INVESTIGATING THE INFLUENCE OF ENDURANCE TRAINING ON CHRONIC RESISTANCE TRAINING OUTCOMES

The influence of short-term aerobic training on muscle hypertrophy and satellite cell content following resistance training in healthy young men and women.

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LAY ABSTRACT

Resistance exercise training is the most effective and accepted strategy for increasing skeletal muscle mass and strength. Yet, there is tremendous individual variability in the adaptive response to exercise and the source(s) contributing to this variability are largely unknown. Recently, evidence has emerged suggesting that capillaries may be a potential target for enhancing the adaptive response to chronic resistance exercise training. Research has only begun to characterize the extent to which microvascular perfusion (capillarization and blood flow to the muscle) plays a role in muscle health and resistance training outcomes. Currently, it is unknown if elevating microvascular perfusion is enough to facilitate greater accretion (hypertrophy) of muscle mass and strength following resistance training. Therefore, the current study hypothesized that increased microvascular perfusion induced by a pre-conditioning period of aerobic training, lasting 6-weeks, would be sufficient to enhance muscle accretion (hypertrophy) and elevate muscle stem cell content following resistance exercise training. To examine this, a cohort of young men and women performed 6 weeks of unilateral (single-leg) cycling following by 10 weeks of bilateral (both legs) resistance exercise training. Results demonstrated an increased oxidative capacity and capillary perfusion in the aerobically-trained limb following single-leg cycling, as expected. Consistent with our initial hypothesis, we observed superior muscle hypertrophy of type-II muscle fibres (increased fibre cross-sectional area), in the aerobically-conditioned limb following resistance training. The results suggest that muscle capillarization may be a determinant and facilitator of adaptation to resistance training and its outcomes.

ABSTRACT

Resistance exercise training is the most effective and accepted strategy for increasing skeletal muscle mass and strength. There is tremendous individual variability in the adaptive response to exercise and the source(s) contributing to this variability are largely unknown. Recent evidence in the literature supports the notion that capillaries may be a potential target for improving outcomes to chronic resistance exercise. Aerobic exercise training is a proven stimulus for eliciting angiogenesis and increasing capillary content. Therefore, we hypothesize that completing a period of aerobic training prior to resistance training will result in a greater increase in fibre cross sectional area (CSA) compared to resistance training alone. Fourteen participants (8M, 6F) completed 6 weeks of unilateral single leg aerobic training prior to undergoing 10 weeks of bilateral lower body resistance exercise training. Performance and anthropometric measures were completed at baseline, post aerobic training and post resistance training. Skeletal muscle biopsies were obtained from the vastus lateralis and immunofluorescent staining of muscle cross sections was completed to determine fibre CSA and satellite cell content. Following unilateral aerobic training, single leg V_{O_2} work peak (*Watts*) ($p<0.001$), and oxygen consumption ($O_2\, mL \cdot min^{-1}$) ($p=.0033$) was significantly higher in the aerobically trained limb (EX) versus the control (CTL) limb. Capillary to perimeter fibre exchange index (CFPE) ($p<0.05$), a measure of microvascular perfusion, was significantly higher in the EX versus CTL limb following unilateral aerobic training. Resistance training resulted in increases in 1-repetition maximum of both squat ($p<0.0001$) and leg press ($p<0.0001$). A

main effect of time was observed for limb fat free mass ($p<0.0001$) as determined via DEXA. Type-II fibre CSA of the EX limb was greater ($p<0.05$) versus CTL limb following resistance exercise training. Type-II fibre associated satellite cell content of the CTL limb was elevated ($p<0.01$) following resistance training. Results suggest that a period of unilateral aerobic training elevates the aerobic capacity and relative microvascular perfusion of the trained leg significantly in comparison to the non-aerobically conditioned limb. Subsequent resistance training, bilateral leg strength increased post resistance training while type II CSA increased in the aerobically pre-conditioned limb following resistance training. Collectively, these results suggest that a period of aerobic preconditioning may augment the muscle's ability to respond to a hypertrophic stimulus.

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LIST OF ABBREVIATIONS

1-RM	One repetition max
ANOVA	Analysis of variance
AMPK	5' adenosine monophosphate-activated protein kinase
CD31	Platelet endothelial cell adhesion molecule (Cluster of differentiation 31)
CFPE	Capillary-to-fibre perimeter exchange index
CFi	Capillary-to-fibre ratio
CSA	Cross-sectional area
CTL	Control limb
DEXA	Dual x-ray absorptiometry
DAPI	4', 6 - diamidino - 2 - phenylindole
EX	Aerobically conditioned limb
IGF-1	Insulin-like growth factor-1
IL-6	Interluekin-6
HGF	Hepatocyte growth factor
FFM	Fat free mass
MICT	Moderate intensity continuous training
MRF	Myogenic regulatory factor
mRNA	Messenger ribonucleic acid
mTORC-1	Mechanistic target of rapamycin-1
OCT	Optimal cutting temperature
PGC-1α	Peroxisome proliferator activated receptor gamma coactivor-1
P70S6K	Ribosomal protein S6 kinase beta-1
SC	Satellite cell
SIRT-1	NAD-dependent deacetylase sirtuin-1
SIT	Sprint-interval training
Pax7	Paired box transcription factor-7
PostAT	Post aerobic training
PostRT	Post resistance training
TSC2	Tuberous sclerosis complex 2
VEGF	Vascular endothelial growth factor
$\dot{V}O_2$	Incremental ramp exercise test

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DELCARATION OF ACADEMIC ACHIEVEMENT

A. C. Q. Thomas and G. Parise were the principle contributors for conceptualizing the research question, hypothesis and experimental design. A. C. Q. Thomas, A. Brown, A. Hatt, K. Manta and A. Costa-Parke performed data collection and analysis. A. C. Q. Thomas, S. Joanisse and G. Parise interpreted the data.

Introduction

I. Overview

Skeletal muscle comprises ~40% of total body weight in men and women (24) and functions to generate force to produce movement, maintain posture and enable physical activity. Metabolically, skeletal muscle is a significant contributor to basal metabolic rate and produces heat to maintain core body temperature. Further, skeletal muscle serves as the largest reservoir for storage of amino acids, which are utilized to support health of all other organs and to maintain blood glucose levels during times of stress.

Resistance exercise training is the most effective non-pharmacological strategy for increasing skeletal muscle mass (hypertrophy) and strength. Yet, there is tremendous individual variability in the adaptive response to resistance exercise, particularly in terms of hypertrophy, and the source(s) of this variability are largely unknown. Although the majority of the population is responsive to the physiological benefits of resistance exercise training, such as improved insulin sensitivity, increased muscle mass and reduced blood pressure, there exists still a significant proportion of "lower-responders" and "non-responders" to exercise training (77). For some variable outcomes, the percentage of non-responders has been recorded at anywhere between 10 – 20% of individuals under study (37). The basis for variability in hypertrophic responses to resistance training is poorly understood; however, factors such genetic polymorphisms (16), transcriptomic differences (67), the ability to activate specific signaling proteins known to be important in muscle protein synthesis (76), and microRNA expression (19) have all been identified as potential regulatory control points determining resistance exercise-induced hypertrophic responses.

Recent evidence supports the notion that skeletal muscle vascularization may be a potentially modifiable target for enhancing resistance exercise-stimulated outcomes and minimizing the variability in responses following chronic resistance exercise (72). It is well understood and accepted that adequate muscle tissue perfusion is vital to muscle maintenance and health, as it is necessary for the delivery of oxygen, nutrients and growth factors to the muscle fibers (72). Without adequate tissue perfusion there is a potential for a limitation in the delivery of signaling factors critical for adaptation of skeletal muscle. It is unknown whether increasing capillary content in muscle could have positive benefits on muscle health or adaptation to resistance training outcomes.

II. Defining Aerobic and Resistance Exercise

Skeletal muscle tissue is extremely dynamic and is capable of undergoing substantial changes in its phenotype, a phenomenon known as muscle plasticity. Both resistance and endurance exercise are potent stimuli that result in profound remodelling and adaptation. Endurance training can broadly be defined as exercise involving large muscle groups exerting low forces for prolonged periods of time and regular practice of this form of exercise typically results in muscle remodelling to a more oxidative phenotype (20). Although it shares some phenotypic outcome responses with resistance training, endurance exercise-mediated adaptations are primarily elicited via energy sensing pathways (AMPK; PGC-1α), resulting in augmented: muscle capillary density, capacity for fatty acid oxidation, mitochondrial density and size, $\dot{V}O_2$ and lactate threshold (51). In contrast, resistance exercise is characterized by the movement of loads that typically result in

muscular fatigue in a relatively short period of time as compared to endurance exercise. The weight, or overload stimulus of resistance exercise leads to adaptations characterized by increases is muscle mass (hypertrophy) and force generation. The primary mechanism of adaptation to resistance exercise is mediated via anabolic pathways such as the mTORC-1 pathway, increasing muscle protein synthesis, proliferation and activation of satellite cells, ultimately resulting in accretion of muscle mass and increases in myofibre cross-sectional area (84).

Although skeletal muscle is a highly plastic tissue that has the ability to respond to a variety of stimuli, the actual myofibre is post mitotic. Thus, it is proposed that some of the adaptations observed in skeletal muscle are mediated by a specific population of skeletal muscle-resident stem cells commonly referred to as satellite cells (SC).

III. SC Function and Activation

SC are monopotent stem cells that, unlike myofibres, are not post-mitotic. These cells play an indispensable role in muscle regeneration and contribute to growth and remodeling in response to stimuli such as exercise or muscle damage (66). SC reside on the periphery of the myofibre between the basal lamina and sarcolemma. In response to appropriate stimuli, including exercise and associated muscle damage, the resident SC pool proliferates, activates and either returns to quiescence or differentiates, fusing to and donating their nuclei to the existing myofiber (48). The process of SC activation and proliferation is governed by the paired box transcription factor 7 (Pax7) and a series of other transcription factors known as the myogenic regulatory factors (MRFs) (Myf5,

MyoD, Myogenin and Mrf4) (34). Following muscle damage, MRF expression is increased in the SC, coordinating a myogenic response to ultimately repair damaged muscle fibres. Tracking the relative expression of MRFs allows for insight into the timeline of muscle repair and regeneration following damage or exercise (5, 47). It is well established that the upregulation of Myf5 denotes the earliest phase of myogenic commitment, followed promptly by the increased expression of MyoD, which is used commonly used as an indicator of SC activation. Subsequent to increased MyoD expression, SC can either differentiate into mature myoblasts through downregulation of Pax7 or return to a quiescent state by reduction of MyoD expression. Using the Pax7 and MyoD transcription factors, SC can be routinely quantified based on both content and activation employing methods such as immunohistochemistry and flow cytometry. Through these techniques, it is possible to then elucidate what proteins or other factors are sufficient and necessary for eliciting a pronounced SC response subsequent to muscle damage or external stimuli. Examples of previously identified compounds known to influence and dictate SC activity include several inflammatory cytokines and growth factors such as insulin-like growth factor-1 (IGF-1), hepatocyte growth factor (HGF), interleukin 6 (IL-6) and myostatin (71). In addition to circulating factors, structural (i.e., extracellular protein lattice) and local cell-based compounds (i.e., paracrine effects) operating within the SC niche have recently been hypothesized to regulate SC activity. In 2016, Garg and Boppart identified a handful of structural proteins that may dictate SC activity, proliferation and pool expansion. Structural components such as proteins of the extracellular matrix i.e. laminin, fibronectin, collagen VI and tenascin C have all been postulated to mediate an aspect of SC activity (26). In

addition to structural proteins, recent literature from our lab has further characterized and highlighted the role that capillaries, and the SC proximity to them, may play in coordinating SC activity and dictating function.

IV. Satellite Cells and Aerobic Training

In comparison to resistance training, there is a relative paucity in the literature regarding the effects of aerobic training on SC content and activity. In addition, the vast majority of research regarding aerobic activity and SC has been characterized in rodent models. Human research in this topic has not yet been extensively studied and results to date are inconsistent. This inconsistency is likely due to varying participant demographics being studied or the variation in the exercise training regimes utilized (i.e. duration, frequency, intensity or interval pattern). Yet, when studied in a rodent model, endurance exercise training results in augmentation of SC content without myofibre hypertrophy (44). Furthermore, increases in SC content were found to be better correlated with intensity as opposed to duration of aerobic activity (49). As a general rule, endurance activity is not a significant stimulus for myofibre hypertrophy (30). Therefore, elevation of SC content with endurance exercise, without a concomitant increase in myofibre cross-sectional area, is suggestive of a role for SC that is not solely related to mediation of muscle growth and repair but potentially also playing a role in muscle remodelling and adaptation. While no study has purposely used exercise as an intervention designed to alter mitochondrial content in order to study its effect on SC function, several *in vivo* and *in vitro* models have highlighted the significance of mitochondria in relation to myofibrillar regeneration and

repair. For example, Jash and Adhya (41), were able to enhance muscle regeneration in rodents by polycistronic RNA administration, a model designed to restore mitochondrial function in injured tissue. Jash and colleagues attributed the result to an enhanced SC proliferation observed following the restoration of mitochondrial function. Furthermore, supporting this relationship, when the mitochondrial modulator SIRT-1 was ablated in rodents, muscle regeneration was severely impaired (87). In addition to mitochondria, capillary content has also been postulated to mediate SC activity and myofibre regeneration. Recent literature supports this notion as Joanisse *et al*. (44) observed that 8 weeks of aerobic training in older mice was sufficient for accelerating the regenerative timeline in comparison to older sedentary mice following cardiotoxin injection of the *tibialas anterior*. To date, rodent models have provided key insights towards characterizing the efficacy of endurance exercise in modulating SC activity and by association, muscle regeneration. Further exploring this relationship and the mechanisms promoting SC function following damage may be critical for enhancing the efficiency of muscle repair.

Studies in humans examining the influence of aerobic exercise on SC function have utilised various models of aerobic training (moderate vs. high intensity) in several different populations (young vs. old, men vs. woman, healthy vs. diseased). However, viewed in totality, the majority of evidence from humans shows that aerobic exercise augments SC function (basal activity and activation in response to muscle damage) but not necessarily SC content (44). Some studies in older men have shown that aerobic exercise results in an increase in SC content, but only in type-II associated SC (11, 82); however, type-IIa fibre hypertrophy also occurred as a result of training and therefore the increase in SC content

may have played a role in mediating the observed accretion of muscle mass (44). Further considering the effects of aerobic activity, when examining a young healthy population, no significant increases in total (all fibre types) SC content can be found (44). Although total SC content remains unchanged, Joannisse *et al.* (42) demonstrated that 6 weeks of aerobic training elevated content and activity of SC associated with hybrid fibres (containing both myosin heavy chain type-I and type-II isoforms). This SC response associated with hybrid fibres may be necessary for myofibrillar remodelling and adaptation to aerobic exercise-mediated stress (42). In addition, both moderate continuous and sprint-interval training (SIT) have been shown to elevate basal SC activity following 6 weeks of training in young men and women (43). These findings have been attributed to the concomitant increases in mitochondrial content, function, as well as augmented capillary density commonly elicited as a result of aerobic training (42 - 44). To date there is no comprehensive understanding of how aerobic training effects SC content and function in humans. However, age and intensity of exercise appear to be important considerations when examining SC content following prolonged periods of aerobic training. In totality, there is reasonable evidence to suggest that aerobic training increases the ability to mobilize SC, allowing for more efficient repair and regeneration of damage fibres. Although, aerobic exercise is not a potent stimuli for increasing SC content, future studies are required to determine SC role in adaptation to aerobic exercise and why some populations may see an increase in content following aerobic training, while others do not.

V. Satellite Cells and Resistance Exercise Training

Each myonuclei within the muscle, is postulated to govern a specific volume of myofibrillar cytoplasm, which is a concept commonly referred to as the myonuclear domain theory (3). This theory suggests that myofibrillar hypertrophy beyond a certain range is impossible without the addition of new nuclei donated by SC (3). However, there is not a consensus on whether the myonuclear domain theory is operational and the topic is still highly debated. For example, early studies examining the role of myonuclei and SC for skeletal muscle hypertrophy employed irradiation models in rodents, where SC were ablated by gamma irradiation. As hypothesized, the muscles of gamma irradiated rodents did not respond (i.e., hypertrophy) to overload training, whereas hypertrophy was elicited in the non-gamma irradiated control group (2). However, this finding (2) answers the important, but not necessarily relevant, question of whether hypertrophy in the absence of SC can occur. What it does not tell us, is whether or not, and to what extent, SC play a role in hypertrophy. Contrary to these findings (2), newer models achieving near complete (>90%) ablation of SC content in mice prior to 6 weeks of muscle overload, demonstrated a sustained ability to respond to overload stimuli. The muscles of these rodents demonstrate equivalent muscle hypertrophy as control animals (54). While marginal hypertrophy in the absence of functioning SC may be possible, a more recent study using the same conditional SC-ablation model indicated that SC are required for sustained muscle growth, as results demonstrated blunted hypertrophy following 8 weeks of overload in mice (25). Altogether, these results suggest SC activity and subsequent myonuclear addition may not be required for early (2-6 weeks) hypertrophy following overload in mice. However, longer periods of overload (>8 weeks) may require SC for sustained fibre growth. Future research in animal

models should focus more on examining prolonged periods of overload in SC ablated skeletal muscle to better understand if hypertrophy is mediated by SC content. Although insightful, SC ablation in rodent models represents a non-physiological approach, therefore more studies characterizing the association between SC content and hypertrophy in humans are required for better understanding the true relationship. Translating rodent model findings to human physiology remains a challenge, however, descriptive studies can be performed in humans by analysing correlations between the changes in myonuclear content, SC number, and muscle fibre hypertrophy in response to anabolic stimuli.

In humans the best non-pharmacological stimulus for inducing muscular hypertrophy is resistance exercise training. In support of some previous mouse studies, Fry and colleagues demonstrated increases in type-IIa myofibre cross-sectional area following 12 weeks of aerobic training in middle-aged men and women absent of any change in SC content (25). Arguably, these findings may be explained by existing myonuclei, which are able to increase transcriptional activity, supporting the small gains in fibre cross-sectional area. Contrary to Fry *et al*. (25), there is an expanding body of evidence illustrating the notion that increases in myofibre size are concomitant with an increase in SC content, and/or myonuclear content following resistance exercise training (18, 45, 75, 79, 87). In addition, multiple studies have described positive correlations between muscle fibre hypertrophy and SC content following extended periods of resistance exercise training in a variety of diverse populations (5, 45, 80).

While the relationship between resistance training and SC content is becoming more apparent in humans, the effect of prolonged resistance exercise training on basal SC

activity and their ability to respond to muscle damage is less clear. A recent study by Nederveen and colleagues (61) aimed to better characterize basal SC activity and the response to muscle damage following prolonged resistance exercise training. A group of young men undertook resistance training for 16 weeks, and the SC response to an acute bout of exercise, resulting in muscle damage, before and after 16 weeks of training was examined. At rest, resistance training elicited no difference in the proportion of active SC. However, prolonged resistance training was effective in augmenting the number of damage induced proliferating ($MyoD^+$) SC at 24 and 72 hours, as well as peak SC content following an acute bout of resistance exercise (61). Nederveen *et al.* (61) attributed the observed increase in SC activation to a concomitant increase in capillary density that occurred over the 16 weeks of training. Contrasting these results (61), Damas *et al*. (18) resistance trained young men for 10 weeks and showed no increase in SC content 48 hours following an acute bout of resistance exercise. Yet it is important to note the timing of the post-training acute exercise bout at which biopsy samples were collected in these studies, as this could potentially explain the contrasting results. Damas and colleagues only measured SC content up to 48 hours following exercise, observing no significant increase (relative to pre-damage) after 10 weeks of training. Consistent with this (18), Nederveen and colleagues observed no significant changes in SC content until 72 hours post-acute exercise (61). Although peak SC content and activation following muscle damage has been recorded as early as 24hrs and as late as 72hrs, it is possible that Damas and colleagues could have observed similar results if timepoints were better matched. Additionally, Damas and colleagues do not report SC activation ($MyoD^+$) data following the acute bout

of resistance exercise. This detail would provide valuable insight on the role SC play subsequent to prolonged resistance training. Taken altogether, chronic resistance training appears to augment SC content and activity, adapting skeletal muscle to better respond to acute bouts of exercise and damage.

VI. Satellite Cells, Vascularization and Hypertrophy

The concept that vascularization is important for overall health and regulation of the stem cell niche is not uncommon and has been well described in haematopoetic and neural stem cell models, however, the musculo-vascular SC niche remains to be well characterized (50). This relationship was first explored by Christov *et al*. (14), who observed "a non-random spatial association between capillaries and SC", as they often reside in close proximity to one another (14). In addition, Christov *et al*. also noted that individuals with a higher capillary density also had an elevated SC content, independent of fibre type. The non-random spatial link between SC and capillaries was further elucidated by Nederveen *et al.,* (59) who observed that active SC ($MyoD^{+}$) are situated in closer proximity to their nearest capillary in comparison to their quiescent ($MyoD^{-}$) counterparts. Nederveen *et al.* (59) suggested that SC that lie closer to capillaries are potentially exposed to higher concentrations of blood borne signaling factors, dictating greater potential for proliferation and activation in response to a stimuli. In addition, the same authors demonstrated that young men with high relative type-II microvascular perfusion elicit a quicker and more pronounced SC response following exercise-induced muscle damage in comparison to their low-perfusion counterparts (61). Previous studies support the

observations of Nederveen *et al.* (61), such as a study by McKay *et al*. (55) that also examined the SC response to exercise induced muscle damage in older and younger men. McKay *et al*. demonstrated that older men experienced impaired SC activation following an acute bout of resistance exercise training. It is important to note that there is a well-documented age associated loss of capillary content surrounding type-II muscle fibres (68, 72). In contrast there was no difference between type-I associated SC responses in younger and older men (55). Although disparate SC responses in younger and older men may be multifactorial in nature, the blunted SC response in old men observed exclusively in type-II associated SC indicates that capillary perfusion may be a primary contributor to this phenomenon (**Figure 1**). Collectively, these results suggest that, independent of age, an adequate level of microvascular perfusion may be necessary for retaining and eliciting a pronounced and significant SC response to muscle damage. An attenuated microvasculature perfusion has been recently hypothesized in the literature as a rationale for diminished SC content and impaired activation following a bout of acute resistance exercise (55, 61). A diminished SC response would in theory delay or prevent the efficient repair of damaged fibers following damage and may therefore also reduce or delay the degree of muscle adaptation and hypertrophy. The implications of an impaired SC content and/or blunted activation upon stimulation are suggested to be detrimental, and may contribute to increased rates of muscle loss in aging (i.e., sarcopenia) and be part of what is known as anabolic resistance (an impaired ability to respond to anabolic stimuli).

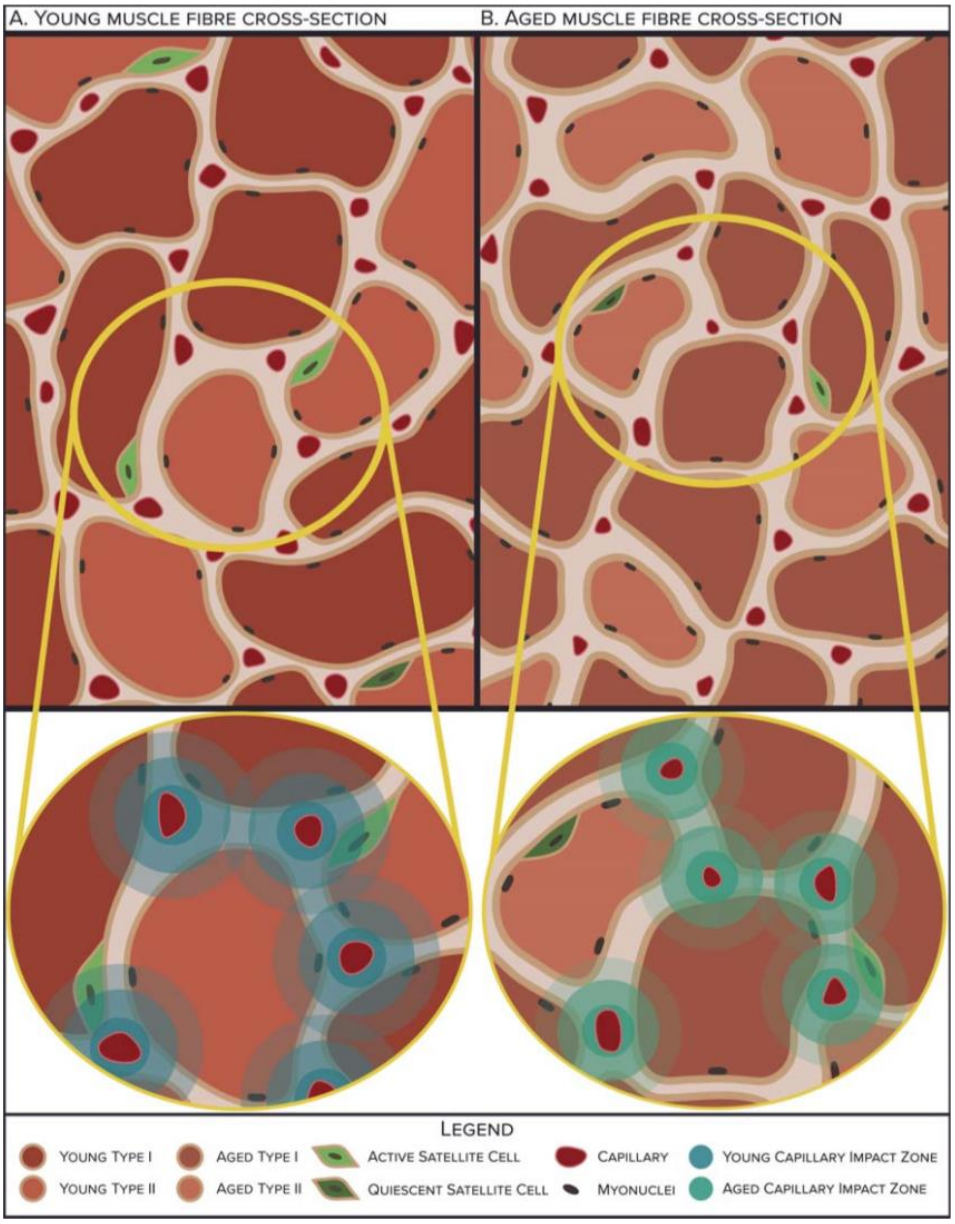

Figure 1; *Capillary impact zone*. Adapted from Joanisse *et al.* (2016). Schematic representation of muscle fibre cross sections taken from **(A)** young and **(B)** older individuals. Aged muscle is characterized by reduced capillary content, type-II fibre cross-sectional area, SC content and thicker basal lamina.

Recent advances have demonstrated a clear link between SC content and activity to both the age-related decline in muscle mass (sarcopenia), as well as the hypertrophic potential of resistance exercise training, demonstrating the significant role SC have in dictating muscle size (5, 7, 18, 79). A recent study by Snijders *et al*. (72) demonstrated that elderly men with the highest muscle fibre capillary perfusion, determined via muscle capillary-to-fibre perimeter exchange index, prior to 24 weeks of resistance exercise training, achieved the greatest degree of myofibrillar hypertrophy. While correlational in nature, this observation indicates that microvascular perfusion may be contributing to anabolic potential and a loss of microvascular perfusion may further contribute to age-related muscle loss (72). Interestingly, SC content only increased in the high perfusion group following 24 weeks of training, further supporting the notion that microvascular perfusion may mediate SC function. Snijders and colleagues suggested that enhanced perfusion was a permissive factor that allowed for greater hypertrophy in comparison to those with low perfusion and that this was a SC-based phenomenon (72). Characteristics of this capillary-SC relationship also hold true when examined in a young healthy population. Recently, muscle capillary content was shown to potentially be a limiting factor for SC activation and subsequent muscle hypertrophy following a period of resistance exercise training in young men (61). Sufficient SC content and activation is known to be critical for optimal and sustained hypertrophy following resistance exercise training; thus, it is possible that the resistance exercise training-induced increase in muscle CSA and strength may be further augmented by elevating the number of capillaries and the basal SC population within the muscle prior to resistance exercise training. Understanding

the roles that SC and microvasculature have in muscle repair and regeneration may aid in understanding the heterogeneity of hypertrophy in response to resistance exercise. Supporting evidence reported that individuals with a greater increase in SC content "pre" to "post" chronic resistance training, also experienced a higher degree of hypertrophy in comparison to individuals that showed little-to-no change in SC content (5). Furthermore Damas *et al*. proposed that the elevated SC pool size observed with resistance exercise training, is likely to have a positive impact on muscle repair and regeneration in the early phase of resistance training. Possessing a greater number of SC may aid the muscle response to acute damage and is likely critical for supporting future increases in muscle fibre cross-sectional area by donating additional myonuclei (18). Together, these data suggest that muscle microvascular perfusion is a key factor in driving the repair response to damage, adaptation to exercise and may even be a determinant of muscle hypertrophy.

VII. Concurrent Training

Concurrent training is the application of both aerobic and resistance exercise incorporated into one training program. Concurrent training protocols can either consist of aerobic and resistance exercise completed on the same or separate days. While concurrent training may elicit many of the previously discussed skeletal muscle adaptations (i.e. increased capillary and SC content) in a young population, previous studies have shown concurrent training may be suboptimal for a sustained trajectory of hypertrophy (>8 weeks) (4). Outcomes of concurrent training were first characterized in 1980 when Hickson *et al*. demonstrated attenuated adaptations of strength and hypertrophy to resistance exercise

training in subjects who also completed aerobic training in parallel (35). Although the mechanisms responsible for these outcomes have not been completely elucidated, it has been postulated that the molecular responses (either AMPK, SIRT1 and/or the unfolded protein response) shortly following aerobic training negatively impact hypertrophic adaptations. This proposed "interference effect" of aerobic exercise on hypertrophic adaptations has been attributed to activation of energy sensors inhibiting activation of the mTORC-1 complex (4). Effective activation of mTORC-1 is critical for resistance exercise-mediated hypertrophy (74); thus, interference would act to inhibit or blunt downstream muscle protein synthesis (4). In-line with Hickson's findings, compromised anabolic molecular events have been reported when aerobic exercise precedes resistance exercise (17). Other studies however, have recorded no hinderance of muscle protein synthesis when 90-minutes of strenuous aerobic activity was performed immediately prior to resistance exercise (10). In contrast to the previous two studies (10, 17), Lundburg *et al.* (51) showed that an acute bout of concurrent exercise elicited greater mTORC-1 and P70S6K, a downstream target of mTORC, phosphorylation in comparison to resistance exercise alone (51). Lundburg and colleagues followed up these findings by investigating outcomes of prolonged concurrent and resistance exercise using the same training modality and timing as their previous study (52). They observed that chronic concurrent exercise training augmented muscle hypertrophy relative to resistance exercise alone (52). Interpreting the conflicting results of acute time-course models in relation to chronic outcomes, the relative timing of concurrent exercise may be significant for better understanding the hypothesized interference mechanism at play. Some previous concurrent

exercise studies in which aerobic activity preceded resistance exercise by less than 3-hours tended to show an interference effect (10, 17). In support of this, elevated AMPK phosphorylation, commonly elicited following endurance exercise has been postulated to interfere with anabolic signalling pathways, specifically TSC2 and raptor complexes (30, 39). In addition, examining the molecular responses 15 minutes and 3 hours post concurrent exercise showed that aerobic exercise preceding resistance exercise caused an immediate (15 minutes post exercise) decrease in signalling markers of translation initiation and ribosome biogenesis, albeit no difference in response of the same markers at the 3 hour time point (31). These results suggest that the effect of aerobic activity on skeletal muscle signalling following resistance exercise was likely minimal as signals are restored within 3 hours (31). Altogether, considering the acute and chronic effects of aerobic training preceding resistance training, it is tempting to speculate that timing of aerobic exercise prior to resistance exercise should be factored into any exercise program that aims to optimize hypertrophy if endurance exercise is included.

VIII. The Unilateral Exercise Model

Unilateral within-subject study designs are a model in the field of exercise physiology, useful for examining peripheral physiological changes to stimuli such as exercise or disuse. A unilateral design permits the comparison of two distinct conditions within the same subject and serves to reduce the time and cost involved in executing a study. In addition, the unilateral model greatly increases statistical power, reducing the number of subjects necessary to observe a significant effect as a result of the intervention.

Another advantage of utilizing the unilateral model when studying skeletal muscle physiology is being able to control for diet and nutritional status. The nutritional state of one limb matches the other, eliminating a common major confounding variable of the between subject design.

