Physiological Mechanisms of Exercise-Induced Hypoxemia in Athletes

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Abstract— Exercise-induced arterial hypoxemia (EIAH), defined as a significant decrease in oxygen saturation (<95%) during maximal and sub-maximal exercise, is a phenomenon observed in moderately and highly trained athletes. The consequences of EIAH on exercise performance relate to its negative influence on maximal O2 uptake (VO2 max) and impairment of oxygen delivery. The causes of EIAH are yet to be completely elucidated. Proposed mechanisms include ventilation/perfusion inequality, relative alveolar hypoventilation, right-to-left shunt, and diffusion limitation. We hypothesized that development of interstitial pulmonary edema during maximal exercise triggers the physiological mechanisms leading to EIAH. Eleven subjects, who had previously developed EIAH during a similar testing protocol, performed an incremental cycling or running protocol to exhaustion, and pre- and post-exercise lungs scanned using computed tomography. Scans were analyzed both qualitatively and quantitatively for the development of pulmonary edema. We employed two different procedures for lung density assessment, specifically, lung sampling technique (Method A) and whole lung measurements (Method B). The lung density measurements were as follows: 0.088±0.008 g/cm^3 pre-exercise, 0.090±0.008 g/cm^3 post-exercise (p=0.27) with Method A, and 0.190±0.018 g/cm^3 pre-exercise, 0.178±0.010 g/cm^3 post-exercise (p=0.94) with Method B. These results do not support the presence of interstitial pulmonary edema in individuals known to develop EIAH. Development of interstitial pulmonary edema cannot be conclusively identified as a significant cause of EIAH in moderately and highly trained athletes.

Keywords— Exercise-induced arterial hypoxemia, EIAH, desaturation in athletes, exercise limitation, interstitial pulmonary edema

I. Introduction

While traditional theory accepts that exercise performance is limited and can be improved by cardiac fitness, research has shown that highly trained endurance athletes reach a fitness level where the respiratory system may become the limiting factor [1], [2]. Aerobic metabolism and the cardiovascular system adapt highly to conditions of endurance training, whereas the respiratory system is limited in its ability to expand [3]. Lowered blood oxygen concentrations during maximal and sub-maximal exercise, an interesting phenomenon designated exercise-induced arterial hypoxemia (EIAH), have been reported in many highly trained endurance athletes.

EIAH manifests as reduced blood oxygen, measured as hemoglobin oxygen saturation (SaO2) or partial pressure of arterial oxygen (PaO2), and can be classified as mild (93-95% SaO2), moderate (88-93% SaO2) or severe (<88% SaO2) [4]. SaO2 is characterized by the oxygen-hemoglobin dissociation curve, which reflects saturation as a measure of PaO2. PaO2 itself is determined by the partial pressure of oxygen in alveolar gas (PAO2) and the alveolar-to-arterial oxygen gradient (A-aDO2). Under constant atmospheric conditions, PAO2 represents the maximum pressure attained by arterial blood. The difference between PAO2 and PaO2 is defined as A-aDO2, a measure of the gas exchange efficiency of the lungs. Typically, A-aDO2 increases from 5-10 Torr at rest to 20-25 Torr at maximal exercise, but there is a proportional increase in ventilation such that EIAH is prevented [4]. However, many healthy, well- trained athletes develop increasing A-aDO2 accompanied by a failure to compensate with hyperventilation (i.e., relative hypoventilation), resulting in a significant decrease in SaO2 [1], [5], [6]. These effects are most significant at or near VO2 max, representing an individual's aerobic capacity. Prolonged moderate- intensity exercise (<80% VO2 max) rarely causes EIAH, and may be explained by hyperventilatory compensation for longer duration of exercise [4].

The prevalence of EIAH in young male athletes has been reported as ~50% [1], [7]. A major consequence of EIAH is its effect on VO2 max and delivery of oxygen to the exercising muscles and other organ systems, leading to limitations in maximal exercise intensity [4]. Improvements in VO2 max have been reported when subjects experiencing EIAH are administered 100% oxygen, indicating that lower SaO2 is responsible for the decreased exercise intensity due to reduced availability of oxygen to the muscle mitochondria [8], [9]. No specific links between VO2 max and exercise performance have been established to date. However, an earlier study by Koskolou & McKenzie [10] specifically focusing on the effects of EIAH on power output reported a significant reduction in exercise performance at SaO2 of <87%, as measured using maximum wattage in a cycling protocol. While their findings were not statistically significant, the authors

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proposed that in terms of exercise, even minor changes in oxygenation have drastic effects.

