EFFECTS OF HELIOX ON RESPIRATORY MECHANICS AND SENSORY RESPONSES DURING EXERCISE IN ENDURANCE-TRAINED MEN AND WOMEN

by

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B.H.K., The University of British Columbia, 2010

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in

THE FACULTY OF GRADUATE STUDIES

(Kinesiology)

THE UNIVERSITY OF BRITISH COLUMBIA
(Vancouver)

September 2012

ABSTRACT

Mechanical ventilatory constraints have been shown to develop in healthy endurance-trained (ET) men, and both ET and untrained women due to structural and functional sex-based differences with respect to the pulmonary system. The purpose of this study was to compare the effects of unloading the respiratory system using a heliox ($He-O_2$) inspirate on expiratory flow limitation (EFL), the work of breathing (WOB), operational lung volumes and sensory responses (leg and breathing discomfort) between men and women. It was hypothesized that $He-O_2$ would reduce EFL, operational lung volumes, the WOB and sensory responses while increasing airflow rates, minute ventilation (V'_E) and exercise performance. The aforementioned changes would occur to a greater extent in women and those developing EFL breathing room air (RA). Endurance trained men (*n* = 11) and women (*n* = 11) competitive cyclists completed two 5 km time trials (TT), breathing either RA or $He-O_2$. The maximum expiratory flow-volume (MEFV) curve method was used to determine EFL. An esophageal balloon catheter was used to measure the WOB as determined by transpulmonary pressure (the difference between esophageal and mouth pressures). Sensory responses were recorded throughout the TTs. Both sexes had a small (albeit non-significant) 2.3% improvement in power output breathing $He-O_2$. During the RA TT, 60% of women and 36% of men developed EFL. Heliox significantly increased the MEFV curve for both sexes however 40% of women and 45% of men still developed EFL. The magnitude of EFL was variable throughout both TT's for all subjects due to alterations in end expired lung volume and expiratory flow rates, as subjects utilized the $He-O_2$ induced enhanced ventilatory reserve. Despite significantly lower V'_E, women had similar WOB and operational lung volumes as men. Sensory responses were not affected by sex, inspirate, or presence of EFL. Collectively these findings suggest that EFL occurs to various extents throughout endurance exercise in both sexes and may limit endurance performance. Sex-based differences in pulmonary structure and function predispose women to mechanical ventilatory constraints breathing RA and increase women's relative cost of breathing compared to men.

PREFACE

Research ethics was approved by the UBC Clinical Research Ethics Board, CREB Number H11-02521.

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LIST OF ABBREVIATIONS

EFL	Expiratory Flow Limitation
EELV	End Expired Lung Volume
EILV	End Inspiratory Lung Volume
ET	Endurance Trained
$\mathbf{E_{tot}}$	Expiratory Total
FAM	Familiarization time trial
$\mathbf{f_b}$	frequency of breathing
FEV	Forced Expiratory Volume
FRC	Functional Residual Capacity
FVC	Forced Vital Capacity
He	Helium
$\mathbf{He\text{-}O_2}$	Heliox
HR	Heart Rate
$\mathbf{I_{el}}$	Inspiratory elastic
$\mathbf{I_{res}}$	Inspiratory resistive
IC	Inspiratory Capacity
M	Men
MEF	Maximum Expiratory Flow
MEFV	Maximum Expiratory Flow Volume
NEFL	Non-Expiratory Flow Limitation
NEP	Negative Expiratory Pressure
$\mathbf{N_2}$	Nitrogen
$\mathbf{P_E}$	Esophageal Pressure
$\mathbf{P_M}$	Mouth Pressure
PAV	Proportional Assist Ventilator

PEF	Peak Expiratory Flow
RA	Room Air
RER	Respiratory Exchange Ratio
RPE	Rating of Perceived Exertion
RPM	Revolutions Per Minute
TLC	Total Lung Capacity
TT	Time Trial
$\mathbf{V'_{E}}$	Minute Ventilation
$\mathbf{V'_{E\ CAP}}$	Ventilatory Capacity
$\mathbf{V'O_2}$	Oxygen consumption
$\mathbf{V'O_{2MAX}}$	Maximal oxygen consumption
$\mathbf{V'O_{2RM}}$	Maximal oxygen consumption by the respiratory muscles
$\mathbf{V'O_{2TOT}}$	Total Body maximal oxygen consumption
$\mathbf{V'CO_2}$	Carbon dioxide production
$\mathbf{V_T}$	Tidal Volume
W	Women
WOB	Work of Breathing

ACKNOWLEDGEMENTS

I would like to thank Dr. Bill Sheel, Dr. Michael Koehle and Dr. Ben Sporer for serving on my committee and providing insight and advice to enhance my study. I am especially grateful to my supervisor Dr. Bill Sheel for his guidance. The knowledge and skills I have acquired as a graduate student will benefit me in my future research and life endeavors.

I am grateful to all the past and present members of the Health and Integrative Pulmonary Laboratory for the education and assistance they provided throughout my master's degree: Jordan Guenette, Paolo Dominelli, Glen Foster, Bill Henderson, Jordan Querido, Josh McKay, Meaghan MacNutt, Jill Kennedy, and Simone Tomczak. Thank you to Melina Mirzaei and the graduate students in the Environmental Physiology Laboratory and the Genes, RNA, Informatics, and Protein Laboratory for their assistance with this study.

I would like to offer special thanks to the subjects who volunteered their time. Thank you to Dr. Don McKenzie for the use of the VeloTron cycle ergometer, and to Sid Reeve for helping construct the equipment shelving.

This study and my degree would not have been possible without funding from the National Sciences and Engineering Research Council of Canada and the University of British Columbia.

Finally, thank you to my family and friends for supporting my academic pursuits.

INTRODUCTION

Endurance training causes changes to the cardiovascular and metabolic systems to meet the augmented aerobic energy requirements (26, 42, 72, 73). Despite high ventilatory rates to enhance oxygen delivery over prolonged periods of time, beneficial effects to the lungs and airways have not been directly demonstrated with endurance training (51, 70). As such, increased demands from the enhanced cardiovascular (cardiac output and stroke volume) and metabolic systems (skeletal muscles vascularity and oxidative capacity) have been shown to exceed the capabilities of the respiratory system in healthy individuals during progressive exercise. By way of expiratory flow limitation (EFL), an increased work of breathing (WOB), diaphragm fatigue, sensations of breathlessness, and decrements in arterial blood gas status, the respiratory system is able to limit exercise performance (21, 32, 35, 44, 53).

To achieve the high minute ventilation (V'_E) required by heavy exercise, both tidal volume (V_T) and breathing frequency (f_b) must increase. These increases are met by increasing expiratory and inspiratory flow rates. Unlike inspiratory flow, expiratory flow at mid and low lung volumes is independent of effort and dependent on the intrinsic properties of the lungs. Healthy individuals exercising near maximal capacity can reach their maximal expiratory flow rates (45). When maximal expiratory flow rates are reached, expiration becomes flow limited. For a given lung volume, no further increases in expiratory airflow rate can be achieved despite an increase in pleural pressure. In order to achieve a further increase in expiratory flow rates and V'_E, end expired lung volume (EELV) is increased to take advantage of higher flow rates available at higher operating lung volumes. As operational lung volumes increase, the shortened inspiratory muscles are at a mechanical disadvantage. An elevated end inspiratory lung volume (EILV) increases the elastic WOB as the lungs are no longer operating on the most compliant portion of the pressure-volume curve. The WOB demanded by heavy exercise appears to cause a redistribution of blood flow away from the locomotor muscles, compromising aerobic capacity and exercise performance (35). If V'_E is mechanically constrained by way of EFL, alveolar ventilation could potentially be limited. Consequently the arterial partial pressure of oxygen would decrease, leading to exercise induced arterial hypoxemia and subsequently a reduced exercise capacity. Concurrent with the onset of EFL and changes in operational lung volumes, there appears to be an accompanying increased sensation of breathlessness (‘exertional’ dyspnea) (37, 54).

The aforementioned findings are predominantly based on data obtained in ET men during heavy or maximal exercise. There is growing evidence however, that mechanical ventilatory constraints may be more predominant in women as a result of sex-based differences in lung structure and function. Structurally, for a given height, women have smaller lung volumes and less alveoli with a reduced alveolar surface area (82). When matched for lung volume, women typically have smaller diameter airways compared to men (56, 77). Functionally, diffusion capacity is reduced due to the smaller alveolar surface area, while smaller airway diameters increase airflow resistance and reduce maximal expiratory flow rates compared to age and height matched men, even when matched for total lung capacity (TLC) (30, 52, 77). Due to a lower ventilatory reserve, EFL has shown to be more prevalent in women despite lower maximal V'_E, (32).

Lung and airway size appear to play a key role in the susceptibility of EFL within women. Specifically, reduced vital capacities (based on predictive normative values) and high V'_E achieved by ET women appear to increase EFL susceptibility (23, 53). Women with forced vital capacities (FVC) much larger than predicted values have greater ventilatory reserves allowing the generation of high flow rates less likely to encroach on the maximal expiratory flow-volume (MEFV) curve (32).

The ventilatory reserve can be increased with a helium-oxygen inspirate (heliox, $He\text{-}O_2$). Helium's (He) lower density and higher viscosity compared to nitrogen (N_2) reduces airflow turbulence, reducing the flow-resistive WOB and increasing the MEFV curve compared to room air (RA) (13, 85). As a result EFL, EELV and the resistive WOB have been shown to decrease in trained male cyclists when breathing $He\text{-}O_2$ compared to RA (54). Elite female runners inspiring $He\text{-}O_2$ have also shown reductions in EFL and operational lung volumes with increases in V'_E. However V'_E only increased for women that had no longer developed EFL when breathing $He\text{-}O_2$ (53) suggesting that limitations to the MEFV curve constrain V'_E. Accordingly, the goal of the present study was to directly compare the effects of unloading the respiratory system using a $He\text{-}O_2$ inspirate between men and women. Specifically, this study aimed at determining: 1) if reducing airflow resistance (by way of $He\text{-}O_2$) will reduce EFL, operational lung volumes, and the WOB while increasing V'_E and exercise performance (5 kilometer (km) time trial (TT)) compared to RA 2) if the aforementioned changes will occur to a greater extent in ET women compared to ET men 3) if sensations of breathlessness will be affected by $He\text{-}O_2$ and potentially the reduced mechanical ventilatory constraints and 4) if breathing $He\text{-}O_2$ in comparison to RA will induce an increase in 5 km TT performance.

REVIEW OF LITERATURE

It is widely accepted that endurance training causes adaptations to the cardiovascular and metabolic systems, with little direct evidence of change to the pulmonary system (70). As such, oxygen transport and utilization, by the cardiovascular system (cardiac output and stroke volume) and skeletal muscles (vascularity and oxidative capacity) were the more plausible factors limiting aerobic capacity. More recently however, young healthy men and women have been shown to reach the limits of their respective pulmonary systems during heavy exercise. The lungs and airways by way of expiratory flow limitation (EFL), increased operational lung volumes, elevated work of breathing (WOB) and heightened sensations of leg and/or breathing discomfort may be the factors limiting exercise performance. This is in stark contrast to previous beliefs that the pulmonary system was 'overbuilt' and the maximal capacity to generate ventilation would never be reached during rigorous exercise in healthy individuals (65).

Development of EFL and elevated operational lung volumes during maximal exercise have been shown in endurance trained (ET) men (1, 32, 44, 60). Endurance trained women have been shown to be more susceptible to EFL, with higher relative operational lung volumes and a greater WOB for a given minute ventilation (V'_E) compared to their male counterparts (32). Sex-based differences in pulmonary structure and function are likely the cause of women's augmented mechanical ventilatory constraints. Structurally women have smaller lung volumes for a given standing height and comparatively smaller diameter airways when matched for lung volume relative to men (55, 82). The smaller diameter airways increase airway resistance, reducing expiratory airflow generating a smaller ventilatory capacity. Despite reaching lower metabolic rates, not only ET but also untrained women develop mechanical ventilatory constraints (23, 53).

To alleviate mechanical ventilatory constraints, researchers have attempted to unload the respiratory system using: mechanical ventilation (proportional assist ventilation (PAV), inspiratory pressure support, and continuous positive airway pressure), bronchodilators and heliox ($He\text{-}O_2$). Healthy ET men cycling at a sustained heavy workload under mechanical ventilation (PAV) have shown increased time-to-exhaustion and V'_E, with decreased oxygen consumption ($V'O_2$) and sensory perceptions of leg and breathing discomfort for a given workload compared to unassisted breathing (37).

Bronchodiators, short and long-acting B_2-agonists, assist in expiration by dilating the conducting airways increasing the forced expiratory volume in 1 sec (FEV_1) and V'_E in individuals with exercise-induced asthma as well as healthy controls (15). However, endurance performance was not improved by inhalation of a B_2-agonist in studies with strong internal validity using athletes with normal pulmonary function (15, 81). Bronchodilators have alleviated EFL for chronic obstructive pulmonary disease

(COPD) patients, but increases in $FEV_{1.0}$ and inspiratory capacity (IC) developed irrespective of EFL occurrence (20).

Helium's (He) lower density relative to nitrogen (N_2) decreases airflow resistance. For a given lung volume airflow rates are higher breathing He-O_2 thereby expanding the maximum expiratory flow-volume (MEFV) curve. Increases in V'_E and decreases in EFL and end expired lung volume (EELV) resulting in performance improvements, have been shown in healthy ET individuals and individuals suffering from diseases such as COPD inspiring He-O_2 (13, 25, 53, 67).

The current literature is lacking in a direct comparison between men and women matched for aerobic capacity, on the ventilatory effect of mechanically unloading the respiratory muscles. Potentially a sex-based difference in the susceptibility and magnitude of EFL would cause different V'_E and performance responses when mechanically unloaded.

The purpose of this review is to examine the existing literature for 1) sex-based differences in pulmonary mechanics, and 2) the effects of He-O_2 as an inspirate on lung mechanics, sensory responses and performance. Mechanical ventilatory constraints effect on blood gases have been thoroughly investigated elsewhere and therefore will not be discussed in the following literature review (22).

NORMAL RESPIRATORY RESPONSE TO EXERCISE

At rest V'_E occurs around functional residual capacity (FRC), where lung compliance is the greatest and a balance occurs between the lungs' inward elastic recoil and the chest wall's tendency to spring outward. Inspiration is initiated when the diaphragm contracts bringing the abdominal contents downward, decreasing pressure within the thorax causing air to flow into the lungs. Expiration is passive as the lung and chest wall return to their equilibrium positions at FRC. During quiet breathing resistance to airflow is low because flow is laminar with high axial flow rates proportional to pressure development. Progressive exercise increases the metabolic rate of the exercising muscles. For which oxygen consumption and removal are met by increasing V'_E. The external intercostals and accessory respiratory muscles (scalene and sternocleidomastoid) assist in inspiration, by further expanding the rib cage generating a greater drop in pressure enhancing the rate of airflow into the lungs. Expiration becomes active as the abdominals and internal intercostals contract, increasing intra-abdominal pressure pushing the diaphragm upwards while pulling the rib cage down, forcing air out of the lungs. The work done by the muscles of expiration act to decrease EELV below resting FRC, lengthening the inspiratory muscles to enhance the skeletal muscles length-tension relationship and optimize force output (88). A reduced EELV allows tidal volume (V_T) to increase while keeping end inspired lung volume (EILV) under 90% of total lung capacity (TLC); minimizing the elastic WOB while remaining on the most compliant portion of the lungs pressure-volume curve. When V_T reaches 50-60% of vital capacity, further increases in V'_E are met by increasing breathing frequency (f_b) which optimizes the elastic WOB by using energy stored and recovered in the lungs and chest wall. Elevated flow rates come at the expense of a turbulent flow pattern in the larger conducting airways increasing the resistive WOB. Coincidentally, the laryngeal and tracheal diameters increase (bronchodilation), to decrease resistance and increase airflow rate. Overall the ventilatory pattern and operational lung volumes function at the lowest possible metabolic cost, using less than 10% of total body $V'O_2$ (1).

Exceptions – Endurance-trained Athletes

Endurance-trained athletes demand high inspiratory and expiratory flow rates to meet their elevated ventilatory demands during exercise. Higher flow rates are achieved by generating greater intra-thoracic pressure. However, unlike inspiration, active expiration is effort independent such that a critical pressure exists at which point maximal expiratory flow is reached. The critical pressure and maximal expiratory flow rates can be met by ET athletes. At this point any effort to generate an intra-thoracic pressure exceeding the critical pressure will not increase expiratory flow rate. Rather, expiratory flow rate can even be reduced as airways downstream from the EFL segment undergo dynamic compression. At this point, expiratory flow rates can only be increased by increasing EELV to take advantage of higher flow rates available at higher lung volumes. This action shortens the inspiratory muscles, which are no longer at an optimal length to produce force and have a reduced contractility time due to a higher f_b. Increasing EELV and V_T increases EILV which has been shown to exceed 90% of TLC, greatly increasing the elastic WOB. The resistive WOB is also increased as expiratory flow rates increase and take on a more turbulent pattern in the smaller airways. Increases in operational lung volumes and/or dynamic compression may cause a reflex inhibition of the hyperventilatory response and alter breathing pattern (69). An increased WOB will require more oxygen and blood flow, likely taking a larger percentage of total body blood flow away from the exercising muscles (35). An increased WOB could lead to diaphragm fatigue, increased perceptions of breathing and limb discomfort, and/or blood redistribution, ultimately limiting aerobic exercise capacity.

MECHANICAL VENTILATORY CONSTRAINT IN MEN

Expiratory Flow Limitation - Susceptibility

Highly trained young men ($V'O_{2MAX} > 60$ ml·kg^{-1}·min^{-1}) with normal pulmonary function have the ability to reach the limits of their pulmonary systems by way of EFL during sustained heavy exercise.

Expiratory flow limitation was found in 3 of 8 highly trained male cyclists tested by Guenette *et al.* (32), all 8 competitive distance runners tested by Johnson *et al.* (44), and only 1 of 10 competitive cyclist tested by Mota *et al.* (60). All men in these studies were of similar age, possessed exceedingly high aerobic capacities (average $V'O_{2MAX}$: 70, 73, 72 $ml \cdot kg^{-1} \cdot min^{-1}$ respectively), and thus reached similar maximal V'_E (average V'_E: 161, 186, 147 $l \cdot min^{-1}$ respectively) whether EFL or non-EFL (NEFL). The vast discrepancy in susceptibility of EFL is interesting since subject characteristics were homogenous with the only differences between studies being testing methodologies and exercise modalities. The forward lean adopted during running facilitates higher flow rates (compared to standing upright) which increase the MEFV curve (33). The accentuated trunk flexion and arm bracing of cyclists enhances the ability of the accessory muscles of respiration to expand the rib cage, increasing vital capacity (8). Yet, discrepancies in body position do not account for the differences in EFL susceptibility between the two cycling studies.

Johnson *et al.* (44) tested EFL by the MEFV curve technique and by athletes meeting or exceeding maximal effective pleural pressure. Tidal volume impinging on the MEFV curve in addition to attainment of maximal effective pleural pressure appeared to justify a finding of 100% EFL in subjects. Furthermore, when Johnson *et al.* (44) gave subjects a chemical stimulus (3% CO_2 or hypoxia) to breathe during exercise, sub-maximal exercise V'_E increased, but at high work rates where EFL occurred, V'_E failed to increase. Respiratory muscle fatigue was unlikely since peak esophageal pressure increased during the end of exercise and expiratory pressure generation was less than a third of that generated during the maximal voluntary ventilation test performed at rest.

The negative expiratory (NEP) technique was used by Guenette *et al.* (2007) and Mota *et al.* (1999), however Guenette *et al.* (2007) obtained 3 NEP tests during the final workload whereas Mota *et al.* (1999) obtained only 1 NEP test during the last minute of each stage. Potentially during the final minute of exercise Mota *et al.* (1999) subjects altered their EELV and thus removed the EFL. Overall determination of EFL is highly sensitive to the measurement techniques, and extreme care must be taken to accurately detect EFL.

Expiratory Flow Limitation - Magnitude

The magnitude of EFL in male endurance athletes varies from 12-76% (44) to 25-100% (1) V_T overlapping the MEFV curve. The discrepancy in the magnitude of EFL appears to be a result of the V'_E the athletes reach during maximal exercise. For example, the cyclist with 100% V_T EFL at maximal exercise was ventilating at 185 $l \cdot min^{-1}$ whereas the individuals with 25% V_T EFL had maximal V'_E of 162 $l \cdot min^{-1}$.

McClaran *et al.* (54) tested highly trained male cyclists breathing a hyperoxic mixture (26% O_2-N_2) and found all 6 subjects developed EFL during heavy and maximal exercise. When the chemoreceptor drive to breathe was increased via increased V_T, by added dead space, the magnitude of EFL was elevated in all subjects. Overall it appears as V'_E increases so does the susceptibility and magnitude of EFL. In the aforementioned studies athletes were reaching average V'_E of 160-170 $l \cdot min^{-1}$, far exceeding the V'_E of an untrained individual.

During heavy exercise, when EFL occurs, V_T has been shown to decrease with increases in EELV (32, 53, 54, 60). This is in contrast to the usual plateau in V_T at high V'_E, with increases in V'_E brought about by increasing f_b. Increases in EELV (potentially in excess of FRC) allow generation of higher expiratory flows at higher lung volumes, however, it comes at the expense of an elevated EILV (90% TLC), thereby increasing the elastic WOB (44). The increase in operational lung volumes augment inspiratory muscle pressure which can exceed 80% maximal dynamic capacity (1, 44).

Pelligrino *et al.* (69) showed further evidence for a correlation between changes in operational lung volumes and EFL in which an expiratory threshold load was applied to both EFL and non-EFL subjects. The expiratory threshold load decreased expiratory flow rates and increased expiratory time for both groups. However, EELV decreased in EFL subjects because it took longer for EFL subjects to reach flow rates causing EFL, therefore a relative decrease in EELV occurred. In contrast the NEFL subjects EELV increased, by way of a smaller increase in expiratory time; for the same given V'_E less air was expired causing increases in EELV.

SEX-BASED DIFFERENCES IN PULMONARY STRUCTURE AND FUNCTION

Structural

Dysanapsis, or unequal growth between lung parenchyma size and airway (intra-thoracic trachea and large bronchi) size was first introduced by Green *et al.* (28). Mead (1980) went on to show that dysanapsis occurs to a greater extent in young boys and women who have airway diameters 17% smaller than men when matched for lung size, with the difference in growth occurring later in life (56). Acoustic reflectance estimates have shown healthy women's tracheal cross-sectional areas are 29% less than men matched for TLC (52). Recently computed tomographic imaging has found the larger conducting airways in women are significantly smaller than those of men matched for lung size, as are the luminal areas (77). The larger lungs possessed by men for a given height result in larger lung volumes and alveolar surface areas, and therefore a greater number of alveoli (82). Consequently, at rest, women have a lower diffusing capacity for oxygen and carbon monoxide (66).

Functional

Structural sex-based differences in the diameter of the large conducting airways and lung volumes translate into differences in pulmonary function. When airway diameter is reduced, resistance to airflow markedly increases based on Poiseuile's law. As airway resistance increases, flow rate decreases; women's smaller diameter airways reduce maximal expiratory flow rates and maximal expiratory flow at 25% TLC ($MEF_{25\%}$) compared to men when matched for TLC (52) with an overall reduced capacity to generate V'_E. Reduced maximal V'_E based on lower achievable metabolic rates by women compared to men led researchers to believe women would not reach their maximal capacity to ventilate. However, ET women and even untrained women are capable of reaching V'_E high enough to impede on their relatively reduced ventilatory reserve (32, 53).

Female Sex Hormones

Evidence of increased resting V'_E during the luteal phase due to elevated progesterone (74) led researchers to believe that female steroid hormones could affect ventilatory mechanics. However, the elevated V'_E across cycle phase has only been shown to affected exercise performance in regularly menstruating 'non-athletes', not regularly menstruating or amenorrheic 'athletes'; the discrepancy in exercise tolerance could be due to subjective sensations of dyspnea (74). Lebrun *et al.* (47) found the magnitude of the effect of female sex hormones on indices of performance shows tremendous variability between subjects and appears to be more relevant on an individual basis. A recent study from our research group (46) found menstrual cycle phase did not have any effect on exercise V'_E. This finding is consistent with several previous studies which failed to find an effect of menstrual cycle phase on the integrated ventilatory response to exercise (9, 10, 18). Our research group also found vast heterogeneity in the cyclical hormone profiles of a relatively homogeneous subject group. Menstrual cycles appear to occur along a continuum of the phases; a 'normal' cycle with discrete phases is not always apparent.

MECHANICAL VENTILATORY CONSTRAINTS IN WOMEN

A reduced ventilatory capacity combined with high V'_E would in theory predispose women to mechanical ventilatory constraints – EFL and relative hyperinflation, at a lower V'_E and $V'O_2$ compared to men. The lone female subject studied by Aaron *et al.* (1) had the greatest magnitude of EFL (60% of V_T), despite a V'_E (139 $l \cdot min^{-1}$) much lower than the male subjects. All the ET women with normal pulmonary function tested by Guenette *et al.* (32) developed EFL during maximal exercise while reaching high V'_E (120 $l \cdot min^{-1}$). In contrast to men, EFL is not exclusive to ET women; development of EFL has been shown in healthy women of varying aerobic capacities during maximal and sub-maximal exercise at V'_E of only 98 $l{\cdot}min^{-1}$ (23, 53, 84, 86).

The magnitude of EFL in women has been shown to range from 0 (NEFL) to 58% V_T overlapping the MEFV curve. At an equivalent V'_E (< 115 $l{\cdot}min^{-1}$) men do not develop EFL, thus making the magnitude of EFL in women much greater. Overall men develop EFL over a greater % V_T (up to 100% V_T) compared to women, however these particular men were reaching substantially higher V'_E in excess of 180 $l{\cdot}min^{-1}$ (1, 44).

Walls *et al.* (84) found, EFL was related to absolute V'_E in a group of untrained women. Despite relatively lower aerobic capacities ($V'O_{2MAX}$: 47 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$), the women with the greatest % V_T EFL at maximal exercise were also EFL during sub-maximal exercise (92 and 93% $V'O_{2MAX}$). This is in stark contrast to men; whereby only men with large aerobic capacities ($V'O_{2MAX}$ > 55 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$) reaching exceedingly high V'_E (160 $l{\cdot}min^{-1}$) develop EFL during maximal exercise. However, McClaran *et al.* (53) found the magnitude of EFL and changes in operational lung volumes were related to aerobic capacity whereby highly trained female runners ($V'O_{2MAX}$ > 57 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$) developed more EFL (32% V_T), compared to relatively untrained women ($V'O_{2MAX}$ < 56 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$; 10% V_T) and had higher EELV (trained: 48 *vs.* untrained: 53% TLC) and EILV (87 *vs.* 90% TLC) than their less fit counterparts. The significantly higher V'_E and flow rates the fitter women generated at the elevated work rates would encroach to a greater extent on their MEFV loop compared to women with the same size MEFV loop that reach lower V'_E.

Size versus Fitness

Exceedingly high V'_E attained by ET women compiled with smaller diameter airways and lung volumes further exacerbates EFL. However, women with abnormally large vital capacities (as percent predicted) and high expiratory flow rates do not develop EFL, nor do they show relative hyperinflation despite V'_E comparable to other women (1, 32). These women with enhanced pulmonary structures have unusually large MEFV curves providing a greater ventilatory reserve. The lone ET women studied by Guenette *et al.* (32) to not develop EFL possessed an FVC 134% predicted; this women could generate expiratory flow rates demanded by her high work rate without encroaching on her MEFV curve. Therefore, absolute lung structure, not just sex, appears to have the greatest impact on respiratory mechanics.

Recently, our research group showed, EFL was more prevalent in women with smaller lung volumes and diameter airways, and occurred regardless of aerobic capacity (22, 83). Larger aerobic capacities possessed by ET athletes will necessitate heightened V'_E responses that could lead to EFL in both men and women. However sex-based differences in ventilatory capacity and expiratory flow rates could predispose even untrained women with small aerobic capacities and low V'_E to EFL.

Operational Lung volumes

Akin to men, women decrease EELV at the onset of exercise, but when exercise intensities approach maximal, women increase EELV and consequently EILV to a significantly greater extent than men. The additional hyperinflation demonstrated by women may be the result of a reflex response brought about by their increased prevalence of EFL (32) to avoid dynamic airway compression and take advantage of higher flow rates available at higher lung volumes.

The increase in EELV causes women's V_T to be at a higher percent of TLC, where lung compliance is reduced and the elastic WOB increases to a greater extent than men. In an effort to prevent EFL or possibly because V_T is mechanically constrained and cannot be further increased, it appears women alter their breathing pattern, relying more on increases in f_b than V_T to increase V'_E (32, 53). By utilizing the tachypneic breathing pattern, women are able to decrease the elastic WOB using energy stored in the tissues.

WORK OF BREATHING

To increase V'_E as one transitions from rest to exercise requires an increase in intra-thoracic pressure development. To develop sufficient pressure, the inspiratory and expiratory muscles of respiration must generate greater muscular contractions, which increase the WOB. The WOB is comprised of an elastic and a resistive component: the elastic component must overcome the elastic properties of the lungs to recoil inward during inspiration, and the outward recoil of the chest wall during expiration; impediments to airflow through the tracheobronchial tree comprise the resistive component.

When V'_E occurs on the compliant portion of the lung's pressure-volume curve the elastic WOB is minimized. Increases in the elastic WOB occur when operational lung volumes increase, especially when EELV exceeds resting FRC and EILV is in excess of 80% TLC. At elevated lung volumes, the shortened inspiratory muscles are at a mechanical disadvantage. A greater intra-thoracic pressure, and thereby muscular contraction, is required to elicit a given volume change which can reach 89% of maximal dynamic capacity (44).

At rest and during low intensity exercise airflow is laminar, EELV is near resting FRC, and the total WOB for a given V'_E is similar in men and women. During progressive exercise as V'_E increases so does the WOB for men and women. For a given V'_E, women's WOB increases to a greater extent and has shown to be twice that of men at V'_E above 90 $l \cdot min^{-1}$ (32). To determine what component of the WOB was contributing to the sex-based differences Guenette *et al.* (30) measured the elastic and resistive components of the WOB during exercise in male and female ET athletes. An increased resistance was found to account for the total elevated WOB for a given V'_E in women. When both sexes were performing the same relative external muscle work, the total WOB was higher in women due to elevated inspiratory and expiratory resistive WOB components. The elevated resistive WOB in women was inversely related to lung size, and presumably airway size.

Women's smaller conducting airway diameters and relatively smaller lung volumes increase resistance to airflow, causing a reduced flow rate for a given driving pressure (ventilatory muscular contraction) (14). When V'_E increases and airflow is predominated by turbulent characteristics, women's resistive WOB is augmented and requires substantially greater external muscle work.

As a consequence of smaller airway diameters, increased airflow resistance, and likely EFL, women engage in a different breathing pattern than men. The higher frequency breathing pattern reduces the elastic WOB by taking advantage of energy stored in the tissues. This is adopted because V'_E occurs at a higher percentage of TLC at the expense of reduced lung compliance. Thus for an absolute V_T women's elastic WOB is higher than men's but due to the tachypneic breathing pattern, for a given V'_E the inspiratory and expiratory elastic WOB is similar to men's (30). One could speculate that an increased WOB in women associated with increases in operational lung volumes and EFL would result in a greater oxygen cost of breathing.

CONSEQUENCES OF MECHANICAL VENTILATORY CONSTRAINTS

Increased Oxygen Cost of Breathing

There is strong evidence to suggest the oxygen cost of exercise hyperpnea appears to be increased in those susceptible to EFL. Without mechanical constraint, the respiratory muscle's oxygen cost of V'_E ($V'O_{2RM}$) during maximal exercise has shown to be ~10% of total body $V'O_2$ ($V'O_{2TOT}$). When EFL develops and inspiratory muscle pressure is near capacity, $V'O_{2RM}$ increases to ~13-15% of $V'O_{2TOT}$ (1). This data was obtained in men, the lone women tested by Aaron *et al.* (1) developed substantial EFL (60% V_T), and had the highest WOB and the highest $V'O_{2RM}$ (15.4% $V'O_{2TOT}$) despite a lower maximal V'_E than men. Presumably women's oxygen cost of V'_E is greater than men's.

As V'_E and the WOB increase, blood flow to the exercising locomotor muscles has been shown to decrease in trained male cyclists possessing a leg $V'O_2$ of 81% $V'O_{2TOT}$ when breathing room air. When the WOB was artificially increased by imposing a resistive load to the respiratory muscles, leg $V'O_2$ decreased to 71% $V'O_{2TOT}$ and increased (89% $V'O_{2TOT}$) when respiratory muscles were unloaded with PAV (35). A correlation between norepinephrine spillover and leg vascular resistance suggests changes in leg blood flow and oxygen delivery are sympathetically mediated and triggered by changes in the WOB, possibly via the respiratory muscle chemoreflex effect. During maximal exercise in highly trained men, Harms *et al.* (36) found the respiratory muscles used up to 14-16% of cardiac output. While EFL was not measured in this study, it is likely those with an elevated WOB due to mechanical constraints would require a larger percentage of cardiac output to meet the increased metabolic demands of their respiratory muscles. Likely when EFL develops and $V'O_{2RM}$ is further augmented greater amounts of blood flow to the exercising locomotor muscles would be redirected to the respiratory muscles.

A reduction in leg blood flow due to a high WOB occurring during heavy exercise appears to reduce exercise performance in highly trained men. When respiratory muscles were unloaded (PAV), and the WOB decreased, exercise performance increased by 14%, whereas when respiratory muscles were loaded (resistive) performance decreased by 15% compared to a no load trial (37).

If women are predisposed to EFL and thus a greater WOB, it is presumable the proportion of cardiac output directed to the respiratory muscles would be elevated at a cost to leg blood flow. Consequently women would endure greater decrements in exercise performance relative to men. If mechanical ventilatory constraints by way of EFL augment the WOB, researchers then speculate if a point exists at which the diaphragm will begin to fatigue.

Diaphragm Fatigue

A high oxidative capacity and capillary density appeared to make the diaphragm well suited for the high demands imposed by exercise (59). Recent evidence of diaphragm fatigue is proving the diaphragm may not be ideally designed for prolonged heavy exercise. Interestingly, sex-based differences with respect to diaphragm fatigue appear to be prevalent (31)

At high exercise intensities (> 85% $V'O_{2MAX}$) when V'_E is in excess of 120 $l \cdot min^{-1}$, inspiratory flow rates are increased 8-10 times resting levels, indicating an increase in the velocity of inspiratory muscle shortening, with peak diaphragm pressure reaching 60% maximum capacity. The increased elastic loads and velocity of muscle shortening cause substantial increases in the work of the diaphragm. Johnson *et al.* (43) found evidence of diaphragm fatigue in healthy males, by decreases in trans-diaphragmatic pressure when electrically stimulated (Bilateral Phrenic Nerve Stimulation technique) near end exercise. At this point the accessory muscles of inspiration were contributing to a greater extent to maintain V'_E as evident by a plateau in trans-diaphragmatic pressure with increasing V'_E (43).

Compared to men, the female diaphragm appears to be more resilient to fatigue. When diaphragm fatigue was measured in ET men and women during heavy exercise, women showed smaller decrements in trans-diaphragmatic pressure twitch potentiations 10, 30, and 60 minutes post exercise. During exercise, the diaphragm's contribution to total inspiratory force output decreased in male subjects who were more reliant on accessory muscles for inspiration, while the women had little change in diaphragmatic contribution, suggesting women have an increased resistance to fatigue (31).

Despite evidence of diaphragm fatigue, respiratory muscles are still capable of generating high ventilatory rates. Minute Ventilation increased linearly throughout exhaustive exercise in ET men, while ET women's V'_E plateaued at high rates. The plateau in V'_E was likely due to mechanical ventilatory constraints as women's diaphragmatic contributions changed little during exercise (31). Diaphragm fatigue does appear to have an effect on limb blood flow due to its association with a respiratory muscle–limb reflex. This metaboreflex appears to originate in the diaphragm and occur at its peak during fatiguing diaphragmatic contractions (75), causing ischemia, with increases in limb vascular resistance and decreases in resting limb blood flow. High levels of central respiratory motor output did not affect leg blood flow or vascular resistance, supporting the argument for a peripheral cause of exercise termination.

SENSORY RESPONSES

Dyspnea

Traditionally, limb discomfort and whole body fatigue have been the primary factors causing cessation of exercise in healthy individuals (63). The leading source of termination of exercise by individuals suffering from respiratory diseases such as COPD, is dyspnea (63). Dyspnea is "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity. The experience derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioral responses" (4).

Dyspnea increases with increasing exercise intensity, and rises steeply during heavy and maximal exercise in healthy individuals. Although direct evidence relating dyspnea to EFL or hyperinflation in young healthy individuals has yet to be shown in the literature, significant reductions of breathing discomfort during heavy exercise, have been shown when the respiratory muscles were unloaded (37, 71). When a resistive load was added, ratings of dyspnea significantly increased. If EFL and hyperinflation increase the work of breathing, based on the aforementioned studies, perceptions of breathing discomfort would likely also be increased.

Considerable evidence relating mechanical ventilatory constraints to heightened dyspnea exists in individuals suffering from COPD and older populations. Individuals with COPD develop EFL, lung hyperinflation, and an elevated WOB at rest and during exercise. The best predictor of dyspnea in COPD patients appears to be increases in EELV; Marin *et al.* (50) found dyspnea increased when IC decreased (indicator of EFL) during exercise. If similar mechanical ventilatory constraints (increases in operational lung volumes and EFL) are occurring in healthy men and women, dyspnea could potentially cause cessation of exercise via the same mechanism.

This mechanism is brought about by lung hyperinflation and airway dynamic compression which is detected by receptors in the airways, lungs, and respiratory muscles and relayed to the somatosensory cortex within the brain. The somatosensory cortex compares the afferent feedback with the efferent information (copy of the respiratory motor output) from the motor cortex. If the ventilatory motor output does not match the efferent sensory information (i.e., hyperinflation) neuro-mechanical uncoupling occurs, increasing dyspnea (4, 76).

Sex-based differences in pulmonary structure and function appear to increase dyspnea ratings in older women and women with COPD. Despite both men and women undergoing the same age-related declines in lung structure and function, for a given $V'O_2$, healthy older women report significantly higher ratings of dyspnea, and a significantly greater number of older women report dypnea as the reason for exercise cessation (64). Similarly, for a given airway obstruction, women suffering from COPD report higher dyspnea (19).

Evaluating dyspnea provides insight into the interconnection between the psychological and physiological changes occurring during exercise (62). Potentially, mechanical ventilatory constraints could decrease exercise capacity by way of perceptions of discomfort, which may be higher in women (54).

Leg Discomfort

As previously mentioned, diaphragm fatigue appears to trigger a metaboreflex causing vasoconstriction of locomotor muscles, ultimately reducing limb blood flow. When respiratory muscle work was reduced (PAV) and diaphragm fatigue no longer occurred, sensations of leg discomfort were reduced (37, 71). When the resistive ventilatory load was increased, further exacerbating diaphragm fatigue, leg fatigue and ratings of leg discomfort were augmented.

HELIOX

Helium has a density a third that of N_2 and a higher viscosity. When the driving pressure to generate ventilation is low, both He and N_2 flow patterns are laminar (streamline with high axial flow rates). When the driving pressure to breathe is increased, the density and viscosity differences between the gases emerge. Viscous forces dominate in He due to a low Reynold's number, so flow remains laminar to a greater extent at high flow rates in the smaller airways. Nitrogen, however, takes on a more turbulent flow pattern with eddy formations at junctions in the tracheobronchial tree due to the dominance of inertial forces characteristic of a high Reynold's number. Breathing heliox (He-O_2) instead of room air (RA) will allow higher flow rates directly proportional to the pressure gradient generated by the thoracic cavity. The lower resistance of He-O_2 will require smaller increases in trans-pulmonary pressure to generate high expiratory flows; a lower intra-thoracic pressure will decrease dynamic compression of the airways. Any effect He has on increasing V'_E and exercise capacity should be caused by its physical properties (i.e., lower density) as it has no direct positive metabolic action at the cellular level (12).

At low exercise intensities below the ventilatory threshold, He-O_2 has not been shown to affect V'_E. Low V'_E requires a low driving pressure, so airflow (both RA and He-O_2) is laminar. During heavy exercise when intrapleural pressures increase and V'_E exceeds the ventilatory threshold, the density induced differences in airflow characteristics between RA and He-O_2 emerge; RA with a more turbulent flow pattern and He-O_2 with a predominantly laminar flow pattern. It is at elevated V'_E and flow rates where EFL develops when breathing RA. For a given lung volume, He-O_2 increases airflow rate enabling generation of larger V_T, potentially eliminating EFL and the likely ensuing cascade of events – increases in operational lung volumes, WOB, and likely dyspnea.

Above the ventilatory threshold, and above 70-85% $V'O_{2MAX}$, increases in V'_E when inspiring He-O_2 have been shown in both healthy young men and women (6, 13, 53, 79, 87). Although EFL was not measured in all studies, it could be presumed the differences in V'_E only occurred during heavy exercise when V'_E was potentially mechanically constrained during RA breathing by EFL.

McClaran *et al.* (53) showed in a group of highly trained female runners, only those that developed EFL during RA breathing increased their V'_E and maximal expiratory flow rates when breathing He-O_2 while running at maximal capacity. Heliox, as an inspirate, reduced EFL by increasing the MEFV curve; relatively smaller increases in EELV occurred and subjects were able to increase both V_T and f_b. Inspiring He-O_2 had no effect on V'_E or operational lung volumes in the women that did not develop EFL breathing RA presumably because the NEFL women could achieve the highest V'_E they required without mechanical constraint.

The chemical drive to breathe can be increased by inspiring 3% CO_2. When a group of untrained young healthy individuals inspired a hypercapnic gas mixture (3% CO_2 - 21% O_2 - 76% N_2) maximal V'_E was increased to the same extent as when He-O_2 (79% He - 21% O_2) was inspired. However, the magnitude of EFL at maximal exercise was increased during the 3% CO_2 trial (16% V_T *vs.* He-O_2 5% V_T), because 3% CO_2 was not capable of enhancing the ventilatory capacity (6). When the same protocol was used on older men, EFL occurred to a greater extent during 3% CO_2 (22% V_T) than RA (12% V_T) or He-O_2 (10% V_T). Above the ventilatory threshold, V'_E increased more so when breathing He-O_2 compared to RA or 3% CO_2, due to age-induced mechanical limitations (7). It is likely the young subjects were able to increase their V'_E to the same level when inspiring 3% CO_2 as when inspiring He-O_2 because of the lower maximal V'_E (100 $l \cdot min^{-1}$) their untrained aerobic capabilities demanded. If the young subject group had been ET as studied by Johnson *et al.* (44), substantially higher V'_E would likely not have been achievable when inspiring 3% CO_2 due to mechanical constraint by the relatively reduced ventilatory capacity.

Adding dead space to the breathing apparatus increases the chemoreceptor drive to breathe through increases in V_T. When McClaran *et al.* (54) had ET male cyclists inspire N_2O_2, EELV increased and V_T decreased at maximal exercise. When dead space was added to the N_2O_2, V_T was elevated but could not be maintained during maximal exercise due to impedance with the MEFV curve. A He-O_2 inspirate increased the athlete's MEFV curve, preventing EFL and preserving V_T (plateau) during maximal exercise with a lower EELV. When dead space was added to the He-O_2 condition, greater increases in V_T were capable with smaller increases in EELV at higher V'_E due to removal of EFL.

Performance

Increases in time-to-exhaustion, and maximal workloads achieved at a lower $V'O_2$ and $V'O_{2MAX}$ have been shown in healthy individuals when breathing He-O_2 (7, 13). The performance improvement is likely due to the greater V'_E and flow rates achievable; a result of the enhanced ventilatory capacity and reduced EFL. Unloading the respiratory muscles allows a significantly lower ventilatory mass to be moved during He-O_2 breathing compared to RA (87). The reduced oxygen cost of inspiring He-O_2 could increase locomotor blood flow (via the metaboreflex) and thus increase exercise performance.

During high-intensity exercise, COPD patients breathing He-O_2 were able to increase their endurance capacity via increases in V'_E brought about by reduction in lung dynamic hyperinflation, allowing increases in IC (67). The He-O_2 induced performance improvements occur only during maximal exercise whereby development of EFL is prevented and V'_E is not restricted due to a limited V_T (13).

Sensory Perceptions

Heliox has been shown to reduce breathing discomfort in healthy young ET individuals and healthy older individuals compared to RA breathing by reducing the load on the respiratory muscles, the degree of dynamic hyperinflation and EELV (7, 54). However, this is not a universal finding, as other studies have failed to find a difference in dyspnea during maximal exercise (6). Individual dyspnea ratings compared to EFL susceptibility were not provided, so it is unclear whether differences in dyspnea occurred in those that developed EFL compared to those that did not.

Individuals suffering from respiratory diseases have lower ratings of dyspnea when inspiring He-O_2. When the WOB is reduced in individuals with COPD by breathing He-O_2, increases in exercise tolerance and reduced rating of dyspnea arise (25, 63, 67). It should be noted that there are conflicting results with respect to He-O_2 alleviating dyspnea and EFL in COPD patients. However, the discrepancies could be a result of the different mechanisms causing EFL in COPD patients. Heliox has no effect on dynamic hyperinflation if EFL is caused by mucous (viscous) rather than the density independent mechanism occurring in healthy populations (17).

The effect of He-O_2 on leg fatigue in COPD patients varies from no effect to reduced ratings (25, 67). In healthy young individuals leg discomfort was not affected by He-O_2 (6) while leg discomfort decreased in older individuals (7). The current literature is lacking in a measure of leg fatigue for a He-O_2 inspirate in healthy individuals.

Work of Breathing, Diaphragm Fatigue, and Oxygen Cost of Inspiring Heliox

Due to the reduced airflow resistance, a given V'_E with He-O_2 will require less muscular effort than that of RA, reducing the WOB (13). Wilson and Welch (87) found a significantly lower ventilatory mass was moved while inspiring He-O_2 than 20% O_2 - 80% N_2 despite significantly higher V'_E due to He's lower density. The WOB, diaphragm fatigue, and oxygen cost of breathing have yet to be measured during exercise with He-O_2 in healthy ET individuals.

CONCLUSION

A balance between the chemical drive to breathe and mechanical constraints appear to regulate V'_E. Expiratory flow limitation and an increased WOB have been shown to develop in healthy ET men and both ET and untrained women. Why EFL develops in some individuals and not others, along with its affect on sensory perceptions is not completely understood. No studies have compared the effect of unloading the respiratory muscles with He-O_2 on EFL between ET men and women. The existing literature indicates that women are more susceptible to developing EFL, as are individuals with extraordinarily high ventilatory requirements. The differences in mechanical ventilatory constraints appear to be a result of structural and functional sex-based differences with respect to the pulmonary system. Exercise performance could be at risk due to mechanical ventilatory constraints elevating the WOB leading to diaphragm fatigue and/or a reduction in limb blood flow.

HYPOTHESES

1. During exercise with a He-O_2 inspirate EFL (susceptibility and magnitude), operational lung volumes and the WOB will be reduced while expiratory flow rates and V'_E will be increased in the men and women that develop EFL when breathing RA.
2. Sensations of breathlessness will be reduced by breathing He-O_2 to a greater extent in those experiencing mechanical ventilatory constraints during RA breathing.
3. Increases in TT performance (power) will occur when the load on the respiratory system is reduced with a He-O_2 inspirate.
4. It is expected the He-O_2 induced changes will occur to a larger extent in women, as they will undergo greater mechanical ventilatory constraints during RA breathing.

METHODS

SUBJECTS

Twenty-seven (15 men and 12 women) competitive cyclists and/or triathletes were recruited to participate in this study. Subjects were required to be 19-40 years of age (inclusive), free of cardiopulmonary disease, nonsmoking with normal pulmonary function as per % predicted values for age and gender (excluding asthmatics) (3). In order to be considered 'competitive', subjects must have been regularly competing in cycling and/or triathlon races and possess an aerobic capacity greater than 50 or 60 $ml \cdot kg^{-1} \cdot min^{-1}$ (women and men respectively). Two men and one woman were excluded due to inadequate maximal aerobic fitness. A third man was excluded as a result of poor pulmonary function (Forced Expiratory Volume in 1 sec ($FEV_{1.0}$) < 80 % predicted). A fourth man endured an injury preventing him from performing the final test. In total 11 men and 11 women completed the entire experimental protocol. Women were tested randomly throughout their menstrual cycle, as female sex hormones do not appear to consistently affect exercise V'_E (9, 10, 18, 49) or endurance performance (17, 44).

EXPERIMENTAL PROTOCOL

All testing occurred at the Health and Integrative Physiology Laboratory at the University of British Columbia. Prior to testing, subjects provided written informed consent to participate, completed a Physical Activity Readiness Questionnaire (PAR-Q) (16), and completed a medical, menstrual, and activity history questionnaire (refer to *Appendix C*). All procedures were approved by the Clinical Research Ethics Board at the University of British Columbia (H11-02521). Testing took place over 3 days, from 1 week to slightly over a month apart. Subjects were either in or out of competition season for both TTs and asked to keep their training regimes consistent prior to each TT (refer to Training Log *Appendix C*), refraining from caffeine 4 hrs prior to testing. On Day 1 anthropometric measures were collected and pulmonary function measures were performed prior to an incremental cycle test to exhaustion to determine $V'O_{2MAX}$. When subjects deemed themselves sufficiently recovered (5-30 min) a familiarization (FAM) 5 km TT was performed. A randomized cross-over design was used for the following 2 TTs. Each subject was instrumented with an esophageal balloon-tipped catheter on Days 2 and 3 before completing a 5 km TT while breathing either humidified compressed RA or He-O_2. Subjects were blinded to the gas mixture they were breathing. Day 3 was identical to Day 2 with subjects breathing the other gas type.

Incremental Exercise Test

All exercise was performed on a cycle ergometer (VeloTron Pro, RacerMate Inc, Seattle, WA, USA). Following a self-selected warm-up (range: 5-30 min), the incremental exercise test started at 260 Watts (W) for men and 160 W for women, with the workload increasing stepwise by 30 W every 3 min (VeloTron Coaching Software, version 1.6.458 RacerMate Inc.) until volitional exhaustion or when pedaling cadence fell below 60 revolutions per min (RPM). The exercise protocols differed depending on sex, to ensure that both men and women exercised for approximately the same duration. During the test subjects were verbally encouraged to achieve their maximal capacity. The amount of recovery time following the $V'O_{2MAX}$ test and prior to the FAM 5 km TT was at each subject's discretion. One FAM TT was required based on highly reproducible performance in competitively trained cyclists (80). Subjects were instructed to give their best effort on the TT, given the condition that they had just performed an exhaustive exercise bout. The practice 5 km TT was administered in the same manner as the experimental 5 km TTs (see below) with the exception of the esophageal balloon and humidified compressed RA (or $He\text{-}O_2$).

Experimental 5 km TTs

Environmental conditions were kept as consistent as possible by having subjects perform both experimental TTs at the same time of day (morning or afternoon). Additionally, on Day 2, subjects completed a food and activity log for that day and 3 prior days. This log was provided to subjects who were asked to keep their nutrition and activity as consistent as possible for Day 3 (refer to *Appendix C*). The esophageal balloon was inserted after which 5 min of resting metabolic data was collected with subjects on the cycle ergometer in a standardized race position. The experimental 5 km TTs were performed breathing either humidified compressed RA or $He\text{-}O_2$ (21% O_2 - 79% He). The percent O_2 in the $He\text{-}O_2$ was tightly controlled and ranged from 20.87% - 21.04%. Following a self-selected warm-up similar to Day 1, both TTs began at a still start with subjects either in or out of the saddle. If subjects chose to start out of the saddle they were required to get in the saddle within a few seconds and remain in the saddle for the duration of the test. The initial gearing combination chosen by each subject on Day 2 was used again at the start of Day 3, but subjects were allowed to adjust the gears throughout each TT. Upper body position was also standardized such that subject's hands were to remain on the brake-hoods at all times during testing. The straight, flat 5 km TT course was created and operated using commercially available software (VeloTron 3D, version 3, RacerMate Inc.) During the TT, subjects watched a monitor displaying their distance covered, time elapsed, and cadence. During the test the experimenter did not verbally encourage subjects. The exact bike set-up (seat and handle-bar positions) on Day 2 was recorded and subjects were required to ride in the identical position on Day 3 and warm-up for the same duration.

MEASUREMENTS

Pulmonary Function Testing

On Day 1, forced vital capacity (FVC), $FEV_{1.0}$ and $FEV_{1.0}$/FVC were determined using a portable spirometer (Spirolab II, Medical International Research, Vancouver BC, Canada) according to recommended guidelines (3). Subjects were familiarized with the graded FVC maneuvers to be performed before and after the 5 km TTs to appropriately account for bronchodilation and thoracic gas compression as previously described (29). Inspiratory capacity (IC) maneuvers were also practiced as they were to be performed at each km during the 5 km TTs. Subjects were shown their flow-volume traces on a computer monitor and verbally coached on the maneuvers until successful completion was independently attained.