With this approach, two limbs of an individual are randomly subjected to separate interventions and so the impact of the interventions can be studied concurrently or sequentially dependant on the nature of the treatments (53). The primary assumptions required for application of the unilateral model are that each limb of a subject are equally responsive to potential treatments and there is no cross-over of treatment effects to the contralateral limb via systemic circulation, or neural adaptation. It is also important to note that each limb under study should be well matched physiologically to the contralateral limb at baseline to ensure a similar response to treatments. A sufficient body of literature exists supporting the notion that limbs at baseline are similar in both biochemical properties and functional measurements (53). There is good evidence to suggest that histological and biochemical outcomes such as muscle cross-sectional area, mitochondrial content and respiration, capillary content, mRNA abundance and signalling protein phosphorylation are all similar between limbs of an individual at baseline (53). In addition, functional measures such as aerobic capacity and strength (1-repetition max via leg extension) are also generally not significantly different between limbs of the same individual at baseline. Previous literature has noted marginal differences in muscle power between limbs, however, this inequality becomes exaggerated when legs are grouped according to dominance (52).

Randomization of limbs into treatment groups would, however, be an effective strategy to allay the concern of limb dominance influencing study outcomes.

A major concern of the unilateral model is transfer or cross-over effect of one treatment to the contralateral limb. While possible, this phenomenon appears to depend on the nature of the outcome being studied. Resistance exercise is known to elicit transient increases of anabolic hormones into circulation, the effect of which in theory could confound physiological responses in the contralateral limb (84). This thesis appears highly unlikely, however, as it has been shown that systemic circulating levels of hormones do not have a significant effect for eliciting change in skeletal muscle protein synthesis or muscle fibre cross-sectional area (84). In addition, although myokines and cytokines released from skeletal muscle during exercise can also in theory enter circulation and alter the biochemical environment of the contralateral limb, the concentration would likely be too low to elicit meaningful phenotypic changes (85). As for other biochemical and molecular evidence, an extensive review of the literature indicated a lack of skeletal muscle adaption transfer between limbs for outcomes such as mitochondrial content, muscle capillarization, local hemodynamics, metabolic adaptations to submaximal exercise (lactate accumulation and fatty acid utilization), skeletal muscle protein synthesis and muscle hypertrophy (53). However, for some outcomes, cross-over effects have been commonly demonstrated, increased strength in the untrained arm following unilateral resistance training is a prime example of cross education (63); however, observations of cross-over resulting in increased strength are likely due to neuromuscular as opposed to biochemical adaptation.

The unilateral model is not without hindrance, with several drawbacks limiting the scope of research that it can be applied to. A primary disadvantage of the unilateral exercise model is the applicability and relatability of findings to bilateral tasks. Comparably little is known regarding prescription of relative intensities for unilateral, in comparison to bilateral, exercise training. As such, more research is required to affirm comparable genetic and phenotypic responses of unilateral resistance and aerobic training are similar to results using bilateral exercise. Second, central adaptation (such as cardiac output) to treatments cannot be examined as it would be impossible to determine the contribution of each limb to central changes. Third, there are distinct physiological mechanisms that limit bilateral and unilateral aerobic exercise capacity. As such, due to central limitations constraining bilateral maximal aerobic exercise, greater workloads, on a per leg basis, are achievable with unilateral activity (46, 64). The dissimilar capacity, and relative intensity, in aerobic exercise could provide a greater stimulus for muscle when performing unilateral vs. bilateral exercise. In fact, greater skeletal muscle adaptation has been observed in unilateral cycling when comparing high intensity interval training outcomes between unilateral and bilateral groups matched for relative work (1).

The unilateral design is a powerful model for studying the effects of skeletal muscle adaption to stimuli such as exercise. Elimination of confounding variables, that are often problematic with between subject study designs, allows for a significant increase in statistical power, offsetting many limitations to the design. Future research should focus on elucidating comparable relative workloads for unilateral and bilateral exercise, as this may be a conflicting factor when interpreting unilateral exercise results.

IV. Objectives and Hypotheses

It is well established that endurance exercise protocols are potent in their ability to increase capillary content within skeletal muscle of both young and older individuals (13, 37). Linking previous literature that denotes the significance of capillary content to SC content, function and hypertrophy following resistance exercise, it can be postulated that an increased capillary network may augment SC function, enhancing skeletal muscle repair and hence amplifying the accretion of muscle mass in response to resistance exercise. However, it is unknown if a period of aerobic training, and subsequent oxidative adaptations, are capable of facilitating augmented accretion of muscle mass and strength following a subsequent period of resistance training. The purpose of the current study was to examine the impact that a period of aerobic pre-conditioning has on muscle hypertrophy following resistance training. We hypothesize that unilateral aerobic training will augment capillary content relative to the control (sedentary) limb. We also hypothesize that completing a period of unilateral endurance training prior to commencing bilateral resistance exercise, will permit larger gains in muscle mass in comparison to resistance training alone. Lastly, we hypothesize that SC content after resistance exercise training will be greater in the aerobically trained limb in comparison to control.

Methods

Experimental Outline

Fourteen young men (n=8) and women (n=6) who were healthy but otherwise not engaged in any formal resistance training protocols were recruited to participate in this study. Subjects aerobically trained one leg (randomly selected) on a cycle ergometer adapted for single-leg cycling for a period of 6 weeks, 3 times per week in an endurance training protocol, following this, participants performed bilateral lower body resistance exercise for 10 weeks, 3 times per week (**Figure 2 & 3**).

Figure 2: ***Experimental Summary***

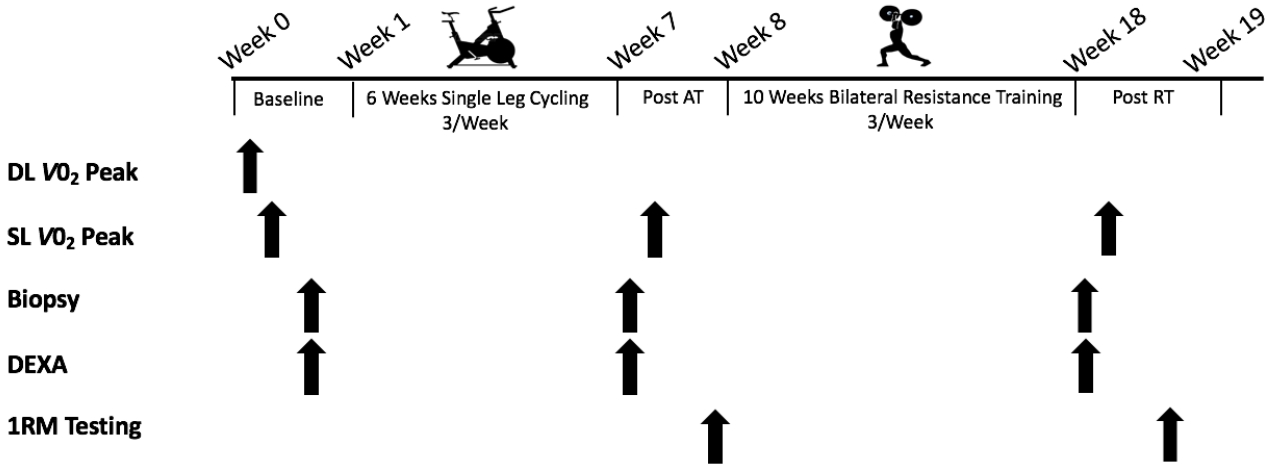

Figure 3: ***Timepoint Summary***

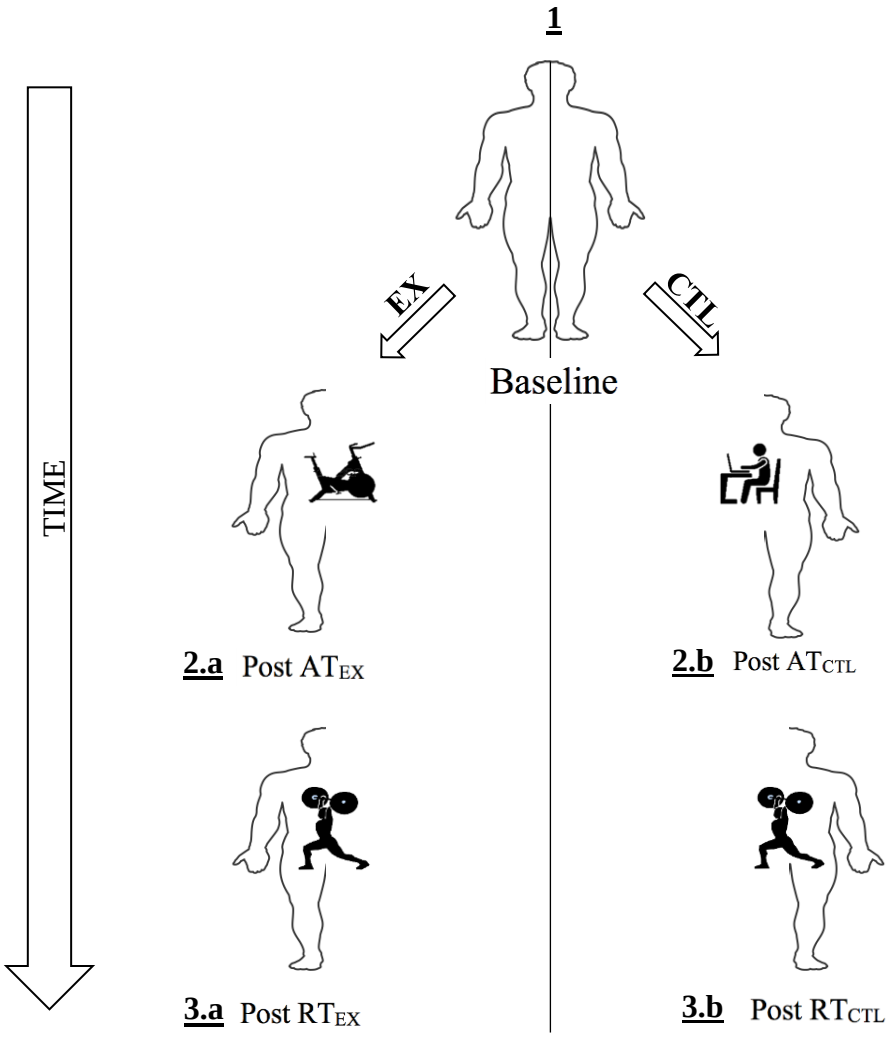

Figure 3; Timepoint Summary

1. Baseline
2. Post Aerobic Training (Post AT): Post 6 weeks unilateral aerobic exercise training
    a. Post AT_{EX}
    b. Post AT_{CTL}
3. Post Resistance Training (Post RT): Post 10 weeks bilateral resistance exercise training
    a. Post RT_{EX}
    b. Post RT_{CTL}

Subjects

A total of fourteen (8M & 6F) young, healthy participants were recruited to participate in this study (**Table 1**). All participants were recreationally active with no formal weight training experience in the previous 6 months. Exclusion criteria included smoking, diabetes, the use of non-steroidal anti-inflammatory drugs or statins, and history of respiratory disease and/or any major orthopaedic disability. Female menstrual cycle and oral contraceptive use was not taken into account as sex differences were not a hypothesized primary outcome of this current study. Participants were informed about the nature and risks of the experimental procedures before their written consent was obtained. The study was approved by the Hamilton Health Sciences Integrated Research Ethics Board (HiREB Number; 3885) and conformed to the guidelines outlined in the Declaration of Helsinki. Participants gave their informed written consent before their inclusion to the study.

Baseline Demographic

Characteristic	*N=14*
Age (years)	21.1 ± 1.6
Height (cm)	169.8 ± 8.6
Weight (kg)	74.1 ± 17.6
BMI ($kg \cdot m^{-2}$)	25.4 ± 4.5
VO_2 Work Peak (watts)	271.6 ± 66.5
VO_2 Relative ($ml \cdot min^{-1} \cdot kg^{-1}$)	39.1 ± 7.1
Single Leg VO_2 Work Peak (watts)	146.5 ± 37.7
Single Leg VO_2 Relative ($ml \cdot min^{-1} \cdot kgFFM_{Limb}{}^{-1}$)	31.4 ± 5.9

Table 1; *Baseline participant demographic.* Values presented as mean ± SD.

V_{O_2} peak and Anthropometric Measurements

Double-leg V_{O_2} peak

After being enrolled in the study, subjects initially performed a standard (double-legged) ramp test to volitional exhaustion on an electronically-braked cycle ergometer (Excalibur Sport, version 2.0; Lode, Groningen, The Netherlands) to determine whole-body peak oxygen uptake (V_{O_2} peak) and peak power output (*Watts*). Following a 1-minute warm-up at 50 *Watts*, workload was increased 1 *Watt* every 2 seconds until the subject reached volitional exhaustion or cadence decreased below 60 revolutions per minute (rpm). Expired gases were analysed using an online gas collection system (Moxus modular oxygen uptake system; AEI Technologies, Pittsburgh, PA, USA) and the V_{O_2} peak was determined from the greatest 30s average of V_{O_2} peak.

Single-leg V_{O_2} peak

At least 48 hours following the double-legged ramp test, subjects were familiarized with a single-leg cycling technique modelled after previous work (1, 8 & 53). One crank on an electronically-braked cycle ergometer (Velotron; RacerMate, Seattle, WA, USA) was fitted with a custom-machined pedal that held an 11.4 kg counterweight (**Figure 4**). Subjects pedalled using one leg, with the non-exercising leg resting on a stationary platform. The counterweight assisted with the upstroke phase of the revolution, eliminating the need to pull up on the pedal. Using this set-up, subjects performed an incremental exercise test to volitional exhaustion with each leg. The single-leg tests were similar to the double-legged tests, except the rate at which the workload increased was reduced by half

(i.e. 1 *Watt* every 4 seconds). Randomization determined order of which leg was tested, followed 10 minutes later by the contralateral leg, given previous data showing that fatigue does not transfer to the non-exercising leg (22). Subjects repeated single-leg V_{O_2} peak testing for each leg at the PostAT and PostRT timepoints.

Figure 4; *Single-leg cycle ergometer set-up.* Velotron, RacerMate cycle ergometer specially adapted with 11.4kg counterweight.

Muscle Biopsy Sampling

A total of 5 percutaneous needle biopsies were taken from the mid portion of the *vastus lateralis* under local anesthetic (1% lidocaine (lignocaine)) using a 5-mm Bergstrom needle adapted for manual suction (6). One muscle biopsy was obtained pre-training (baseline) at rest from a randomized leg. This biopsy was used for baseline measures. After 6 weeks of single-leg aerobic training, biopsies were obtained from the aerobically trained and untrained legs (PostAT). Following 10 weeks of resistance training (PostRT) a final biopsy was obtained from both legs. Approximately 150 mg of muscle tissue was collected from each biopsy. Following collection of the sample, the muscle was dissected free of adipose and connective tissue and flash-frozen in liquid nitrogen, then stored at −80°C for later analysis. For immunohistochemistry, a fresh piece of muscle (approximately 50 mg) was dissected from the biopsies, orientated in cross-section, mounted in OCT compound (Tissue-Tek, Sakura Finetek, USA) and frozen in isopentane cooled with liquid nitrogen. The mounted samples were stored at −80°C and then sectioned (7 μm) at −20°C. The cross-sections were mounted on slides and stored at −80°C for later immunohistochemical analysis.

Body Composition

Whole-body and regional lean soft tissue mass (i.e., fat-free and bone-free mass), fat mass, and bone mineral content were measured with the use of dual energy X-ray absorptiometry (DEXA) (GE-Lunar iDXA; Aymes Medical) after a 10- to 12-h overnight fast. Body composition was measured at Baseline, PostAT and PostRT timepoints.

Aerobic Training

All aerobic training was performed on the same cycle-ergometer adapted for single-leg as that used for baseline single-leg V_{O_2} peak testing (Excalibur Sport, version 2.0; Lode, Groningen, The Netherlands). Random assignment determined which leg would complete the aerobic training protocol while the other would remain sedentary (untrained). Participants completed 18 · 45-minute sessions of progressive moderate intensity continuous training (MICT) over a period of 6 weeks. 6 weeks of aerobic training was chosen as this has been demonstrated to be a sufficient period of time for increasing capillary content in sedentary individuals with aerobic training (37). Initial workload was determined by 50% of the average work peak (*Watts*) achieved in the participants single-leg V_{O_2} peak test. Participants progressed in wattage at a rate of 2-4% every 4 sessions. All training sessions included a 3-minute warm-up (25 watts) followed by 40-minutes of MICT during which participants were instructed to maintain a cadence of approximate 80-90 rpm, concluded by a 2-minute cool-down (25 watts). Heart rate and rating of perceived exertion were recorded during each session at the 2, 7, 40 and 44-minute timepoints.

Resistance Exercise Training

Participants performed progressive bilateral lower body resistance training 3 times per week for 10 weeks, specifically targeting the thigh (quadriceps) muscle. On each visit, participants completed 5 lower body exercises: leg extension, leg press, calf raises, hamstring curls and squats. For leg extension, leg press and squat participants performed 3 sets of 10-12 repetitions at 70-80% of their 1-reptition max (1-RM) with the last set

completed to failure for each exercise. For calf raise exercise, 3 sets of 10-12 repetitions with 20lb dumbbells was performed. Lastly for hamstring curl exercise, 3 sets of 10-12 repetitions were performed at a weight aimed to elicit failure between the 9th and 11th repetition of the third set.

Muscle Strength

Bilateral 1-RM testing was performed according to national strength and conditioning (NSCA) guidelines for leg extension, leg press and squat exercise prior to and post resistance training.

Supplementation

Immediately following each resistance exercise training session, 25g of whey protein isolate (including 2.7g leucine) (Ascent, Vanilla Bean) was ingested by each participant to support optimal adaptation to resistance exercise.

Immunofluorescence

Muscle cross sections (7µm) were prepared from unfixed OCT embedded samples, allowed to air dry for 30 minutes and stored at - 80˚C. Samples were stained with antibodies against Pax7, myosin heavy chain type-I, myosin heavy chain type-II, laminin and CD31. For immunofluorescent detection, appropriate secondary antibodies were used. Detailed antibody information can be found in **Table 2**. Nuclei were labelled with DAPI (4',6 - diamidino - 2 - phenylindole) (1:20000, Sigma - Aldrich, Oakville, ON, Canada), prior to

cover slipping with fluorescent mounting media (DAKO, Burlington, ON, Canada). The staining procedures were verified using negative controls, in order to ensure appropriate specificity of staining. Slides were viewed with the Nikon Eclipse Ti Microscope (Nikon Instruments, Inc. USA), equipped with a high-resolution Photometrics CoolSNAP HQ2 fluorescent camera (Nikon Instruments, Melville, NY, USA). Images were captured and analyzed using the Nikon NIS Elements AR 3.2 software (Nikon Instruments, Inc., USA). All images were obtained with the 20x objective, and ≥ 200 muscle fibres/subject/time point were included in the analyses for SC content (i.e., $DAPI^+$/ $Pax7^+$ cells) and fibre cross-sectional area. The quantification of muscle fibre SC content was performed by identifying the number of SC (i.e. $Pax7^+$ colocalized with DAPI) per 100 myofibers within the muscle sample. The quantification of muscle fibre capillaries was performed on 60 muscle fibres/subject/time point. Based on the work of Hepple *et al.* the capillary-to-fibre ratio on an individual fibre basis (CF*i*) and the capillary-to-fibre perimeter exchange index (CFPE) was calculated as an estimate of the capillary-to-fibre surface area (33) as a proxy measure of perfusion. All immunofluorescent analysis were completed in a blinded fashion.

Antibody	Species	Source	Details	Primary	Secondary
Anti-Pax7	Mouse	DSHB	Pax7	*Neat*	Alexa Fluor 594 goat anti-mouse 1:500
Anti-laminin	Rabbit	Abcam	Ab11575	1:500	Alexa Fluor 488, 647 goat anti-rabbit 1:500
Anti-MHCI	Mouse	DSHB	A4.951 Slow isoform	*Neat*	Alexa Fluor 488 goat anti-mouse 1:500
Anti-MHCII	Rabbit	Abcam	Ab51263	1:1000	Alexa Fluor 647 goat anti-rabbit 1:500
Anti-CD31	Rabbit	Abcam	Ab 28364	1:50	Alexa Fluor 594 goat anti-rabbit 1:500

Table 2; Detailed information on primary and secondary antibodies and dilutions used for immunofluorescent staining of the frozen muscle cross sections.

Detailed Antibody Information

Statistical Testing

Muscle data were analyzed using a one-way repeated measures analysis of variance (ANOVA) to compare biopsy samples (Baseline, $PostAT_{CTL}$, $PostAT_{EX}$, $PostRT_{CTL}$, $PostRT_{EX}$). These tests were performed to assess the following; the change in capillarization following aerobic training (CFi and CFPE), the change in fibre CSA following resistance training (CSA), and the change in SC content following aerobic and resistance training (SC). Upon detection of significance, pre-planned post hoc testing, involving Holm-Sidak's multiple comparison tests, were performed.

Pre-planned Post Hoc Comparisons for one-way ANOVA Testing

- CFi
    a. Baseline *vs.* $PostAT_{CTL}$
    b. Baseline *vs.* $PostAT_{EX}$
    c. $PostAT_{CTL}$ *vs.* $PostAT_{EX}$

- CFPE:
    a. Baseline *vs.* $PostAT_{CTL}$
    b. Baseline *vs.* $PostAT_{EX}$
    c. $PostAT_{CTL}$ *vs.* $PostAT_{EX}$

- CSA:
    a. $PostAT_{CTL}$ *vs.* $PostAT_{EX}$
    b. $PostAT_{CTL}$ *vs.* $PostRT_{CTL}$
    c. $PostAT_{EX}$ *vs.* $PostRT_{EX}$
    d. $PostRT_{CTL}$ *vs.* $PostRT_{EX}$

- SC content
    a. Baseline *vs.* $PostAT_{EX}$

b. $PostAT_{CTL}$ *vs.* $PostAT_{EX}$
c. $PostAT_{CTL}$ *vs.* $PostRT_{CTL}$
d. $PostAT_{EX}$ *vs.* $PostRT_{EX}$
e. $PostRT_{CTL}$ *vs.* $PostRT_{EX}$

A two-factor ANOVA, time (Baseline, PostAT and PostRT) and condition (CTL or EX) was used to analyze data from single-leg $\dot{V}O_2$ peak testing and DEXA measures. Prior to this, a Shapiro-Wilk test was performed on the data to test normality. Wilcoxon signed-rank tests were used to assess indices of muscle strength, 1-RM leg press and squat. Lastly, Pearson's r correlation was utilised to observe the relationship between fibre specific CFPE and change (delta) in myofibre CSA pre-to-post resistance training. Analysis were conducted using GraphPad Prism 8.0 (GraphPad Software, La Jolla, CA, USA). Statistical significance was set at $p<0.05$ for all measures. All $\dot{V}O_2$ exercise test data are represented as mean ± standard error of mean (SEM). Biopsy and Strength data are presented as box and whisker plots, for each, the box denotes the median, 25^{th} and 75^{th} percentiles, the cross represents the mean value and whiskers represent the maximum and minimum values.

Results

V_{O_2} Absolute $(ml \cdot min^{-1})$

A significant interaction ($p<0.01$) between condition (CTL vs. EX) and time (Baseline, PostAT and PostRT) was observed for V_{O_2} peak ($ml \cdot min^{-1}$) (**Figure 5A**). Post hoc testing revealed that single-leg cycling increased V_{O_2} peak ($ml \cdot min^{-1}$) from Baseline in the EX limb (Baseline: 2330 ± 611 to PostAT: 2603 ± 712 $ml \cdot min^{-1}$; $p=0.05$). V_{O_2} peak ($ml \cdot min^{-1}$) tended to be greater in the EX limb in comparison to CTL at the PostAT (2603 ± 711 vs. 2415 ± 668 $ml \cdot min^{-1}$; $p=0.06$) and PostRT timepoints (2571 ± 723 vs. 2404 ± 694 $ml \cdot min^{-1}$; $p<0.05$).

V_{O_2} Relative to Limb Fat Free Mass ($ml \cdot min^{-1} \cdot kgFFM_{Limb}^{-1}$)

A significant interaction ($p<0.01$) between condition (CTL vs. EX) and time (Baseline, PostAT and PostRT) was observed for pulmonary V_{O_2} peak relative to leg fat free mass ($ml \cdot min^{-1} \cdot kgFFM_{Limb}^{-1}$) (**Figure 5B**). Post hoc testing revealed that single-leg cycling increased V_{O_2} peak relative to leg fat free mass ($ml \cdot min^{-1} \cdot kgFFM_{Limb}^{-1}$) from Baseline in the EX limb (Baseline: 256 ± 38 to PostAT: 285 ± 47 $ml \cdot min^{-1} \cdot kgFFM_{Limb}^{-1}$;

p<0.05). V_{O_2} peak relative to leg fat free mass was greater in the EX limb in comparison to CTL at the PostAT (285 ± 47 vs. 266 ± 42 $ml \cdot min^{-1} \cdot kgFFM_{Limb}^{-1}$; p=0.0231) and PostRT timepoints (260 ± 45 vs. 246 ± 47 $ml \cdot min^{-1} \cdot kgFFM_{Limb}^{-1}$; p=0.03).

V_{O_2} Work Peak (*Watts*)

A significant interaction (p<0.0004) between condition (CTL vs. EX) and time (Baseline, PostAT and PostRT) was observed for V_{O_2} work peak (peak power output), recorded in watts (**Figure 5C**). Post hoc testing revealed that single-leg cycling increased work peak from Baseline in the EX limb (Baseline: 148 ± 40 to PostAT: 167 ± 35 *Watts*; p<0.0046). Work peak was greater in the EX limb in comparison to CTL at the PostAT (167 ± 35 vs. 148 ± 34 *Watts*; p=0.0008) and PostRT timepoints (161 ± 32 vs. 150 ± 31 *Watts*; p=0.0145).

Limb Fat Free Mass

No interaction was detected (p>0.05) for limb fat free mass (**Figure 5D**). However, a main effect of time (p<0.0001) was observed. Post hoc testing revealed that limb fat free mass was elevated at the PostRT (9901 ± 2494 *g*) timepoint in comparison to both Baseline (9173 ± 2426 *g*; p<0.0001) and PostAT (9134 ± 2420 *g*; p<0.0001) timepoints.

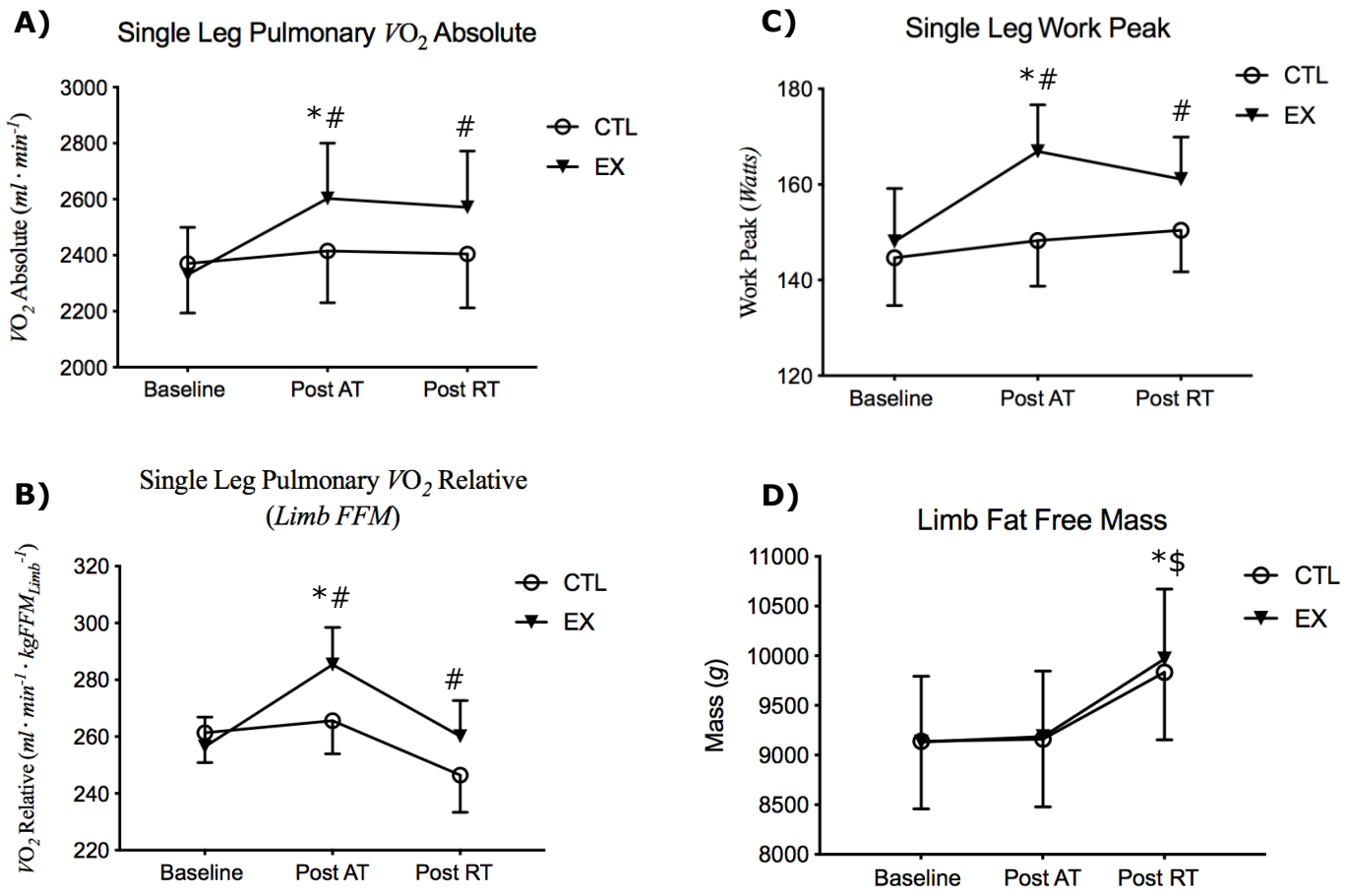

Figure 5; *Single Leg Pulmonary VO_2, Work Peak and Limb Fat Free Mass Measures.* Single leg performance test values for **(A)** pulmonary VO_2 absolute, **(B)** pulmonary VO_2 relative (Limb FFM) and **(C)** work peak data from incremental ramp tests. **(D)** Limb fat free mass data measured via DEXA. Data collected at Baseline, PostAT and PostRT timepoints; mean ± SEM. *$p<0.05$ for significant difference from Baseline. #$p<0.05$ for significant difference between CTL vs. EX. \$$p<0.05$ for significant difference from Post AT.

CFi

One-way repeated measures ANOVA indicated significant differences between means in CFi within type-I ($p<0.001$) (**Figure 6A**) and type-II ($p<0.01$) (**Figure 6B**) fibres. Post hoc testing revealed that in comparison to Baseline (1.27 ± 0.25), aerobic training elevated type-I CFi of both CTL (1.61 ± 0.42) ($p<0.05$) and EX (1.81 ± 0.39) ($p<0.001$) limbs. No differences in type-I CFi between the CTL and EX limbs was observed at PostAT (1.61 ± 0.42 vs. 1.81 ± 0.39; $p>0.05$). Additionally, post hoc comparisons demonstrated that aerobic training increased type-II CFi of both CTL (1.56 ± 0.49) ($p<0.05$) and EX (1.69 ± 0.24) ($p<0.001$) from Baseline (1.21 ± 0.29). No differences in type-II CFi between CTL and EX was observed at PostAT (1.56 ± 0.49 vs. 1.69 ± 0.24) ($p>0.05$).

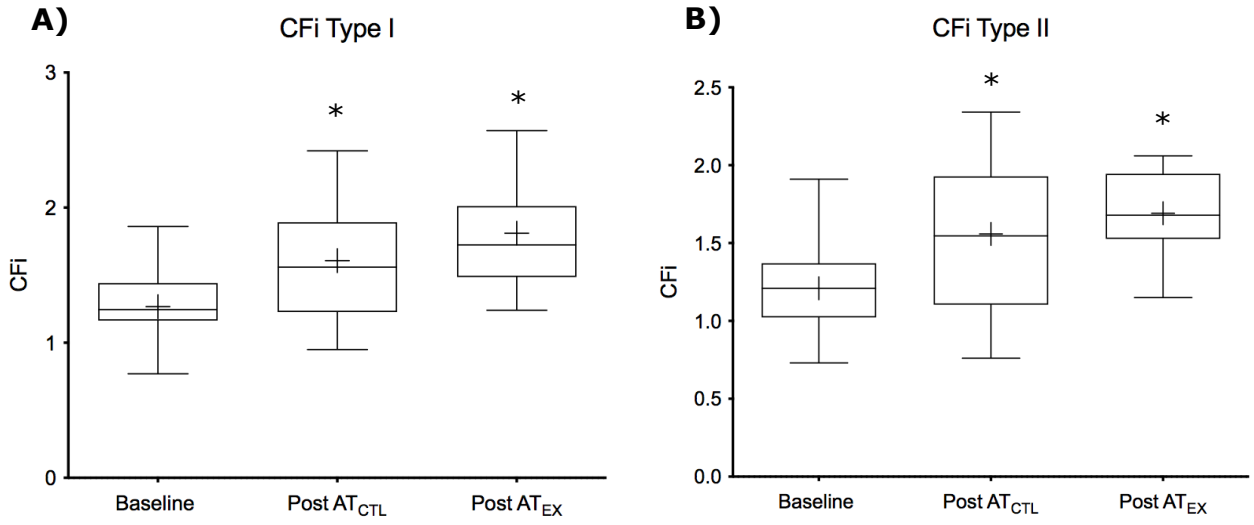

Figure 6; *Capillary Content Expressed as CFi Following Aerobic Training*. CFi of **(A)** type-I and **(B)** type-II associated fibres, measured at Baseline and PostAT analyzed using immunohistochemical staining. *$p<0.05$ for significant difference from Baseline. Values are presented as box and whisker plot, cross indicates the mean and line as the median, boxes denote the 25th and 75th percentile, whiskers represent the minimum and minimum values.