II. Mechanisms of EIAH

The precise mechanisms underlying EIAH are not known at present. A number of physiologic theories implicate inadequate hyperventilatory compensation widened A-a DO2 gradient, and expiratory flow limitation (EFL), but definitive evidence is lacking.

A. Inadequate Hyperventilatory Compensation

Current hypotheses on the role of ventilatory compensation tend to focus on ventilatory drive during exercise. As metabolic demand increases during exercise, individuals are expected to exhibit elevated ventilation to compensate for the gas exchange requirements. During heavy exercise, an increase in PAO2 is required to maintain the level to correct for lower venous PO2 and reduced pulmonary red blood cell transit time [1]. Relative hypoventilation, defined as alveolar ventilation below the rate required to maintain arterial blood gases at physiologically normal levels [11], is characterized by PAO2<110 mmHg and PaCO2>35 mmHg [12]. In healthy untrained individuals, the ventilatory capacity of the lungs is viewed as overbuilt for exercise, being able to maintain blood gases when approaching VO2 max. However, endurance-trained athletes are able to achieve significantly higher metabolic rates that cannot be matched by compensatory hyperventilation, which leads to relative hypoventilation [5].

B. Increase A-aDO2 Gradient

As mentioned above, the A-aDO2 gradient is a measure of the gas exchange efficiency of the lungs. During exercise, values above 25 Torr are considered excessive, and those above 35 Torr severe. Assuming constant PAO2, a widening A-aDO2 gradient causes a decrease in PaO2. These effects are most marked as workloads approach VO2 max [11], [12]. If widened A-aDO2 were to coincide with inadequate hyperventilatory response, the effects would compound to produce significant EIAH. Abnormally widened A-aDO2 gradient may be induced by ventilation and perfusion (VA/Q) inequalities and poor diffusion from the alveoli to pulmonary capillaries, among other effects [11].

VA/Q inequality is described as changes in ventilation in relation to perfusion, which lead to insufficient availability of ventilation for adequate oxygenation of some regions of pulmonary capillaries. As a result, average oxygenation of blood leaving the lungs is reduced in comparison to the expected levels for a given PAO2. Although specific areas within the lung may display PaO2 reflecting adequate ventilation, as a whole, PaO2 is such that abnormally widened A-aDO2 is observed, possibly leading to EIAH development. Oxygen diffusion across the alveolar-capillary membrane is related to the exposure time of red blood cells (RBCs) in pulmonary capillaries or changes in the alveolar-capillary membrane [13]. The transit time of RBCs decreases with increasing cardiac output, and the alveolar-capillary membrane can be influenced by factors, such as development of interstitial pulmonary edema, which increases the diffusion distance [5].

The lung is ~80% water by weight, and between 30% and 50% of the aqueous content is extracellular, consisting of interstitial fluid and lymph, respectively [14]. Transient interstitial edema during exercise could partly explain the widened A-aDO2 observed during exercise in subjects displaying EIAH. Interstitial pulmonary edema, measured as extravascular lung water (EVLW) and caused by increase in the filtration of fluid from the pulmonary capillaries into interstitial space, may interfere with gas exchange, thus leading to widened A-aDO2. Pulmonary edema may occur through changes in Starling forces (pulmonary capillary leakage) and/or the structure of the capillary membrane (pulmonary capillary stress failure) [15]. Both of these mechanisms are possibly associated with increased fluid permeability at maximal exercise when increased cardiac output and pulmonary pressure occur [16]–[18].