Metabolic Data

Inspired and expired gases, pressure and flow values were measured using previously described hardware and software (23, 29, 30, 86). In brief, ventilatory and mixed expired metabolic parameters were collected using a customized metabolic cart consisting of two calibrated pneumotachographs (model 3813, Hans Rudolph, Kansas City, MO) to measure inspiratory and expiratory flow, and calibrated O_2 and CO_2 analyzers (Model S-3-A/I and Model CD-3A, respectively, Applied Electrochemistry, Pittsburgh, PA). Carbon dioxide could not be measured during the He-O_2 trials due to He interfering with the infrared signal used by the CO_2 analyzer to determine CO_2 concentration. The pneumotachographs were independently calibrated using a 3 l calibration syringe for both RA and He-O_2. Volumes were obtained by numerical integration of the flow signals. Due to He's lower heat capacity and higher thermal conductivity relative to N_2, a low-resistance spirometry filter (PDS8505, Roxon, Vancouver) was placed before the expired pneumotachograph and the heater was increased to 43°C (RA TT temperature - 37°C). The filter and elevated temperature were used to prevent moisture build-up on the pneumotachograph causing false measures of flow rates. The spirometry filter was present in both trials to maintain a consistent set-up and external resistance. Heliox expired ventilation was temperature corrected off-line during subsequent data analysis to take into account the vapour pressure of water at 43°C. The humidified gases were inspired via a 2-way breathing valve connected to a continuously filled 200 l meteorological balloon (1197-25, VacuMed, Ventura, CA, USA) via a water-filled basin. All raw data during the exercise test was recorded continuously at 200 Hz (PowerLab/16SP model ML 796, AD

Instruments, Colorado Springs, CO, USA) and stored on a computer for later analysis (Bibo, LabChart v6.1.3, AD Instruments, Colorado Springs, CO, USA).

Heart Rate

A heart-rate monitor (S610i, Polar Electro, Kempele, Finland) was worn on the chest, and heart rate was recorded at rest, at every min during the incremental test, and at every 500 meters during the TTs.

Sensory Responses

Ratings of perceived exertion (RPE) for leg and breathing discomfort were determined using a 10-point category ratio scale (11), with '0, representing no breathing (or leg) discomfort' and '10, representing the most severe breathing (or leg) discomfort one has experienced or could imagine experiencing'. Ratings were recorded at rest and every min during the incremental test and every km during the TTs. At exercise cessation, subjects were asked to state their main reason for stopping (incremental test) or not cycling faster (TT): leg, respiratory, combination, or other, as well as what relative percentages of leg and breathing discomfort contributed to exercise termination. The RPEs recorded during the 5 km TTs were repeated back to each subject post exercise to confirm the correct ratings were obtained. Subjects raised their right hand in the same manner during both TTs to the RPE scale suspended approximately 5 centimeters (cm) directly in front of the right handle bar. The collection of RPEs on Day 1 during both the $V'O_{2MAX}$ test and FAM 5 km TT served as a familiarization procedure, enabling subjects to become accustomed to reporting how their legs and breathing feel during exercise.

Expiratory Flow Limitation

Forced Vital Capacities and Graded FVCs were performed pre and post (within 2 min) exercise while ICs were performed at the end of each km. On Day 1, FVCs and graded FVCs were performed as a familiarization for the forthcoming experimental 5 km TTs. During the $V'O_{2MAX}$ test, ICs were performed during the last 30 sec of each stage. If adequate IC maneuvers were not performed during the $V'O_{2MAX}$ test, subjects were given appropriate feedback during the recovery time to correct their ICs for the FAM 5 km TT.

The highest flows recorded for a given volume from the FVCs and graded FVCs were compiled to form the outer boundary of the MEFV curve to account for thoracic gas compression and bronchodilation as previously described by Guenette *et al.* (29). Expiratory flow limitation was determined by superimposing the expiratory portion of a tidal breath for each km within the MEFV curve.

The tidal breath was an ensemble average of approximately 10 tidal breaths preceding the IC maneuver performed at the end of every km during the 5 km TTs. The magnitude of EFL was calculated as the volume of tidal breath overlapping the MEFV curve divided by the tidal volume during each km.

Operational Lung Volumes

End expired lung volume (EELV) was measured by subtracting the IC from the resting FVC. Exercise tidal volume (ensemble average of 10 tidal breaths preceding the IC) was added to EELV to determine end inspired lung volume (EILV). Inspiratory capacity was considered accurate when peak inspiratory esophageal pressure reached or exceeded that obtained during rest (29, 45).

Ventilatory Capacity

Ventilatory capacity ($V'_{E\ CAP)}$ was estimated for each subject breathing both RA and He-O_2. The $V'_{E\ CAP}$ is an estimate of the maximal expiratory flows an individual is theoretically capable of attaining for their chosen breathing pattern (49). Exercise flow-volume loops were placed with the MEFV loop, and the tidal breath was divided into equal 40 ml segments. For each segment, the change in volume was divided by the highest expiratory flows attained to determine an expiratory duration. The expiratory durations for the all segments were summed to estimated minimal expiratory duration. Inspiratory time was calculated based on the ratio of inspiratory-to-total breathing cycle time ratio. Maximal breathing frequency was calculated based on the minimum tidal breath. Estimated $V'_{E\ CAP}$ is the product of maximal breathing frequency and tidal volume. Ventilatory reserve is the difference between $V'_{E\ CAP}$ and the subject's V'_{E}.

Work of Breathing

Prior to the insertion of a balloon-tipped esophageal catheter (no. 47-9005-RO, Ackrad, Trumbull, CT), subjects sniffed 1 ml of xylocaine viscous 2% to minimize discomfort. While the subject sipped water through a straw, the catheter was inserted ~45 cm down the nasal passage. The catheter was then connected to a 3-way stopcock that connected to a pressure transducer (Validyne, MCI-10, Northridge, CA, USA). Subjects performed a Valsalva maneuver to expel all air from the balloon. One ml of air, as per manufacturer specifications, was injected into the balloon via the 3-way stopcock. As the subjects took sharp sniffs, the catheter was slowly pulled out of the nose (thereby out of the stomach and esophagus) until the first negative pressure deflection occurred (indicating the balloon had surpassed the level of the diaphragm). The catheter was then pulled-up an additional 10 cm, approximately at the level of the heart and sufficiently above the diaphragm. Validity of the balloon placement was determined by having the subject expire against an occluded airway (dynamic occlusion test); if transpulmonary pressure remained constant while airway opening pressure increased, catheter placement was considered correct (58). Depth markings on the catheter allowed the exact balloon placement to be recorded and replicated for the subsequent test. Ample surgical tape was used to secure the balloon to the nose in order to prevent movement during exercise. Mouth pressure was measured at a port in the mouthpiece connected to another pressure transducer. Transpulmonary pressure was calculated as the difference between esophageal and mouth pressures. The pressure transducers were calibrated using a mercury manometer; signals were amplified (gain P_M: 10, P_E: 25), filtered (P_M and P_E: 200 Hz), and connected to the previously described data acquisition system whereby the signal was converted from volts into cmH_2O.

The WOB was determined by taking the integral of an ensemble average of several transpulmonary pressure volume loops using a customized software program as previously described (30, 83). The WOB was multiplied by the frequency of breathing (f_b) to determine the work done per min by the respiratory system and converted into joules per min ($J \cdot min^{-1}$).

Performance

The VeloTron is a cycle ergometer directly measuring power from which speed is calculated. As such, improvements in performance were determined from power output over the course of the 5 km and at each km. Cadence, speed and time were also taken into consideration.

Statistical Analysis

A sample size of 16 was selected based on an 80% power to detect a significant difference in dyspnea intensity at a standardized time during the TT via a relevant difference in Borg rating (±1) (64). However a sample size of 11 was achieved due to the response of adequate subjects willing to volunteer for the study. As a result the study was likely underpowered to detect a significant difference in sensory responses or performance.

Unpaired *t*-tests were used to examine descriptive characteristics, pulmonary function and maximal exercise data between men and women. Repeated measures ANOVA (Statistica 6.1, Stat Soft Inc., Tulsa, OK, USA) were used to compare the effects of RA versus $He\text{-}O_2$ between men and women for: metabolic and cycling variables, EFL (magnitude), WOB, RPE and operational lung volumes. If significant *F*-ratios were detected, Tukey's post hoc test was applied to determine where the differences occurred. Linear regression analysis was used to determine the relationship between EFL, performance and the selected respiratory parameters. The level of significance was set at $P < 0.05$ for all statistical comparisons.

Performance data from the 2 TTs were analyzed using paired *t*-tests and the magnitude-based inferences approach (41). Coefficients of variation (CV) for time and power were determined using previously reported variations for elite cyclists during indoor cycling due to the effects of environmental factors on outdoor cycling performance. The typical variation in indoor cycling TT performance time in elite cyclists is thought to be approximately 1% (0.7 – 1.1%) (68, 78, 80). Using the more liberal 0.7% CV the smallest worthwhile change in performance would be 0.21% or a 1.04 sec improvement. A conservative CV (1.1%) results in the smallest worthwhile change in performance time of 0.33% (1.64 sec improvement) (40). On an indoor cycle ergometer, the CV for power (W) has shown to be between 1.9 – 2.1% (78, 80). The smallest worthwhile changes in power would be 0.57% (1.31 W) and 0.63% (1.45 W) for CV of 1.9 and 2.1% respectively (40).

RESULTS

SUBJECT CHARACTERISTICS AND RESTING PULMONARY FUNCTION

Descriptive and anthropometric data for subjects completing the entire experimental protocol are presented in table 1. Men were on average older than the women, but both groups were under 40 years of age. Normal pulmonary function was present in all subjects as per the predicted equations set by the American Thoracic Society and European Respiratory Society (3) with $FEV_{1.0}$/FVC > 80% predicted (table 2).

Table 1 - Descriptive and Anthropometric Data

	Men (n = 11)	Women (n = 11)	*P* value
Age (yr)	30.5 ± 5.3 (22 – 39)	26.3 ± 4.3 (19 – 34)	0.05
Height (cm)	180.4 ± 6.5 (170 – 187)	167.8 ± 6.4 (159 – 179)	< 0.001
Weight (kg)	73.7 ± 6.5 (60.1 – 84.8)	59.0 ± 6.1 (50.2 – 70.6)	< 0.001

Values are means ± SD (range).

Table 2 - Pulmonary Function Data

	Men (n = 11)	Women (n = 11)	*P* value
FVC (l)	5.7 ± 0.7 (4.5 – 6.6)	4.3 ± 0.7 (3.0 – 5.5)	< 0.001
FVC (% predicted)	108 ± 8 (96 – 118)	111 ± 11 (85 – 125)	0.48
$FEV_{1.0}$ (l)	4.5 ± 0.6 (3.6 – 5.6)	3.5 ± 0.6 (2.5 – 4.4)	< 0.001
$FEV_{1.0}$ (% predicted)	102 ± 11 (82 – 118)	105 ± 9 (94 – 122)	0.38
$FEV_{1.0}$/FVC (%)	79.7 ± 3.6 (74.8 – 85.2)	81.1 ± 4.2 (74.6 – 88.1)	0.22
$FEV_{1.0}$/FVC (% predicted)	98 ± 4 (92 – 103)	97 ± 5 (89 – 104)	0.90
PEF ($l \cdot sec^{-1}$)	11.2 ± 1.3 (9.8 – 13.0)	7.5 ± 1.1 (5.6 – 9.0)	< 0.001
PEF (% predicted)	112 ± 11 (99 – 130)	102 ± 15 (78 – 123)	0.08

FVC, forced vital capacity; $FEV_{1.0,}$ forced expired volume in 1 sec; PEF, peak expiratory flow. Values are means ± SD (range).

All subjects met the ‘competitive’ cyclist criteria, and were actively involved in road, mountain, cyclo-cross and/or triathlon, with some athletes competing in more than one discipline (table 3). Subjects competed at a variety of levels ranging from regional to international competitions. National or international level competitors did so as ‘age-groupers’ with the exception of 2 women. One woman was a member of the provincial road cycling team and the other was a professional Ironman triathlete. Due to the timing and duration of testing, 13 subjects were ‘in’ competition season and 9 subjects were ‘out’ of competition season, but all were actively training (table 3).

Table 3 - Cycling Background Experience

	Discipline				Competition Level				Competition Status	
	Road	Triathlon	Mountain	Cyclo-cross	Regional	Provincial	National	International	In-season	Off-season
Men (n = 11)	6	3	2	1	5	2	3	1	7	4
Women (n = 11)	5	6	1	2	5	1	2	3	6	5

INCREMENTAL CYCLE TEST

Maximal oxygen consumption and cycling parameters during the incremental cycle test are presented in table 4. All women met the required $V'O_{2MAX}$ of 50 ml·kg·min^{-1} (55.9 ± 3.1 ml·kg·min^{-1}). Seven men met the $V'O_{2MAX}$ criteria of 60 ml·kg·min^{-1} (60.8 ± 3.8 ml·kg·min^{-1}), and 4 men were within 5 ml·kg·min^{-1} of the standard. On average men achieved significantly higher $V'O_{2MAX}$ (relative and absolute), $V'CO_2$, V'_E and V_T than women. However, women’s $V'O_{2MAX}$ values reached a significantly higher percentage of their predicted maximal aerobic capacities (women: 148 ± 14 *vs.* men: 134 ± 11 % predicted) (46). Breathing frequency and HR were comparable between men and women ($P > 0.05$). The peak power attained my men was significantly higher than women (men: 361 ± 24 *vs.* women: 283 ± 34 W, $P < 0.001$), but this difference was no longer present when expressed relative to body weight (men: 4.9 ± 0.4 *vs.* women: 4.8 ± 0.4 W·kg^{-1}, $P = 0.50$). The incremental cycle test lasted approximately the same duration for both men and women (women: 835.6 ± 224.1, range: 601.2 – 1217.4 *vs.* men: 723.9 ± 142.3, range: 607.2 – 1013.4 sec, $P = 0.18$) with all subjects cycling to volitional exhaustion, as indicated by similar respiratory exchange ratios (RER) (men: 1.11 ± 0.03 *vs.* women: 1.08 ± 0.04, $P = 0.12$). At the end of the incremental cycle test men’s RPE for leg discomfort was significantly higher than women’s (men: 9 ± 0.6 and women: 7.5 ± 1.9, $P = 0.002$). Breathing discomfort was also significantly higher for men (men: 8.5 ± 0.7 *vs.* women: 7.3 ± 1.7, $P = 0.009$). However no sex differences emerged for the relative contribution of leg (men: 56 ± 12 *vs.* women: 65 ± 9%, $P = 0.41$) or breathing (men: 44 ± 12 *vs.* women: 35 ± 9%, $P = 0.41$) discomfort contributing to exercise termination. The main reason for exercise termination was leg discomfort (men: $n = 7$ and women: $n = 7$) followed by a combination of leg and breathing discomfort (men: $n = 3$ and women: $n = 3$) and breathing discomfort (men: $n = 1$ and women: $n = 1$). The FAM 5 km TT was performed in a significantly faster time by the men (477.7 ± 15.6 sec) than it was by the women (534.8 ± 36.9 sec, $P = 0.01$).

Table 4 - Maximal Values from Incremental Cycle Test to Exhaustion

	Men	Women	*P* value
$V'O_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	60.8 ± 3.8 (55.3 – 67.0)	55.9 ± 3.1 (51.8 – 61.3)	< 0.05
$V'O_2$ ($l \cdot min^{-1}$)	4.47 ± 0.40 (3.80 – 4.98)	3.29 ± 0.40 (2.89 – 3.88)	< 0.05
$V'O_2$ (% predicted)	134 ± 11 (118 – 151)	148 ± 14 (131–173)	< 0.05
$V'CO_2$ ($l \cdot min^{-1}$)	4.90 ± 0.40 (4.12 – 5.44)	3.55 ± 0.40 (3.12 – 4.21)	< 0.001
V'_E ($l \cdot min^{-1}$)	140.2 ± 11.7 (117.9 – 163.4)	100.7 ± 13.6 (83.7 – 132.9)	< 0.001
f_b ($l \cdot min^{-1}$)	58 ± 14 (34 – 78)	57 ± 9 (46 – 72)	0.75
V_T (l)	2.88 ± 0.50 (2.35 – 4.01)	2.10 ± 0.40 (1.44 – 2.75)	< 0.001
RER	1.11 ± 0.03 (1.07 – 1.15)	1.08 ± 0.04 (1.03 – 1.14)	0.12
HR ($beats \cdot min^{-1}$)	193 ± 16 (178 – 233)	185 ± 11 (168 – 204)	0.22
Peak Power (Watts)	361 ± 24 (320 – 410)	283 ± 34 (250 – 340)	< 0.001
Peak Power ($Watts \cdot kg^{-1}$)	4.9 ± 0.4 (4.5 – 5.5)	4.8 ± 0.4 (4.3 – 5.6)	0.50
Duration (sec)	723.9 ± 142.3 (525.0 – 1013.4)	835.58 ± 224.1 (601.2 – 1217.4)	0.18

$V'O_2$, oxygen consumption; $V'CO_2$, carbon dioxide production; RER, respiratory exchange ratio; V'_E, minute ventilation; V_T, tidal volume; f_b, frequency of breathing; HR, heart rate. Values are means ± SD (range).

EXPERIMENTAL 5 KM TIME TRIALS

Performance – Power

Heliox was associated with a 2.3% improvement in average power output over the 5 km (~5.3 W, $F(1) = 3.98$, $P = 0.06$) compared to the RA trial for men and women combined. Using the magnitude-based inferences approach with a liberal threshold of performance improvement (1.31 W, refer to *Methods*) the chances the effect of He-O_2 is beneficial/trivial/harmful are 95.5/2.2/2.3%. Similarly the more conservative performance improvement threshold (1.45 W) finds the chances of the effect beneficial/trivial/harmful to be 95.3/2.5/2.2%. Based on a 95% CI [-0.2, 10.7] for men and women combined. The 'true' effect of He-O_2 on performance could be slightly worse (-0.2 W) or definitely worthwhile (+10.7 W) (figure 1 and table 5).

Men's power output was on average 1.6% higher on the $He\text{-}O_2$ TT than the RA TT (~5.0 W, t (10) = 1.29, P = 0.23, d = 0.39). Using the more liberal threshold of wattage improvement (1.78 W), the chances that the effect of $He\text{-}O_2$ is beneficial/trivial/harmful are 31.7/67.7/0.6% using the magnitude-based inferences of performance improvement. With a more conservative (1.97 W) for performance improvement, the chances are 25.6/74.0/0.4%. Based on the men's 95% CI [-2.7, 12.7], the 'true' effect of $He\text{-}O_2$ on power could be slightly worse (-2.7 W) or definitely worthwhile (+12.7 W).

Women's power output was on average 2.9% higher on the $He\text{-}O_2$ TT than the RA TT (~5.5 W, t (10) = 1.54, P = 0.15, d = 0.47). Using the more liberal threshold of power improvement (1.08 W), the chances that the effect of $He\text{-}O_2$ is beneficial/trivial/harmful are 67.4/31.3/1.3% using the magnitude-based inferences of performance improvement. With a more conservative (1.19 W) for performance improvement, the chances are 63.5/35.4/1.0%. Based on the women's 95% CI [-2.3, 13.2], the 'true' effect of $He\text{-}O_2$ on wattage could be slightly worse (-2.3 W) or definitely worthwhile (+13.2 W).

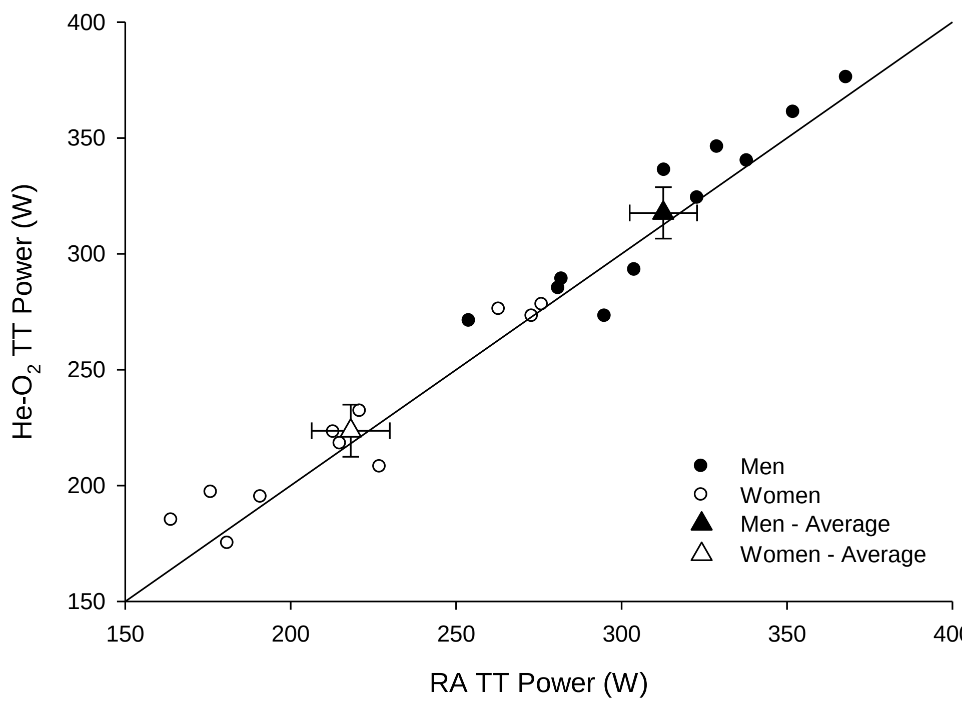


Figure 1 - Men and Women TT Performance - Power

Nine men and 8 women had a higher power output on average during the He-O_2 TT compared to the RA TT (men: 9.8 ± 7.6; women: 10.6 ± 7.5 W); 2 men and 2 women produced more power breathing RA (men: 16.5 ± 7.8; women: 12.5 ± 9.3 W); 1 women's power was not affected by He-O_2 (table 6). Men produced significantly more power than women for both RA (men: 312.6 ± 33.8 *vs*. women: 218.2 ± 39.1 W, $P = 0.002$) and He-O_2 (men: 317.6 ± 36.9 *vs*. women: 223.6 ± 37.2 W, $P = 0.002$) TTs.

Performance - Time

Heliox was associated with a 0.9% improvement in performance time (~4.5 sec, F (1) = 4.05, $P = 0.058$) compared to the RA trial for men and women combined. Using the magnitude-based inferences approach with a liberal threshold of performance improvement (1.04 sec) the chances that the effect of He-O_2 is beneficial/trivial/harmful are 96.1/1.6/2.3%. The conservative performance improvement threshold (1.64 sec) results in 95.2/2.8/2.1% chances that the effect is beneficial/trivial/harmful. Based on a 95% CI [-0.2, 9.1] for men and women combined. The 'true' effect of He-O_2 on performance could be slightly worse (-0.2 sec) or definitely worthwhile (+ 9.1 sec) (table 5).

Men completed the He-O_2 TT an average of 0.7% faster than the RA TT (~3.2 sec, t (10) = 1.42, $P = 0.32$, d = 0.43). With a liberal threshold of performance improvement (0.96 sec), the chances the effect of He-O_2 is beneficial/trivial/harmful are 67.4/30.7/1.9% using the magnitude-based inferences of performance improvement. With a more conservative approach (1.5 sec) for performance improvement, the chances are 46.8/52.4/0.8%. Based on the men's 95% CI [-3.4, 9.7], the 'true' effect of He-O_2 on performance could be slightly worse (-3.4 sec) or definitely worthwhile (+9.7 sec).

Women were on average 1.1% faster on the He-O_2 TT than the RA TT (~5.8 sec, t (10) = 1.50, $P = 0.16$, d = 0.45). With a liberal threshold of performance improvement (1.1 sec), the chances the effect of He-O_2 is beneficial/trivial/harmful are 65.1/33.6/1.3% using the magnitude-based inferences of performance improvement. With a more conservative (1.7 sec) for performance improvement, the chances are 41.2/58.3/0.5%. Based on the women's 95% CI [-0.8, 12.3], the 'true' effect of He-O_2 on performance could be slightly worse (-0.8 sec) or definitely worthwhile (+12.3 sec).

Eight men and 8 women completed the He-O_2 TT faster than the RA TT (men: 6.8 ± 3.7; women: 11.2 ± 9.4 sec); 3 men and 3 women were faster breathing RA (men: 6.4 ± 6.3; women: 8.7 ± 8.6 sec) (table 6). Men were significantly faster than women for both RA (men: 461.8 ± 19.5 *vs*. women: 532.0 ± 36.7 sec, $P = 0.002$) and He-O_2 (men: 458.6 ± 20.2 *vs*. women: 526.2 ± 32.5 sec, $P = 0.003$) TTs.

Table 5 - Summary of 5 km TT Performance Data (Performance Time and Power Output)

Subject Group	Treatment Intervention	Performance Time			Power Output			Effect of Intervention
		Mean (sec) ± SD	95% CI (sec)	*P*	Mean (W) ± SD	95% CI (W)	*P*	
Men & Women	RA	496.9 ± 45.9	± 4.7 [-0.2, 9.1]	0.06	265.4 ± 60.1	± 5.5 [-0.2,10.7]	0.06	unclear
	$He-O_2$	492.4 ± 43.5			270.6 ± 60.2			
Men	RA	461.8 ± 19.5	± 6.6 [-3.4, 9.7]	0.32	312.6 ± 34.0	± 7.7 [-2.7,12.7]	0.23	unclear
	$He-O_2$	458.6 ± 20.2			317.6 ± 36.9			
Women	RA	532.0 ± 36.7	± 6.6 [-0.8, 12.3]	0.16	218.2 ± 39.1	± 7.8 [-2.3, 13.2]	0.15	unclear
	$He-O_2$	526.2 ± 32.5			223.6 ± 37.2			

Table 6 - TT Performance Improvement

	Higher Power Output TT $He-O_2$				Higher Power Output TT RA			
	Subjects (*n*)	Performance Improvement (W)	Test Order (*n*) 1st	2nd	Subjects (*n*)	Performance Improvement (sec)	Test Order (*n*) 1st	2nd
Men	9	9.8 ± 7.6 (1.0 – 23.0)	4	5	2	16.5 ± 7.8 (3.0 – 21.0)	1	1
Women	8	10.6 ± 7.5 (3.0 – 21.0)	4	4	2	12.5 ± 9.3 (6.0 – 9.0)	1	1

Values are means ± SD (range).

The TT with the highest power output was performed 1st for nearly half of the subjects accordingly test order did not appear to have an effect on performance (table 6). Women had a significantly longer duration between Day 2 and Day 3 tests (men: 7.7 ± 4.1 *vs.* women: 15.3 ± 10.5 days, $P = 0.04$).

Average speed, power, and cadence over the RA and $He-O_2$ TTs are presented in table 7. Men cycled significantly faster ($km \cdot hr^{-1}$) on average throughout both 5 km TTs compared to women ($P < 0.05$) and produced a significantly greater amount of absolute power ($P < 0.05$). Power in relation to body weight ($W \cdot kg^{-1}$) was not affected by sex or inspirate ($P > 0.05$). There were no sex-based differences in RPM during either TT ($P > 0.05$).

The 5 km TT average speed ($km \cdot hr^{-1}$) for men and women combined was significantly greater on $He-O_2$ than on RA (RA: 36.6 ± 3.3 *vs.* $He-O_2$: 36.9 ± 3.2 $km \cdot hr^{-1}$, $P = 0.04$). However $He-O_2$ had no effect on men or women's speed as individual groups (men: $P = 0.49$, women: $P = 0.35$). Combined or separate, men's and women's RPM over the 5 km TT's were not affected by $He-O_2$ (combined: $P = 0.35$, men: $P = 0.94$, women: $P = 0.86$).

Table 7 - Average Speed, Power and Cadence over the RA and He-O_2 5 km TTs

	RA	He-O_2	*P* Value
Speed (Average km·hr^{-1})			
Combined	36.6 ± 3.2	36.9 ± 3.2	0.04
Men	39.1 ± 1.6	39.4 ± 1.7	0.49
Women	34.1 ± 2.4	34.4 ± 2.2	0.35
Power (Average W)			
Combined	265.4 ± 60.1	270.6 ± 60.2	0.06
Men	312.6 ± 33.8	317.6 ± 36.9	0.54
Women	218.2 ± 39.0	223.6 ± 37.2	0.47
Power (Average W·kg^{-1})			
Combined	4.0 ± 0.6	4.1 ± 0.6	0.06
Men	4.3 ± 0.5	4.3 ± 0.6	0.68
Women	3.7 ± 0.5	3.8 ± 0.5	0.38
Cadence (Average RPM)			
Combined	102 ± 7	103 ± 9	0.35
Men	106 ± 8	107 ± 9	0.94
Women	98 ± 5	100 ± 7	0.86

Values are means ± SD.

Performance data for each km is presented in figure 2. Men cycled at a significantly faster speed (km·h^{-1}) and produced a significantly greater amount of power than women at each km throughout both the He-O_2 and RA 5 km TT. On He-O_2, women cycled at a significantly faster speed (km·h^{-1}) compared to RA at 3 km, while men displayed no differences between the 2 TTs. On RA men completed the 1st, 3rd, 4th and 5th km significantly faster than women, while on He-O_2 the 1st, 4th and 5th km were performed significantly faster by men than women. RPMs were not affected by sex or inspirate throughout the TTs.

Familiarization TT

The men's experimental TTs were completed significantly faster than their respective FAM TTs ($P < 0.001$). Women completed the experimental TTs faster but did not reach statistical significance (RA *vs.* FAM, $P = 0.96$; He-O_2 *vs.* FAM, $P = 0.13$).

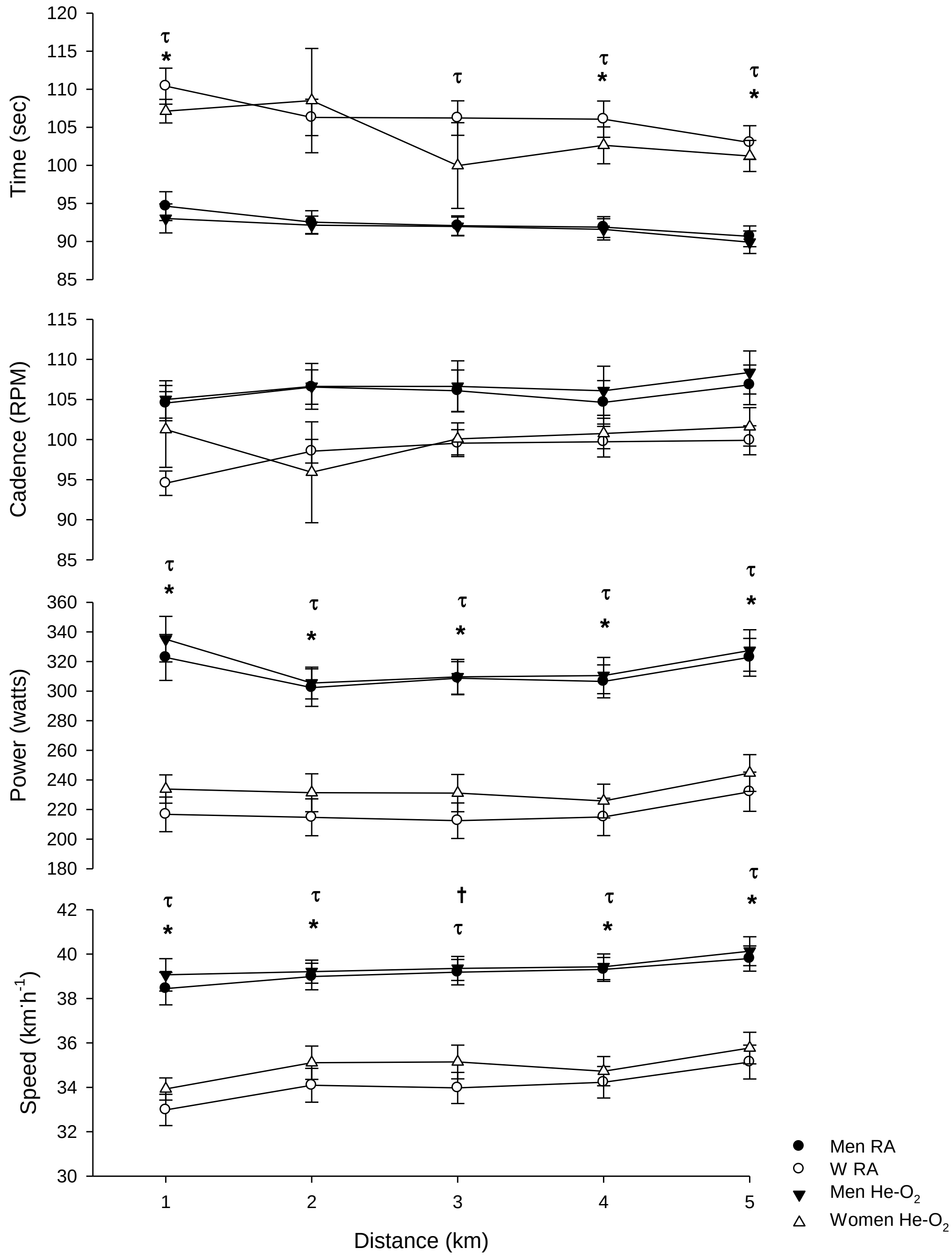


Figure 2 - Time, Cadence, Power and Speed for men and women during the RA and He-O_2 TTs. τ significantly different RA TT men *vs.* women, * Significantly different He-O_2 TT men *vs*. women, † significantly different RA *vs*. He-O_2 TT for women. Data are presented as means ± SE. Statistical significance is set at the level of $P < 0.05$.

Metabolic Data & Breathing Pattern

Metabolic data for each TT is presented in table 8 (RA) and table 9 (He-O_2). Throughout the entire RA and He-O_2 TTs, men reached significantly higher V'O_2 (l·min^{-1}), V'CO_2 (RA only), V'_E and V'_T than women. Frequency of breathing, V'O_2 (ml·kg·min^{-1}), RER (RA only), and HR were not significantly different between men and women at rest or during either TT.

The ventilatory response to exercise is presented in figure 3, panel A, B and C. Women breathed at a significantly higher frequency during the He-O_2 TT, while men had a significantly higher f_b at 4 km on He-O_2 compared to RA. At 5 km, sex appeared to play a role on V_T whereby men's V_T increased on He-O_2 and women's decreased (P = 0.02). There were no significant differences in V'O_2, V'_E or HR between the RA and He-O_2 TTs for men or women.

Bronchodilation occurred in all subjects as determined by visual inspection. Post exercise FVC and graded FVC's were performed with higher expiratory flow rates generating a larger post exercise MEFV curve. Refer to *Appendix B* for individual figures.

Heliox significantly increased peak expiratory flow and maximal expiratory flow at 50% of vital capacity for men and women (table 10). Exercise expiratory flow rates were significantly higher on He-O_2 compared to RA for men and women combined (RA: 5.72 ± 1.25 *vs.* He-O_2: 7.05 ± 1.80 l·sec^{-1}, P < 0.001). As a group, men's maximal expiratory flow rates were significantly higher on He-O_2 compared to RA (RA: 6.65 ± 0.90 *vs.* He-O_2: 7.25 ± 8.57 l·sec^{-1}, P < 0.001), as were women's (RA: 4.78 ± 0.73 *vs.* He-O_2: 5.27 ± 5.52 l·sec^{-1}, P = 0.002). Men's expiratory flow rates increased to a significantly greater extent than women's (Men: 9% *vs.* women: 5%, P < 0.001).

Table 8 - Room Air TT Metabolic Data

RA		Rest	1 km	2 km	3 km	4 km	5 km
$V'O_2$ ($l{\cdot}min^{-1}$)	Men	0.38* ± 0.08 (0.25 – 0.56)	3.42* ± 0.43 (2.46 – 4.14)	3.82* ± 0.49 (3.10 – 4.78)	4.01* ± 0.50 (3.33 – 4.93)	4.14* ± 0.54 (3.40 – 5.06)	4.21* ± 0.56 (3.54 – 5.17)
	Women	0.26* ± 0.10 (0.11 – 0.43)	2.66* ± 0.40 (2.11 – 3.13)	2.84* ± 0.44 (2.35 – 3.49)	2.95* ± 0.50 (2.35 – 3.68)	2.98* ± 0.53 (2.33 – 3.70)	3.04* ± 0.55 (2.26 – 3.78)
$V'O_2$ ($ml{\cdot}kg^{-1}{\cdot}min^{-1}$)	Men	5.16 ± 1.12 (3.31 – 6.93)	46.68 ± 6.31 (31.77 – 54.64)	51.91 ± 6.17 (40.00 – 63.16)	54.57 ± 5.98 (42.99 – 65.07)	56.23 ± 6.11 (43.92 – 66.74)	57.19 ± 6.40 (45.70 – 68.23)
	Women	4.36 ± 1.23 (1.92 – 6.16)	44.92 ± 3.35 (40.10 – 51.52)	48.00 ± 4.03 (42.57 – 55.28)	49.74 ± 5.17 (42.71 – 58.74)	50.35 ± 5.68 (41.61 – 58.70)	51.32 ± 5.84 (41.13 – 58.68)
$V'CO_2$ ($l{\cdot}min^{-1}$)	Men	0.36* ± 0.09 (0.25 – 0.54)	3.32* ± 0.56 (2.17 – 3.81)	4.47* ± 0.61 (5.42 – 3.47)	4.46* ± 0.47 (3.76 – 5.46)	4.49* ± 0.47 (3.73 – 5.52)	4.57* ± 0.56 (3.79 – 5.65)
	Women	0.26* ± 0.11 (0.10 – 0.50)	2.51* ± 0.38 (1.93 – 2.98)	3.11* ± 0.53 (2.26 – 3.86)	3.09* ± 0.55 (2.17 – 3.73)	3.08* ± 0.54 (2.20 – 3.80)	3.14* ± 0.53 (2.33 – 3.93)
V'_E ($l{\cdot}min^{-1}$)	Men	11.5 ± 3.4 (8.5 – 19.4)	83.3* ± 18.0 (50.9 – 103.4)	113.6* ± 19.3 (73.3 – 136.8)	121.1* ± 18.7 (86.9 – 151.4)	126.9* ± 15.3 (103.3 – 155.3)	134.4* ± 12.7 (115.8 – 157.3)
	Women	9.4 ± 5.8 (3.6 – 25.3)	65.2* ± 10.6 (42.9 – 76.0)	83.1* ± 14.0 (55.1 – 93.5)	87.0* ± 15.2 (60.0 – 103.8)	90.3* ± 16.4 (57.5 – 109.5)	94.4* ± 17.8 (56.7 – 117.6)
f_b ($breaths{\cdot}min^{-1}$)	Men	13 ± 3 (11 – 19)	37 ± 10 (23 – 50)	44 ± 11 (28 – 58)	47 ± 12 (31 – 64)	50 ± 12 (35 – 69)	55 ± 12 (39 – 76)
	Women	13 ± 5 (7 – 25)	39 ± 8 (29 – 52)	48 ± 13 (33 – 76)	51 ± 12 (36 – 76)	52 ± 9 (42 – 66)	54 ± 10 (44 – 72)
V_T (l)	Men	1.0 ± 0.3 (0.7 – 1.6)	2.7* ± 0.5 (2.1 – 3.7)	3.1* ± 0.6 (2.5 – 4.3)	3.1* ± 0.6 (2.5 – 4.4)	3.0* ± 0.6 (2.4 – 4.4)	2.9* ± 0.6 (2.3 – 4.2)
	Women	0.8 ± 0.2 (0.6 – 1.2)	2.0* ± 0.4 (1.3 – 2.5)	2.2* ± 0.5 (1.0 – 3.0)	2.1* ± 0.5 (1.0 – 3.0)	2.1* ± 0.5 (1.1 – 2.9)	2.1*± 0.4 (1.3 – 2.8)
RER	Men	0.98 ± 0.14 (0.82 – 1.31)	0.99 ± 0.15 (0.65 – 1.14)	1.18 ± 0.15 (0.87 – 1.34)	1.12 ± 0.11 (0.96 – 1.27)	1.09 ± 0.11 (0.96 – 1.30)	1.09 ± 0.12 (0.96 – 1.38)
	Women	1.00 ± 0.32 (0.80 – 1.94)	0.96 ± 0.08 (0.88 – 1.11)	1.10 ± 0.10 (0.96 – 1.29)	1.05 ± 0.09 (0.92 – 1.18)	1.03 ± 0.08 (0.94 – 1.18)	1.04 ± 0.08 (0.95 – 1.21)
HR ($beats{\cdot}min^{-1}$)	Men	61 ± 4 (55 – 69) (n=9)	165 ± 12 (138 – 177)	171 ± 11 (147 – 181)	175 ± 8 (161 – 184)	179 ± 6 (169 – 187)	184 ± 6 (173 – 192)
	Women	63 ± 7 (56 – 74)	163 ± 11 (147 – 178)	168 ± 12 (150 – 184)	172.4 ± 10 (157 – 186)	175 ± 10 (158 – 188)	181 ± 10 (166 – 195)

$V'O_2$, oxygen consumption; $V'CO_2$, carbon dioxide production; RER, respiratory exchange ratio; V'_E, minute ventilation; V_T, tidal volume; f_b, frequency of breathing; HR, heart rate; Values are means ± SD (ranges). *Significantly differences between men and women.

Table 9 - Heliox TT Metabolic Data

$He\text{-}O_2$		Rest	1 km	2 km	3 km	4 km	5 km
$V'O_2$ ($l \cdot min^{-1}$)	Men	0.34 ± 0.09 (0.24 – 0.53)	3.48* ± 0.52 (2.75 – 4.26)	3.72* ± 0.38 (3.10 – 4.31)	3.90* ± 0.42 (3.28 – 4.57)	4.07* ± 0.44 (3.42 – 4.86)	4.15* ± 0.45 (3.47 – 4.93)
	Women	0.28 ± 0.10 (0.03 – 0.39)	2.54* ± 0.35 (2.15 – 3.11)	2.70* ± 0.41 (2.17 – 3.38)	2.85* ± 0.45 (2.17 – 3.56)	2.84* ± 0.47 (2.22 – 3.69)	2.89* ± 0.49 (2.21 – 3.65)
$V'O_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	Men	4.64 ± 1.11 (3.18 – 7.04)	47.32 ± 6.22 (35.94 – 55.31)	50.63 ± 4.81 (43.42 – 59.18)	52.99 ± 4.86 (45.09 – 61.37)	55.33 ± 4.38 (48.74 – 62.42)	56.40 ± 4.39 (49.36 – 64.11)
	Women	4.66 ± 1.76 (0.52 – 7.12)	42.99 ± 3.29 (38.93 – 50.64)	45.44 ± 4.37 (39.37 – 51.34)	47.90 ± 5.43 (39.35 – 55.92)	48.09 ± 5.73 (40.52 – 57.33)	48.92 ± 6.00 (40.13 – 58.36)
V'_E ($l \cdot min^{-1}$)	Men	10.5 ± 3.4 (6.5 – 17.1)	85.3* ± 16.3 (54.1 – 113.5)	116.0* ± 19.2 (83.5 – 144.4)	122.9* ± 17.4 (95.3 – 149.2)	131.0* ± 13.1 (110.0 – 149.8)	141.6* ± 12.6 (123.4 – 160.7)
	Women	9.2 ± 4.3 (0.9 – 19.4)	66.3* ± 9.5 (46.2 – 78.3)	83.9* ± 14.8 (63.5 – 109.0)	89.2* ± 17.2 (60.8 – 115.8)	92.4* ± 16.5 (64.3 – 117.4)	97.3* ± 18.2 (63.7 – 120.3)
f_b ($breaths \cdot min^{-1}$)	Men	13 ± 4 (8 – 18)	41 ± 11 (28 – 58)	49 ± 12 (34 – 65)	53 ± 13 (37 – 74)	57 ± 13 (41 – 78)	62 ± 13 (41 – 82)
	Women	14 ± 6 (2 – 23)	47 ± 14 (32 – 78)	54 ± 13 (40 – 77)	58 ± 12 (45 – 80)	63 ± 15 (48 – 98)	67 ± 17 (52 – 113)
V_T (l)	Men	1.07* ± 0.33 (0.57 – 1.61)	2.70* ± 0.46 (2.12 – 3.59)	3.13* ± 0.46 (2.51 – 3.95)	3.07* ± 0.46 (2.55 – 3.90)	3.03* ± 0.52 (2.41 – 4.09)	3.02* ± 0.59 (2.26 – 4.31)
	Women	0.83* ± 0.16 (0.64 – 1.09)	1.93* ± 0.46 (1.06 – 2.53)	2.10* ± 0.50 (1.07 – 2.78)	2.05* ± 0.50 (1.05 – 2.67)	1.97* ± 0.50 (1.05 – 2.67)	1.95* ± 0.48 (1.15 – 2.59)
HR ($beats \cdot min^{-1}$)	Men	68 ± 16 (52 – 95)	164 ± 21 (109 – 183)	174 ± 10 (150 – 185)	178 ± 8 (158 – 188)	182* ± 7 (167 – 190)	187 ± 5 (177 – 194)
	Women	62 ± 7 (50 – 72)	164 ± 8 (152 – 175)	170 ± 9 (158 – 179)	173 ± 9 (162 – 186)	175* ± 8 (166 – 186)	181 ± 10 (170 – 192)

$V'O_2$, oxygen consumption; V'_E, minute ventilation; V_T, tidal volume; f_b, frequency of breathing; HR, heart rate; Values are means ± SD (ranges). *Significantly differences between men and women.

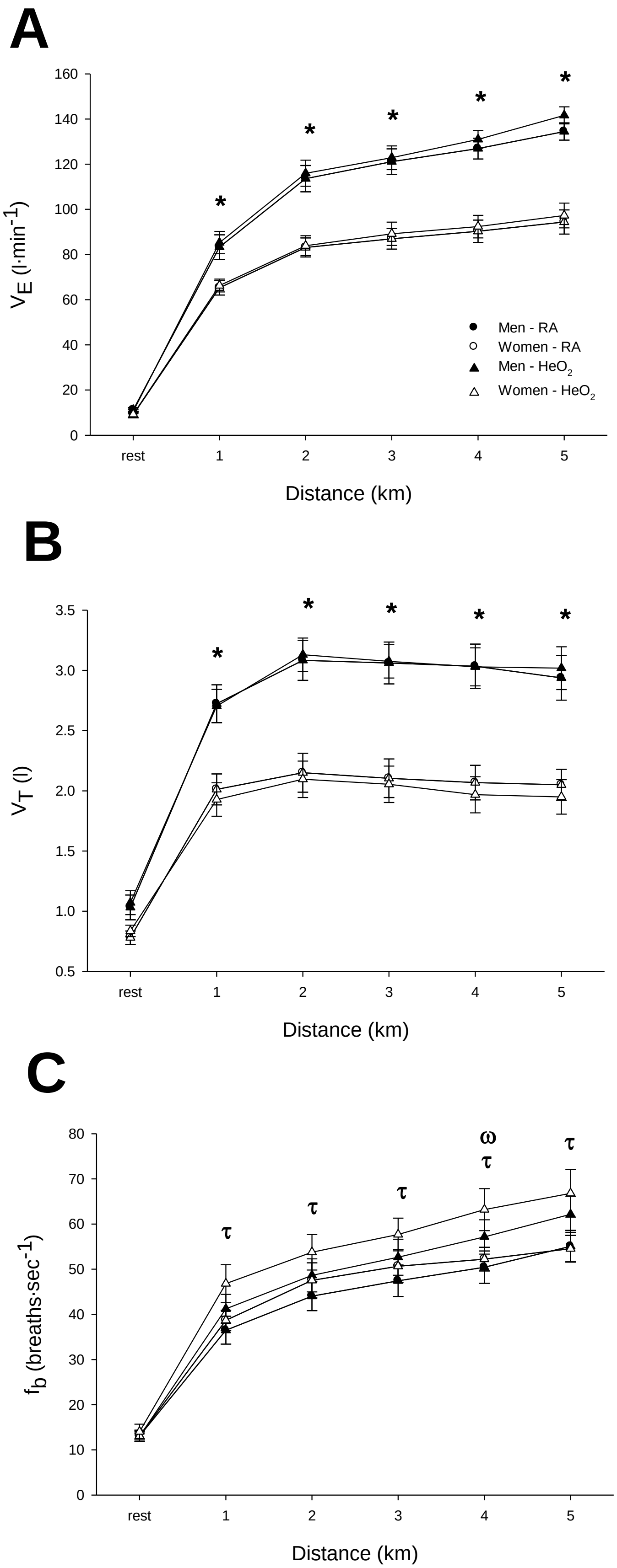


Figure 3 – Ventilatory response for men and women breathing RA and He-O_2 (A) V'_E (B) V_T (C) f_b. ***** Significant differences between men and women during RA and He-O_2 TTs. **ω** Significant difference between men RA *vs.* He-O_2. **τ** Significant differences between women RA *vs.* He-O_2. Data are presented as means ± SE. Statistical significance is set at the level of $P < 0.05$.

Table 10 - Maximal Expiratory Flow Rates and Maximal Expiratory Flow at 50% Vital Capacity

	MEF ($l \cdot sec^{-1}$)	*P* value	MEF-50% ($l \cdot sec^{-1}$)	*P* value
Men & Women – RA	9.60 ± 2.20	< 0.001	5.71 ± 1.27	< 0.001
Men & Women – He-O_2	12.70 ± 3.25		7.76 ± 1.99	
Men - RA	11.39 ± 1.08	< 0.001	6.46 ± 0.99	< 0.001
Men – He-O_2	15.43 ± 1.73		8.92 ± 1.84	
Women - RA	7.63 ± 1.12	< 0.001	4.89 ± 1.03	< 0.001
Women – He-O_2	9.70 ± 1.06		6.49 ± 1.27	

MEF, Maximal Expiratory Flow; MEF-50%, Maximal Expiratory Flow at 50 % Vital Capacity. Values are means ± SD.

Operational Lung Volumes – Sex Differences

When breathing RA men's absolute EELV and EILV's were significant greater than women's at rest and throughout the entire 5 km TT. With a He-O_2 inspirate, men's EELV was significantly greater than women's only at rest while men's EILV was significantly greater than women's at rest and throughout the 5 km TT. When EELV and EILV were compared between men and women as percentages of their FVCs no significant differences in operational lung volumes occurred for either condition at any point during the TTs (table 11 and 12, figure 4). An interaction effect occurred for EELV at 1 and 4 km whereby men had significantly greater EELV breathing RA. As the TTs progressed no significant differences in operational lung volumes occurred for men and women.

Operational Lung Volumes – Effect of Helium

Men's and women's combined operational lung volumes were significantly reduced with the He-O_2 inspirate. In absolute values EELV (l) was significantly less at rest and at each km ($P < 0.05$), and EILV (l) was significantly reduced breathing He-O_2 at rest, at 1 km, and at 4 km. In relation to vital capacity (% FVC), EELV for men and women was significantly less at 1 km (RA: 36.8 ± 6.0 *vs.* He-O_2: 30.7 ± 10.0%, $P = 0.01$), 4 km (RA: 38.9 ± 7.9 *vs.* He-O_2: 35.0 ± 8.5%, $P = 0.008$) and 5 km (RA: 39.5 ± 8.3 *vs.* He-O_2: 32.8 ± 10.2%, $P = 0.02$). End inspired lung volume (% FVC) was significantly reduced breathing He-O_2 compared to RA at 4 km (RA: 38.9 ± 7.9 *vs.* He-O_2: 35.0 ± 8.5%, $P = 0.008$).

Men's absolute EELV (l) was significantly lower from 3 to 5 km, with the He-O_2 inspirate. As a % FVC, EELV was significantly lower at 1 and 4 km. Absolute EILV (l) at rest, at 1 km and at 4 km was significantly lower compared to RA. Expressed as % FVC, EILV was not affected by He-O_2. Women's operational lung volumes were not different on He-O_2 compared to RA (tables 11 and 12, and figure 4).

Table 11 - Room Air Operational Lung Volumes

		Rest	1 km	2 km	3 km	4 km	5 km
EELV (l)	Men (*n* = 11)	2.76* ± 0.60	2.02* ± 0.37	1.91* ± 0.41	2.01*† ± 0.31	2.14*† ± 0.42	2.14*† ± 0.50
	Women (*n* = 10)	1.87* ± 0.44	1.39* ± 0.41	1.47* ± 0.43	1.43* ± 0.56	1.47* ± 0.43	1.53* ± 0.48
EELV (% FVC)	Men (*n* = 11)	46 ± 16	37† ± 7	35 ± 8	33 ± 13	39† ± 8	39 ± 9
	Women (*n* = 10)	45 ± 17	35 ± 6	33 ± 12	32 ± 14	37 ± 8	39 ± 9
EILV (l)	Men (*n* = 11)	3.68*† ± 0.59 (*n*=10)	4.81*† ± 0.29	4.79* ± 0.50	4.91* ± 0.49	4.97*† ± 0.53	4.84* ± 0.63
	Women (*n* = 10)	2.55* ± 0.46	3.39* ± 0.64	3.61* ± 0.71	3.50* ± 0.80	3.40* ± 0.70	3.46* ± 0.72
EILV (% FVC)	Men (*n* = 11)	61 ± 21	88 ± 7	87 ± 6	80 ± 27	91 ± 5	88 ± 6
	Women (*n* = 10)	61 ± 21	86 ± 4	82 ± 28	79 ± 27	87 ± 5	88 ± 1

EELV, End expired lung volume; EILV; End inspired lung volume. Values are means ± SD. * Significantly different lung volumes between sexes, $P < 0.05$. † Significantly different lung volumes between men, $P < 0.05$.