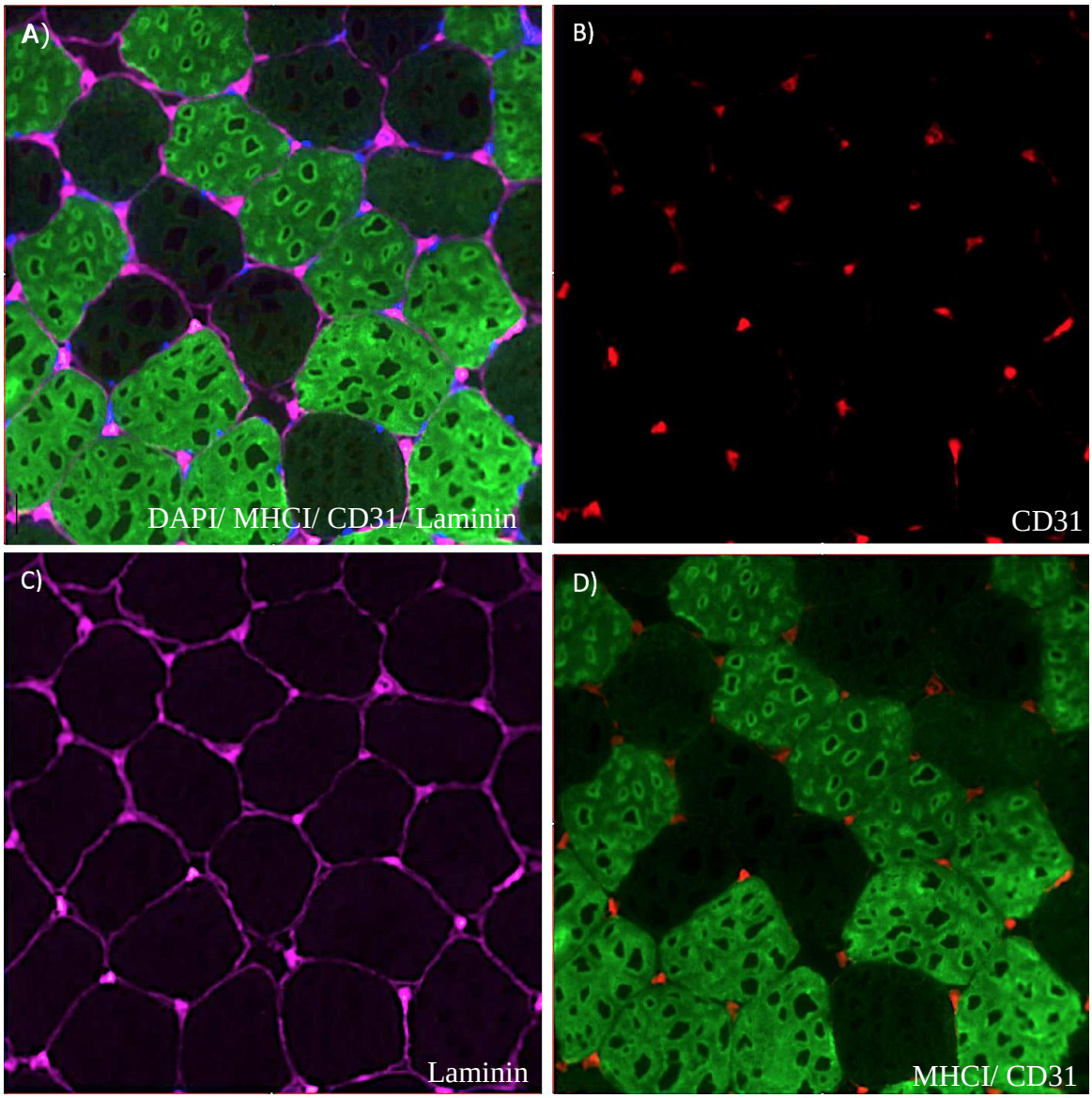

Figure 7; Representative image of DAPI/ MHCI/ CD31/ Laminin immunohistochemical stain. **(A)** DAPI/ MHCI/ CD31/ Laminin **(B)** CD31 **(C)** Laminin **(D)** MHCI/ CD31.

CFPE

One-way repeated measures ANOVA indicated significant differences between means in CFPE within type-I ($p<0.001$) (**Figure 8A**) and type-II ($p<0.05$) (**Figure 8B**) fibres. Post hoc comparisons revealed that PostAT type-I fibre CFPE was elevated in both the CTL (5.56 ± 1.06) ($p<0.05$) and EX (6.96 ± 1.19) ($p<0.0001$) limb in comparison to Baseline (4.93 ± 0.78). In addition, post hoc testing revealed that type-I fibre CFPE of the EX limb was greater relative to CTL at PostAT (5.56 ± 1.06 vs. 6.96 ± 1.19; $p<0.01$). In comparison to Baseline, type-II CFPE was elevated in the EX limb following aerobic training (4.63 ± 1.02 vs. 5.62 ± 1.15; $p<0.05$). No difference was observed between type-II CFPE of CTL and EX limbs following aerobic training (4.84 ± 1.12 vs. 5.62 ± 1.15; $p>0.05$).

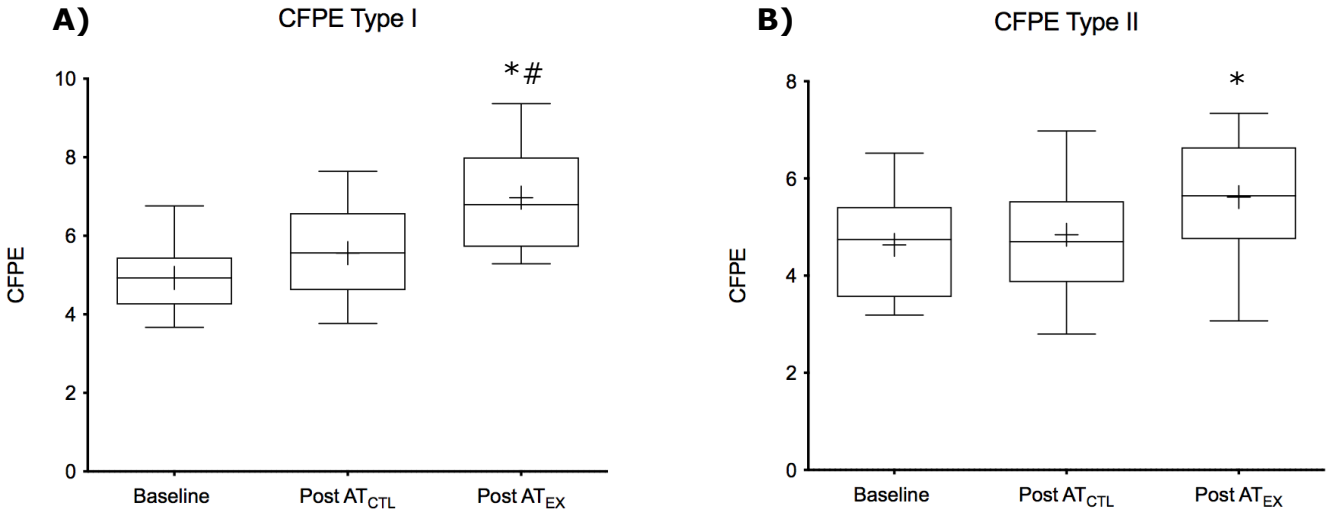

Figure 8; *Capillary Content Expressed as CFPE Following Aerobic Training*. CFPE of **(A)** type-I and **(B)** type-II associated fibres, measured at Baseline and PostAT analyzed using immunohistochemical staining. *$p<0.05$ for significant difference from Baseline. #$p<0.05$ for significant difference between CTL and EX. Values are presented as box and

whisker plot, cross indicates the mean and line as the median, boxes denote the 25th and 75th percentile, whiskers represent the minimum and minimum values.

SC Content

One-way repeated measures ANOVA indicated significant differences between means in SC content of type-I ($p<0.05$) (**Figure 9A**) and type-II ($p<0.05$) (**Figure 9B**) fibres. Despite significance being reported in ANOVA testing of type-I fibres, post hoc testing revealed no significant differences in SC content. However, type-II fibre SC content of the CTL limb was elevated following resistance training (4.03 ± 1.61 vs. 6.74 ± 1.96; $p<0.01$). No difference in type-II fibre SC content was observed between CTL and EX limbs at either PostAT (4.03 ± 1.61 vs. 4.12 ± 1.70; $p>0.05$) or PostRT (6.74 ± 1.96 vs. 8.59 ± 5.53; $p>0.05$) timepoints.

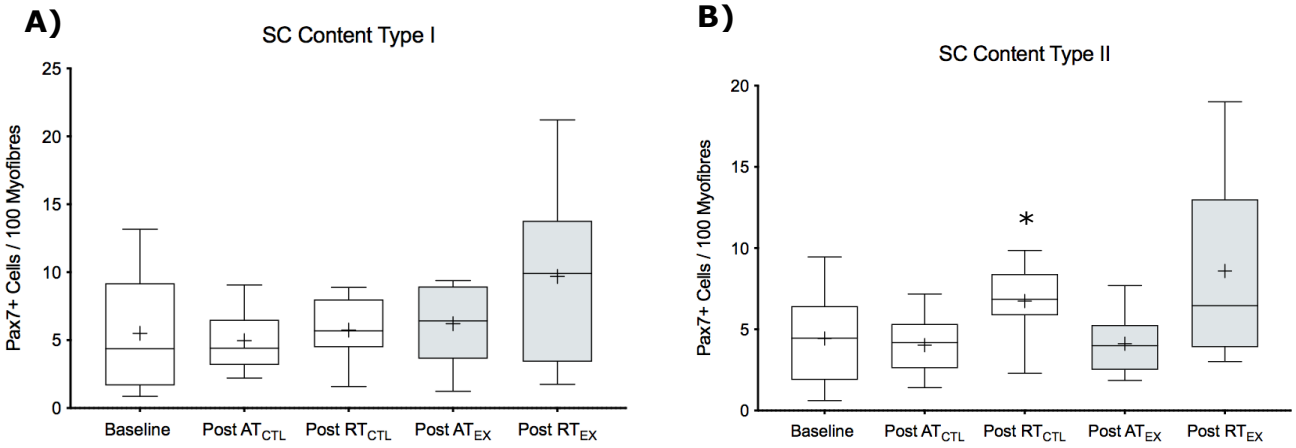

Figure 9; *SC Content Following Aerobic and Resistance Training*. SC content determined via immunohistochemical staining at Baseline, PostAT and PostRT in CTL and EX limbs for **(A)** type-I and **(B)** type-II fibres. *$p<0.05$ for difference pre-to-post resistance training, within limb (CTL or EX). Values are presented as box and whisker plot, cross indicates the mean and line as the median, boxes denote the 25th and 75th percentile, whiskers represent the minimum and minimum values.

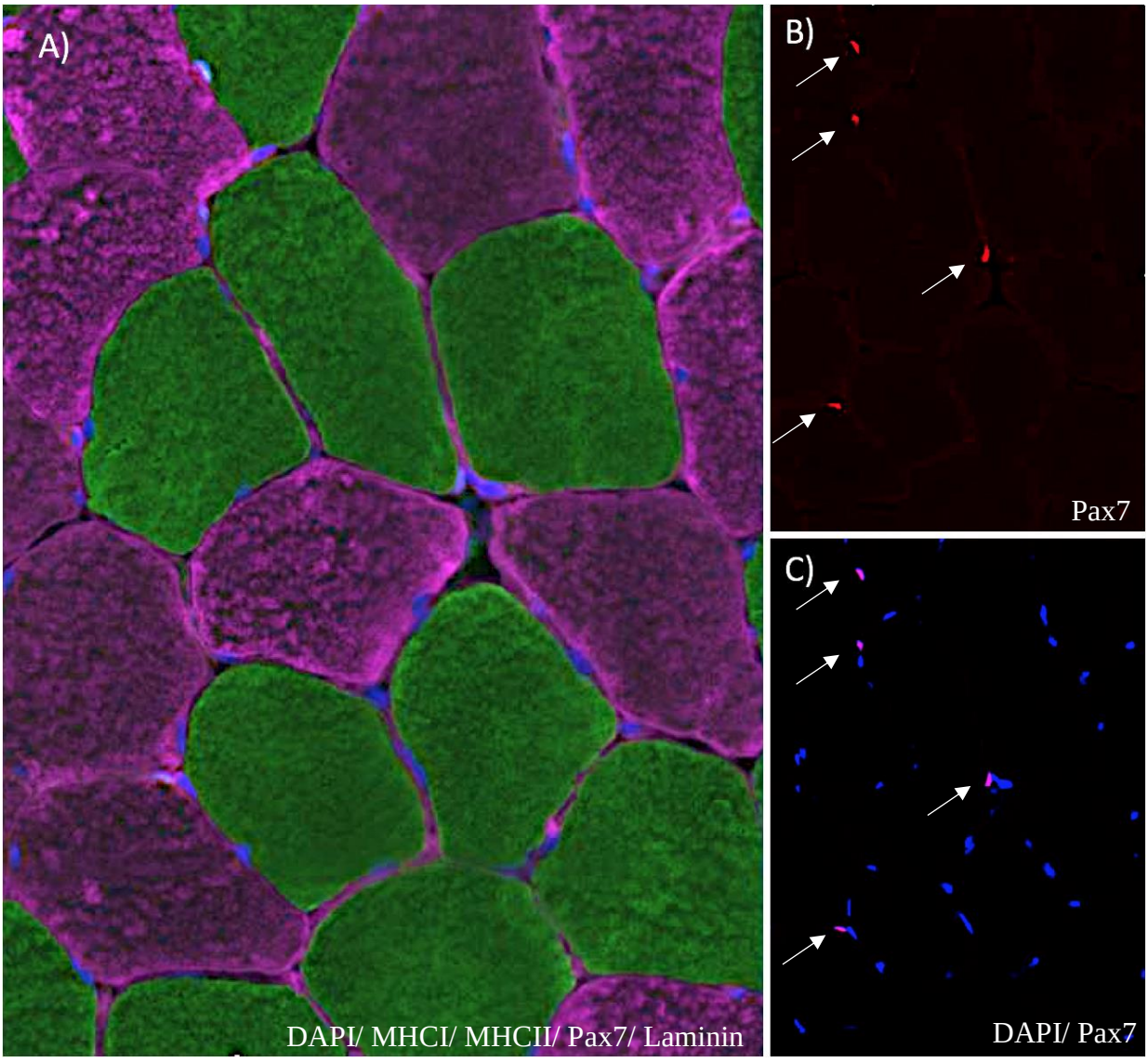

Figure 10; Representative Image of Pax7/ MHCI/ MHCII/ DAPI/ Laminin immunohistochemical stain. **(A)** DAPI/ MHCI/ MHCII/ Pax7/ Laminin **(B)** Pax7 **(C)** DAPI/ Pax7.

CSA

One-way repeated measures ANOVA indicated significant differences between means in CSA within type-I ($p<0.05$) (**Figure 11A**) and type-II ($p<0.05$) (**Figure 11B**) fibres. Further post hoc testing did not reveal any difference in type-I fibre CSA pre-to-post resistance training in either the EX (5150 ± 1429 vs. 6147 ± 1471 μm^2; $p=0.10$) or CTL (5149 ± 1077 vs. 5241 ± 1033 μm^2; $p=0.65$) limb. However, resistance training led to an increase in type-II fibre CSA of the EX limb between PostAT (5050 ± 1619 μm^2) to PostRT (7072 ± 2931 μm^2) ($p\leq0.05$). No difference in either type-I or type-II fibres was detected between CTL and EX limb at the PostRT timepoint ($p>0.05$).

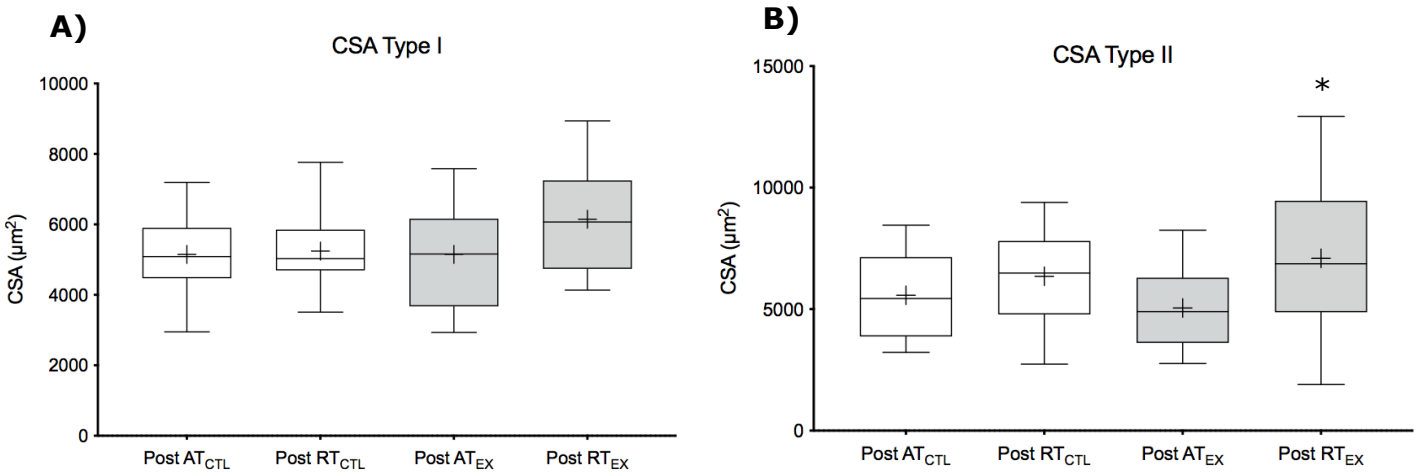

Figure 11; *Individual CSA Following Resistance Training.* Immunohistochemical analysis of fibre CSA pre-to-post resistance training for **(A)** type-I and **(B)** type-II fibres. *$p<0.05$ for difference pre-to-post resistance training, within limb (CTL or EX). Values are presented as box and whisker plot, cross indicates the mean and line as the median, boxes denote the 25th and 75th percentile, whiskers represent the minimum and minimum values.

Strength

Wilcoxon signed-rank test indicated an increase from pre-to-post resistance training in 1-RM strength for squat (192 ± 84 vs. 252 ± 85 *lbs*; p<0.0001) (**Figure 12A**) and leg-press (384 ± 179 vs. 523 ± 209 *lbs*; p<0.0001) (**Figure 12B**).

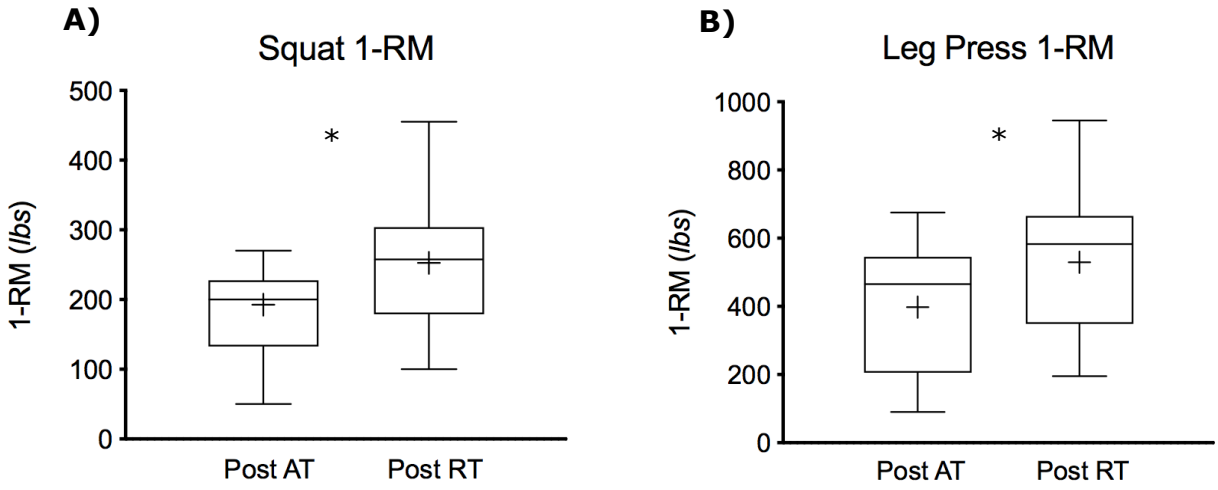

Figure 12; *One-Repetition Maximum for Squat and Leg Press Exercises Pre and Post Resistance Training*. Bilateral 1-RM measures pre-to-post resistance training for **(A)** squat and **(B)** leg press exercises. *p<0.05 for difference pre-to-post resistance training. Values are presented as box and whisker plot, cross indicates the mean and line as the median, boxes denote the 25th and 75th percentile, whiskers represent the minimum and minimum values.

Discussion

The current investigation is the first to assess the influence of an aerobic exercise preconditioning period on resistance exercise training and its associated outcomes. Both aerobic and resistance exercise are potent stimuli and induce a myriad of physiological responses, ultimately transforming muscle's phenotype. Inter-individual variability in response to resistance training adaptation in a young healthy population is readily reported in the literature (77). Recent work has highlighted the importance of muscle capillarization to support muscle adaption elicited via resistance exercise such as increased fibre CSA and SC content (56, 73). It has therefore been hypothesized that muscle capillary content may be a limiting factor for adaptation to resistance exercise training. The current study aimed to isolate the influence a period of unilateral aerobic training exhibits on muscle capillarization and the subsequent impact on muscle accretion and SC content following resistance exercise training. To date, research examining the effect of aerobic training on resistance training outcomes have utilized concurrent (aerobic immediately prior to resistance training within the same session) training models. Results are equivocal with some groups reporting increased acute anabolic signaling, while others report an attenuation in acute anabolic signaling following a concurrent training session (4, 16, 51). When extrapolating acute findings in attempt to examine long-term concurrent training outcomes the results appear inconsistent, some studies report blunted hypertrophy while others have reported no interference of combined aerobic and resistance training (35, 52). Therefore, the novelty of this study lies in its unique study design, whereby we utilized a pre-conditioning period of unilateral aerobic training to examine its influence on resistance

exercise training induced outcomes. A sequential, as opposed to concurrent study design, allowed us to examine the impact of aerobic training on muscle capillarization and the subsequent effect on muscle mass and SC content following a distinct resistance exercise training period.

Effect of unilateral aerobic training on muscle capillarization

In the present study we observed an overall increase in muscle capillarization (CFi and CFPE) in the EX limb following unilateral aerobic training (**Figure 6 & 8**). Specifically, we observed an elevation of type-I (20%) and type-II (21%) fibre CFPE of the EX limb following aerobic training and were found to be greater than CTL of type-I fibres, which demonstrated no change in CFPE from baseline (**Figure 8)**. These findings are consistent with previous literature as rises in capillarization have been reported anywhere between 10-30% in untrained individuals following 6-8 weeks of aerobic training (27), aligning well with previous studies that demonstrate aerobic exercise is a potent stimulus for increasing microvascular content (37). Interestingly, CFi increased in both the CTL (27%) and EX (41%) limb following aerobic training. Capillarization within skeletal muscle is primarily driven by frictional force (sheer stress) of blood applied to the luminal wall of the vessels (21). Subsequent downstream signalling elicited via sheer stress upregulates the production of angiogenic factors such as vascular endothelial growth factor (VEGF), secreted by the muscle fibre into the interstitium (21, 37). VEGF among others, is imperative and the most efficacious factor for increasing capillary content (21). Although not anticipated, the resulting increase of CFi in the CTL limb following aerobic

training could be due to either a systemic increase of pro-angiogenic factors from the EX limb leading to a "cross-effect" between limbs, or an unforeseen elevation in blood flow to the CTL limb during unilateral aerobic exercise training. Indeed, Kraus *et al.* (2003) demonstrated a rise in circulating VEGF following 1 hour of cycling at 50% $\dot{V}O_2$ work peak in trained and untrained subjects. Similarly, blood samples collected 1 hour following exercise from the femoral artery and femoral vein of an exercised limb demonstrate a negative arteriovenous balance of VEGF protein (36). The elevation in femoral venous, not arterial VEGF protein, is indicative that other tissue, besides the working muscle, may uptake circulating VEGF. Additionally, increases in endurance capacity and maximal blood flow of a resting contralateral limb has been observed following 5 weeks of unilateral upper body hand ergometer training, the effect of which could be potentially additive to cross-education of angiogenic factors (86). Taken together, we demonstrate that capillarization of a non-exercising contralateral limb may be possible with unilateral exercise, however, the degree of capillarization is likely not as robust, as changes in CFPE were only observed in the EX limb (**Figure 8**). To understand the disparate results of CFi vs. CFPE in the present study, it is important to consider how each value is determined. CFi is derived from a calculation that takes into consideration the sum of each capillary's fractional contribution of perfusion to an individual fibre (32). CFPE, going one step further, is calculated by dividing each fibre's CFi by the cross-sectional outer membrane perimeter of that fibre. Thus, CFPE is a better outcome as a proxy for fibre perfusion, representing the two-dimensional capillary-fibre surface area which is proposed to be the greatest point of resistance for nutrient and trophic factor diffusion into the muscle (32, 33).

In the current investigation we report that aerobic training did not alter fibre type distribution or perimeter from baseline measure, nor was there a difference in either measure between CTL and EX limbs following aerobic training. Although an increase in absolute CFi was observed in CTL and EX limbs following unilateral aerobic training, when made relative to their respective fibre perimeter (CFPE) we show that a difference between the CTL and EX limbs becomes more apparent. Following aerobic training, marginally smaller perimeter of type-II ($p=0.08$) and larger CFi of type-I ($p=0.10$) fibres of the EX limb compared to CTL may have emphasized the difference in level of individual fibre perfusion between limbs. More studies employing the use of a unilateral design to determine the influence of aerobic training on capillarization are necessary in order to further understand the implications of potential angiogenic cross-education and alterations in fibre perfusion.

Effect of unilateral training on muscle satellite cell content

In the present study we observed no change of muscle SC content in the CTL or EX limb following 6 weeks of unilateral aerobic training (**Figure 9**). Aerobic training's influence on SC content is not yet fully elucidated. In human models, previous literature in this area has utilised varying participant demographics and vastly divergent training regimes all in an attempt to characterize the SC pool following training. Due to a low degree of study homogeneity, it is not surprising that the results of these studies are inconsistent. The findings of the current investigation align well with previous work from our lab (42, 43), that show no expansion of the SC pool with 6 weeks of aerobic training

(SIT and MICT) in young healthy individuals as well as obese women. It is important to note that neither this investigation nor Joanisse *et al*. (42, 43) observed any myofibre hypertrophy following aerobic training. Previous literature demonstrating a change in SC content with aerobic training also reported a change in muscle CSA, therefore the rise of SC content could have occurred to mediate fibre hypertrophy and the SC pool response to aerobic exercise is likely highly dependent on the intensity of exercise, age and/or the extent to which participants may be sedentary (11, 82). Taken together these results conform well with previous observations demonstrating no change in SC content (with no change in CSA) following aerobic training in young healthy populations.

Effect of resistance training on muscle hypertrophy and bilateral strength

In human skeletal muscle, resistance exercise training is the best non-pharmacological stimulus for inducing muscle hypertrophy. In the present study, we demonstrate that 10 weeks of lower body resistance exercise training resulted in an accretion of limb fat free mass (**Figure 5D**), as well as increases in both squat 1-RM (**Figure 12A**) and leg press (**Figure 12B**). Additionally, we observed an increase of type-II muscle fibre CSA in the EX limb following resistance exercise training, with no difference in type-II muscle fibre CSA reported in the CTL limb. Although non-significant, it is important to note that type-II fibre CSA in the CTL limb tended to increase ($p=0.10$) following resistance exercise training (**Figure 11B**). Whereas many studies with prolonged resistance training protocols report hypertrophy of both fibre types (5, 38, 61), it is not uncommon that type-II fibres preferentially hypertrophy with resistance training, as

observed in the present study. Previous studies (18) with similar resistance training protocols and duration of intervention as the current investigation have also reported type-II fibre specific hypertrophy (18, 72). Current resistance exercise training dogma would suggest high-load (>60% 1-RM) resistance training is necessary to stimulate hypertrophy of type-II fibres due to the high stimulatory threshold of their motor units, exerting a greater stimulus upon type-II fibres and inducing adaptation such as increased CSA (9). However, recent literature (29, 57, 58) have challenged this concept, proposing that type-I and type-II motor unit activation, and subsequent hypertrophy, following resistance training is no different when exercise is performed to volitional muscular failure. In the present investigation, limbs were trained bilaterally to muscular failure (on the last set), subjecting each limb to the same stimulus as the other. Pushing the muscle to volitional failure in only one of three sets may not have subjected type-I fibres to sufficient metabolic stress (calcium flux, lactate, etc.) to induce significant hypertrophic adaptation (83). Additionally, it is possible that the current investigation was underpowered to detect marginal changes in type-I fibre CSA following resistance training, (delta resistance training EX limb type-I CSA; $p=0.10$). Regardless, and despite identical training stimuli in each condition, we report disparate hypertrophic responses between limbs, with the EX limb demonstrating more robust hypertrophy of type-II fibres in comparison to the CTL limb following resistance training. Although resistance exercise training is a potent stimulus for inducing muscle hypertrophy, dissimilar changes in CSA between limbs raises the question of limiting factors that may influence muscle accretion induced via resistance training.

Effect of resistance training on muscle satellite cell content

In the present study we did not observe an increase in type-I fibre associated SC content following resistance training in either the CTL or EX limb (**Figure 9**). We do however report an increase in type-II associated SC of the CTL limb following resistance training and although statistical significance was not reached, it is important to note that type-II SC content in the EX limb tended to increase (p=0.07) following resistance training. Individual responses in the EX limb were highly variable, ranging from 3- type-II SC per 100 fibres to 19- type-II SC per 100 fibres following resistance training. In the current investigation and other recent investigations, expansion of the type-II fibre associated SC pool following resistance training is consistently reported in studies spanning a wide subject demographic (18, 45, 72, 79, 82). SC pool expansion and subsequent myonuclear addition are proposed to be necessary for sustained and robust hypertrophy often associated with resistance exercise training (3, 25). Skeletal muscle is a post-mitotic tissue, therefore, any addition of myonuclei to the myofibre would be derived from a pre-existing SC. Thus, with increasing fibre CSA, such as with resistance training induced myofibre hypertrophy, the domain (volume) of cytoplasm that a single myonuclei can sustain is subjected to transcriptional stress (3, 45). The concept, coined the "myonuclear domain theory" hypothesizes that myonuclear addition, via SC division and fusion, is required to alleviate this transcriptional stress, permitting and supporting further expansion in fibre CSA (3). We, as well as others (18, 72, 81), have demonstrated type-II specific increases in SC content following resistance training, where SC content of type-I associated fibres show no apparent change. Consistent with this, studies, including the current investigation, that

demonstrate no resistance training induced change in type-I SC content also tend not to report increase of type-I fibre CSA. In alignment with the myonuclear domain theory, an increase in SC content is not necessary to increase the transcriptional requirements when hypertrophy has not occurred. Altogether, results from the present study align well with previous literature demonstrating an elevation in type-II associated SC content with type-II specific increases in fibre CSA following a period of prolonged resistance exercise training.