The issue of whether transient interstitial pulmonary edema occurs in association with EIAH has been the focus of a number of studies, but remains unresolved [19]–[21]. In swines subjected to treadmill running for 6–7 min, evidence of pulmonary edema following heavy exercise was obtained microscopically [22]. Pulmonary edema (bilateral pulmonary airspace infiltrates, upper lobe venous congestion, and cardiomegaly) was detected three decades ago in two human subjects following an ultramarathon race [23]. Assessment with modern imaging techniques, including radiography, computerized tomography (CT), and magnetic resonance imaging (MRI), disclosed the presence of transient pulmonary edema in subjects following exercise [19] – [21]. However, one study reported that pulmonary gas exchange is not compromised as a result [24]. Conversely, several other researchers found no evidence of transient pulmonary edema following exercise [25]–[27].

C. Expiratory Flow Limitation

Physical and functional characteristics of individual respiratory systems play a role in limiting the maximum ventilatory capacity. Airway properties and muscle power both play a role in the pressures and volumes generated by the lungs. EFL can be measured as the percentage of the tidal volume (VT) that meets or exceeds the expiratory portion of a maximum flow-volume loop, that vary depending on differing end-expiratory volumes. The reference flow-volume loop is established by maximal effort flow-volume maneuvers performed before and after exercise [5], [35], [36]. As one experiences EFL, larger lung volumes are needed to generate the pressures required for adequate ventilation. During exercise, EFL can manifest such that lung volume approaches the total lung capacity leading to hyperinflation and the tidal volume approaches the residual volume preventing further increases in flow to meet ventilatory demands [35]. Furthermore, the intrathoracic pressures required in the face of EFL cause airway compression and more limited airflow. The resulting increase in ventilatory work induces diaphragm fatigue and ultimately EIAH [37], [38]. As expected the inter individual differences in lung properties play a large role in

EFL. In particular, elderly and female athletes tend to have smaller lung volumes and decreased pressure-generating capabilities when compared to their age-, height-, and weight-matched male counterparts, and are thus more prone to respiratory muscle fatigue and EIAH [36], [38], [39].

The described method of quantifying EFL, comparing tidal volume to volume-specific maximal flow-volume loops, demonstrates that up to 90% of tested subjects experience flow limitation [35], [40], [36]. This procedure has been criticized as being inconsistent and unreliable with a possibility of having overestimated the prevalence of flow limitation [36], [37]. Valta proposed a technique to detect EFL using negative expiratory pressure applied during expiration [37], [41]. Individuals who are not flow limited should demonstrate an increase in flow rates when the negative pressure applied generates an increased pressure gradient between alveolar and airway pressures. Thus, subjects who have negative expiratory pressures applied who do not show an increase in expiratory flow would be evidenced as having EFL. During exercise testing, this method is more reliable than traditional methods in that each breath can be compared to a subsequent breathe where negative pressure is applied. Using this method, significantly lower rates of EFL were detected (10-50%) in highly trained male athletes [35],[9], [36], [5], [42].

Currently, EFL is understood to have a strong association with SaO2, accounting for 30-40% of the variance observed [36], [5]. However, it is still unclear as to the relationship between EFL and the ventilatory response but evidence points toward hyperventilation as a causal factor flow limitation and now the inverse [35], [36].

D. Study Hypothesis

In this study, we proposed that expiratory flow limitation and development of interstitial pulmonary edema both have significant contributions to the phenomenon of EIAH.

III. Material and Methods

A. Study Subjects and Experimental Protocol

Ethical approval was granted by the Biomedical Ethics Board, University of Manitoba, and written informed consent obtained from all study subjects. Eighty-two individuals were recruited prospectively from the local recreational and amateur athletic community. Participants were 19 to 74 years of age, and screened for activity levels as well as cardiac and pulmonary health using a standardized interview. These subjects participated in a screening phase of the study that aimed to establish a more accurate prevalence of EIAH in both the highly- and moderately-trained athletic community. This phase also generated the data used to quantify the contribution of expiratory flow limitation to EIAH. These subjects performed both the cycling and treadmill protocols. Data was gathered before and after exercise, after 5- and 15-minutes, for blood pressure (GE Dinamap Pro 100), SaO2, heart rate (Nellcor N-595 pulse oximeter and OxiMax Max-Fast adhesive forehead reflectance sensor), capillary lactate (Arkray LT1710), arterial blood gases (ABG), and spirometry. Spirometric parameters used to assess the development of expiratory flow limitation and exercise-induced airway hyperresponsiveness included percent predicted forced expiratory flow in 1 second (FEV1 PP), percent predicted forced vital capacity (FVC PP), percent predicted ratio of FEV1/FVC, and percent predicted forced expiratory flow rates at 25% to 75% of FVC (FEF25-75 PP). A 10% decrease in FEV1 post-exercise was considered evidence for exercise-induced bronchoconstriction. SaO2, heart rate and capillary lactate were also measured throughout the exercise protocol