Table 12 - Heliox Operational Lung Volumes

		Rest	1 km	2 km	3 km	4 km	5 km
EELV (l)	Men (*n* = 11)	2.50* ± 0.68	1.65 ± 0.44	1.64 ± 0.48 (*n*=10)	1.62† ± 0.52	1.77† ± 0.53	1.83† ± 0.48 (*n*=10)
	Women (*n* = 10)	1.83* ± 0.30	1.36 ± 0.35	1.40 ± 0.42	1.38 ± 0.40	1.48 ± 0.41	1.42 ± 0.41
EELV (% FVC)	Men (*n* = 11)	46 ± 11	27† ± 11	30 ± 7	30 ± 8	33† ± 9	31 ± 13
	Women (*n* = 10)	47 ± 10	34 ± 8	35 ± 10	35 ± 7	37 ± 6	35 ± 6
EILV (l)	Men (*n* = 11)	3.04*† ± 0.55	4.48*† ± 0.52	4.64* ± 0.64	4.59* ± 0.65	4.61*† ± 0.66	4.80* ± 0.67
	Women (*n* = 10)	2.58* ± 0.27	3.35* ± 0.70	3.40* ± 0.82	3.36* ± 0.82	3.37* ± 0.80	3.27* ± 0.85
EILV (% FVC)	Men (*n* = 11)	57* ± 10	75 ± 25	86 ± 5	85 ± 6	85 ± 9	80 ± 27
	Women (*n* = 10)	66* ± 9	84 ± 7	85 ± 10	84 ± 11	84 ± 8	82 ± 11

EELV, End expired lung volume; EILV; End inspired lung volume. Values are means ± SD. * Significantly different lung volumes between sexes, $P < 0.05$. † Significantly different lung volumes between men, $P < 0.05$.

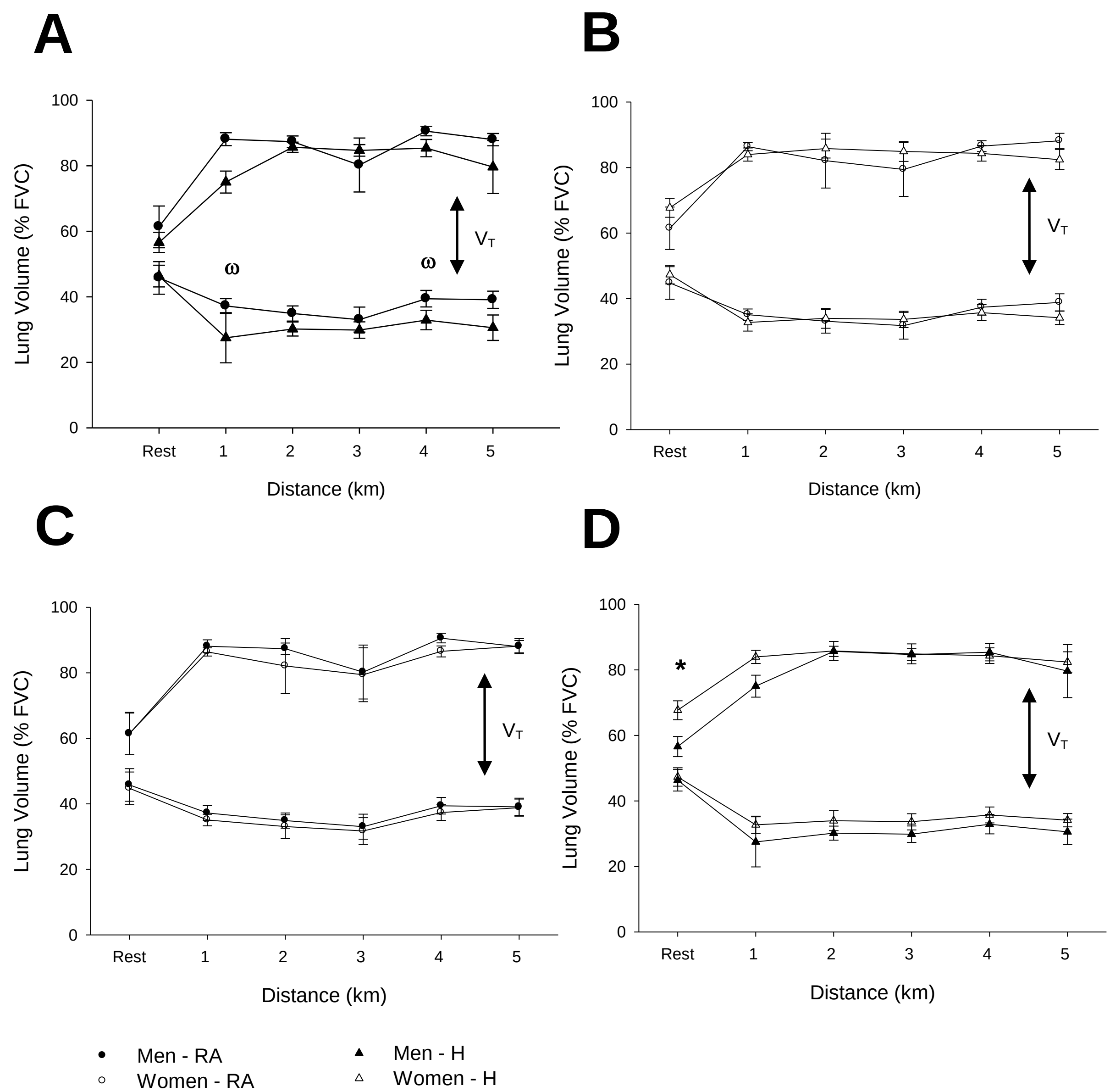


Figure 4 – Operational lung volumes (A) Men RA *vs.* He-O_2 (B) Women RA *vs.* He-O_2 (C) Men *vs.* Women RA (D) Men *vs.* Women He-O_2. **ω** Significant differences in EELV between men RA *vs.* He-O_2. * Significant differences in EILV between men and women breathing He-O_2. Data are presented as means ± SE. Statistical significance is set at the level of $P < 0.05$.

Expiratory Flow Limitation - Susceptibility

Expiratory flow limitation data is reported as averages of all subjects with attainable flow-volume and IC data. Irregular flow rates made analysis of flow-volume breathing loops unviable at rest for 2 subjects breathing RA (subject numbers: 114 and 208). Inaccurate IC maneuvers or inconsistent flows during the 5 km TTs resulted in a lack of EFL data for a small number of subjects at a few km points.

Subject 201 did not perform correct FVC's pre and post exercise during the He-O_2 TT, therefore she is not included in any of the flow-volume relationship data.

Four of 11 men (36%) and 6 of 10 women (60%) developed EFL during the RA 5 km TT. Five of 11 men (45%) and 4 of 10 women (40%) developed EFL during the He-O_2 TT. Three of the 4 EFL-RA men also developed EFL during the He-O_2 TT. Two non-EFL-RA (NEFL) men developed EFL breathing He-O_2. Three of the 6 EFL-RA women developed EFL during the He-O_2 TT. Two women NEFL–RA, developed EFL breathing He-O_2 (table 13 and *Appendix A* - tables 35 and 36 for individual data).

During the 1st km of the RA TT, no subjects developed EFL. Throughout the rest of the TTs, the development of EFL was variable, with some subjects developing EFL early on (1 km – He-O_2; 2 km - RA) and maintaining EFL for the duration of the TT, while others developed EFL intermittently.

Table 13 - Expiratory Flow Limitation - Susceptibility

	EFL susceptibility (*n*)	Rest	1 km	2 km	3 km	4 km	5 km
RA	Men (*n* =11)	0	0	2	3 (*n* = 10)	2	4
	Women (*n* =10)	0	0	1 (*n* = 9)	2 (*n* = 9)	4	4
He-O_2	Men (*n* =11)	0	2 (*n* = 10)	2	3	2	3 (*n* = 10)
	Women (*n* =10)	0	0	2	0	2	2

Values are means of only those subjects having developed EFL.

Expiratory Flow Limitation - Magnitude

The magnitude of EFL varied within and between subjects at each km during both TTs (table 14). Table 15 shows EFL susceptibility and magnitude at 5 km when V'_E was the highest. Four men and 4 women developed EFL breathing RA at 5 km. Development of EFL at 5 km with a He-O_2 inspirate was slightly reduced to 3 men and 2 women. The magnitude of EFL was not different between men and women breathing RA (Men: 48 ± 24, Women: 30 ± 19%, $P = 0.50$) or He-O_2 (Men: 30 ± 7, Women: 45 ± 3%, $P = 0.80$) at 5 km. Heliox did not impact the magnitude of EFL for men, women, or men, and women combined ($P > 0.05$). There appeared to be an association between V'_E and the magnitude of EFL during the RA TT for men and women combined at 2 km (r = 0.55, $P = 0.009$), 4 km (r = 0.51, $P = 0.02$) and 5 km (r = 0.60, $P = 0.01$). For men, an association was found at 4 km (r = 0.71, $P = 0.01$) and 5 km (r = 0.65, $P = 0.03$) breathing RA. However no associations between V'_E and EFL (%V_T) occurred for women breathing RA. During the $He-O_2$ TT no relationships were found for either sex (separate or combined). Fitness as determined by $V'O_{2MAX}$ ($ml \cdot kg^{-1} \cdot min^{-1}$) was only related to the magnitude of EFL for men at 5 km breathing RA (r = 0.78, $P = 0.004$).

Table 14 - Magnitude of EFL for subjects having developed EFL

	EFL magnitude (% V_T)	Rest	1 km	2 km	3 km	4 km	5 km
RA	Men	0	0	26 ± 3	35 ± 20	32 ± 1	48 ± 24
	Women	0	0	21 ± 0	41 ± 33	36 ± 17	30 ± 19
$He-O_2$	Men	0	19 ± 10	30 ± 23	27 ± 27	32 ± 16	30 ± 7
	Women	0	0	16 ± 7	0	42 ± 21	45 ± 3

EFL magnitude; expiratory flow limitation severity (> 5% V_T). Values are means ± SD.

Table 15 - Expiratory Flow Limitation susceptibility and magnitude at 5 km

	n	EFL magnitude at 5 km (% V_T)	*P* value
M-RA	4	48 ± 24	0.50
W-RA	4	30 ± 19	
M-$He-O_2$	3	30 ± 7	0.80
W-$He-O_2$	2	45 ± 3	
M & W – RA	8	39 ± 22	0.39
M & W – $He-O_2$	5	36 ± 10	
M-RA	4	48 ± 24	0.55
M-$He-O_2$	3	30 ± 7	
W-RA	3	30 ± 19	0.77
W-$He-O_2$	2	45 ± 3	

Values are means ± SD.

Expiratory Flow Limitation - Performance

Four of the 9 men with improved $He-O_2$ TT power output developed EFL, and 3 of those 4 also developed EFL during the RA TT. Three of the 8 women who produced more power during the $He-O_2$ TT did so having developed EFL. Those same 3 women also developed EFL during the RA 5 km TT. Two additional women developed EFL during the $He-O_2$ 5 km TT while NEFL when breathing RA.

The 2 men that completed the RA 5 km TT with a higher power output did so having not developed EFL. One of these men did develop EFL during the $He-O_2$ TT. One of the 2 women who performed the RA TT with a higher power output developed EFL breathing RA and $He-O_2$, while EFL could not be determined for the other women (201). The woman with the same power output over the course of the 2 TTs did not develop EFL during either TT.

Expiratory Flow Limitation - Ventilatory Reserve

The ventilatory reserve (V'_E as a percentage of $V'_{E\ CAP}$) was increased with a He-O_2 inspirate in all subjects except 2 men. Men's average RA V'_E utilized 47.4 ± 9.1% of their average RA $V'_{E\ CAP}$ and was significantly reduced to 40.7 ± 10.3% during the He-O_2 TT ($P = 0.002$). Women's average V'_E was 49.0 ± 9.5% of their RA TT $V'_{E\ CAP}$, and was significantly reduced to 40.6 ± 9.1% of their He-O_2 $V'_{E\ CAP}$ ($P = 0.0004$). No significant differences existed between sexes for RA ($P = 0.99$) or He-O_2 ($P = 1.00$). Figure 5 shows the ventilatory reserves for both men and women in relation to their respective TT performances. At 5 km men's and women's combined ventilatory reserve was correlated to the magnitude of EFL for both the RA (r = 0.72, $P = 0.0003$) and He-O_2 (r = 0.61, $P = 0.004$) TT's. Men's RA and He-O_2 5 km ventilatory reserves were correlated to their magnitude of EFL (r = 0.72, $P = 0.02$ and r = 0.79, $P = 0.007$ respectively). At 5 km for women the relationship was significant for the RA TT (r = 0.80, $P = 0.005$), but not the He-O_2 TT (r = 0.51, $P = 0.13$).

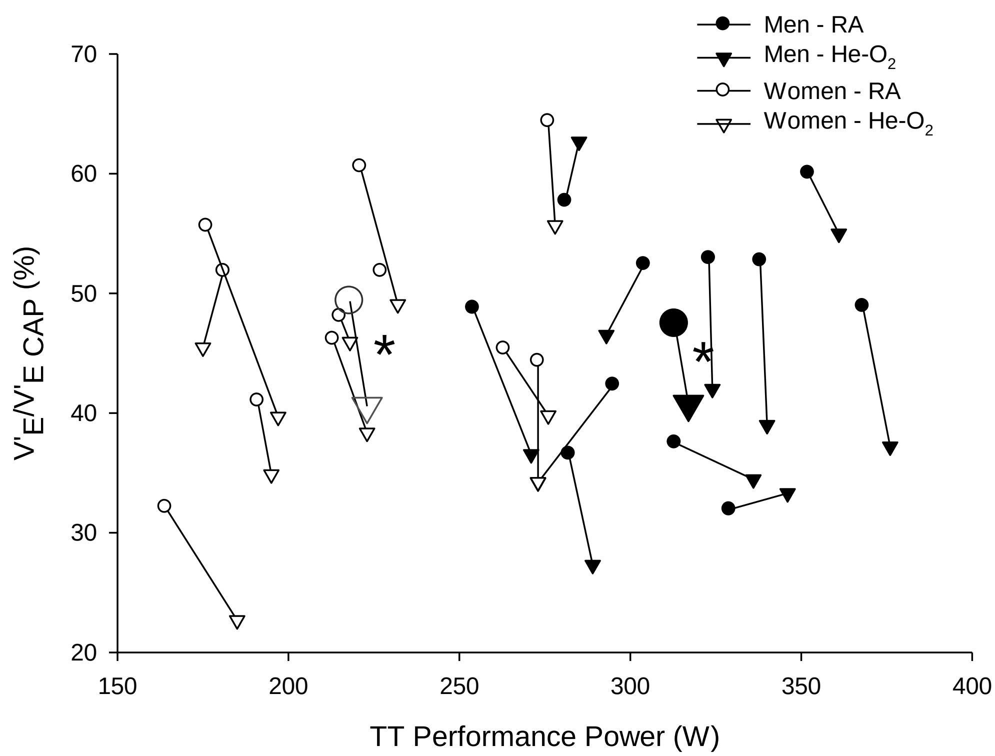


Figure 5 – Average ventilatory reserve throughout the TTs for individual subjects in relation to their TT performances. Group averages are denoted by the larger solid symbols (men) and open symbols (women).
*** S**ignificant differences between RA and He-O_2 ventilatory reserves for both men and women. Statistical significance is set at the level of $P < 0.05$.

Work of Breathing

Men and women's combined total WOB was reduced breathing $He-O_2$ compared to RA from rest to 5 km, with significant reductions at 2 through 5 km ($P < 0.05$) (table 16). Table 17 shows men's and women's separate total WOB. Men's and women's total WOB were not different at rest or at any km throughout either TT ($P > 0.05$) (table 17). However, at each km for an equivalent total WOB to that of men, women had significantly lower V'_E (figure 6). Men's total WOB was reduced at 3 km (M-RA: 299.1 ± 151.9 *vs*. M- $He-O_2$: 221.0 ± 74.0 $J \cdot min^{-1}$, $P = 0.01$). Heliox had no effect on women's total WOB at any km.

Table 16 - Total Work of Breathing - Men and Women Combined

Total Work of Breathing ($J \cdot min^{-1}$)	Rest	1 km	2 km	3 km	4 km	5 km
M & W RA	3.6 ± 3.3	157 ± 72	214* ± 99	242* ± 127	265* ± 117	299* ± 121
M & W $He-O_2$	3.1 ± 2.4	139 ± 60	181* ± 80	192* ± 80	214* ± 90	264* ± 94
P value	0.42	0.06	0.02	0.003	0.003	0.01

Values are means ± SD. * Significantly different total WOB men and women RA *vs*. men and women $He-O_2$ TT

Table 17 - Total Work of Breathing - Men and Women Separate

Total Work of Breathing ($J \cdot min^{-1}$)	Rest	1 km	2 km	3 km	4 km	5 km
M-RA	3.6 ± 3.4	182 ± 92	251 ± 121	299† ± 152	305 ± 141	345 ± 134
W-RA	3.6 ± 3.3	132 ± 31	177 ± 53	191 ± 72	223 ± 67	248 ± 58
P value	1.0	0.53	0.44	0.26	0.49	0.29
M-$He-O_2$	2.5 ± 1.6	157 ± 73	208 ± 82	221† ± 74	250 ± 84	319 ± 79
W-$He-O_2$	3.7 ± 3.0	121 ± 41	153 ± 72	167 ± 79	176 ± 84	204 ± 72
P value	0.88	0.76	0.67	0.78	0.58	0.18
P value M-RA *vs*. $He-O_2$	0.54	0.22	0.11	0.01	0.07	0.46
P value W-RA *vs*. $He-O_2$	1.0	0.81	0.56	0.69	0.18	0.13

Values are means ± SD. † Significantly different total WOB in men RA *vs*. $He-O_2$ TT

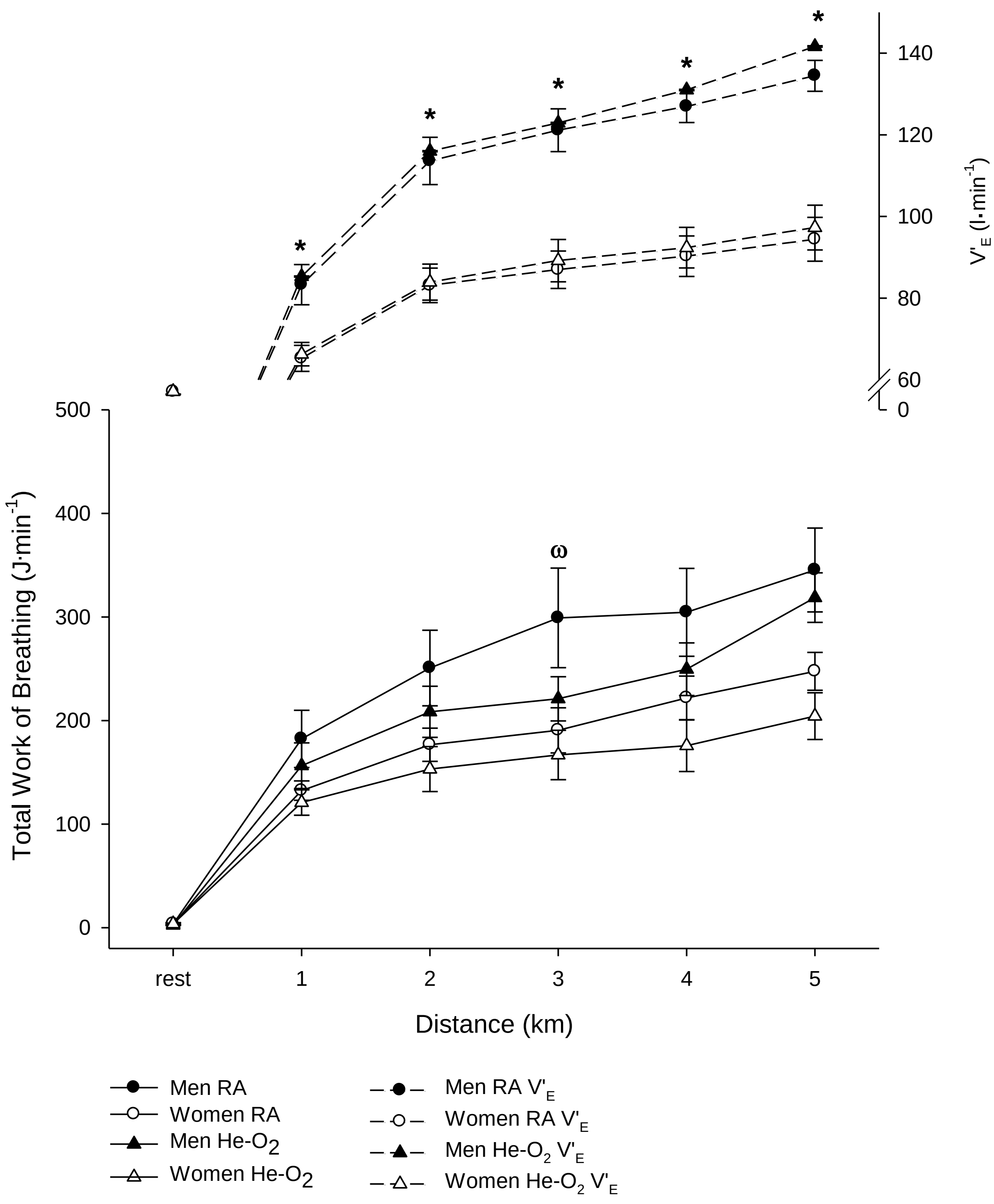


Figure 6 – Total WOB for men and women breathing RA and He-O_2. ***** Significant differences in V'_E between men and women during RA and He-O_2 TTs. **ω** Significant difference between men RA *vs.* He-O_2. Data are presented as means ± SE. Statistical significance is set at the level of $P < 0.05$.

The Ires (inspiratory resistive) WOB was significantly reduced breathing $He\text{-}O_2$ compared to RA for men and women combined throughout the 5 km TT ($P < 0.05$). Figure 7 (Panel A and B) shows the Ires WOB for men and women separately. The Ires WOB was not different between the sexes for either inspirate ($P > 0.05$). Men's Ires WOB was significantly reduced breathing $He\text{-}O_2$ compared to RA at 1 through 5 km (figure 7, Panel B). Women's Ires WOB was significantly reduced breathing $He\text{-}O_2$ compared to RA at 5 km (figure 7, Panel A).

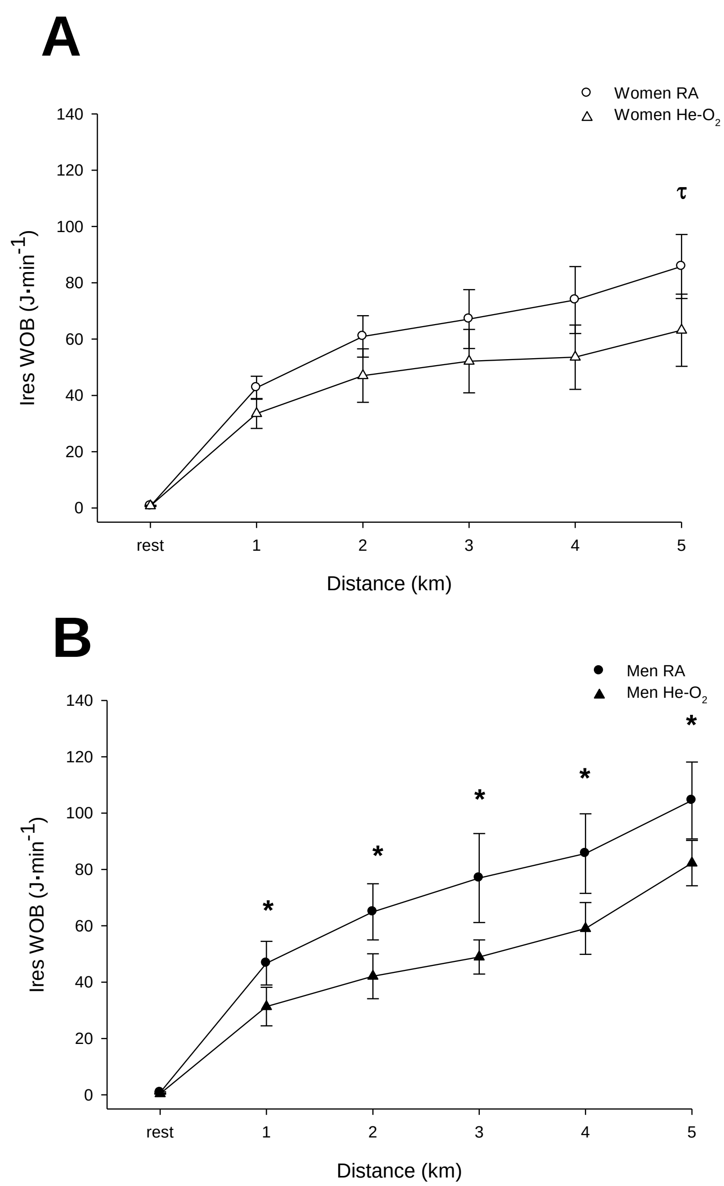


Figure 7 – Ires WOB breathing RA and $He\text{-}O_2$ for women (A) and men (B). **τ** Significant differences between women RA *vs.* $He\text{-}O_2$. ***** Significant differences between men RA *vs.* $He\text{-}O_2$. Data are presented as means ± SE. Statistical significance is set at the level of $P < 0.05$.

Men's and women's combined Iel (inspiratory elastic) WOB during the He-O_2 TT was not statistically different from the RA TT (table 18). Sex had an effect on the Iel WOB only at 5 km breathing He-O_2 (men: 227.2 *vs*. women: 130.1 J·min^{-1}, $P = 0.02$). Separately both women and men's Iel WOB was not affected by the He-O_2 inspirate (table 19).

The Etot (expiratory total) WOB for men and women combined was reduced during the He-O_2 TT compared to the RA TT, reaching statistical significance at 2 and 4 km (RA: 16.2 ± 30.1 *vs*. He-O_2: 2.0 ± 2.8 J·min^{-1}, $P = 0.03$; RA: 24.5 ± 41.4 *vs*.He-O_2: 4.8 ± 6.7 J·min^{-1}, $P = 0.04$, respectively) (table 20). Sex did not affect the Etot WOB nor did inspirate for men and women as separate groups (table 21).

Table 18 - Inspiratory Elastic Work of Breathing **-** Men and Women Combined

Iel Work of Breathing (J·min^{-1}) M & W	Rest	1 km	2 km	3 km	4 km	5 km
RA	2.4 ± 2.2	104 ± 46	135 ± 58	147 ± 62	157 ± 58	176 ± 60
He-O_2	2.4 ± 1.9	105 ± 45	134 ± 59	139 ± 57	152 ± 62	183 ± 67
P value	0.98	0.91	0.97	0.13	0.40	0.27

Values are means ± SD.

Table 19 - Inspiratory Elastic Work of Breathing **-** Men and Women Separate

Iel Work of Breathing (J·min^{-1})	Rest	1 km	2 km	3 km	4 km	5 km
M-RA	2.3 ± 1.5	122 ± 57	160 ± 70	181 ± 69	186 ± 61	208 ± 62
W-RA	2.6 ± 2.8	87 ± 21	109 ± 29	115 ± 32	125 ± 33	140 ± 30
P value	0.99	0.46	0.35	0.18	0.22	0.12
M-HeO_2	2.0 ± 1.2	123 ± 54	163 ± 60	166 ± 55	184 ± 59	227* ± 61
W-HeO_2	2.8 ± 2.2	87 ± 26	105 ± 43	113 ± 43	113 ± 43	130* ± 33
P value	0.90	0.45	0.25	0.34	0.14	0.02
M-RA *vs*. He-O_2 *P* value	0.94	1.00	0.99	0.26	0.99	0.16
W-RA *vs*. He-O_2 *P* value	0.93	1.00	0.99	0.99	0.75	0.95

Values are means ± SD. *Significantly different Ires WOB between men and women on He-O_2.

Table 20 - Expiratory Total Work of Breathing - Men and Women Combined

Etot Work of Breathing ($J \cdot min^{-1}$) M & W	Rest	1 km	2 km	3 km	4 km	5 km
RA	0.08 ± 0.14	8.6 ± 18.1	16.2* ± 30.1	20.2 ± 42.5	24.5* ± 41.4	23.6 ± 40.5
He-O_2	0.03 ± 0.07	1.4 ± 2.2	2.0* ± 2.8	3.0 ± 3.44	4.8* ± 6.7	5.9 ± 7.8
P value	0.59	0.22	0.03	0.31	0.04	0.49

Values are means ± SD. *Significantly different Etot WOB between men and women combined on He-O_2 *vs.* RA.

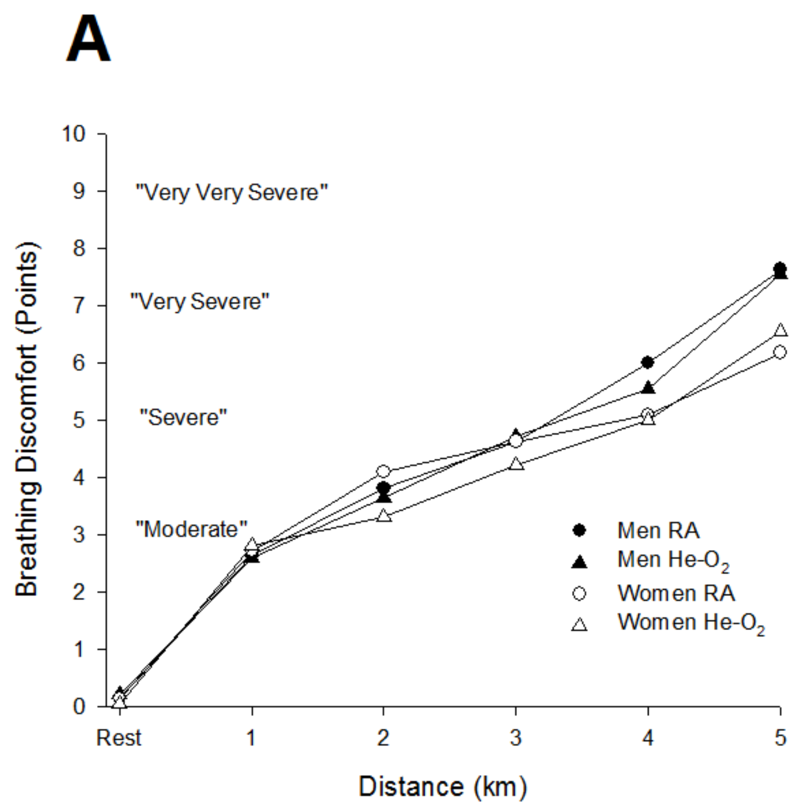
Table 21 - Expiratory Total Work of Breathing - Men and Women Separate

Etot Work of Breathing ($J \cdot min^{-1}$)	Rest	1 km	2 km	3 km	4 km	5 km
M-RA	0.1 ± 0.2	14.0 ± 24.6	25.8 ± 40.7	30.2 ± 57.1	32.8 ± 54.8	32.6 ± 53.8
W-RA	0.1 ± 0.1	3.1 ± 4.1	6.7 ± 7.4	8.4 ± 11.3	14.1 ± 17.0	12.4 ± 14.8
P value	0.95	0.24	0.20	0.43	0.59	0.50
M-HeO_2	0.0 ± 0.1	2.4 ± 2.8	3.2 ± 3.4	4.1 ± 3.8	6.3 ± 7.5	9.2 ± 9.0
W-HeO_2	0.0 ± 0.1	0.4 ± 0.6	0.7 ± 1.3	1.7 ± 2.7	2.9 ± 5.5	1.9 ± 3.9
P value	1.00	0.99	0.99	1.00	1.00	0.95
P value M-RA *vs.* He-O_2	0.46	0.13	0.06	0.18	0.16	0.23
P value W-RA *vs.* He-O_2	0.89	0.95	0.98	0.94	0.76	0.79

Values are means ± SD.

SENSORY RESPONSES

Neither sex nor inspirate affected dyspnea or leg discomfort at rest or at any km during the 5 km TT except at 2 km where men's and women's combined dyspnea ratings were significantly lower when breathing He-O_2 (figure 8). Additionally, the relative contributions of leg and breathing discomfort preventing faster cycling were not affected by sex or gas type (table 22). The main reason for men not cycling faster breathing RA was leg discomfort (n = 6), followed by a combination of leg and respiratory discomfort (n = 3), and lastly respiratory discomfort (n = 2). With a He-O_2 inspirate, 7 men reported their performance was limited by their legs and 4 by a combination of legs and breathing. Women's reasons for not cycling faster during the RA TT were equally distributed between leg discomfort and a combination of leg and breathing discomfort, with one woman rating 'other' inhibiting her performance. Women's ratings were similar during the He-O_2 TT with 6 women claiming leg discomfort and 5 reporting a combination of leg and breathing discomfort (table 22).



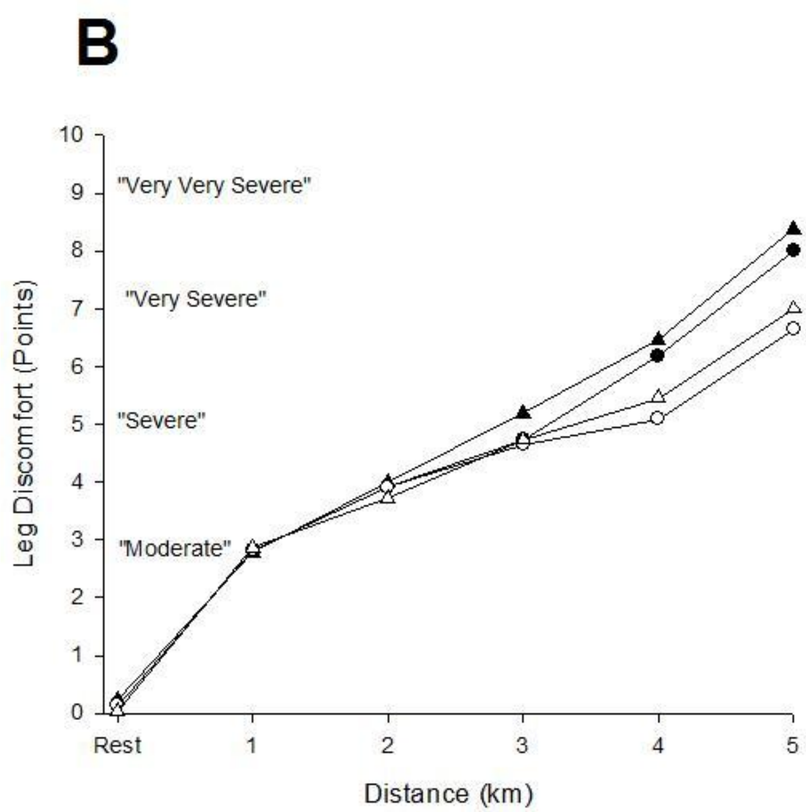


Figure 8 – Breathing (A) and Leg (B) discomfort for men and women breathing RA and He-O_2.

Table 22 - Ratings of Perceived Exertion at TT Completion

RA	Men (*n* = 11)	Women (*n* = 11)	*P* value
Reason for not going faster:			
Respiratory	2	0	
Leg	6	5	
Combination	3	5	
Other	0	1	
Relative Contributions preventing faster TT:			
% respiratory discomfort	44 ± 17 (30 – 85)	36 ± 21 (0 – 70)	0.14
% leg discomfort	56 ± 17 (15 – 70)	64 ± 21 (30 – 100)	0.14
He-O_2			
Reason for not going faster:			
Respiratory	0	0	
Leg	7	6	
Combination	4	5	
Other	0	0	
Relative Contributions preventing faster TT:			
% respiratory discomfort	37 ± 8.8	33 ± 13.1	0.40
% leg discomfort	63 ± 8.8	67 ± 13.1	0.40

Values are means ± SD (ranges).

DISCUSSION

The main findings of this investigation were: 1) the exercise performance improvements when breathing He-O_2 were modest, variable between subjects and equally variable between men and women; 2) women were more susceptible to EFL than men breathing RA, and the effects of He-O_2 on EFL development were equally variable for both men and women; 3) for a significantly lower V'_E, women had the same total WOB and operational lung volumes as men; 4) sensory responses were similar for men and women regardless of inspirate or EFL.

The collective findings from this study suggest that the reduced density of He relative to N_2 may not necessarily unload the respiratory system of sufficient magnitude to remove EFL and reduce the total WOB, to enable large and consistent gains in exercise performance. It appears EFL (susceptibility and magnitude) is not an all-or-none phenomenon and can occur to varying extents in both sexes during rigorous exercise. Sex-based differences in pulmonary structure and function predispose women to mechanical ventilatory constraints breathing RA. Ventilatory capacity in conjunction with changes in EELV and expiratory flow rates are likely the main contributors to avoiding and/or removing EFL. Sensory responses are not affected by sex-based differences in pulmonary structure or function, nor are they affected by He-O_2 or the development of EFL.

PERFORMANCE EFFECTS OF HELIOX

Endurance trained cyclists/triathletes were tested because their elevated metabolic demands require greater V'_E despite possessing resting pulmonary function values (lung size and flow rates) that are similar to untrained individuals. As such, this makes ET athletes more likely to develop EFL (70). To date there is no evidence that cycling training regimes and/or fitness level positively affect pulmonary function (44, 51, 57, 61). Men and women in this study are comparable to ET cyclists/triathletes studied by others (31, 32, 44, 53), and previous racing experience meant the athletes could perform reproducible TTs. Both men and women in this study had pulmonary function values that met or exceeded predicted values (3). Men's lung volumes and peak expiratory flow rates were significantly higher than women's suggesting the men had larger diffusion surfaces (82) and airway diameters (55).

The He-O_2 TT was completed faster and at a higher power output than the RA TT although neither variable reached statistical significance (P = 0.06). Despite this the observed performance improvements are scientifically meaningful although mechanistically unclear as the likely range of the true values (95% CI) results in both performance enhancement and decrement. A greater performance improvement would likely be observed with a larger sample size as similar (non-significant) improvements in time-to-exhaustion have been reported for men with a 20% O_2 – 80% He inspirate compared to RA (87). The performance improvement can be attributed to the effects of He's reduced density on ventilatory mechanics (refer to *Lung Mechanics*). This is because He has no known metabolic affects for individuals with healthy pulmonary systems (12). Helium's relatively high thermal conductivity does not appear to have an effect on body temperature when used as an inspirate or on bronchodilation in individuals without asthma (87).

Over the course of each TT, men and women cycled at a consistent cadence and speed. Men on average completed the RA and He-O_2 TTs faster than women, however not all men outperformed women on either trial (refer to *Methodological Considerations*). Cycling improvements were attributed to He-O_2 because almost half of the TTs with a higher power output were performed 1st eliminating a potential 'learning effect', and the duration between tests had no bearing on performance. The 'training log' (*Appendix C*) assured training (volume and intensity), nutrition, and sleep were consistent between trials so as to minimize any confounding effects.

The FAM TT was expectedly slower than the experimental TTs since it was performed shortly after the incremental cycle test, but subjects pushed themselves to volitional exhaustion. By providing subjects an opportunity to become accustomed to the ergometers gearing, and their desired pacing strategy, the FAM TT limited any 'learning effect' that could have potentially confounded any observed performance related changes.

EXPIRATORY FLOW LIMITATION

Susceptibility & Magnitude

Consistent with previous findings, women in the present study were more susceptible to developing EFL compared to men during RA exercise despite having significantly lower V'_E and expiratory flow rates (23, 32, 44, 53, 86). Sex-based differences in pulmonary structure (lung and airway size) (55) and function (MEFV curve) (51) are likely the cause for the differences. As such, women have relatively less ventilatory reserve within their MEFV curve to accommodate exercise-induced increases in V'_E. Previous research has revealed women that possess FVC (32) and dysanapsis ratios similar in size to that predicted for men (23) are less susceptible to developing EFL. The enhanced lung volumes and airflow rates possessed by these women greatly expand their MEFV curves and thus increase their ventilatory capacities decreasing their propensity to develop mechanical ventilatory constraints. Accordingly the subjects in this study utilizing a greater percentage of their ventilatory capacity developed EFL of a greater magnitude.

Helium was used in place of N_2 in an attempt to increase airflow rate thereby lessening or eliminating EFL due to He's substantial affects on both the inspiratory and expiratory portions of the maximal flow-volume curve. Expiratory flow limitation was not substantially affected in either sex compared to RA, because for a similar lung volume subjects utilized the greater ventilatory reserve by increasing exercise expiratory flow rates until the MEFV curve was intersected. Men increased their expiratory flow rates by a significantly greater amount compared to women (men: 22% *vs.* women: 13%) and in doing so a greater number of men developed EFL during the He-O_2 TT compared to women (45% men *vs.* 40% women).

Changes in EELV and expiratory flow rates had the greatest impact on the magnitude of EFL for each subject breathing RA or He-O_2, regardless of an increased MEFV curve. A strong relationship existed between the magnitude of EFL and ventilatory capacity at 5 km for both RA and He-O_2. Heliox slightly increased V'_E however the magnitude of EFL was slightly decreased at 5 km for men and increased at 5 km for women. This is in contrast to McClaran *et al.* (53) who found the He-O_2 induced increases of the MEFV curve reduced EFL in women. However a He-O_2 inspirate has not always demonstrated a reduction in the development of EFL (6). In support of previous research in our laboratory, fitness was not related to the magnitude of EFL in women. Presumably women's lung and airway size play a bigger role in the susceptibility of EFL than fitness and V'_E alone (23).

Impending EFL

There is growing evidence supporting the concept of EFL as a continuum rather than an all-or-none phenomenon. Impending EFL occurs when the exercise flow-volume loop follows (but does not intersect) the MEFV curve, and EELV increases towards resting (54). Nearly all NEFL subjects in this study exhibited the characteristics of impending EFL. Given that the presence or absence of EFL did not directly affect operational lung volumes, presumably impending EFL regulates EELV. Changes in EELV were variable between subjects, as each subject attempted to maximize expiratory flow rates at the lowest EELV (i.e., the diaphragm's optimal length-tension relationship) without developing EFL. It has been suggested that EFL (full or impending) causes a reflex inhibition of expiration, causing premature inspiration and increases in EELV (54, 69). This phenomenon has been shown in a group of healthy moderately active men studied by Younes and Kivinen (88) that did not development EFL (due to relatively low V'_E) but showed relative lung hyperinflation as maximal exercise capacity was approached. In the present study, EFL had variable effects on performance for both sexes, with subjects performing better on the RA or He-O_2 TTs despite EFL development. Potentially, alterations in lung volumes brought about by *impending* EFL have a profound effect on performance in addition to the presence or absence of *full* EFL.

RESPIRATORY MECHANICS

Metabolic Data and Breathing Pattern

The larger stature and greater metabolic requirements of men in the present study resulted in a higher V'_E compared to women. Men were able to increase their V'_E through increases in V_T made possible through their relatively larger vital capacities. Consistent with previous findings in ET women (30), the women in this study adopted a different breathing pattern relying to a greater extent on f_b to elevate V'_E. This 'tachypneic' breathing pattern reduces the Iel WOB by recovering energy used during expiration. Previous studies have shown women to have significantly higher operational lung volumes compared to men and thus explaining the tachypneic breathing pattern. Although sex-based differences in operational lung volumes were not shown in this study it is likely the women were trying to reduce their total WOB by reducing their Iel WOB. Over the last 2 km's during both TTs, men's V_T decreased as EILV approached 90% of FVC. At this point men utilized the tachypneic pattern to decrease the metabolic cost of breathing (Iel WOB) as lung volumes encroached on the non-compliant portion of the lungs' pressure-volume curve. It is also believed the lungs' stretch receptors inhibit inspiration, constraining the ventilatory response when EILV approaches 90% FVC (54). A reduced contribution of V_T near maximal exercise is consistent with the finding of other highly trained cyclists (48, 54).

Heliox caused a small (non-significant) increase in V'_E regardless of EFL development or attenuation. This is in contrast to previous reports whereby in healthy young men and women V'_E increased *only* for those that underwent reductions (susceptibility or magnitude) in EFL from RA to He-O_2 (53, 54). Older individuals with mild chronic airflow limitation have shown increases in V'_E at ventilatory threshold and maximal exercise despite no changes in EFL susceptibility or magnitude (5). It appears the He-O_2 induced resistive unloading of the pulmonary system allowed for increases in V'_E. However, women's flow rates were likely not high enough for He-O_2 to greatly affect the resistive unloading of the airways enabling women to increase V'_E through increases in V_T (increasing alveolar V'_E). Thus women's f_b was significantly higher during the He-O_2 TT.

Operational Lung Volumes

Operational lung volumes were similar between sexes when breathing RA. This is in contrast to Guenette *et al.* (30) who found that EELV and EILV (expressed as % FVC) were significantly higher in women. Nevertheless, the general operational lung volume strategy was consistent with that previously reported in the literature (23, 32, 69, 86, 88). All subjects reduced their EELV at the beginning of both TTs from resting levels via active expiration to facilitate inspiration by optimizing diaphragmatic length. By doing so expiration is performed primarily by elastic work from chest wall recoil, of which some energy is recovered for the preceding inspiration. Breathing at lower operational lung volumes retains lung compliance. During the RA TT, men and women continued to reduce their EELV from 1 – 3 km for the aforementioned reasons. At 4 km both sexes increased their EELV (men: 6%, women: 5%); and at 5 km women increased (2%), while men maintained, their EELV taking advantage of higher flow rates available at higher operational lung volumes, preventing dynamic airway compression, and potentially reducing, removing or avoiding EFL (figure 9).

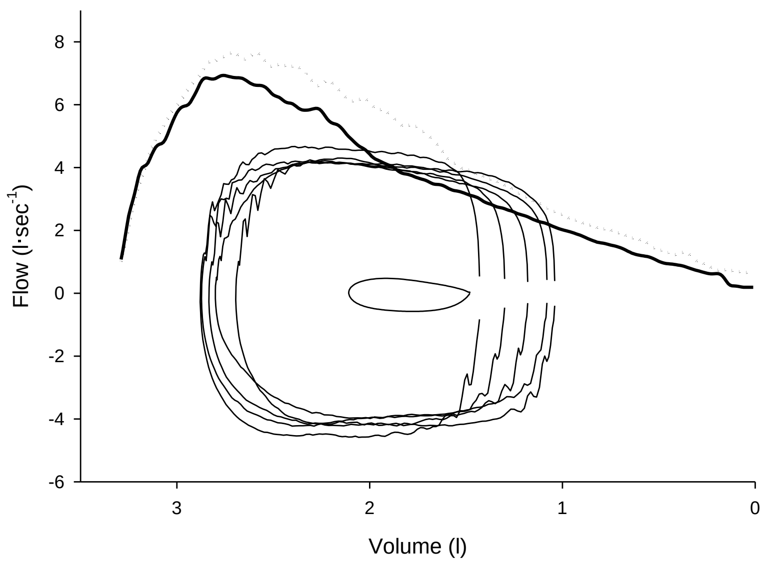


Figure 9 – Representative subject demonstrating increasing EELV as EFL developed throughout the TT.

Both men and women underwent non-significant similar changes for operational lung volumes breathing He-O_2 compared to RA (except men's EELV at 1 and 4 km); however, the general trend is worth noting. Men and women slightly *increased* their EELV from 2 – 4 km. At 5 km both men and women *reduced* their EELV because of the extra expiratory flow reserve brought from the increased MEFV curve. This allowed the preservation of expiratory flow rates at a lower EELV and thus reduced metabolic cost (i.e., optimal diaphragmatic position for force generation and most favorable lung compliance). Men's EELV was slightly lower throughout the He-O_2 TT compared to RA. This was likely because men's significantly higher flow rates benefited to a greater extent from the reduced resistance of $He\text{-}O_2$. At a lower lung volume, men accordingly have more ventilatory reserve than women.

Changes in EILV followed that of EELV and were not different between sexes or influenced by inspirate. Throughout both TTs, EILV reached or exceeded 80% FVC increasing the elastic WOB by way of shifting V_T to the less compliant portion of the pressure-volume curve. However, EILV remained for the most part below 90% FVC to avoid excessively elevating the elastic WOB. A constant EILV from RA to $He\text{-}O_2$ is supported by others (5).

Resting operational lung volumes were not significantly different between RA and $He\text{-}O_2$ for men and women. At rest subjects are overly conscious of their breathing pattern and performing the IC maneuver so resting V'_E is highly susceptible to irregular breathing through uncharacteristic alterations in f_b, V_T, and flow rates. During timed exercise, performance motivation, physical exertion and mental exhaustion act to distract subjects from overanalyzing their respective breathing patterns.

Due to the variability in the susceptibility and magnitude of EFL over the course of the TT, EFL had no consistent effect on operational lung volumes. The maintenance of EELV occurred regardless of EFL development and is in contrast to McClaran *et al.* (53) who found that EELV was lower in women only when $He\text{-}O_2$ significantly reduced EFL.

Work of Breathing

Helium caused a lower WOB at every km despite a higher V'_E. However, the WOB reductions with He administration were similar between men and women. Women's V'_E was significantly lower than men's breathing RA or $He\text{-}O_2$ despite a similar WOB. Thus, for a given V'_E women had a greater WOB. A higher physiological cost of breathing for women has previously been reported in our laboratory (32), with the sex-based differences rising exponentially at V'_E above 90 $l \cdot min^{-1}$. Over the second half of the TTs in this study, V'_E exceeded 90 $l \cdot min^{-1}$. The greater sex-based disparity in the total WOB as V'_E increases appears to be a result of differences in the work to overcome airflow resistance. Guenette *et al.* (30) found the Ires WOB was the main cause for women's relatively higher total WOB. Women's significantly smaller conducting airways (52, 77) exponentially increase airflow resistance based on Poiseuille's law. As such, the women in this study had a similar Ires WOB despite significantly lower expiratory flow rates compared to their male counterparts. Tidal volume was also significantly lower for women despite a similar Iel WOB. Although the Iel WOB has not shown sex-based differences (30), women in this and other studies (23, 30, 53) utilized a tachypneic ventilatory pattern to minimize the Iel WOB since previously discussed anatomical differences limit women's ability to reduce their resistive

WOB. As such, women's expiratory resistive WOB would have been the major cause of their relatively higher Etot WOB.

Heliox reduced the Ires WOB for men throughout the TT and women at 5 km in spite of both sexes obtaining significantly higher expiratory flow rates. Men's V'_E was high enough for $He\text{-}O_2$ to have a significant effect on the airflow characteristics (turbulent *vs.* laminar). Women's V'_E was likely not high enough for the density and viscosity differences between He and N_2 to emerge until 5 km, at which point V'_E exceeded 90 $l \cdot min^{-1}$ and the Ires WOB was significantly reduced. Tidal volumes and operational lung volumes were not affected by $He\text{-}O_2$ for either men or women, and thus the Iel WOB was unchanged with $He\text{-}O_2$. The Etot WOB was reduced breathing $He\text{-}O_2$ for men and women combined at 2 and 4 km, likely due to the decreased expiratory airflow resistance. For each sex however, the Etot WOB was similar between $He\text{-}O_2$ and RA despite significantly higher $He\text{-}O_2$ expiratory flow rates, presumably because of the reduced airflow resistance.

Expiratory flow limitation increases the WOB for a given V'_E. When EFL develops, the rate of expiratory airflow is constrained, and attempts to increase expiratory airflow (and V'_E) by generating greater trans-pulmonary pressures are ineffective. Generation of trans-pulmonary pressures in excess of the maximal effective pressures (critical pressure at iso-lung volume resulting in maximal expiratory flow) can occur and due to airway compression potentially decrease expiratory airflow (60). Due to the variability in the susceptibility and magnitude of EFL, and the V'_E at which EFL occurred over the course of the 2 TTs, discerning the effects of mechanical ventilatory constraints on the WOB in this study is problematic.

Proportional-assist ventilation unloads the inspiratory muscles, and in doing so improves time-to-exhaustion and attenuate the respiratory muscle metaboreflex decreasing sensory perceptions of respiratory and leg discomfort in healthy male athletes (37). Obese individuals and those suffering from disease such as COPD have shown improvements in exercise performance and attenuations in dyspnea with PAV (24, 39) Both $He\text{-}O_2$ and PAV reduce the expiratory WOB to a similar extent, however PAV unloads inspiration by a substantially greater amount compared to $He\text{-}O_2$ (2). The present study aimed to disrupt inspiration as little as possible thereby facilitating the analysis of EFL's affect on V'_E. The V'_E of a cyclist during a TT involving non-uniform gearing ratios and power output can cause PAV to disrupt the athlete's preferred breathing pattern (35, 37). It is tremendously difficult to blind subjects to PAV and minimize confounding errors with negligible disruption to subject's normal breathing and cycling responses thus making PAV a poor methodological choice (Refer to *Methodological Considerations*).