Effect of capillarization on SC content following resistance training

The present study is the first to examine the influence of capillarization on SC content following resistance training between limbs of an individual. We observe that elevated CFPE of the EX limb did not affect the gain in SC content following resistance training, when compared to the CTL limb. Together, these results suggest that increased CFPE in the EX limb did not dictate expansion of the SC pool with resistance training. A foundational study first characterizing the relationship between capillary and SC content demonstrated that a greater number of capillaries surrounding a fibre correlated well with the likelihood that a SC would be found associated with that fibre (14). Additionally, it was reported that a non-random spatial relationship existed between SC and capillaries and proposing the idea of a "juxta-vascular" SC niche (14). More recently, work from our lab has significantly contributed to understanding and further characterizing the capillary-to-SC relationship. Nederveen and colleagues (2018) demonstrated that young individuals with high relative CFPE had a more pronounced increase in SC content and activity, in

comparison to those with low relative CFPE, following a bout of eccentric contractions. Additionally, following 16 weeks of resistance training, expansion of capillary content (CFi and CFPE) did not alter the basal SC content, however, higher CFPE did augment the SC response to a single bout of resistance exercise (61). Taken together, these results demonstrate a potential for capillaries to regulate SC content acutely through paracrine or endocrine signalling in response to muscle damage. Although not observed in a young healthy population, data in elderly individuals suggests that a diminished network of capillaries occurs concomitant with a loss of SC content, selectively in type-II muscle fibres (17, 68). In an attempt to further characterize the implication of this phenomenon, 24 weeks of resistance training in an elderly population revealed that only individuals with high baseline CFPE were able to augment basal SC content, whereas low CFPE individuals showed no change in SC content following resistance training (72, 73). These data suggest retention of capillary content in older individuals is important for mediating the basal SC pool content with age. Collectively, the present study demonstrates no clear relationship between capillary content or perfusion (CFi or CFPE) and SC pool content following resistance training. Putting this finding into context, we hypothesize that in young individuals (<30 y.o.), capillary content may play a more "permissive" role in mediating basal SC content, therefore increasing capillary content above a given threshold does not augment basal SC content any further. Additionally, we propose an increase of capillary content in young individuals is an effective strategy for augmenting SC activation and proliferation in response to muscle damage due to higher concentrations and exposure to regulatory factors upregulated following damage (62). We also suggest that the capillary-

to-SC relationship changes with age, as studies have shown in older adults (>60 y.o.) that the decline in capillary content occurs concomitantly with basal SC content and a reduced SC activation in response to muscle damage (72, 73). This alteration, although likely multifactorial in nature, could be a result of increased fibrosis commonly reported in aging muscle (Boppart 2016), favouring type-II fibres and conceivably hampering paracrine signalling. Future research in this area should continue to explore how the capillary-to-SC dynamic changes in aging muscle, what factors may be influencing this and the implications to muscle health.

Effect of capillarization on hypertrophy following resistance training

The current investigation demonstrates a greater capacity for perfusion of type-I and type-II fibres in the EX limb following unilateral aerobic training. Similarly, we observe type-II fibre hypertrophy in the EX limb with no change reported in the CTL limb (type-I or II CSA) following resistance training. Additionally, we observe that the degree of muscle perfusion prior to commencement of resistance training is positively correlated, regardless of fibre-type, with the gain in muscle fibre CSA observed pre-to-post resistance training (**Figure 13**). The current study is not the first to suggest or provide evidence towards the notion that muscle capillarization may be a determining factor of hypertrophy following resistance training (72). Studies observing a change in capillary content in both younger and older men have demonstrated resistance training to be an effective intervention for elevating muscle perfusion (38, 60, 81). Whereas some studies in older men have suggested that sufficient capillarization may be a pre-requisite for supporting hypertrophy,

researchers have demonstrated that adequate perfusion of type-II muscle fibres is necessary prior to increasing CSA with resistance exercise training (25, 72).

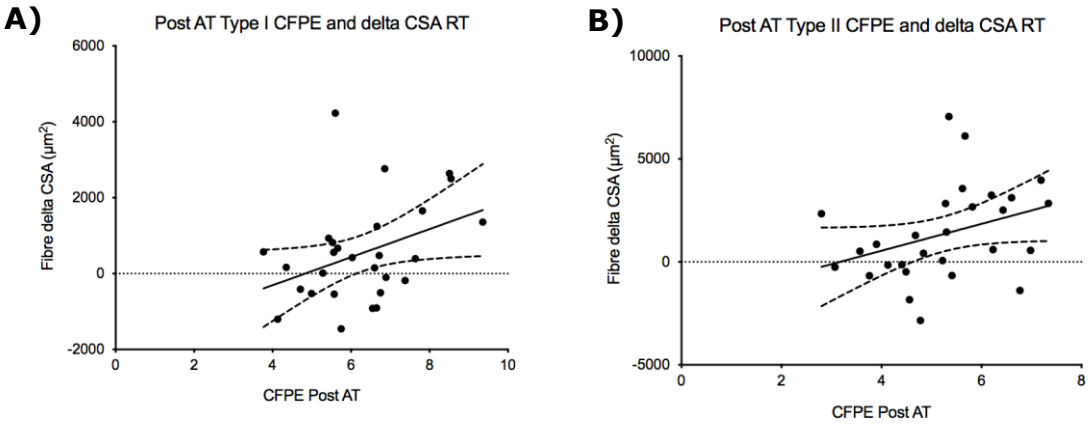

Figure 13; *Capillary Perfusion Prior to, and Change in Fibre CSA Following Resistance Training*. Characterization of relationship between CFPE prior to resistance training and change in **(A)** type-I ($r = 0.38$, $p<0.05$) and **(B)** type-II ($r = 0.35$, $p<0.05$) fibre CSA following resistance training.

Based on current evidence, it would appear that muscle capillarization has a degree of underlying influence on fibre size and the ability to respond to resistance exercise training stimuli, the effect of which may become more apparent and exaggerated with age. In addition, SC proliferation induced in response to muscle damage is necessary to support the efficient repair and maintenance of myofibers (62). Studies in young and older individuals have demonstrated that high perfusion (CFPE) of skeletal muscle evokes a greater expansion of SC content and activation in comparison to lower perfused skeletal muscle following a single bout of muscle damage (5, 62, 71). Extrapolating these results over weeks of repetitive muscle damage in the form of resistance exercise training, the relationship between capillaries and hypertrophic potential becomes more apparent in an

aging population. The present study provides initial evidence of this relationship holding true in a young healthy population, where an elevated fibre perfusion of the EX limb may have contributed towards augmented hypertrophy of type-II fibres. Additionally, The current investigation is the first to demonstrate evidence that elevating capillary perfusion in young healthy individuals may be an effective strategy for augmenting muscle hypertrophy following resistance training. More studies examining the influence of capillarization on resistance training outcomes in young individuals are required to better understand the proposed relationship.

Conclusion

In conclusion, results from the present study indicate that 6 weeks of unilateral aerobic training is an effective conditioning strategy for increasing skeletal muscle capillary perfusion and subsequently may benefit resistance training outcomes such as augmented hypertrophy of type-II muscle fibres. We demonstrate that capillary content nor perfusion alters SC accretion following a period of prolonged resistance exercise training in young healthy men and women.

Limitation of the current investigation and potential future directions

The objective of the current investigation was to assess the influence of a prolonged period of aerobic training prior to resistance training and its associated outcomes using a unique unilateral design. We successfully demonstrated disparate outcomes of gains in muscle CSA between limbs of an individual despite an identical (bilateral) resistance

exercise training intervention. A limitation of the present study is the exclusion of unilateral strength data due to technical challenges. Additionally, the relative work-loads and intensity of single-leg cycling is not yet well characterized or documented in the literature in relation to double-leg cycling exercise prescription. The current investigation is limited therefore by the unknown relative work intensity participants trained at during the period of single-leg cycling. A future direction of this research is to follow-up in an elderly and ageing population to determine if aerobic activity improves resistance training outcomes, such an augmentation of fibre CSA observed in the present study. Additionally, the acute damage-induced increase in SC content following aerobic exercise should be explored to determine if oxidative adaption of muscle can influence the inter-individual SC response to muscle damage. Lastly, immunohistochemical analysis of SC activation ($MyoD^{+}$) following aerobic and resistance training would lend further insight into the capillary-to-SC relationship.

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APPENDIX A: Raw Data

Table 1. Baseline Anthropometric Characteristics and V_{O_2} Raw Data for Men

		Males										
	Subject Blind #	Age	Height (cm)	Weight (Kg)	BMI (Kg/m^2)	DL Watt Pk	DL V02_Relative	Single Leg Watt Pk (Avg)	(Trained) - (Untrained) Watt Pk	AVG SL V02_Relative	(Trained) - (Untrained) SL V02_Relative (llbm)	AVG SL V02_Relative (llbm)
PRE	S01	22.00	177.00	110.70	35.33	382.00	30.61	208.00	11.800	27.60	-24.14	237.62
	S03	23.00	174.00	104.20	34.42	387.00	43.07	196.00	18.900	28.72	-26.60	243.37
	S09	21.00	176.50	71.20	22.86	319.00	44.71	180.00	-7.000	38.90	-8.33	260.16
	S10	19.00	167.00	74.90	26.86	270.00	38.83	147.00	7.000	32.74	27.27	264.24
	S11	20.00	177.50	71.12	22.57	299.00	44.28	149.00	20.000	35.41	14.24	235.98
	S12	18.00	178.00	75.90	23.96	286.00	43.71	133.00	10.000	26.41	29.51	222.73
	S13	23.00	182.00	95.25	28.76	306.00	36.75	167.00	-7.000	28.50	-0.79	230.74
	S14	22.00	171.00	69.90	23.90	301.00	56.20	190.00	0.000	46.83	8.73	335.20
	Average	21.00	175.38	84.15	27.33	318.75	42.27	171.25	6.71	33.14	2.49	253.76
	SD	1.73	4.34	15.51	4.77	40.27	6.94	24.89	9.89	6.55	20.01	33.47

Table 2. Baseline Anthropometric Characteristics and V_{O_2} Raw Data for Women

		Females										
	Subject Blind #	Age	Height (cm)	Weight (Kg)	BMI (Kg/m^2)	DL Watt Pk	DL V02_Relative	Single Leg Watt Pk (Avg)	(Trained) - (Untrained) Watt Pk	AVG SL V02_Relative	(Trained) - (Untrained) SL V02_Relative (llbm)	AVG SL V02_Relative (llbm)
PRE	S02	21.00	163.00	64.40	24.24	266.00	39.78	142.00	4.90	32.27	-1.79	308.58
	S04	23.00	172.00	60.60	20.48	217.00	36.57	120.00	9.90	31.30	-45.36	284.00
	S05	20.00	152.00	50.21	21.73	173.00	31.24	76.00	-3.60	21.61	-0.46	202.13
	S06	19.00	162.50	62.40	23.63	183.00	29.29	88.00	-10.00	26.67	-21.26	238.31
	S07	23.00	155.00	49.00	20.40	173.00	40.91	117.00	-14.00	31.36	-18.58	253.20
	S15	20.00	170.00	77.10	26.68	241.00	30.84	138.00	7.00	31.48	-0.80	308.54
	Average	21.00	162.42	60.62	22.86	208.83	34.77	113.50	-0.97	29.11	-14.71	265.80
	SD	1.53	7.23	9.42	2.24	35.60	4.55	24.23	8.89	3.82	16.13	38.63

Table 3. Post AT Anthropometric Characteristics and V_{O_2} Raw Data for Men

		Females										
	Subject Blind #	Age	Height (cm)	Weight (Kg)	BMI (Kg/m^2)	/	/	Single Leg Watt Pk (Avg)	(Trained) - (Untrained) Watt Pk	AVG SL V02_Relative	(Trained) - (Untrained) SL V02_Relative (llbm)	AVG SL V02_Relative (llbm)
MID	S02	21.00	163.00	63.80	24.01			149.50	26.20	40.57	33.65	378.33
	S04	23.00	172.00	60.20	20.35			135.35	23.10	29.36	9.67	259.15
	S05	20.00	152.00	50.80	21.99			107.80	34.80	28.85	0.90	256.00
	S06	19.00	162.50	63.30	23.97			113.00	10.00	29.14	10.93	265.08
	S07	23.00	155.00	50.70	21.10			113.00	8.00	29.27	33.61	246.04
	S15	20.00	170.00	78.70	27.23			138.50	27.00	29.29	24.84	290.40
	Average	21.00	162.42	61.25	23.11			126.19	21.52	31.08	18.93	282.50
	SD	1.53	7.23	9.46	2.29			15.63	9.54	4.25	12.53	44.96

Table 4. Post AT Anthropometric Characteristics and V_{O_2} Raw Data for Women

	Males											
MID	Subject Blind #	Age	Height (cm)	Weight (Kg)	BMI (Kg/m^2)	/	/	Single Leg Watt Pk (Avg)	(Trained) - (Untrained) Watt Pk	AVG SL V02_Relative	(Trained) - (Untrained) SL V02_Relative (llbm)	AVG SL V02_Relative (llbm)
	S01	22.00	177.00	112.50	35.91			224.50	29.40	31.27	59.50	270.33
	S03	23.00	174.00	104.60	34.55			196.10	12.00	31.26	-2.51	241.32
	S09	21.00	176.50	69.67	22.36			188.00	26.00	38.05	42.09	257.48
	S10	19.00	167.00	76.20	27.32			162.00	18.00	34.43	32.14	278.38
	S11	20.00	177.50	69.80	22.15			175.00	34.00	38.43	14.23	259.61
	S12	18.00	178.00	77.20	24.37			169.00	7.00	32.15	0.57	267.52
	S13	23.00	182.00	95.70	28.89			139.50	-6.00	27.58	-1.93	216.38
	S14	22.00	171.00	69.80	23.87			195.00	12.00	51.75	18.40	370.95
	Average	21.00	175.38	84.43	27.43			181.14	16.55	35.61	20.31	270.25
	SD	1.73	4.34	16.15	5.00			24.05	12.26	6.98	21.20	42.17

Table 5. Post RT Anthropometric Characteristics and V_{O_2} Raw Data for Men

	Males											
POST	Subject Blind #	Age	Height (cm)	Weight (Kg)	BMI (Kg/m^2)	/	/	Single Leg Watt Pk (Avg)	(Trained) - (Untrained) Watt Pk	AVG SL V02_Relative	(Trained) - (Untrained) SL V02_Relative (llbm)	AVG SL V02_Relative (llbm)
	S01	22.00	177.00	118.40	37.79			216.65	24.30	27.995	38.152	248.565
	S03	23.00	174.00	108.30	35.77			194.05	12.30	27.845	-14.701	229.098
	S09	21.00	176.50	71.40	22.92			162.5	15.00	35.75	20.750	221.040
	S10	19.00	167.00	76.60	27.47			154	16.00	37.75	14.900	267.360
	S11	20.00	177.50	69.80	22.15			172.5	15.00	36.165	16.870	218.700
	S12	18.00	178.00	78.40	24.74			135	8.00	26.695	8.400	184.360
	S13	23.00	182.00	95.80	28.92			179	-14.00	33.69	25.750	262.670
	S14	22.00	171.00	72.40	24.76			191	2.00	53.09	-5.200	359.350
	Average	21.00	175.38	86.39	28.07			175.59	9.83	34.87	13.12	248.89
	SD	1.73	4.34	17.49	5.46			23.90	10.84	7.97	15.79	48.70

Table 6. Post RT Anthropometric Characteristics and V_{O_2} Raw Data for Men

	Females											
POST	Subject Blind #	Age	Height (cm)	Weight (Kg)	BMI (Kg/m^2)	/	/	Single Leg Watt Pk (Avg)	(Trained) - (Untrained) Watt Pk	AVG SL V02_Relative	(Trained) - (Untrained) SL V02_Relative (llbm)	AVG SL V02_Relative (llbm)
	S02	21.000	163.000	63.300	23.825			160.250	13.500	36.755	5.113	329.980
	S04	23.000	172.000	59.700	20.180			129.500	9.000	27.835	17.911	236.486
	S05	20.000	152.000	51.340	22.221			120.500	23.000	26.950	4.729	227.146
	S06	19.000	162.500	65.500	24.805			112.000	12.000	26.760	10.850	205.690
	S07	23.000	155.000	48.700	20.271			114.000	0.000	34.775	29.709	273.858
	S15	20.000	170.000	78.500	27.163			140.000	14.000	30.845	18.550	273.090
	Average	21.00	162.42	61.17	23.08			129.38	11.92	30.65	14.48	257.71
	SD	1.53	7.23	9.81	2.49			16.75	6.83	3.90	8.72	40.44

Table 7. Raw Data for V_{O_2} Relative to Whole Body Mass ($ml \cdot min^{-1} \cdot kg^{-1}$)

V02 mL/min/ KG		SL V02			SL V02			SL V02	
Subject	DL V02	Pre_T	Pre_UT		Mid_T	Mid_UT		Post_T	Post_UT
S01	30.61	26.05	29.15		34.56	27.98		30.47	25.52
S02	39.78	32.18	32.35		42.98	38.15		37.35	36.16
S03	43.07	25.21	32.23		30.81	31.71		26.65	29.04
S04	36.57	30.51	32.09		31.28	27.44		29.42	26.25
S05	31.24	22.41	20.80		29.13	28.57		27.86	26.04
S06	29.29	25.14	28.20		29.73	28.54		27.56	25.96
S07	40.91	29.56	33.15		30.67	27.87		35.72	33.83
S09	44.71	38.21	39.59		40.63	35.46		37.87	33.63
S10	38.83	34.46	31.02		37.63	31.23		36.30	39.20
S11	44.28	36.51	34.31		38.84	38.01		37.41	34.92
S12	43.71	29.78	27.21		28.36	26.79		27.96	25.43
S13	36.75	25.98	26.84		32.39	31.91		35.50	31.88
S14	56.20	47.49	46.16		51.96	51.53		53.17	53.01
S15	30.84	31.62	31.33		30.25	28.33		31.40	30.29

Table 8. Raw Data for V_{O_2} Work Peak (Watts)

W_Peak		SL V02			SL V02			SL V02	
Subject	DL V02	Pre			Mid			Post	
S01	382.30	213.80	202.00		239.20	209.80		228.80	204.50
S02	265.50	144.90	140.00		162.60	136.40		167.00	153.50
S03	387.50	205.70	186.80		202.10	190.10		200.20	187.90
S04	217.00	124.90	115.00		146.90	123.80		134.00	125.00
S05	173.30	74.10	77.70		125.20	90.40		132.00	109.00
S06	183.00	83.00	93.00		118.00	108.00		118.00	106.00
S07	172.40	110.00	124.00		117.00	109.00		114.00	114.00
S09	319.00	176.00	183.00		201.00	175.00		170.00	155.00
S10	270.00	150.00	143.00		171.00	153.00		162.00	146.00
S11	299.00	159.00	139.00		192.00	158.00		180.00	165.00
S12	286.00	138.00	128.00		143.00	136.00		139.00	131.00
S13	306.00	163.00	170.00		166.00	172.00		172.00	186.00
S14	301.00	190.00	190.00		201.00	189.00		192.00	190.00
S15	241.00	141.00	134.00		152.00	125.00		147.00	133.00

Table 9. Raw Data for V_{O_2} Relative to Limb Fat Free Mass ($ml \cdot min^{-1} \cdot kgFFM_{Limb}^{-1}$)

V02 mL/min/llbm		SL V02			SL V02			SL V02	
Subject	DL V02	Pre_T	Pre_UT		Mid_T	Mid_UT		Post_T	Post_UT
S01	167.60	225.55	249.69		300.08	240.58		267.64	229.49
S02	189.78	307.68	309.47		395.16	361.51		332.54	327.42
S03	167.99	230.08	256.67		240.07	242.57		221.75	236.45
S04	165.05	261.32	306.69		263.98	254.31		245.44	227.53
S05	140.04	201.90	202.36		256.45	255.55		229.51	224.78
S06	130.86	227.69	248.94		270.55	259.62		211.11	200.26
S07	165.89	243.91	262.49		262.85	229.23		288.71	259.00
S09	149.55	256.00	264.33		278.52	236.43		231.41	210.67
S10	155.96	277.88	250.61		294.44	262.31		283.81	268.91
S11	149.09	243.09	228.86		266.72	252.50		227.14	210.26
S12	180.86	245.49	215.98		216.67	216.10		188.56	180.16
S13	153.87	222.34	223.13		266.56	268.48		275.55	249.80
S14	205.55	339.56	330.83		380.15	361.75		356.75	361.95
S15	149.52	308.14	308.94		302.82	277.98		282.37	263.81

Table 10. Raw Data for Limb Fat Free Mass

LLBM (g)								
Subject	Double Limb BL	Pre_T	Pre_UT		Mid_T	Mid_UT		Post_T	Post_UT
S01	25805	12831	12964		12953	13089		13477	13164
S02	13674	6939	6734		6939	6734		7112	6994
S03	27162	13639	13523		13417	13670		13565	13301
S04	13626	7133	6492		7133	6492		7130	6865
S05	11454	5775	5678		5775	5678		6235	5948
S06	13962	6913	7094		6960	6964		8441	8389
S07	12080	5916	6164		5916	6164		6051	6386
S09	21290	10629	10661		10168	10447		11676	11397
S10	18652	9425	9425		9737	9546		10803	10561
S11	21121	10572	10548		10389	10503		11579	11676
S12	18771	9210	9561		10103	9565		11625	11068
S13	22760	11217	11545		11626	11375		12339	12306
S14	19100	9739	9721		9533	9935		10792	10601
S15	15730	7912	7817		7942	8112		8744	9014

Table 11. Raw Data for Muscle Fibre Cross-Sectional Area

	Timepoint	S01	S02	S03	S04	S05	S06	S07	S09	S10	S11	S12	S13	S14	S15
Type 1	Pre	5213.0	4777.2	4954.565	3440.13	3913.93	4065.64	4329.555	8378.735	4756.1	5165.4	4797.965	4365.5	4902.155	3526.1
	Mid_UT	6619.5	5834.0	5432.645	3787.12333	5334.54	4840.07667	7192.855	6108.37667	4820.3	5610.2	4744.88	4536.85333	4283.51	2949.28667
	Mid_T	6162.0	5906.4	4616.573333	3486.885	6173.2563	3738.41	4646	6162.42	7579.9	7324.2	3385	5674.58	4315.11	2933
	Post_UT	6076.8	4633.6	4906.065	4717.98	4920.87333	5438.8	7767.075	6502.13	5241.5	5104.8	3828.145	5782.34	4952.535	3508.415
	Post_T	6638.0	4450.6	8846.605	5985.825	6188.225	4557.33	4797.705	5259.195	8937.3	7225.8	6147.7	7327	4134.04	5573.095
	Timepoint	S01	S02	S03	S04	S05	S06	S07	S09	S10	S11	S12	S13	S14	S15
Type 2	Pre	7391.0	5642.1	7823.2	2964.0	2671.9	4703.4	4006.8	8681.0	8757.7	8247.9	7193.44	4985	5372.545	4106.705
	Mid_UT	8459.5	5465.5	7403.7	3311.6	3224.1	3967.2	7051.5	7621.3	4854.0	6817.8	4255.04333	6617.87667	5411.29	3595.37
	Mid_T	8251.0	5302.6	5875.4	2760.2	4742.4	3060.6	3746.0	7121.1	7172.5	5049.8	3976.5	6024.69	4415.18	3199
	Post_UT	6621.1	4793.8	7278.5	4765.0	2740.5	6356.4	9398.7	8182.7	7687.1	6882.7	4855.33	9136.09333	6271.715	4011.34
	Post_T	7593.5	5051.9	12936.8	6734.2	1897.5	4347.7	6421.5	6966.5	10014.3	11168.6	7091.6	9271.5	3022.535	6764.015

Table 12. Raw Data for Muscle Satellite Cell Content (Pax7^{+} Cells/ 100 Myofibres)

Raw Values

	Subject	1	2	3	4	5	6	7	9	10	11	12	13	14	15
TYPE 1	Pre	13.16	2.28	1.77	1.00	7.76	0.86	5.14	8.44	11.44	5.28	11.50	1.35	3.61	3.43
	Mid UnT	3.84	3.41	9.07	2.21	5.84	6.84	6.04	3.85	8.62	4.97	2.73	6.39	3.33	2.37
	24_UnT	6.99	6.46	10.00	6.73	3.55	2.99	10.14	7.11	10.66	7.74	6.84	7.58	7.05	5.67
	48_UnT	8.25	8.57	6.27	4.20	6.35	10.47	12.63	10.22	12.57	5.44	9.24	8.25	4.81	8.23
	Mid T	5.69	3.76	9.32	2.15	9.25	8.67	3.28	8.36	8.86	6.11	9.39	6.72	1.24	4.13
	24_T	6.45	14.39	23.12	5.57	9.61	8.40	5.37	22.81	11.30	19.09	8.34	11.11	6.25	6.56
	48_T	13.78	13.26	13.42	5.54	13.18	6.44	6.66	5.74	9.77	10.56	15.83	8.68	9.77	4.17
	Post_UT	1.58	7.63	8.05	4.76	5.75	5.75	7.99	3.64	8.89	5.00	5.62	8.07	5.54	2.15
	Post_T	10.53	1.75	21.21	15.15	13.33	6.64	9.29	3.54	1.87	3.02	18.27	8.48	11.02	11.46

Raw Values

	Subject	1	2	3	4	5	6	7	9	10	11	12	13	14	15
TYPE 2	Pre	4.43	3.07	4.15	0.61	4.49	1.60	4.71	9.46	8.00	6.08	4.82	1.16	7.49	1.98
	Mid UnT	4.40	1.41	7.17	2.67	2.42	3.45	5.85	4.35	6.12	4.03	1.85	5.16	4.33	3.23
	24_UnT	12.55	4.15	10.57	5.28	7.35	4.95	6.59	14.77	11.35	13.66	3.66	6.66	9.02	5.24
	48_UnT	13.02	9.71	10.17	2.99	2.57	6.59	10.68	8.98	12.52	15.49	8.00	8.73	6.39	6.35
	Mid T	3.87	2.28	5.82	1.86	4.17	2.58	2.90	2.26	6.92	4.12	5.08	7.70	3.70	4.40
	24_T	13.76	5.25	6.50	2.77	3.91	5.24	3.09	12.12	4.13	6.50	5.37	11.52	6.21	4.67
	48_T	20.38	10.80	14.06	4.57	6.10	7.28	4.16	8.01	16.72	14.13	19.35	10.54	10.85	4.89
	Post_UT	2.30	6.96	9.86	7.35	4.64	6.74	6.74	8.36	6.65	8.54	8.98	7.11	6.27	3.83
	Post_T	12.07	4.24	19.01	18.51	3.27	6.50	11.09	6.41	3.60	3.02	8.59	4.20	4.01	15.79

Table 13. Raw Data for Muscle Fibre Perimeter

	Timepoint	S01	S02	S03	S04	S05	S06	S07	S09	S10	S11	S12	S13	S14	S15
Relative T1 Perimeter	Pre	269.65144	250.61462	268.42738	230.27111	248.26322	297.86544	225.5395	337.76544	340.62044	272.73222	239.43863	214.14233	265.4	254.679
	Mid_UT	347.33224	349.86333	286.8241	236.15833	288.191	233.43317	332.92211	288.775	291.72183	273.28983	236.3477	258.03378	296.49289	208.726
	Mid_T	331.03567	285.861	261.75392	225.48444	290.37905	221.89042	262.22722	286.87367	317.11517	261.97528	235.95875	257.67744	249.66717	268.3
	Post_UT	273.9	252.64869	303.53133	274.54683	289.73485	273.9	244.27117	286.08833	345.688	257.5175	235.39592	303.48828	271.46683	222.72133
	Post_T	260.82278	258.17767	322.94422	280.78262	220.54731	233.00233	331.0785	292.3	405.66786	385.20711	292.3	301.02011	235.96024	272.52075
Relative T2 Perimeter	Pre	332.45833	272.73184	336.47817	211.67878	211.66189	299.5012	209.5	351.053	356.57433	328.37489	261.80854	248.863	284.7	280.62025
	Mid_UT	287.32873	347.43563	334.60222	219.12456	232.75789	217.87933	328.46289	322.755	332.12767	321.12667	234.37017	297.30211	297.702	236.52383
	Mid_T	263.5	282.10978	308.09042	216.73256	259.00218	202.34633	236.33536	304.61144	307.30044	325.77717	250.78	298.81078	247.93	185.96511
	Post_UT	352.51367	266.56667	374.51256	270.2165	220.01133	297.3	274.79333	322.66333	332.46406	287.05367	263.8915	361.06382	293.73333	245.28322
	Post_T	317.73217	283.75753	389.21733	292.13567	215.16067	238.16896	336.20211	317.3	410.958	461.34433	317.3	334.55544	223.23389	305.55788

Table 14. Raw Data for Muscle Fibre CFi

	Timepoint	S01	S02	S03	S04	S05	S06	S07	S09	S10	S11	S12	S13	S14	S15
Relative T1 CFi	Pre	1.86	1.19	1.09	1.24	1.21	1.22	0.77	1.46	1.27	1.44	1.25	1.45	1.34	0.96
	Mid_UT	1.12	1.44	1.41	1.25	1.32	0.95	1.16	2.22	2.42	1.86	1.87	1.68	1.88	1.93
	Mid_T	2.23	1.60	1.45	1.94	1.50	1.24	1.70	1.88	2.57	1.68	1.75	1.93	2.51	1.37
	Post_UT	1.50	1.60	1.66	1.28	1.39	1.47	1.58	1.11	1.02	1.76	1.67	1.34	1.78	1.39
	Post_T	1.63	1.79	1.23	1.06	0.82	1.14	0.91	1.30	1.36	1.36	1.45	1.17	1.06	0.88

	Timepoint	S01	S02	S03	S04	S05	S06	S07	S09	S10	S11	S12	S13	S14	S15
Relative T2 CFi	Pre	1.21	1.50	1.05	1.07	1.07	0.94	0.73	1.21	1.91	1.40	1.36	1.35	1.27	0.87
	Mid_UT	1.38	1.53	1.47	1.16	0.93	0.76	0.90	2.26	2.34	1.66	1.56	1.84	2.19	1.83
	Mid_T	2.01	1.43	1.58	1.63	1.15	1.69	1.53	1.74	2.06	1.96	1.67	1.78	1.94	1.52
	Post_UT	1.19	1.43	1.70	1.17	0.97	1.37	1.71	1.34	0.87	1.78	1.38	1.16	1.84	1.31
	Post_T	1.62	1.69	1.25	1.13	0.77	1.15	0.86	1.32	1.33	1.59	1.66	1.35	0.94	0.82

Table 15. Raw Data for Muscle Fibre Type Distribution

	Timepoint	S01	S02	S03	S04	S05	S06	S07	S09	S10	S11	S12	S13	S14	S15
Type I Proportion	Pre	40.7	50.1	38.5	56.6	24.3	27.9	27.3	25.9	42.6	21.7	44.7	35.5	51.0	52.0
	Mid_UT	38.5	45.3	27.9	36.0	28.5	44.5	30.8	24.5	37.5	16.7	41.8	38.9	57.7	53.8
	Mid_T	41.5	46.4	31.0	38.3	27.9	30.7	32.7	27.7	40.9	24.7	40.7	55.3	46.0	50.6
	Post_UT	51.2	61.6	38.4	42.6	37.3	40.8	30.4	38.2	35.1	24.5	46.6	31.5	34.8	58.6
	Post_T	50.2	58.1	46.2	50.2	28.0	35.3	35.4	27.5	38.6	29.1	41.6	31.4	44.4	47.4

	Timepoint	S01	S02	S03	S04	S05	S06	S07	S09	S10	S11	S12	S13	S14	S15
Type II Proportion	Pre	59.3	49.9	61.5	43.4	75.7	72.1	72.7	74.1	57.4	78.3	55.3	64.5	49.0	48.0
	Mid_UT	61.5	54.7	72.1	64.0	71.5	55.5	69.2	75.5	62.5	83.3	58.2	61.1	42.3	46.2
	Mid_T	58.5	53.6	69.0	61.7	72.1	69.3	67.3	72.3	59.1	75.3	59.3	44.7	54.0	49.4
	Post_UT	48.8	38.4	61.6	57.4	62.7	59.2	69.6	61.8	64.9	75.5	53.4	68.5	65.2	41.4
	Post_T	49.8	41.9	53.8	49.8	72.0	64.7	64.6	72.5	61.4	70.9	58.4	68.6	55.6	52.6

Table 16. Raw Data for Muscle Fibre CFPE

	Timepoint	S01	S02	S03	S04	S05	S06	S07	S09	S10	S11	S12	S13	S14	S15
Relative T1 CFPE	Pre	5.89	4.93	4.16	5.40	4.50	4.28	3.67	4.55	4.93	5.19	5.60	6.76	5.09	4.07
	Mid_UT	5.57	4.13	4.99	5.43	4.71	4.35	3.77	7.64	6.03	6.75	6.55	6.66	5.66	5.56
	Mid_T	6.72	5.75	5.60	8.55	5.28	5.53	6.60	6.65	9.36	6.89	6.86	7.82	7.38	8.51
	Post_UT	4.35	6.13	5.62	4.91	4.83	5.46	6.50	4.04	3.19	6.81	7.39	4.44	6.58	6.17
	Post_T	6.02	6.88	6.52	4.15	3.94	5.14	2.79	4.72	6.01	3.67	3.48	3.91	5.36	3.45

	Timepoint	S01	S02	S03	S04	S05	S06	S07	S09	S10	S11	S12	S13	S14	S15
Relative T2 CFPE	Pre	6.52	4.98	3.37	4.86	5.02	3.19	3.60	3.77	6.25	4.37	5.40	5.46	4.63	3.45
	Mid_UT	4.56	3.76	4.41	5.30	4.49	3.57	2.80	6.98	5.28	5.22	6.23	6.43	3.90	4.84
	Mid_T	5.41	3.07	5.35	7.19	4.78	4.68	5.82	4.13	7.34	5.67	6.60	6.20	6.77	5.62
	Post_UT	3.39	4.86	4.60	4.67	4.16	4.77	7.14	3.92	2.94	6.19	5.17	3.34	6.42	5.14
	Post_T	4.19	5.33	4.72	5.21	3.82	4.81	2.41	4.05	4.29	3.63	3.18	3.82	4.24	3.02