From the first phase, eleven subjects were recruited for the CT scan phase. These subjects were aged between 20 and 57 years, and included both males and females. Subjects were known to desaturate based on previous testing, and it was expected that their EIAH could be reproduced. These participants underwent pre- and post-exercise uninfused high resolution computed tomography (HRCT) scanning of the thorax at full inspiration. Experiments were planned according to CT scanner availability. The time between the end of exercise and beginning of the CT scan was not recorded, but the goal was to keep it under 30 minutes. Measurements at rest before exercise and immediately after exercise included blood pressure, oxygen saturation via forehead oximetry, capillary lactate, and ABG. All subjects were continuously monitored for heart rate and oxygen saturation via forehead oximetry. All subjects but one was subjected to a cycling protocol. The remaining individual performed a treadmill protocol. Protocols were consistent with the published research exercise methods that are able to effectively produce pulmonary edema (maximal or near-maximal) [20], [21].

B. CT scanning

CT scan data were analyzed using two different protocols. The first population of 6 individuals was analyzed both qualitatively and quantitatively for the development of pulmonary edema (Method A), while the second population of 5 individuals underwent quantitative analysis only (Method B). Qualitative analysis involved two blinded, independent radiologists monitoring pre-defined signs of pulmonary edema. For the first population (Method A), scans were obtained for every 10 mm of lung parenchyma with 1 mm thickness, totaling 16 to 18 slices for each experiment (GE Lightspeed 16 slice scanner). These sections represented three standardized slice levels at the apex, carina, and lower pulmonary artery (lung sampling technique, Method A). Quantitative analysis was performed by comparing pre- and post-exercise lung parenchymal densities. The second cohort was subjected to quantitative analysis by measuring lung parenchyma density for the entire lung (whole lung measurement, Method B). Patients were scanned (GE Lightspeed 64 slice scanner) in the supine position, and 1.25 mm contiguously acquired axial slices obtained from apex to diaphragm in inspiration. A large field of view was used. Exposure settings were 140 kvp and 200 mA, with a 0.6 sec tube rotation. The lung parenchyma was mapped every 4 slices in the axial view and cascaded in between by the software. (GE Advantage Workstation).

Corrections were made for considerable errors. Structures representing the mediastinum, vessels, and airways were more precisely identified using different views to facilitate their omission from analysis. Method consistency was ensured for pre- and post-exercise scans for the same subject. Figure 1 shows one representative subject subjected to measurements according to Method B. The images illustrate a 3D reconstruction of the thorax after the elimination of irrelevant structures and typical mapping out of one slice.

The CT scan expresses regional attenuation in Hounsfield units (HU), a relative scale whereby -1000 represents the density of air and 0 the density of water. Density was calculated from HU using the following formula: d = (HU/1000) + 1 [28], while mass was determined using the equation: Mass = Volume * Density. Increased lung density and mass were considered radiographic evidence for the development of pulmonary edema.

IV. Results

Demographics of subjects from the screening phase are listed in Table 1. Data for the spirometry measurements are presented in Table 3.

The spirometric data, demonstrated no significant signs for the development of expiratory flow limitation between subjects who desaturated versus normal saturators. The mean FEV1 PP, FVC PP, FEV1/FVC ratio and FEF25-75 PP measurements at 5 minutes post-exercise for individuals who desaturated were 99.0±22.4, 104.4±25.1, 92.0±19.0, 87.9±20.6 versus 92.7±32.7, 97.6±34.7, 86.7±30.2, 89.2±22.5, respectively, for subjects who did not desaturate. No individuals in either group developed a decrease in FEV1 by 10%, indicating lack of exercise-induced airway hyperresponsiveness.

Demographic data obtained using Methods A and B are listed in Tables 2a and 2b, respectively. Values for lung volume, density, and mass are presented in Tables 4a and 4b for Methods A and B, respectively.