Body Position

Body position was identical during both TTs to avoid confounding lung mechanics and sensory responses. However, respiratory changes induced by cycling position are worth noting especially when comparing lung mechanics of a cyclist to those of upright exercise disciplines. Trunk flexion causes abdominal compression which has been shown to increase V'_E through f_b as the diaphragm is restricted in its ability to descend and expand lung volume (27). Diaphragmatic restrictions rather than EFL would potentially cause EELV to increase. However, EELV in this study was not different from that of runners (44, 53) so presumably abdominal compression was not the cause. Furthermore, EELV was regulated by proximity of expiratory flows to the MEFV curve and subjects were not positioned in the more aggressive 'drops' or 'aerobars', which further increase abdominal compression. Rather the hands were placed on the 'brake-hoods' allowing for arm bracing which improves the function of the accessory muscles to expand the rib cage and increase vital capacity (8).

SENSORY EFFECTS

This study supports previous findings that leg discomfort is the main symptom limiting exercise in most healthy men and women (34). Leg discomfort was rated higher as the limiting factor to exercise performance both as an absolute cause and as a relative contribution in the present study. There is belief dyspnea may be higher in young women compared to young men due to anatomical differences (smaller airway diameters) which increases airway resistance (76). This is based on significantly different dyspnea ratings between older healthy men and women (64) and those suffering from clinical illness such as chronic obstructive pulmonary disease (19). However there were no sex-based differences in dyspnea during either TT in this study. Similar non-significant findings have been reported by others comparing ET men and women during sustained heavy exercise (31). Expiratory flow limitation did not affect sensory responses for either sex in this study and is consistent with previous findings in our laboratory (23, 86). Dyspnea is not likely the symptom limiter of exercise in healthy individuals (34).

Heliox did not affect sensory responses for either sex. Within the literature, $He\text{-}O_2$ has not made a significant impact on dyspnea rating during rigorous exercise in men and women of average fitness (6) or highly trained men (54). Babb (5) also failed to find a difference in dyspnea rating in a group of older individuals with a $He\text{-}O_2$ inspirate.

Men and women's sensory responses post RA and $He\text{-}O_2$ TTs were significantly lower than after the $V'O_{2MAX}$ test. Significant sex-based differences in RPE at the end of the incremental exercise test with no differences during constant load exercise have been shown before (31). Possibly, the ability of subjects to control the intensity, and thereby their effort during the TTs, caused the reduced RPEs relative to the computer controlled incremental cycle test.

METHODOLOGICAL CONSIDERATIONS

The IC and MEFV curve method of detecting EFL, when done correctly, can be accurate despite its caveats. Using an IC to measure EELV could be problematic because the mere action of performing an IC could alter EELV either before or after the IC is performed (60). By having subjects practice the maneuver and observing a few tidal breaths before the IC, normal breathing can be ensured. The IC maneuver does require subject motivation; if subjects do not give their best effort they may not fully inspire to TLC. A continuous measure of esophageal pressure confirmed that maximal inspiratory pressure (same as at rest) was achieved to perform the IC (32, 45). Measurement of EFL is limited in that it cannot be measured continuously during exercise, only at the end of a specified time period (each km). Due to changes in operational lung volumes throughout the TT, the susceptibility and magnitude of EFL may have been underestimated.

The negative expiratory pressure technique (NEP) allows for a continuous measure of EFL susceptibility throughout exercise but it does not provide an indication of impending EFL an important variable in this study. In addition NEP may cause collapse of the upper airways potentially causing a reflexive increase in EELV confounding comparisons to RA trials.

Using esophageal balloons to measure the WOB does not take into account the flow-resistive work done on the tissues of the thorax and abdomen. The amount of work is small at low V'_E and increases at higher V'_E, which would increase the total WOB. Unlike PAV where the degree of inspiratory unloading can be adjusted, the precise amount of respiratory unloading that He-O_2 provides is unknown. Heliox unloads both the inspiratory and expiratory side of V'_E. Therefore consideration needs to be taken if changes to the inspiratory WOB were a direct result of He-O_2 or the secondary effects of alleviated expiratory mechanical ventilatory constraints.

Cycling does recruit less muscle mass than running or cross-country skiing, therefore theoretically requiring a lower V'_E to sustain exercise. However, studies using ET cyclists (32) have found V'_E comparable to those achieved by elite runners (44). Healthy young men have been shown to develop EFL during heavy exercise at V'_E in excess of 120 $l \cdot min^{-1}$ (44). The men in this study reached V'_E in excess of 120 $l \cdot min^{-1}$ from 3 to 5 km. Furthermore both sex's V'_E at 5 km during the TTs were similar to their respective V'_E at $V'O_{2MAX,}$ assuring subjects were reaching their full ventilatory capacities. The controlled setting provided by the cycle ergometer allowed for the collection of data with fewer artifacts (compared to tread-mill) and also provided insight into ventilatory constraints affecting cyclists with a high degree of trunk flexion.

The maximal power output achieved on the incremental test is likely an underrepresentation of the athlete's true capabilities due to the abrupt wattage increments characteristic of the step-wise protocol. Women were at a higher percentage of their predicted $V'O_{2MAX}$ compared to men. This was likely the result of 4 men slightly below the $V'O_{2MAX}$ criteria, and possibly the prediction equation (46) (created 25 years ago) underestimating the women's predicted $V'O_{2MAX}$. However men and women were similar based upon power-to-weight ratios. Three women produced more power than 1 man breathing RA, and 2 of those women again produced more power than 2 men breathing He-O_2. The 2 'less powerful' men both exceeded the $V'O_{2MAX}$ criteria and were experienced in road and mountain cycling respectively. The 3 'more powerful' women competed at the highest level of all subjects and reached a power output on the $V'O_{2MAX}$ comparable with most men. Recruitment strived to attain the fittest cyclists/triathletes with ample race experience. However, women were on average more aerobically fit (as determined by $V'O_{2MAX}$ as percent predicted) and subjects were not TT specialists, which could have been why some women outperformed men. Also, the CVs for indoor cycling were based on elite cyclists and thus may have been slightly misrepresentative. A few FAM TTs to determine a CV for each individual subject would have given more precise insight into each individual subject's performance improvement. However there was no difference in performance between the 1st and 2nd TT so it appears that the learning or knowledge of time (as displayed on the monitor) did not affect performance.

Subject 108's (man) exercise inspiratory flow-volume loops revealed a saw tooth pattern during the RA TT that was no longer present breathing He-O_2 (Refer to *Appendix C, Figure 35)*. The saw tooth pattern, determined by visual inspection of fluctuations in inspiratiory flow, is characteristic of vocal cord dysfunction (38). However, the degree of irregular inspiratory flow exhibited by subject 108 was less than half of that shown in previous reports (38). Furthermore, inspiratory and expiratory flow rates were not affected. This subject did not have severe dyspnea ratings or rate dyspnea as his exercise symptom limiting factor. Breathing He-O_2 appeared to remove the saw tooth pattern however no changes in dyspnea resulted.

FUTURE CONSIDERATIONS

A larger sample size of elite men and women TT specialists would help clarify whether He-O_2 can induce a true performance improvement, as the current study was underpowered. Development of a method with the ability to unload only expiration (undetectable by subjects) would isolate and clarify how the effects of EFL, operational lung volumes, the WOB, and potentially sex affect endurance performance. Potentially TTs of a longer duration involving short sprints would generate V'_E high enough for EFL to develop while determining the effects of endurance exercise (an hour or more) on the WOB, sensory responses and diaphragm fatigue. A 3rd TT could be performed to determine if the ventilatory drive could be increased without manipulating the MEFV curve and the subsequent effects on performance. This could be done by increasing the chemical drive to breath via CO_2 loading (44).

Structural and functional sex-based differences with respect to the pulmonary system could be further analyzed by comparing a group of men and women matched for height and a group of men and women matched for lung size.

CONCLUSION

Based on the results from this study, the effects of He-O_2 on cycling performance appear small and are variable between subjects. Further testing of a larger sample size is required to say with certainty whether the effects of He-O_2 do or do not improve performance. The susceptibility of EFL was found to be higher in women breathing RA, however the magnitude was comparable between the sexes and not affected by He-O_2. This was because throughout both TTs men and women took full advantage of their MEFV curve. As such, nearly all subjects demonstrated impending EFL. By regulating their EELV subjects strived to achieve the highest expiratory flows possible, free of mechanical ventilatory constraint. It was also observed that He-O_2 does not appear to reduce airflow resistance enough to substantially reduce the total WOB compared to RA in men or women. Women demonstrated a significantly greater WOB compared to men for a similar V'_E, which is likely due to women's inherently smaller diameter airways and lower maximal flow rates. Despite the greater absolute cost of breathing, men and women have similar sensory responses regardless of inspirate, potentially attributed to differences in psychosocial factors or stoicism. Further research with the ability to unloading expiration and isolate the effects of expiratory mechanical ventilatory constraints on endurance performance is necessary to understand how EFL, operational lung volumes, the WOB, and potentially sex affect endurance performance.

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APPENDIX A - INDIVIDUAL DATA – TABLES

Table 23 - Individual descriptive and anthropometric data

	Age (yr)	Height (cm)	Mass (kg)
Men			
104	27	187.2	84.8
105	38	186.0	77.9
106	29	186.0	77.3
107	30	187.0	77.4
108	36	171.5	67.5
109	32	175.0	69.0
110	39	178.0	71.1
111	22	181.0	75.2
112	28	170.0	60.1
114	30	186.0	75.8
115	25	177.0	74.9
Women			
201	26	171.0	54.7
202	19	160.0	55.2
203	22	171.5	58.6
204	30	166.0	60.2
205	28	163.0	50.2
206	34	159.0	55.0
207	24	166.0	58.1
208	24	170.0	58.9
210	31	176.0	70.6
211	24	179.0	69.6
212	27	164.0	58.2

Table 24 - Individual pulmonary function data. FVC, forced vital capacity; $FEV_{1.0,}$ forced expired volume in 1 sec; PEF, peak expiratory flow.

	FVC (l)	FVC (% predicted)	$FEV_{1.0}$ (l)	$FEV_{1.0}$ (% predicted)	$FEV_{1.0}$/FVC (%)	$FEV_{1.0}$/FVC (% predicted)	PEF ($l \cdot sec^{-1}$)	PEF (% predicted)
Men								
104	6.61	115	5.63	118	85.2	103	11.6	111
105	5.50	102	4.54	103	82.5	103	13.0	130
106	6.45	115	5.28	113	81.9	100	10.8	104
107	6.37	113	5.08	109	79.7	97	12.6	122
108	4.46	96	3.64	82	81.6	101	9.8	107
109	5.77	118	4.32	105	74.9	92	10.2	108
110	5.32	109	3.98	99	74.8	93	12.0	127
111	5.32	97	4.13	89	77.6	93	10.6	102
112	4.67	99	3.72	93	79.7	97	9.8	104
114	6.46	116	4.87	105	75.4	92	12.9	121
115	5.34	102	4.45	101	83.3	101	9.9	99
Women								
201	4.34	108	3.48	99	80.2	95	8.0	106
202	4.31	116	3.52	109	81.7	96	7.1	100
203	5.03	122	3.79	105	75.3	89	7.6	100
204	4.16	113	3.53	110	84.9	102	8.5	119
205	3.05	85	2.45	96	80.3	96	5.6	79
206	3.58	109	3.06	107	85.5	103	8.2	123
207	3.76	98	3.14	94	83.5	99	6.5	88
208	4.87	121	4.29	122	88.1	104	9.0	120
210	4.48	109	3.34	94	74.6	90	6.0	78
211	5.52	125	4.44	115	80.4	95	8.3	103
212	4.02	110	3.43	107	85.3	102	7.4	104

Table 25 - Individual cycling experience

	Discipline				Highest Level of Competition				Training Status	
	Road	Triathlon	Mountain	Cyclo-cross	Regional	Provincial	National	International	In-season	Off-season
Men										
104	X				X					X
105	X				X					X
106	X				X				X	
107		X					X			X
108		X					X		X	
109	X						X		X	
110		X						X	X	
111			X			X			X	
112	X			X	X				X	
114	X				X				X	
115			X			X				X
Women										
201		X				X				X
202		X			X					X
203	X		X	X			X			X
204		X			X					X
205	X			X	X					X
206		X						X	X	
207	X				X				X	
208	X							X	X	
210		X						X	X	
211	X				X				X	
212		X					X		X	

Table 26 - Individual Day 1 maximal exercise data. $V'O_2$, oxygen consumption; $V'CO_2$, carbon dioxide production; RER, respiratory exchange ratio; V'_E, minute ventilation; V_T, tidal volume; f_b, frequency of breathing; HR, heart rate.

	$V'O_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	$V'O_2$ ($l \cdot min^{-1}$)	$V'O_2$ (% predicted)	$V'CO_2$ ($l \cdot min^{-1}$)	RER	V'_E ($l \cdot min^{-1}$)	fb ($breaths \cdot min^{-1}$)	V_T (l)	HR ($beats \cdot min^{-1}$)	Duration (sec)	Power (Watts)	Power ($Watts \cdot kg^{-1}$)
Men												
104	58.7	5.0	133	5.4	1.08	138	43	3.4	192	853.2	380	4.5
105	61.8	4.8	140			144	57	2.9	190	607.2	350	4.5
106	55.3	4.3	118	4.7	1.10	132	46	3.3	233	640.8	350	4.5
107	56.0	4.3	118	4.8	1.12	143	63	2.7	178	704.4	350	4.5
108	60.7	4.1	145	4.7	1.15	148	65	2.6	190	637.8	350	5.2
109	67.0	4.6	151	5.0	1.07	138	57	2.8	196	868.2	380	5.5
110	63.7	4.5	148	4.9	1.09	163	77	2.4	180	786.0	380	5.3
111	60.1	4.5	127	5.2	1.14	148	78	2.3	n/a	631.2	350	4.7
112	63.2	3.8	130	4.1	1.09	130	64	2.3	189	525.0	320	5.3
114	65.6	5.0	137	5.4	1.10	118	34	4.0	180	1013.4	410	5.4
115	57.1	4.3	129	4.8	1.13	140	56	2.9	197	695.4	350	4.7
Women												
201	57.5	3.1	131	3.6	1.14	98	48	2.4	189	795.6	280	5.1
202	54.8	3.0	149	3.2	1.07	89	72	1.4	177	610.2	250	4.5
203	56.0	3.3	131	3.4	1.03	95	52	2.1	190	841.2	280	4.8
204	58.3	3.5	169	4.0	1.13	106	62	2.0	168	786.6	280	4.7
205	59.5	3.0	151	3.3	1.11	84	52	1.9	185	789.6	280	5.6
206	52.6	2.9	173	3.2	1.11	94	61	1.8	186	601.2	250	4.5
207	51.8	3.0	137	3.1	1.04	107	64	1.9	196	652.8	250	4.3
208	61.3	3.6	151	4.0	1.10	109	46	2.7	194	1096.2	310	5.3
210	54.6	3.9	153	4.0	1.03	105	51	2.4	168	1217.4	340	4.8
211	56.3	3.9	139	4.2	1.09	133	66	2.3	204	1159.8	340	4.9
212	52.5	3.1	149	3.2	1.06	89	50	2.1	178	640.8	250	4.3

Table 27 - Individual overall TT performance data

	Performance Time (sec)		Amount Faster (sec)		Faster TT order (first or second)	Time between tests (days)
	RA	He-O_2	RA	He-O_2		
Men						
104	452.1	442.3		9.8	1	6
105	470.2	483.2	13.0		1	7
106	458.7	447.7		11.0	1	7
107	481.0	475.2		5.7	2	7
108	466.1	471.9	5.8		2	7
109	439.7	435.4		4.2	2	2
110	453.3	453.7	0.5		2	7
111	497.1	485.0		12.1	2	9
112	481.6	476.4		5.3	1	7
114	433.5	429.0		4.5	2	19
115	446.9	445.2		1.7	2	7
Women						
201	519.7	536.96	17.3		1	35
202	591.0	564.1		26.9	2	3
203	523.8	513.69		10.1	1	7
204	531.2	527.01		4.2	2	14
205	533.1	523.48		9.6	2	24
206	565.7	574.46	8.7		2	7
207	573.2	548.77		24.4	1	21
208	492.7	485.95		6.7	1	25
210	482.0	480.6		1.4	1	4
211	483.9	484.0	0.1		1	21
212	555.7	549.4		6.3	2	7

Table 28 - Individual RA TT performance data

	1 km				2 km				3 km				4 km				5 km			
	Speed ($km \cdot h^{-1}$)	Power (Watts)	Cadence (RPM)	time (sec)	Speed ($km \cdot h^{-1}$)	Power (Watts)	Cadence (RPM)	time (sec)	Speed ($km \cdot h^{-1}$)	Power (Watts)	Cadence (RPM)	time (sec)	Speed ($km \cdot h^{-1}$)	Power (Watts)	Cadence (RPM)	time (sec)	Speed ($km \cdot h^{-1}$)	Power (Watts)	Cadence (RPM)	time (sec)
Men																				
104	35.9	262	93	101.1	39.5	316	97	90.6	40.7	337	98	88.2	40.7	337	96	88.2	42.7	393	101	84.0
105	40.4	368	111	89.6	37.6	268	109	95.6	37.8	279	110	95.2	38.2	281	110	94.8	38.0	279	110	95.2
106	38.2	306	104	95.0	39.2	304	110	91.6	39.3	311	110	92.0	39.7	315	108	90.3	40.6	329	113	89.8
107	33.0	218	104	109.3	36.2	248	114	100.0	37.9	284	115	94.2	39.3	302	111	91.6	41.1	358	111	85.8
108	39.0	342	103	92.7	39.2	302	103	92.6	38.8	295	100	92.7	38.2	289	102	94.3	38.3	292	107	93.9
109	40.3	361	107	90.2	41.3	353	109	86.6	41.4	348	108	88.1	41.0	342	108	87.4	41.5	356	108	87.4
110	39.9	349	96	91.0	40.1	325	94	89.2	39.7	316	95	91.3	39.5	310	91	90.9	39.8	315	94	90.9
111	37.0	287	121	98.3	36.2	245	119	99.7	35.7	242	120	100.1	36.3	246	120	100.1	36.3	250	120	98.9
112	37.7	308	105	95.7	37.1	262	105	97.5	37.4	282	93	96.2	37.0	260	93	97.9	38.3	293	94	94.3
114	40.5	366	104	89.8	41.9	368	108	86.2	42.1	373	112	85.3	42.3	373	112	84.9	41.2	360	114	87.4
115	41.0	383	102	88.5	40.6	335	104	88.4	40.2	329	106	89.6	40.2	317	100	90.4	40.0	326	103	90.0
Women																				
201	35.0	249	101	103.7	35.4	235	105	101.9	33.4	200	106	107.1	34.2	212	108	106.1	35.5	239	105	100.9
202	29.3	159	99	123.9	29.7	151	101	121.3	30.4	161	103	118.0	30.6	161	101	118.5	32.5	188	96	109.3
203	32.6	205	93	111.3	34.4	215	99	105.1	34.7	219	102	103.6	34.7	225	102	102.7	36.1	241	104	101.2
204	33.7	234	98	107.6	33.9	212	106	106.2	34.1	211	108	105.7	33.9	203	108	106.6	34.4	215	110	105.2
205	31.4	187	92	115.7	33.8	207	96	106.5	34.1	215	97	104.9	34.7	223	99	105.0	35.5	233	96	101.1
206	32.3	202	92	112.4	32.3	182	94	111.4	31.7	177	93	113.0	31.7	171	89	115.0	31.5	173	92	114.0
207	30.0	171	86	120.2	32.0	179	92	112.3	31.6	175	92	113.9	31.6	171	90	114.0	32.3	184	95	112.8
208	36.9	286	100	97.9	36.9	266	100	98.3	35.7	237	103	101.1	36.1	247	105	99.3	37.4	279	107	96.1
210	34.5	239	99	105.1	37.7	277	103	95.8	38.2	285	101	93.6	38.0	283	101	94.5	39.1	296	101	93.1
211	35.3	254	89	102.9	37.1	262	95	97.0	37.4	273	98	96.1	38.2	279	98	95.2	38.5	297	100	92.6
212	31.8	198	91	114.0	31.8	176	93	113.5	32.4	184	92	111.5	32.8	190	96	110.0	33.7	207	93	106.8

Table 29 - Individual He-O_2 TT performance data

	1 km				2 km				3 km				4 km				5 km			
	Speed ($km \cdot h^{-1}$)	Power (Watts)	Cadence (RPM)	time (sec)	Speed ($km \cdot h^{-1}$)	Power (Watts)	Cadence (RPM)	time (sec)	Speed ($km \cdot h^{-1}$)	Power (Watts)	Cadence (RPM)	time (sec)	Speed ($km \cdot h^{-1}$)	Power (Watts)	Cadence (RPM)	time (sec)	Speed ($km \cdot h^{-1}$)	Power (Watts)	Cadence (RPM)	time (sec)
Men																				
104	38.6	317	98	94.1	40.0	323	104	89.9	41.4	353	101	87.5	41.6	359	97	86.7	42.4	378	105	84.2
105	37.5	297	110	96.9	36.3	249	116	98.7	37.5	267	119	96.9	37.5	275	119	96.0	38.2	277	121	94.7
106	40.3	364	101	89.4	39.5	308	103	91.4	40.2	330	108	89.8	40.8	334	104	88.9	40.7	344	109	88.2
107	33.5	224	108	108.5	37.5	270	112	95.7	38.2	286	113	94.0	39.2	308	111	90.9	41.6	357	106	86.1
108	39.0	336	104	92.5	39.0	302	108	92.9	37.8	277	109	95.1	37.8	269	111	96.4	37.9	281	108	95.0
109	42.3	407	110	85.8	41.5	353	108	86.9	41.3	350	109	87.8	40.9	342	109	87.7	41.5	353	109	87.4
110	40.6	373	94	89.0	39.8	315	94	91.0	39.3	308	91	91.9	39.5	308	93	91.0	39.8	316	93	91.0
111	38.5	322	122	94.2	37.3	266	124	96.4	37.0	258	123	97.7	36.4	250	119	99.5	36.8	259	122	97.2
112	37.5	299	98	96.5	38.3	285	90	94.7	37.9	280	88	95.1	37.9	276	88	95.1	37.9	285	96	95.1
114	40.7	367	108	88.9	41.7	361	110	86.8	42.1	373	109	85.6	42.7	379	113	84.5	43.3	400	115	83.3
115	41.2	380	102	87.7	40.4	328	104	89.3	40.2	324	103	90.5	39.4	316	103	90.9	41.3	352	108	86.8
Women																				
201	32.7	211	108	110.1	34.1	209	108	106.8	33.4	204	108	107.6	33.4	196	108	108.2	34.4	220	113	104.2
202	31.6	196	145	114.7	31.2	168	35	175.7	31.7	176	90	53.7	32.3	184	94	112.1	33.2	201	91	107.9
203	33.9	227	90	106.8	34.9	225	92	103.5	35.9	238	94	100.2	34.9	226	92	103.5	35.9	244	92	99.7
204	34.4	240	106	105.7	34.8	222	110	103.3	34.0	210	108	106.2	33.6	204	108	107.2	34.7	214	108	104.7
205	32.2	199	95	111.8	34.4	217	99	105.0	35.1	229	100	102.5	35.1	227	98	103.1	35.7	243	98	101.1
206	32.0	196	96	113.1	31.6	174	102	114.2	31.2	167	99	115.7	30.8	163	99	116.8	31.4	175	94	114.7
207	31.6	189	90	114.1	33.2	197	96	109.5	33.0	193	96	129.1	32.6	193	94	90.1	34.1	213	99	106.1
208	36.6	294	98	98.8	38.2	284	100	94.8	37.7	274	99	95.2	36.3	256	103	99.8	36.7	272	105	97.4
210	34.7	243	99	104.4	37.9	281	111	94.5	38.4	286	111	94.6	38.2	290	111	93.3	38.8	290	113	93.7
211	34.5	238	94	104.7	37.9	282	98	94.8	38.0	278	99	95.3	36.8	258	101	97.9	39.3	309	103	91.3
212	31.7	193	92	113.7	32.7	189	96	110.7	33.1	194	94	109.2	33.3	196	98	108.7	33.7	203	95	107.2

Table 30 - Individual RA TT metabolic data. $V'O_2$, oxygen consumption; $V'CO_2$, carbon dioxide production; RER, respiratory exchange ratio; V'_E, minute ventilation; V_T, tidal volume; f_b, frequency of breathing; HR, heart rate.

Rest	$V'O_2$ (l·min^{-1})	$V'CO_2$ (l·min^{-1})	RER	V'_E (l·min^{-1})	f_b (breaths·min^{-1})	V_T (l)	HR (beats·min^{-1})
Men							
104	0.4	0.3	0.82	9	13	0.8	
105	0.6	0.5	0.98	15	11	1.6	
106	0.4	0.4	0.96	13	13	1.2	65
107	0.3	0.3	0.84	10	16	0.7	55
108	0.3	0.3	1.00	10	16	0.7	57
109	0.3	0.3	0.91	9	11	1.0	61
110	0.4	0.3	0.88	11	12	1.1	60
111	0.2	0.3	1.01	9	16	0.7	57
112	0.4	0.5	1.31	19	14	1.6	63
114	0.4	0.3	0.92	9	11	0.9	63
115	0.4	0.3	0.86	9	11	1.0	69
Women							
201	0.3	0.5	1.82	22	22	1.1	
202	0.1	0.1	0.93	4	7	0.6	
203	0.3	0.3	0.86	9	16	0.7	74
204	0.3	0.3	1.06	12	14	1.0	58
205	0.2	0.2	0.89	6	12	0.6	56
206	0.2	0.2	1.09	8	10	0.9	60
207	0.2	0.2	0.91	8	15	0.6	71
208	0.2	0.2	0.91	5	8	0.9	65
210	0.4	0.3	0.80	9	13	0.8	56
211	0.4	0.4	0.82	11	16	0.8	69
212	0.3	0.2	0.86	6	12	0.6	61

1 km	$V'O_2$ (l·min^{-1})	$V'CO_2$ (l·min^{-1})	RER	V'_E (l·min^{-1})	fb (breaths·min^{-1})	V_T (l)	HR (beats·min^{-1})
Men							
104	3.4	2.2	0.65	50.9	24	2.5	148
105	3.7	3.8	1.06	92.0	31	3.4	176
106	3.8	3.3	0.87	81.1	28	3.3	172
107	2.5	2.3	0.94	52.2	29	2.1	138
108	3.3	3.6	1.14	96.3	50	2.2	173
109	3.4	3.6	1.07	95.8	40	2.8	177
110	3.3	3.7	1.14	100.1	45	2.6	162
111	3.4	3.6	1.08	90.5	50	2.1	161
112	3.2	3.5	1.11	103.4	48	2.5	166
114	4.1	3.5	0.87	74.6	23	3.7	165
115	3.6	3.4	0.97	79.2	34	2.7	174
Women							
201	2.5	2.6	1.03	74.1	37	2.3	177
202	2.3	2.0	0.89	51.0	47	1.3	151
203	2.6	2.3	0.89	63.2	33	2.3	161
204	2.8	2.6	0.95	63.0	41	1.8	154
205	2.1	1.9	0.92	42.9	29	1.7	156
206	2.2	2.5	1.11	74.8	52	1.7	169
207	2.3	2.0	0.88	64.3	49	1.5	170
208	3.0	2.9	1.02	76.0	35	2.5	174
210	3.2	2.9	0.92	73.6	35	2.4	147
211	3.3	3.0	0.92	72.1	34	2.4	178
212	2.7	2.7	1.05	62.7	34	2.1	157

Table 30 - Individual RA TT metabolic data, continued…

2 km	$V'O_2$ ($l\cdot min^{-1}$)	$V'CO_2$ ($l\cdot min^{-1}$)	RER	V'_E ($l\cdot min^{-1}$)	fb ($breaths\cdot min^{-1}$)	V_T (l)	HR ($beats\cdot min^{-1}$)
Men							
104	4.0	3.5	0.87	73.3	28	3.1	157
105	4.2	4.8	1.15	124.2	41	3.6	180
106	4.4	4.3	0.99	104.5	34	3.6	181
107	3.1	3.7	1.20	85.3	36	2.7	147
108	3.5	4.7	1.34	130.2	58	2.6	177
109	3.8	5.0	1.30	136.8	52	3.0	178
110	3.6	4.6	1.28	128.4	52	2.9	168
111	3.5	4.3	1.21	115.5	52	2.6	166
112	3.4	3.8	1.13	115.4	54	2.5	174
114	4.8	5.4	1.14	113.8	30	4.3	170
115	3.7	4.9	1.33	121.9	46	3.1	178
Women							
201	2.7	3.3	1.22	93.5	44	2.5	184
202	2.3	2.3	0.96	62.0	75	1.0	150
203	3.0	3.1	1.02	88.5	44	2.3	171
204	3.3	3.7	1.11	91.4	48	2.2	161
205	2.4	2.6	1.10	55.1	33	2.0	170
206	2.4	2.8	1.20	89.8	59	1.8	171
207	2.6	2.6	1.03	88.1	62	1.7	173
208	3.0	3.9	1.29	92.8	36	3.0	176
210	3.5	3.5	1.01	90.6	42	2.5	151
211	3.4	3.6	1.06	93.5	43	2.5	182
212	2.6	2.8	1.06	69.1	37	2.1	158

3 km	$V'O_2$ ($l\cdot min^{-1}$)	$V'CO_2$ ($l\cdot min^{-1}$)	RER	V'_E ($l\cdot min^{-1}$)	fb ($breaths\cdot min^{-1}$)	V_T (l)	HR ($beats\cdot min^{-1}$)
Men							
104	4.5	4.3	0.96	86.9	31	3.3	168
105	4.3	4.4	1.03	123.6	42	3.4	183
106	4.6	4.5	0.97	106.8	34	3.6	179
107	3.3	4.2	1.26	101.2	42	2.8	161
108	3.7	4.4	1.16	131.9	60	2.6	178
109	4.0	4.9	1.22	139.9	54	3.0	184
110	3.7	4.6	1.22	151.4	64	2.7	169
111	3.7	3.9	1.06	111.0	52	2.5	167
112	3.6	3.8	1.05	118.6	56	2.5	177
114	4.9	5.5	1.11	124.8	33	4.4	174
115	3.8	4.8	1.27	136.3	54	2.9	182
Women							
201	2.7	3.1	1.14	92.7	44	2.4	186
202	2.4	2.2	0.92	60.0	76	1.0	159
203	3.2	3.2	0.99	92.3	48	2.3	177
204	3.5	3.7	1.04	103.8	56	2.2	167
205	2.5	2.9	1.16	63.0	36	2.0	176
206	2.3	2.7	1.13	92.5	62	1.7	171
207	2.6	2.5	0.97	85.4	62	1.6	177
208	3.2	3.7	1.18	97.3	38	3.0	177
210	3.7	3.6	0.98	96.9	47	2.4	157
211	3.6	3.7	1.04	101.0	46	2.5	186
212	2.7	2.7	0.99	71.6	41	2.0	163

Table 30 - Individual RA TT metabolic data, continued…

4 km	$V'O_2$ ($l \cdot min^{-1}$)	$V'CO_2$ ($l \cdot min^{-1}$)	RER	V'_E ($l \cdot min^{-1}$)	fb ($breaths \cdot min^{-1}$)	V_T (l)	HR ($beats \cdot min^{-1}$)
Men							
104	4.9	4.8	1.00	103.3	35	3.5	175
105	4.4	4.4	0.99	129.7	45	3.4	183
106	4.7	4.5	0.96	112.0	36	3.6	183
107	3.4	4.4	1.30	116.6	47	2.9	169
108	3.9	4.2	1.08	133.7	62	2.5	180
109	4.0	4.8	1.19	140.9	58	2.8	187
110	3.8	4.5	1.17	155.3	69	2.6	170
111	3.9	4.0	1.01	113.1	54	2.4	172
112	3.7	3.7	1.01	121.2	58	2.4	184
114	5.1	5.5	1.09	130.4	35	4.4	179
115	3.8	4.6	1.21	139.9	56	2.9	183
Women							
201	2.8	3.0	1.08	92.4	46	2.3	188
202	2.3	2.2	0.94	57.5	62	1.1	161
203	3.4	3.3	0.97	95.2	49	2.2	182
204	3.5	3.5	1.00	107.8	62	2.1	170
205	2.5	3.0	1.18	70.8	42	1.9	180
206	2.3	2.6	1.12	93.7	66	1.7	174
207	2.6	2.5	0.95	85.0	61	1.6	177
208	3.2	3.6	1.13	104.8	43	2.9	182
210	3.7	3.7	0.98	100.0	49	2.3	158
211	3.7	3.8	1.04	109.5	50	2.5	186
212	2.8	2.8	0.99	76.2	44	2.0	166

5 km	$V'O_2$ ($l \cdot min^{-1}$)	$V'CO_2$ ($l \cdot min^{-1}$)	RER	V'_E ($l \cdot min^{-1}$)	fb ($breaths \cdot min^{-1}$)	V_T (l)	HR ($beats \cdot min^{-1}$)
Men							
104	5.0	5.3	1.06	127.8	47	3.2	187
105	4.4	4.3	0.97	132.0	45	3.4	189
106	4.8	4.6	0.96	116.9	39	3.6	187
107	3.5	4.9	1.38	137.9	54	3.0	178
108	4.0	4.2	1.06	137.0	64	2.5	185
109	4.1	4.8	1.17	142.5	64	2.6	192
110	3.9	4.5	1.14	157.3	76	2.4	173
111	3.9	3.9	1.00	115.8	57	2.4	173
112	3.8	3.8	1.01	123.8	62	2.3	189
114	5.2	5.7	1.09	144.7	39	4.3	182
115	3.7	4.4	1.18	143.2	60	2.8	185
Women							
201	2.9	3.1	1.10	98.8	50	2.3	194
202	2.4	2.3	0.97	56.7	50	1.3	174
203	3.4	3.4	0.98	99.7	51	2.3	188
204	3.6	3.5	0.99	116.4	72	1.9	174
205	2.5	3.0	1.21	74.8	45	1.9	183
206	2.3	2.5	1.12	95.8	69	1.6	176
207	2.7	2.5	0.95	90.3	65	1.6	183
208	3.3	3.6	1.10	102.4	44	2.8	189
210	3.8	3.7	0.98	103.3	52	2.3	166
211	3.7	3.9	1.05	117.6	55	2.5	195
212	2.9	2.9	1.00	82.7	48	2.0	173

Table 31 - Individual He-O_2 TT metabolic data. $V'O_2$, oxygen consumption; $V'CO_2$, carbon dioxide production; RER, respiratory exchange ratio; V'_E, minute ventilation; V_T, tidal volume; f_b, frequency of breathing; HR, heart rate.

Rest	$V'O_2$ ($l\cdot min^{-1}$)	$V'CO_2$ ($l\cdot min^{-1}$)	RER	V'_E ($l\cdot min^{-1}$)	f_b ($breaths\cdot min^{-1}$)	V_T (l)	HR ($beats\cdot min^{-1}$)
Men							
104	0.5			12	14	1.0	84
105	0.4			13	13	1.3	
106	0.4			13	11	1.6	60
107	0.4			11	17	0.9	
108	0.3			8	18	0.6	55
109	0.2			6	9	1.0	77
110	0.3			7	8	1.0	56
111	0.2			8	16	0.6	52
112	0.3			13	15	1.1	95
114	0.5			17	14	1.6	63
115	0.3			7	9	1.1	84
Women							
201	0.4			19	23	1.1	66
202	0.0			1	2	0.7	
203	0.4			10	15	0.9	72
204	0.3			9	11	1.1	50
205	0.3			8	13	0.7	58
206	0.2			8	10	1.0	63
207	0.3			10	20	0.7	71
208	0.3			10	15	0.8	65
210	0.3			9	15	0.8	54
211	0.3			10	15	0.8	54
212	0.2			8	15	0.6	67

1 km	$V'O_2$ ($l\cdot min^{-1}$)	$V'CO_2$ ($l\cdot min^{-1}$)	RER	V'_E ($l\cdot min^{-1}$)	f_b ($breaths\cdot min^{-1}$)	V_T (l)	HR ($beats\cdot min^{-1}$)
Men							
104	4.3			84.6	34	2.9	161
105	3.0			71.3	31	2.9	166
106	3.3			81.8	34	3.1	179
107	2.8			54.1	33	2.1	142
108	3.2			90.5	50	2.2	174
109	3.8			113.5	49	3.0	183
110	3.6			100.0	53	2.5	109
111	3.6			101.0	58	2.3	177
112	2.8			88.9	50	2.3	167
114	4.2			78.8	28	3.6	170
115	3.8			73.8	33	2.8	171
Women							
201	2.3			66.9	42	2.0	163
202	2.3			64.1	78	1.1	157
203	2.5			64.5	34	2.4	170
204	2.6			65.3	64	1.4	152
205	2.3			46.2	32	1.8	166
206	2.2			74.2	52	1.8	168
207	2.3			68.0	53	1.6	175
208	3.0			76.6	44	2.3	174
210	3.1			78.3	39	2.5	153
211	3.1			70.7	38	2.4	166
212	2.3			54.1	38	1.8	159

Table 31 - Individual He-O_2 TT metabolic data, continued…

2 km	$V'O_2$ (l·min^{-1})	$V'CO_2$ (l·min^{-1})	RER	V'_E (l·min^{-1})	f_b (breaths·min^{-1})	V_T (l)	HR (beats·min^{-1})
Men							
104	4.2			97.4	37	3.1	172
105	3.4			105.0	40	3.5	170
106	3.7			107.2	38	3.7	183
107	3.4			83.5	38	2.9	150
108	3.3			136.3	64	2.7	179
109	4.1			144.4	55	3.4	184
110	3.8			141.5	63	2.9	173
111	3.8			126.1	65	2.5	185
112	3.1			115.4	56	2.6	172
114	4.3			106.6	35	4.0	170
115	3.8			112.3	45	3.2	177
Women							
201	2.5			84.7	48	2.3	168
202	2.2			63.7	77	1.1	159
203	2.7			87.7	46	2.5	178
204	2.8			96.1	71	1.8	158
205	2.6			63.5	41	2.0	174
206	11.3			89.3	59	1.9	167
207	2.3			85.7	70	1.6	179
208	3.0			109.0	50	2.8	179
210	3.4			89.8	44	2.6	161
211	3.2			89.8	46	2.5	181
212	2.4			63.8	41	2.0	161

3 km	$V'O_2$ (l·min^{-1})	$V'CO_2$ (l·min^{-1})	RER	V'_E (l·min^{-1})	f_b (breaths·min^{-1})	V_T (l)	HR (beats·min^{-1})
Men							
104	4.5			111.8	41	3.2	177
105	3.5			106.4	42	3.3	174
106	3.9			112.1	41	3.5	184
107	3.7			95.3	42	2.9	158
108	3.4			143.1	68	2.6	179
109	4.2			144.7	54	3.4	187
110	3.9			149.2	74	2.6	172
111	3.9			131.5	67	2.6	188
112	3.3			121.4	61	2.5	176
114	4.6			112.4	37	3.9	179
115	4.0			123.6	50	3.2	180
Women							
201	2.6			86.5	50	2.2	172
202	2.2			60.8	73	1.1	162
203	2.9			98.5	52	2.4	186
204	2.9			103.4	80	1.7	163
205	2.8			70.2	45	2.0	182
206	8.9			89.9	64	1.8	168
207	2.4			85.6	70	1.6	180
208	3.2			115.8	55	2.7	180
210	3.6			99.8	50	2.6	165
211	3.4			103.0	51	2.6	184
212	2.5			67.5	45	1.9	165

Table 31 - Individual He-O_2 TT metabolic data, continued…

4 km	$V'O_2$ ($l \cdot min^{-1}$)	$V'CO_2$ ($l \cdot min^{-1}$)	RER	V'_E ($l \cdot min^{-1}$)	f_b ($breaths \cdot min^{-1}$)	V_T (l)	HR ($beats \cdot min^{-1}$)
Men							
104	4.9			131.3	46	3.3	183
105	3.8			118.0	47	3.2	189
106	4.1			121.2	45	3.5	185
107	3.9			110.0	48	3.0	167
108	3.5			147.5	73	2.6	181
109	4.3			149.8	62	3.1	189
110	4.0			145.6	78	2.4	175
111	4.0			130.0	69	2.4	190
112	3.4			120.8	62	2.5	181
114	4.7			129.0	41	4.1	181
115	4.1			137.4	58	3.1	183
Women							
201	2.7			86.0	52	2.1	175
202	2.3			64.3	79	1.1	168
203	2.9			100.2	55	2.4	186
204	2.9			109.3	98	1.5	166
205	2.9			79.2	52	2.0	183
206	2.2			86.8	67	1.7	168
207	2.4			88.3	76	1.5	181
208	3.3			117.4	56	2.7	182
210	3.7			108.1	57	2.4	167
211	3.4			102.8	54	2.4	183
212	2.6			73.6	48	2.0	167

5 km	$V'O_2$ ($l \cdot min^{-1}$)	$V'CO_2$ ($l \cdot min^{-1}$)	RER	V'_E ($l \cdot min^{-1}$)	f_b ($breaths \cdot min^{-1}$)	V_T (l)	HR ($beats \cdot min^{-1}$)
Men							
104	4.9			143.8	50	3.4	188
105	3.8			128.6	52	3.2	188
106	4.2			135.4	51	3.5	188
107	4.1			134.2	55	3.2	177
108	3.6			153.6	75	2.6	186
109	4.3			160.7	74	2.8	194
110	4.2			156.6	82	2.5	179
111	4.0			131.4	75	2.3	194
112	3.5			123.4	64	2.5	186
114	4.9			137.4	41	4.3	188
115	4.2			152.8	65	3.0	188
Women							
201	2.8			93.6	58	2.1	180
202	2.3			63.7	71	1.1	173
203	3.0			103.4	59	2.3	192
204	2.9			120.3	113	1.4	170
205	2.9			84.1	54	2.0	187
206	2.2			90.8	77	1.5	173
207	2.5			92.0	74	1.6	190
208	3.3			119.7	59	2.6	187
210	3.6			108.3	60	2.3	170
211	3.6			116.2	59	2.5	196
212	2.6			78.0	52	1.9	169

Table 32 – Individual expiratory flow rates. MEF, Maximal Expiratory Flow; MEF-50%, Maximal Expiratory Flow at 50 % Vital Capacity; MEF-exercise, maximal expiratory flow achieved during the time trial.

Subject	MEF ($l \cdot sec^{-1}$)		MEF-50 % ($l \cdot sec^{-1}$)		MEF-exercise ($l \cdot sec^{-1}$)	
	RA	He-O_2	RA	He-O_2	RA	He-O_2
Men						
104	11.76	16.40	7.21	10.00	6.58	9.01
105	12.99	17.71	7.52	10.91	7.44	8.60
106	11.86	14.41	7.94	10.63	5.28	7.40
107	12.19	17.13	6.69	7.75	6.42	7.98
108	10.74	13.73	5.50	6.46	6.54	8.52
109	10.02	13.33	5.38	7.02	7.27	9.74
110	13.19	16.82	6.69	8.67	7.21	8.74
111	10.56	14.47	6.12	9.34	5.29	7.44
112	10.38	12.72	4.59	6.06	5.97	7.12
114	10.50	16.75	6.52	11.05	8.17	9.64
115	11.11	16.22	6.89	10.27	7.00	10.12
Women						
202	6.81	10.10	4.74	7.25	3.12	4.63
203	7.58	10.18	4.17	5.43	5.42	6.35
204	9.38	11.78	6.68	8.26	5.37	6.64
205	5.77	8.59	4.04	5.00	4.03	5.10
206	7.65	9.69	4.73	6.40	4.67	4.63
207	6.84	8.74	4.17	6.11	4.80	5.28
208	9.35	10.81	6.46	8.26	5.51	5.98
210	7.26	8.64	3.85	5.10	5.15	6.55
211	8.22	9.75	5.73	7.56	5.43	6.09
212	7.45	8.74	4.37	5.48	4.53	4.49

Table 33 - Individual RA TT operational lung volumes. EELV, End expired lung volume; EILV; End inspired lung volume.

Rest	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	2.7	44.0	3.9	62.2
105	2.5	43.7	3.7	64.7
106	3.6	57.2	4.6	73.6
107	3.8	59.7	4.6	71.6
108	2.7	54.5	3.3	67.8
109	3.0	54.6	3.7	67.3
110	2.8	55.2	3.6	69.6
111	1.9	40.5	2.6	54.8
112	2.0	44.0	3.4	75.4
114				
115	2.6	50.1	3.5	67.8
Women				
201	1.5	41.2	2.6	74.4
202	1.9	57.9	2.4	74.8
203	2.4	54.5	3.1	70.8
204	1.4	36.6	2.2	58.1
205	1.8	59.9	2.3	76.8
206	1.5	45.0	2.1	63.8
207	1.5	45.0	2.1	62.1
208				
210	2.2	51.6	2.9	68.1
211	2.7	54.6	3.5	70.0
212	1.9	45.6	2.4	57.2

1 km	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	2.4	38.3	4.9	78.1
105	1.5	25.5	4.9	85.5
106	2.0	31.7	5.1	81.7
107	2.8	43.7	5.2	80.9
108	2.2	44.5	4.6	93.7
109	1.8	32.7	4.8	88.0
110	2.2	42.3	4.8	93.8
111	2.1	45.8	4.4	95.1
112	2.0	44.5	4.5	98.5
114	1.7	27.1	5.3	86.5
115	1.7	33.0	4.6	87.7
Women				
201	0.8	22.4	3.2	89.5
202	1.4	43.3	2.7	83.5
203	1.6	36.7	3.8	87.0
204	1.2	30.5	3.0	79.3
205	0.9	31.6	2.7	92.3
206	1.1	32.8	2.8	85.1
207	1.2	34.3	2.8	83.1
208	2.2	42.2	4.4	85.2
210	1.7	38.4	4.0	93.5
211	1.7	34.7	4.2	84.1
212	1.6	38.6	3.7	87.3

2 km	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	2.3	36.6	5.0	80.5
105	1.6	27.1	4.8	84.4
106	2.0	31.8	5.4	86.0
107	2.7	41.7	5.3	82.4
108	2.1	42.9	4.6	92.9
109	2.1	38.0	5.0	90.3
110	1.5	29.8	4.2	82.7
111	1.4	30.6	3.9	82.4
112	2.2	49.6	4.5	100.2
114	1.4	23.0	5.6	90.5
115	1.7	32.8	4.6	88.1
Women				
201	1.1	31.3	3.3	93.5
202		0.0		0.0
203	1.5	35.5	3.8	88.6
204	1.1	28.6	3.2	85.4
205	1.0	34.7	3.0	99.3
206	1.0	31.6	2.7	82.1
207	1.2	36.7	2.9	86.4
208	2.2	42.2	4.9	93.8
210	1.8	40.5	4.1	95.6
211	2.0	39.5	4.4	87.7
212	1.8	42.8	3.8	90.4

Table 33 - Individual RA TT operational lung volumes, continued…

3km	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	2.2	34.6	5.0	79.9
105	1.6	27.8	4.9	84.8
106	2.1	33.9	5.5	88.1
107	2.6	40.4	5.3	82.6
108	2.0	40.8	4.4	89.0
109	2.1	38.9	5.0	90.3
110	1.6	31.2	4.2	81.3
111		0.0		0.0
112	2.2	48.9	4.5	100.4
114	1.7	27.2	5.7	93.5
115	2.1	39.5	4.8	92.5
Women				
201	0.8	21.3	3.0	84.9
202		0.0		0.0
203	1.5	35.5	3.6	84.5
204	0.8	22.3	2.8	73.5
205	0.9	30.6	2.9	97.0
206	1.2	35.9	2.8	86.0
207	1.1	31.1	2.7	78.7
208	2.0	39.1	4.8	93.1
210	1.6	38.0	3.9	89.4
211	2.3	45.4	4.6	92.9
212	2.1	49.6	4.0	93.4

4 km	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	2.1	34.1	5.1	82.8
105	1.8	31.1	5.0	87.8
106	1.9	30.9	5.3	85.4
107	3.1	48.3	5.9	91.7
108	2.5	51.0	4.9	99.0
109	2.4	43.6	5.0	90.5
110	2.1	40.5	4.5	88.3
111	1.8	37.5	4.1	87.6
112	2.2	48.2	4.3	95.8
114	1.6	25.3	5.6	92.0
115	2.2	43.0	5.0	95.6
Women				
201	1.0	28.1	3.1	88.1
202	1.6	49.5	2.8	86.9
203	1.4	32.5	3.6	82.6
204	0.9	24.4	2.8	72.9
205	0.9	29.3	2.7	89.6
206	1.3	39.5	2.9	87.2
207	1.4	41.7	2.9	84.3
208	1.8	35.1	4.4	85.4
210	1.8	42.1	4.0	93.5
211	2.1	41.9	4.5	90.1
212	2.0	46.6	3.9	91.1

5km	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	2.2	35.7	5.3	85.7
105	1.8	31.8	5.1	88.6
106	2.0	32.3	5.0	80.2
107	3.1	48.0	5.9	92.0
108	2.6	53.3	5.0	101.0
109	2.7	48.9	5.1	93.1
110	2.1	40.9	4.3	84.6
111	1.7	36.4	3.9	83.9
112	1.6	34.7	3.7	81.9
114	1.5	24.0	5.1	83.7
115	2.3	43.8	4.9	93.1
Women				
201	1.0	28.1	3.1	89.2
202	1.6	49.5	3.0	92.5
203	1.6	36.7	3.7	86.8
204	0.8	21.2	2.6	67.6
205	1.0	33.0	2.8	94.9
206	1.4	43.5	2.9	87.5
207	1.4	39.9	2.9	85.8
208	2.2	42.8	4.7	90.2
210	1.9	43.3	4.0	93.5
211	2.0	39.7	4.3	86.5
212	2.1	49.4	4.0	94.8

Table 34 - Individual He-O_2 TT operational lung volumes. EELV, End expired lung volume; EILV; End inspired lung volume.