APPENDIX B: Statistical Outputs

Table 1.1 1-Way ANOVA Output for Type I Cross-Sectional Area

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	CSA Type I				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	3.167				
6	P value	0.0429				
7	P value summary	*				
8	Statistically significant (P < 0.05)?	Yes				
9	Geisser-Greenhouse's epsilon	0.6508				
10	R square	0.1959				
11						
12	**Was the matching effective?**					
13	F	3.104				
14	P value	0.0018				
15	P value summary	**				
16	Is there significant matching (P < 0.05)?	Yes				
17	R square	0.3842				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	14872489	4	3718122	F (2.603, 33.84) = 3.167	P=0.0429
21	Individual (between rows)	47372663	13	3644051	F (13, 52) = 3.104	P=0.0018
22	Residual (random)	61048434	52	1174008		
23	Total	123293586	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 1.2 Post Hoc: Holm-Sidak Comparison for Type I Cross-Sectional Area

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	3							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons te**	**Mean Diff.**	**Significan**	**Summary**	**Adjusted P Value**				
6	Post AT_{CTL} vs. Post RT_{CTL}	-91.92	No	ns	0.6551	B-D			
7	Post AT_{EX} vs. Post RT_{EX}	-997.5	No	ns	0.1052	C-E			
8	Post RT_{CTL} vs. Post RT_{EX}	-906.2	No	ns	0.2010	D-E			
9									
10	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
11	Post AT_{CTL} vs. Post RT_{CTL}	5150	5242	-91.92	201.1	14	14	0.4571	13
12	Post AT_{EX} vs. Post RT_{EX}	5150	6148	-997.5	427.6	14	14	2.333	13
13	Post RT_{CTL} vs. Post RT_{EX}	5242	6148	-906.2	522.0	14	14	1.736	13
14									

Table 2.1 1-Way ANOVA Output for Type II Cross-Sectional Area

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	CSA Type II				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	3.733				
6	P value	0.0258				
7	P value summary	*				
8	Statistically significant (P < 0.05)?	Yes				
9	Geisser-Greenhouse's epsilon	0.6347				
10	R square	0.2231				
11						
12	**Was the matching effective?**					
13	F	6.330				
14	P value	<0.0001				
15	P value summary	****				
16	Is there significant matching (P < 0.05)?	Yes				
17	R square	0.5515				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	33766603	4	8441651	F (2.539, 33.00) = 3.733	P=0.0258
21	Individual (between rows)	186072593	13	14313276	F (13, 52) = 6.330	P<0.0001
22	Residual (random)	117575591	52	2261069		
23	Total	337414788	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 2.2 Post Hoc: Holm-Sidak Comparison for Type II Cross-Sectional Area

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	3							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Post AT_{CTL} vs. Post RT_{CTL}	-780.4	No	ns	0.1062	B-D			
7	Post AT_{EX} vs. Post RT_{EX}	-2042	No	ns	0.0550	C-E			
8	Post RT_{CTL} vs. Post RT_{EX}	-735.8	No	ns	0.3179	D-E			
9									
10	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
11	Post AT_{CTL} vs. Post RT_{CTL}	5575	6356	-780.4	369.5	14	14	2.112	13
12	Post AT_{EX} vs. Post RT_{EX}	5050	7092	-2042	760.0	14	14	2.687	13
13	Post RT_{CTL} vs. Post RT_{EX}	6356	7092	-735.8	708.5	14	14	1.039	13

Table 3.1 1-Way ANOVA Output for Type I CFi

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	Type I CFi				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	8.792				
6	P value	0.0002				
7	P value summary	***				
8	Statistically significant (P < 0.05)?	Yes				
9	Geisser-Greenhouse's epsilon	0.7024				
10	R square	0.4035				
11						
12	**Was the matching effective?**					
13	F	1.868				
14	P value	0.0566				
15	P value summary	ns				
16	Is there significant matching (P < 0.05)?	No				
17	R square	0.2179				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	3.296	4	0.8241	F (2.809, 36.52) = 8.792	P=0.0002
21	Individual (between rows)	2.276	13	0.1751	F (13, 52) = 1.868	P=0.0566
22	Residual (random)	4.874	52	0.09373		
23	Total	10.45	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 3.2 Post Hoc: Holm-Sidak Comparison for Type I CFi

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	3							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Baseline vs. Post AT_{EX}	-0.5429	Yes	***	0.0002	A-C			
7	Baseline vs. Post AT_{CTL}	-0.3400	Yes	*	0.0423	A-B			
8	Post AT_{CTL} vs. Post AT_{EX}	-0.2029	No	ns	0.1087	B-C			
9									
10	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
11	Baseline vs. Post AT_{EX}	1.268	1.811	-0.5429	0.09635	14	14	5.634	13
12	Baseline vs. Post AT_{CTL}	1.268	1.608	-0.3400	0.1300	14	14	2.615	13
13	Post AT_{CTL} vs. Post AT_{EX}	1.608	1.811	-0.2029	0.1178	14	14	1.722	13

Table 4.1 1-Way ANOVA Output for Type II CFi

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	Type II CFi				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	6.675				
6	P value	0.0020				
7	P value summary	**				
8	Statistically significant (P < 0.05)?	Yes				
9	Geisser-Greenhouse's epsilon	0.6301				
10	R square	0.3393				
11						
12	**Was the matching effective?**					
13	F	2.745				
14	P value	0.0049				
15	P value summary	**				
16	Is there significant matching (P < 0.05)?	Yes				
17	R square	0.3120				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	2.362	4	0.5905	F (2.520, 32.76) = 6.675	P=0.0020
21	Individual (between rows)	3.157	13	0.2428	F (13, 52) = 2.745	P=0.0049
22	Residual (random)	4.600	52	0.08846		
23	Total	10.12	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 4.2 Post Hoc: Holm-Sidak Comparison for Type II CFi

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	3							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons te**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Baseline vs. Post AT_{EX}	-0.4821	Yes	****	<0.0001	A-C			
7	Baseline vs. Post AT_{CTL}	-0.3479	Yes	*	0.0111	A-B			
8	Post AT_{CTL} vs. Post AT_{EX}	-0.1343	No	ns	0.2547	B-C			
9									
10	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
11	Baseline vs. Post AT_{EX}	1.210	1.692	-0.4821	0.07275	14	14	6.627	13
12	Baseline vs. Post AT_{CTL}	1.210	1.558	-0.3479	0.1049	14	14	3.315	13
13	Post AT_{CTL} vs. Post AT_{EX}	1.558	1.692	-0.1343	0.1127	14	14	1.192	13

Table 5.1 1-Way ANOVA Output for Type I CFPE

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	Type I CFPE				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	7.870				
6	P value	0.0003				
7	P value summary	***				
8	Statistically significant (P < 0.05)?	Yes				
9	Geisser-Greenhouse's epsilon	0.7565				
10	R square	0.3771				
11						
12	**Was the matching effective?**					
13	F	0.7761				
14	P value	0.6808				
15	P value summary	ns				
16	Is there significant matching (P < 0.05)?	No				
17	R square	0.1078				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	43.17	4	10.79	F (3.026, 39.34) = 7.870	P=0.0003
21	Individual (between rows)	13.84	13	1.064	F (13, 52) = 0.7761	P=0.6808
22	Residual (random)	71.31	52	1.371		
23	Total	128.3	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 5.2 Post Hoc: Holm-Sidak Comparison for Type I CFPE

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	3							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Baseline vs. Post AT_{CTL}	-0.6271	Yes	*	0.0333	A-B			
7	Baseline vs. Post AT_{EX}	-2.034	Yes	***	0.0001	A-C			
8	Post AT_{CTL} vs. Post AT_{EX}	-1.407	Yes	**	0.0024	B-C			
9									
10	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
11	Baseline vs. Post AT_{CTL}	4.930	5.557	-0.6271	0.2635	14	14	2.380	13
12	Baseline vs. Post AT_{EX}	4.930	6.964	-2.034	0.3378	14	14	6.022	13
13	Post AT_{CTL} vs. Post AT_{EX}	5.557	6.964	-1.407	0.3417	14	14	4.118	13

Table 6.1 1-Way ANOVA Output for Type II CFPE

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	Type II CFPE				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	3.371				
6	P value	0.0274				
7	P value summary	*				
8	Statistically significant (P < 0.05)?	Yes				
9	Geisser-Greenhouse's epsilon	0.7585				
10	R square	0.2059				
11						
12	**Was the matching effective?**					
13	F	0.6638				
14	P value	0.7880				
15	P value summary	ns				
16	Is there significant matching (P < 0.05)?	No				
17	R square	0.1164				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	17.58	4	4.395	F (3.034, 39.44) = 3.371	P=0.0274
21	Individual (between rows)	11.25	13	0.8654	F (13, 52) = 0.6638	P=0.7880
22	Residual (random)	67.80	52	1.304		
23	Total	96.63	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 6.2 Post Hoc: Holm-Sidak Comparison for Type II CFPE

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	3							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Baseline vs. Post AT_{CTL}	-0.2071	No	ns	0.5712	A-B			
7	Baseline vs. Post AT_{EX}	-0.9829	Yes	*	0.0432	A-C			
8	Post AT_{CTL} vs. Post AT_{EX}	-0.7757	No	ns	0.1446	B-C			
9									
10	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
11	Baseline vs. Post AT_{CTL}	4.634	4.841	-0.2071	0.3565	14	14	0.5810	13
12	Baseline vs. Post AT_{EX}	4.634	5.616	-0.9829	0.3492	14	14	2.814	13
13	Post AT_{CTL} vs. Post AT_{EX}	4.841	5.616	-0.7757	0.4010	14	14	1.934	13

Table 7.1 1-Way ANOVA Output for Type I Satellite Cell Content

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	Type I SC Content				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	3.581				
6	P value	0.0377				
7	P value summary	*				
8	Statistically significant (P < 0.05)?	Yes				
9	Geisser-Greenhouse's epsilon	0.5439				
10	R square	0.2160				
11						
12	**Was the matching effective?**					
13	F	1.271				
14	P value	0.2601				
15	P value summary	ns				
16	Is there significant matching (P < 0.05)?	No				
17	R square	0.1995				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	197.5	4	49.38	F (2.176, 28.28) = 3.581	P=0.0377
21	Individual (between rows)	227.9	13	17.53	F (13, 52) = 1.271	P=0.2601
22	Residual (random)	717.0	52	13.79		
23	Total	1142	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 7.2 Post Hoc: Holm-Sidak Comparison for Type I Satellite Cell Content

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	5							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Baseline vs. Post RT_{CTL}	-0.2429	No	ns	0.8667	A-C			
7	Post AT_{CTL} vs. Post RT_{CTL}	-0.7793	No	ns	0.2494	B-C			
8	Post AT_{CTL} vs. Post AT_{EX}	-1.244	No	ns	0.2345	B-D			
9	Post RT_{CTL} vs. Post RT_{EX}	-3.939	No	ns	0.2021	C-E			
10	Post AT_{EX} vs. Post RT_{EX}	-3.474	No	ns	0.2345	D-E			
11									
12	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
13	Baseline vs. Post RT_{CTL}	5.501	5.744	-0.2429	1.419	14	14	0.1712	13
14	Post AT_{CTL} vs. Post RT_{CTL}	4.965	5.744	-0.7793	0.4871	14	14	1.600	13
15	Post AT_{CTL} vs. Post AT_{EX}	4.965	6.209	-1.244	0.6553	14	14	1.899	13
16	Post RT_{CTL} vs. Post RT_{EX}	5.744	9.683	-3.939	1.768	14	14	2.228	13
17	Post AT_{EX} vs. Post RT_{EX}	6.209	9.683	-3.474	1.721	14	14	2.019	13

Table 8.1 1-Way ANOVA Output for Type II Satellite Cell Content

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	Type II SC Content				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	5.602				
6	P value	0.0158				
7	P value summary	*				
8	Statistically significant (P < 0.05)?	Yes				
9	Geisser-Greenhouse's epsilon	0.3999				
10	R square	0.3011				
11						
12	**Was the matching effective?**					
13	F	0.9332				
14	P value	0.5266				
15	P value summary	ns				
16	Is there significant matching (P < 0.05)?	No				
17	R square	0.1402				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	227.8	4	56.96	F (1.599, 20.79) = 5.602	P=0.0158
21	Individual (between rows)	123.4	13	9.489	F (13, 52) = 0.9332	P=0.5266
22	Residual (random)	528.7	52	10.17		
23	Total	879.9	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 8.2 Post Hoc: Holm-Sidak Comparison for Type II Satellite Cell Content

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	5							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Baseline vs. Post RT_{CTL}	-2.306	No	ns	0.0552	A-C			
7	Post AT_{CTL} vs. Post RT_{CTL}	-2.706	Yes	**	0.0047	B-C			
8	Post AT_{CTL} vs. Post AT_{EX}	-0.08714	No	ns	0.8547	B-D			
9	Post RT_{CTL} vs. Post RT_{EX}	-1.856	No	ns	0.4754	C-E			
10	Post AT_{EX} vs. Post RT_{EX}	-4.475	No	ns	0.0561	D-E			
11									
12	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
13	Baseline vs. Post RT_{CTL}	4.432	6.738	-2.306	0.8138	14	14	2.833	13
14	Post AT_{CTL} vs. Post RT_{CTL}	4.031	6.738	-2.706	0.6368	14	14	4.250	13
15	Post AT_{CTL} vs. Post AT_{EX}	4.031	4.119	-0.08714	0.4664	14	14	0.1868	13
16	Post RT_{CTL} vs. Post RT_{EX}	6.738	8.594	-1.856	1.631	14	14	1.138	13
17	Post AT_{EX} vs. Post RT_{EX}	4.119	8.594	-4.475	1.672	14	14	2.676	13

Table 9.1 2-Way ANOVA Output for V_{O_2} Work Peak (Watts)

2way ANOVA ANOVA results						
1	Table Analyzed	VO2 Watt Peak Pre-Post				
2						
3	**Two-way RM ANOVA**	Matching: Both factors				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Source of Variation**	**% of total variation**	**P value**	**P value summary**	**Significant?**	**Geisser-Greenhouse's epsilon**
8	Time	1.884	0.0081	**	Yes	0.7638
9	Training Status	2.339	0.0005	***	Yes	1.000
10	Time x Training Status	0.7587	0.0004	***	Yes	0.7046
11	Subject x Time	3.483				
12	Subject x Training Status	1.458				
13	Subject	89.43				
14						
15	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
16	Time	2025	2	1012	F (1.528, 19.86	P=0.0081
17	Training Status	2514	1	2514	F (1.000, 13.00	P=0.0005
18	Time x Training Status	815.2	2	407.6	F (1.409, 18.32	P=0.0004
19	Subject x Time	3742	26	143.9		
20	Subject x Training Status	1566	13	120.5		
21	Subject	96085	13	7391		
22	Residual	697.3	26	26.82		
23						
24	**Difference between column means**					
25	Mean of Control	147.8				
26	Mean of Aero Pre -Trained	158.7				
27	Difference between means	-10.94				
28	SE of difference	2.395				
29	95% CI of difference	-16.12 to -5.766				
30						
31	**Data summary**					
32	Number of columns (Training Status)	2				
33	Number of rows (Time)	3				
34	Number of subjects (Subject)	14				
35	Number of missing values	0				

Table 9.2 Post-Hoc: Holm-Sidak Comparison for Work Peak (Watts)

2way ANOVA Multiple comparisons									
1	Compare cell means regardless of rows and columns								
2									
3	Number of families	1							
4	Number of comparisons per family	15							
5	Alpha	0.05							
6									
7	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
8									
9	Baseline :Control vs. Baseline :Aero Pre -Trained	-3.421	No	ns	0.6810				
10	Baseline :Control vs. Post AT:Control	-3.571	No	ns	0.6711				
11	Baseline :Control vs. Post AT:Aero Pre -Trained	-22.25	Yes	**	0.0040				
12	Baseline :Control vs. Post RT :Control	-5.743	No	ns	0.6677				
13	Baseline :Control vs. Post RT :Aero Pre -Trained	-16.46	Yes	*	0.0453				
14	Baseline :Aero Pre -Trained vs. Post AT:Control	-0.1500	No	ns	0.9601				
15	Baseline :Aero Pre -Trained vs. Post AT:Aero Pre -Trained	-18.83	Yes	**	0.0046				
16	Baseline :Aero Pre -Trained vs. Post RT :Control	-2.321	No	ns	0.8359				
17	Baseline :Aero Pre -Trained vs. Post RT :Aero Pre -Trained	-13.04	No	ns	0.1020				
18	Post AT:Control vs. Post AT:Aero Pre -Trained	-18.68	Yes	***	0.0008				
19	Post AT:Control vs. Post RT :Control	-2.171	No	ns	0.8344				
20	Post AT:Control vs. Post RT :Aero Pre -Trained	-12.89	Yes	*	0.0229				
21	Post AT:Aero Pre -Trained vs. Post RT :Control	16.51	Yes	*	0.0158				
22	Post AT:Aero Pre -Trained vs. Post RT :Aero Pre -Trained	5.786	No	ns	0.2714				
23	Post RT :Control vs. Post RT :Aero Pre -Trained	-10.72	Yes	*	0.0145				
24									
25									
26	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**N1**	**N2**	**t**	**DF**
27									
28	Baseline :Control vs. Baseline :Aero Pre -Trained	144.7	148.1	-3.421	2.832	14	14	1.208	13.00
29	Baseline :Control vs. Post AT:Control	144.7	148.3	-3.571	2.641	14	14	1.352	13.00
30	Baseline :Control vs. Post AT:Aero Pre -Trained	144.7	166.9	-22.25	4.538	14	14	4.903	13.00
31	Baseline :Control vs. Post RT :Control	144.7	150.4	-5.743	3.930	14	14	1.461	13.00
32	Baseline :Control vs. Post RT :Aero Pre -Trained	144.7	161.1	-16.46	4.903	14	14	3.358	13.00
33	Baseline :Aero Pre -Trained vs. Post AT:Control	148.1	148.3	-0.1500	2.944	14	14	0.05095	13.00
34	Baseline :Aero Pre -Trained vs. Post AT:Aero Pre -Trained	148.1	166.9	-18.83	3.928	14	14	4.793	13.00
35	Baseline :Aero Pre -Trained vs. Post RT :Control	148.1	150.4	-2.321	4.258	14	14	0.5452	13.00
36	Baseline :Aero Pre -Trained vs. Post RT :Aero Pre -Trained	148.1	161.1	-13.04	4.558	14	14	2.861	13.00
37	Post AT:Control vs. Post AT:Aero Pre -Trained	148.3	166.9	-18.68	3.174	14	14	5.886	13.00
38	Post AT:Control vs. Post RT :Control	148.3	150.4	-2.171	2.793	14	14	0.7775	13.00
39	Post AT:Control vs. Post RT :Aero Pre -Trained	148.3	161.1	-12.89	3.416	14	14	3.774	13.00
40	Post AT:Aero Pre -Trained vs. Post RT :Control	166.9	150.4	16.51	4.104	14	14	4.023	13.00
41	Post AT:Aero Pre -Trained vs. Post RT :Aero Pre -Trained	166.9	161.1	5.786	2.598	14	14	2.227	13.00
42	Post RT :Control vs. Post RT :Aero Pre -Trained	150.4	161.1	-10.72	2.605	14	14	4.116	13.00

Table 10.1 2-Way ANOVA Output for $\dot{V}O_2$ Relative ($ml \cdot min^{-1} \cdot kgFFM_{Limb}^{-1}$)

2way ANOVA ANOVA results						
1	Table Analyzed	VO2 Relative (LBM) Pre-Post				
2						
3	**Two-way RM ANOVA**	Matching: Both factors				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Source of Variation**	**% of total variation**	**P value**	**P value summary**	**Significant?**	**Geisser-Greenhouse's epsilon**
8	Time	4.452	0.0199	*	Yes	0.8763
9	Training Status	1.135	0.0070	**	Yes	1.000
10	Time x Training Status	1.376	0.0072	**	Yes	0.7256
11	Subject x Time	11.73				
12	Subject x Training Status	1.442				
13	Subject	77.49				
14						
15	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
16	Time	7453	2	3726	F (1.753, 22.78) = 4.935	P=0.0199
17	Training Status	1900	1	1900	F (1.000, 13.00) = 10.23	P=0.0070
18	Time x Training Status	2303	2	1151	F (1.451, 18.86) = 7.532	P=0.0072
19	Subject x Time	19634	26	755.1		
20	Subject x Training Status	2414	13	185.7		
21	Subject	129719	13	9978		
22	Residual	3975	26	152.9		
23						
24	**Difference between column means**					
25	Mean of Control	257.8				
26	Mean of Aero Pre -Trained	267.3				
27	Difference between means	-9.513				
28	SE of difference	2.974				
29	95% CI of difference	-15.94 to -3.088				
30						
31	**Data summary**					
32	Number of columns (Training Status)	2				
33	Number of rows (Time)	3				
34	Number of subjects (Subject)	14				
35	Number of missing values	0				

Table 10.2 Post-Hoc: Holm-Sidak Comparison for $\dot{V}O_2$ relative ($ml \cdot min^{-1} \cdot kgFFM_{Limb}^{-1}$)

2way ANOVA Multiple comparisons									
1	Compare cell means regardless of rows and columns								
2									
3	Number of families	1							
4	Number of comparisons per family	15							
5	Alpha	0.05							
6									
7	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
8									
9	Baseline :Control vs. Baseline :Aero Pre -Trained	4.883	No	ns	0.9235				
10	Baseline :Control vs. Post AT:Control	-4.281	No	ns	0.9552				
11	Baseline :Control vs. Post AT:Aero Pre -Trained	-24.00	No	ns	0.1739				
12	Baseline :Control vs. Post RT :Control	14.89	No	ns	0.6817				
13	Baseline :Control vs. Post RT :Aero Pre -Trained	1.193	No	ns	0.9552				
14	Baseline :Aero Pre -Trained vs. Post AT:Control	-9.164	No	ns	0.8623				
15	Baseline :Aero Pre -Trained vs. Post AT:Aero Pre -Trained	-28.89	Yes	*	0.0446				
16	Baseline :Aero Pre -Trained vs. Post RT :Control	10.01	No	ns	0.8623				
17	Baseline :Aero Pre -Trained vs. Post RT :Aero Pre -Trained	-3.690	No	ns	0.9552				
18	Post AT:Control vs. Post AT:Aero Pre -Trained	-19.72	Yes	*	0.0231				
19	Post AT:Control vs. Post RT :Control	19.17	No	ns	0.0690				
20	Post AT:Control vs. Post RT :Aero Pre -Trained	5.474	No	ns	0.9258				
21	Post AT:Aero Pre -Trained vs. Post RT :Control	38.90	Yes	***	0.0006				
22	Post AT:Aero Pre -Trained vs. Post RT :Aero Pre -Trained	25.20	Yes	*	0.0231				
23	Post RT :Control vs. Post RT :Aero Pre -Trained	-13.70	Yes	*	0.0299				
24									
25									
26	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**N1**	**N2**	**t**	**DF**
27									
28	Baseline :Control vs. Baseline :Aero Pre -Trained	261.4	256.5	4.883	5.635	14	14	0.8666	13.00
29	Baseline :Control vs. Post AT:Control	261.4	265.6	-4.281	9.070	14	14	0.4720	13.00
30	Baseline :Control vs. Post AT:Aero Pre -Trained	261.4	285.4	-24.00	9.145	14	14	2.625	13.00
31	Baseline :Control vs. Post RT :Control	261.4	246.5	14.89	9.301	14	14	1.601	13.00
32	Baseline :Control vs. Post RT :Aero Pre -Trained	261.4	260.2	1.193	9.296	14	14	0.1283	13.00
33	Baseline :Aero Pre -Trained vs. Post AT:Control	256.5	265.6	-9.164	7.906	14	14	1.159	13.00
34	Baseline :Aero Pre -Trained vs. Post AT:Aero Pre -Trained	256.5	285.4	-28.89	8.323	14	14	3.471	13.00
35	Baseline :Aero Pre -Trained vs. Post RT :Control	256.5	246.5	10.01	8.251	14	14	1.213	13.00
36	Baseline :Aero Pre -Trained vs. Post RT :Aero Pre -Trained	256.5	260.2	-3.690	8.610	14	14	0.4286	13.00
37	Post AT:Control vs. Post AT:Aero Pre -Trained	265.6	285.4	-19.72	4.996	14	14	3.947	13.00
38	Post AT:Control vs. Post RT :Control	265.6	246.5	19.17	6.014	14	14	3.188	13.00
39	Post AT:Control vs. Post RT :Aero Pre -Trained	265.6	260.2	5.474	7.492	14	14	0.7306	13.00
40	Post AT:Aero Pre -Trained vs. Post RT :Control	285.4	246.5	38.90	6.463	14	14	6.018	13.00
41	Post AT:Aero Pre -Trained vs. Post RT :Aero Pre -Trained	285.4	260.2	25.20	6.389	14	14	3.943	13.00
42	Post RT :Control vs. Post RT :Aero Pre -Trained	246.5	260.2	-13.70	3.673	14	14	3.730	13.00

Table 11.1 2-Way ANOVA Output for V_{O_2} Absolute ($ml \cdot min^{-1}$)

2way ANOVA ANOVA results						
1	Table Analyzed	VO2 Absolute Pre-Po				
2						
3	**Two-way RM ANOVA**	Matching: Both factors				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Source of Variation**	**% of total variation**	**P value**	**P value summary**	**Significant?**	**Geisser-Greenhouse's epsilon**
8	Time	1.066	0.0605	ns	No	0.7712
9	Training Status	0.5867	0.0086	**	Yes	1.000
10	Time x Training Status	0.5633	0.0094	**	Yes	0.6352
11	Subject x Time	3.971				
12	Subject x Training Status	0.7983				
13	Subject	92.06				
14						
15	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
16	Time	417508	2	208754	F (1.542, 20.05) = 3.490	P=0.0605
17	Training Status	229808	1	229808	F (1.000, 13.00) = 9.553	P=0.0086
18	Time x Training Status	220641	2	110320	F (1.270, 16.52) = 7.692	P=0.0094
19	Subject x Time	1555405	26	59823		
20	Subject x Training Status	312720	13	24055		
21	Subject	36063807	13	2774139		
22	Residual	372901	26	14342		
23						
24	**Difference between column means**					
25	Mean of Control	2397				
26	Mean of Aero Pre -Trained	2501				
27	Difference between means	-104.6				
28	SE of difference	33.85				
29	95% CI of difference	-177.7 to -31.49				
30						
31	**Data summary**					
32	Number of columns (Training Status)	2				
33	Number of rows (Time)	3				
34	Number of subjects (Subject)	14				
35	Number of missing values	0				

Table 11.2 Post-Hoc: Holm-Sidak Comparison for V_{O_2} Absolute ($ml \cdot min^{-1}$)

2way ANOVA Multiple comparisons									
1	Compare cell means regardless of rows and columns								
2									
3	Number of families	1							
4	Number of comparisons per family	15							
5	Alpha	0.05							
6									
7	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
8									
9	Baseline :Control vs. Baseline :Aero Pre -Trained	39.86	No	ns	0.9427				
10	Baseline :Control vs. Post AT:Control	-45.46	No	ns	0.9570				
11	Baseline :Control vs. Post AT:Aero Pre -Trained	-232.6	No	ns	0.1290				
12	Baseline :Control vs. Post RT :Control	-34.71	No	ns	0.9570				
13	Baseline :Control vs. Post RT :Aero Pre -Trained	-201.2	No	ns	0.3693				
14	Baseline :Aero Pre -Trained vs. Post AT:Control	-85.31	No	ns	0.8323				
15	Baseline :Aero Pre -Trained vs. Post AT:Aero Pre -Trained	-272.5	No	ns	0.0555				
16	Baseline :Aero Pre -Trained vs. Post RT :Control	-74.57	No	ns	0.9109				
17	Baseline :Aero Pre -Trained vs. Post RT :Aero Pre -Trained	-241.1	No	ns	0.1422				
18	Post AT:Control vs. Post AT:Aero Pre -Trained	-187.2	No	ns	0.0613				
19	Post AT:Control vs. Post RT :Control	10.74	No	ns	0.9570				
20	Post AT:Control vs. Post RT :Aero Pre -Trained	-155.8	No	ns	0.2170				
21	Post AT:Aero Pre -Trained vs. Post RT :Control	197.9	No	ns	0.1594				
22	Post AT:Aero Pre -Trained vs. Post RT :Aero Pre -Trained	31.43	No	ns	0.9570				
23	Post RT :Control vs. Post RT :Aero Pre -Trained	-166.5	Yes	*	0.0395				
24									
25									
26	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**N1**	**N2**	**t**	**DF**
27									
28	Baseline :Control vs. Baseline :Aero Pre -Trained	2370	2330	39.86	49.53	14	14	0.8046	13.00
29	Baseline :Control vs. Post AT:Control	2370	2416	-45.46	73.05	14	14	0.6223	13.00
30	Baseline :Control vs. Post AT:Aero Pre -Trained	2370	2603	-232.6	79.07	14	14	2.942	13.00
31	Baseline :Control vs. Post RT :Control	2370	2405	-34.71	89.28	14	14	0.3888	13.00
32	Baseline :Control vs. Post RT :Aero Pre -Trained	2370	2571	-201.2	95.89	14	14	2.098	13.00
33	Baseline :Aero Pre -Trained vs. Post AT:Control	2330	2416	-85.31	66.99	14	14	1.274	13.00
34	Baseline :Aero Pre -Trained vs. Post AT:Aero Pre -Trained	2330	2603	-272.5	78.32	14	14	3.479	13.00
35	Baseline :Aero Pre -Trained vs. Post RT :Control	2330	2405	-74.57	73.95	14	14	1.008	13.00
36	Baseline :Aero Pre -Trained vs. Post RT :Aero Pre -Trained	2330	2571	-241.1	84.80	14	14	2.843	13.00
37	Post AT:Control vs. Post AT:Aero Pre -Trained	2416	2603	-187.2	55.25	14	14	3.388	13.00
38	Post AT:Control vs. Post RT :Control	2416	2405	10.74	46.68	14	14	0.2301	13.00
39	Post AT:Control vs. Post RT :Aero Pre -Trained	2416	2571	-155.8	62.42	14	14	2.495	13.00
40	Post AT:Aero Pre -Trained vs. Post RT :Control	2603	2405	197.9	72.53	14	14	2.729	13.00
41	Post AT:Aero Pre -Trained vs. Post RT :Aero Pre -Trained	2603	2571	31.43	54.55	14	14	0.5762	13.00
42	Post RT :Control vs. Post RT :Aero Pre -Trained	2405	2571	-166.5	45.04	14	14	3.697	13.00

Table 12.1 2-Way ANOVA Output for Limb Fat Free Mass

2way ANOVA
ANOVA results

1	Table Analyzed	LLBM				
2						
3	**Two-way RM ANOVA**	Matching: Both factors				
4	Assume sphericity?	Yes				
5	Alpha	0.05				
6						
7	**Source of Variation**	**% of total variation**	**P value**	**P value summary**	**Significant?**	
8	Time	2.032	<0.0001	****	Yes	
9	Training Status	0.01060	0.3350	ns	No	
10	Time x Training Status	0.01521	0.2629	ns	No	
11	Subject x Time	1.102				
12	Subject x Training Status	0.1375				
13	Subject	96.56				
14						
15	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
16	Time	10439298	2	5219649	F (2, 26) = 23.98	P<0.0001
17	Training Status	54468	1	54468	F (1, 13) = 1.002	P=0.3350
18	Time x Training Status	78125	2	39063	F (2, 26) = 1.407	P=0.2629
19	Subject x Time	5658696	26	217642		
20	Subject x Training Status	706348	13	54334		
21	Subject	495999573	13	38153813		
22	Residual	721914	26	27766		
23						
24	**Difference between column means**					
25	Mean of Control	9378				
26	Mean of Aero Pre -Trained	9429				
27	Difference between means	-50.93				
28	SE of difference	50.87				
29	95% CI of difference	-160.8 to 58.96				
30						
31	**Data summary**					
32	Number of columns (Training Status)	2				
33	Number of rows (Time)	3				
34	Number of subjects (Subject)	14				
35	Number of missing values	0				