Qualitative analysis of the CT scans revealed no significant signs of pulmonary edema. Each radiologist found one scan with minimal signs of pulmonary edema or increased pulmonary water content. There was no concordance between the two radiologists.

Among the Method A subjects, 4 showed increases in both lung density and mass between pre- and post- exercise ($p=0.27$, $p=0.06$), while only one of the subjects in the Method B group displayed increased lung density and mass ($p=0.94$, $p=0.26$). However, these differences were not statistically significant ($p= 0.8$). Notably, 4 of these subjects displayed a slight (non-significant) increase in mass.

This increase may be attributed to a >2% increase in lung volume, and does not represent a finding of interstitial pulmonary edema.

A comparison of the performance of individuals subjected to Method B (Part 2) with their original screening performance in the epidemiology study is presented in Table 5. Only three of the subjects displayed desaturation, while two subjects reached saturation equal to or less than original values. The subjects displaying desaturation were the only individuals able to reach or exceed their original maximum wattage.

V. Discussion

Our spirometric results did not indicate any significant contribution of EFL to desaturation in our study population. Previous investigations of EFL have been inconclusive, with evidence both for [1], [5] and against [35] an impact on EIAH. EFL has been shown to occur in a proportion of both male and female athletes [35], [36], but to date there is no evidence linking it to EIAH. Reviewers might identify our simplistic measurements as evidence for EFL as a weakness. We argue that the conventional method of comparing tidal to maximal flow-volume curves is quite invasive and cumbersome to perform and tends to overestimate EFL [36], [37]. Further, our data did not suggest any evidence of EFL and did not indicate a need for more invasive testing. This also holds true for the proposed use of negative expiratory pressure to identify EFL. This method, which tends to assess a lower prevalence of EFL in trained athletes, would undoubtedly find that the true prevalence of EFL in our study population does not exceed that which we detected to any significant degree. Our results conclusively demonstrate the absence of airway hyperresponsiveness in both the desaturating population and individuals who did not desaturate.

Our results showed no evidence of increased lung density or mass post-maximal exercise in the study subjects to indicate development of interstitial pulmonary edema. We utilized two different techniques, specifically, lung sampling and whole lung measurements. Other authors have reported a 65% chance of clinical pulmonary edema development during exercise classified as maximal or near-maximal [21]. Our findings appear consistent with data obtained using this type of exercise protocol. However, very few studies have used the same exercise protocols, which limit the ability to draw direct comparisons. Reviews in this area tend to group various types of exercise protocols together, but these classifications do not necessarily encompass all the differences within the same group. Our exercise protocol was evidently of sufficient intensity to produce EIAH, but interstitial pulmonary edema was not induced for unknown reasons.

Many reviewers will criticize that we employed two different techniques to analyze the CT scans. Notably, both methods yielded similar results, although a trend towards increased density was observed with Method A ($p=0.27$). Our sample size for Method A may have been insufficient to disclose statistically significant differences. However, we were limited by the fact that St. Boniface General Hospital has replaced the scanners used for Method A, and were therefore unable to include additional subjects in this group. Both of these methods have been employed previously, with comparable results to ours [25], [27]. While Caillaud et al. reported significant evidence of increased lung density after maximal exercise [25], Manier and co-workers argued that generalization of results from selected slices analyzed with methods that do not involve the entire lung is difficult [27]. Indeed, minor changes in a few slices are amplified when taken as a representative of the whole lung, since other areas

of the lung with normal or decreased densities attenuate the overall findings. However, another study has provided evidence supporting the use of representative slices rather than the whole lung to determine changes in lung density [5]. We did not observe different density gradients that fluctuated with exercise when comparing various regions of the lung. Thus, comparison of the same areas pre- and post- exercise should yield representative density data. Nonetheless, there is no conclusive evidence that either analysis is more valid than the other? Since both methods are acceptable, this corroborates our conclusion that lung density is not increased following exercise.

In subjects of the Method B group, lowered performance was generally observed. Several studies have shown that the development of pulmonary edema is not significantly related to power output [24], [29]. Therefore, similar amounts of pulmonary edema would be expected to develop between both trials. There is no strong indication that edema would be more prominent if these individuals were to desaturate to the previous levels.

