.

**Compensation**

- You will be compensated for your time in the form of a gift card and a DXA scan.

If you are eligible and interested please contact Angelina Curiel , angelina@ou.edu or Dr. Chris Black (Primary Investigator), cblack@ou.edu

The University of Oklahoma is an equal opportunity institution.