Rest	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	2.2	36.8	3.0	49.0
105	2.1	39.0	2.9	53.6
106	3.9	67.6	2.2	38.5
107	3.5	55.8	4.3	67.9
108	2.4	50.6	2.9	60.8
109	2.7	49.3	3.4	62.2
110	2.8	55.1	3.4	66.7
111	1.7	36.0	2.4	50.5
112	2.1	46.3	3.0	68.1
114	1.8	29.3	2.7	43.2
115	2.3	43.6	3.2	62.0
Women				
201	1.6	49.2	2.6	82.6
202	2.2	70.9	2.6	84.6
203	1.9	43.9	2.9	66.3
204	1.5	41.1	2.4	65.9
205	1.7	56.3	2.3	76.3
206	1.3	36.7	2.3	67.3
207	1.7	49.4	2.3	65.7
208	2.1	41.1	2.9	57.3
210	1.9	43.6	2.7	61.6
211	2.2	43.9	3.0	59.3
212	1.9	44.0	2.5	57.6

1km	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	2.0	33.1	5.0	82.1
105	1.2	21.7	4.2	77.5
106	1.2	21.3	4.3	74.0
107	2.6	41.8	5.2	82.6
108	1.9	38.8	4.3	89.8
109	1.5	28.4	4.7	86.9
110				
111	1.3	28.2	3.7	78.5
112	1.3	28.8	3.7	83.1
114	1.7	26.8	5.0	79.7
115	1.8	33.7	4.7	90.6
Women				
201	0.6	17.4	2.6	80.8
202	1.5	50.0	2.7	86.6
203	1.3	30.0	3.8	87.5
204	0.9	24.3	2.5	66.8
205	0.8	27.7	2.8	93.0
206	1.0	28.3	2.8	81.2
207	1.4	41.0	3.0	86.9
208	1.7	33.5	4.3	84.8
210	1.4	32.9	3.9	88.1
211	1.9	37.9	4.3	85.4
212	1.6	36.8	3.5	82.4

2km	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	1.9	31.8	5.0	82.0
105	1.2	21.4	4.0	73.5
106	1.2	21.3	5.1	88.5
107	2.8	45.1	5.6	89.3
108	1.8	37.5	4.4	91.5
109	1.5	28.4	4.7	86.9
110	1.7	33.7	4.4	86.5
111	1.5	32.4	4.0	84.4
112	1.1	24.7	3.6	80.9
114	1.7	26.5	5.6	89.3
115	1.5	29.1	4.7	89.3
Women				
201	0.7	20.5	2.9	90.5
202	1.6	52.9	2.7	87.3
203	1.6	36.0	4.0	92.8
204	0.8	20.7	2.3	62.4
205	1.0	33.0	2.9	98.0
206	0.8	22.0	2.6	74.9
207	1.4	40.4	2.9	82.8
208	1.7	33.5	4.5	88.6
210	1.5	33.1	4.0	90.9
211	1.9	38.5	4.4	87.8
212	1.8	42.9	3.7	87.6

Table 34 - Individual He-O_2 TT operational lung volumes, continued…

3km	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	1.8	30.0	5.1	84.9
105	1.1	19.5	4.0	73.3
106	1.3	22.5	4.7	81.5
107	2.9	46.1	5.7	90.6
108	1.8	36.7	4.2	87.9
109	1.7	31.0	5.0	93.0
110	1.9	37.1	4.3	85.1
111	1.4	29.7	3.9	81.5
112	1.0	22.7	3.5	79.6
114	1.2	19.8	5.2	82.5
115	1.8	33.5	4.8	91.6
Women				
201	0.7	20.8	2.9	89.9
202	1.5	49.7	2.5	82.4
203	1.6	36.0	4.0	92.8
204	0.8	20.7	2.3	63.8
205	1.0	34.7	3.0	101.0
206	1.1	30.6	2.8	79.5
207	1.0	29.9	2.6	75.3
208	1.9	37.4	4.5	88.4
210	1.6	36.8	4.1	92.7
211	1.9	38.5	4.4	87.4
212	1.5	34.7	3.4	80.6

4km	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	1.8	29.3	5.1	83.8
105	1.2	21.9	3.7	67.4
106	1.2	20.2	4.3	75.6
107	2.8	45.3	5.7	90.7
108	2.4	49.2	4.8	100.4
109	2.1	37.8	4.9	90.8
110	1.8	35.7	4.2	81.4
111	1.9	40.6	4.2	88.0
112	1.2	26.5	3.7	83.1
114	1.4	22.0	5.4	86.6
115	1.7	33.3	4.8	91.4
Women				
201	0.6	19.6	2.6	83.3
202	1.4	46.4	2.5	82.7
203	1.3	29.6	3.5	81.8
204	1.0	27.8	2.5	67.6
205	1.1	35.7	2.9	96.3
206	1.1	30.6	2.6	74.6
207	1.4	41.3	2.9	85.2
208	2.0	39.2	4.6	91.1
210	1.6	36.8	3.8	87.7
211	2.2	43.9	4.5	89.6
212	1.8	41.9	3.8	87.8

5km	EELV (l)	EELV (% FVC)	EILV (l)	EILV (% FVC)
Men				
104	1.9	31.8	5.5	91.4
105	1.3	24.7	4.4	81.2
106	1.6	27.9	4.9	85.0
107	2.7	43.2	5.9	94.3
108				
109	2.4	44.5	5.1	93.7
110	2.0	39.4	4.4	87.1
111	2.1	43.8	4.2	89.3
112	1.3	29.9	3.8	85.8
114	1.4	22.2	5.4	86.4
115	1.5	28.9	4.3	81.6
Women				
201	0.7	22.4	2.8	87.1
202	1.3	42.5	2.5	81.0
203	1.6	36.0	3.7	86.4
204	0.9	24.3	2.2	59.9
205	0.9	30.7	2.9	96.0
206	1.2	33.2	2.5	73.1
207	1.0	29.7	2.5	72.1
208	2.0	39.8	4.4	87.2
210	1.7	38.8	4.0	91.3
211	1.8	36.7	4.4	87.0
212	1.8	41.2	3.6	85.2

Table 35 - RA TT individual EFL susceptibility and magnitude

	Rest (%V_T)	1km (%V_T)	2km (%V_T)	3km (%V_T)	4km (%V_T)	5km (%V_T)
Men						
104	0	0	0	0	0	0
105	0	0	0	0	0	0
106	0	0	0	0	0	0
107	0	0	0	0	0	0
108	0	0	0	0	0	0
109	0	0	28	51	31	60
110	0	0	0	41	0	12
111	0	0	0		0	0
112	0	0	0	0	1	60
114		0	24	13	33	60
115	0	0	0	0	0	0
Women						
201	0	33	27	44	35	37
202	0	0			0	0
203	0	0	0	0	37	24
204	0	0	0	4	25	44
205	0	0	0	0	21	3
206	0	0	21	0	0	0
207	0	0	0	18	0	5
208		0	0	0	0	0
210	0	0	1	65	60	45
211	0	0	0	0	0	0
212	0	0	0	0	0	0

Table 36 – He-O_2 TT individual EFL susceptibility and magnitude

	Rest (%V_T)	1km (%V_T)	2km (%V_T)	3km (%V_T)	4km (%V_T)	5km (%V_T)
Men						
104	0	0	0	0	0	0
105	0	0	0	0	0	0
106	0	0	0	0	0	0
107	0	0	0	0	0	0
108	0	0	0	12	0	
109	0	26	14	10	21	0
110	0		0	0	0	0
111	0	0	0	0	0	0
112	0	12	46	57	43	35
114	0	0	0	0	1	22
115	0	0	0	0	0	32
Women						
201	0	0	0	0	0	0
202	0	0	0	0	0	0
203	0	0	0	0	28	42
204	0	0	0	0		47
205	0	0	0	0	0	0
206	0	0	21	0	0	0
207	0	0	0	0	0	0
208	0	0	0	0	0	0
210	0	0	10	0	60	0
211	0	0	0	0	0	0
212	0	0	0	0	0	0

Table 37 - Individual RA TT work of breathing data. Iel, inspiratory elastic work of breathing; Ires, inspiratory resistive work of breathing; Exp total, total expiratory work of breathing; WOB, work of breathing (inspiratory and expiratory); F_b, frequency of breathing; WOB, work of breathing (inspiratory and expiratory); V'_E, minute ventilation.

Rest – RA

	Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})		Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})
Men									Women								
104	1.8	0.0	0.0	1.6	11	0.8	1.7	11	201	4.1	0.9	0.0	5.0	24	1.1	11.9	25
105	2.7	0.6	0.0	3.3	13	1.6	4.1	15	202	1.5	0.6	0.1	2.1	23	0.6	4.7	10
106	2.2	1.1	0.0	3.3	13	1.2	4.1	13	203	0.6	0.0	0.0	0.6	15	0.7	1.0	10
107	1.1	0.6	0.0	1.7	19	0.7	3.3	14	204						1.0		
108	0.7	0.2	0.0	0.9	15	0.7	1.3	18	205	0.9	0.7	0.2	1.8	19	0.6	3.2	8
109	0.5	0.3	0.3	1.0	13	1.0	1.3	9	206	1.7	0.3	0.0	2.0	12	0.9	2.4	7
110	1.1	0.2	0.0	1.3	11	1.1	1.4	7	207	1.3	0.2	0.0	1.6	21	0.6	3.1	11
111	1.2	0.9	0.0	2.1	24	0.7	4.7	15	208						0.9		
112	4.2	1.8	0.4	6.4	14	1.6	8.9	17	210	1.0	0.7	0.0	1.8	14	0.8	2.5	9
114						0.9			211	1.2	0.5	0.0	1.8	16	0.8	2.8	11
115	1.8	-0.1	0.0	1.6	10	1.0	1.7	11	212	0.0	0.3	0.2	0.6	13	0.6	0.7	7

1 km – RA

	Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})		Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})
Men									Women								
104	12.3	3.5	0.1	15.9	29	2.5	44.5	63	201	20.4	6.2	0.0	26.7	37	2.3	97.8	79
105	33.3	16.9	0.5	50.7	35	3.4	174.0	111	202	16.1	9.9	0.6	26.5	53	1.3	137.4	63
106	32.2	10.6	1.6	44.5	31	3.3	134.1	87	203	17.5	14.4	3.4	35.2	38	2.3	132.3	75
107	14.7	10.1	0.0	24.8	29	2.1	70.1	62	204	14.2	10.7	1.6	26.5	45	1.8	117.3	80
108	43.5	9.7	0.3	53.5	53	2.2	278.7	119	205	19.6	6.1	0.1	25.7	31	1.7	77.1	49
109	43.0	19.1	19.1	81.3	44	2.8	354.0	122	206	20.5	8.2	0.1	28.8	55	1.7	153.9	84
110	29.0	9.4	0.3	38.7	45	2.6	171.4	108	207	18.3	10.5	0.6	29.4	49	1.5	140.8	74
111	20.8	8.4	1.6	30.8	47	2.1	142.2	98	208	24.3	12.5	0.0	36.8	35	2.5	125.9	82
112	30.4	19.4	4.6	54.4	53	2.5	280.3	118	210	32.7	17.0	1.8	51.5	39	2.4	195.2	83
114	52.2	15.7	2.5	70.3	27	3.7	184.3	91	211	25.5	9.7	0.2	35.4	35	2.4	122.9	79
115	31.8	8.2	6.4	46.4	38	2.7	171.6	98	212	30.1	11.0	0.1	41.2	38	2.1	154.8	74

Table 37 - Individual RA TT work of breathing data, continued…

2 km – RA

	Iel (cmH$_2$O)	Ires (cmH$_2$O)	Exp total (cmH$_2$O)	WOB (cmH$_2$O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})		Iel (cmH$_2$O)	Ires (cmH$_2$O)	Exp total (cmH$_2$O)	WOB (cmH$_2$O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})
Men									Women								
104	10.9	5.2	0.1	16.1	27	3.1	42.3	74	201	19.7	9.2	0.0	28.9	45	2.5	128.7	96
105	35.0	20.6	1.0	56.5	43	3.6	237.4	125	202	7.8	5.5	0.7	14.0	101	1.0	138.7	69
106	40.2	12.2	1.7	54.1	34	3.6	180.6	106	203	21.3	18.0	5.8	45.1	42	2.3	187.3	89
107	20.9	13.0	0.5	34.4	37	2.7	126.5	88	204	21.0	13.3	2.7	36.9	50	2.2	182.8	96
108	49.1	11.1	0.7	60.9	59	2.6	349.3	131	205	23.1	7.1	0.7	30.9	33	2.0	100.1	57
109	43.0	25.1	25.1	93.2	55	3.0	500.4	144	206	20.3	9.5	0.4	30.2	62	1.8	183.2	91
110	38.1	11.1	0.6	49.8	52	2.9	253.1	128	207	24.3	12.7	0.6	37.7	59	1.7	216.5	91
111	26.4	8.0	2.4	36.9	53	2.6	190.3	117	208	46.8	31.3	2.6	80.7	35	3.0	275.4	93
112	27.0	17.1	4.6	48.8	56	2.5	270.0	117	210	33.8	20.5	2.6	56.8	43	2.5	239.6	91
114	68.5	16.8	9.4	94.8	31	4.3	284.9	118	211	26.5	13.6	0.1	40.2	44	2.5	172.1	97
115	37.8	18.2	13.6	69.6	47	3.1	323.3	123	212	24.0	8.0	0.1	32.2	38	2.1	118.5	67

3 km – RA

	Iel (cmH$_2$O)	Ires (cmH$_2$O)	Exp total (cmH$_2$O)	WOB (cmH$_2$O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})		Iel (cmH$_2$O)	Ires (cmH$_2$O)	Exp total (cmH$_2$O)	WOB (cmH$_2$O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})
Men									Women								
104	19.2	5.3	1.0	25.5	36	3.3	89.5	93	201	19.7	8.1	0.0	27.8	45	2.4	122.0	91
105	31.9	18.3	0.3	50.5	42	3.4	209.1	126	202	7.9	5.2	0.5	13.6	102	1.0	135.6	71
106	42.9	13.8	2.3	58.9	35	3.6	201.5	107	203	25.8	25.0	7.2	58.0	51	2.3	287.8	99
107	25.2	14.2	1.7	41.1	43	2.8	173.5	105	204	21.1	14.4	1.9	37.3	63	2.2	231.1	111
108	44.3	15.3	1.0	60.5	61	2.6	362.3	133	205	26.6	8.1	0.6	35.2	35	2.0	122.0	62
109	46.8	35.5	35.5	117.9	55	3.0	630.4	141	206	18.6	8.0	0.4	27.0	59	1.7	157.6	88
110	39.6	11.5	0.2	51.3	65	2.7	327.4	156	207	21.1	12.8	0.8	34.7	58	1.6	196.3	84
111						2.5			208	40.9	24.5	1.8	67.2	41	3.0	267.3	105
112	27.0	18.5	4.0	49.6	56	2.5	274.1	122	210	33.5	21.3	4.8	59.6	50	2.4	293.1	101
114	68.1	17.3	5.8	91.2	34	4.4	300.6	128	211	26.2	15.7	0.1	42.0	48	2.5	198.2	104
115	40.2	24.1	13.8	78.2	55	2.9	422.6	139	212	16.4	3.3	0.0	19.8	44	2.0	85.1	75

Table 37 - Individual RA TT work of breathing data, continued…

4 km – RA

	Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'$_E$ (l·min^{-1})		Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'$_E$ (l·min^{-1})
Men									Women								
104	22.6	9.1	0.4	32.2	37	3.5	117.3	112	201	18.4	9.0	9.0	36.5	49	2.3	175.2	97
105	31.7	18.4	2.4	52.5	44	3.4	227.2	126	202	15.4	9.5	0.2	25.1	58	1.1	143.8	71
106	44.9	15.6	1.9	62.4	36	3.6	221.5	112	203	25.4	25.2	9.7	60.4	50	2.2	293.8	96
107	33.5	14.3	1.3	49.1	47	2.9	226.8	121	204	22.5	15.8	1.9	40.3	69	2.1	272.4	115
108	44.1	14.6	0.8	59.6	63	2.5	365.4	133	205	23.4	9.5	2.4	35.3	46	1.9	158.6	74
109	43.2	31.1	31.1	105.4	61	2.8	634.1	144	206	18.9	8.8	0.1	27.8	65	1.7	176.6	97
110	37.0	10.3	0.5	47.8	68	2.6	318.7	154	207	15.5	10.8	1.1	27.4	61	1.6	163.2	80
111	25.9	8.4	1.1	35.4	54	2.4	185.9	115	208	37.8	27.3	1.8	66.9	43	2.9	284.0	108
112	24.6	17.5	4.7	46.8	63	2.4	291.1	125	210	35.7	22.7	4.6	63.0	52	2.3	323.8	104
114	66.4	17.1	12.7	96.2	35	4.4	325.6	132	211	27.3	17.9	0.2	45.4	51	2.5	227.3	113
115	40.4	27.4	11.3	79.1	56	2.9	435.7	141	212						2.0		

5 km – RA

	Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'$_E$ (l·min^{-1})		Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'$_E$ (l·min^{-1})
Men									Women								
104	32.6	17.4	2.8	52.7	48	3.2	246.8	136	201	18.1	15.2	0.1	33.4	52	2.3	170.6	105
105	33.0	14.9	1.7	49.6	46	3.4	223.3	136	202	18.3	11.7	1.9	31.9	52	1.3	162.6	66
106	40.3	14.3	2.5	57.0	41	3.6	226.8	118	203	24.1	23.0	10.1	57.1	52	2.3	291.7	103
107	41.6	21.6	1.8	65.0	57	3.0	365.2	148	204	22.8	14.7	1.5	38.9	77	1.9	293.5	125
108	45.7	15.9	1.9	63.5	64	2.5	397.0	136	205	26.8	12.7	2.0	41.5	48	1.9	194.1	80
109	41.7	29.2	29.2	100.2	65	2.6	640.2	147	206	19.1	9.6	0.1	28.8	78	1.6	219.7	103
110	34.3	10.9	0.5	45.7	75	2.4	335.8	159	207	22.3	12.8	2.2	37.3	67	1.6	246.6	101
111	23.9	7.8	1.1	32.7	56	2.4	179.6	115	208	37.9	28.2	3.4	69.5	46	2.8	311.7	104
112	22.8	20.2	5.5	48.5	62	2.3	294.6	123	210	32.6	23.2	4.1	59.9	53	2.3	314.1	104
114	62.6	27.2	3.5	93.3	45	4.3	415.0	147	211	28.0	20.2	0.4	48.6	57	2.5	270.9	122
115	41.6	29.0	10.5	81.1	60	2.8	474.2	142	212						2.0		

Table 38 - Individual He-O_2 TT work of breathing data. Iel, inspiratory elastic work of breathing; Ires, inspiratory resistive work of breathing; Exp total, total expiratory work of breathing; WOB, work of breathing (inspiratory and expiratory); F_b, frequency of breathing; WOB, work of breathing (inspiratory and expiratory); V'_E, minute ventilation.

Rest – He-O_2

Men	Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})	Women	Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})
104	0.8	0.1	0.0	1.0	18	1.0	1.7	12	201	3.9	1.0	0.0	4.9	23	1.1	11.2	20
105	1.5	0.2	0.0	1.7	16	1.3	2.7	12	202	0.7	0.0	0.0	0.7	2	0.7	1.5	1
106	4.9	1.0	0.0	5.9	10	1.6	6.0	14	203	3.1	1.1	0.0	4.2	12	0.9	4.9	9
107	0.7	0.0	0.0	0.7	20	0.9	1.4	13	204	2.0	0.8	0.0	2.8	12	1.1	3.2	9
108	0.4	0.0	0.0	0.3	25	0.6	0.8	10	205	1.0	0.5	0.0	1.5	15	0.7	2.2	7
109	1.3	0.5	0.0	1.8	11	1.0	1.9	8	206	3.1	0.6	0.3	4.0	9	1.0	3.7	8
110	0.8	0.2	0.0	1.0	13	1.0	1.3	8	207	1.1	0.2	0.0	1.3	22	0.7	2.8	9
111	1.2	0.6	0.0	1.8	23	0.6	4.1	13	208	1.5	0.4	0.0	1.9	16	0.8	2.9	10
112	1.6	0.5	0.1	2.2	15	1.1	3.2	12	210	1.5	0.6	0.0	2.0	14	0.8	2.8	9
114						1.6			211	1.2	0.4	0.0	1.6	17	0.8	2.7	12
115	2.1	0.3	0.0	2.4	9	1.1	2.0	7	212	0.9	0.3	0.0	1.2	15	0.6	1.7	7

1 km – He-O_2

Men	Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})	Women	Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})
104	22.4	4.9	0.0	27.3	33	2.9	88.4	79	201	14.2	3.4	0.0	17.6	44	2.0	76.5	73
105	23.7	3.9	0.0	27.6	36	2.9	98.2	86	202	7.6	1.8	0.0	9.4	88	1.1	81.2	78
106	29.3	6.9	0.2	36.4	38	3.1	134.8	88	203	28.7	16.7	0.2	45.5	38	2.4	168.7	77
107	16.8	6.5	0.0	23.3	32	2.1	74.0	66	204	10.6	5.4	0.0	16.0	62	1.4	96.9	69
108	30.5	6.9	0.0	37.5	59	2.2	218.6	119	205	21.7	3.2	0.0	24.9	37	1.8	89.4	56
109	44.9	15.8	0.9	61.6	54	3.0	325.5	133	206	19.7	6.2	0.0	25.9	56	1.8	143.0	82
110	33.3	5.2	0.0	38.5	55	2.5	206.2	123	207	12.5	6.7	0.0	19.2	63	1.6	118.4	80
111	21.6	3.5	1.4	26.4	59	2.3	153.0	112	208	29.1	10.1	0.2	39.4	47	2.3	183.4	97
112	20.1	9.6	0.6	30.3	57	2.3	170.1	110	210	29.5	14.6	0.5	44.6	41	2.5	179.7	85
114	35.8	14.6	2.0	52.3	29	3.6	149.3	86	211	16.2	8.6	0.0	24.8	41	2.4	100.4	80
115	27.8	0.4	0.9	29.1	36	2.8	103.1	81	212	19.4	4.7	0.2	24.3	39	1.8	92.3	60

Table 38 - Individual He-O_2 TT work of breathing data, continued…

2 km – He-O_2

	Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})		Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})
Men									Women								
104	24.4	5.5	0.1	30.1	39	3.1	114.7	96	201	16.7	4.0	0.1	20.8	49	2.3	99.5	86
105	23.9	5.0	0.0	28.8	42	3.5	117.8	108	202	6.8	1.9	0.1	8.8	89	1.1	76.4	74
106	48.1	9.0	0.7	57.9	35	3.7	197.3	109	203	28.8	21.2	0.3	50.3	49	2.5	242.7	93
107	20.6	8.1	0.3	28.9	40	2.9	113.0	90	204	11.8	4.4	0.0	16.2	87	1.8	138.6	104
108	33.6	9.2	0.0	42.9	66	2.7	277.5	144	205	22.3	5.0	0.1	27.3	43	2.0	114.8	65
109	49.6	19.1	0.8	69.5	55	3.4	371.6	145	206	19.7	5.5	0.0	25.2	63	1.9	156.8	94
110	34.2	7.0	0.0	41.2	70	2.9	284.0	151	207	12.0	6.1	0.0	18.1	76	1.6	135.5	89
111	24.2	3.1	0.7	28.0	67	2.5	183.1	135	208	39.1	18.9	0.1	58.0	51	2.8	289.9	111
112	23.9	11.4	1.5	36.8	59	2.6	213.4	118	210	32.6	18.2	1.0	51.8	47	2.6	239.2	97
114	57.8	14.4	1.3	73.6	34	4.0	248.2	110	211	11.6	7.9	0.0	19.4	49	2.5	93.8	100
115	33.6	3.2	2.1	39.0	45	3.2	172.0	112	212	17.4	5.6	0.0	23.0	43	2.0	97.4	67

3 km – He-O_2

	Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})		Iel (cmH_2O)	Ires (cmH_2O)	Exp total (cmH_2O)	WOB (cmH_2O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})
Men									Women								
104	27.4	9.5	0.5	37.4	37	3.2	136.5	102	201	16.8	3.8	0.0	20.6	49	2.2	100.1	85
105	24.4	6.8	0.0	31.2	42	3.3	129.1	107	202	5.9	1.6	0.1	7.5	85	1.1	62.4	70
106	38.3	10.4	0.7	49.3	41	3.5	196.9	109	203	31.9	23.4	1.0	56.3	53	2.4	292.7	103
107	22.8	10.0	0.2	33.0	44	2.9	143.3	104	204	12.9	5.6	0.1	18.5	88	1.7	160.6	111
108	32.0	10.3	0.2	42.6	71	2.6	298.3	147	205	23.6	3.8	0.6	28.0	47	2.0	130.1	74
109	46.8	17.7	1.4	65.9	54	3.4	351.0	145	206	16.9	4.7	0.0	21.6	66	1.8	139.8	90
110	29.4	5.3	0.0	34.7	76	2.6	260.1	153	207	12.7	6.8	0.0	19.6	71	1.6	136.7	88
111	23.2	5.1	1.0	29.3	67	2.6	192.7	129	208	35.4	18.2	0.0	53.6	57	2.7	296.9	120
112	22.3	10.7	1.9	34.9	61	2.5	208.6	124	210	31.3	17.7	1.6	50.6	51	2.6	253.0	100
114	57.2	14.0	1.6	72.7	38	3.9	270.6	116	211	18.2	12.3	0.0	30.5	54	2.6	160.4	108
115	34.0	6.8	1.2	42.0	52	3.2	215.9	128	212	18.3	5.2	0.1	23.6	44	1.9	101.7	68

Table 38 - Individual $He\text{-}O_2$ TT work of breathing data, continued…

4 km – $He\text{-}O_2$

	Iel (cmH₂O)	Ires (cmH₂O)	Exp total (cmH₂O)	WOB (cmH₂O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})		Iel (cmH₂O)	Ires (cmH₂O)	Exp total (cmH₂O)	WOB (cmH₂O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})
Men									Women								
104	31.3	9.4	0.3	41.1	46	3.3	186.5	121	201	14.6	3.7	0.0	18.3	55	2.1	99.0	90
105	19.1	4.2	0.0	23.3	48	3.2	110.5	119	202	7.9	2.2	0.1	10.2	93	1.1	92.8	85
106	38.1	10.7	1.0	49.8	52	3.5	252.9	128	203	27.8	19.6	2.6	50.0	57	2.4	278.5	103
107	27.6	10.0	0.0	37.6	50	3.0	185.8	114	204	11.5	4.6	0.2	16.3	95	1.5	152.9	112
108	33.6	11.2	0.3	45.0	76	2.6	334.7	154	205	21.9	4.1	0.0	26.0	53	2.0	135.6	83
109	40.9	19.2	0.9	61.0	68	3.1	407.0	154	206	14.0	4.2	0.0	18.2	73	1.7	129.9	89
110	27.6	6.2	0.0	33.8	81	2.4	268.0	152	207	11.4	6.6	0.0	18.0	72	1.5	127.5	86
111	18.9	4.8	0.7	24.5	71	2.4	170.9	126	208	32.6	18.5	0.2	51.3	57	2.7	285.2	120
112	23.9	14.2	3.8	41.9	60	2.5	248.6	122	210	30.3	18.5	2.2	51.0	64	2.4	319.1	116
114	60.6	17.5	2.2	80.3	40	4.1	318.2	132	211	14.8	10.6	0.0	25.4	55	2.4	136.5	102
115	37.0	6.2	3.1	46.3	58	3.1	262.0	138	212	17.7	4.8	0.0	22.5	48	2.0	106.5	75

5 km – $He\text{-}O_2$

	Iel (cmH₂O)	Ires (cmH₂O)	Exp total (cmH₂O)	WOB (cmH₂O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})		Iel (cmH₂O)	Ires (cmH₂O)	Exp total (cmH₂O)	WOB (cmH₂O)	F_b (breaths·min^{-1})	V_T (l)	WOB (J·min^{-1})	V'_E (l·min^{-1})
Men									Women								
104	37.5	16.0	4.6	58.1	46	3.4	262.3	134	201	18.6	4.5	0.0	23.2	59	2.1	134.9	98
105	29.5	11.2	0.0	40.8	55	3.2	219.2	133	202	9.7	2.0	0.0	11.7	90	1.1	104.1	87
106	45.3	12.3	0.4	58.1	55	3.5	310.4	142	203	28.0	21.9	2.2	52.1	62	2.3	314.8	109
107	37.2	11.4	0.4	49.0	59	3.2	283.5	152	204	12.1	4.1	0.0	16.2	121	1.4	191.0	123
108	36.9	11.5	0.5	48.9	79	2.6	378.6	157	205	24.9	5.7	0.6	31.2	57	2.0	174.9	88
109	38.7	18.6	1.5	58.8	75	2.8	431.8	163	206	13.7	4.0	0.0	17.7	88	1.5	152.4	98
110	32.3	8.8	0.0	41.1	84	2.5	338.6	164	207	13.3	7.8	0.0	21.2	87	1.6	179.9	102
111	18.6	5.2	1.1	24.9	79	2.3	192.5	135	208	30.1	20.2	0.1	50.3	63	2.6	309.2	122
112	25.1	16.8	4.6	46.5	62	2.5	283.1	127	210	28.0	17.9	0.7	46.6	59	2.3	270.4	112
114	61.9	23.8	2.9	88.6	45	4.3	389.1	145	211	20.6	14.7	0.0	35.3	61	2.5	211.5	128
115	41.0	12.8	1.6	55.4	77	3.0	416.2	169	212	16.1	4.0	0.0	20.1	53	1.9	104.0	77

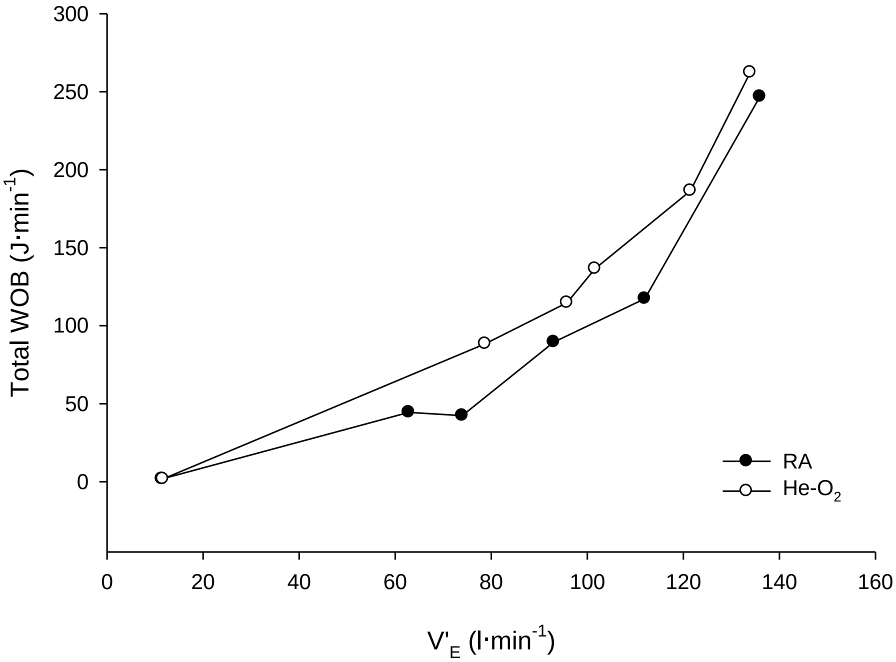
Table 39 - Individual RA TT Ratings of Perceived Exertion

	Rest		1 km		2 km		3 km		4 km		5 km		Reason for not cycling faster				Relative Contribution	
	Dyspnea	Leg	Dyspnea	Leg	Dyspnea	Leg	Dyspnea	Leg	Dyspnea	Leg	Dyspnea	Leg	Breathing	Leg	Combination	Other	Breathing (%)	Leg (%)
Men																		
104	0	0	2	2	3	3	3	3	3	3	4	4		X			40	60
105	0	0	3	3	4	4	5	5	5	5	7	7			X		40	60
106	1	1	3	3	4	4	4	4	5	5	7	6	X				70	30
107	0	0	1	3	2	4	3	5	5	7	9	10		X			30	70
108	0	0.5	2	2	4	4	4	5	6	6	7	9			X		30	70
109	0.5	0	4	4	6	5	7	5	9	6	9	6	X				85	15
110	0	0	5	5	6	6	8	8	8	8	9	9			X		45	55
111	0	0	1	1	1	1	4	4	6	6	7	8		X			40	60
112	0	0	2	2	3	3	3	3	4	6	8	9		X			40	60
114	0	0	3	3	5	5	5	5	7	8	8	10		X			30	70
115	0	0	3	3	4	4	5	5	8	8	9	10		X			40	60
Women																		
201	0	0	0.5	0.5	1	1	1	1	2	2	2	2		X			30	70
202	0.5	0.5	3	3	5	6	6	6	6	6	7	7				X	40	60
203	0	0	4	3	4	4	4	5	6	6	8	9		X			40	60
204	0	0	4	5	5	5	6	6	7	7	9	9			X		30	70
205	0	0.5	3	4	5	5	7	7	7	7	7	8			X		35	65
206	0	0	1	1	3	2	3	3	3	3	4	4		X			0	100
207	0	0	4	4	6	6	8	8	8	8	8	8			X		50	50
208	0	0	5	5	8	6	8	6	8	6	9	10		X			50	50
210	0	0	2	2	4	4	4	4	5	5	8	8			X		45	55
211	0.5	0.5	3	3	3	3	3	3	3	4	5	5			X		70	30
212	0.5	0	0.5	0.5	1	1	1	2	1	2	1	3		X			2	98

Table 40 - Individual He-O_2 TT Ratings of Perceived Exertion

	Rest		1 km		2 km		3 km		4 km		5 km		Reason for not cycling faster				Relative Contribution	
	Dyspnea	Leg	Dyspnea	Leg	Dyspnea	Leg	Dyspnea	Leg	Dyspnea	Leg	Dyspnea	Leg	Breathing	Leg	Combination	Other	Breathing (%)	Leg (%)
Men																		
104	0	0	0.5	0.5	2	2	4	4	5	5	5	5		X			30	70
105	1	1	3	3	4	4	4	4	4	5	6	7		X			40	60
106	0	0	2	2	3	3	5	5	5	5	8	7		X			30	70
107	0.5	0.5	2	2	3	4	4	5	5	7	9	10		X			30	70
108	0	0.5	3	3	3	3	4	4	6	6	8	8			X		50	50
109	0.5	0	4	4	5	6	5	6	7	8	8	8			X		50	50
110	0	0	5	5	6	7	7	8	7	8	8	9			X		35	65
111	0	0	2	2	4	4	6	6	6	9	6	9		X			35	65
112	0	0	2	3	2	3	4	5	5	6	7	9		X			30	70
114	0	0	3	4	5	5	6	7	7	8	10	10			X		50	50
115	0.5	0.5	2	2	3	3	3	3	4	4	8	10		X			30	70
Women																		
201	0	0	1	1	2	3	2	3	2	3	2	3		X			30	70
202	0.5	0.5	4	4	4	4	5	5	7	7	8	8		X			30	70
203	0	0	4	3	3	2	4	4	5	5	9	9		X			40	60
204	0	0	4	4	4	5	5	6	6	7	8	9			X		40	60
205	0	0	4	4	4	4	7	7	7	7	10	10			X		30	70
206	0	0	0.5	0.5	2	2	2	2	4	4	4	4		X			0	100
207	0	0	4	4	4	5	5	6	6	7	8	9		X			40	60
208	0	0	6	6	7	7	9	9	8	9	9	9			X		40	60
210	0	0	1	1	3	3	4	4	5	5	7	7			X		50	50
211	0	0	2	2	3	4	3	3	3	3	5	5			X		40	60
212	0	0	0.5	2	0.5	2	0.5	3	2	3	2	4		X			25	75

APPENDIX B - INDIVIDUAL DATA – FIGURES



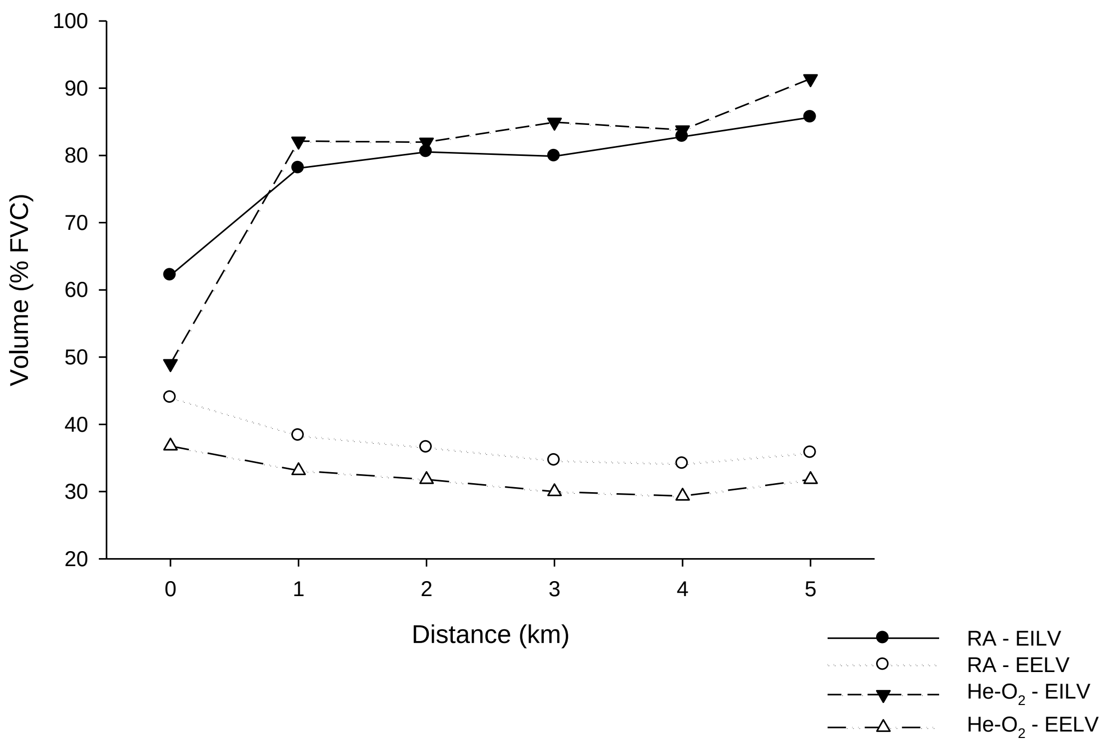


Figure 10 – Subject 104 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs**.**

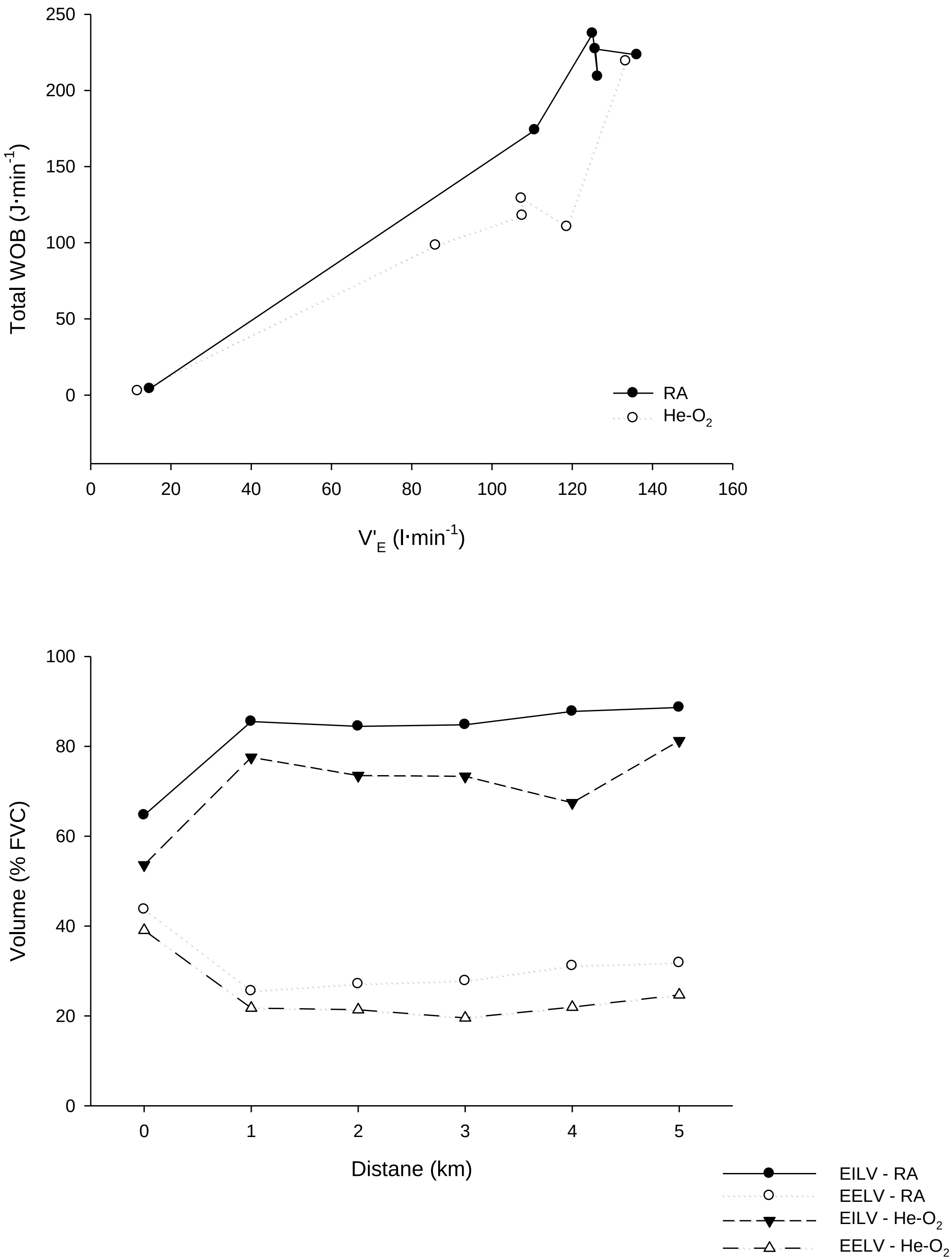


Figure 11 – Subject 105 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs

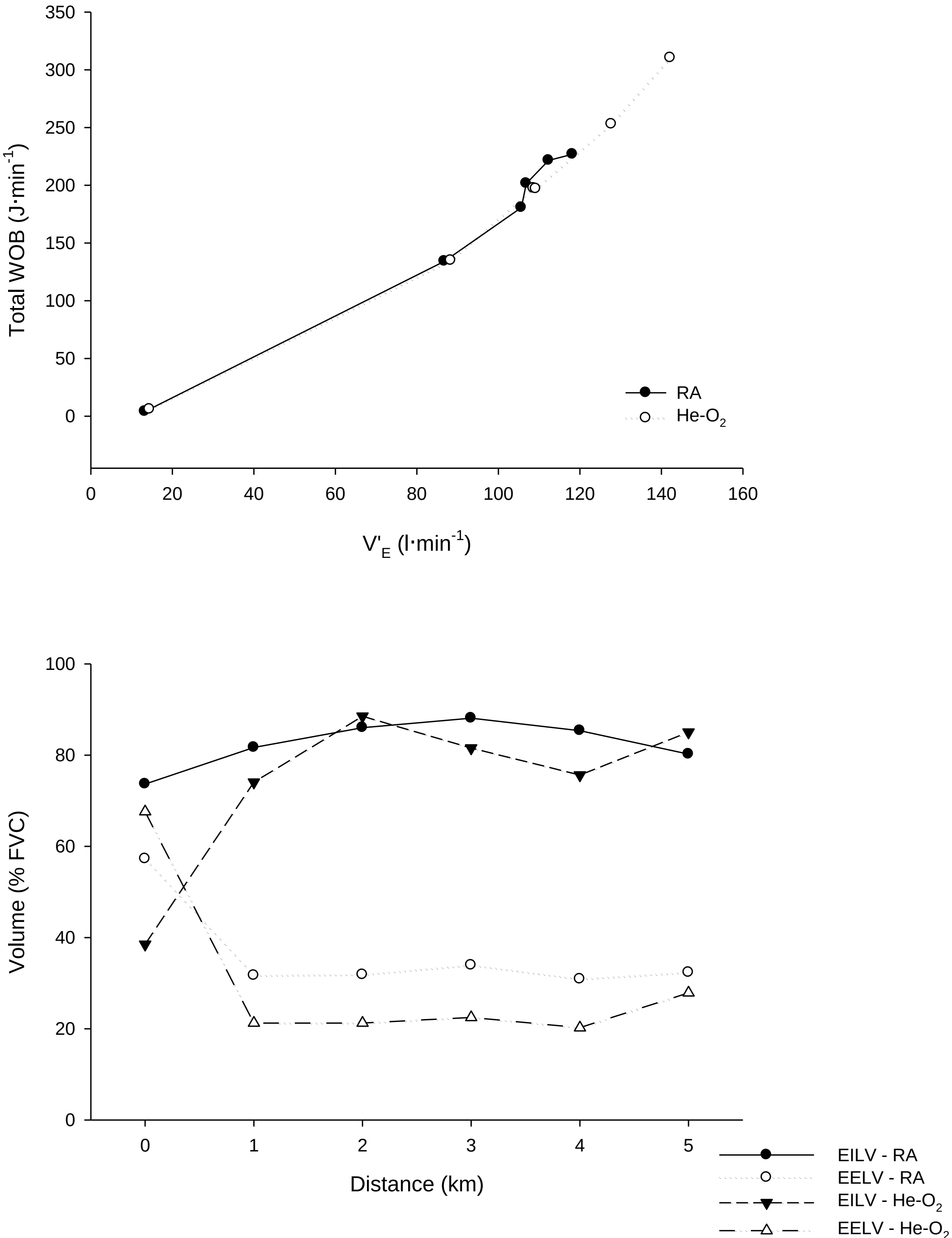
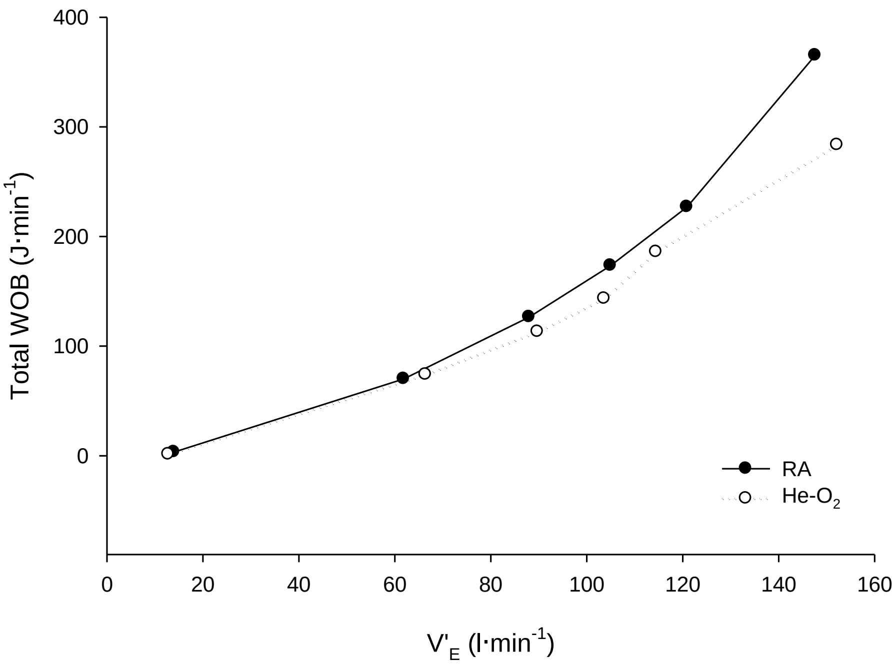


Figure 12 – Subject 106 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs



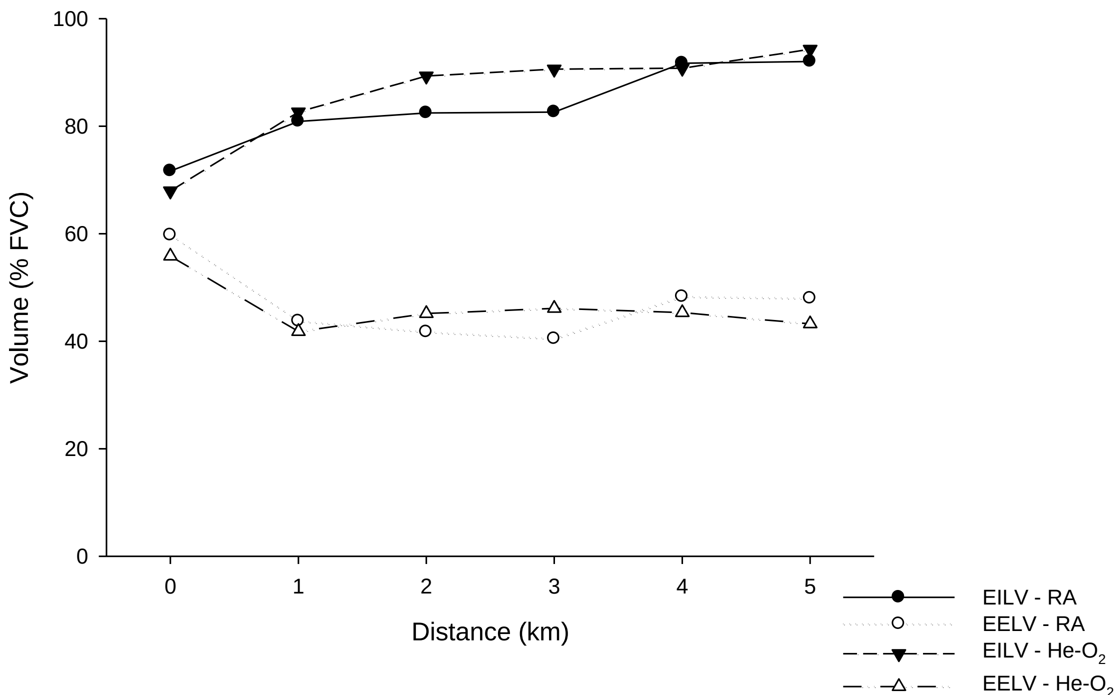


Figure 13 – Subject 107 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs

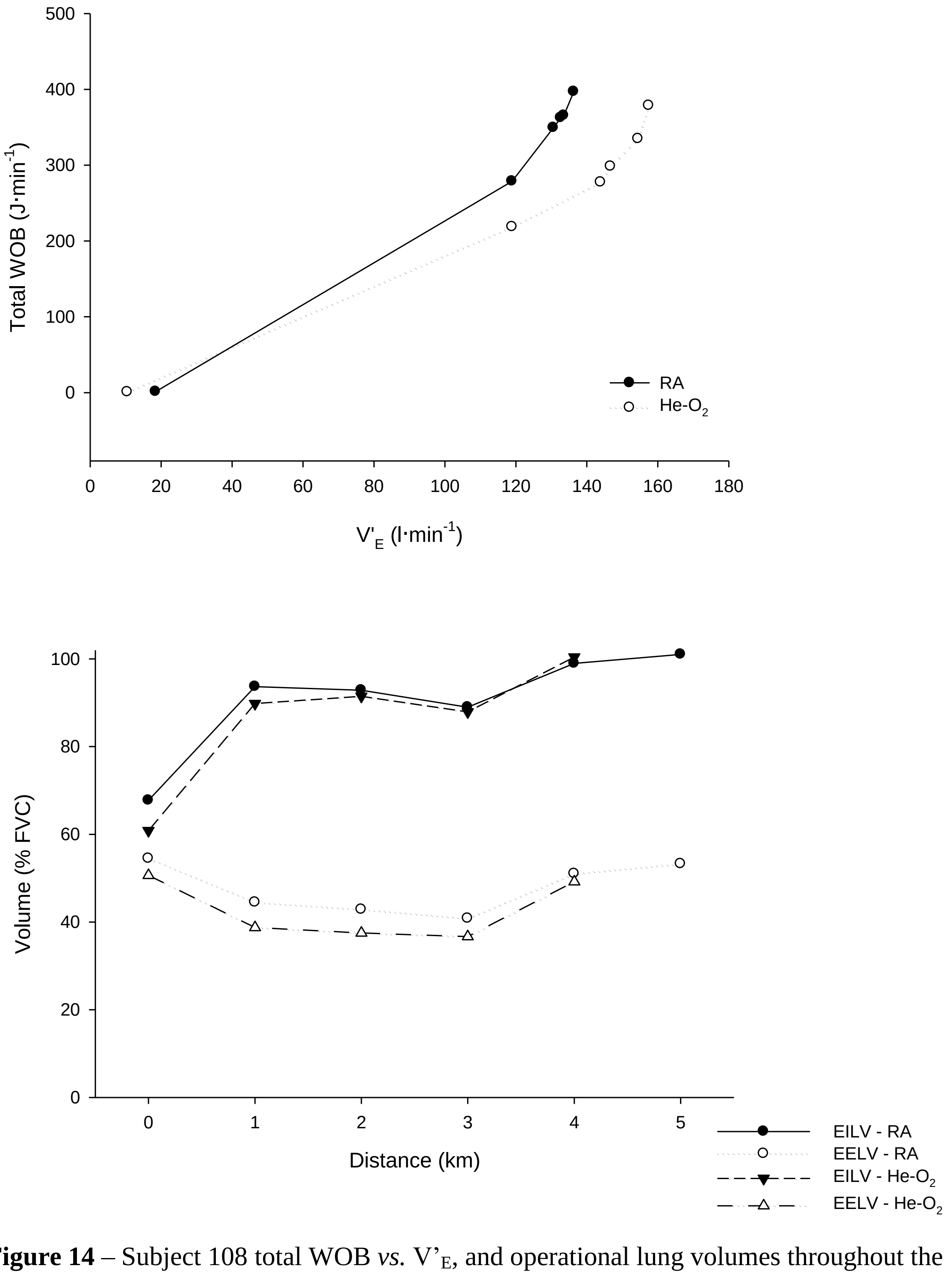
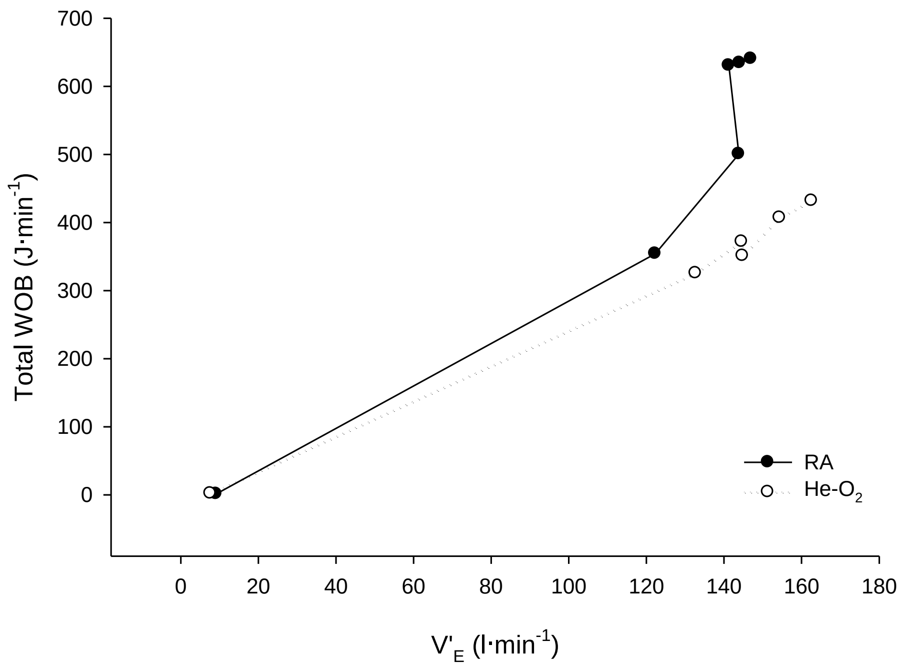