While qualitative analysis of the CT scans may seem unreliable, our use of two blinded investigators removed any observer bias. Various studies focusing solely on qualitative analysis for pulmonary edema [16], [24] have used similar techniques to blind their investigators, with good results. We believe that our application of this method is in keeping with the accepted standards and our findings are reliable.

CT scan is an effective indicator of interstitial pulmonary edema. The technique is comparable to plain radiographs and MRI, but has the added advantage over plain films in that quantitative analysis of lung density and mass can be performed [21], [27]. Furthermore, this quantitative analysis may be used to detect minor changes in lung water [27, 28]. Previous research reveals no added advantages in employing other modes of imaging for pulmonary edema detection. We suspect that other imaging techniques, such as MRI scan, would yield similar results.

Some investigators have performed imaging at functional residual capacity rather than total lung capacity, but it is suggested that lung volumes can be reproduced reliably at full inhalation [30]. We selected full inhalation for imaging, and subjects were instructed by the CT technologists to inspire maximally for the duration of the scan. While we feel that this has yielded favorable results in terms of consistent lung volumes, Caillaud and co-workers went so far as to train their subjects for the full inspiration maneuver to generate better results [25]. In our opinion, prior training for full inspiration hold would not have led to considerably different outcomes for our subjects.

While we did not officially record the time between the end of exercise and imaging, earlier studies have reported wait times from 2 minutes [26] to 2 hours [23], with little differences in the pulmonary edema findings. Moreover, research suggests that sufficient wait time (>30 min) must be ensured to allow for pulmonary blood flow and volume to return to normal in order to avoid false-positive findings of pulmonary edema [31]. Zavorsky reported consistent findings of pulmonary edema despite varying wait times, indicating that pulmonary edema is not influenced by the time elapse between exercise and imaging [21]. Our wait times were approximately 30 minutes, consistent with the published literature. The time between exercise and imaging in our study did not appear to influence the results of CT scans.

Previous research suggests that interstitial pulmonary edema occurs during and not after exercise, since lungs can rapidly recover post-exercise [21]. This rapid recovery is still in concordance with the variable wait times between exercise and imaging, but may lead to underestimation of the actual prevalence of exercise-induced pulmonary edema. While evidence of pulmonary edema at varying times post-exercise has been recorded [16], [24], [25], [29], [32], it is arguable whether the amount of edema detected after exercise truly represents the quantity that would have been detected during exercise. Indeed, all our subjects may have developed significant pulmonary edema during exercise but recovered satisfactorily immediately following exercise, thus presenting no findings. Currently, it is difficult to measure changes in lung density during exercise in a non-invasive manner. Advances in technology may show that edema occurs with greater frequency and lower exercise intensities than currently estimated, implying that pulmonary edema plays a limited role in producing EIAH. Certainly, factors that are thought to exacerbate pulmonary edema have partial effects on oxygen saturation [33]–[38]. Repeated bouts of exercise may trigger or aggravate pulmonary edema due to changes in the alveolar-capillary membrane. These experiments revealed no correlation between interstitial pulmonary edema scores from radiographs and arterial blood gas status. There is growing evidence that EIAH is not significantly associated with the development of interstitial pulmonary edema. The lack of significant interstitial pulmonary edema observed in our qualitative and quantitative analyses of CT scans further discredits theories linking it to EIAH.

VI. Conclusion

In conclusion, our experiments failed to demonstrate a significant role for EFL contributing to EIAH despite the presence of EFL in some athletes. Additionally, there was no evidence to support the presence of interstitial pulmonary edema following maximal intensity exercise in athletes who developed EIAH. While the exercise protocols utilized in our study have been shown to induce EIAH and edema by earlier investigators, our findings are consistent with research that points to no correlation between the two phenomena. These results add to the accumulating evidence that interstitial pulmonary edema is not a significant contributor to EIAH development. Further conclusive evidence supportive of our findings would involve measurement of lung densities during exercise, for which resources are not yet available.