Table 12.2 Post-Hoc: Holm-Sidak Comparison for Limb Fat Free Mass

2way ANOVA
Multiple comparisons

1	Compare cell means regardless of rows and columns								
2									
3	Number of families	1							
4	Number of comparisons per family	15							
5	Alpha	0.05							
6									
7	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
8									
9	Baseline :Control vs. Baseline :Aero Pre -Trained	5.500	No	ns	0.9822				
10	Baseline :Control vs. Post AT:Control	-24.79	No	ns	0.9822				
11	Baseline :Control vs. Post AT:Aero Pre -Trained	-47.43	No	ns	0.9571				
12	Baseline :Control vs. Post RT :Control	-695.9	Yes	****	<0.0001				
13	Baseline :Control vs. Post RT :Aero Pre -Trained	-831.6	Yes	****	<0.0001				
14	Baseline :Aero Pre -Trained vs. Post AT:Control	-30.29	No	ns	0.9822				
15	Baseline :Aero Pre -Trained vs. Post AT:Aero Pre -Trained	-52.93	No	ns	0.9571				
16	Baseline :Aero Pre -Trained vs. Post RT :Control	-701.4	Yes	****	<0.0001				
17	Baseline :Aero Pre -Trained vs. Post RT :Aero Pre -Trained	-837.1	Yes	****	<0.0001				
18	Post AT:Control vs. Post AT:Aero Pre -Trained	-22.64	No	ns	0.9822				
19	Post AT:Control vs. Post RT :Control	-671.1	Yes	****	<0.0001				
20	Post AT:Control vs. Post RT :Aero Pre -Trained	-806.8	Yes	****	<0.0001				
21	Post AT:Aero Pre -Trained vs. Post RT :Control	-648.5	Yes	****	<0.0001				
22	Post AT:Aero Pre -Trained vs. Post RT :Aero Pre -Trained	-784.1	Yes	****	<0.0001				
23	Post RT :Control vs. Post RT :Aero Pre -Trained	-135.6	No	ns	0.2524				
24									
25									
26	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**N1**	**N2**	**t**	**DF**
27									
28	Baseline :Control vs. Baseline :Aero Pre -Trained	9138	9132	5.500	62.98	14	14	0.08733	26.00
29	Baseline :Control vs. Post AT:Control	9138	9162	-24.79	62.98	14	14	0.3935	26.00
30	Baseline :Control vs. Post AT:Aero Pre -Trained	9138	9185	-47.43	62.98	14	14	0.7531	26.00
31	Baseline :Control vs. Post RT :Control	9138	9834	-695.9	62.98	14	14	11.05	26.00
32	Baseline :Control vs. Post RT :Aero Pre -Trained	9138	9969	-831.6	62.98	14	14	13.20	26.00
33	Baseline :Aero Pre -Trained vs. Post AT:Control	9132	9162	-30.29	62.98	14	14	0.4809	26.00
34	Baseline :Aero Pre -Trained vs. Post AT:Aero Pre -Trained	9132	9185	-52.93	62.98	14	14	0.8404	26.00
35	Baseline :Aero Pre -Trained vs. Post RT :Control	9132	9834	-701.4	62.98	14	14	11.14	26.00
36	Baseline :Aero Pre -Trained vs. Post RT :Aero Pre -Trained	9132	9969	-837.1	62.98	14	14	13.29	26.00
37	Post AT:Control vs. Post AT:Aero Pre -Trained	9162	9185	-22.64	62.98	14	14	0.3595	26.00
38	Post AT:Control vs. Post RT :Control	9162	9834	-671.1	62.98	14	14	10.66	26.00
39	Post AT:Control vs. Post RT :Aero Pre -Trained	9162	9969	-806.8	62.98	14	14	12.81	26.00
40	Post AT:Aero Pre -Trained vs. Post RT :Control	9185	9834	-648.5	62.98	14	14	10.30	26.00
41	Post AT:Aero Pre -Trained vs. Post RT :Aero Pre -Trained	9185	9969	-784.1	62.98	14	14	12.45	26.00
42	Post RT :Control vs. Post RT :Aero Pre -Trained	9834	9969	-135.6	62.98	14	14	2.154	26.00

Table 14. Wilcoxon Students T-Test: 1 Repetition Max for Squat

1	Table Analyzed	Strength - Squat
2		
3	Column B	Post RT
4	vs.	vs.
5	Column A	Post AT
6		
7	**Wilcoxon matched-pairs signed rank test**	
8	P value	<0.0001
9	Exact or approximate P value?	Exact
10	P value summary	****
11	Significantly different (P < 0.05)?	Yes
12	One- or two-tailed P value?	One-tailed
13	Sum of positive, negative ranks	105.0 , 0.000
14	Sum of signed ranks (W)	105.0
15	Number of pairs	14
16	Number of ties (ignored)	0
17		
18	**Median of differences**	
19	Median	50.00
20		
21	**How effective was the pairing?**	
22	rs (Spearman)	0.8273
23	P value (one tailed)	0.0002
24	P value summary	***
25	Was the pairing significantly effective?	Yes

Table 15. Wilcoxon Students T-Test: 1 Repetition Max for Leg Press

1	Table Analyzed	Strength - Press
2		
3	Column B	Post RT
4	vs.	vs.
5	Column A	Post AT
6		
7	**Wilcoxon matched-pairs signed rank test**	
8	P value	0.0001
9	Exact or approximate P value?	Exact
10	P value summary	***
11	Significantly different (P < 0.05)?	Yes
12	One- or two-tailed P value?	One-tailed
13	Sum of positive, negative ranks	91.00 , 0.000
14	Sum of signed ranks (W)	91.00
15	Number of pairs	14
16	Number of ties (ignored)	1
17		
18	**Median of differences**	
19	Median	115.0
20		
21	**How effective was the pairing?**	
22	rs (Spearman)	0.9184
23	P value (one tailed)	<0.0001
24	P value summary	****
25	Was the pairing significantly effective?	Yes

Table 16.1 1-Way ANOVA Output for Type I Fibre Perimeter

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	Type I Perimeter				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	1.315				
6	P value	0.2848				
7	P value summary	ns				
8	Statistically significant (P < 0.05)?	No				
9	Geisser-Greenhouse's epsilon	0.6777				
10	R square	0.09184				
11						
12	**Was the matching effective?**					
13	F	2.725				
14	P value	0.0052				
15	P value summary	**				
16	Is there significant matching (P < 0.05)?	Yes				
17	R square	0.3822				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	6484	4	1621	F (2.711, 35.24) = 1.315	P=0.2848
21	Individual (between rows)	43677	13	3360	F (13, 52) = 2.725	P=0.0052
22	Residual (random)	64124	52	1233		
23	Total	114285	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 16.2 Post-Hoc: Holm-Sidak Comparison for Type I Fibre Perimeter

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	5							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Baseline vs. Post RT_{CTL}	-8.535	No	ns	0.6289	A-C			
7	Post AT_{CTL} vs. Post RT_{CTL}	6.658	No	ns	0.6289	B-C			
8	Post AT_{CTL} vs. Post AT_{EX}	12.28	No	ns	0.5785	B-D			
9	Post RT_{CTL} vs. Post RT_{EX}	-18.39	No	ns	0.5785	C-E			
10	Post AT_{EX} vs. Post RT_{EX}	-24.01	No	ns	0.5298	D-E			
11									
12	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
13	Baseline vs. Post RT_{CTL}	265.4	273.9	-8.535	9.615	14	14	0.8877	13
14	Post AT_{CTL} vs. Post RT_{CTL}	280.6	273.9	6.658	13.16	14	14	0.5058	13
15	Post AT_{CTL} vs. Post AT_{EX}	280.6	268.3	12.28	8.971	14	14	1.369	13
16	Post RT_{CTL} vs. Post RT_{EX}	273.9	292.3	-18.39	14.22	14	14	1.293	13
17	Post AT_{EX} vs. Post RT_{EX}	268.3	292.3	-24.01	15.28	14	14	1.571	13

Table 17.1 1-Way ANOVA Output for Type II Fibre Perimeter

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	Type II Perimet				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	4.099				
6	P value	0.0117				
7	P value summary	*				
8	Statistically significant (P < 0.05)?	Yes				
9	Geisser-Greenhouse's epsilon	0.7757				
10	R square	0.2397				
11						
12	**Was the matching effective?**					
13	F	6.453				
14	P value	<0.0001				
15	P value summary	****				
16	Is there significant matching (P < 0.05)?	Yes				
17	R square	0.5509				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	21589	4	5397	F (3.103, 40.34) = 4.099	P=0.0117
21	Individual (between rows)	110466	13	8497	F (13, 52) = 6.453	P<0.0001
22	Residual (random)	68469	52	1317		
23	Total	200523	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 17.2 Post-Hoc: Holm-Sidak Comparison for Type II Fibre Perimeter

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	5							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Baseline vs. Post RT_{CTL}	-12.58	No	ns	0.5941	A-C			
7	Post AT_{CTL} vs. Post RT_{CTL}	-10.90	No	ns	0.5941	B-C			
8	Post AT_{CTL} vs. Post AT_{EX}	22.87	No	ns	0.0827	B-D			
9	Post RT_{CTL} vs. Post RT_{EX}	-20.04	No	ns	0.5941	C-E			
10	Post AT_{EX} vs. Post RT_{EX}	-53.81	Yes	*	0.0124	D-E			
11									
12	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
13	Baseline vs. Post RT_{CTL}	284.7	297.3	-12.58	11.59	14	14	1.085	13
14	Post AT_{CTL} vs. Post RT_{CTL}	286.4	297.3	-10.90	12.59	14	14	0.8653	13
15	Post AT_{CTL} vs. Post AT_{EX}	286.4	263.5	22.87	8.742	14	14	2.616	13
16	Post RT_{CTL} vs. Post RT_{EX}	297.3	317.3	-20.04	17.00	14	14	1.179	13
17	Post AT_{EX} vs. Post RT_{EX}	263.5	317.3	-53.81	14.40	14	14	3.736	13

Table 18.1 1-Way ANOVA Output for Type I Fibre Proportion

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	Type I Proporti				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	0.7706				
6	P value	0.5156				
7	P value summary	ns				
8	Statistically significant (P < 0.05)?	No				
9	Geisser-Greenhouse's epsilon	0.7373				
10	R square	0.05596				
11						
12	**Was the matching effective?**					
13	F	9.968				
14	P value	<0.0001				
15	P value summary	****				
16	Is there significant matching (P < 0.05)?	Yes				
17	R square	0.7017				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	121.4	4	30.35	F (2.949, 38.34) = 0.7706	P=0.5156
21	Individual (between rows)	5104	13	392.6	F (13, 52) = 9.968	P<0.0001
22	Residual (random)	2048	52	39.39		
23	Total	7274	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 18.2 Post-Hoc: Holm-Sidak Comparison for Type I Fibre Proportion

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	5							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Baseline vs. Post RT_{CTL}	2.365	No	ns	0.8551	A-C			
7	Post AT_{CTL} vs. Post RT_{CTL}	3.509	No	ns	0.7194	B-C			
8	Post AT_{CTL} vs. Post AT_{EX}	0.8544	No	ns	0.8929	B-D			
9	Post RT_{CTL} vs. Post RT_{EX}	-0.5893	No	ns	0.8929	C-E			
10	Post AT_{EX} vs. Post RT_{EX}	2.065	No	ns	0.8551	D-E			
11									
12	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
13	Baseline vs. Post RT_{CTL}	61.53	59.16	2.365	2.619	14	14	0.9029	13
14	Post AT_{CTL} vs. Post RT_{CTL}	62.67	59.16	3.509	2.751	14	14	1.276	13
15	Post AT_{CTL} vs. Post AT_{EX}	62.67	61.82	0.8544	1.977	14	14	0.4321	13
16	Post RT_{CTL} vs. Post RT_{EX}	59.16	59.75	-0.5893	1.902	14	14	0.3098	13
17	Post AT_{EX} vs. Post RT_{EX}	61.82	59.75	2.065	2.529	14	14	0.8165	13

Table 19.1 1-Way ANOVA Output for Type II Fibre Proportion

	RM one-way ANOVA ANOVA results					
1	Table Analyzed	Type II Proportion				
2						
3	**Repeated measures ANOVA summary**					
4	Assume sphericity?	No				
5	F	0.7706				
6	P value	0.5156				
7	P value summary	ns				
8	Statistically significant (P < 0.05)?	No				
9	Geisser-Greenhouse's epsilon	0.7373				
10	R square	0.05596				
11						
12	**Was the matching effective?**					
13	F	9.968				
14	P value	<0.0001				
15	P value summary	****				
16	Is there significant matching (P < 0.05)?	Yes				
17	R square	0.7017				
18						
19	**ANOVA table**	**SS**	**DF**	**MS**	**F (DFn, DFd)**	**P value**
20	Treatment (between columns)	121.4	4	30.35	F (2.949, 38.34) = 0.7706	P=0.5156
21	Individual (between rows)	5104	13	392.6	F (13, 52) = 9.968	P<0.0001
22	Residual (random)	2048	52	39.39		
23	Total	7274	69			
24						
25	**Data summary**					
26	Number of treatments (columns)	5				
27	Number of subjects (rows)	14				
28	Number of missing values	0				

Table 19.2 Post-Hoc: Holm-Sidak Comparison for Type II Fibre Proportion

	RM one-way ANOVA Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	5							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	Baseline vs. Post RT_{CTL}	-2.365	No	ns	0.8551	A-C			
7	Post AT_{CTL} vs. Post RT_{CTL}	-3.509	No	ns	0.7194	B-C			
8	Post AT_{CTL} vs. Post AT_{EX}	-0.8544	No	ns	0.8929	B-D			
9	Post RT_{CTL} vs. Post RT_{EX}	0.5893	No	ns	0.8929	C-E			
10	Post AT_{EX} vs. Post RT_{EX}	-2.065	No	ns	0.8551	D-E			
11									
12	**Test details**	**Mean 1**	**Mean 2**	**Mean Diff.**	**SE of diff.**	**n1**	**n2**	**t**	**DF**
13	Baseline vs. Post RT_{CTL}	38.47	40.84	-2.365	2.619	14	14	0.9029	13
14	Post AT_{CTL} vs. Post RT_{CTL}	37.33	40.84	-3.509	2.751	14	14	1.276	13
15	Post AT_{CTL} vs. Post AT_{EX}	37.33	38.18	-0.8544	1.977	14	14	0.4321	13
16	Post RT_{CTL} vs. Post RT_{EX}	40.84	40.25	0.5893	1.902	14	14	0.3098	13
17	Post AT_{EX} vs. Post RT_{EX}	38.18	40.25	-2.065	2.529	14	14	0.8165	13

Table 20.1 Pearson's Correlation for Type I CFPE PostAT and delta CSA pre-to-post RT

Correlation		A
		CFPE at PA vs. Fibre CSA Delta
		Y
1	**Pearson r**	
2	r	0.3830
3	95% confidence interval	0.01154 to 0.6615
4	R squared	0.1467
5		
6	**P value**	
7	P (one-tailed)	0.0221
8	P value summary	*
9	Significant? (alpha = 0.05)	Yes
10		
11	**Number of XY Pairs**	28

Table 20.2 Pearson's Correlation for Type II CFPE PostAT and delta CSA pre-to-post RT

Correlation		A
		CFPE at PA vs. Fibre CSA Delta
		Y
1	**Pearson r**	
2	r	0.3499
3	95% confidence interval	-0.02661 to 0.6395
4	R squared	0.1225
5		
6	**P value**	
7	P (one-tailed)	0.0340
8	P value summary	*
9	Significant? (alpha = 0.05)	Yes
10		
11	**Number of XY Pairs**	28

APPENDIX C: GROUPED MALE AND FEMALE FIGURES AND STATS

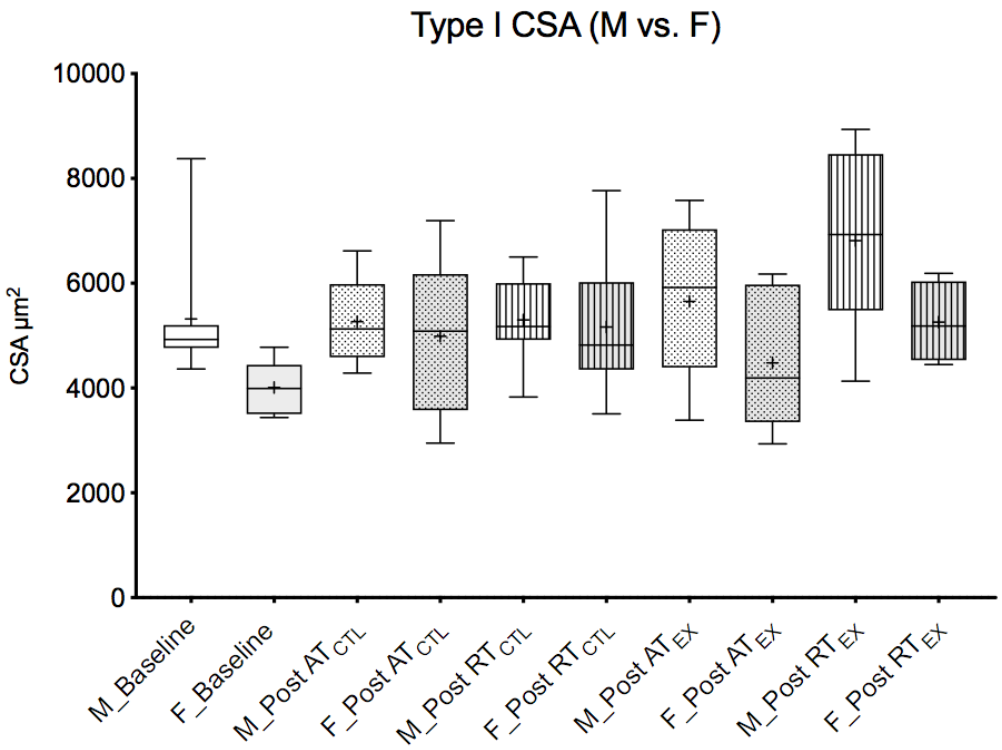

Figure 1.1 Male and Female data for type-I CSA at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX)

Table 1.1 Mixed-effects model statistical analysis of type-I CSA (M vs. F)

1	Table Analyzed	Type I CSA (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsilon**
8	Treatment (between columns)	0.0766	ns	No	F (2.821, 16.61	0.3134
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	332.7	110664			
12	Residual	1176	1382154			
13						
14	**Was the matching effective?**					
15	Chi-square, df	0.7727, 1				
16	P value	0.3794				
17	P value summary	ns				
18	Is there significant matching (P < 0.05)?	No				

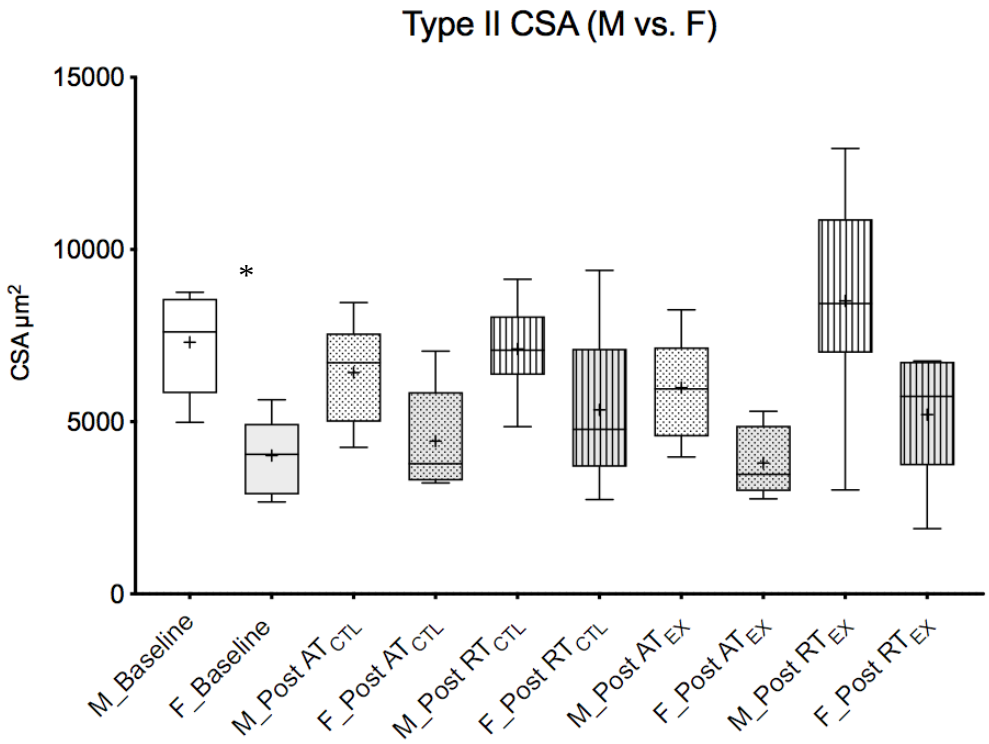

Figure 1.2 Male and Female data for type-II CSA at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX) *p<0.05 between sex (M vs. F) at timepoint within limb (CTL or EX)

Table 1.2 Mixed-effects model statistical analysis of type-II CSA (M vs. F)

1	Table Analyzed	Type II CSA (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsilon**
8	Treatment (between columns)	0.0035	**	Yes	F (3.016, 17.76	0.3351
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	785.3	616766			
12	Residual	1613	2600683			
13						
14	**Was the matching effective?**					
15	Chi-square, df	3.645, 1				
16	P value	0.0562				
17	P value summary	ns				
18	Is there significant matching (P < 0.05)?	No				

	Mixed-effects analysis Multiple comparisons								
1	Number of families	1							
2	Number of comparisons per family	5							
3	Alpha	0.05							
4									
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**				
6	M_Baseline vs. F_Baseline	3291	Yes	*	0.0390	A-B			
7	M_Post AT_{CTL} vs. F_Post AT_{CTL}	1994	No	ns	0.0930	C-D			
8	M_Post RT_{CTL} vs. F_Post RT_{CTL}	1770	No	ns	0.1239	E-F			
9	M_Post AT_{EX} vs. F_Post AT_{EX}	2184	No	ns	0.0901	G-H			
10	M_Post RT_{EX} vs. F_Post RT_{EX}	3305	No	ns	0.1239	I-J			
11									

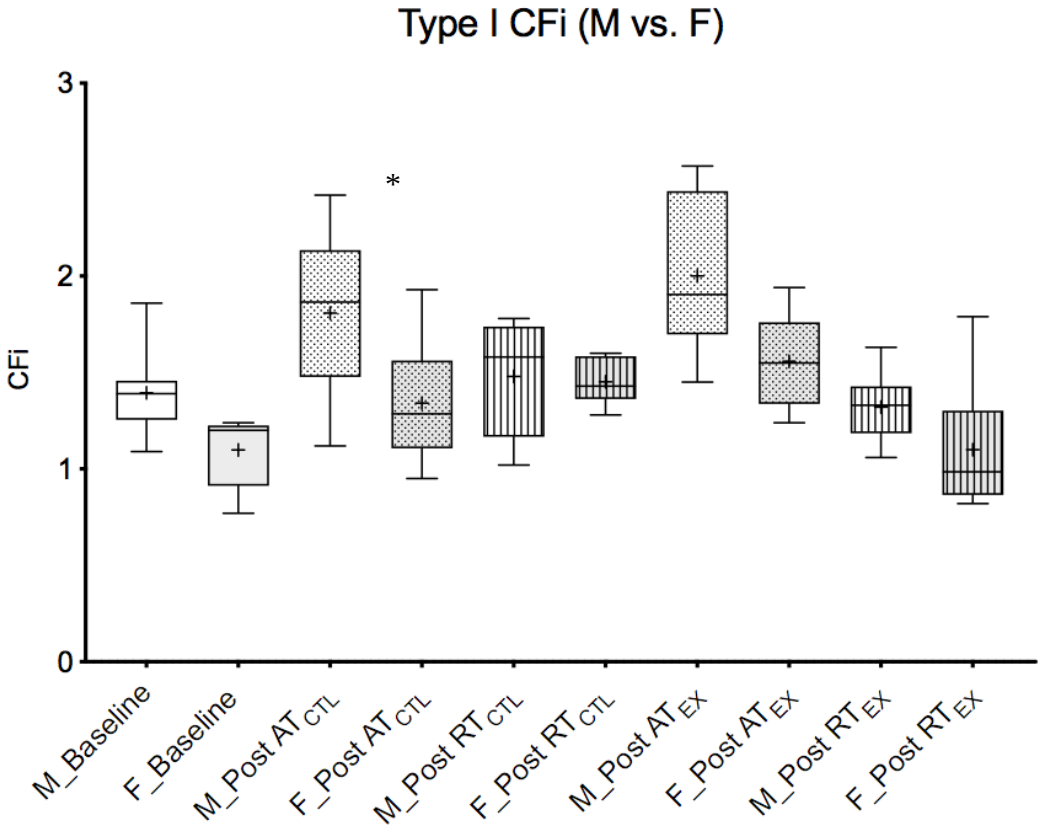

Figure 2.1 Male and Female data for type-I CFi at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX) *p<0.05 between sex (M vs. F) at timepoint within limb (CTL or EX)

Table 2.1 Mixed-effects model statistical analysis of type-I CFi (M vs. F)

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Type I CFi (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P <**	**F (DFn, DFd)**	**Geisser-Greenhouse's eps**
8	Treatment (between columns)	0.0013	**	Yes	F (3.832, 22.57) = 6.608	0.4258
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	0.02539	0.0006448			
12	Residual	0.2952	0.08714			

	Mixed-effects analysis Multiple comparisons					
1	Number of families	1				
2	Number of comparisons per family	5				
3	Alpha	0.05				
4						
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**	
6	M_Baseline vs. F_Baseline	0.2967	No	ns	0.0655	A-B
7	M_Post AT_{CTL} vs. F_Post AT_{CTL}	0.4658	Yes	*	0.0490	C-D
8	M_Post RT_{CTL} vs. F_Post RT_{CTL}	0.02833	No	ns	0.8590	E-F
9	M_Post AT_{EX} vs. F_Post AT_{EX}	0.4417	No	ns	0.1422	G-H
10	M_Post RT_{EX} vs. F_Post RT_{EX}	0.2200	No	ns	0.3251	I-J

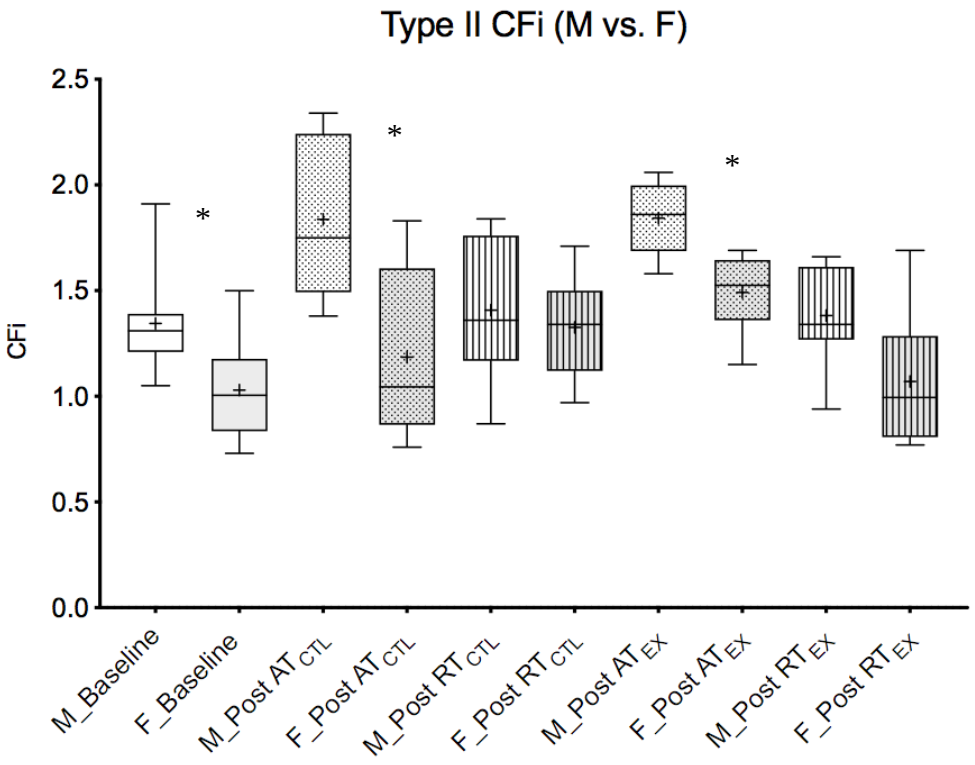

Figure 2.2 Male and Female data for type-II CFi at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX) *p<0.05 between sex (M vs. F) at timepoint within limb (CTL or EX)

Table 2.2 Mixed-effects model statistical analysis of type-II CFi (M vs. F)

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Type II CFi (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P**	**F (DFn, DFd)**	**Geisser-Greenhouse's eps**
8	Treatment (between columns)	0.0016	**	Yes	F (3.459, 20.37) = 6.904	0.3843
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	0.07742	0.005994			
12	Residual	0.2833	0.08026			

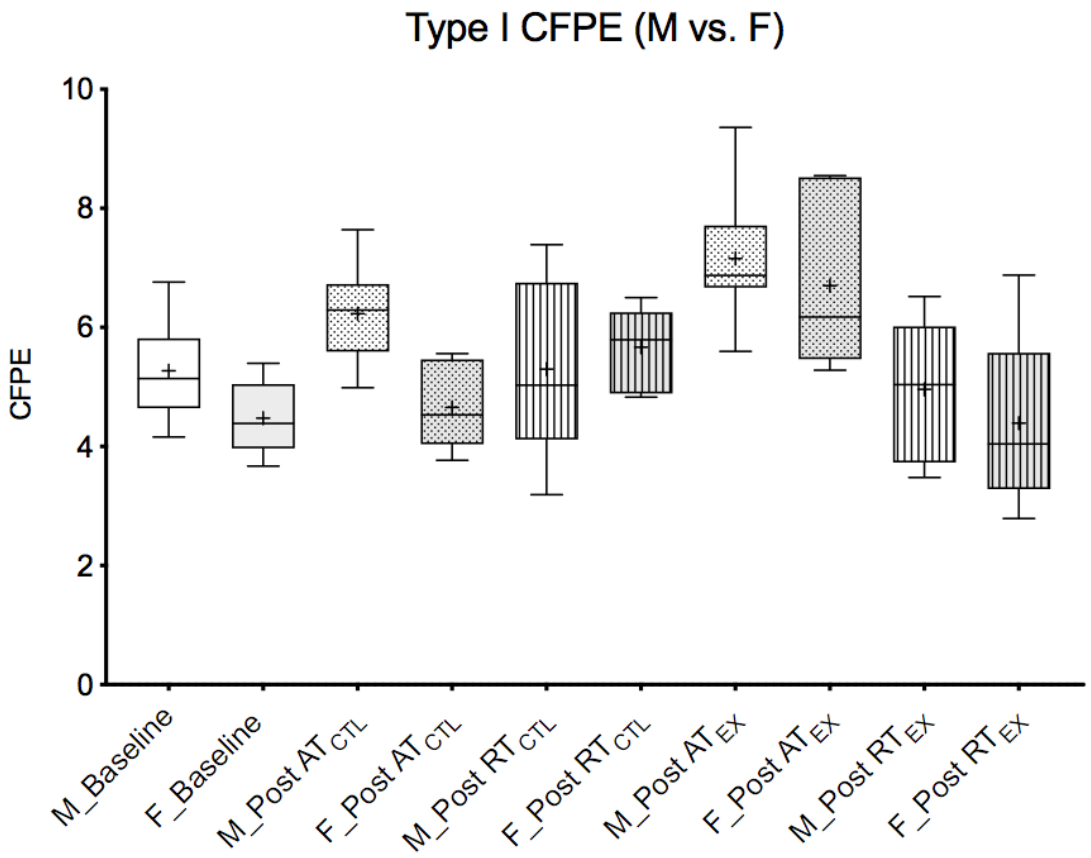

Figure 3.1 Male and Female data for type-I CFPE at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX)

Table 3.1 Mixed-effects model statistical analysis of type-I CFPE (M vs. F)

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Type I CFPE (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsilon**
8	Treatment (between columns)	0.0044	**	Yes	F (3.669, 24.46	0.4077
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	0.000	0.000			
12	Residual	1.097	1.203			

	Mixed-effects analysis Multiple comparisons					
1	Number of families	1				
2	Number of comparisons per family	5				
3	Alpha	0.05				
4						
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**	
6	M_Baseline vs. F_Baseline	0.7963	No	ns	0.3688	A-B
7	M_Post AT_{CTL} vs. F_Post AT_{CTL}	1.573	No	ns	0.0591	C-D
8	M_Post RT_{CTL} vs. F_Post RT_{CTL}	-0.3642	No	ns	0.8115	E-F
9	M_Post AT_{EX} vs. F_Post AT_{EX}	0.4567	No	ns	0.8115	G-H
10	M_Post RT_{EX} vs. F_Post RT_{EX}	0.5696	No	ns	0.8115	I-J

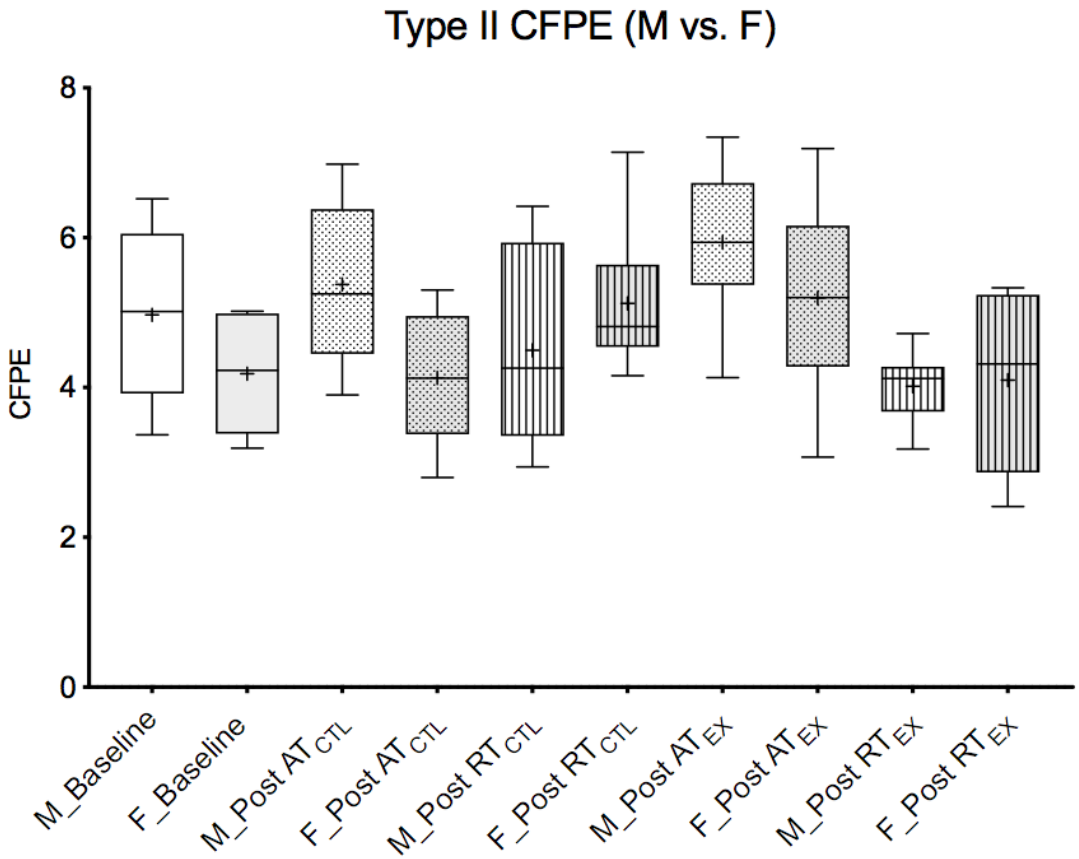

Figure 3.2 Male and Female data for type-II CFPE at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX)

Table 3.2 Mixed-effects model statistical analysis of type-II CFPE (M vs. F)

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Type II CFPE (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (**	**F (DFn, DFd)**	**Geisser-Greenhouse's e**
8	Treatment (between columns)	0.0635	ns	No	F (3.222, 21.48) = 2.763	0.3579
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	0.000	0.000			
12	Residual	1.067	1.139			
13						

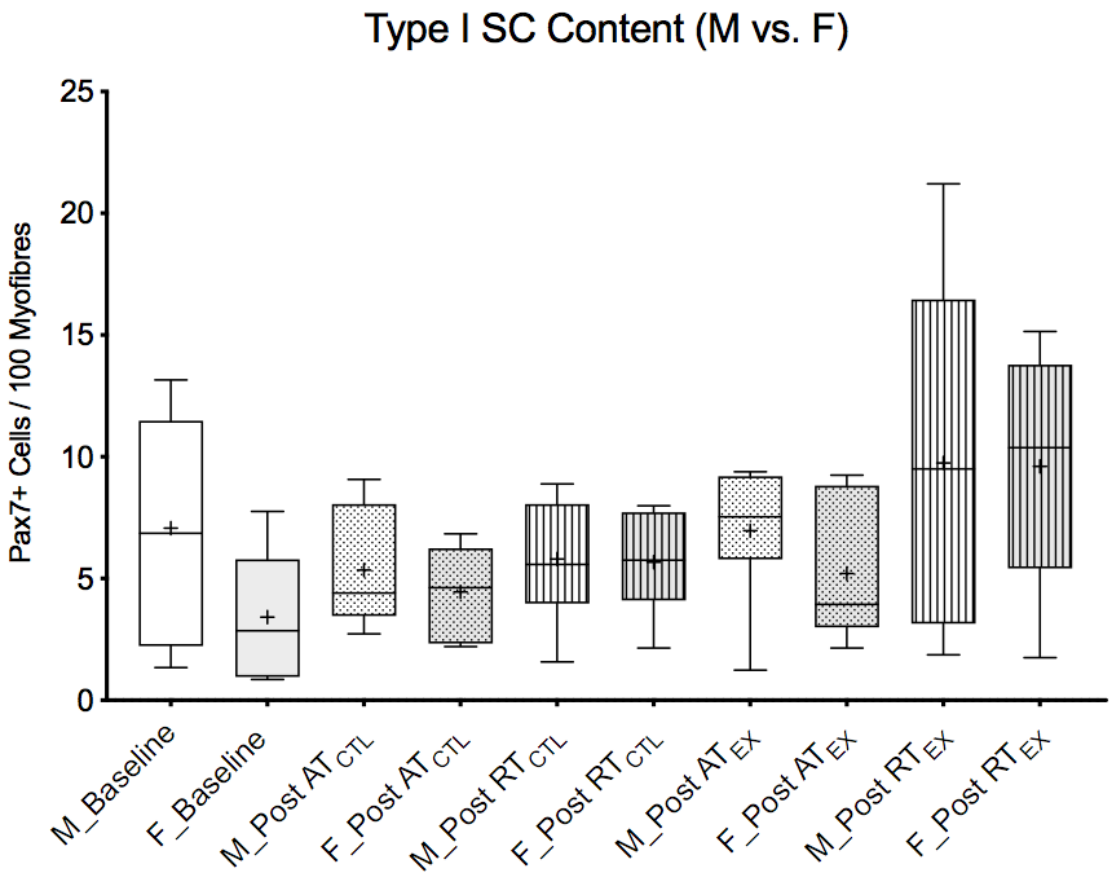

Figure 4.1 Male and Female data for type-I SC content at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX)

Table 4.1 Mixed-effects model statistical analysis of type-I SC content (M vs. F)

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Type I SC Content (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsilon**
8	Treatment (between columns)	0.1490	ns	No	F (2.837, 16.71) = 2.042	0.3152
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	0.9785	0.9574			
12	Residual	3.719	13.83			
13						

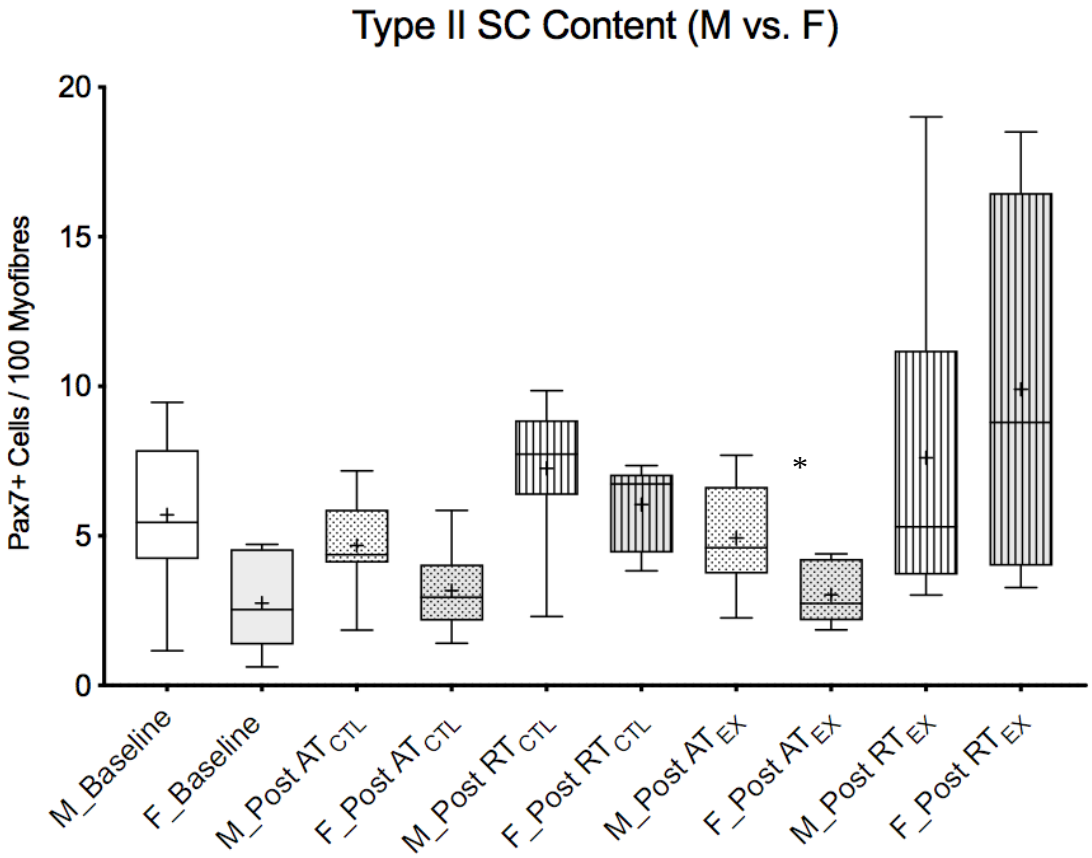

Figure 4.2 Male and Female data for type-II SC content at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX) *p<0.05 between sex (M vs. F) at timepoint within limb (CTL or EX)

Table 4.2 Mixed-effects model statistical analysis of type-II SC content (M vs. F)

Mixed-effects analysis
Tabular results

1	Table Analyzed	Type II SC Content (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P <**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsi**
8	Treatment (between columns)	0.0370	*	Yes	F (2.927, 19.51) = 3.465	0.3252
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	0.000	0.000			
12	Residual	3.106	9.650			
13						

Mixed-effects analysis
Multiple comparisons

1	Number of families	1				
2	Number of comparisons per family	5				
3	Alpha	0.05				
4						
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**	
6	M_Baseline vs. F_Baseline	2.955	No	ns	0.2830	A-B
7	M_Post AT_{CTL} vs. F_Post AT_{CTL}	1.505	No	ns	0.5150	C-D
8	M_Post RT_{CTL} vs. F_Post RT_{CTL}	1.215	No	ns	0.5323	E-F
9	M_Post AT_{EX} vs. F_Post AT_{EX}	1.902	Yes	*	0.0228	G-H
10	M_Post RT_{EX} vs. F_Post RT_{EX}	-2.286	No	ns	0.5323	I-J
11						

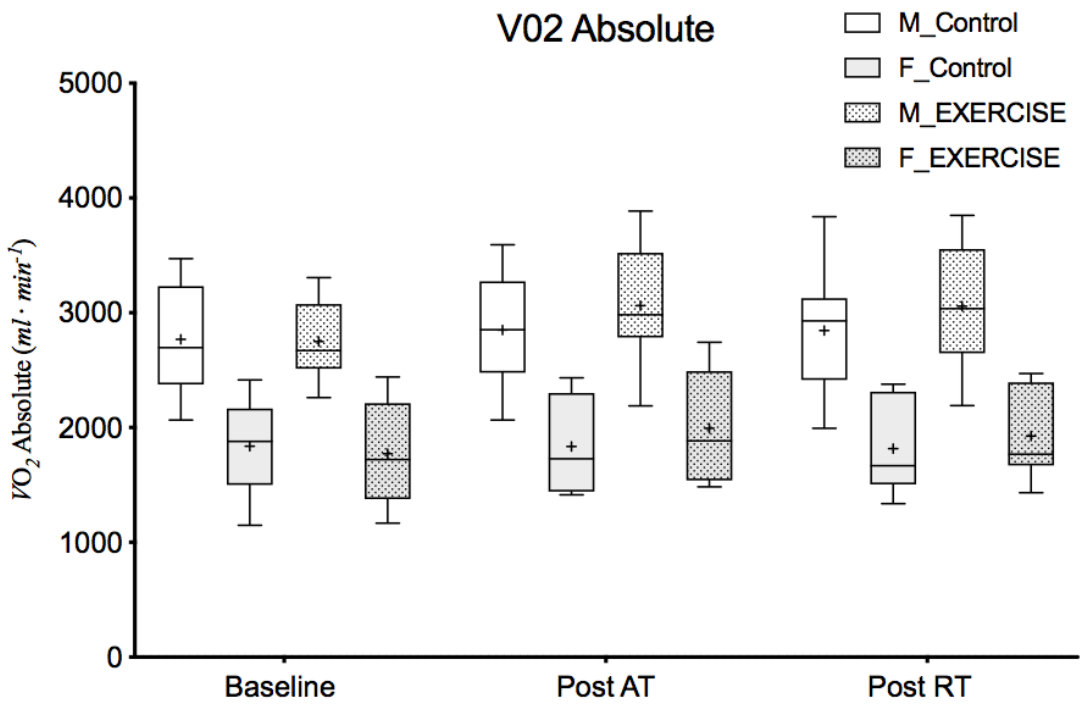

Figure 5.1 Male and Female data for VO_2 at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX)

Table 5.1 Mixed-effects model statistical analysis of V02 absolute (M vs. F)

	Mixed-effects analysis Tabular results				
1	Table Analyzed	V02 Absolute			
2					
3	**Mixed-effects model (REML)**	Matching: Both factors			
4	Assume sphericity?	Yes			
5	Alpha	0.05			
6					
7	**Fixed effects (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**
8	Time	0.0794	ns	No	F (2, 14) = 3.05
9	Sex+TS	<0.0001	****	Yes	F (3, 21) = 15.2
10	Time x Sex+TS	0.1507	ns	No	F (6, 30) = 1.72

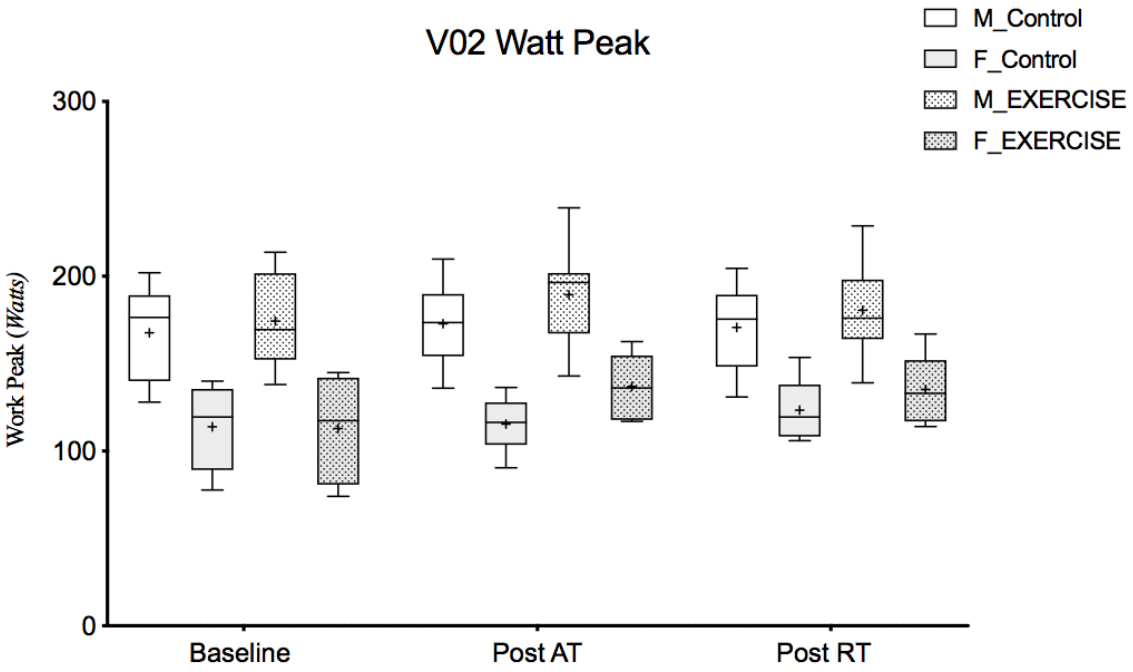

Figure 6.1 Male and Female data for VO_2 watt peak at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX)

Table 6.1 Mixed-effects model statistical analysis of V02 work peak (M vs. F)

	Mixed-effects analysis Tabular results				
1	Table Analyzed	V02 Watt Peak			
2					
3	**Mixed-effects model (REML)**	Matching: Both factors			
4	Assume sphericity?	Yes			
5	Alpha	0.05			
6					
7	**Fixed effects (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**
8	Time	0.0084	**	Yes	F (2, 14) = 6.85
9	Sex+TS	<0.0001	****	Yes	F (3, 21) = 22.9
10	Time x Sex+TS	0.0008	***	Yes	F (6, 30) = 5.33
11					

7	Holm-Sidak's multiple comparisons test	Summary	Adjusted P Value
8			
9	Baseline :M_Control vs. Baseline :F_Control	****	<0.0001
10	Baseline :M_Control vs. Baseline :M_EXERCISE	ns	0.9853
11	Baseline :M_Control vs. Baseline :F_EXERCISE	****	<0.0001
12	Baseline :M_Control vs. Post AT:M_Control	ns	0.9665
13	Baseline :M_Control vs. Post AT:F_Control	***	0.0002
14	Baseline :M_Control vs. Post AT:M_EXERCISE	ns	0.2163
15	Baseline :M_Control vs. Post AT:F_EXERCISE	ns	0.2581
16	Baseline :M_Control vs. Post RT :M_Control	ns	0.9963
17	Baseline :M_Control vs. Post RT :F_Control	**	0.0035
18	Baseline :M_Control vs. Post RT :M_EXERCISE	ns	0.8844
19	Baseline :M_Control vs. Post RT :F_EXERCISE	ns	0.1731
20	Baseline :F_Control vs. Baseline :M_EXERCISE	****	<0.0001
21	Baseline :F_Control vs. Baseline :F_EXERCISE	ns	0.9988
22	Baseline :F_Control vs. Post AT:M_Control	****	<0.0001
23	Baseline :F_Control vs. Post AT:F_Control	ns	0.9988
24	Baseline :F_Control vs. Post AT:M_EXERCISE	****	<0.0001
25	Baseline :F_Control vs. Post AT:F_EXERCISE	ns	0.3069
26	Baseline :F_Control vs. Post RT :M_Control	****	<0.0001
27	Baseline :F_Control vs. Post RT :F_Control	ns	0.6754
28	Baseline :F_Control vs. Post RT :M_EXERCISE	****	<0.0001
29	Baseline :F_Control vs. Post RT :F_EXERCISE	ns	0.4181
30	Baseline :M_EXERCISE vs. Baseline :F_EXERCISE	****	<0.0001
31	Baseline :M_EXERCISE vs. Post AT:M_Control	ns	0.9988
32	Baseline :M_EXERCISE vs. Post AT:F_Control	****	<0.0001
33	Baseline :M_EXERCISE vs. Post AT:M_EXERCISE	*	0.0435
34	Baseline :M_EXERCISE vs. Post AT:F_EXERCISE	*	0.0408
35	Baseline :M_EXERCISE vs. Post RT :M_Control	ns	0.9988
36	Baseline :M_EXERCISE vs. Post RT :F_Control	***	0.0003
37	Baseline :M_EXERCISE vs. Post RT :M_EXERCISE	ns	0.9418
38	Baseline :M_EXERCISE vs. Post RT :F_EXERCISE	*	0.0238
39	Baseline :F_EXERCISE vs. Post AT:M_Control	****	<0.0001
40	Baseline :F_EXERCISE vs. Post AT:F_Control	ns	0.9988
41	Baseline :F_EXERCISE vs. Post AT:M_EXERCISE	****	<0.0001
42	Baseline :F_EXERCISE vs. Post AT:F_EXERCISE	***	0.0005
43	Baseline :F_EXERCISE vs. Post RT :M_Control	****	<0.0001
44	Baseline :F_EXERCISE vs. Post RT :F_Control	ns	0.9665
46	Baseline :F_EXERCISE vs. Post RT :F_EXERCISE	Yes	**	0.0015
47	Post AT:M_Control vs. Post AT:F_Control	Yes	****	<0.0001
48	Post AT:M_Control vs. Post AT:M_EXERCISE	No	ns	0.5077
49	Post AT:M_Control vs. Post AT:F_EXERCISE	Yes	*	0.0435
50	Post AT:M_Control vs. Post RT :M_Control	No	ns	0.9988
51	Post AT:M_Control vs. Post RT :F_Control	Yes	***	0.0005
52	Post AT:M_Control vs. Post RT :M_EXERCISE	No	ns	0.9852
53	Post AT:M_Control vs. Post RT :F_EXERCISE	Yes	*	0.0403
54	Post AT:F_Control vs. Post AT:M_EXERCISE	Yes	****	<0.0001
55	Post AT:F_Control vs. Post AT:F_EXERCISE	No	ns	0.3351
56	Post AT:F_Control vs. Post RT :M_Control	Yes	****	<0.0001
57	Post AT:F_Control vs. Post RT :F_Control	No	ns	0.8844
58	Post AT:F_Control vs. Post RT :M_EXERCISE	Yes	****	<0.0001
59	Post AT:F_Control vs. Post RT :F_EXERCISE	No	ns	0.5186
60	Post AT:M_EXERCISE vs. Post AT:F_EXERCISE	Yes	****	<0.0001
61	Post AT:M_EXERCISE vs. Post RT :M_Control	No	ns	0.4181
62	Post AT:M_EXERCISE vs. Post RT :F_Control	Yes	****	<0.0001
63	Post AT:M_EXERCISE vs. Post RT :M_EXERCISE	No	ns	0.6232
64	Post AT:M_EXERCISE vs. Post RT :F_EXERCISE	Yes	****	<0.0001
65	Post AT:F_EXERCISE vs. Post RT :M_Control	No	ns	0.1231
66	Post AT:F_EXERCISE vs. Post RT :F_Control	No	ns	0.9145
67	Post AT:F_EXERCISE vs. Post RT :M_EXERCISE	Yes	**	0.0048
68	Post AT:F_EXERCISE vs. Post RT :F_EXERCISE	No	ns	0.9988
69	Post RT :M_Control vs. Post RT :F_Control	Yes	***	0.0007
70	Post RT :M_Control vs. Post RT :M_EXERCISE	No	ns	0.9418
71	Post RT :M_Control vs. Post RT :F_EXERCISE	Yes	*	0.0498
72	Post RT :F_Control vs. Post RT :M_EXERCISE	Yes	****	<0.0001
73	Post RT :F_Control vs. Post RT :F_EXERCISE	No	ns	0.9418
74	Post RT :M_EXERCISE vs. Post RT :F_EXERCISE	Yes	**	0.0015

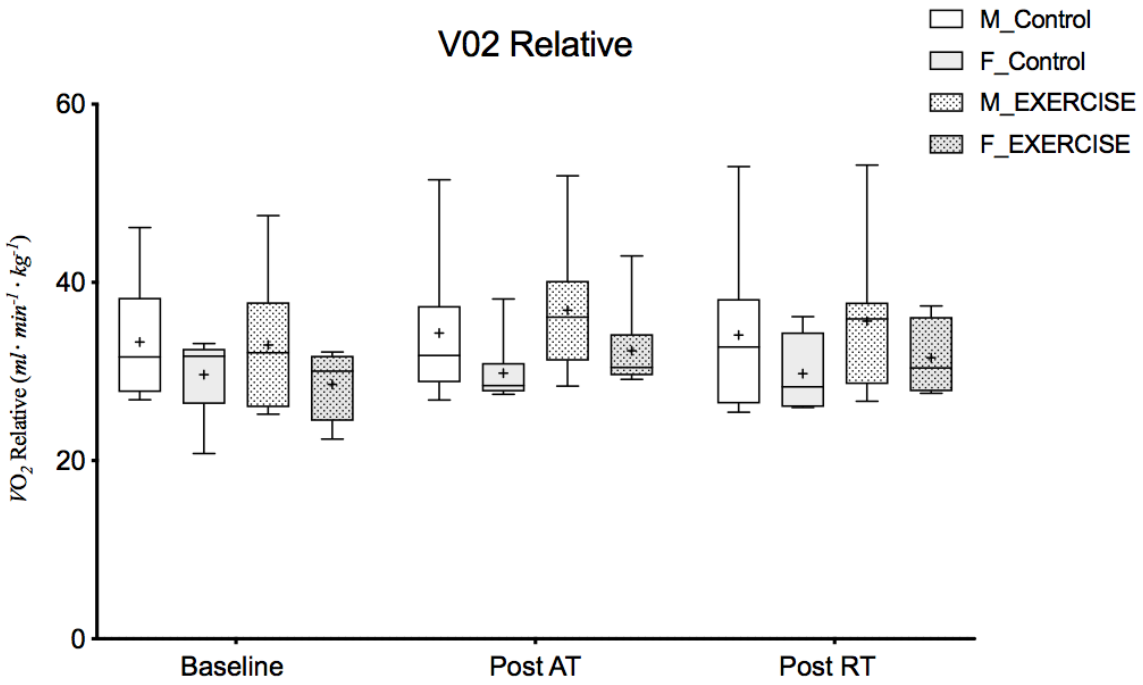

Figure 7.1 Male and Female data for VO_2 relative peak at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX)

Table 7.1 Mixed-effects model statistical analysis of V02 relative (M vs. F)

	Mixed-effects analysis Tabular results				
1	Table Analyzed	V02 Relative (Whole body)			
2					
3	**Mixed-effects model (REML)**	Matching: Both factors			
4	Assume sphericity?	Yes			
5	Alpha	0.05			
6					
7	**Fixed effects (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**
8	Time	0.0942	ns	No	F (2, 14) = 2.80
9	Sex+TS	0.3303	ns	No	F (3, 21) = 1.21
10	Time x Sex+TS	0.2039	ns	No	F (6, 30) = 1.52
11					

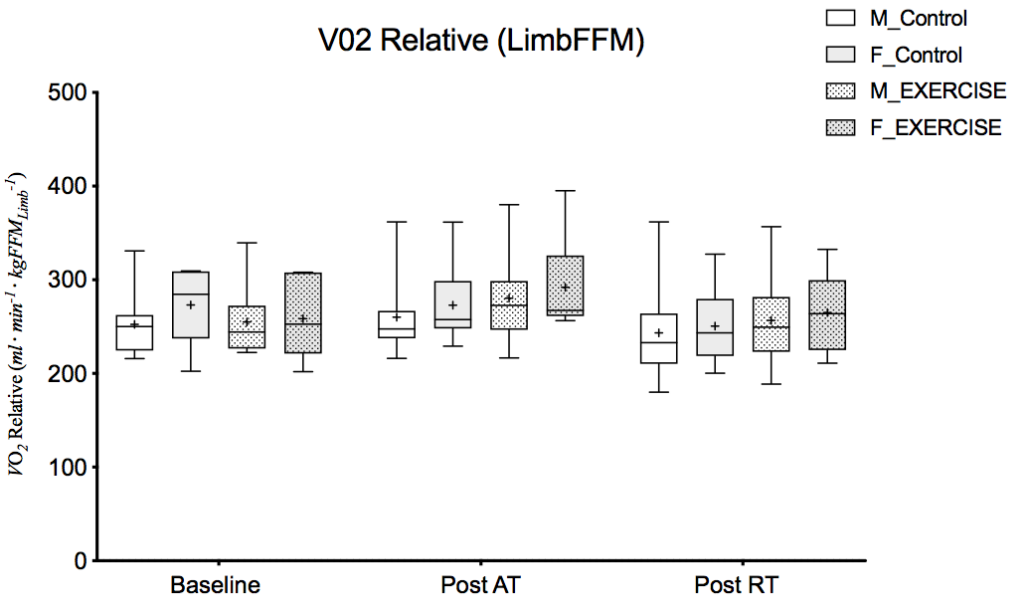

Figure 8.1 Male and Female data for VO_2 relative to limb fat free mass at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX)

Table 8.1 Mixed-effects model statistical analysis of V02 relative to limb fat free mass (M vs. F)

	Mixed-effects analysis Tabular results				
1	Table Analyzed	V02 Relative (LimbFFM)			
2					
3	**Mixed-effects model (REML)**	Matching: Both factors			
4	Assume sphericity?	Yes			
5	Alpha	0.05			
6					
7	**Fixed effects (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**
8	Time	0.0482	*	Yes	F (2, 14) = 3.796
9	Sex+TS	0.3198	ns	No	F (3, 21) = 1.241
10	Time x Sex+TS	0.1435	ns	No	F (6, 30) = 1.751
11					
12	**Random effects**	**SD**	**Variance**		
13	Subject	33.04	1092		
14	Subject x Time	14.65	214.5		
15	Subject x Sex+TS	29.47	868.6		
16	Residual	16.06	258.0		

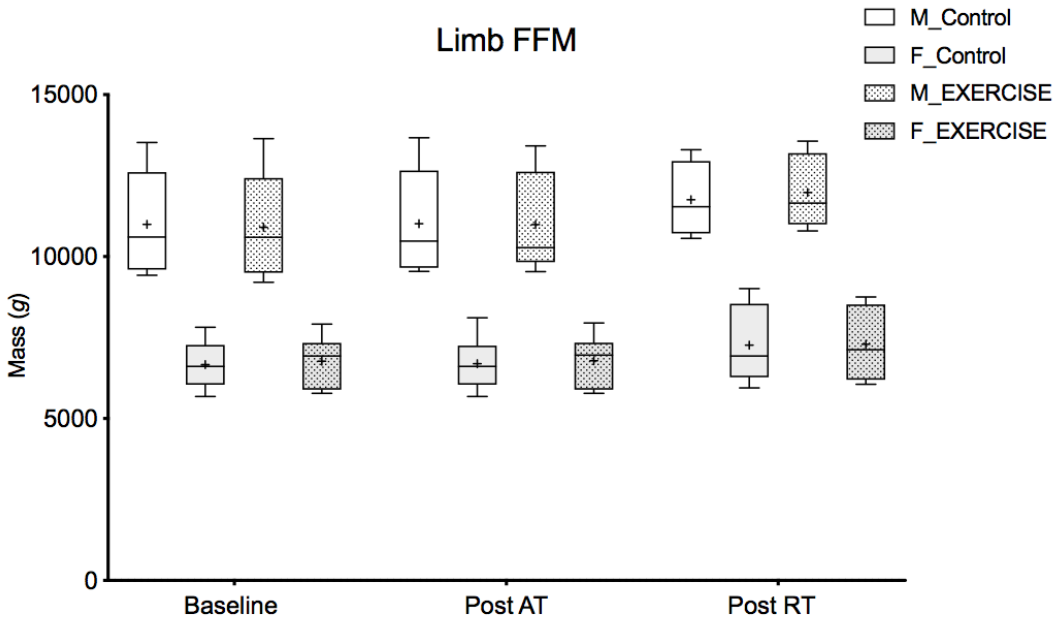

Figure 9.1 Male and Female data for limb fat free mass at each of the timepoints (Baseline, Post AT and Post RT) for each limb (CTL and EX)

Table 9.1 Mixed-effects model statistical analysis of fat free mass (M vs. F)

	Mixed-effects analysis Tabular results				
1	Table Analyzed	Limb FFM			
2					
3	**Mixed-effects model (REML)**	Matching: Both factors			
4	Assume sphericity?	Yes			
5	Alpha	0.05			
6					
7	**Fixed effects (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**
8	Time	0.0002	***	Yes	F (2, 14) = 16.24
9	Sex+TS	<0.0001	****	Yes	F (3, 21) = 46.36
10	Time x Sex+TS	0.0301	*	Yes	F (6, 30) = 2.746
11					
12	**Random effects**	**SD**	**Variance**		
13	Subject	820.2	672678		
14	Subject x Time	250.0	62512		
15	Subject x Sex+TS	906.6	821942		
16	Residual	231.0	53339		
17					