Figure 14 – Subject 108 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs



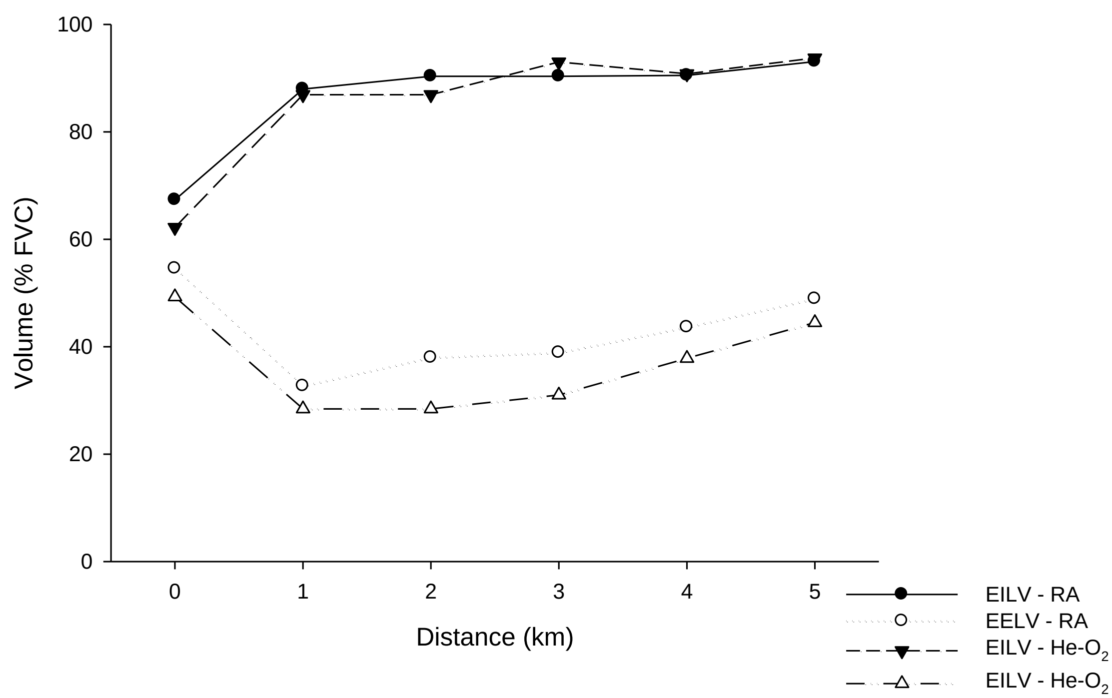


Figure 15 – Subject 109 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs

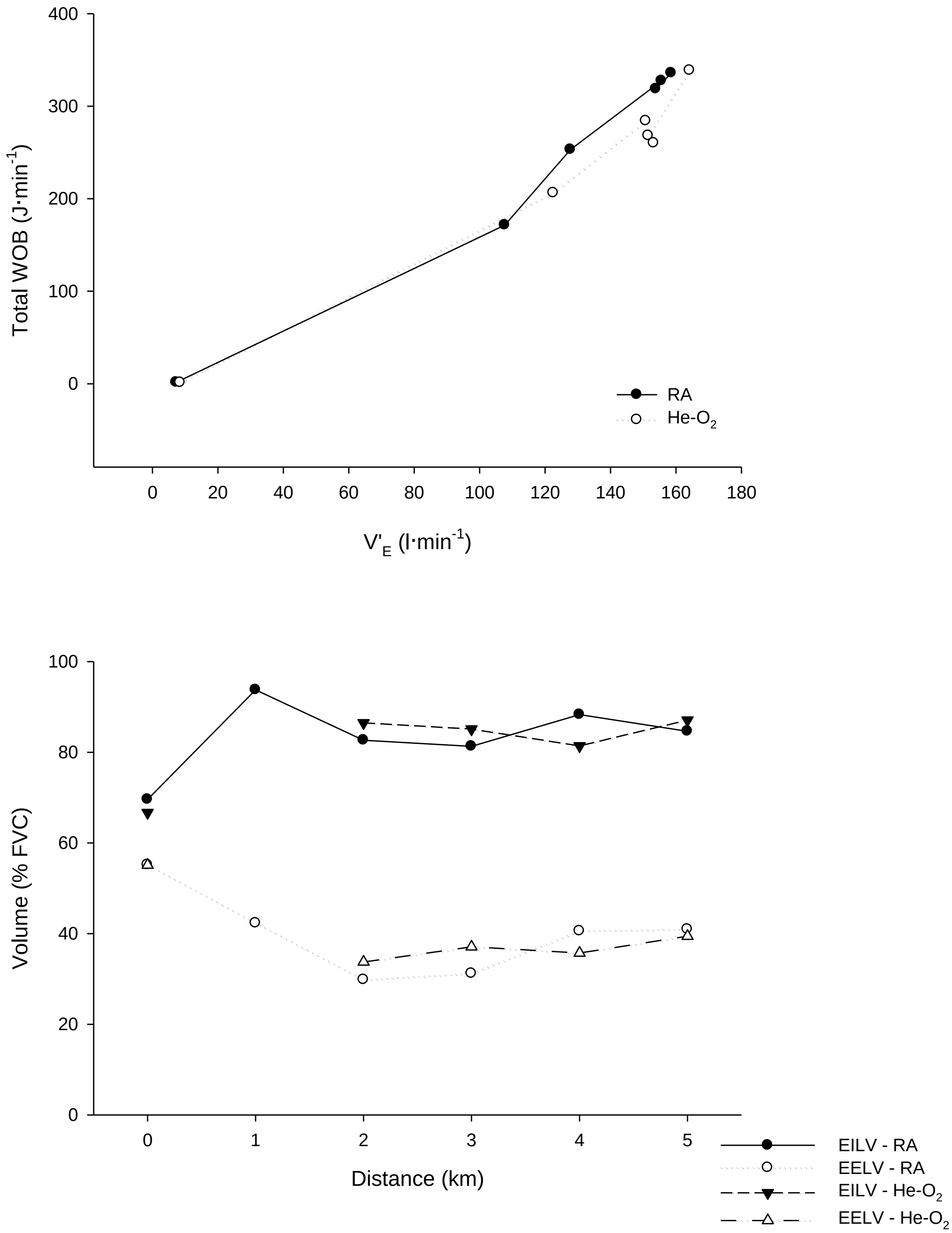
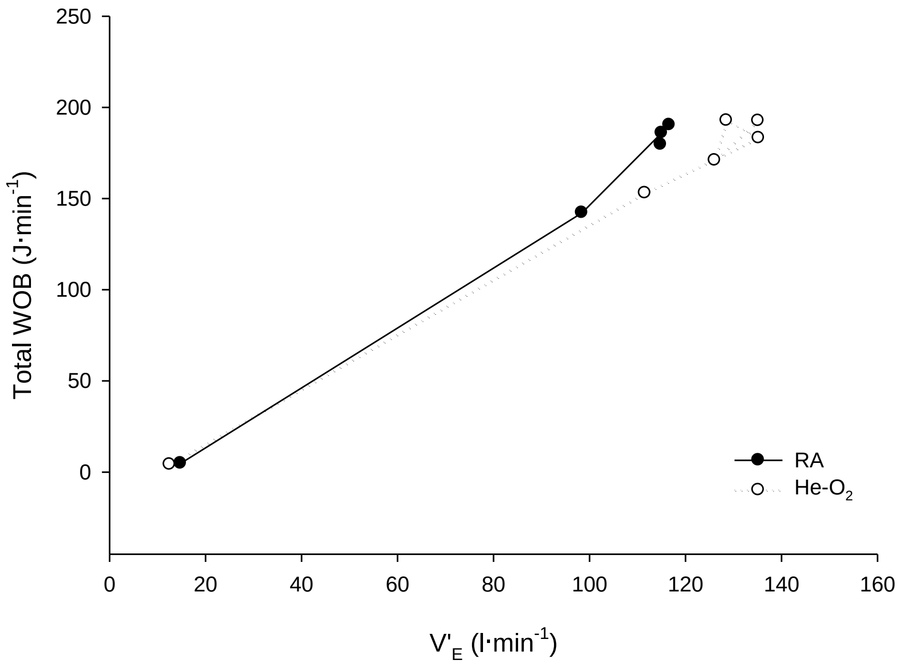


Figure 16 – Subject 110 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs



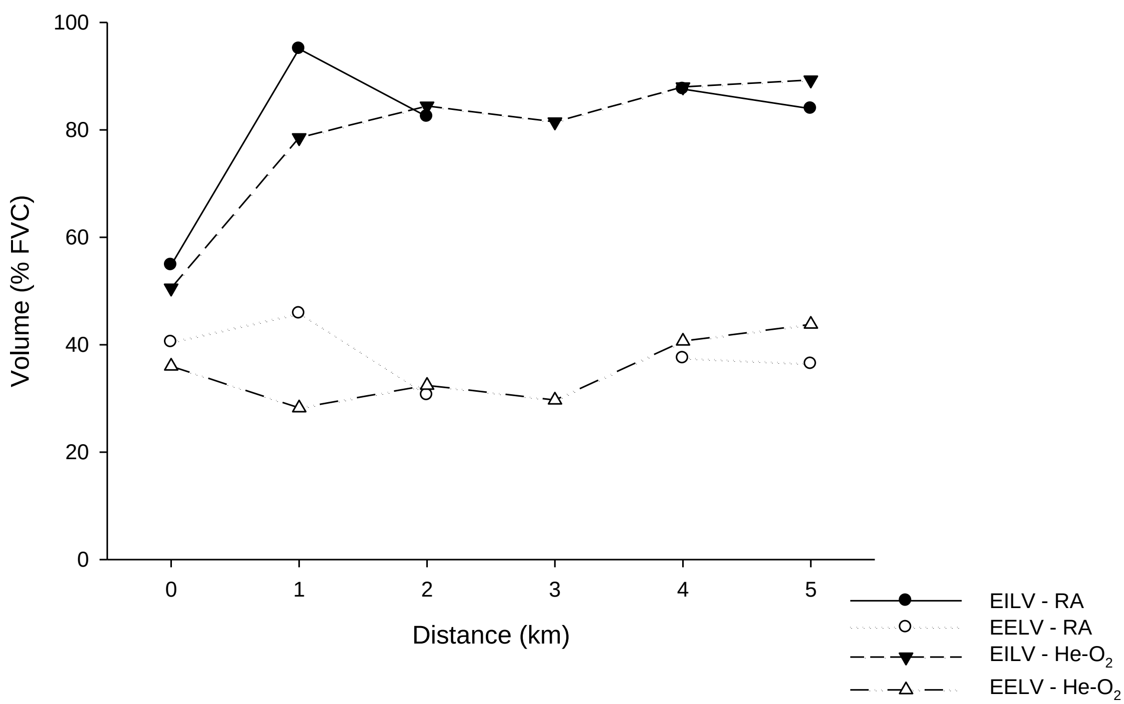
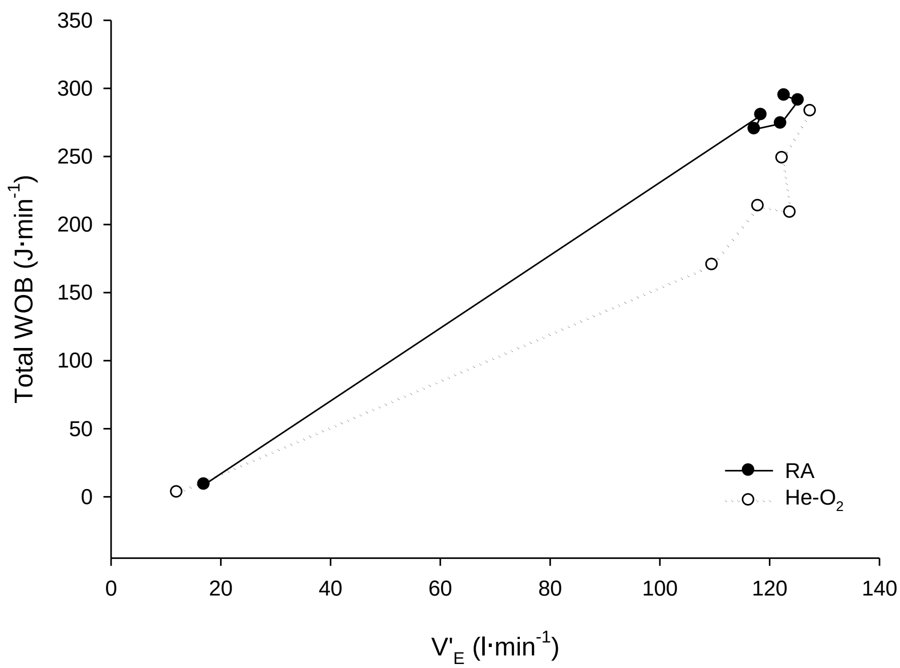


Figure 17 – Subject 111 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs



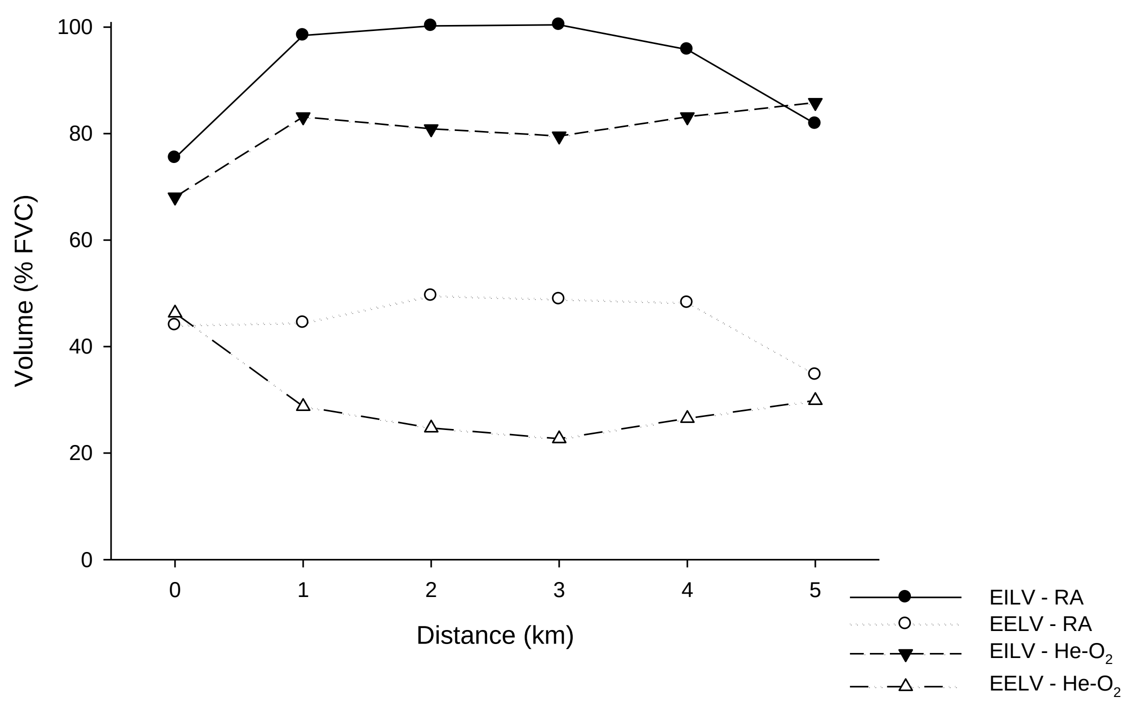


Figure 18 – Subject 112 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs

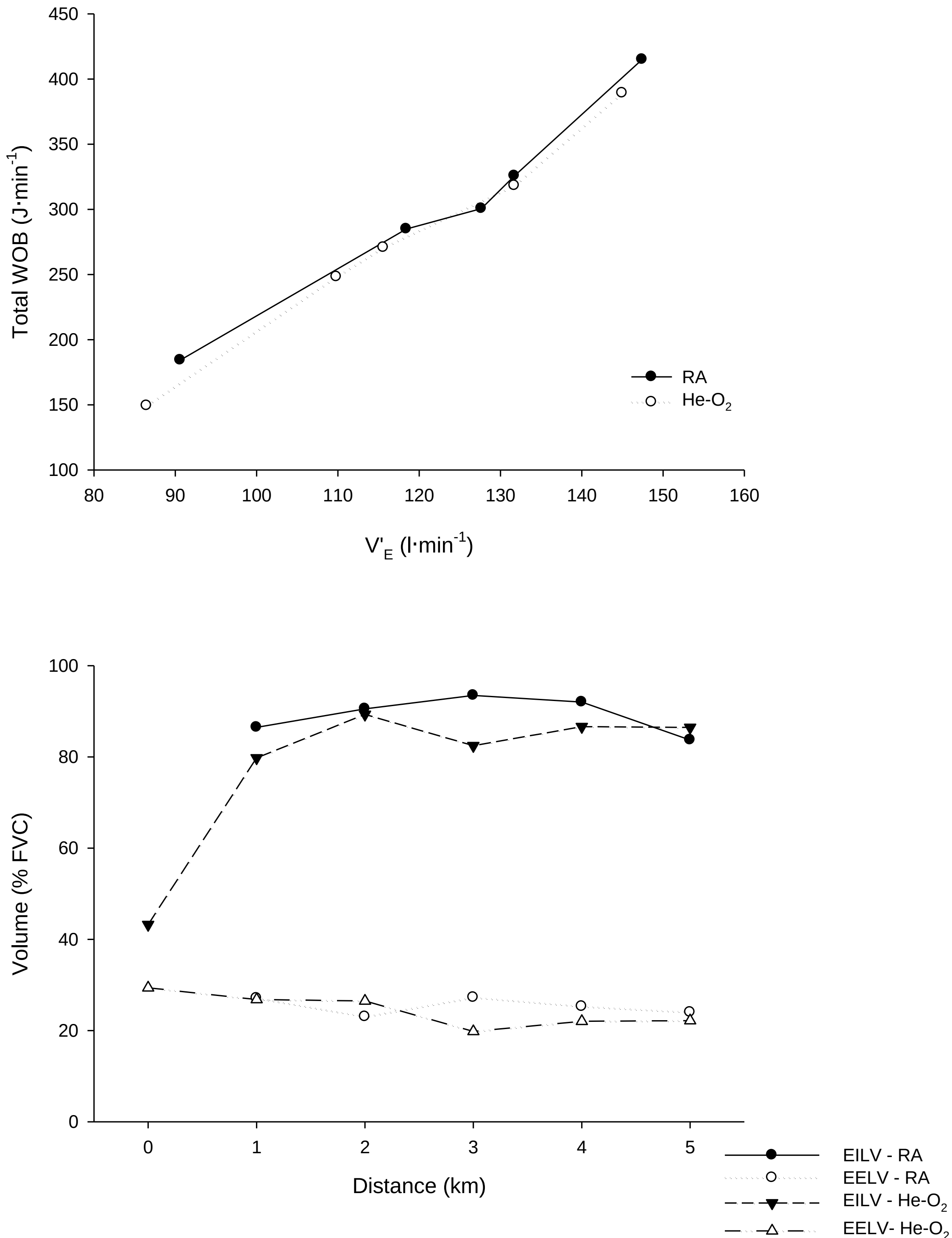
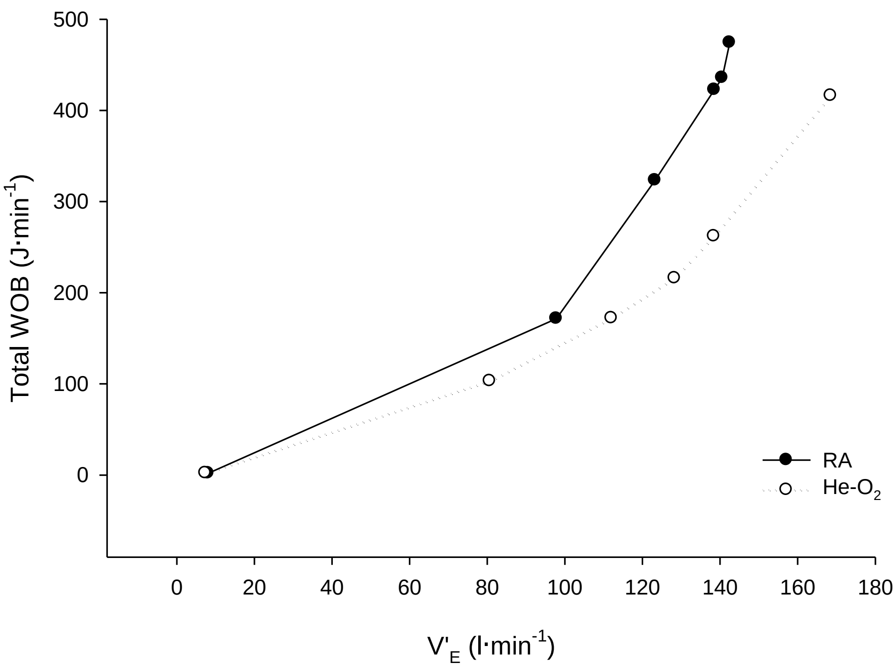


Figure 19 – Subject 114 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs



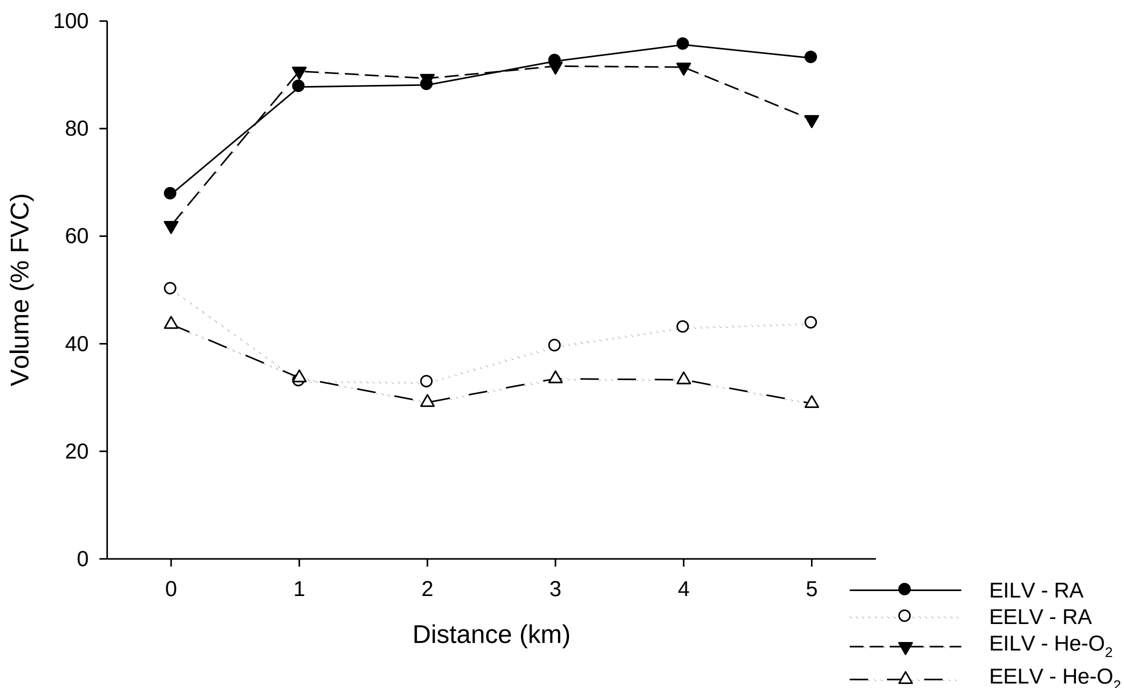


Figure 20 – Subject 115 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs

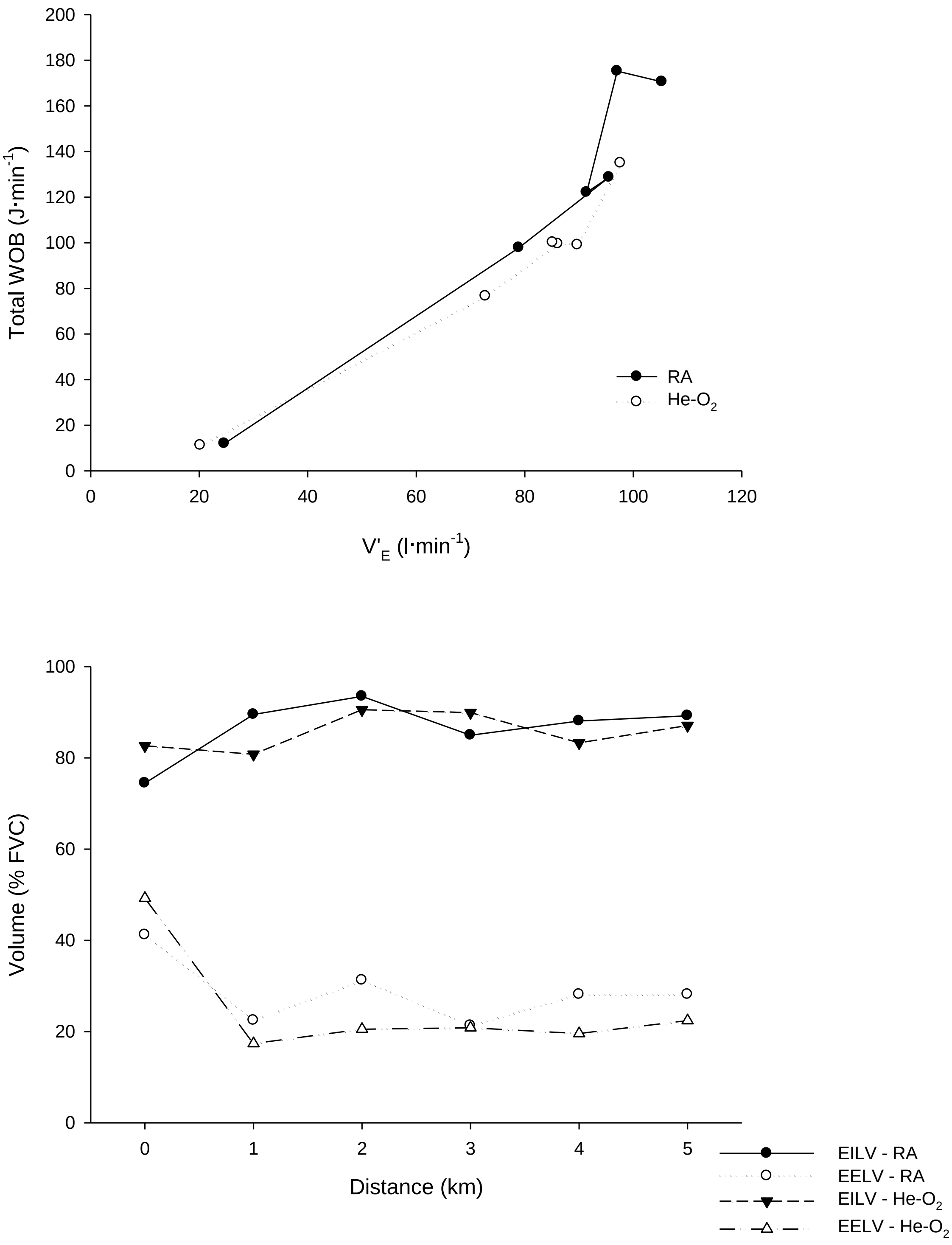


Figure 21 – Subject 210 total WOB *vs.* V'$_E$, and operational lung volumes throughout the TTs

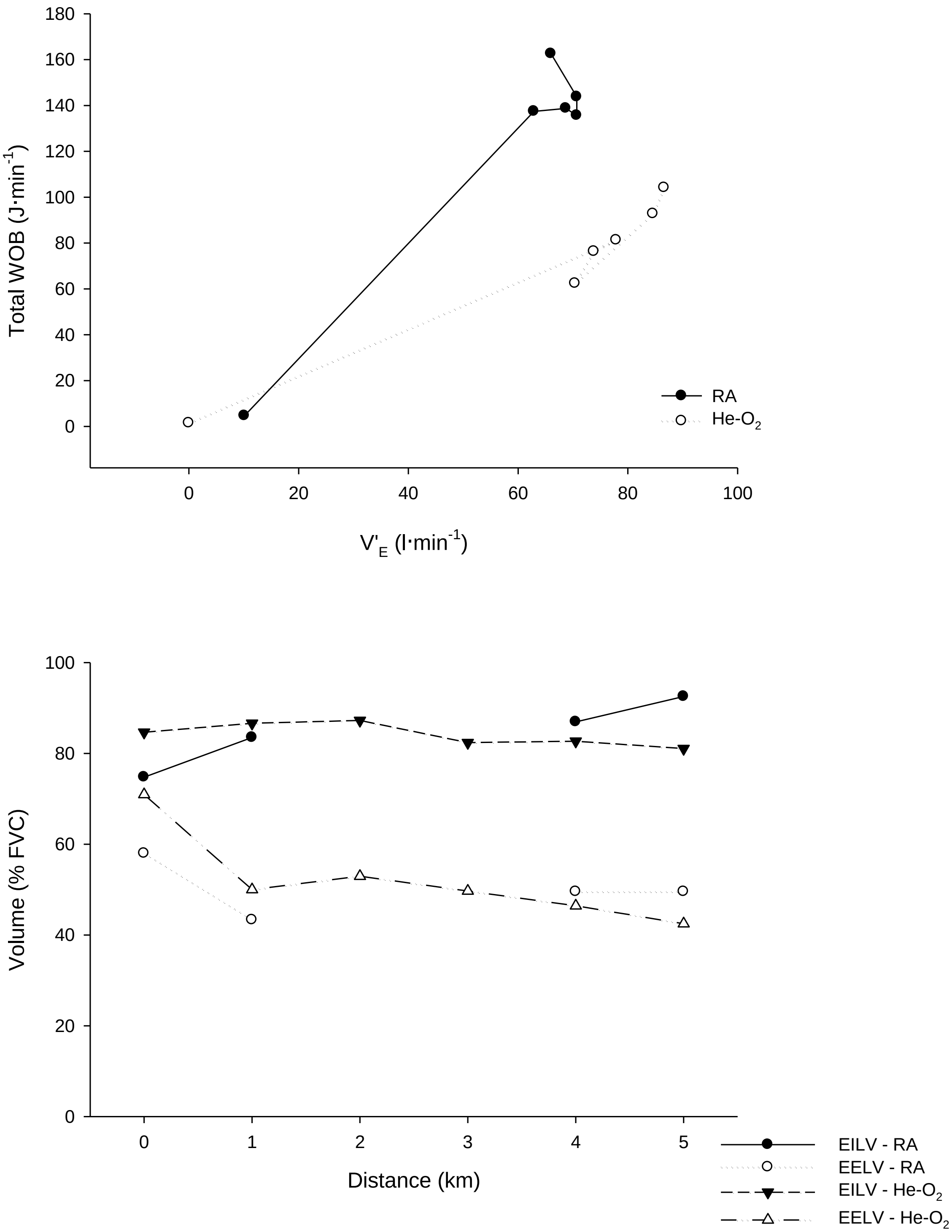


Figure 22 – Subject 202 total WOB *vs.* V'$_E$, and operational lung volumes throughout the TTs

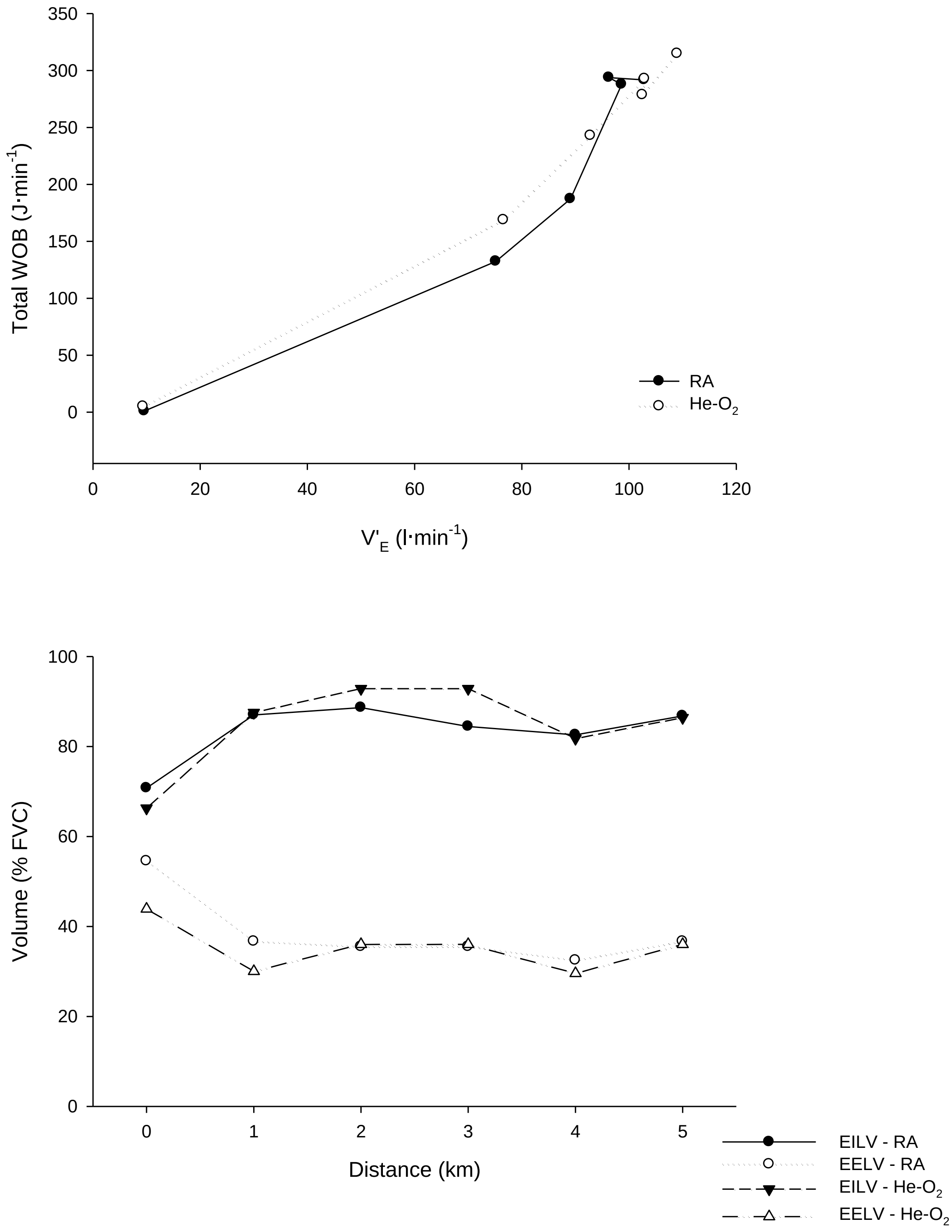


Figure 23 – Subject 203 total WOB *vs.* V'$_E$, and operational lung volumes throughout the TTs

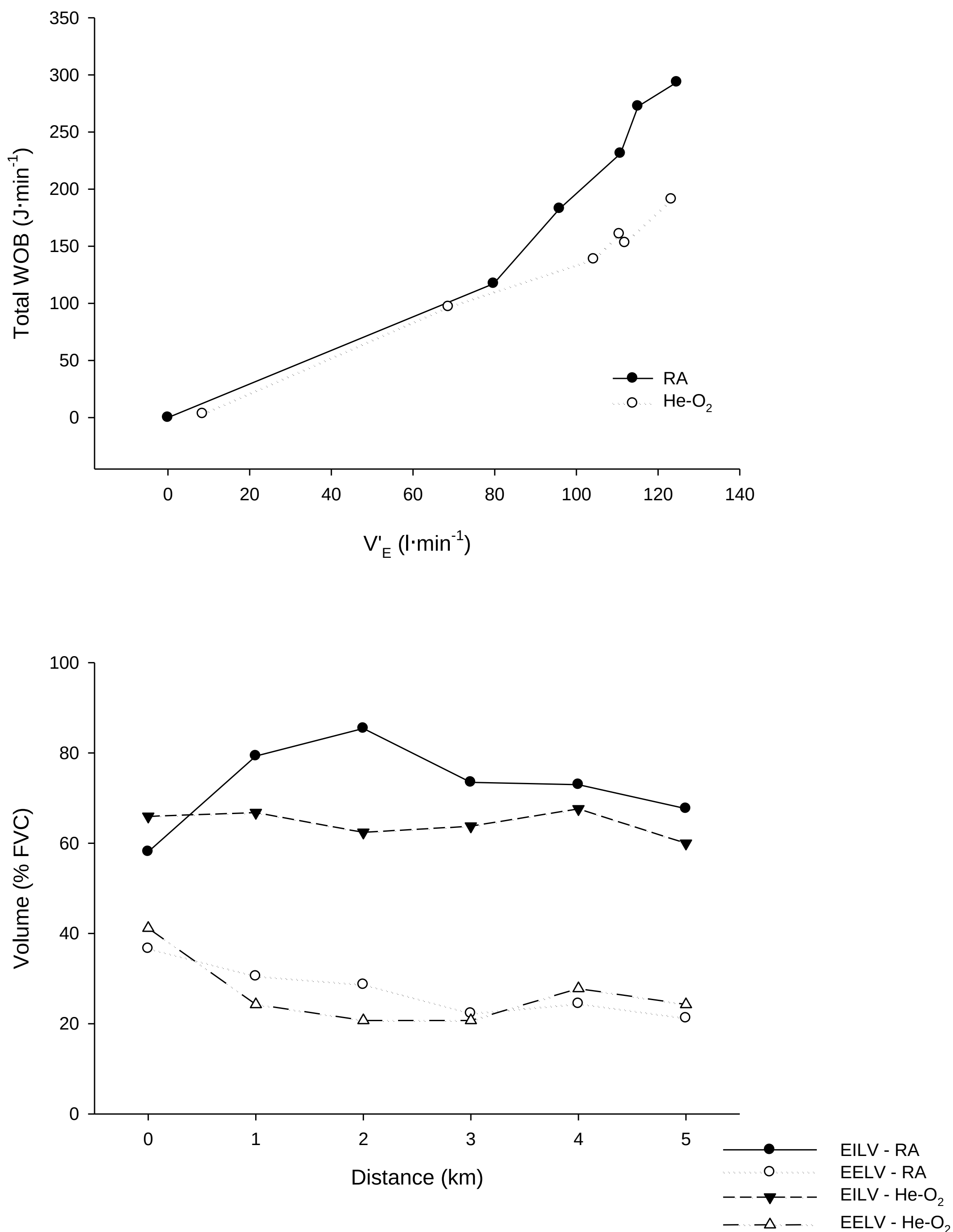


Figure 24 – Subject 204 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs

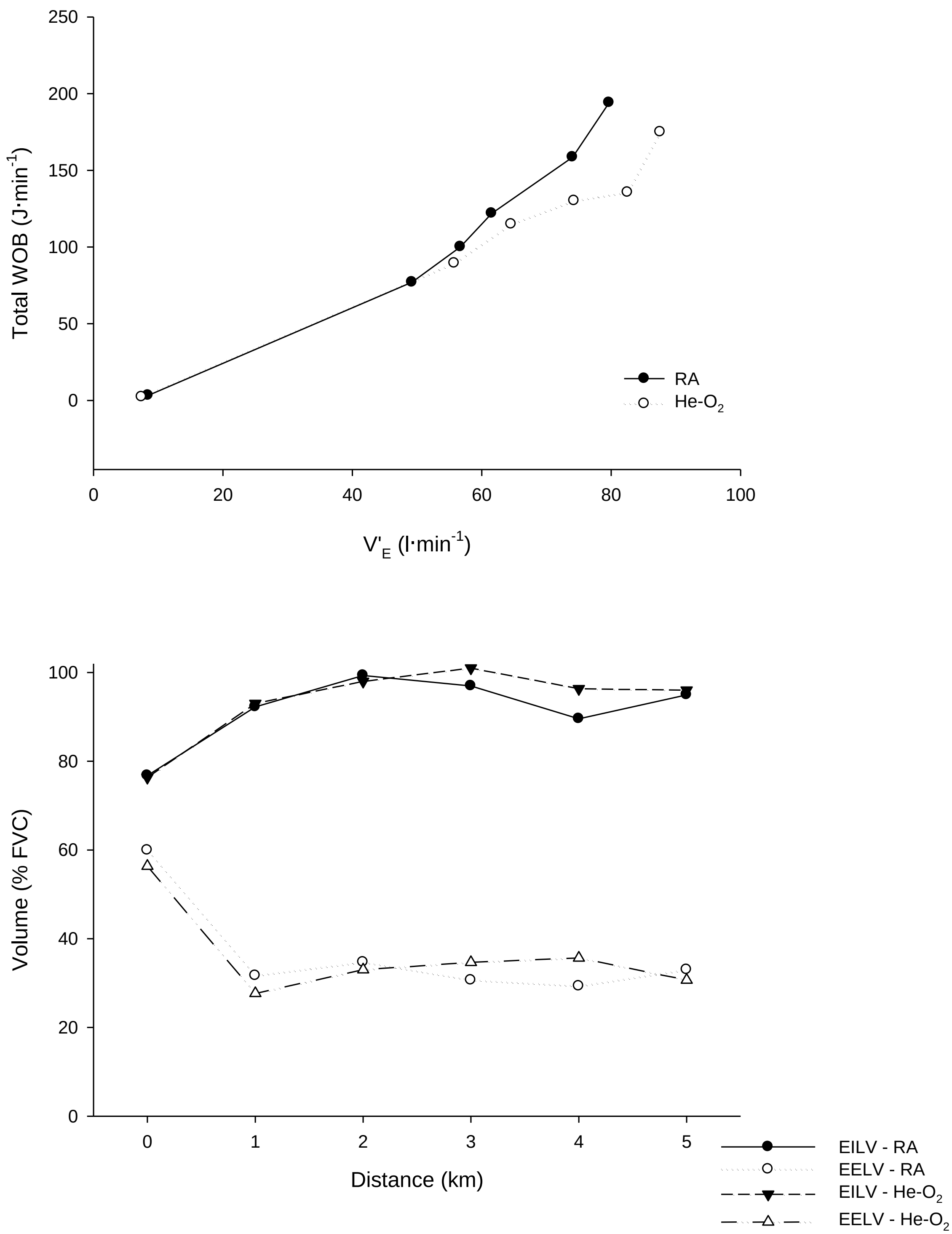


Figure 25 – Subject 205 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs

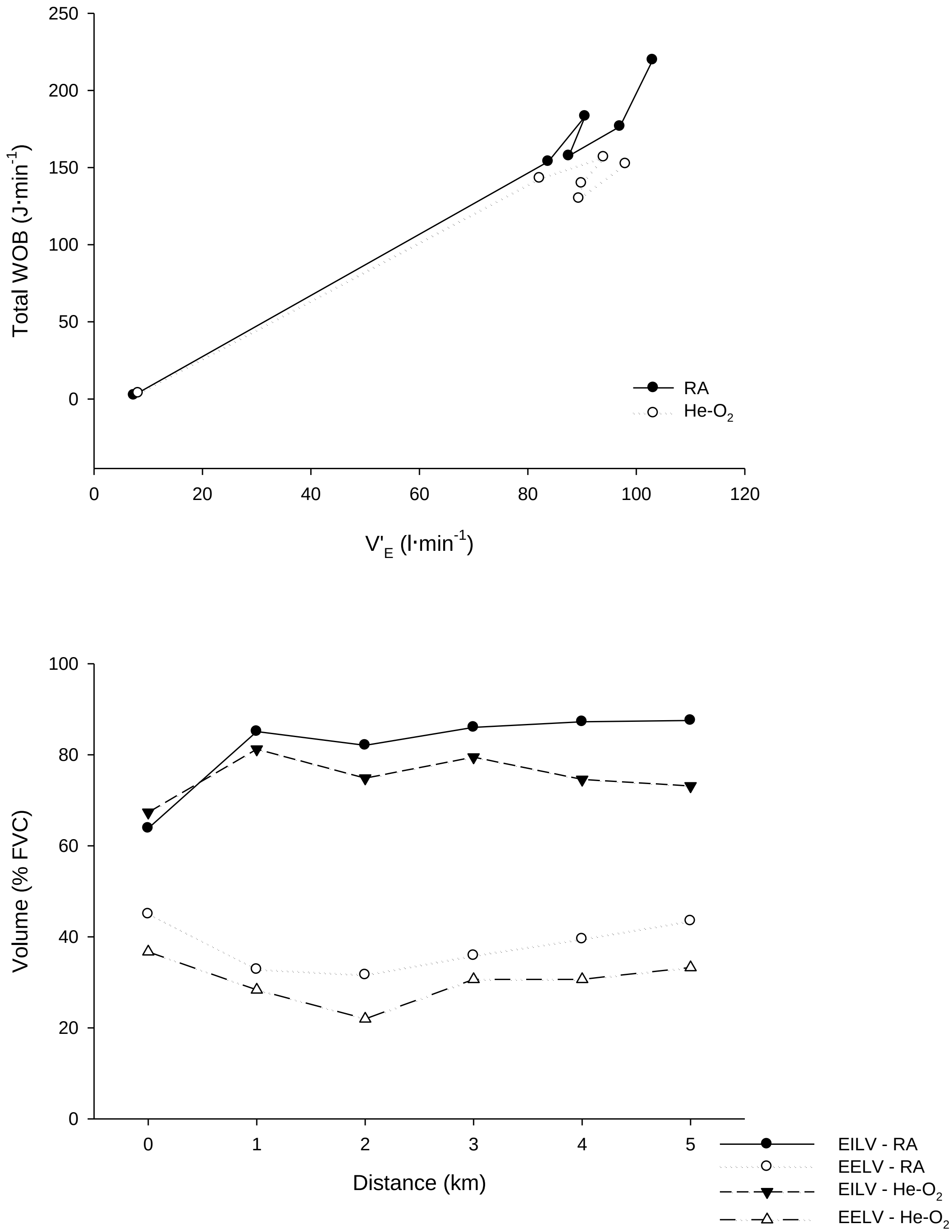


Figure 26 – Subject 206 total WOB *vs.* V’$_E$, and operational lung volumes throughout the TTs

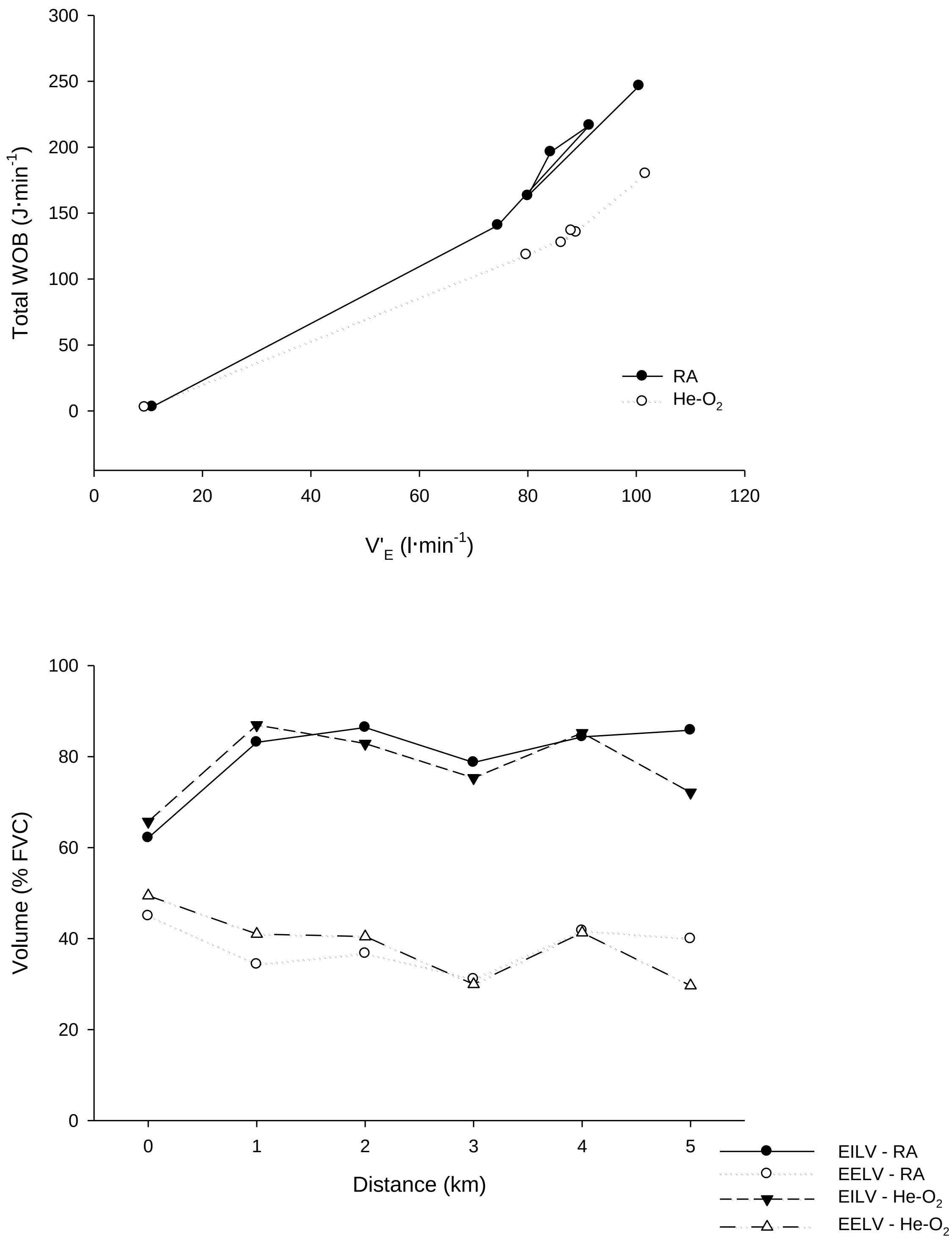


Figure 27 – Subject 207 total WOB *vs.* V'$_E$, and operational lung volumes throughout the TTs