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Table 1 *Average of demographic data for subjects in screening phase*

	n	%	Age yr	Height cm	Weight kg	Exercise/week hr	Consistent Exercise yr
Total Population	82	100	36.4±13.0	175.3±8.9	74.9±8.9	7.9±3.8	13.5±10.9
Normal Saturators	53	64.6	37.2±13.1	175.0±9.0	74.3±11.9	7.3±3.5	14.5±11.5
Desaturators	29	35.4	35.0±12.7	175.8±8.8	75.9±10.9	8.9±4.2	11.6±8.7

Mean±SD

Table 2a. *Average of demographic data for subjects undergoing CT analysis by Method A*

		Mean±SD
Age	yr	34.4 ±12.1
Height	cm	177.9 ±11.3
Weight	kg	78.0 ±6.1
Est. $VO_{2\ max}$	ml/kg/min	53.1 ±12.4
Training	times/wk	6.9 ±2.4
	hr/wk	7.8 ±2.9
Consistent exercise	yr	12.0 ±9.9
Competitions	/yr	7.5 ±11.0

Table 2b. *Demographic data for each subject undergoing CT analysis by Method B*

Subject No.	Age yr	Sex	Height cm	Weight kg	Est. $VO_{2\ max}$ ml/kg/min	Training times/wk	Training hr/wk	Consistent exercise yr	Competitions /yr
171	22	M	183.5	93.0		5	6	16	0
172	34	M	189.0	74.5	65	4	8	4	6
173	48	M	167.0	64.0	59	5	10	3	10
174	22	M	181.0	79.5	65	6	20	17	40
179	20	M	172.0	73.0	41	4	6	7	0
Mean±SD	29.2±11.9		178.5±8.9	76.8±10.6	57.5±11.4	4.8±0.8	10.0±5.8	9.4±6.7	11.2±16.6

Table 3 *Average spirometric volume and flows*

	%-Predicted FVC			%-Predicted FEV1			%-Predicted FEV1/FVC			%-Predicted FEF 25-75%		
	Resting	5-min Post	15-min Post	Resting	5-min Post	15-min Post	Resting	5-min Post	15-min Post	Resting	5-min Post	15-min Post
Total Population	100.0±25.9	100.0±31.7	102.7±23.9	94.2±24.3	94.9±29.5	98.0±22.5	89.9±21.8	88.6±26.7	92.4±19.7	82.9±22.0	88.8±21.8	89.1±19.4
Normal Saturators	97.1±30.9	97.6±34.7	100.0±28.0	91.5±28.9	92.7±32.7	95.8±26.2	87.6±26.5	86.7±30.2	90.9±24.1	83.2±23.6	89.2±22.5	90.1±19.6
Desaturators	105.3±10.7	104.4±25.1	107.6±12.8	99.2±11.2	99.0±22.4	102.2±12.9	94.3±6.8	91.9±19.0	95.1±6.0	82.4±18.8	87.9±20.6	86.9±19.2
Mean±SD												

Table 4a. *CT analysis for volume, density, and mass for each subject undergoing CT analysis by Method A*

	Volume, cm3		Density				Mass, g	
			Hounsfield units		g/cm^3			
CT Subject No.	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	325.5	360.3	-897	-909	0.103	0.091	33.53	32.79
2	255.3	255.3	-914	-906	0.086	0.094	21.96	24.00
3	396.9	400.8	-917	-908	0.083	0.092	32.94	36.87
4	366.2	386.9	-916	-925	0.084	0.075	30.76	29.02
5	356.4	381.9	-911	-902	0.089	0.098	31.72	37.43
6	400.7	425.3	-919	-908	0.081	0.092	32.46	39.13
Mean±SD	350.2±54.1	368.4±59.4	-912±8.0	-909±7.9	0.088±0.008	0.090±0.008	30.6±4.3	33.2±5.8

Table 4b. *CT analysis for volume, density, and mass for each subject undergoing CT analysis by Method B*