7	Holm-Sidak's multiple comparisons test	Summary	Adjusted P Value
8			
9	Baseline :M_Control vs. Baseline :F_Control	****	<0.0001
10	Baseline :M_Control vs. Baseline :M_EXERCISE	ns	>0.9999
11	Baseline :M_Control vs. Baseline :F_EXERCISE	****	<0.0001
12	Baseline :M_Control vs. Post AT:M_Control	ns	>0.9999
13	Baseline :M_Control vs. Post AT:F_Control	****	<0.0001
14	Baseline :M_Control vs. Post AT:M_EXERCISE	ns	>0.9999
15	Baseline :M_Control vs. Post AT:F_EXERCISE	****	<0.0001
16	Baseline :M_Control vs. Post RT :M_Control	**	0.0014
17	Baseline :M_Control vs. Post RT :F_Control	****	<0.0001
18	Baseline :M_Control vs. Post RT :M_EXERCISE	ns	0.6390
19	Baseline :M_Control vs. Post RT :F_EXERCISE	****	<0.0001
20	Baseline :F_Control vs. Baseline :M_EXERCISE	****	<0.0001
21	Baseline :F_Control vs. Baseline :F_EXERCISE	ns	>0.9999
22	Baseline :F_Control vs. Post AT:M_Control	****	<0.0001
23	Baseline :F_Control vs. Post AT:F_Control	ns	>0.9999
24	Baseline :F_Control vs. Post AT:M_EXERCISE	****	<0.0001
25	Baseline :F_Control vs. Post AT:F_EXERCISE	ns	>0.9999
26	Baseline :F_Control vs. Post RT :M_Control	****	<0.0001
27	Baseline :F_Control vs. Post RT :F_Control	ns	0.1263
28	Baseline :F_Control vs. Post RT :M_EXERCISE	****	<0.0001
29	Baseline :F_Control vs. Post RT :F_EXERCISE	ns	0.9987
30	Baseline :M_EXERCISE vs. Baseline :F_EXERCISE	****	<0.0001
31	Baseline :M_EXERCISE vs. Post AT:M_Control	ns	>0.9999
32	Baseline :M_EXERCISE vs. Post AT:F_Control	****	<0.0001
33	Baseline :M_EXERCISE vs. Post AT:M_EXERCISE	ns	>0.9999
34	Baseline :M_EXERCISE vs. Post AT:F_EXERCISE	****	<0.0001
35	Baseline :M_EXERCISE vs. Post RT :M_Control	ns	0.8246
36	Baseline :M_EXERCISE vs. Post RT :F_Control	****	<0.0001
37	Baseline :M_EXERCISE vs. Post RT :M_EXERCISE	****	<0.0001
38	Baseline :M_EXERCISE vs. Post RT :F_EXERCISE	****	<0.0001
39	Baseline :F_EXERCISE vs. Post AT:M_Control	****	<0.0001
40	Baseline :F_EXERCISE vs. Post AT:F_Control	ns	>0.9999
41	Baseline :F_EXERCISE vs. Post AT:M_EXERCISE	****	<0.0001
42	Baseline :F_EXERCISE vs. Post AT:F_EXERCISE	ns	>0.9999
43	Baseline :F_EXERCISE vs. Post RT :M_Control	****	<0.0001
44	Baseline :F_EXERCISE vs. Post RT :F_Control	ns	0.9998
45	Baseline :F_EXERCISE vs. Post RT :M_EXERCISE	****	<0.0001
46	Baseline :F_EXERCISE vs. Post RT :F_EXERCISE	ns	0.3221
47	Post AT:M_Control vs. Post AT:F_Control	****	<0.0001
48	Post AT:M_Control vs. Post AT:M_EXERCISE	ns	>0.9999
49	Post AT:M_Control vs. Post AT:F_EXERCISE	****	<0.0001
50	Post AT:M_Control vs. Post RT :M_Control	**	0.0020
51	Post AT:M_Control vs. Post RT :F_Control	****	<0.0001
52	Post AT:M_Control vs. Post RT :M_EXERCISE	ns	0.6616
53	Post AT:M_Control vs. Post RT :F_EXERCISE	****	<0.0001
54	Post AT:F_Control vs. Post AT:M_EXERCISE	****	<0.0001
55	Post AT:F_Control vs. Post AT:F_EXERCISE	ns	>0.9999
56	Post AT:F_Control vs. Post RT :M_Control	****	<0.0001
57	Post AT:F_Control vs. Post RT :F_Control	ns	0.1805
58	Post AT:F_Control vs. Post RT :M_EXERCISE	****	<0.0001
59	Post AT:F_Control vs. Post RT :F_EXERCISE	ns	0.9990
60	Post AT:M_EXERCISE vs. Post AT:F_EXERCISE	****	<0.0001
61	Post AT:M_EXERCISE vs. Post RT :M_Control	ns	0.9066
62	Post AT:M_EXERCISE vs. Post RT :F_Control	****	<0.0001
63	Post AT:M_EXERCISE vs. Post RT :M_EXERCISE	****	<0.0001
64	Post AT:M_EXERCISE vs. Post RT :F_EXERCISE	****	<0.0001
65	Post AT:F_EXERCISE vs. Post RT :M_Control	****	<0.0001
66	Post AT:F_EXERCISE vs. Post RT :F_Control	ns	0.9998
67	Post AT:F_EXERCISE vs. Post RT :M_EXERCISE	****	<0.0001
68	Post AT:F_EXERCISE vs. Post RT :F_EXERCISE	ns	0.3663
69	Post RT :M_Control vs. Post RT :F_Control	****	<0.0001
70	Post RT :M_Control vs. Post RT :M_EXERCISE	ns	>0.9999
71	Post RT :M_Control vs. Post RT :F_EXERCISE	****	<0.0001
72	Post RT :F_Control vs. Post RT :M_EXERCISE	****	<0.0001
73	Post RT :F_Control vs. Post RT :F_EXERCISE	ns	>0.9999
74	Post RT :M_EXERCISE vs. Post RT :F_EXERCISE	****	<0.0001

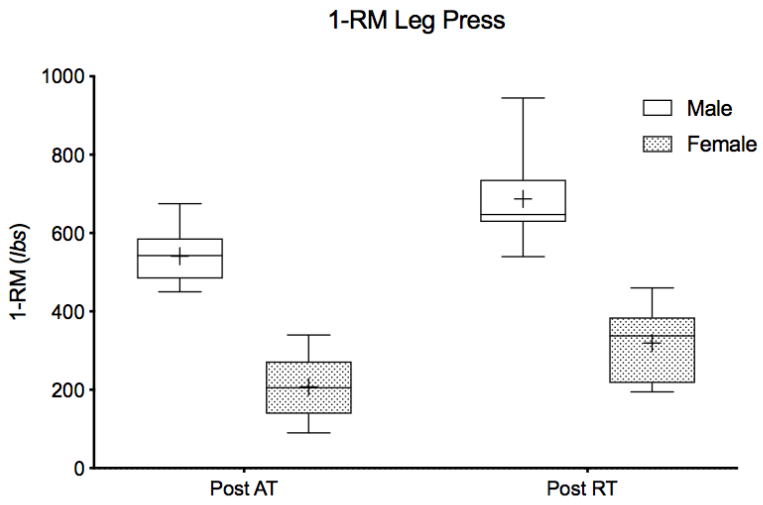

Figure 10.1 Male and Female data for 1-RM leg press at each of the timepoints (Post AT and Post RT)

Table 10.1 Mixed-effects model statistical analysis of 1-RM leg press (M vs. F)

	Mixed-effects analysis Tabular results				
1	Table Analyzed	1RM Leg Press			
2					
3	**Mixed-effects model (REML)**	Matching: Both factors			
4	Assume sphericity?	Yes			
5	Alpha	0.05			
6					
7	**Fixed effects (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**
8	Time	0.0003	***	Yes	F (1, 7) = 42.19
9	Sex	0.0002	***	Yes	F (1, 7) = 53.99
10	Time x Sex	0.4479	ns	No	F (1, 3) = 0.758
11					
12	**Random effects**	**SD**	**Variance**		
13	Subject	0.000	0.000		
14	Subject x Time	0.000	0.000		
15	Subject x Sex	80.46	6474		
16	Residual	51.99	2703		
17					

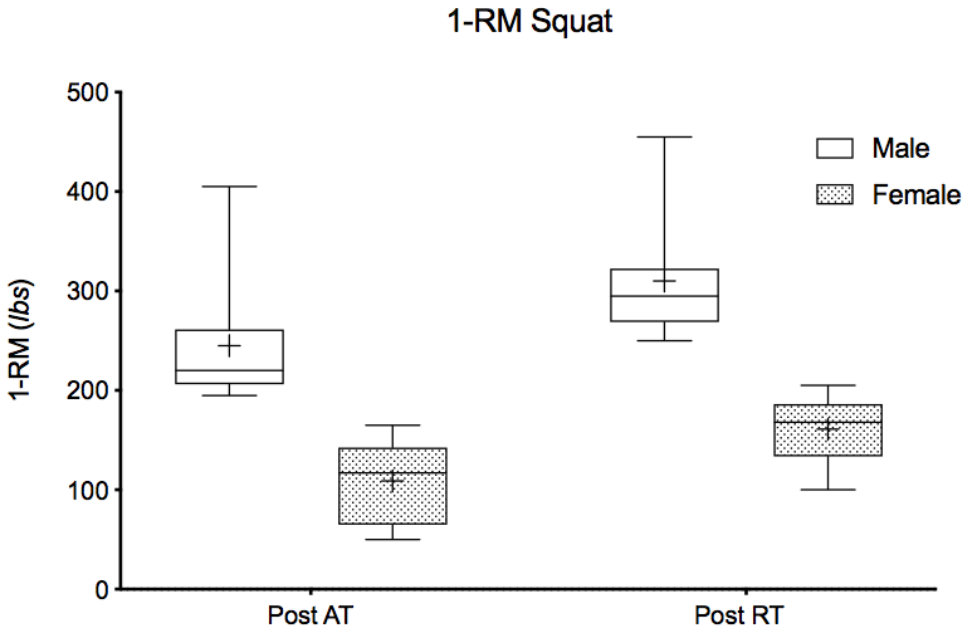

Figure 11.1 Male and Female data for 1-RM squat at each of the timepoints (Post AT and Post RT)

Table 11.1 Mixed-effects model statistical analysis of 1-RM squat (M vs. F)

	Mixed-effects analysis Tabular results				
1	Table Analyzed	1RM Squat			
2					
3	**Mixed-effects model (REML)**	Matching: Both factors			
4	Assume sphericity?	Yes			
5	Alpha	0.05			
6					
7	**Fixed effects (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**
8	Time	0.0001	***	Yes	F (1, 7) = 57.59
9	Sex	0.0006	***	Yes	F (1, 7) = 34.60
10	Time x Sex	0.4610	ns	No	F (1, 3) = 0.711
11					
12	**Random effects**	**SD**	**Variance**		
13	Subject	44.05	1941		
14	Subject x Time	0.000	0.000		
15	Subject x Sex	36.79	1354		
16	Residual	20.19	407.5		
17					

APPENDIX D: MALE AND FEMALE DETLA CHANGE FIGURES WITH STATS FOR IMMUNOHISTOCHEMICAL DATA

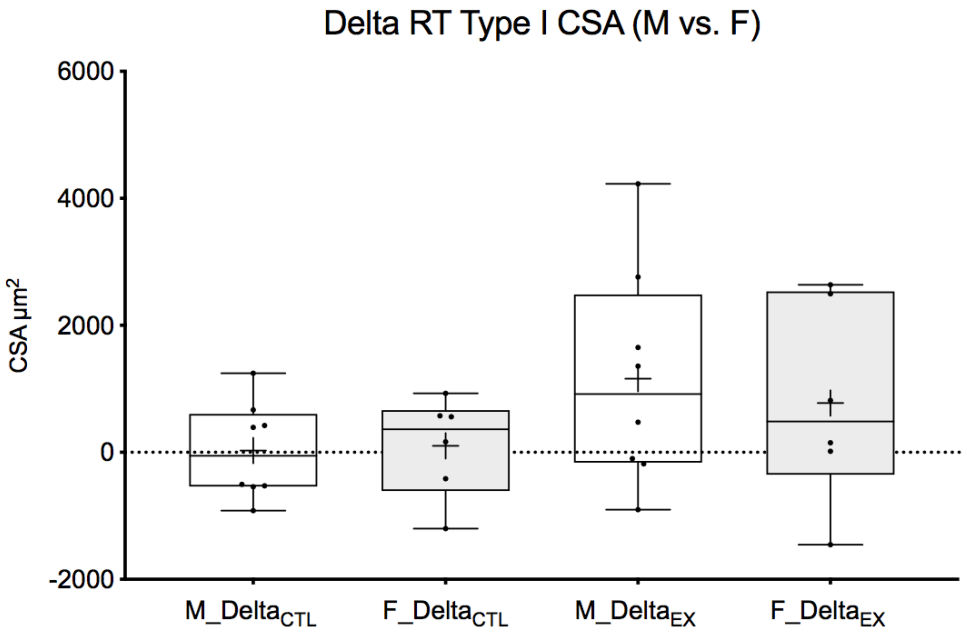

Figure 1.1 Male and Female data for type-I CSA delta changes across the RT period for each limb (CTL and EX)

Table 1.1

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Delta RT Type II CSA (M vs				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P**	**F (DFn, DFd)**	**Geisser-Greenhouse's eps**
8	Treatment (between columns)	0.3352	ns	No	F (1.947, 15.57) = 1.169	0.6489
9						

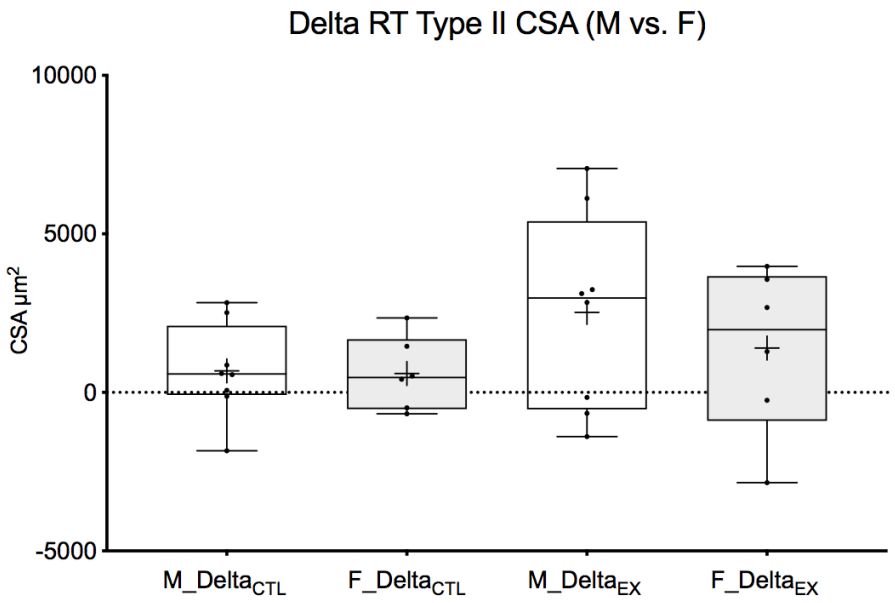

Figure 1.2 Male and Female data for type-II CSA delta changes across the RT period for each limb (CTL and EX)

Table 1.2

	Mixed-effects analysis Tabular results					
1	Table Analyzed	****Delta RT Type I CSA (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsilon**
8	Treatment (between columns)	0.2895	ns	No	F (1.576, 12.61	0.5252
9						

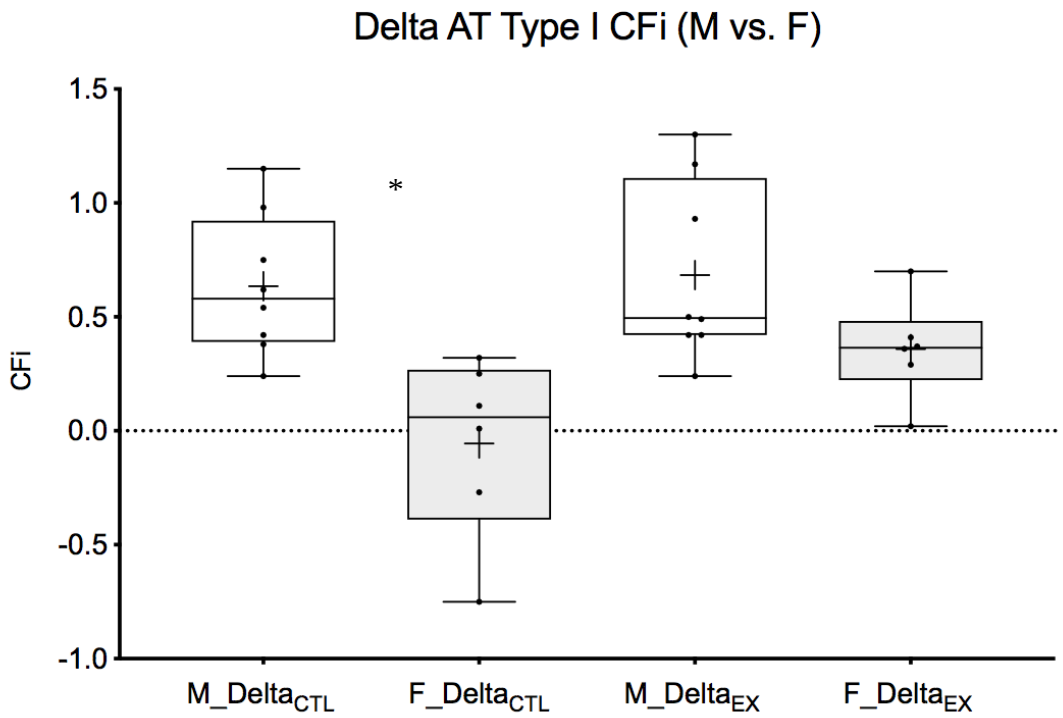

Figure 2.1 Male and Female data for type-I CFi delta changes across the AT period for each limb (CTL and EX) *p<0.05 between M vs. F within limb (CTL or EX)

Table 2.1

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Delta AT Type I CFi (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsilon**
8	Treatment (between columns)	0.0081	**	Yes	F (2.028, 11.49	0.6759
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	0.1434	0.02057			
12	Residual	0.3083	0.09507			
13						

	Mixed-effects analysis Multiple comparisons					
1	Number of families	1				
2	Number of comparisons per family	2				
3	Alpha	0.05				
4						
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**	
6	M_Delta_{CTL} vs. F_Delta_{CTL}	0.6900	Yes	**	0.0027	A-B
7	M_Delta_{EX} vs. F_Delta_{EX}	0.3254	No	ns	0.1402	C-D
8						

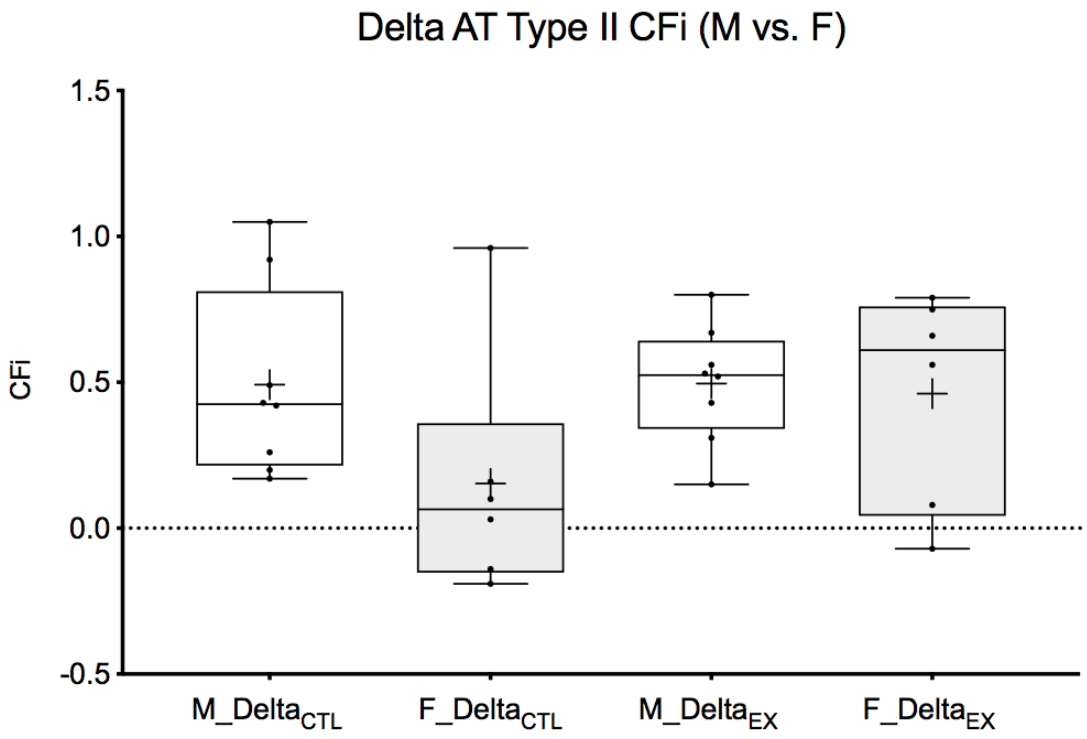

Figure 2.2 Male and Female data for type-II CFi delta changes across the AT period for each limb (CTL and EX)

Table 2.2

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Delta AT Type II CFi (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsilon**
8	Treatment (between columns)	0.2063	ns	No	F (2.628, 14.89	0.8759
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	0.1106	0.01224			
12	Residual	0.3082	0.09498			
13						

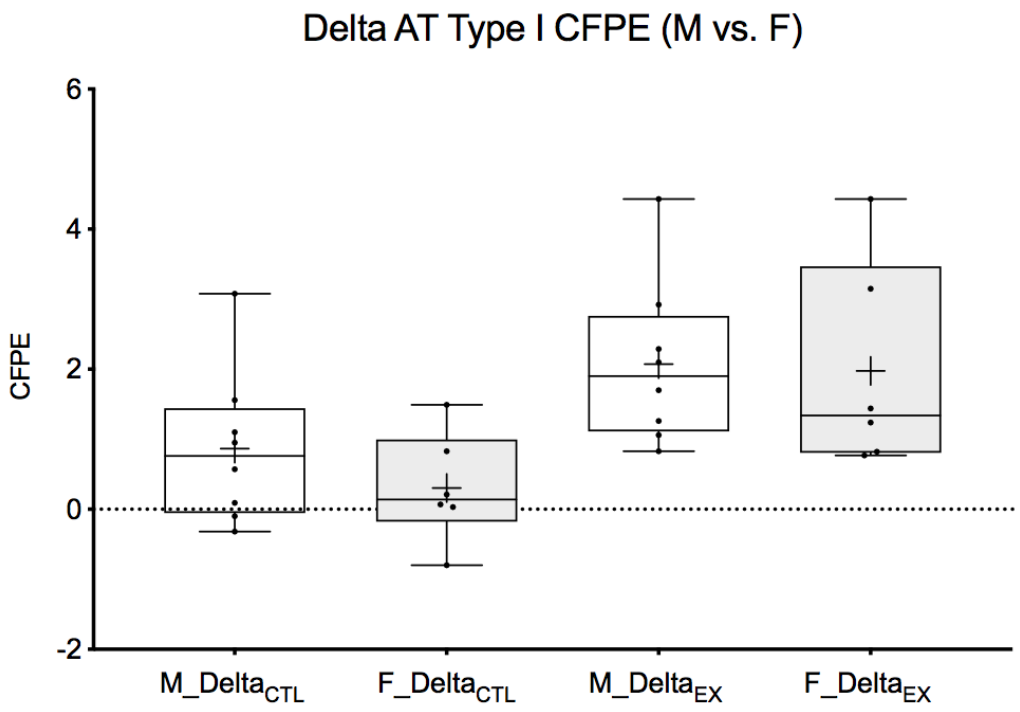

Figure 3.1 Male and Female data for type-I CFPE delta changes across the AT period for each limb (CTL and EX)

Table 3.1

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Delta AT Type I CFPE				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significa**	**F (DFn, DFd)**	**Geisser-Greenhouse**
8	Treatment (between columns)	0.0048	**	Yes	F (2.545, 14.42) = 7.1	0.8484
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	0.7796	0.6077			
12	Residual	0.8535	0.7285			
13						

	Mixed-effects analysis Multiple comparisons					
1	Number of families	1				
2	Number of comparisons per family	2				
3	Alpha	0.05				
4						
5	**Holm-Sidak's multiple comparisons test**	**Mean Diff.**	**Significant?**	**Summary**	**Adjusted P Value**	
6	M_Delta_{CTL} vs. F_Delta_{CTL}	0.5613	No	ns	0.4992	A-B
7	M_Delta_{EX} vs. F_Delta_{EX}	0.09875	No	ns	0.8165	C-D
8						

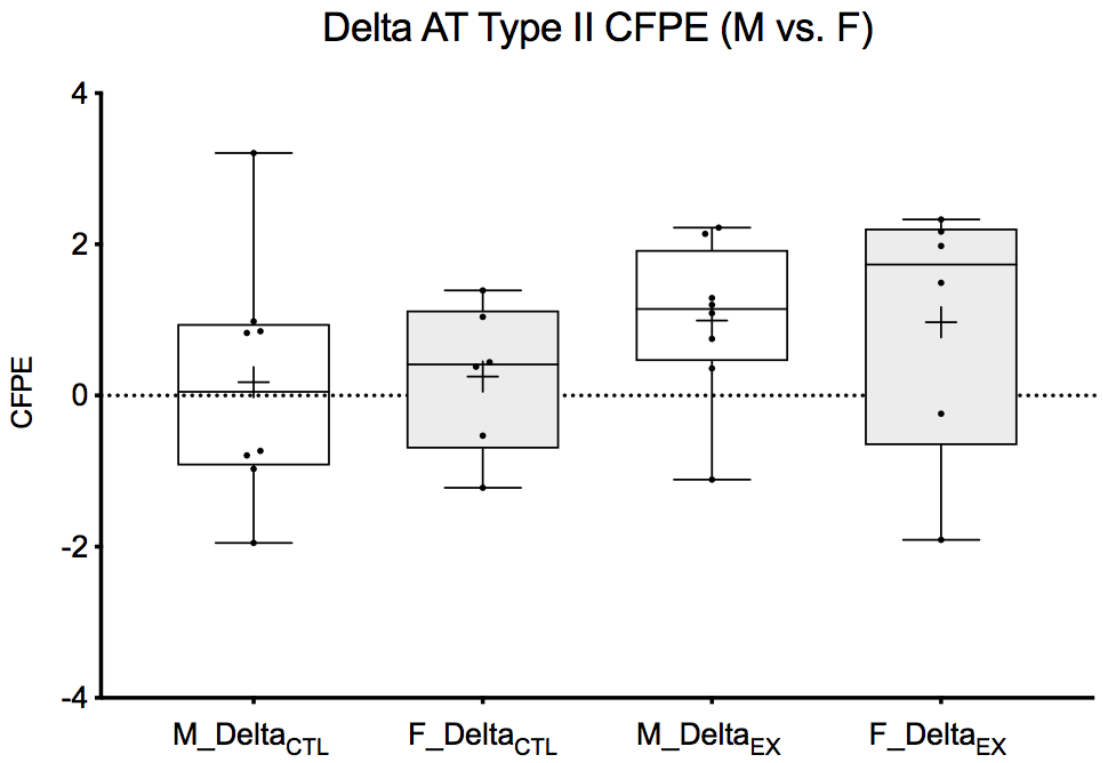

Figure 3.2 Male and Female data for type-II CFPE delta changes across the AT period for each limb (CTL and EX)

Table 3.2

Mixed-effects analysis Tabular results						
1	Table Analyzed	Delta AT Type II CFPE (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.(**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsilon**
8	Treatment (between columns)	0.4161	ns	No	F (1.889, 10.70) = 0.9382	0.6297
9						

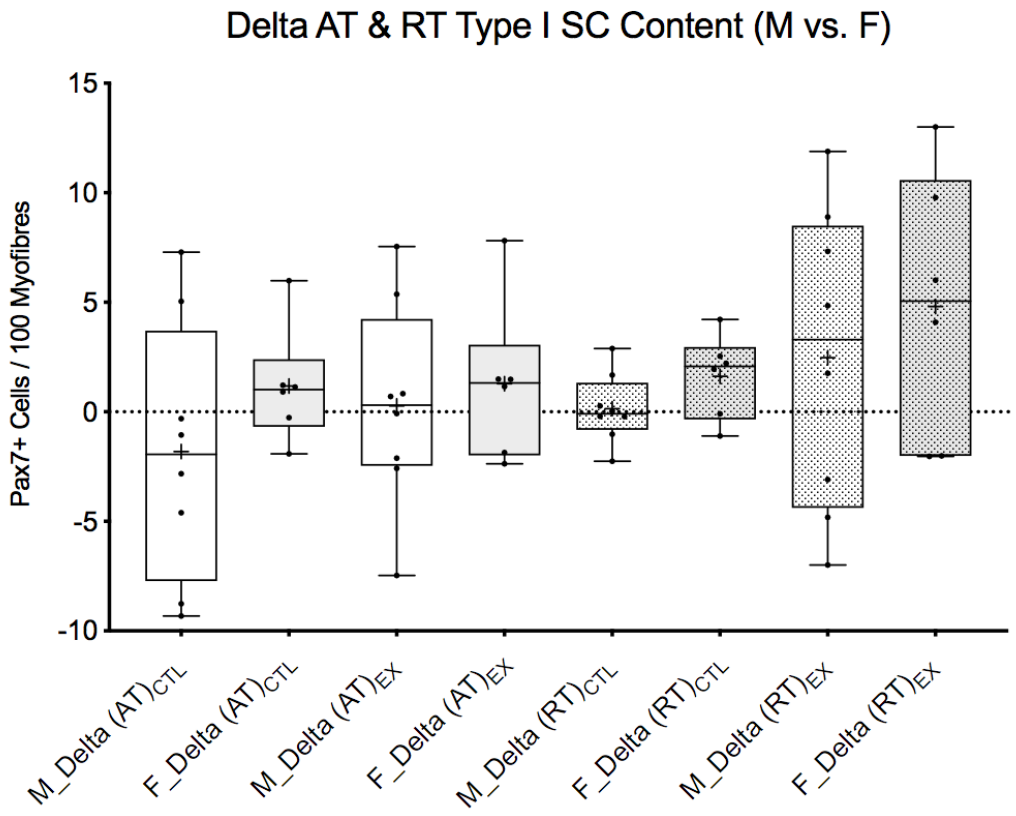

Figure 4.1 Male and Female data for type-I SC content delta changes across the AT & RT periods for each limb (CTL and EX)

Table 4.1

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Delta RT Type-I SC Content (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsilon**
8	Treatment (between columns)	0.3447	ns	No	F (2.368, 13.87	0.3383
9						
10	**Random effects**	**SD**	**Variance**			
11	Individual (between rows)	0.2779	0.07720			
12	Residual	4.682	21.92			

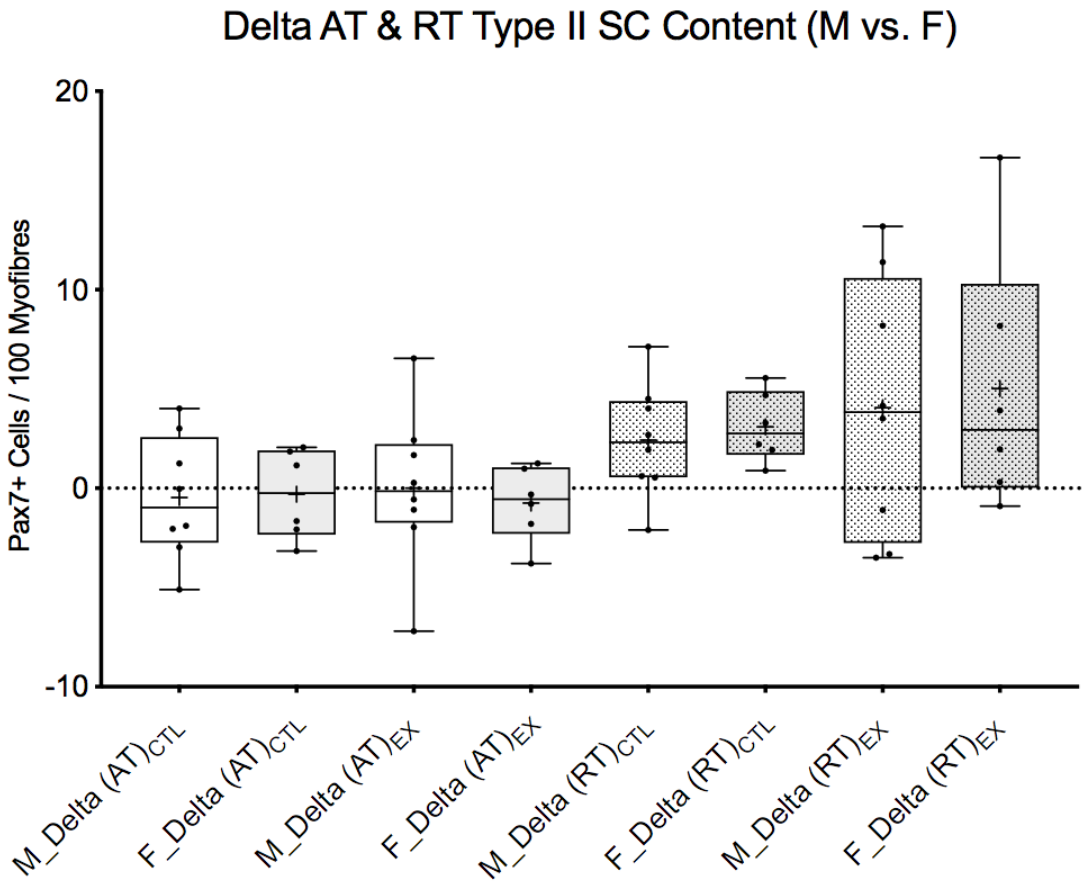

Figure 4.2 Male and Female data for type-II SC content delta changes across the AT & RT periods for each limb (CTL and EX)

Table 4.2

	Mixed-effects analysis Tabular results					
1	Table Analyzed	Delta RT Type II SC Content (M vs. F)				
2						
3	**Mixed-effects model (REML)**	Matching: Across row				
4	Assume sphericity?	No				
5	Alpha	0.05				
6						
7	**Fixed effect (type III)**	**P value**	**P value summary**	**Statistically significant (P < 0.05)?**	**F (DFn, DFd)**	**Geisser-Greenhouse's epsilon**
8	Treatment (between columns)	0.1175	ns	No	F (3.005, 17.60) = 2.256	0.4293
9						