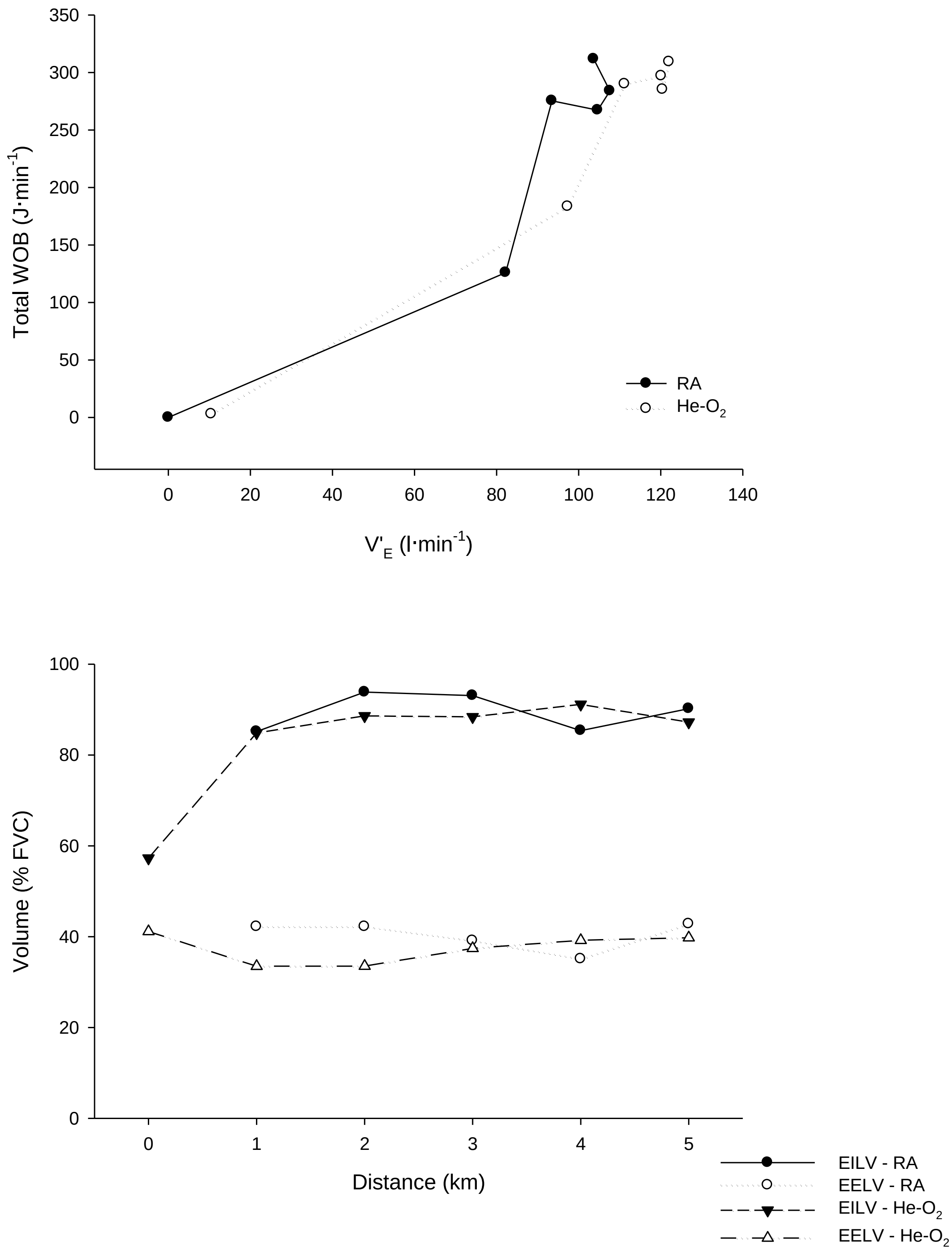


Figure 28 – Subject 208 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs

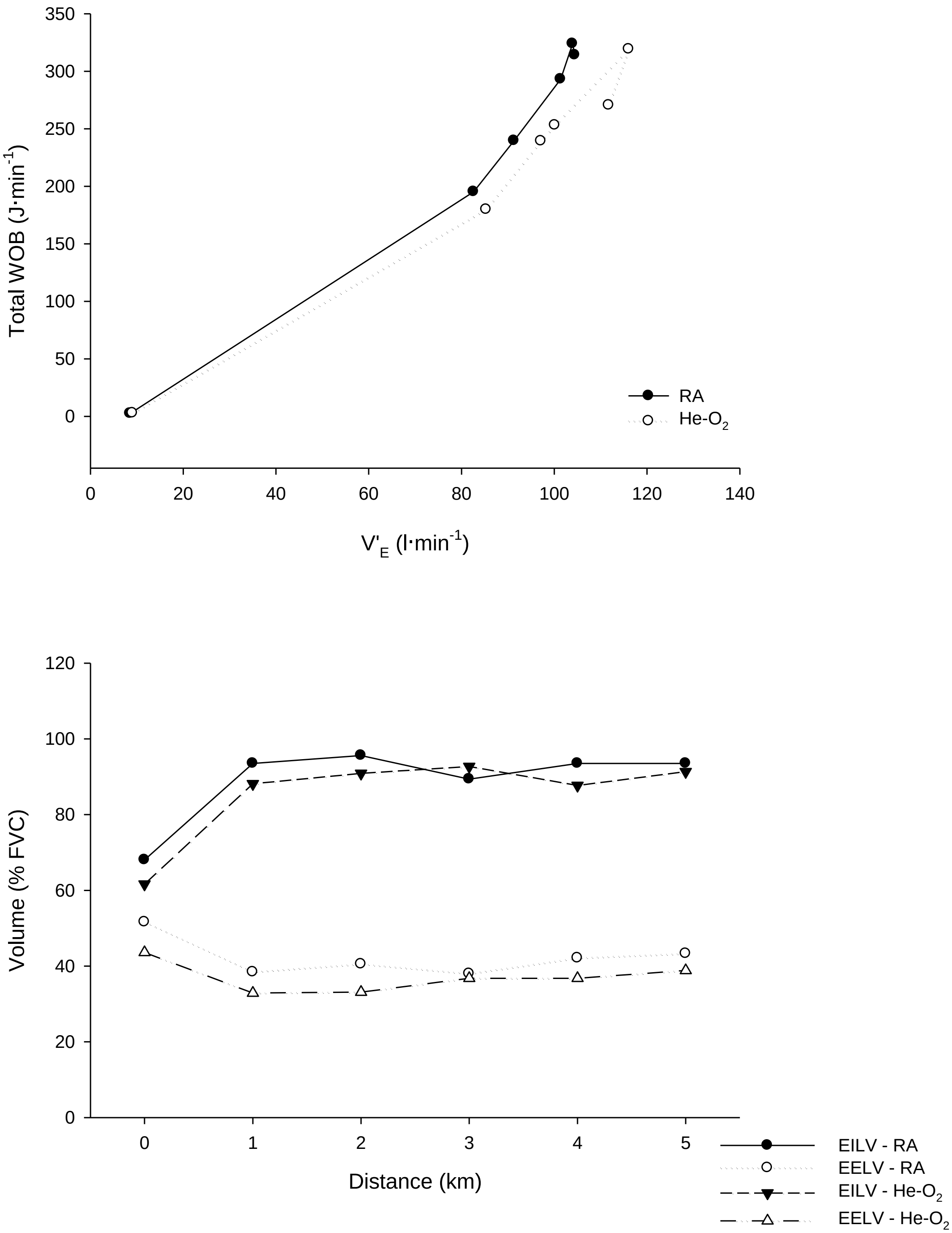
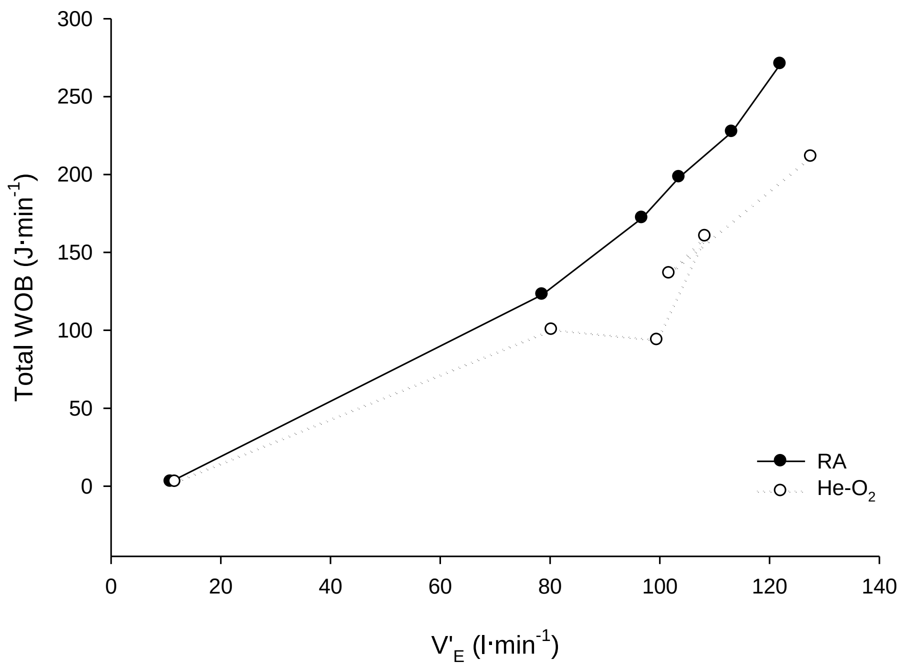


Figure 29 – Subject 210 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs



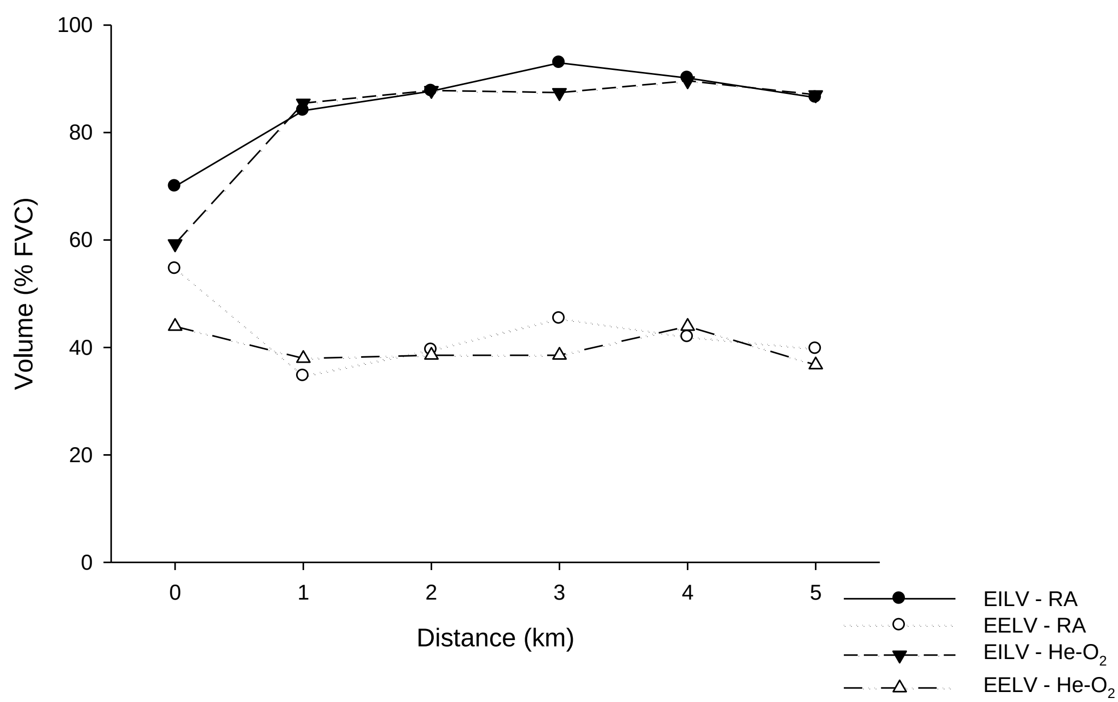
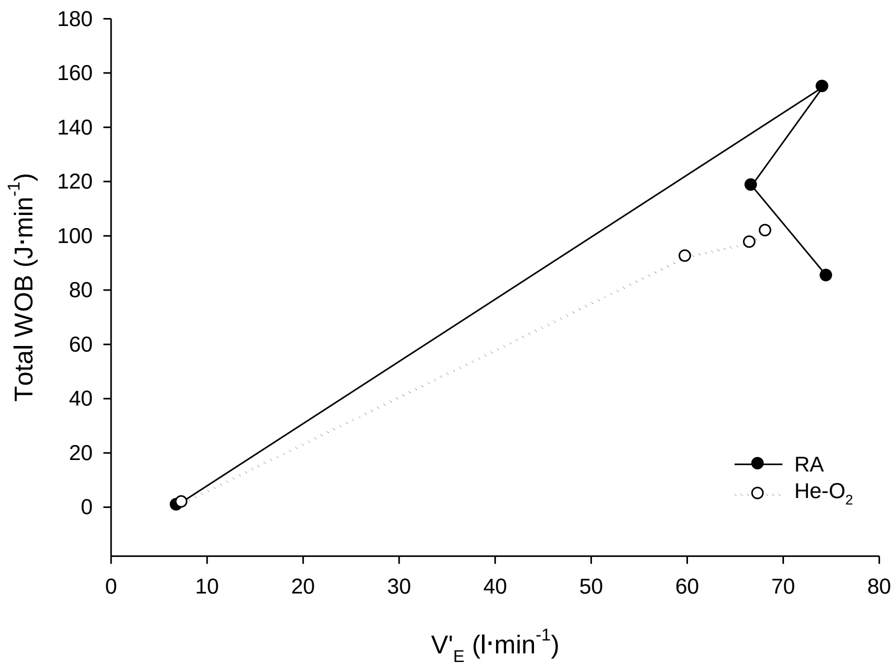


Figure 30 – Subject 211 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs



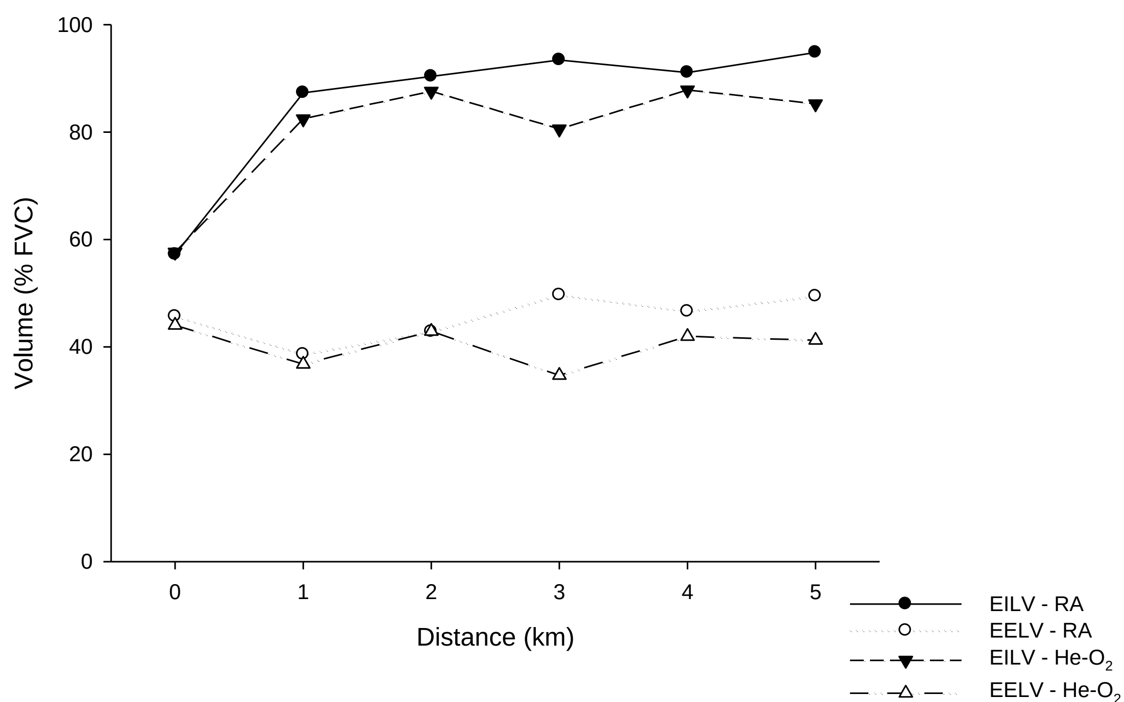


Figure 31 – Subject 211 total WOB *vs.* V'_E, and operational lung volumes throughout the TTs