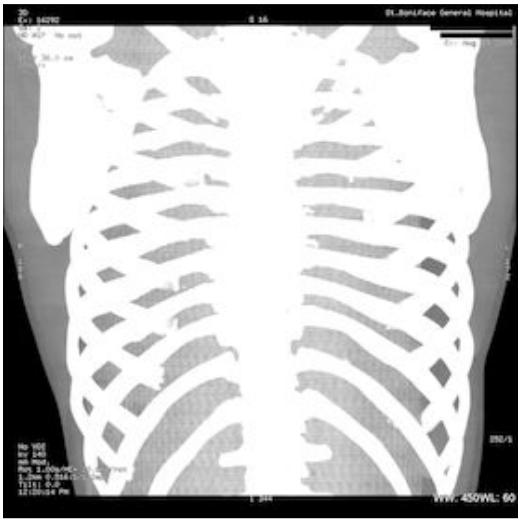
	Volume, cm3		Density				Mass, g	
			Hounsfield units		g/cm^3			
Subject No.	Pre	Post	Pre	Post	Pre	Post	Pre	Post
171	6120.4	7580.9	-789	-824	0.211	0.176	1291.4	1334.2
172	8692.0	9303.8	-811	-821	0.189	0.179	1642.8	1665.4
173	6163.1	6381.2	-836	-833	0.164	0.167	1010.8	1065.7
174	7823.0	7996.4	-815	-826	0.185	0.174	1447.3	1391.4
179	5091.4	5299.0	-798	-805	0.202	0.195	1028.5	1033.3
Mean±SD	6778.0±1450.0	7312.3±1535.1	-810±17.9	-822±10.4	0.190±0.018	0.178±0.010	1284.1±271.8	1298.0±259.3

Table 5. *Comparison of exercise performance between screening and CT protocol for each subject undergoing CT analysis by Method B*

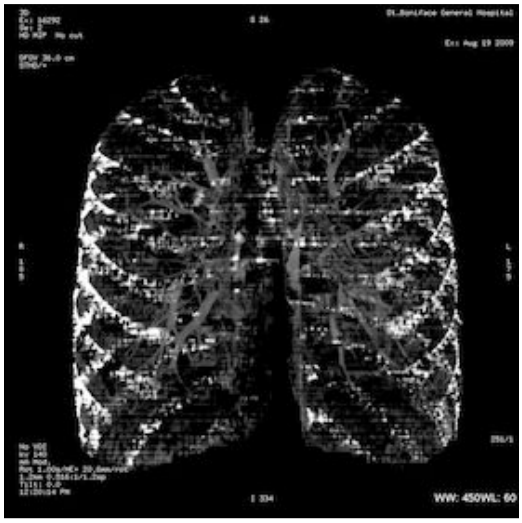
.	Lowest O2 Sat		Max HR		Watts Final Stage		Watts/kg	
Subject No	Part 1	Part 2	Part 1	Part 2	Part 1	Part 2	Part 1	Part 2
171	91	95	205	201	400	375	4.3	4.0
172	94	92	194	195	440	450	5.9	6.0
173	93	93	183	180	370	375	5.7	5.9
174	87	93	190	185	490	460	6.2	5.8
179	94	95	192	173	220	200	3.0	2.7
Mean±SD	91.8±2.95	93.6±1.34	192.8±7.98	186.8±11.28	384.0±102.1	372.0±104.2	5.0±1.3	4.9±1.5

Figure 1. *CT scans of subject No. 179. a. 3D reconstruct of thorax before analysis b. 3D reconstruct of thorax after analysis c. Axial slice of thorax to be manually highlighted d. Red line enclosing areas to be analyzed as lung parenchyma*

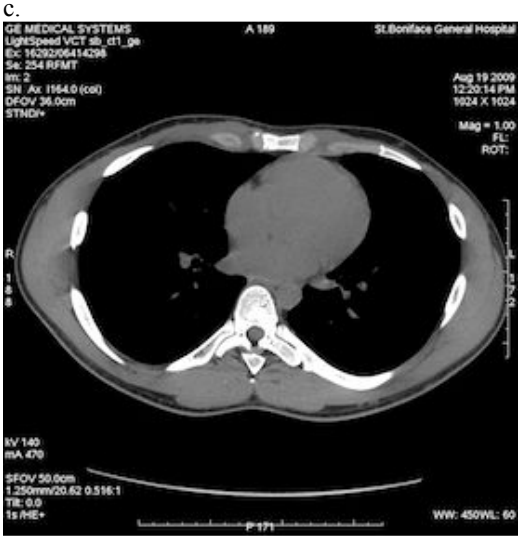
a.



b.



c.



d.