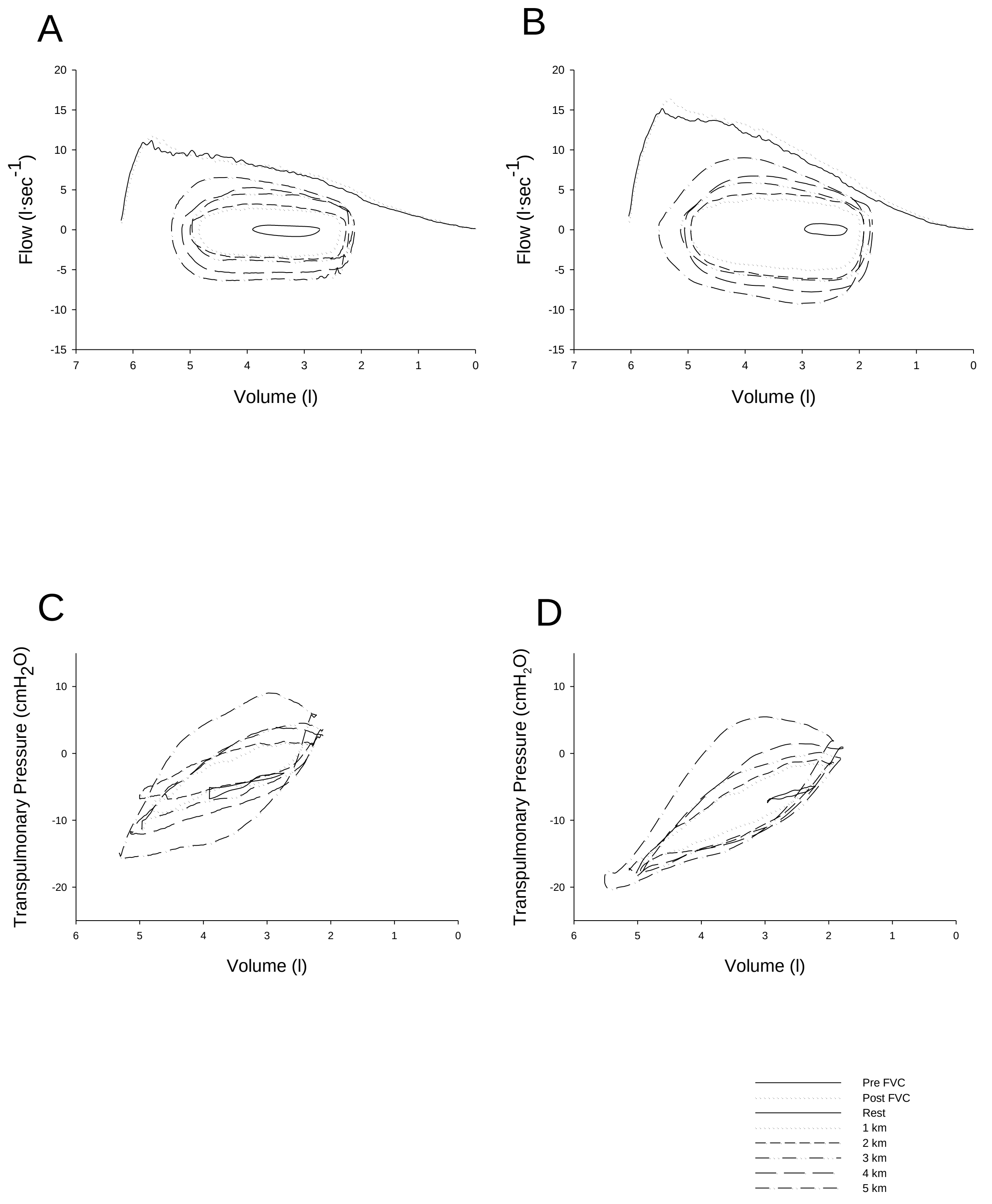


FIGURE 32 – Subject 104 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

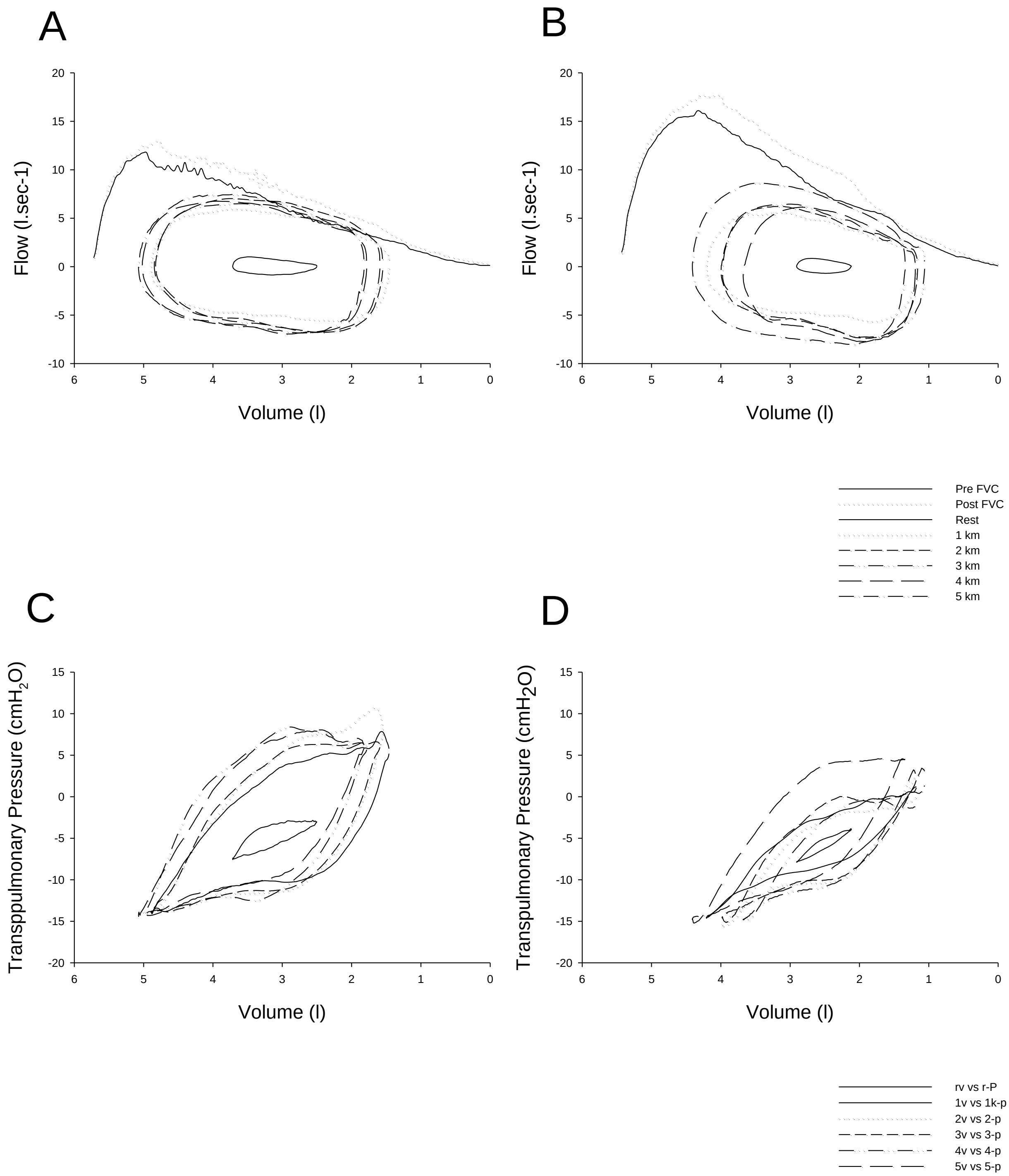


FIGURE 33 – Subject 105 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

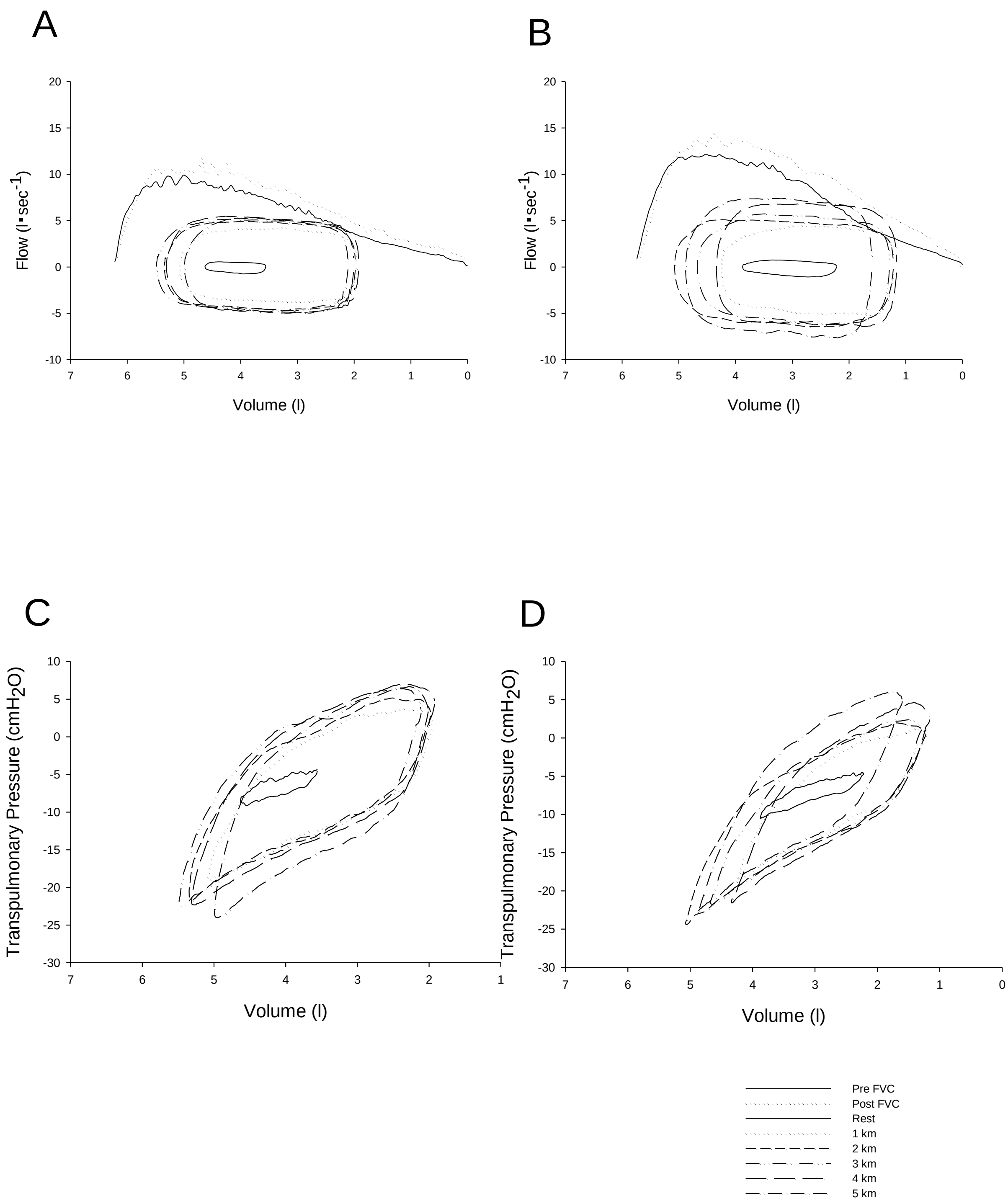


FIGURE 34 – Subject 106 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

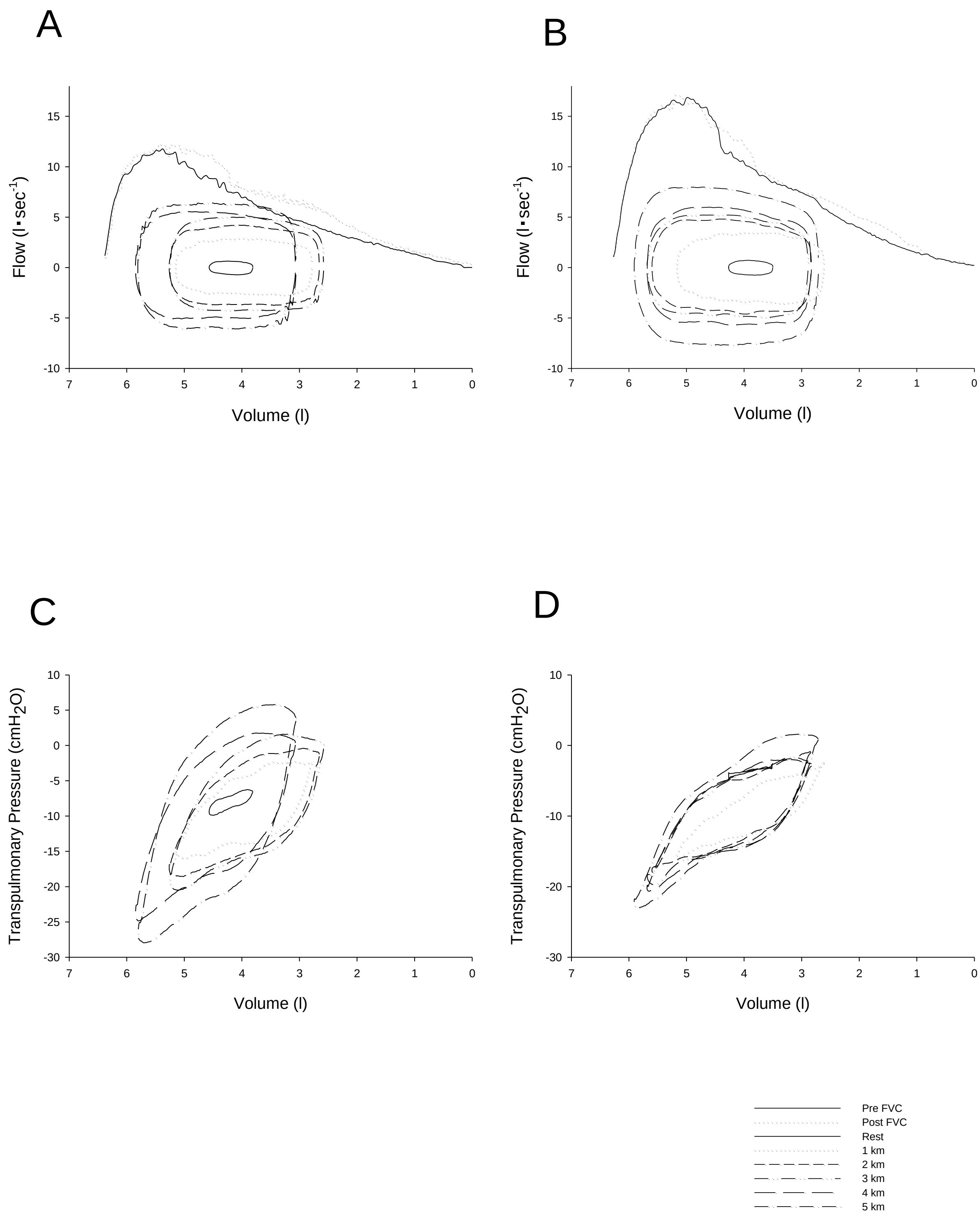


FIGURE 35 – Subject 107 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

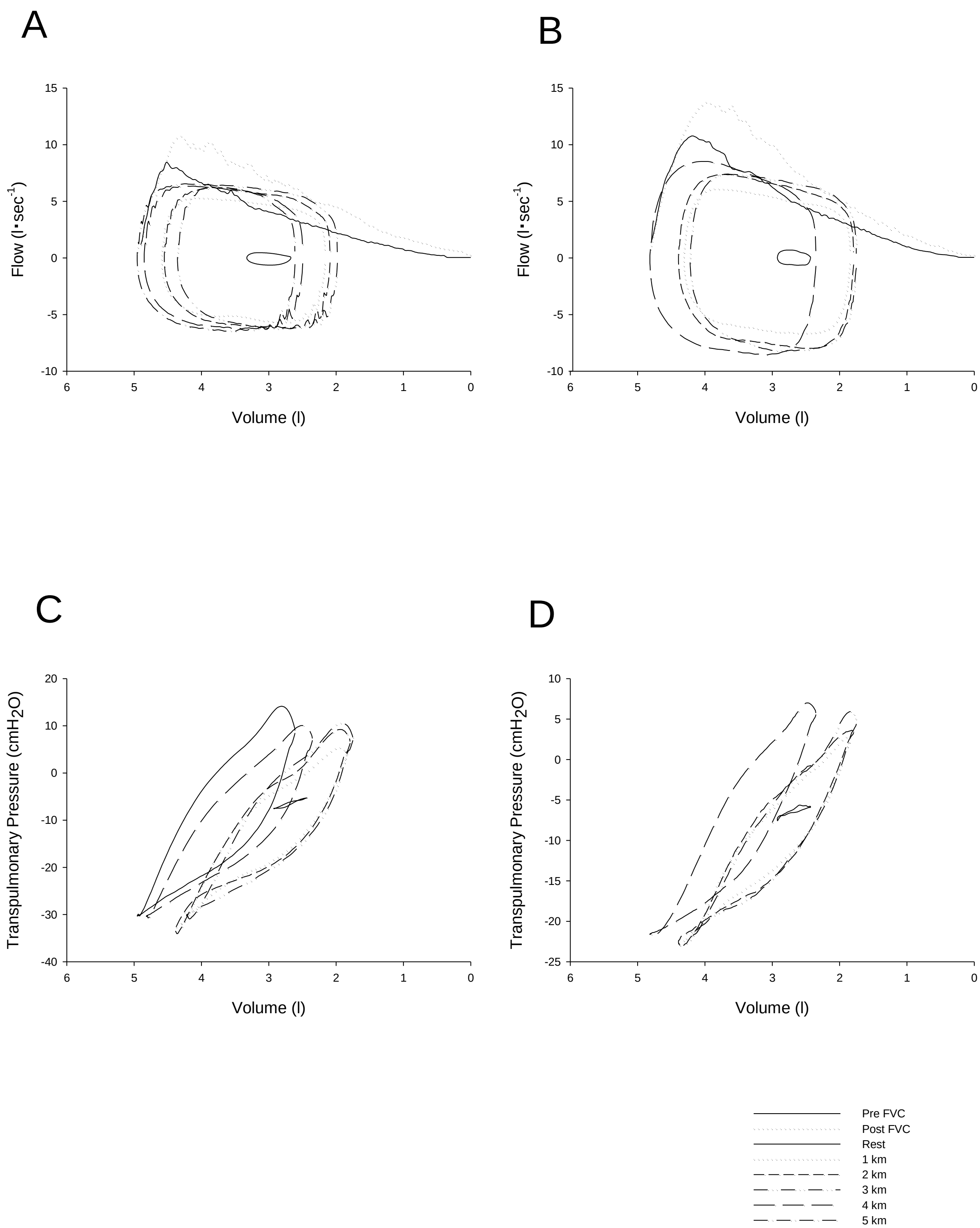


FIGURE 36 – Subject 108 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

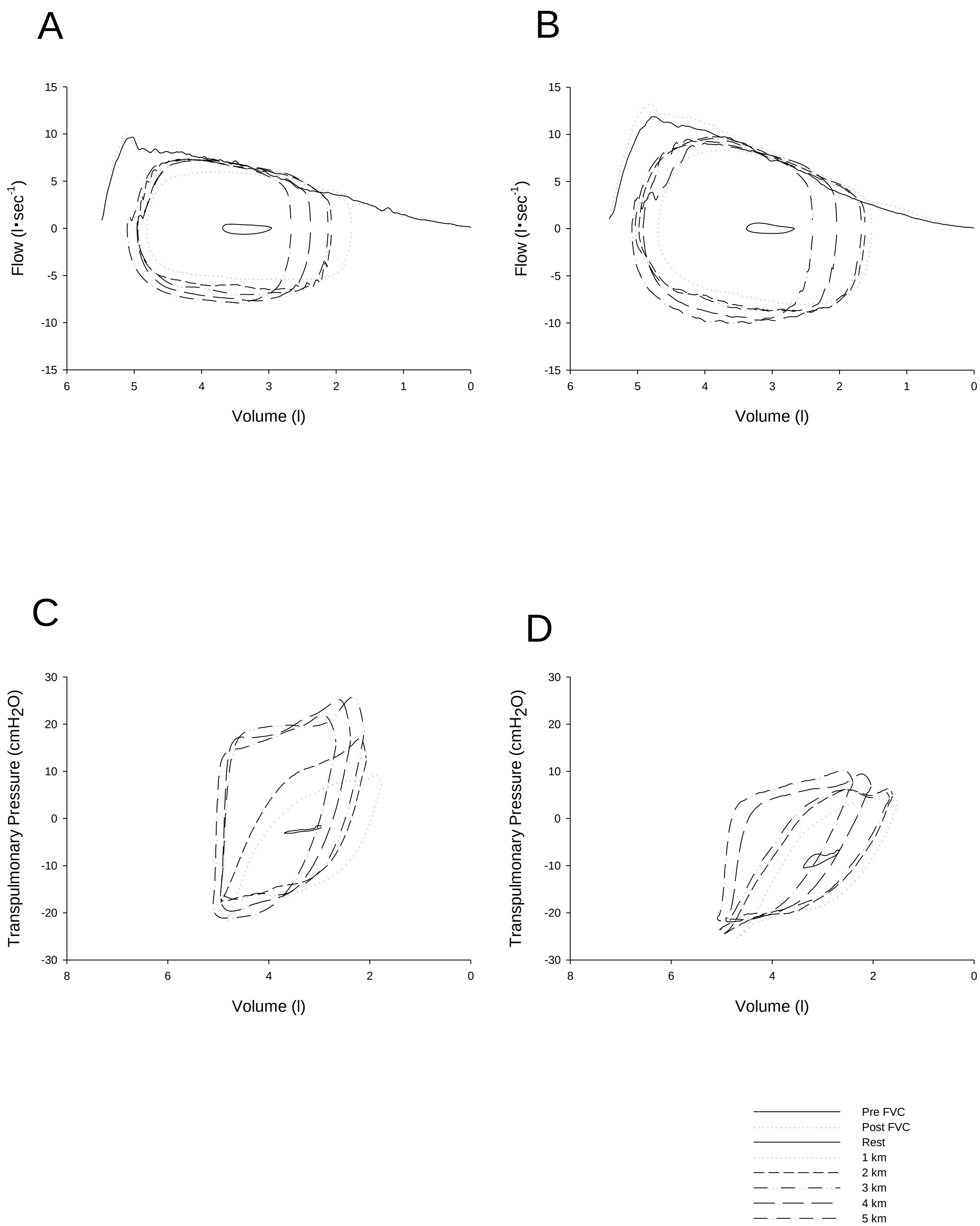


FIGURE 37 – Subject 109 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

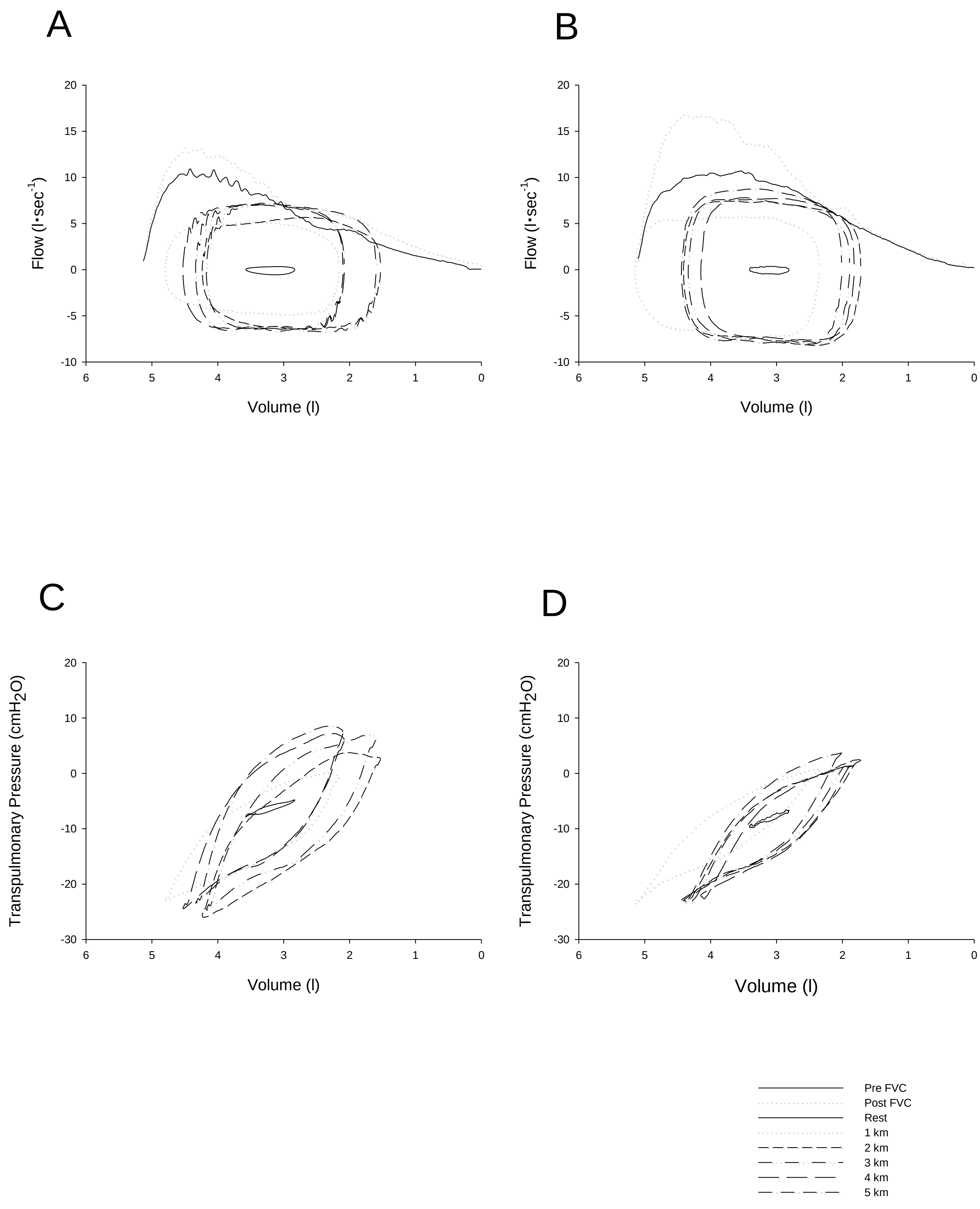


FIGURE 38 – Subject 110 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

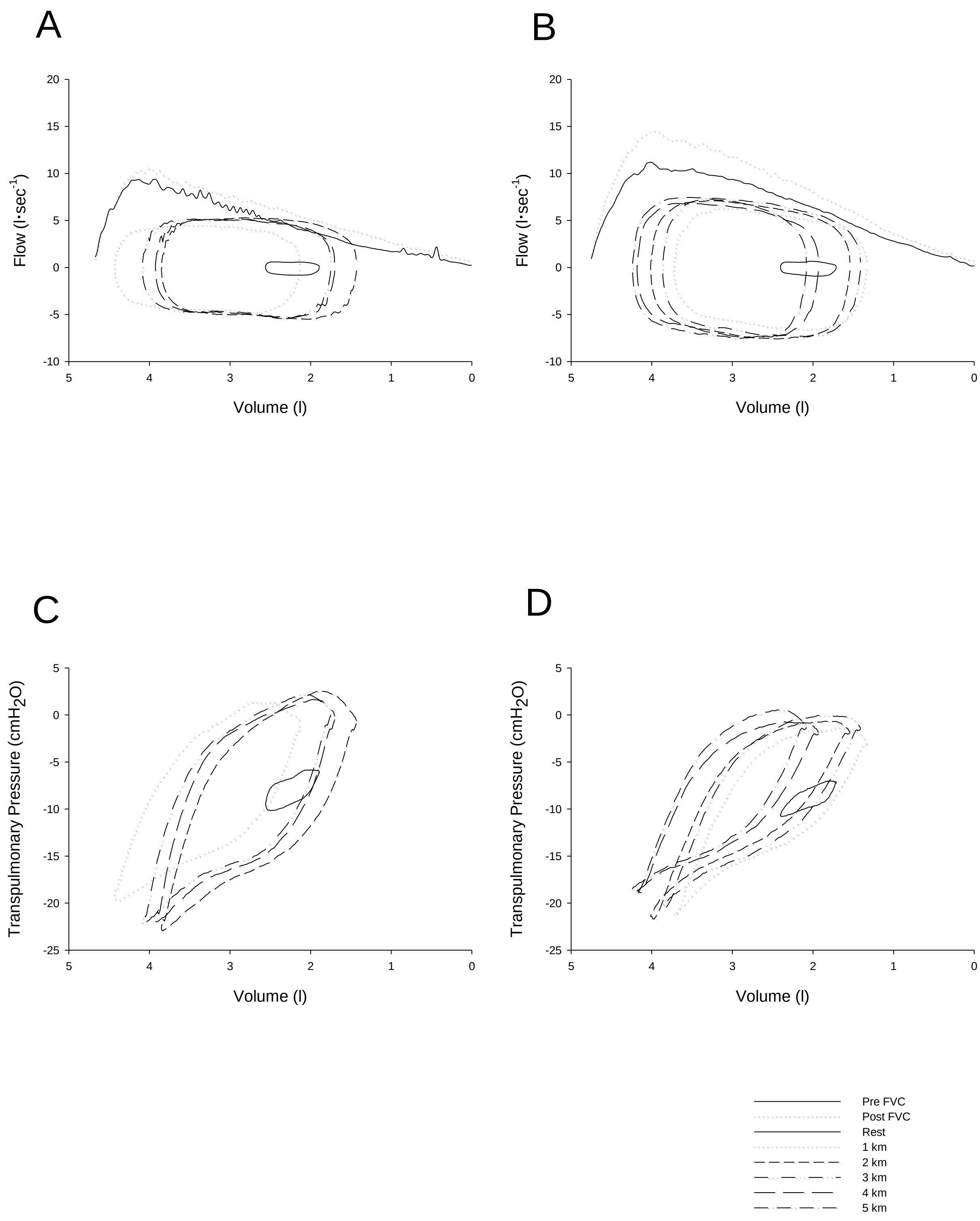


FIGURE 39 – Subject 111 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

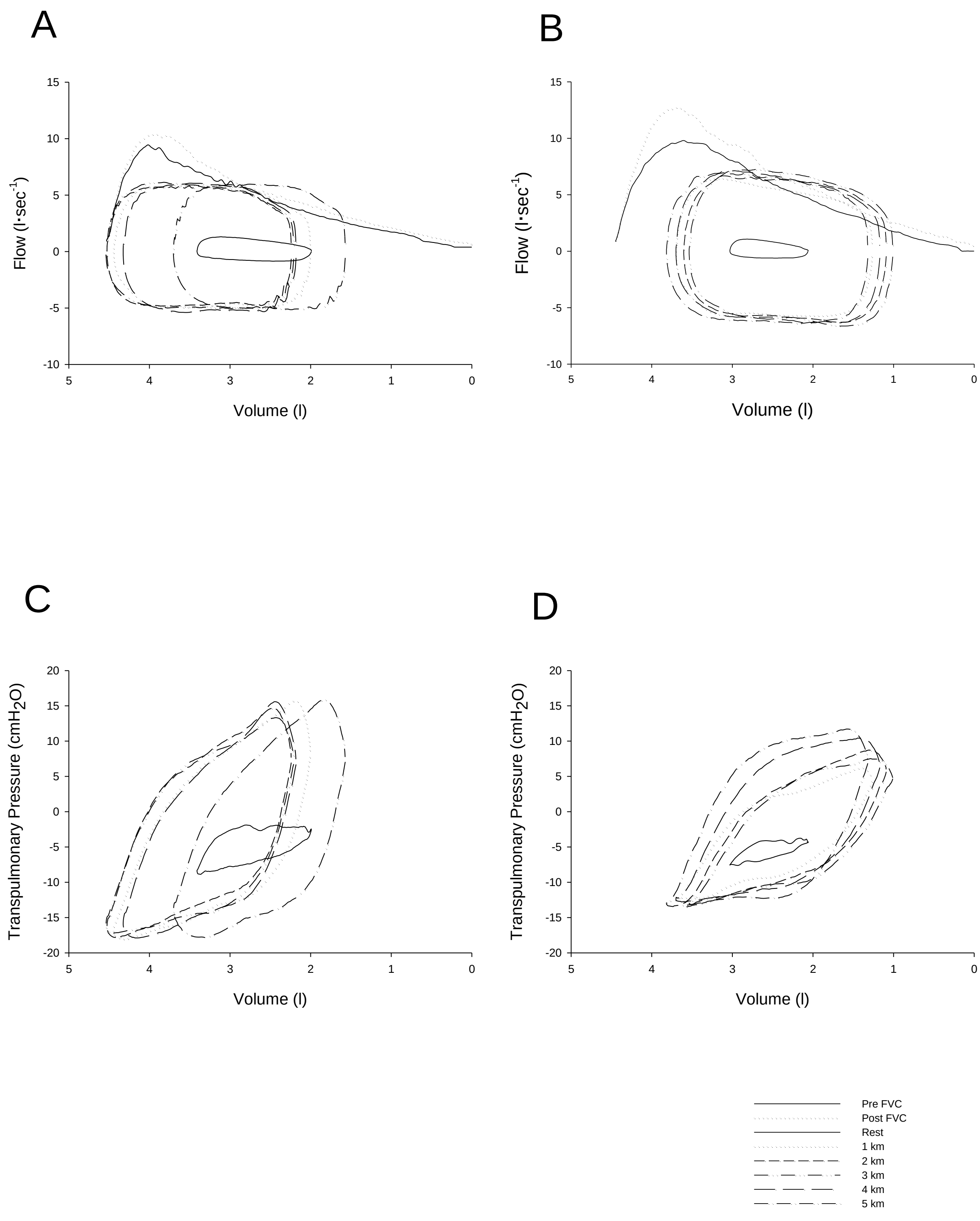


FIGURE 40 – Subject 112 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

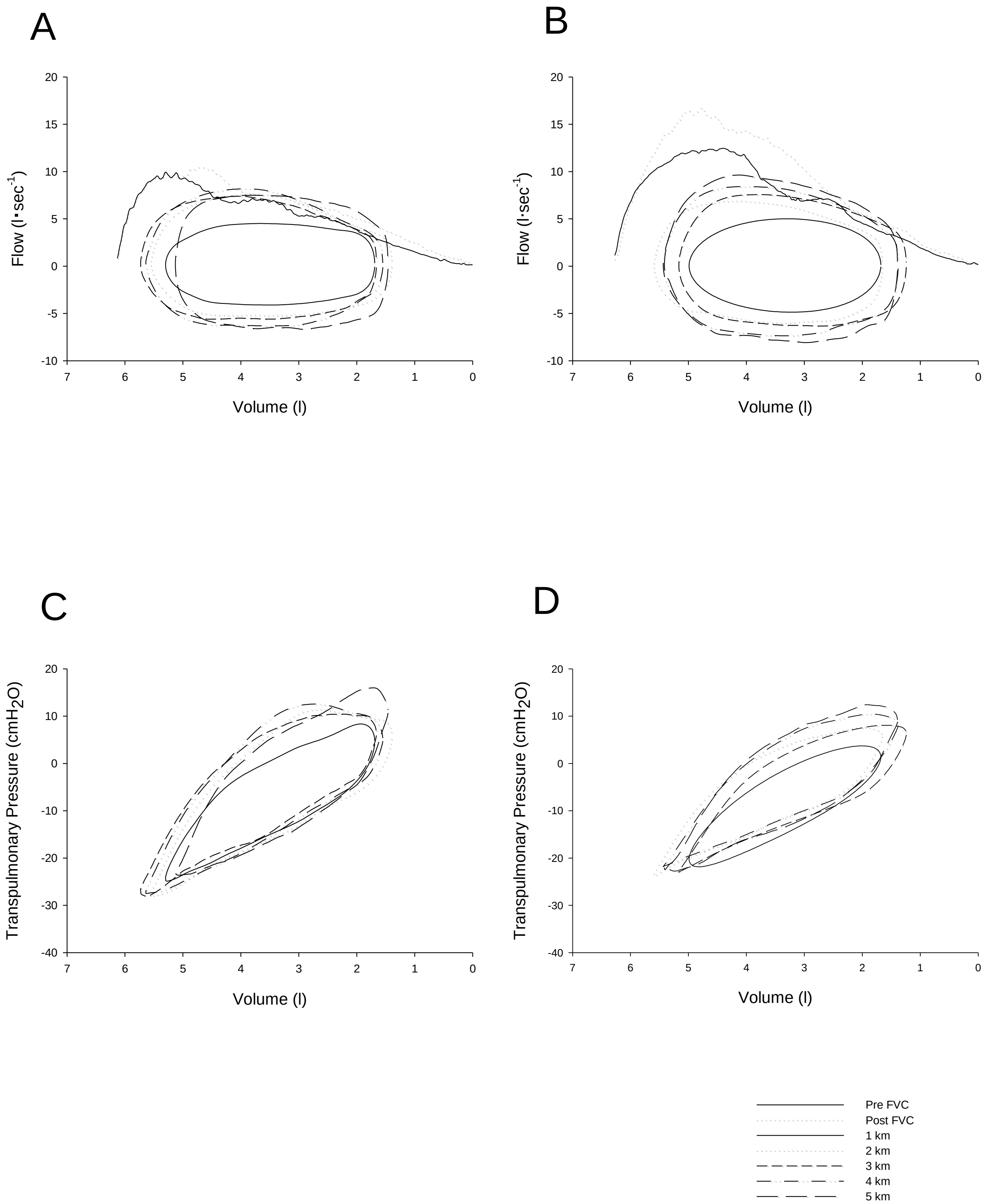


FIGURE 41 – Subject 114 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

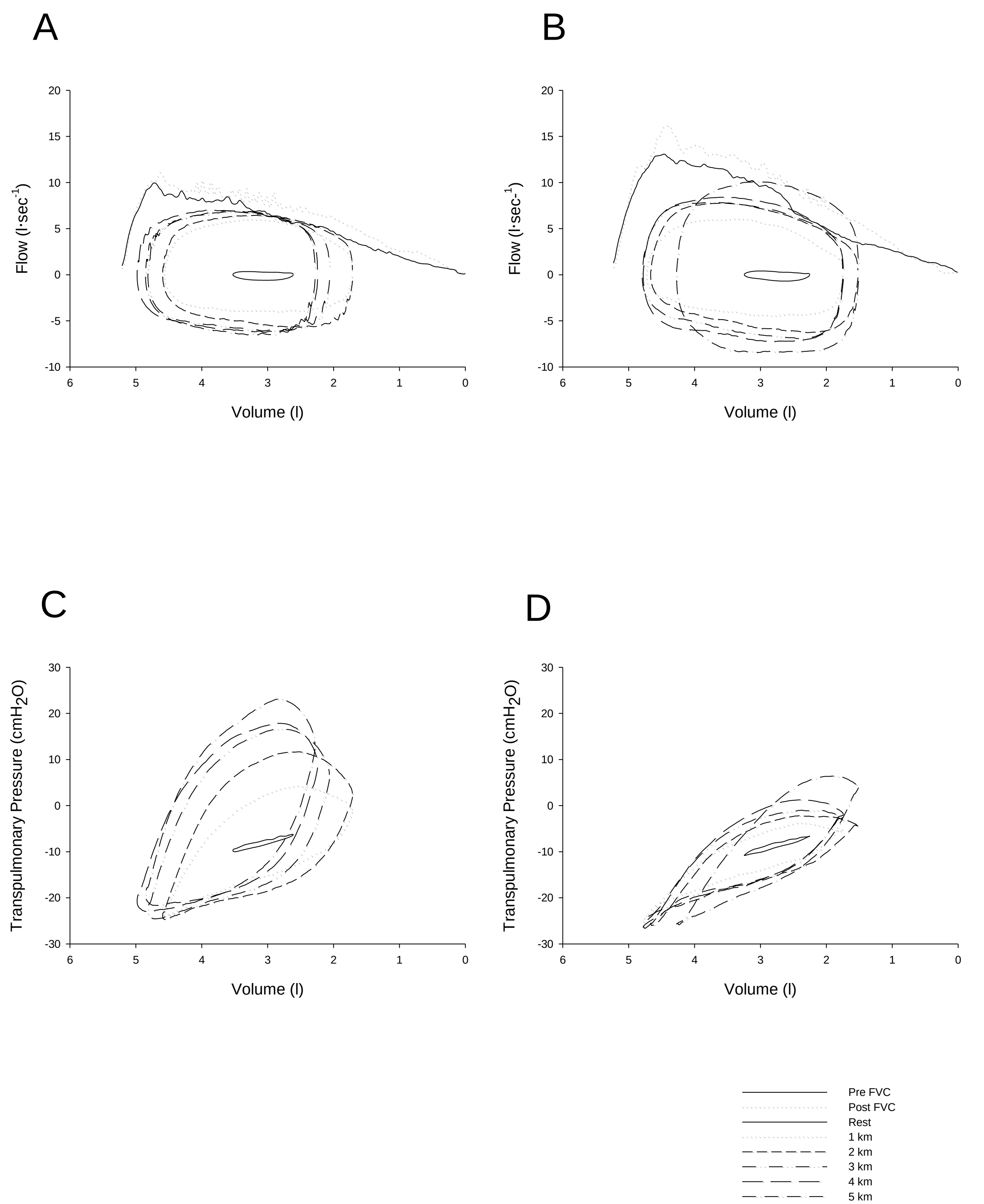


FIGURE 42 – Subject 115 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

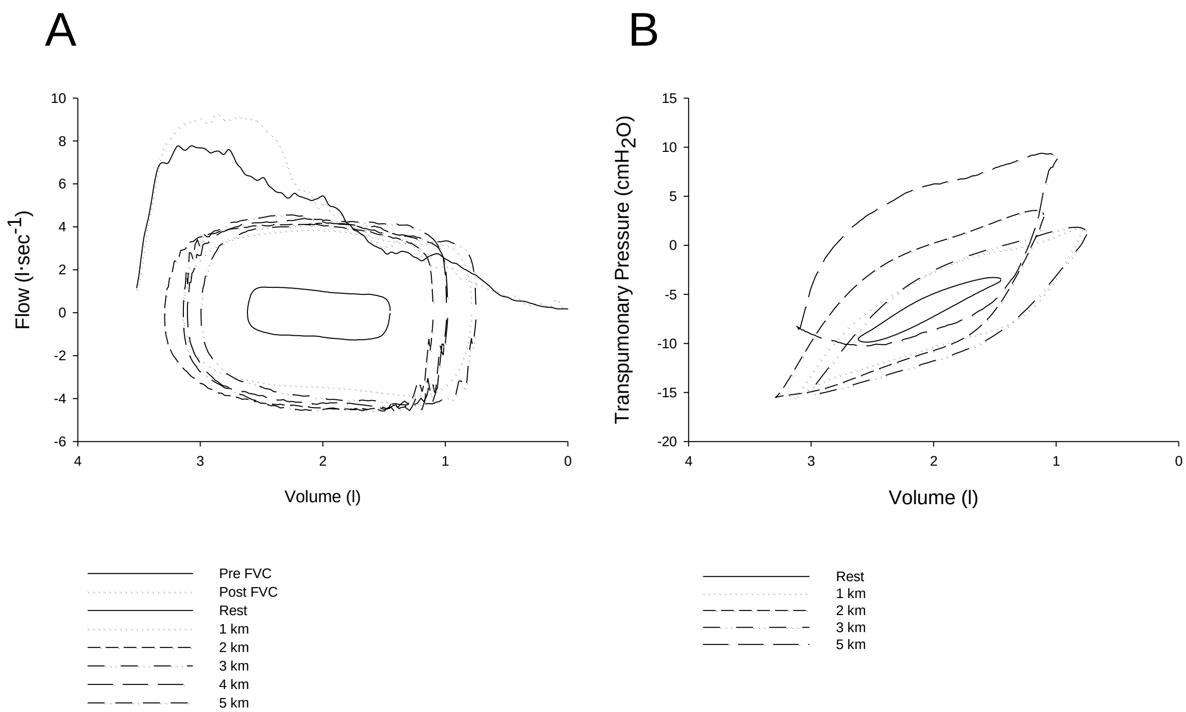


FIGURE 43 – Subject 201 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

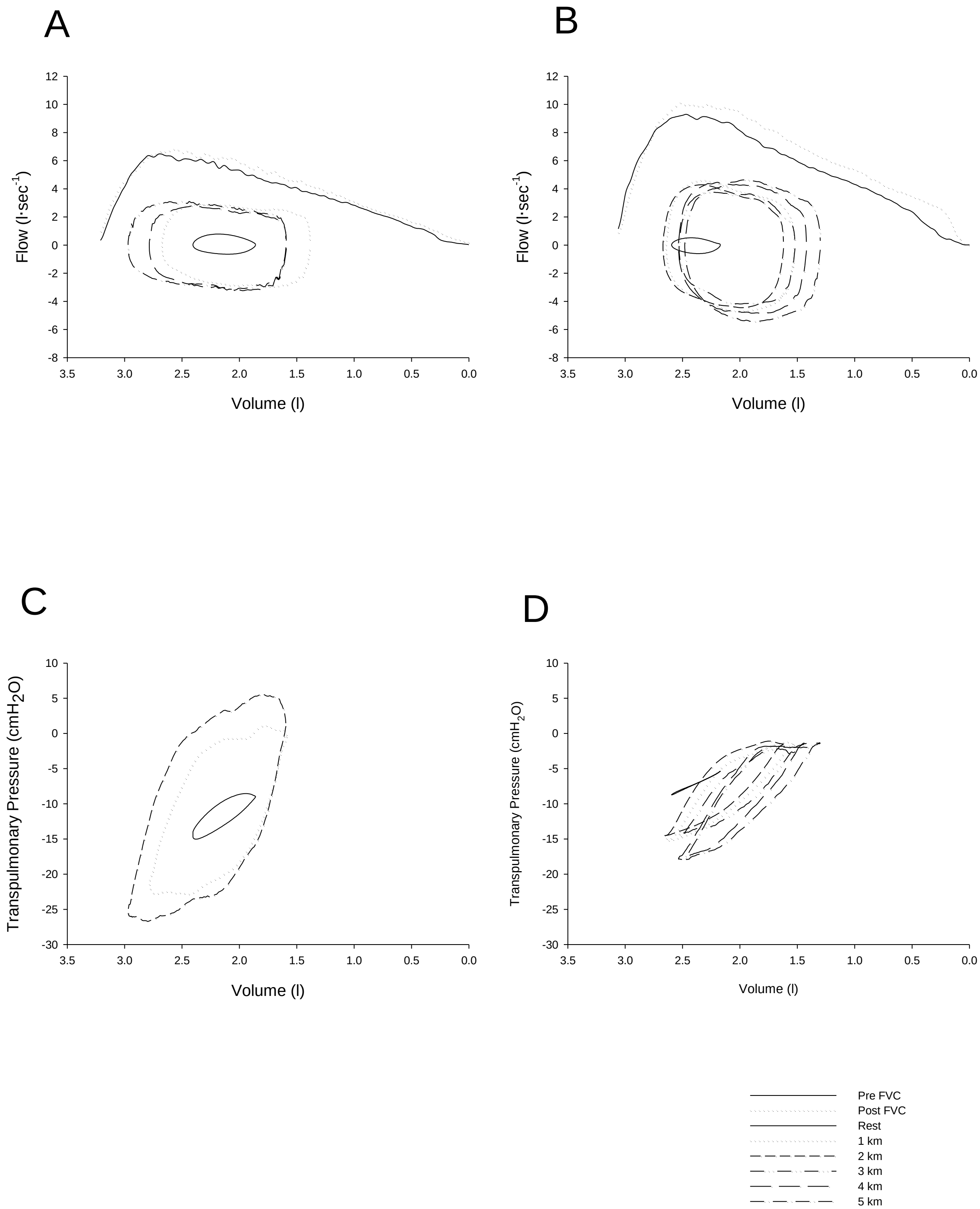


FIGURE 44 – Subject 202 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

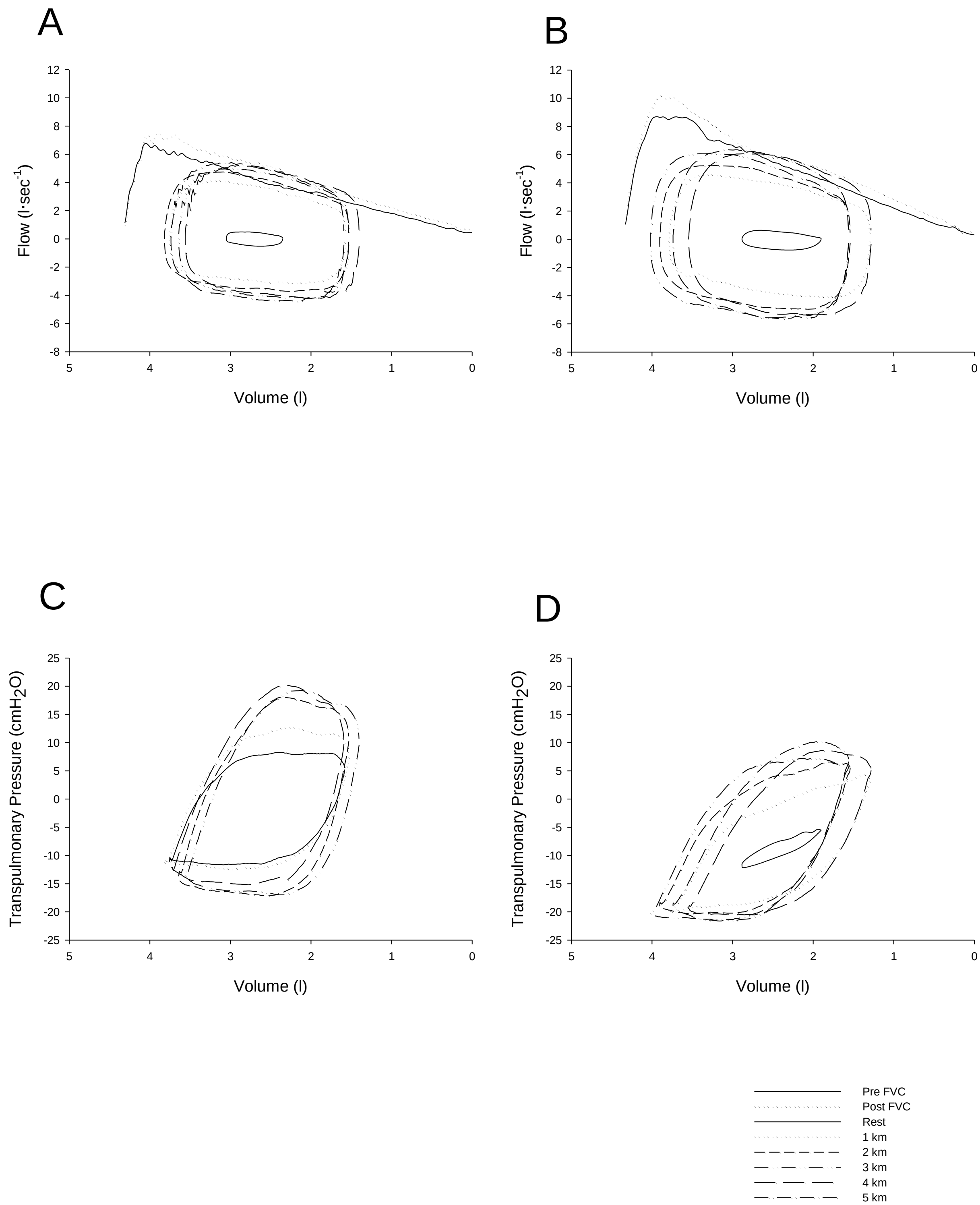


FIGURE 45 – Subject 203 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

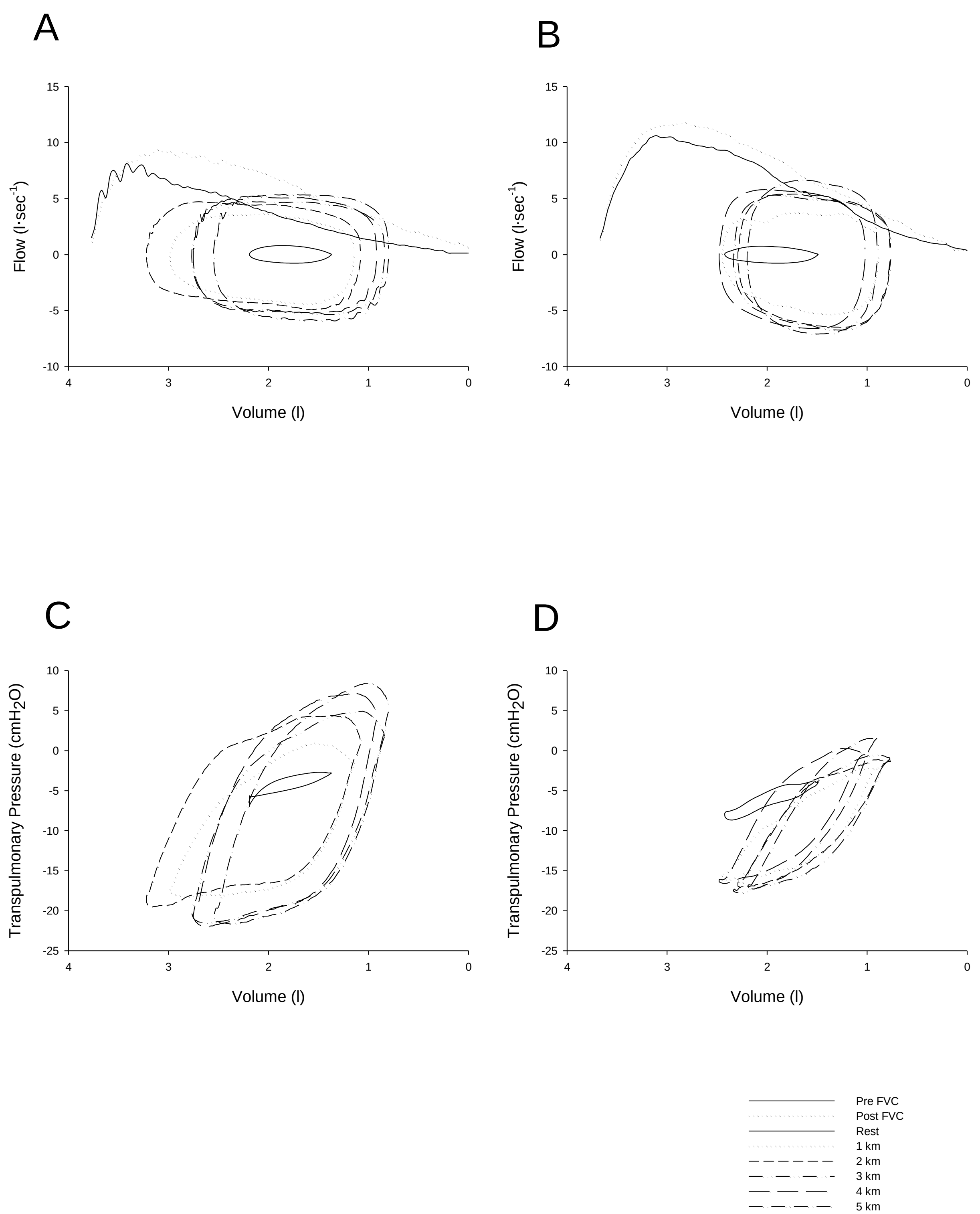


FIGURE 46 – Subject 204 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

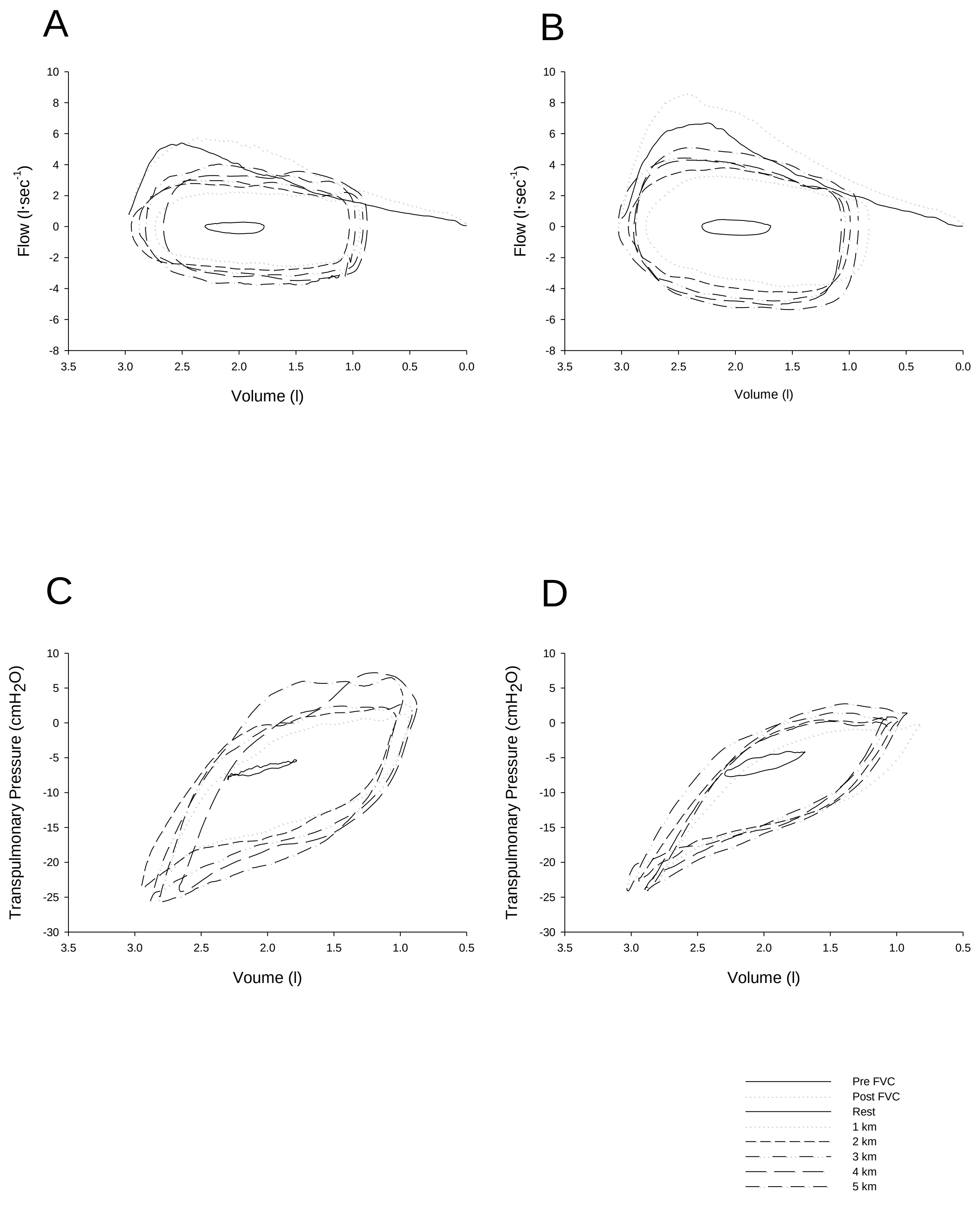


FIGURE 47 – Subject 205 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

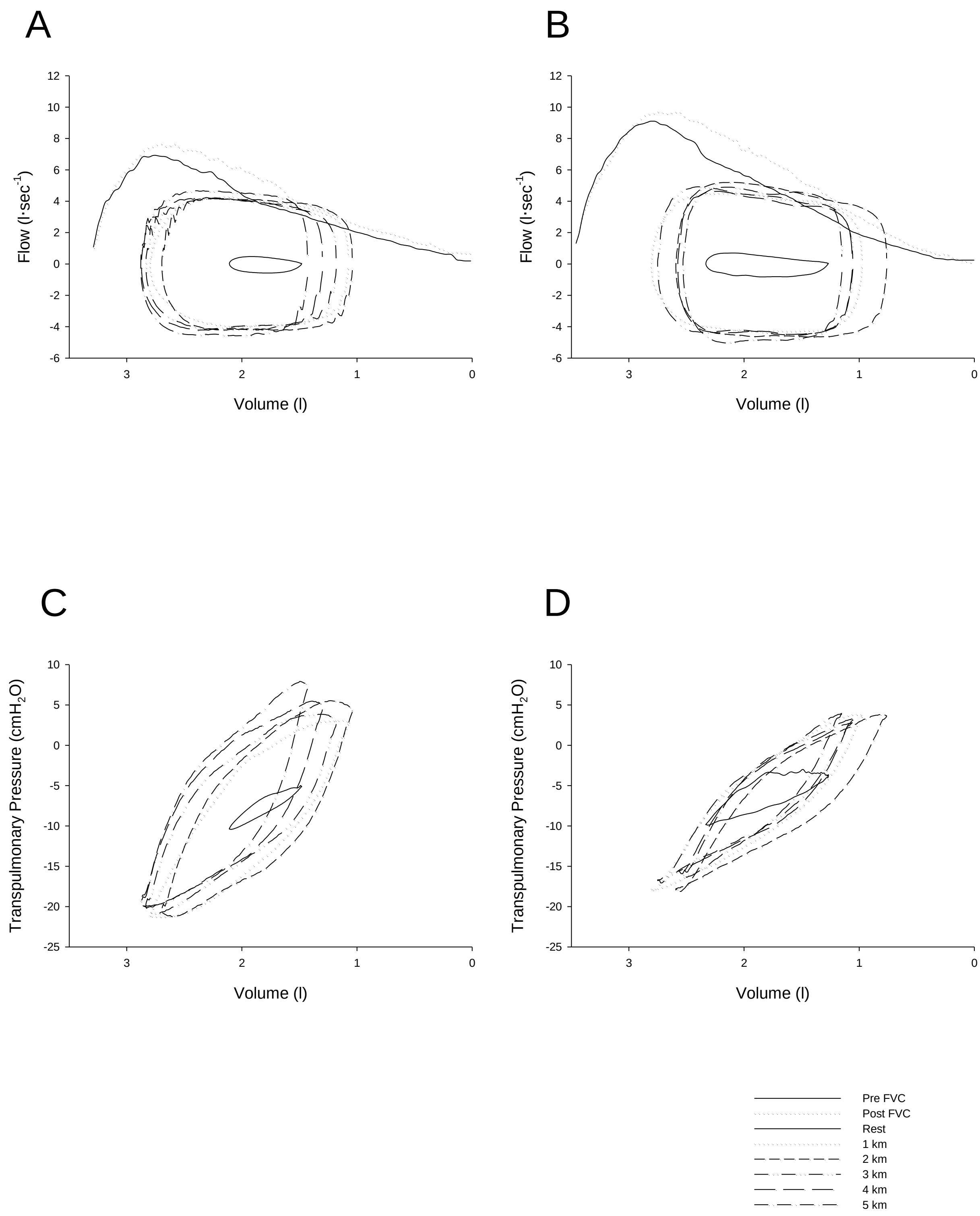


FIGURE 48 – Subject 206 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

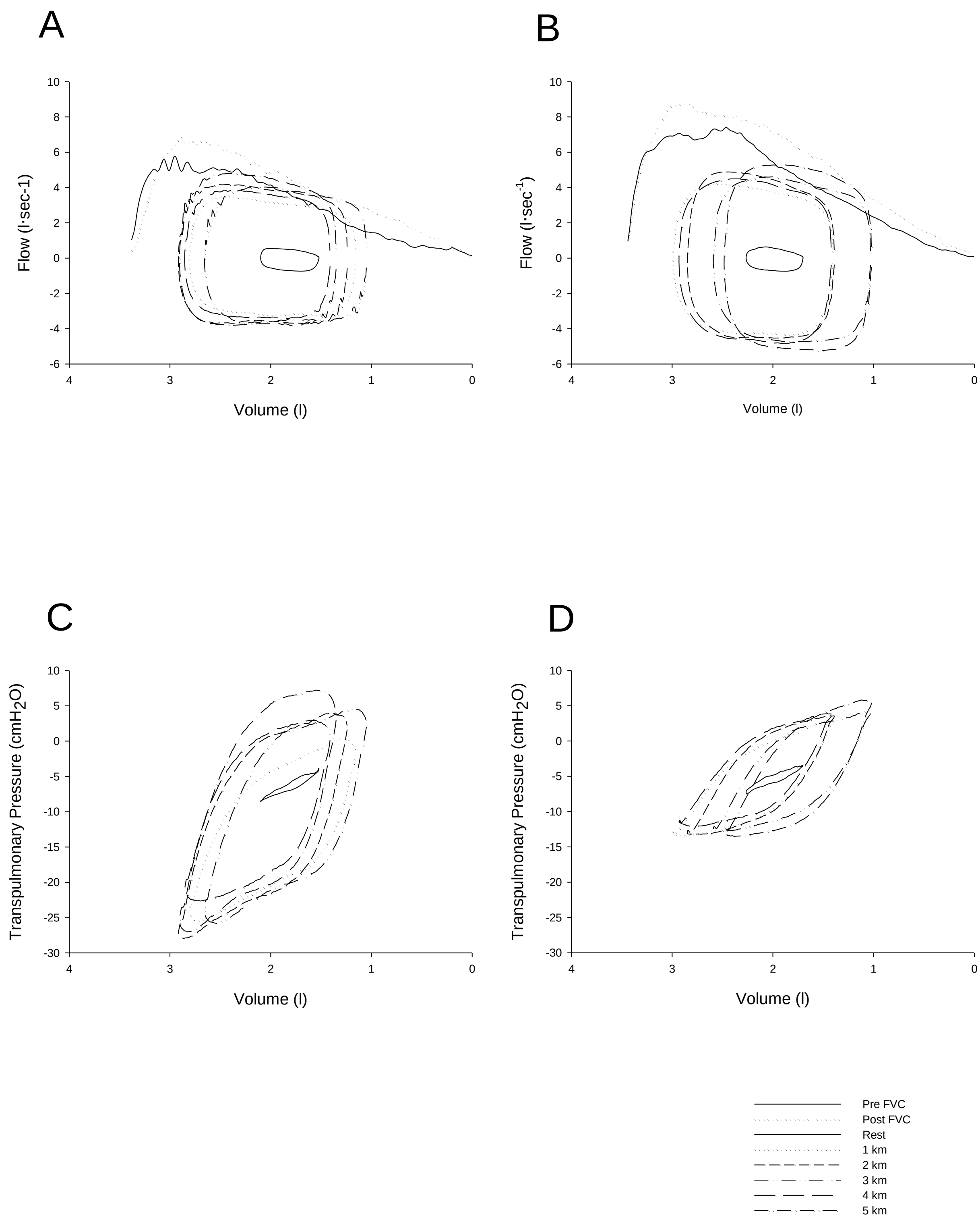


FIGURE 49 – Subject 207 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

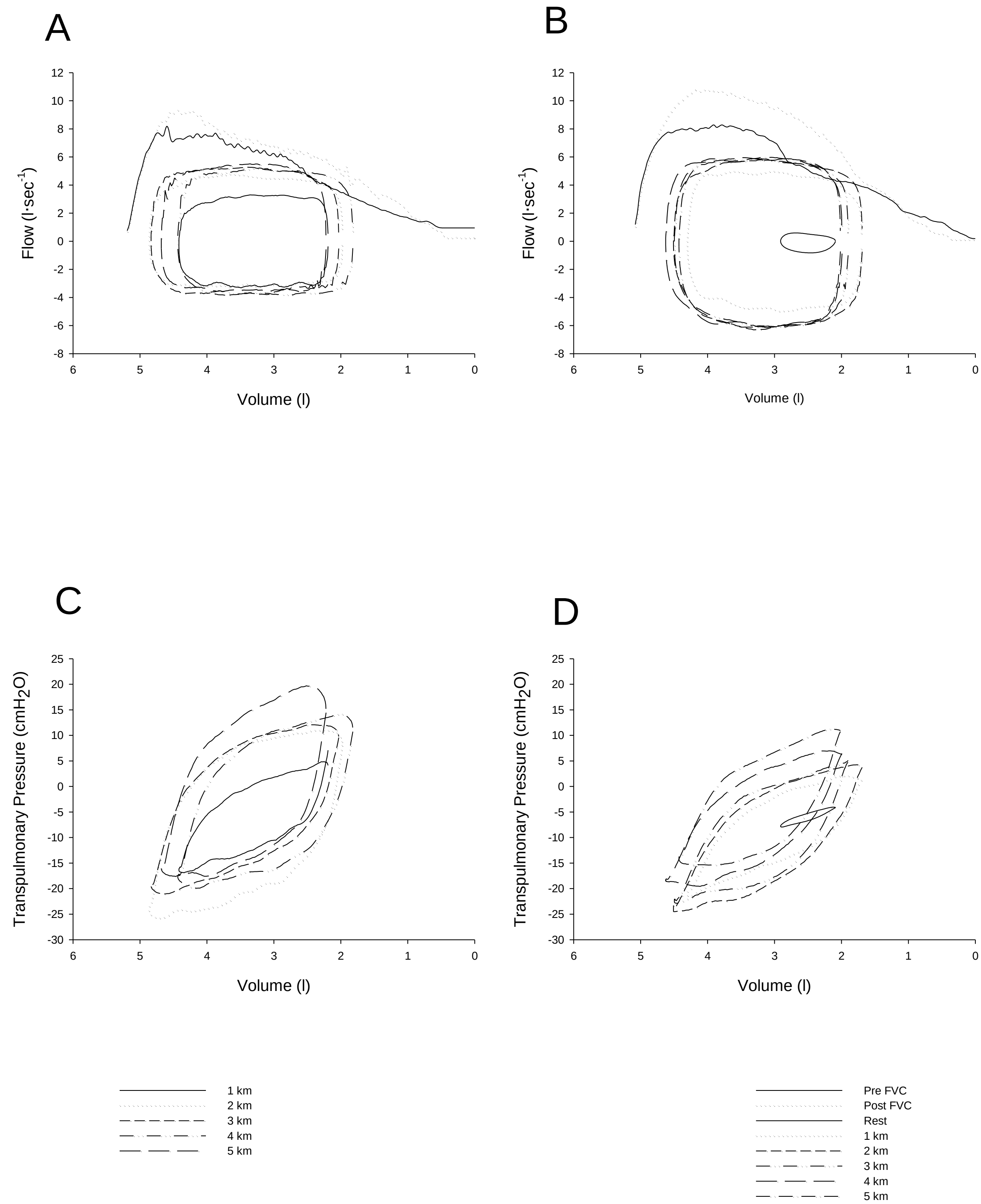


FIGURE 50 – Subject 208 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

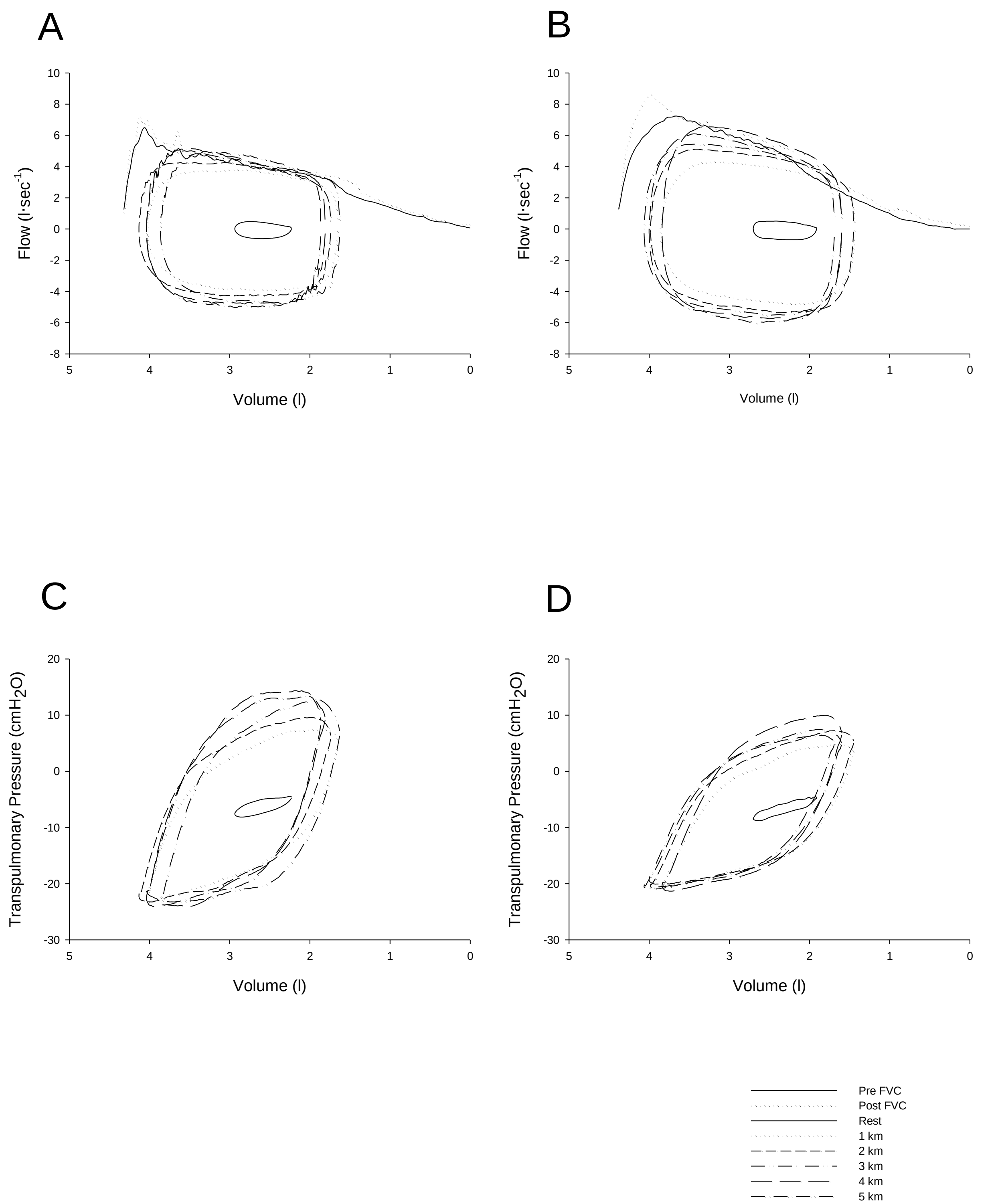


FIGURE 51 – Subject 210 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

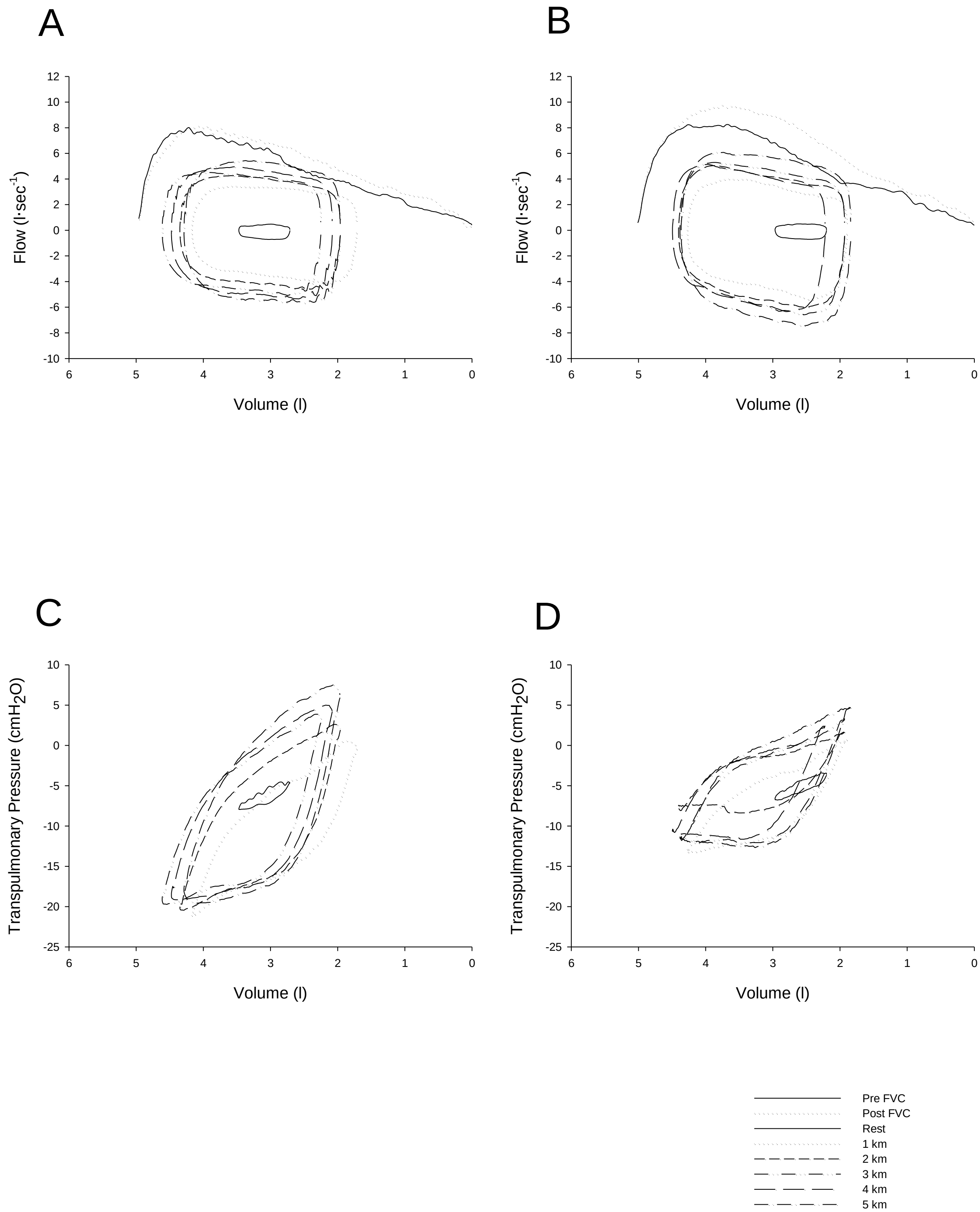


FIGURE 52 – Subject 211 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

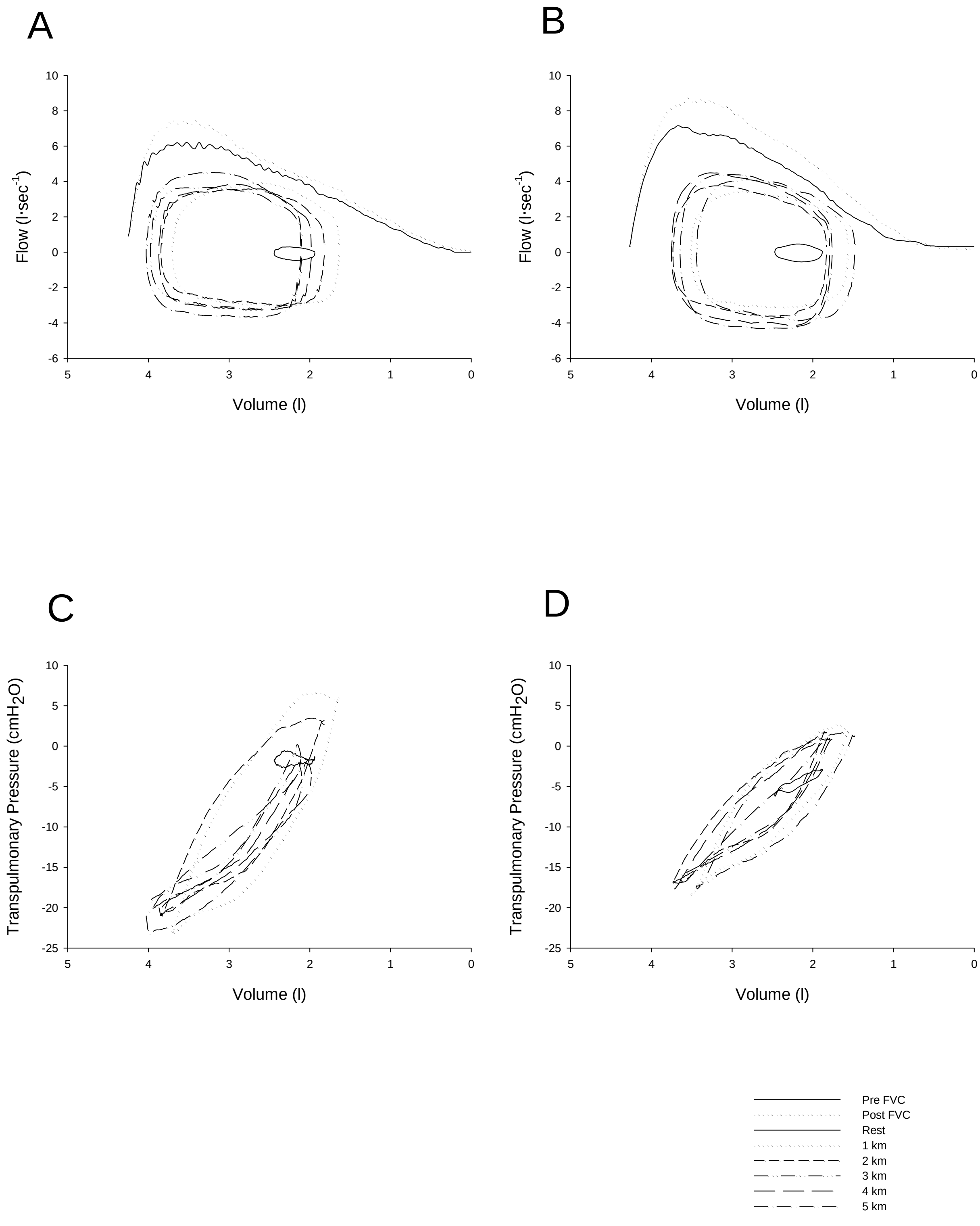


FIGURE 53 – Subject 212 flow-volume RA (Panel A) and He-O_2 (Panel B), and transpulmonary pressure-volume RA (Panel C) and He-O_2 (Panel D) traces.

APPENDIX C – QUESTIONNAIRES

Effect of Heliox on Respiratory Mechanics, Sensory Responses, and Performance during Exercise in Endurance-Trained Men and Women

Subject Identifier:

Medical History

1. Are you currently taking any medications (excluding oral contraceptives)?

   Please List: ____

2. Do you currently smoke? YES/NO

3. Are you a past smoker? YES/NO

4. When was the last time you had a cold? ____________________

5. Do you have asthma, other lung problems or significant illness? Please List:

   ____

6. Have you had recent nasopharyngeal surgery? YES/NO

7. Do you have an ulcer or tumour in your esophagus? YES/NO

8. Are you sensitive to local anaesthetics or do you have allergies to latex? YES/NO

9. Are you pregnant or is there any chance you could be pregnant? YES/NO

Menstrual History Questionnaire:

1. Are you having regular periods? YES/NO

2. How long is your cycle length? __________ (days)

3. How many days long is your flow? __________ (days)

4. Can you usually tell, by the way you feel, that your period is coming? YES/NO

5. Do you usually experience the following symptoms?

   Breast tenderness YES/NO
   Appetite changes YES/NO
   Mood changes YES/NO
   Fluid retention YES/NO

6. How many times did you menstruate in the past year? __________

7. How many periods have you missed in the last five years? __________

8. Are you currently taking oral contraceptives? YES/NO

If yes, for how long? ____________

What is the name of the oral contraceptive pill which you are taking?

____

9. When was the last start date of your period (DAY 1; i.e., when you began to menstruate)? ____________

Physical Activity History

Type of Physical Activity: ____

Volume per week: ____

Are you: in-season or off-season? ____

Highest level of competition:____

$V'O_{2MAX}$ (if known): ______________date: ________________exercise modality:_________________

Last cycling race:______________ distance: _________time: ___________date: ________________

Cycling Category (if applicable): ____________________

PAR-Q+

The Physical Activity Readiness Questionnaire for Everyone

Regular physical activity is fun and healthy, and more people should become more physically active every day of the week. Being more physically active is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

SECTION 1 - GENERAL HEALTH

Please read the 7 questions below carefully and answer each one honestly: check YES or NO.	YES	NO
1) Has your doctor ever said that you have a heart condition **OR** high blood pressure?	☐	☐
2) Do you feel pain in your chest at rest, during your daily activities of living, **OR** when you do physical activity?	☐	☐
3) Do you lose balance because of dizziness **OR** have you lost consciousness in the last 12 months? Please answer **NO** if your dizziness was associated with over-breathing (including during vigorous exercise).	☐	☐
4) Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)?	☐	☐
5) Are you currently taking prescribed medications for a chronic medical condition?	☐	☐
6) Do you have a bone or joint problem that could be made worse by becoming more physically active? Please answer **NO** if you had a joint problem in the past, but it does not limit your current ability to be physically active. For example, knee, ankle, shoulder or other.	☐	☐
7) Has your doctor ever said that you should only do medically supervised physical activity?	☐	☐

If you answered NO to all of the questions above, you are cleared for physical activity. Go to Section 3 to sign the form. You do not need to complete Section 2.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow Canada's Physical Activity Guidelines for your age (www.csep.ca/guidelines).
- You may take part in a health and fitness appraisal.
- If you have any further questions, contact a qualified exercise professional such as a CSEP Certified Exercise Physiologist® (CSEP-CEP) or a CSEP Certified Personal Trainer® (CSEP-CPT).
- If you are over the age of 45 yr and **NOT** accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered YES to one or more of the questions above, please GO TO SECTION 2.

Delay becoming more active if:

- You are not feeling well because of a temporary illness such as a cold or fever - wait until you feel better
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ before becoming more physically active OR
- Your health changes - please answer the questions on Section 2 of this document and/or talk to your doctor or qualified exercise professional (CSEP-CEP or CSEP-CPT) before continuing with any physical activity programme.

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SECTION 2 - CHRONIC MEDICAL CONDITIONS

1. Do you have Arthritis, Osteoporosis, or Back Problems?

YES ☐ If yes, answer questions 1a-1c **NO** ☐ If no, go to question 2

1a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
1b.	Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/or spondylolysis/pars defect (a crack in the bony ring on the back of the spinal column)?	YES ☐ NO ☐
1c.	Have you had steroid injections or taken steroid tablets regularly for more than 3 months?	YES ☐ NO ☐

2. Do you have Cancer of any kind?

YES ☐ If yes, answer questions 2a-2b **NO** ☐ If no, go to question 3

2a.	Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and neck?	YES ☐ NO ☐
2b.	Are you currently receiving cancer therapy (such as chemotheraphy or radiotherapy)?	YES ☐ NO ☐

3. Do you have Heart Disease or Cardiovascular Disease? *This includes Coronary Artery Disease, High Blood Pressure, Heart Failure, Diagnosed Abnormality of Heart Rhythm*

YES ☐ If yes, answer questions 3a-3e **NO** ☐ If no, go to question 4

3a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
3b.	Do you have an irregular heart beat that requires medical management? (e.g., atrial fibrillation, premature ventricular contraction)	YES ☐ NO ☐
3c.	Do you have chronic heart failure?	YES ☐ NO ☐
3d.	Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer **YES** if you do not know your resting blood pressure)	YES ☐ NO ☐
3e.	Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?	YES ☐ NO ☐

4. Do you have any Metabolic Conditions? *This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes*

YES ☐ If yes, answer questions 4a-4c **NO** ☐ If no, go to question 5

4a.	Is your blood sugar often above 13.0 mmol/L? (Answer **YES** if you are not sure)	YES ☐ NO ☐
4b.	Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, and the sensation in your toes and feet?	YES ☐ NO ☐
4c.	Do you have other metabolic conditions (such as thyroid disorders, pregnancy-related diabetes, chronic kidney disease, liver problems)?	YES ☐ NO ☐

5. Do you have any Mental Health Problems or Learning Difficulties? *This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome)*

YES ☐ If yes, answer questions 5a-5b **NO** ☐ If no, go to question 6

5a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
5b.	Do you also have back problems affecting nerves or muscles?	YES ☐ NO ☐

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6. Do you have a Respiratory Disease? *This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure*

YES ☐ If yes, answer questions 6a-6d **NO** ☐ If no, go to question 7

6a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
6b.	Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy?	YES ☐ NO ☐
6c.	If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice in the last week?	YES ☐ NO ☐
6d.	Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?	YES ☐ NO ☐

7. Do you have a Spinal Cord Injury? *This includes Tetraplegia and Paraplegia*

YES ☐ If yes, answer questions 7a-7c **NO** ☐ If no, go to question 8

7a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
7b.	Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?	YES ☐ NO ☐
7c.	Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?	YES ☐ NO ☐

8. Have you had a Stroke? *This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event*

YES ☐ If yes, answer questions 8a-c **NO** ☐ If no, go to question 9

8a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
8b.	Do you have any impairment in walking or mobility?	YES ☐ NO ☐
8c.	Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?	YES ☐ NO ☐

9. Do you have any other medical condition not listed above or do you live with two chronic conditions?

YES ☐ If yes, answer questions 9a-c **NO** ☐ If no, read the advice on page 4

9a.	Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months **OR** have you had a diagnosed concussion within the last 12 months?	YES ☐ NO ☐
9b.	Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?	YES ☐ NO ☐
9c.	Do you currently live with two chronic conditions?	YES ☐ NO ☐

Please proceed to Page 4 for recommendations for your current medical condition and sign this document.

PAR-Q+

If you answered NO to all of the follow-up questions about your medical condition, you are ready to become more physically active:

- It is advised that you consult a qualified exercise professional (e.g., a CSEP-CEP or CSEP-CPT) to help you develop a safe and effective physical activity plan to meet your health needs.
- You are encouraged to start slowly and build up gradually - 20-60 min of low to moderate intensity exercise, 3-5 days per week including aerobic and muscle strengthening exercises.
- As you progress, you should aim to accumulate 150 minutes or more of moderate intensity physical activity per week.
- If you are over the age of 45 yr and **NOT** accustomed to regular vigorous physical activity, please consult a qualified exercise professional (CSEP-CEP) before engaging in maximal effort exercise.

If you answered **YES** to **one or more of the follow-up questions** about your medical condition:

You should seek further information before becoming more physically active or engaging in a fitness appraisal.
It is recommended strongly that you complete the specially designed online screening and exercise recommendations program (i.e., the ePARmed-X+; www.eparmedx.com) and/or visit a qualified exercise professional (CSEP-CEP) for further information.

Delay becoming more active if:

- You are not feeling well because of a temporary illness such as a cold or fever - wait until you feel better
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ before becoming more physically active OR
- Your health changes - please talk to your doctor or qualified exercise professional (CSEP-CEP) before continuing with any physical activity programme.

SECTION 3 - DECLARATION

- You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
- The PAR-Q+ Collaboration, the Canadian Society for Exercise Physiology, and their agents assume no liability for persons who undertake physical activity. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.
- If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

- Please read and sign the declaration below:

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that a Trustee (such as my employer, community/fitness centre, health care provider, or other designate) may retain a copy of this form for their records. In these instances, the Trustee will be required to adhere to local, national, and international guidelines regarding the storage of personal health information ensuring that they maintain the privacy of the information and do not misuse or wrongfully disclose such information.

NAME ____ DATE ______________________________

SIGNATURE ____________________________________ WITNESS ___________________________

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER ____

For more information, please contact

www.eparmedx.com or
Canadian Society for Exercise Physiology
www.csep.ca

Citation for PAR-Q+
Warburton DER, Jamnik VK, Bredin SSD, and Gledhill N on behalf of the PAR-Q+ Collaboration. The Physical Activity Readiness Questionnaire (PAR-Q+) and Electronic Physical Activity Readiness Medical Examination (ePARmed-X+). Health & Fitness Journal of Canada 4(2):3-23, 2011.

The PAR-Q+ was created using the evidence-based AGREE process (1) by the PAR-Q+ Collaboration chaired by Dr. Darren E. R. Warburton with Dr. Norman Gledhill, Dr. Veronica Jamnik, and Dr. Donald C. McKenzie (2). Production of this document has been made possible through financial contributions from the Public Health Agency of Canada and the BC Ministry of Health Services. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada or BC Ministry of Health Services.

Key References
1. Jamnik VJ, Warburton DER, Makarski J, McKenzie DC, Shephard RJ, Stone J, and Gledhill N. Enhancing the effectiveness of clearance for physical activity participation; background and overall process. APNM 36(S1):S3-S13, 2011.
2. Warburton DER, Gledhill N, Jamnik VK, Bredin SSD, McKenzie DC, Stone J, Charlesworth S, and Shephard RJ. Evidence-based risk assessment and recommendations for physical activity clearance; Consensus Document. APNM 36(S1):S266-s298, 2011.

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Today's Date:
Food Consumption: What: Time:
Activity: Type: Duration: Intensity:
Caffeine: YES / NO If yes, when:
Hours of Sleep:

1 Day Prior:
Food Consumption: What: Time:
Activity: Type: Duration: Intensity:

2 Days Prior:
Activity: Type: Duration: Intensity:

3 Days Prior:
Activity: Type: Duration: Intensity:

Today's Date:
Food Consumption: What: Time:
Activity: Type: Duration: Intensity:
Caffeine: YES / NO If yes, when:
Hours of Sleep:

1 Day Prior:
Food Consumption: What: Time:
Activity: Type: Duration: Intensity:

2 Days Prior:
Activity: Type: Duration: Intensity:

3 Days Prior:
Activity: Type: Duration: Intensity: