LungFIT: Validating a Smartphone Application for Pulmonary Rehabilitation

by

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Abstract

Introduction: Chronic Obstructive Pulmonary Disease (COPD) symptoms of dyspnea, exercise intolerance, and reduced health related quality of life are best treated with pulmonary rehabilitation (PR). Despite benefits, transportation, availability of PR programs, and social support barriers limit PR access. Telerehabilitation (TR) may provide the solution by utilizing pulse oximetry to monitor patient oxygen saturation (SpO_2) and heart rate (HR), along with measures of exercise intensity to ensure patient safety during home-based, unsupervised rehabilitation exercise. Study Purpose: To test the validity and reliability of a smartphone system called LungFIT in measuring heart rate, oxygen saturation, and distance in a healthy population. The LungFIT's functionality was also assessed. Methods: Functionality of the LungFIT was assessed by a time-to-complete test and the adapted Mobile Phone Usability Questionnaire (MPUQ). SpO_2 and HR measurements by 3 different LungFIT probes (Nonin, Masimo, and LionsGate Technologies) were evaluated during 5-minute cycle ergometry (50 watts at 60-70 revolutions/minute) and treadmill walking tests (3km/hr). Both tests were repeated 3 times. Distance measurements were assessed by outdoor walking tests of a 1 city block course. Results: SpO_2 measurements were valid with mean biases ranging between -0.93% and 0.88% and limits of agreement no greater than ±3.78% over the 3 LungFIT probes. The Masimo probe had the smallest mean biases ranging from 0.18% to 0.74% and mean limits of agreement ranging from ±1.94% (±0.93% 95% confidence interval) to ±2.79% (±1.34% 95% confidence interval). All probes had moderate to good SpO2 measurement reliability (ICCs between 0.65-0.87) with the Masimo probe performing the best (all ICCs ≥ 0.82). During exercise, HR measurements were invalid (mean limits of agreement > 10.00 beats/min), but reliable (ICCs between 0.87-0.97). Time-to-complete assessments found no software issues, but revealed 4 instances of navigation

or setup issues. The MPUQ showed ease of use despite lack of interface appeal. Conclusion:

During exercise, the 3 LungFIT probes were reliable in measuring SpO_2 and HR, but only valid

in measuring SpO_2. Overall, the Masimo probe was the most valid and reliable of the 3 probes

tested. Future LungFIT prototypes will improve user interface and accuracy of distance

measurements.

Preface

        The process of developing this project entitled LungFIT: Validation of a Smartphone Application for Pulmonary Rehabilitation began with the success of the Phone Oximeter developed by Dr. Mark Ansermino and Dr. Guy Dumont. Dr. Pat Camp became interested in the Phone Oximeter as it could accurately measure oxygen saturation and heart rate at rest. Thus, there was potential in the Phone Oximeter to monitor chronic lung disease patients without access to a conventional program during home based pulmonary rehabilitation.

        In order to develop the Phone Oximeter into the LungFIT as a Master's of Rehabilitation Sciences thesis project, an initial supervisory committee was established with the developers of the Phone Oximeter, Drs. Mark Ansermino and Guy Dumont. Supervisory Committee member Dr. Linda Li provided guidance in knowledge translation issues and additional clinical expertise. With the permission of the Phone Oximeter team, the idea of the LungFIT was brought to a telehealth convention called Hacking Health 2012. At the event, smartphone application designers and programmers collaborated to draft the initial mock-ups and functions of the LungFIT application. For the ideas and progress made, the project was awarded the Microsoft and Best Allied Care Project Awards, building good momentum to progress the project further.

        With the help of Peter Chen, a programmer with the Electrical & Computer Engineering in Medicine research group, the current LungFIT application prototype was designed. I then designed a study protocol based off typical pulmonary rehabilitation exercise intensities in order to assess and further develop the LungFIT for this population and use. The University of British Columbia's Ethics Board issued an Ethics Certificate Number of H13-03091 for this project. Lastly, Bland-Altman analyses for this project were completed by the Centre for Health Evaluation and Health Outcome Sciences.

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List of Abbreviations

%	percent
6MWT	6-Minute Walk Test
AECOPD	acute exacerbations of chronic obstructive pulmonary disease
BMI	body mass index
CAT	Chronic Obstructive Pulmonary Disease Assessment Tool
CI	95% confidence interval
COPD	chronic obstructive pulmonary disease
CRQ	chronic respiratory questionnaire
ECG	electrocardiogram
FEV_1	forced expiratory volume in one second
FVC	forced vital capacity
GOLD	The Global Initiative for Chronic Obstructive Lung Disease
GPS	global positioning system
HR	heart rate
HRQL	health related quality of life
ICC	intraclass correlation coefficient
IQR	interquartile range
LED	light emitting diodes
LoA	limits of agreement
m	metres
mMRC	modified British Medical Research Council Dyspnoea Scale
mL	milliliters
MPUQ	Mobile Phone Usability Questionnaire
Nm	nanometer
PAR-Q	The Physical Activity Readiness Questionnaire for Everyone
PLC	product life cycle
PR	pulmonary rehabilitation
r	Pearson's product moment coefficient of correlation
RPE	rate of perceived exertion scale
Rpm	revolutions per minute
SD	standard deviation
SGRQ	St. George's Respiratory Questionnaire
SpO2	pulse oximeter measured oxygen saturation
TR	telerehabilitation
W	watts

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I thank Dr. Mark Ansermino for his guidance and vision to produce a successful project that can potentially lead to better care for thousands of people. I thank and acknowledge Dr. Guy Dumont's thought provoking feedback and support throughout the project that kept me motivated in researching different aspects of the project. Thank you to Dr. Linda Li for her expertise and thoroughness that has taught me about different research approaches and ensuring clarity in my scientific work.

Dedication

A very special thank you to my parents for all their support and belief in me in every

challenge I give myself.

1. Introduction

1.1 Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is an irreversible disease characterized by pulmonary airflow limitation[1, 2]. This is an irreversible disease as it is progressive with no cure or treatment to completely reverse effects. COPD affects multiple systems of the body, but is mainly characterized by two distinct phenotypes, chronic bronchitis and emphysema[3]. Clinically, chronic bronchitis is defined as persistent and long-term increase in mucous production spanning a minimum of 3 consecutive months over 2 years[4]. Emphysema is the destruction of alveoli and alveolar surfaces, resulting in decreased elastic recoil and reduced surface area for gas exchange[3]. The result of these two phenotypes is an increased work of breathing and risk of infection for people with COPD[5]. As disease severity worsens, symptoms can significantly decrease quality of life and ability to perform daily activities[5].

1.2 Chronic Obstructive Pulmonary Disease Diagnosis

COPD is diagnosed by identifying a person's medical history, symptoms and signs, and using spirometry to determine airflow obstruction[5]. Factors for diagnosis coming from one's history include being a smoker or ex-smoker, 35 years or older, and family history of COPD[5, 6]. Symptoms and signs that may be present at diagnosis are: persistent or easily induced breathlessness, chronic cough, continuous sputum production, wheezing, frequent respiratory infections to the chest, peripheral edema, cyanosis, cachexia or unintentional weight loss, reduced activity tolerance, and hyperinflated lungs[5-7]. However, many of these symptoms may not be present early in the disease.

Spirometry is used to determine the level of airflow obstruction. Spirometry is a pulmonary function test that measures lung function by measuring air volume and flow under

different conditions. The key measurements used in diagnosing COPD from spirometry are forced expiratory volume in one second (FEV_1) and FEV_1/FVC (forced vital capacity) ratio[7, 8]. FEV_1 is a measurement of the total amount of air exhaled during the first second of exhalation during a forceful and maximal exhalation maneuver. FVC is the maximum amount of air one can exhale after a complete inhalation. This serves as a measure of a person's total usable lung volume for breathing, as in theory, only one's residual lung volume would remain in their lungs after a FVC maneuver. One criterion for a person to be diagnosed with COPD is if their FEV_1/FVC ratio is below 0.70, indicating obstruction in a person's airway[7, 8]. Predicted values are standardized based on a person's age and height. In combination with a low FEV_1/FVC value, FEV_1 values less than 80% predicted[8] demonstrate greater disease severity. Combined with other diagnostic factors, these spirometry values help determine a COPD diagnosis. To ensure optimal performance and standardization, spirometry measurements for COPD are taken post-bronchodilator use[5].

1.3 The Global Initiative for Chronic Obstructive Lung Disease Classifications

COPD severity is classified according to The Global Initiative for Chronic Obstructive Lung Disease (GOLD). Traditionally, COPD is classified by 4 stages from GOLD stage 1 to 4, with 1 being mild, then ranging to very severe in stage 4[8]. All stages indicate a FEV_1/FVC ratio less than 0.70, but differentiate severity by FEV_1 predicted values[7, 8]. Stage 1 is defined as mild COPD in which FEV_1 is greater than or equal to 80% predicted. Stage 2 or moderate COPD is characterized by an FEV_1 between 50 and 80% predicted. A FEV_1 between 30 and 50% predicted corresponds to stage 3 or severe COPD, and very severe or stage 4 is given if FEV_1 is less than 30% predicted or a FEV_1 less than 50% predicted but with chronic respiratory failure. Chronic respiratory failure is defined by GOLD as having an arterial partial pressure of O_2 less

than 60 mm Hg, regardless of hypercapnia while breathing ambient air[8]. In order to improve the classification of COPD severity, GOLD updated their guidelines in 2011 to include frequency of exacerbations, modified British Medical Research Council Dyspnoea Scale (mMRC) score[9], and COPD Assessment Tool (CAT) score[6, 10]. The mMRC is a five grade scale that assesses the degree of breathlessness associated with daily activities ranging from strenuous exercise to dressing in the morning[6, 9]. The CAT is an eight question test used to determine the level of impact on daily activities from COPD[10]. Those of GOLD stages of 1 and 2 with less than 1 exacerbation per year are characterized as being low risk of future exacerbations and mortality[7]. A label of fewer symptoms is given for mMRC scores at 1 or less, along with having a CAT score below 10[7]. Patient categories are then split into 4 categories[7] with category A being the most mild category consisting of patients with low risk and less symptoms. Category B designates those with low risk but more symptoms, while category C is for those with high risk but fewer symptoms. Patient category D is given to the most severe patients with high risk and more symptoms. A summary of the four patient categories can be found in Table 1.

1.4 Chronic Obstructive Pulmonary Disease Systemic System Effects

Exercise or strenuous activities are especially difficult for people with COPD because of a compromised pulmonary system that is compounded by a higher ventilation requirement[2]. This is a result of two phenotypes: first, emphysema reduces lung elasticity and surface area for gas exchange. Second, chronic bronchitis further increases the work of breathing by narrowing airways and increasing mucous. This can be augmented by static and dynamic lung hyperinflation, which positions respiratory muscles in biomechanically inefficient positions for breathing[2]. Furthermore, weakened inspiratory muscle strength, endurance, and function contribute and worsen the ability to efficiently breathe[2, 11]. Those with COPD experience a

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higher ventilation requirement during exercise due to hypoxia and lactic acidemia[2]. Emphysema and chronic bronchitis also alter gas exchange between terminal alveoli and pulmonary capillaries to become less efficient compared to a healthy adult of the same age[2]. Not having adequate gas exchange results in decreased oxygen saturation within blood designated to be used in the systemic system, or hypoxia. Hypoxia from exercise can also lead to lactic acidemia, or an excess of lactic acid, from inadequate oxygen delivery to peripheral muscles. The result of these two factors is an increase demand for ventilation. When combined with an increased work of breathing, trying to breathe during exercise can be incredibly uncomfortable.

In addition to pulmonary system changes of ventilation constraints and dyspnea[2], peripheral muscle dysfunction[12] and cardiac dysfunction factors also influence the systemic system leading to exercise intolerance in COPD patients. COPD-specific structural changes to lower limb muscles include atrophy and weakness especially in the quadriceps muscles, mitochondrial dysfunction, reduced oxidative capacity, and a shift to more type 1 muscle fibers[12]. In COPD patients, these muscle dysfunctions are associated with increased risk for mortality, uses of health care resources, and reduced quality of life[12]. In addition, dysfunction of lower limb muscles and associated feelings of dyspnea are other key factors for exercise intolerance in COPD patients[2, 11]. "Interactions among multiple physiological, psychological, social, and environmental factors,"[13] contribute to the commonly experienced feelings of dypsnea and muscular fatigue during exercise. Lifestyle factors associated with peripheral muscle dysfunction are deconditioning from inactivity, poor nutrition, and smoking[2]. COPD-induced factors include systemic inflammation, impaired gas exchange, oxidative stress, side effects from corticosteroid use[14], and lactic acidosis[2, 15]. Lactic acidosis is increased lactic acid production

during a given workload, which increases the drive for oxygen and breathing[15]. Therefore, for those with COPD, dyspnea is a common limiting factor to exercise, as muscles have become deconditioned and weakened, which is augmented by inefficient breathing mechanics that cannot meet the increased oxygen demands from exercising muscles.

The systemic system of those with COPD also can be impaired from cardiovascular dysfunction in the form of pulmonary arterial hypertension[2], and other cardiovascular diseases like hypoxic vasoconstriction, vascular injury, vascular remodeling, and erythrocythosis[2]. Pulmonary arterial hypertension is defined as a progressively elevated pulmonary vascular resistance[2, 16]. This can also lead to an increased right ventricular afterload if the entire volume of blood in the right ventricle is unable to pass through into pulmonary circulation. Furthermore, long-term right ventricular afterload leads to the development of right ventricular hypertrophy, which further impairs efficiency of the cardiac system. By impairing the delivery of oxygenated blood to systemic circulation, cardiac dysfunction also acts to compound problems of hypoxia and dyspnea. Table 2 summarizes the systemic factors related to COPD and exercise.

1.5 Chronic Obstructive Pulmonary Disease Etiology

The burden of COPD is high, with a prevalence of 65 million people worldwide [17, 18]. In 2010, Canada had a total of greater than 800 000 people diagnosed with COPD, with 106 073 diagnoses from British Columbia alone[19]. Spirometry data estimated that these figures may be higher with about 13% of all Canadians between the ages of 35 and 79 potentially having undiagnosed COPD[20, 21]. Furthermore, COPD will be the third leading cause of death by 2020 according to the World Health Organization[17, 18]. The prevalence of COPD is high because of a number of factors that accelerate the normal decline in lung function associated with age. These

factors include cigarette smoking, pollution, genetics, and infections[5, 22-24]. About 80% of COPD

cases are be associated with lifelong smoking[3]. Table 3 outlines the key components of each

etiology related to COPD development.

1.5.1 Chronic Obstructive Pulmonary Disease Etiology - Smoking

Lifetime smoking is the most common etiology of COPD with the risk of developing

COPD increasing with each year a person smokes cigarettes. A study by Lokke et al in 2006[25]

looked at data from an epidemiological study called the Copenhagen City Heart Study, and

found that smoking cigarettes for 25 years results in a 30 to 40% chance of developing COPD.

Smoking increases the risk of COPD as it has been shown to significantly accelerate lung

function decline associated with age[26], as shown by Figure 1. Naturally from aging, FEV_1

declines by about 20 to 30 milliliters (mL) per year as adults. This natural decline does not result

in lung function that would disable or limit a person's daily activities[22]. Conversely, the curve

associated with smoking for 25 years, shows a much steeper decline in FEV_1 that can potentially

lead to severely debilitating levels associated with GOLD stages 3 and greater. Smokers who

develop COPD can experience a mean annual FEV_1 decline of 80 to 100 ml/year[22].

1.5.2 Chronic Obstructive Pulmonary Disease Etiology -Genetics

A caveat to cigarette smoking accelerating FEV_1 decline, is whether a person is

susceptible to developing COPD or not[26], as there are about 60 to 70% of lifetime smokers that

do not develop COPD. Non-susceptible smokers may experience a much milder decline in FEV_1

at 30 to 45 ml/year. Susceptibility is believed to be strongly related to genetic history. One

genetic factor associated with susceptibility has been α1- antitrypsin deficiency found in 2% of

COPD patients[27]. The result of α1- antitrypsin deficiency is tissue being more prone to damage

from cigarette smoke[27, 28]. Thus far, studies on genetic factors for COPD have not been able to

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produce good reproducibility or replication as population studies on different ethnicities and geographic origins can result in false-positive findings if not all population factors are considered.

1.5.3 Chronic Obstructive Pulmonary Disease Etiology - Pollution

Another etiology for developing COPD is exposure to environmental and domestic pollutions. A systematic review of 14 papers on air pollution and COPD by Schikowski et al in 2013[24] found no conclusive results for a direct cause of pollutants leading to COPD. However, associations can still be made with a number of different pollutants[24, 29, 30]. Studies examining the association between air pollution and COPD rates have identified particles of less than 10 μm dynamic diameter termed PM_{10}, as a potential key pathogen to COPD[31]. In theory, exposure to high concentrations of these small molecules can cause oxidative stress to the pulmonary and systemic systems as their small size allow for deeper penetration into human tissue[24]. This would result in increased inflammation, damage to cilia, increased bronchial sensitivity, increased risk of viral infection, and decline in lung function[24]. Domestic exposures to burning biomass fuels and woods also increases the risk for COPD, as long-term exposure to burning biomass fuels and wood has been shown to increase risk by an odds ratio of 2.49 (95% confidence interval (CI) = 1.54 to 4.01) and 4.29 (95% CI=1.35 to13.70), respectively[32].

1.5.4 Chronic Obstructive Pulmonary Disease Etiology – Acute Exacerbations

Once diagnosed with COPD, illnesses resulting in prolonged and amplified symptoms called acute exacerbations of COPD (AECOPD) become significant events that worsen disease severity, decrease quality of life and increases mortality risk[23, 33, 34]. Exacerbations are defined as having two consecutive days in which two major symptoms and one minor symptom are increased[35]. Major symptoms include increased dyspnea, sputum purulence, and sputum

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amount[35]. Minor symptoms include wheezing, sore throat, cough, and nasal congestion or

discharge[35]. The frequency of exacerbations experienced by COPD patients is a strong indicator

of health status and relative risk for mortality[23]. As shown in Figure 2, the hazard ratio increases

significantly with each additional AECOPD per year. Compared to a person with no

exacerbations, those who experienced more than three AECOPD per year had a 4.3 (2.62-7.02)

times greater mean chance of mortality[23]. An AECOPD increases the risk for mortality as it has

been shown to significantly accelerate the rate of decline in a person's lung function. In a study

conducted by Donaldson et al in 2002[33] that tracked 109 COPD patients over 4 years, it was

found that those with more than 3 exacerbations per year declined in their FEV_1 by 8ml more

than those with less than 3 exacerbations, along with a 2.94 l/min decline per year in peak

expiratory flow. Peak expiratory flow is defined as the maximum speed at which one can expire

air. Thus, frequent exacerbations increases mortality as each exacerbation further accelerates a

decline in lung function and increases debilitating symptoms[36].

Frequent AECOPDs also significantly worsens a patient's quality of life compared to

those with less frequent exacerbations, as measured by questionnaires[34, 37]. In studies using the

St. George's Respiratory Questionnaire (SGRQ), those with more frequent exacerbations have

reported worse scores in all three of the questionnaires domains on symptoms, activities, and

impact[34, 37, 38]. A study using the health related quality of life (HRQL) questionnaire found

similar results in which those with 3 or more exacerbations per year scored almost 2 points worse

than those with fewer exacerbations[34, 39].

Those with COPD are also at an increased risk of respiratory infections due to

compromised immunity by the pulmonary system. Smokers who experience even just one lower

respiratory infection have shown an additional decline of 7 ml in their FEV$_1$[40]. Furthermore, those with frequent exacerbations have significantly higher rates of experiencing symptoms of dyspnea and wheezing during daily living. Therefore, frequent acute exacerbations are not only acutely detrimental to lung function and health, but further compound and accelerate COPD severity. Although treated with antibiotics while exacerbated, further rehabilitation intervention is required to stop the accelerated rates of decline from an AECOPD.

1.6 COPD Therapies

The first stage of managing the progression of COPD is through smoking cessation[1]. Medication therapy is also very commonly prescribed in the form of inhaled or oral medications that improve symptoms of quality of life, quality of sleep, breathlessness, and exacerbations[41]. However, several side effects to the pulmonary and gastrointestinal systems[41] exist from these medications. For those with severe pulmonary limitations in which hypoxemia is a concern, long-term supplemental oxygen therapy is used[1]. Lung volume reduction or transplantation surgery can also be performed for those with the worse lung conditions that qualify for surgery[1]. Lastly, all COPD patients can be well managed and treated with pulmonary rehabilitation[1].

1.7 Pulmonary Rehabilitation

1.7.1 Pulmonary Rehabilitation – Logistics

In combination with smoking cessation and medications, COPD is best treated with an intervention called pulmonary rehabilitation (PR). PR is defined as "a multidisciplinary programme of care for patients with chronic respiratory impairment that is individually tailored and designed to optimise physical and social performance and autonomy"[42]. PR typically consists of two main components, an exercise program and self-management education sessions. After completing an initial assessment by a physiotherapist or physician, patients are prescribed

an individualized exercise program based on their maximum exercise capacity[2]. Maximal

exercise capacity can be assessed directly by a maximal cardiopulmonary exercise test.

However, these can be difficult for people with severe COPD to complete and tolerate. Thus,

alternatively, sub-maximal exercise tests can also be used to determine exercise capacity. The 6-

Minute Walk Test (6MWT) is a commonly used functional walk test to estimate maximum

functional capacity and ability to perform daily activities in clinical populations [43]. The test is

used as it is easy to administer and is well tolerated by functionally limited populations, like

those with COPD. It involves walking as quickly as possible for 6 minutes around a 100 foot or

30 meter pathway[43]. Tests similar to the 6MWT that are also commonly used for assessments in

PR are the 12-minute walk test and shuttle walk test. The 12-minute walk test is the same as the

6MWT except patients are asked to walk for 12 minutes instead of 6 minutes. The shuttle walk

test involves walking back and forth between two markers at an increasing pace until exhaustion.

From the current guidelines[1, 2, 5, 11, 44, 45], PR exercise programs are advised to be at least 4

weeks, with longer programs shown to be more effective in producing short and long-term

improvements to exercise tolerance. PR exercise sessions should occur at least 3 times per week

with exercise lasting at least 30 minutes. Finally, exercise intensities should be between 60 to

80% of maximum capacity. This would correspond to a Borg Breathlessness Scale level of

about 4 to 6 or Rating of Perceived Exertion Scale (RPE) of 12 to 14. Exercise sessions consist

of both aerobic or endurance exercise, and strength training. Aerobic activities can be performed

using machines such as a treadmill, stationary cycle ergometer, or rowing ergometer and

typically target the muscles of locomotion[2]. Intensity for aerobic exercise can be set based on

any one of a number of different measures, including peak oxygen consumption, walking speed,

RPE, or power output[2]. Strength training is performed to increase the muscle mass and strength of patients. With a focus on upper extremities, an increase in upper limb strength can help decrease dyspnea as breathing and sustaining exercise may become easier[2]. Strength training can be performed using a hand ergometer, light free weights, body weight, and elastic bands[2]. For strength training exercises, 2 to 4 sets of 6 to 12 repetitions at 50 to 85% of the patient's one-repetition maximum is recommended[2, 11]. A one-repetition maximum is the most resistance a person can sustain for one repetition using good technique, for a given exercise. Since each patient has different needs, it is important for practitioners to follow the above guideline to tailor exercise prescriptions that are appropriate for each patient.

Different strategies can be used by practitioners administering PR to personalize exercise prescriptions for patients. In order to optimize potential benefits from exercise, PR programs should have a minimum of 20 total sessions with high exercise intensities and durations[2]. However, continuous and high intensity exercise can be unsafe or difficult for many people with COPD. For example, although performing at least 30 minutes of continuous aerobic exercise is ideal, many COPD patients cannot sustain exercise for that long. Thus, a technique called interval training can be used instead[2, 11]. Interval training is an effective strategy to maintain exercise intensities by segmenting continuous exercise into several shorter bouts with rest periods in between each bout.

In addition to muscular fatigue limiting exercise intensities, airway obstruction and limitation associated with COPD can interfere with exercise performance. Thus, bronchodilators can be used prior to exercise sessions to help reduce dyspnea and airway restriction[2, 5]. Patients on long-term oxygen therapy are advised to increase their flow rate of oxygen supplement during

exercise as well in an attempt to optimize their exercise tolerance[2]. However, current evidence is inconclusive on whether or not supplemental oxygen improves exercise tolerance regardless if one becomes hypoxic from exercise[46-50]. A final component that can be used alongside exercise sessions for those with especially poor inspiratory muscle strength is inspiratory muscle training[11]. This training can be performed by using inspiratory resistive training, threshold loading, or normocapnic hyperpnea[11]. Current literature on these three techniques has not determined one to be more effective than another[11].

Practitioners supervising exercise sessions monitor patients by periodically measuring oxygen saturation, heart rate, and level of perceived exertion[2]. Oxygen saturation and heart rate are measured using a pulse oximeter that attaches to a patients finger. Exertion level can be measured using the Borg Scale or the RPE[11]. It is important to monitor these measures to ensure the safety and intensity of exercise. Monitoring oxygen saturation is especially important for people with COPD as oxygen desaturation can occur with exercise and daily activities, leading to hypoxia and tissue damage if not intervened upon[2, 47-50]. A healthy individual will generally maintain an oxygen saturation above 95% saturation at all times, including during exercise. If a patient's oxygen saturation drops below 88% during PR, supplemental oxygen to increase and stabilize oxygen saturation is provided before exercise can resume[2, 5, 46]. However, oxygen desaturation can be prevented by using oxygen supplementation for patients with exercise-induced hypoxemia[11].

A final component of PR is self-management education sessions. These sessions provide education on nutrition, smoking cessation, and other self-management strategies related to

having COPD[2]. Education sessions along with practitioner supervision during exercise sessions provide psychosocial support, which can be a key factor in PR adherence and effectiveness[51].

1.7.2 Pulmonary Rehabilitation – Qualifying Criteria

An individual with COPD qualifies for PR after experiencing an acute exacerbation, or if they have experienced a decrease in exercise capacity and/or ability to perform daily activities[5, 11]. An increased feeling of dyspnea or fatigue during daily living also qualifies one for PR.

1.7.3 Pulmonary Rehabilitation – Evidence-Based Outcomes

The evidence supporting exercise prescription guidelines is well established in PR with a number of societies and associations having consensus parameters for exercise guidelines[2, 5, 52-54] including the Canadian Thoracic Society[53], British Thoracic Society[55], American Thoracic Society[2], and American College of Chest Physicians[56]. Pulmonary rehabilitation along with smoking cessation[57] has been shown to be the most effective intervention for COPD[58, 59]. Although PR cannot reverse declines in lung function, smoking cessation with PR can significantly improve the rate of decline to rates similar to those of the same age without COPD[26, 57]. Pulmonary rehabilitation improves exercise capacity, quality of life, and mortality. A Cochrane review by Lacasse et al in 2006[59] reviewed studies on PR for people with COPD. Evidence from 16 studies confirmed that PR improves 6-minute walk distance, based on a reported weighted mean difference of 48 metres with a CI from 32 – 65 meters [59]. Another Cochrane Review was conducted by Puhan et al in 2011[58] on the effects of PR after an AECOPD. Based on 6 studies, 6MWT scores improved by a weighted mean of 77.7 metres with a 95% CI from 12.21 – 143.2 metres[58]. A minimal clinically significant improvement is 35 to 54 metres[60, 61], thus, both reviews found impactful improvements. Exercise capacity improvements

were further confirmed by the Puhan et al[58] review that found a mean improvement of 64.35 metres (95% CI 41.28 - 87.43 metres) in shuttle walk test performance over 3 studies.

Health related quality of life is often assessed in PR by the Chronic Respiratory Questionnaire[62-64] (CRQ) and the St. George Respiratory Questionnaire[62, 65] (SGRQ). The CRQ utilizes questions to probe domains on dyspnea, fatigue, emotional function, and mastery. The minimal clinically significant improvement in the CRQ is set at 0.5 for each domain[66]. The review by Puhan et al[58] identified 5 studies on PR after AECOPD that used the CRQ and found clinically significant improvements in all four domains. Looking at the mean differences between baseline and post-PR, dyspnea improved by 0.97 (95% CI 0.35 - 1.58), fatigue improved by 0.81 (95% CI 0.16 - 1.45), emotional function by 0.94 (95% CI 0.46 - 1.42), and mastery by 0.93 (95% CI - 0.13-1.99)[58]. The Lacasse et al[59] review on PR in stable patients analyzed data on 11 studies that used the CRQ and found clinically significant similar improvements in all domains. From the mean differences, improvements were found in dyspnea by 1.06 (95% CI 0.85 - 1.26), fatigue by 0.92 (95% CI 0.71 - 1.13), emotional function by 0.76 (0.52 - 1.00), and mastery by 0.97 (95% CI 0.74 - 1.20)[59].

Although the physiology is not completely well understood[67, 68], improvements in dyspnea perception are linked to improved psychophysical process from PR[69]. Improved psychology in patients from the social and emotional support aspects of practitioner and peer interactions during PR may improve affective factors like fear and anxiety during exercise[68, 70]. Along with improvements in emotional function, self-efficacy to perform exercise, and depression, the perception and awareness of dyspnea may be reduced[68, 69]. Furthermore, improved physical ability from increased exercise tolerance and peripheral muscle function after PR desensitize

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COPD patients to feelings of dyspnea, allowing for better tolerance of breathing discomfort during exercise[67, 70].

The SGRQ assesses health related quality of life using domains on impact, symptoms, activity limitation, and then a total score from the three domains. The minimal clinically significant change to indicate improvements is 4.00 for the SGRQ[71]. Three studies were identified in the review by Puhan et al[58] and found improvements in two of the three domains. From the mean differences, impact improved by -13.94 (95% CI -20.37 – -7.51), activity limitation improved by -9.94 (95% CI -15.98 – -3.89), and effects on symptoms were mixed from score of 0.85 (95% CI -6.82 – 8.82)[58]. Overall, the total score improved by -9.88 (95% CI -14.40 – -5.37)[58]. The review by Lacasse et al[59] also found 6 studies that utilized the SGRQ and improvements were found in all domains. Improvements in mean differences were as follows, impact by -6.27 (95% CI -10.08 – -2.47), activity by -4.78 (95% CI -7.83 – -1.72), symptoms by -4.68 (95% CI -9.61 – 0.25), and total by -6.11 (95% CI -6.98 – -3.24)[59].

As previously mentioned, an AECOPD significantly increases the risk of mortality and hospital re-admissions, thus, the review by Puhan et al[58] analyzed data to determine the effect of PR on these two parameters. Over 3 studies, the odds ratio of mortality after receiving PR after an AECOPD compared to having no intervention was 0.28 (95% CI 0.10-0.84)[58]. Hospital re-admission data after PR for an AECOPD was collected from 5 studies and produced an odds ratio of 0.22 (95% CI 0.08-0.58) over a mean 25 week follow up period[58]. This further demonstrates the impact PR has on mortality as frequent hospital re-admissions have been linked to increased mortality risk in COPD.

1.8 Pulmonary Rehabilitation Barriers

1.8.1 Pulmonary Rehabilitation Barriers – Healthcare System

Despite the well-established research supporting the numerous benefits from PR for

COPD, only 1.2% of Canadians with COPD had access to a PR program in 2005[72]. This data

was from a national survey conducted by Brooks et al in 2005[72] that characterized all the PR

programs in Canada. The survey identified 98 PR programs in 60 facilities, with no programs

identified in Prince Edward Island, Newfoundland, and the three territories[72, 73]. From the 98

programs, the total yearly capacity was 8927 people, thus with about 750 000 Canadians

diagnosed with COPD in 2005[74, 75], only 1.2% of Canadians with COPD received PR that year.

Therefore, there is both an insufficient number of programs and capacity of PR programs.

1.8.2 Pulmonary Rehabilitation Barriers – Patients

In addition to lack of available programs, patient barriers to attend PR also exist. Barriers

include transportation, motivation, health literacy, physical, and safety factors[76, 77]. A systematic

review by Keating et al in 2011[76] found 5 qualitative and 6 quantitative research studies on the

factors affecting PR attendance and completion in a COPD population. The review reported 5

major themes. The most common theme was patients not wanting to disrupt an established daily

routine. This included not wanting to lose time devoted to social activities, work, summer

vacation, and family. The other major themes related to non-attendance included, unfamiliarity

with the doctor, a doctor that did not prescribe PR, a lack of perceived benefits from PR, and

inconvenient times of PR sessions[76]. Furthermore, minor themes identified were previous

negative experiences with health care, a fear of exercise-induced breathlessness, and lack of

knowledge on PR components and scheduling[76]. The review also reported that social support

and motivation played a role in completing PR. For instance, patients living alone or depressed

reported less motivation to complete PR[76]. Additionally, a study done by Hayton et al[77] found

that those who believed their disease was too severe already were less likely to attend PR as they

did not believe it would benefit them.

1.8.3 Pulmonary Rehabilitation Barriers – Geographic

The review by Keating et al[76] also found that travel, transportation and program location

were major factors to not attending PR. Due to COPD consisting of an elderly population,

driving or taking public transportation independently are concerns as well[76]. With a lack of

available programs, some individuals may live too far from a PR program to safely and

consistently find means of transportation. Fan et al in 2008[78] reported that those living 36 miles

from a PR site had an odds ratio to complete PR of 0.49 compared to those living only 6 miles

away. Those with COPD also often face mobility issues that can further augment transportation

problems.

1.9 Pulmonary Rehabilitation Maintenance Program

After completing a pulmonary rehabilitation program, COPD patients are advised to

continue a daily exercise program, but adherence in these maintenance programs can be poor[2, 79-81]. A systematic review by Busby et al[81] on PR maintenance programs found adherence rates to

be too low in some studies and varied overall to make general conclusions on the effectiveness of

maintenance interventions. In addition, exercise prescription and program parameters are not

standardized for PR maintenance programs[79]. Thus, many different types of maintenance

interventions for COPD patients have been studied[81], with few being randomized controlled

trials[79]. Strategies researched have focused on relapse prevention, follow up reminders, and self

monitoring[81]. However, despite a lack of standardization in interventions, COPD patients that

continue to exercise after PR have shown good ability to sustain improvements from PR in

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exercise capacity and health related quality of life[79, 81]. The best results have been shown in interventions with longer maintenance periods that provide supervision during exercise[79, 80, 82]. For example, a study by Foglio et al[82] completed a 7 year intervention in which COPD patients underwent an 8 to 10 week PR program every 12-18 months, while being encouraged to be active in their daily lives. The study found that 6MWT, peak oxygen consumption, dyspnea, and SGRQ scores were stable throughout the 7 years[82]. In addition, FEV_1 only declined by 18 ml/year[82]. This study demonstrates that long term and sustained physical activity by COPD patients is clinically effective in maintaining exercise tolerance.

Despite the benefits of ongoing exercise, the challenge for PR programs is being able to deliver supervised and long-term exercise programs to patients. In interventions where patients were prescribed to perform unsupervised exercise at home, absence of the psychosocial aspect of PR contributes to poor adherence, leading to improvements from PR quickly deteriorating[2, 79-81]. For patients that do not perform maintenance exercise after PR, exercise capacity can return to pre-PR values after 6 to 12 months[81]. To deliver pulmonary rehabilitation to patients without access in their communities, and to provide opportunities for ongoing, supported maintenance programs, telerehabilitation has been suggested as a possible solution[83].

1.10 Telerehabilitation

1.10.1 Telerehabilitation Definition

Telerehabilitation (TR) is defined as home- or community-based rehabilitation delivered using teletechnology[84]. Teletechnology includes telephone landlines, Internet, and cellular phone technologies. The advantage of TR is the ability to utilize tele-technologies to store and

communicate information between a patient and practitioner. In addition, TR technologies allow

for portable devices that are easy and practical to use by patients.

1.10.2 Telerehabilitation for Chronic Obstructive Pulmonary Disease

In 2007, Paré et al[85] published a systematic review on home telemonitoring studies for

patients with chronic pulmonary conditions, diabetes, hypertension, and cardiovascular diseases.

The review included 65 studies, with 18 studies focused on pulmonary conditions of pulmonary

transplantation, asthma, or COPD. Overall, the review found that telemonitoring interventions

were feasible and well accepted as demonstrated by accurate and reliable data communication

and strong levels of satisfaction and acceptance of instruments[85]. Specific to the studies on

pulmonary conditions, telemonitoring tools were effective in identifying changes in patient

symptoms to allow for earlier intervention and avoidance of exacerbations[85]. In addition, these

studies found significant reductions in hospital admissions, visits to the emergency department,

length of hospitalizations[85].

Teletechnology to aid in the management of COPD has been implemented in many

different ways. In 2010, Polisena et al[86] conducted a systematic review and meta-analysis of 10

studies that compared clinical outcomes, quality of life and healthcare use between home

telehealth or telephone support interventions that monitored patient symptoms to usual care for

COPD patients. Similar to the review by Paré et al[85], it was reported that home telehealth and

telephone support interventions were effective in reducing rates of hospitalization and

emergency department use[86]. Three studies on home telehealth interventions reported on quality

of life changes. Two studies found significant improvements in quality of life in the

interventions groups, while the third study found no significant changes[86]. However, quality of

life scores from these studies were similar to usual care scores[86]. Thus, despite a small pool of studies to analyze, the systematic review and meta-analysis demonstrated effectiveness in patient monitoring using teletechnology.

A study by Stickland et al[87] attempted to build upon telemonitoring interventions by researching a pulmonary telerehabilitation program in Edmonton, Canada. Patients travelled to their local health centre where they underwent an initial consultation with the respirologist and participated in education sessions via video-conferencing. Exercise sessions were done at the health centre with in-person supervision by a health care professional. The investigators reported similar improvements in 6MWD and quality of life in the telerehabilitation group compared to those who attended the hospital PR program. Marshall et al[88] investigated the feasibility of a smartphone system to monitor COPD patients participating in an exercise program. The system utilized an application designed using Microsoft (Microsoft, Redmond, USA) programming to be used on two different phones. A Nonin 4100 Bluetooth Pulse Oximeter (Nonin, Plymouth, USA) was used to collect and display measurements on the smartphone. Both heart rate and oxygen saturation were recorded during exercise and data was sent to a secure server either through the mobile network or by connecting the smartphone to an Internet enabled computer. The application contained 12 exercises that were to be performed for 5 minutes each[88]. Although this system was an improvement on previous TR interventions for COPD patients, the application only displayed heart rate despite oxygen saturation being recorded as well. The system was also limited to only being able to administer the 12 pre programmed exercises. Thus, there is still a need for better solutions to provide adequate and safe TR to COPD patients.

TR for cardiovascular patients has been researched more extensively. Worringham et al[89] developed a smartphone system that monitored a cardiac patient's HR, ECG, distance, speed, altitude and location. Subjects used the system for a home-based, outdoor walking program for 6 weeks and 6MWT mean scores improved by 113m[89]. This study reported no adverse events from exercise and only 8% of sessions were cancelled from technical issues[89]. Other studies implementing TR systems that monitor ECG and exercise in cardiac patients have also resulted in improved quality of life measures, VO_2 peak, peak workload, exercise duration, and energy expenditure[90-94]. In addition, none of these studies reported an adverse event during monitored exercise bouts. When compared to usual care cardiac rehabilitation, TR interventions were similarly as effective in improving exercise parameters and quality of life. Quality of life improvements were seen in TR groups despite a lack of interaction with practitioners and other patients during exercise sessions[87, 90, 92].

1.10.3 Telemonitoring in Telerehabilitation for Pulmonary Rehabilitation

Teletechnology in PR must be able to monitor exercise, enable patient education and behavioral modification, and facilitate secure communication between the patient and health care professional. In order to adequately monitor exercise, a TR device should be able to measure all components of the FITT principle[95]. The FITT principle is often used in exercise prescriptions and is an acronym for exercise: Frequency, Intensity, Type, and Time[95]. Frequency refers to the number of times exercise sessions are performed. This component could be tracked by recording each day that an exercise session is completed using the TR device. Exercise intensity refers to the amount of energy and effort required for exercises and could be measured in several ways. Since PR guidelines recommend walking, cycling, or rowing as forms of aerobic activity[2], the TR device could estimate exercise intensity by measuring energy expenditure during these

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activities. Measuring distance travelled, total steps, and/or speed can also be used as if a walking

program is prescribed. PR exercise can consist of a number of different exercises, thus, the TR

device should allow for the type of activities completed to be inputted into the device. Based on

the type of activity, the TR device will need to be able to determine the appropriate energy

expenditure algorithm or exercise intensity measure to use. The total time spent exercising could

be recorded by the TR device by implementing a time counter or stopwatch into the device.

Finally, type of exercise refers to the form of exercise or modalities used and could be recorded

by selecting pre-programmed exercise types on the TR device. A built in exercise diary in the

TR device could also be used to provide more details on exercise types completed.

In addition to monitoring the exercise parameters, a TR device would need to be able to

accurately and consistently monitor a patient's response to exercise. In PR oxygen saturation,

heart rate, the Borg Breathlessness Scale, and the Rating of Perceived Exertion are typical

measures which are monitored by the health care professional during exercise. The accurate

measurement of these parameters ensures safe exercise that is effective at improving health

outcomes. Therefore, it is important to understand the characteristics of this biomonitoring

component and how they would be delivered in a TR setting.

1.11 Pulse Oximetry for Oxygen Saturation and Heart Rate Measurement

During pulmonary rehabilitation, oxygen saturation and heart rate are periodically

monitored to ensure patient safety and assess the intensity of exercise[2]. Oxygen saturation and

heart rate (HR) can be measured by gold standard techniques, arterial blood gas and

electrocardiogram (ECG), respectively. However, these techniques require additional resources,

setup, and training, along with arterial blood gas tests being invasive, as it requires needle

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penetration into an artery. Thus, oxygen saturation (SpO_2) and HR can be conveniently and non-invasively measured using a pulse oximeter.

A pulse oximeter probe is placed on a finger or ear lobe as these areas provide tissue that is rich in arterial blood flow while being relatively thin to allow light to shine through it. Pulse oximeters utilize two light emitting diodes (LED) to emit two wavelengths on one side of the finger or ear probe. Probes then have a photoreceptor on the opposite side of the LEDs in order to receive the unabsorbed light that has passed through a finger or ear. Pulse oximetry utilizes the two wavelengths and the Beer-Lambert Law to determine oxygen saturation levels in tissue[96]. The Beer-Lambert Law states that "the concentration of a solute is related to the intensity of light transmitted through a solution."[96] Using this relationship, absorption of light can be determined when comparing the intensity of light before and after passing through a solute in a solution. The concentration of a solute can then be easily equated for based on the absorption of light using the equation: Concentration of solute = [(path length light is transmitted) x (extinction coefficient of the solute at a specified wavelength)] / (absorption)[96]. When a finger or ear lobe is inserted into a pulse oximeter probe, the solute in the scenario is oxygen and blood is the solution. The path length is a known value based on the size of the oximeter probe. The extinction coefficient of hemoglobin at a specified wavelength is also known as early studies on hemoglobin types have determined absorption rates at specific wavelengths. Current pulse oximeters emit two different wavelengths, one at 660 nanometer (nm) or red light, and 940nm or infrared light[96, 97]. These wavelengths are selected because oxygenated hemoglobin, or oxyhemoglobin, light absorption peaks at 660nm and deoxygenated hemoglobin, or deoxyhemoglobin, peaks at 940nm[96, 98]. Thus, SpO_2 or the concentration of oxygen in blood can

be deduced by comparing the ratios of absorption at 660nm and 940nm to each other and reference values. Reference values are embedded within a pulse oximeter's processor from desaturation studies that compared absorption ratios to arterial blood gas[96, 98].

Pulse oximetry can also indirectly measure heart rate based on arterial pulse waveform. Heartbeat is isolated using the LED and photoreceptor of the pulse oximeter. During a healthy arterial pulse waveform, there is a large and sharp pulsation in the artery with each heartbeat. These blood pulsations produce a change in pressure and are detected by the sensor and amplified to represent a heartbeat. Heart rate is then measured by assessing the time between blood pulsations in the monitored area. Although pulse oximetry has the capability to measure heart rate, studies suggest that measurements are limited in accuracy when compared to electrocardiogram[99-101]. The key reason for potential inaccuracy is from movements of the sensor or person that may alter the detection of a pressure change. High heart rates can also be challenging to detect as some pulse oximeters may not be sensitive enough to differentiate blood pulsations at high frequencies[99]. Thus, fast heart rates can be underestimated by pulse oximetry.

1.11.1 Pulse Oximetry Limitations

Due to pulse oximeters indirectly measuring SpO_2 and HR, measurements face limitations and error. Quality pulse oximeter manufacturers claim one standard deviation or 2% error in SpO_2 values between 70 and 100%[102]. This also indicates that 95% of all SpO_2 measurements are within two standard deviations or 4% SpO_2. Standard error increases to 3% for SpO_2 values between 50 and 70%, with no guaranteed accuracy for values below 50%[102]. Accuracy decreases as SpO_2 decreases because reference values from desaturation studies on humans were limited for values below 70% for ethical reasons[102]. There are also extrinsic factors

that can affect accuracy. Due to the colour and spectra of the wavelengths used, blue, black and

green nail polishes interfere with readings[98]. To prevent error from nail polishes, those using a

finger probe are recommended not to have any nail polish on the finger used for pulse oximetry.

Florescent and xenon lamp light around a probe can also decrease accuracy[98]. Conditions like

hypotension, low cardiac output, vasoconstriction, hypothermia, and other conditions that result

in decreased blood volume and pressure can result in compromised signal strength and quality by

the photoreceptor[98]. Finally, movement of the probe or body while connected to a probe is a

significant source of signal artifact and potentially inaccurate measurements[98].

In addition to understanding the biomonitoring aspect required from a TR device for PR,

awareness of the process of developing a novel TR device is needed in order to ensure its success

into clinical practices.

1.12 Product Life Cycle

To eventually bridge the gap between research and practice, a novel TR device will need

to follow the product life cycle (PLC). The PLC is a model used in economics and marketing

that describes "the evolution of a product, as measured by its sales over time."[103] As shown in

Figure 3, the PLC consists of four main stages, introduction, growth, maturity, and decline [103-105].

These four stages are defined within four main milestone events, catalogue birth, commercial

birth, commercial death, and catalogue death. For healthcare/medical products developed for use

within Canada, Health Canada outlines the need for pre-clinical and clinical studies prior to

submitting the product to Health Canada for approval and evaluation. In addition to being

clinically effective and safe for public use, all other Health Canada Medical Device Regulations

must be met for the product to be released to the public[106]. Evaluation of new medical devices in

order to be granted a Medical Device License is conducted by the Medical Devices Bureau of the Therapeutic Products Directorate[106]. This study was a pre-clinical study of a smartphone system intended for healthcare use. Completion of this pre-clinical study can potentially advance the smartphone system to be tested on appropriate patients/consumers in clinical studies.

One of the finger probes tested in this study was produced by a company called LionsGate Technologies (Vancouver, Canada)[107]. This finger probe is currently in the growth stage of the PLC as it is being sold by LionsGate Technologies as part of smartphone pulse oximeter system called Kenek Edge[107]. The aim of this project was to validate a smartphone system that was innovated from technology used in the Kenek Edge[107]. If the smartphone system tested in this study eventually reaches a catalogue birth, it will face unique challenges during its PLC introduction as it is an innovation of existing medical technology.

Technological innovations in the medical field potentially face special barriers to a successful PLC. One large barrier then can potentially affect the release of a medical innovation into the market is dealing with legalities. This includes issues around patent protection, intellectual property, and regulations[104]. When producing a product that is innovating existing technology, as is the case with this project, it is imperative to ensure legalities over the creation of the product are settled well before catalogue birth to avoid any setbacks or lawsuits while selling the product. Medical innovation products also must face the challenge of competing with the original product on the market[104]. In order to be successful, the new product must have additional benefits from the original product without having an excessively increased cost[104]. Although having great capability in the new product helps lessen this potential barrier, good marketing and supplier competence is needed to convince consumers that the new innovation is

needed. The physical attractiveness of the new product may help with marketing it[104]. One final

potential barrier is anticipating any additional costs to patients[104]. If this project materializes into

a tool to deliver TR, patients must account for additional costs of buying a smartphone and

cellular data plan.

2. Study Purpose

        The purpose of this study was to test the validity and reliability of a smartphone system (termed LungFIT) in measuring heart rate, oxygen saturation, and distance in a healthy population during low intensity exercise. Functionality assessment will be used to further improve the development of the LungFIT.

2.1 Study Objectives

1. To test the validity and reliability of the LungFIT smartphone prototype in measuring heart rate, oxygen saturation, and distance during low intensity exercise in a healthy population.

2. To test the functionality of the LungFIT in a sample of healthy adults.

3. To determine which LungFIT probe is most accurate in measuring heart rate and oxygen saturation in healthy adults.

2.2 Hypotheses

        The LungFIT system sensors will provide valid and reliable (intraclass correlation coefficients ≥ 0.75, $p < 0.05$) measurements of heart rate (valid if, bias $\leq \pm 5$ beats/minute), oxygen saturation (valid if, bias $\leq \pm 3\%$), and distance walked (valid if, difference ≤ 18.10 metres) in a healthy adult population when compared to respective gold standard methods.

3. Methods

3.1 Participant Recruitment

Ethics for this cross-sectional study was approved by the University of British

Columbia's Ethic Board (H13-03091). Participants were recruited from the Institute for Heart

and Lung Health, the University of British Columbia's Rehabilitation Sciences program,

Providence Health, St. Paul's Hospital, West End Community Centre, and the Robert Lee

YMCA. Recruitment was done via posters on staff and community bulletin boards, as well as

postings to staff list services. The study recruited a convenience sample by accepting the first 15

people that reply to an ad and met all the study requirements. Participants volunteered for the

study by contacting the study researcher via telephone or email. The researcher corresponded

with the participant to determine if they met the study criteria, followed by scheduling a testing

time. Participants were screened for the study using a screening form which included all of the

study's inclusion and exclusion criteria.

3.2 Participant Inclusion and Exclusion Criteria

The inclusion criteria for participants interested in the study were: between the age of 35

and 70 years old, able to read and speak English, did not use any form of walking aid, and free of

injuries that would interfere with cycling, walking or placing devices on their arms and body.

Participants were reminded to have trimmed and nail polish-free nails for the day of their study

session. Participants were excluded if they had diagnosed hypertension, cardiovascular disease,

or COPD. Cardiovascular diseases included arrhythmias, prior myocardial infarction, prior

stroke, ischemia, and angina. Participants with severe, uncontrolled or exercise induced asthma

that would require intervention during exercise were excluded. Those who had a respiratory

infection such as pneumonia or an acute respiratory exacerbation within the past year, as well as

having a hand injury or impairment that would influence phone use were excluded also. A final criteria was not answering 'yes' to any questions on The Physical Activity Readiness Questionnaire for Everyone (PAR-Q)[108]. This last criterion was evaluated after study consent was received.

3.3 The Phone Oximeter

The Phone Oximeter was developed to make SpO_2 and heart rate monitoring more readily available and affordable to countries where medical equipment is not widespread[109]. The World Health Organization reported that there are 77 000 operating rooms worldwide without pulse oximetry resulting in death rates 100 to 1000 times greater than operating rooms in high income countries[110]. However, mobile phone use in these poorer countries is high and continuing to rapidly grow. For example, Africa as a whole had a growth rate of 50% per year in subscriptions to mobile phone companies in 2009[111]. Thus, a pulse oximeter that could utilize mobile phones would be able to increase the access of pulse oximetry in these countries. The Phone Oximeter was developed using a modified finger probe and an Apple iOS mobile device[109]. It utilized signals from an oximeter probe that was modified to insert into an Apple iOS mobile device to display SpO_2 and HR on the mobile device screen by running a pulse oximeter application[97, 109]. Thus, the Phone Oximeter only required a compatible mobile phone and a probe with an adapted cable for insertion into the mobile phone, making pulse oximetry more available and inexpensive.

In a usability study of the Phone Oximeter prototype using the Mobile Phone Usability Questionnaire, medical staff in Canada and in the developing country of Uganda produced usability scores of 82% and 78% positive responses respectively[109]. These scores indicated that

the Phone Oximeter could be a functional tool for use in developing countries requiring greater

pulse oximetry use. The prototype of the Phone Oximeter utilized probes that required an

adapter cable in order to attach through the dock connector of an Apple iPhone (Apple Inc., 1

Infinite Loop, Cupertino, California, USA) mobile device. As a way to further decrease costs, a

low cost probe has been developed. The development of this innovative probe was described in

a study by Petersen et al[97]. The low cost finger sensor utilizes a mobile phone's audio interface

rather than the dock connector for power and communication to the Phone Oximeter

application[97]. The forward voltage thresholds for the red and infrared diodes were about 1.3

volts and 1.8 volts respectively, with the Apple high current mobile phone audio output able to

produce much greater voltages[97]. Thus, input from the probe's photoreceptor was amplified[97].

The input signal then went through a demultiplexer and algorithms in order to extract SpO_2 and

HR values[97]. When tested for validity compared to a conventional oximeter, correlation

coefficients were above 0.99 for oxygen saturations ranging from 70 to 100%[97]. Therefore,

future Phone Oximeter models could provide cheap, effective, and available pulse oximetry to

operating rooms and other healthcare environments.

Innovation of the Phone Oximeter for the LungFIT project was based on it being capable

of measuring the main parameters monitored during PR of SpO_2, and HR. This LungFIT project

innovated the Phone Oximeter by adding a distance measurement function to assess exercise

intensity as well as assessing finger probes during exercise scenarios.

3.4 LungFIT Finger Probes

This study tested the use of three different finger probes compatible for use with the

LungFIT. Finger probes were produced by Nonin, Masimo (Masimo Corporation, Irvine,

California, USA), and LionsGate Technologies. The LungFIT Nonin finger probe was a silicone

soft-tip finger sensor (model ASSNN-D1) developed by Acare Technology Co., Ltd (Acare

Technology Co., Ltd, Xinzhuang District, New Taipei City, Taiwan) that was connected to a

Nonin Xpod Low Power External SpO_2 cable. The silicone finger probe was designed to firmly

wrap the user's finger, while the Nonin Xpod cable has been marketed to be able to provide

additional processing for more accurate pulse oximetry measurements during motion and low

perfusion conditions[112]. The Masimo sensor used was the M-LNCS DC-I finger clip sensor. It

was a hard plastic sensor with soft silicone wrapping the finger inside the probe and on the sides

of the finger probe. According to Masimo, this sensor was designed to be able to provide a

secure fit in order to accurately monitor users during motion, low perfusion, and intense ambient

light[113]. Lastly, the LionsGate Technologies probe was a prototype finger probe that utilized the

auditory input of a smartphone. The finger probe was a hard plastic finger clip probe with rubber

inserts surrounding the inside and sides of the probe. This prototype probe did not have a motion

reduction function implemented in it.

3.5 Baseline Measurements

A flow diagram outlining the study methodology can be found in Figure 4. All subjects

provided written and informed consent before any study components began. Upon providing

consent, subjects answered The Physical Activity Readiness Questionnaire for Everyone form

before baseline characteristic measurements were taken. First, subject age and sex were

recorded followed by height and weight being taken using a Detecto (Webb City, USA) standing

scale with participants in their socks. Using height and weight data, Body Mass Index (BMI)

was calculated in order to categorize subjects into standardized health risk groups. Participants

were requested to wear lightweight, exercise-appropriate clothing prior to the study to help

obtain a true body weight as well as to make exercise more comfortable. Participants were instructed to stand straight while their height and weight were measured. An experiment and participant code was used to organize subject data.

The participant then sat down quietly for 10 to 15 minutes. This time allowed the participant to come to a resting state, introduce them to the LungFIT, and ask additional questions on smoking history (pack years), smoking status (active smoker, ex-smoker, never-smoker), self-reported smartphone experience (novice, intermediate, advanced, expert) and any relevant medical history.

After the 10 to 15 minute period, resting HR (beats per minute) and SpO_2 (%) were taken using a Nonin (Plymouth, USA) 8500 pulse oximeter. This pulse oximeter utilized a plastic finger clip sensor validated for use during rest and motion environments[114]. The pulse oximeter took a few seconds to stabilize its measurements, thus, readings were recorded after wearing the device for 1 minute. Finally, the placement of the LungFIT finger probes on either the right or left hand was recorded. Hand selection was determined by alternating allocation for each patient to prevent potential bias from handedness. The Nonin pulse oximeter was used on the opposite hand as the allocated hand for the LungFIT probes.

3.6 Functionality Test

3.6.1 Functionality Test – Original Protocol

While sitting in a resting state, subjects were given an orientation to the LungFIT system on how to use it and its functions. The orientation followed an operation manual that detailed step-by-step instructions for using the iPhone, application, and finger probes. During this time, subjects were free to ask any question as well as try each step themselves. After all the steps in

the operation manual had been explained, subjects were given about three to five minutes to review the manual and practice using the LungFIT alone. Once subjects felt comfortable using the LungFIT, the first part of the two part functionality test was administered using a time-to-complete assessment of tasks involving the LungFIT. The test involved 9 tasks that included, turning the iPhone on and off, accurately connecting the probe, using an armband that holds the iPhone, and maneuvering through the LungFIT application. Subjects' hands were videotaped to monitor their hand gestures and identify errors made. This also allowed for tests to be reviewed afterwards for timing accuracy and detailing errors made. Subjects were also asked to incorporate a think-aloud method in which they verbalized their thoughts and steps while performing tasks. After the time-to-complete assessment, subjects concluded the functionality test by completing a usability questionnaire that evaluated their impressions of the LungFIT system. The questionnaire was an adaptation of the Mobile Phone Usability Questionnaire (MPUQ).

3.6.2 Functionality Test – Advanced Protocol

The purpose of the time-to-complete assessment in the functionality test was to assess for any navigation or function issues, as well as any setup or procedural issues with the LungFIT system. The original protocol, outlined above, was used on the first ten of fifteen subjects in order to assess these issues. With no notable function issues with the LungFIT observed, the protocol for the functionality test was altered slightly for the last five subjects of the study. The test was adjusted to be slightly more difficult and simulate a field test in which the setup of the application and finger probe would be assessed more directly, rather than assessing the use of the iPhone. For this reason, previous iPhone use experience was added as a screening criterion for the last five subjects of the study. For the advanced functionality test, subjects were setup in the

same environment with the same iPhone, finger probe, and armband as the original functionality test. Once seated and comfortable, the subject was given the orientation manual and instructed to read through each step and practice using the LungFIT accordingly without any formal instruction from the researcher. The subject could ask the researcher for a prompt if needed, but were encouraged to try to learn how to use the application, finger probe and armband independently. After about 10 minutes or when the subject felt comfortable using the LungFIT, the time-to-complete assessment was explained. Instead of each task being read aloud, the subject was given a flash card that had general instructions written on it. The instructions were: setup the LungFIT on your arm, determine your heart rate and oxygen saturation, and dissemble and turn off the LungFIT. Subjects were also instructed to use the think-aloud method throughout the test. Subjects were timed from start to finish instead of by per task. Similar to the original test, the research assistant videotaped the subject's hands in order to review afterwards for any hand gestures and movements that resulted in setup errors. Meanwhile, the researcher watched the subject's facial expressions and verbal cues in order to make notes if there were signs of frustration, annoyance, confusion or any other negative emotions associated with using the LungFIT. Subjects then completed the MPUQ to conclude to the functionality test.

3.7 Exercise Protocol

3.7.1 Exercise Protocol – Equipment Setup

Following the functionality test, the subject was fitted with a 12-lead ECG, the Cosmed K4 b2 Metabolic System, a Nonin 8500 pulse oximeter and three LungFIT systems. 12-lead ECGs were placed by a researcher of the same sex as the subject. Ten electrodes were placed on the subject's body followed by connecting each probe to the ECG receiver that was harnessed

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onto the right hip of the subject. Next, the Cosmed K4 b2 was placed on the subject over their clothing. This device involved wearing a device that harnessed around the body, along with wearing a face mask that covered the nose and mouth. It recorded energy expenditure by measuring breath-by-breath measures of oxygen consumption and carbon dioxide production[115, 116]. Once the Cosmed unit was harnessed on the subject, the O_2/CO_2 delay calibration was completed by the subject. This calibration involved the subject syncing their breathing into the face mask to rhythmic signals from the Cosmed. Once this was completed, the subject's exercise characteristics were inputted into the Cosmed in order to begin recording data. Next, three LungFIT systems were placed on the subject. The armbands housing the iPhones were placed in order of the finger sensor connected to it. First, the iPhone connected to the LungFIT Nonin finger probe was placed on the subject's arm just inferior of their shoulder. The iPhone with the Masimo probe was placed below the previous one, such that it was superior of the elbow. Finally, the iPhone with the LionsGate Technologies probe was placed on the forearm, distal from the elbow of the subject. The iPhones were positioned to have their screens facing the lateral side of the subject. Wire slack was wrapped around the subject's armpit area and attached to the Cosmed harness at the shoulder area. Probes were then placed on the subjects hands in a standardized fashion. The LungFIT Nonin probe was worn on the index finger, the Masimo was worn on the middle finger, and the LionsGate Technologies probe was worn on the fourth finger. The Nonin 8500 pulse oximeter finger probe was then placed on the opposite index finger of the LungFIT equipped hand. Probe wires were taped down to the posterior side of the hand. Table 4 and Figure 5 outline all the devices that were used and how they tested the LungFIT for validity.

3.7.2 Exercise Protocol – Cycle Ergometer Test

The subject was fitted on the cycle ergometer. Seat height was determined by ensuring ten to thirty degrees of flexion in the subject's leg when fully extended on the cycle ergometer, while ensuring their hips did not shift upwards and downwards while cycling. The exercise portion of the study was then explained prior to beginning the first cycle ergometer trial. Instructions were standardized according to a script that can be found in appendix A.

For the first test the subject cycled at 60-70 revolutions per minute (RPM) for 5 minutes at an intensity of 50 watts (W), followed by a 3 minute break in a seated position. Breaks were shortened if the subject reached their resting heart rate according to the 12-lead ECG before the end of the 3 minute period. This was performed 2 more times for a total of 3 sets. The Rate of Perceived Exertion (RPE) scale was used to ensure that subjects were not exceeding a score of 4 out of 10. This was to maintain all subjects at a light to moderate exercise intensity. If subjects exceeded a score of 4, the intensity would be decreased to 25 or 0 W. The subject's heart rate and oxygen saturation was recorded after 2 minutes of exercise, the last 30 seconds of exercise, and during the last 30 seconds of each resting period. A marker was put on to the Cosmed system at the start and end of each exercise period so that energy expenditure recordings could be tracked after the study. The total cycling time was 15 minutes.

3.7.3 Exercise Protocol – Treadmill Test

After the cycle ergometer test, the subject walked on a treadmill at 3 km/hr and 0% incline for 5 minutes, followed by a 3 minute break in a sitting position that was identical to the ones given during the cycle ergometer test. Intensity was monitored using the RPE scale to ensure subjects did not exceed a score of 4 out of 10. This was done for a total of 3 sets. Data

was recorded in the same fashion as in the cycle ergometer test. The total treadmill walking time was 15 minutes.

3.7.4 Exercise Protocol – Outdoor Walking Test

This last test was conducted at Nelson Park located at Thurlow Street and Comox Street, Vancouver, British Columbia, Canada. The main purpose of this test was to evaluate the Global Positioning System (GPS) function of the LungFIT. Therefore, the 12-lead ECG, LungFIT finger probes, and Nonin pulse oximeter were removed prior to going outdoors. One iPhone around the triceps of the same arm that previously housed the 3 LungFITs and the Cosmed K4 b2 were worn. The subject walked around a pre-measured, standardized, 1 city block course that was 362 m long. The subject was instructed to walk at their own desired pace while staying to the right of the course path as much as possible. If needed, they were given a 3 minute sitting break after each lap. Once more, a total of 3 sets were completed. The Cosmed K4 b2 was marked at the start and end of each lap and the distance measured from the iPhone was recorded at the completion of each lap. Coordinates of latitude and longitude were recorded at 4 points along the course path as well. The total outdoor walking time was approximately 15 minutes.

Once all tests were completed, the participant was escorted back to the lab to remove the iPhone and Cosmed K4 b2, as well as gather any of their belongings. The participant was thanked for their time and participation. Lab contact information was given to the participant in case they have any further questions.

3.7.5 Exercise Protocol – Gold Standard Devices

The Cosmed K4 b2 Metabolic System has been assessed within the literature to be valid and reliable in measuring energy expenditure[115, 116]. By utilizing a specifically designed face mask, oxygen consumption is directly measured to be calculated into an energy expenditure

value. Both the 12-lead ECG and the Nonin8500 pulse oximeter have been approved for clinical use of Health Canada. 12-lead ECG was considered a direct measure of HR. The Nonin 8500 pulse oximeter was used as it has been used in pulmonary rehabilitation. Measurement errors in this tool will be further discussed. Finally, a high-quality distance measuring wheel was used to accurately measure the distance of the standardized course.

3.8 Data Collection

Subject baseline characteristics, functionality assessment scores, HR, SpO_2, and distance values over a study session were recorded on a data collection form (Appendix B). LungFIT functionality was assessed by recording times of each task during time-to-complete assessments as well as having participants complete the MPUQ. Validity and impacts of reliability of LungFIT probes were assessed by simultaneous measurements of HR and SpO_2 displayed on each iPhone and respective gold standards during the cycle ergometer and treadmill tests that were recorded 30 seconds before each exercise set, 2 minutes into exercise, and 30 seconds before the end of an exercise set by two recorders. One recorder wrote all results from the three iPhones, while the other recorded results from the 12-lead ECG and Nonin 8500 pulse oximeter. These measurements were synchronized using a visual clock in order to match respective HR and SpO_2 measurements. To avoid potential biases, the two recorders stood on opposite sides of the participant during all exercise sets and were sure to avoid any communication about recorded results. Data analyses of HR and SpO_2 measurements between LungFIT probes would identify the most accurate probe of the three tested. Distance was recorded at the end of each completed lap during the outdoor walking test only. These values were compared to the outdoor course distance of 362 m in order to assess measurement validity and reliability.

4. Data Analysis

Written HR and SpO_2 values during exercise tests were entered into a Microsoft Excel spreadsheet. Data analysis of recorded data was performed using the statistical tools R[117] and SAS (SAS Institute Inc., SAS Campus Drive, Cary, North Caroline, USA). Subject characteristics and functionality assessment data was analyzed using descriptive statistics. Validity and reliability of the LungFIT was assessed by analyzing values recorded on data collection forms from the LungFITs to recorded values from 12-lead electrocardiogram for heart rate and Nonin 8500 pulse oximeter for oxygen saturation. Distance measurements from the LungFIT were analyzed by comparing values to the reference value of the outdoor walking test course distance (362 m).

Baseline subject characteristics of age, sex, height, weight, smoking status, smoking history, smartphone experience, resting heart rate, and resting oxygen saturation were reported using descriptive statistics of mean, standard deviation, and range for continuous data, and counts and frequencies for categorical data. Data from functionality assessments were analyzed with descriptive statistics as well. Mean and median times, interquartile range, and standard deviation were calculated for time-to-complete tasks and total times. The main purpose of the time-to-complete assessment and functionality assessment was to identify any software, navigational, or setup issues with the LungFIT application and/or probes. Thus, frequencies of mistakes or issues during the time-to-complete assessment were reported as well. Results from the adapted MPUQ were tallied for each question and the frequency of negative responses for each question was recorded.

During exercise tests, LungFIT readings with low signal quality at measurement time points were not recorded, resulting in missing data. The number of readings with low signal quality were tallied as a frequency and excluded from statistical analyses. Due to each LungFIT probe being manufactured from different companies, they each required different processing by the LungFIT application. For the Nonin and Masimo probes, detected signal qualities below 80% resulted in values to no longer appear on the iPhone screen. The LionsGate Technologies probe continued to display HR and SpO_2 measurements regardless of signal quality, but a signal quality measure between 0 and 100% was displayed. Values with a signal quality below 80% were excluded.

For heart rate and oxygen saturation, associations to gold standard values were assessed by X-Y plots comparing LungFIT and gold standard measurements taken at the end of exercise during the second set of the cycle ergometer and treadmill walking tests. This measurement point was chosen to be representative of measurements made during peak exercise of each exercise test. Values with weak signal quality were excluded from plots. X-Y plots were made by plotting LungFIT measurements on the X-axis and the respective gold standard measurements on the Y-axis. Separate plots were created for each of the three LungFIT probes for heart rate and oxygen saturation during the cycle ergometer and treadmill walking exercise tests. This resulted in 4 plots per LungFIT probe and 12 plots in total.

Due to X-Y plots only visually displaying linear association of devices at one measurement point, validity was assessed using Bland-Altman analyses and plots to determine device agreements through mean differences or biases, 95% limits of agreements, and 95% confidence intervals of the limits of agreement between each LungFIT probe to the respective

gold standard[118]. Plots were created by grouping measurements made at rest and during exercise separately. In addition, oxygen saturation and heart rate measurements were separated, as well as distinguishing between measurements made during either the cycle-ergometer or treadmill walking test. Thus, over the 3 LungFIT probes tests, there were 12 total plots created. A mean difference value of 0 would indicate no overall bias in the LungFIT probe measurements, relative to the gold standard measurements. Limits of agreement (LoA) were calculated by a mixed model to avoid within-subject bias created from grouping data over several trials of the same subjects[118, 119]. The mixed model accounted for this error by computing residual values of within subject and between subject differences for both gold standard and LungFIT probe measurements[119]. LoA were used as they demonstrated that 95% of values measured by a LungFIT probe for each exercise test condition would fall within the calculated range. Validity was determined if bias and limits of agreement were both within manufacturer stated errors for the respective gold standard instrument. For the Nonin 8500 pulse oximeter, ±2% standard deviation or 95% of values within ±4% SpO_2 were considered the reference variation allowed[114]. For heart rate values, 12-lead ECG was considered a direct measure of heart rate and without error. However, since pulse oximetry measurement of heart rate is more varied, limits of agreement within a standard deviation of ±5 beats/minute[114] of 12-lead ECG values were considered valid. This also corresponds to 95% of HR values being within ±10 beats/minute of the mean value. This standard coincided with the manufacturer stated accuracy in heart rates measured during motion by the Nonin 8500 pulse oximeter[114].

Bland-Altman plots were created for each measurement parameter for each exercise test and probe individually. As an example, the analysis performed for the Bland-Altman plot of HR

measured by the Nonin probe at rest during the cycle ergometer test is detailed below and found in appendix C. First, all 15 measurement points, one from each subject, made by the Nonin probe during rest before each cycle ergometer set were grouped into separate columns according to their set number on Microsoft Excel. Respective gold standard HR measurements made by 12-lead ECG were placed adjacent to these columns. Next, a new column labeled 'difference' was placed next the gold standard column. Calculations subtracting Nonin probe values of each subject to the respective 12-lead ECG measurement were inserted into the 'difference' column. With differences still separated by exercise set, mean differences of each set were calculated from the previously calculated differences. Mean LoA and 95% confidence intervals of the LoA were determined by using a statistics package on R designed for models of replicate measurements[119] (Appendix C). The model compensates for the bias created from including several measurements from the same subject by calculating variance of 4 residual components. The 4 residual components were the differences created from between subjects and within subject measurement differences by both the gold standard and LungFIT probe. This variance value was then used to calculate LoA by multiplying it against a t-alpha two-sided score of 2.15. The R package then calculated CI for the LoA using standard error and the t-alpha two-sided score.

Reliability of heart rate and oxygen saturation measurements were assessed with Intraclass Correlation Coefficients (ICC) model 3 of several measurements (3,k). ICCs were calculated for each LungFIT probe by comparing SpO_2 or HR measurements between trials of the same exercise test. Model 3 ICCs was used as it would demonstrate within rater or in this case, probe, reliability of several measurements over repeatable trials on different subjects, in which the probe was a fixed effect but subjects were a random effect[120]. Since there were 3 trials

or judges in this study, the k variable equaled 3. ICC (3,3) values equal to or above 0.75 with statistical significance <0.05 were considered good reliable measures[120, 121]. ICCs between 0.4 and 0.75 were considered modestly reliable. An ICC value of 1.00 signified no variance in measurements[120].

The mean distances measured by the LungFIT were compared to the reference value of 362 m to determine validity. Distances were compared for each of the 3 laps separately as well as the cumulative mean distance from all 3 laps. Validity was determined by no more than 5% (18.10m) differences to 362 m. This is to ensure that the minimal clinically important difference in a 6MWT would be detected if the LungFIT is eventually used to administer the test[60, 61]. Reliability in distance measurements was assessed according to the standard deviation of LungFIT measured distances. Values with less than 5% fluctuation from the mean were considered reliable.

Energy expenditure data from the Cosmed K4 b2 indirect calorimeter and accelerometry data in the x, y, and z-axes by a LungFIT were recorded with the intent of creating an algorithm for the LungFIT to estimate energy expenditure. However, this data was not analyzed for this study due to LungFIT accelerometry data not being time matched to the Cosmed K4 b2 in the first 10 subjects. Additional accelerometer and Cosmed K4 b2 data will be collected in a future study in order to equate an energy expenditure algorithm for the LungFIT.

5. Results

5.1 Subject Characteristics

Data collection on 15 subjects occurred between March and July 2014. A summary of subject characteristics is in Table 5. The average of the sample was 47.2 years old with a standard deviation (SD) of ±7.54 years. There were disproportionately more females than males in the study as 10 of the 15 subjects were females. The average height was 167.33cm (SD ±9.96cm) and the average weight was 73.66kg (SD ±16.25kg). This produced an average BMI of 26.3kg/m^2, corresponding to being classified as overweight. Eight subjects reporting to never smoking, 6 subjects were ex-smokers, and 1 subject was an active smoker. The mean smoking history of smokers and ex-smokers was 3.78 pack years (SD ±5.09 pack years). One subject was a novice or never user of smartphones, one was as an intermediate user, 10 were advanced users who used a smartphone daily, and 3 were expert users of smartphones. Resting oxygen saturation and resting heart rate was measured with the Nonin 8500 pulse oximeter. The mean resting oxygen saturation was 96.4% (SD ±1.4%) and mean resting heart rate was 68.27 beats/min (SD ±14.64 beats/min).

5.2 Functionality Assessment

The functionality assessment component of the study consisted of two parts, a time-to-complete assessment and the adapted Mobile Phone Usability Questionnaire. Results from the time-to-complete assessment can be found in Table 6 and 7. Mean and median times, interquartile ranges, and standard deviations for both time-to-complete assessment protocols are summarized in Table 6. Tasks of "Insert iPhone into the armband and put armband on to arm" and "Put on probe, re-open PC app, and begin recording data." took the longest amounts of time to complete at 20.04 seconds (SD ±7.96 seconds) and 13.16 seconds (SD ±6.26 seconds),

respectively. During the time-to-complete assessments, there were a total of 15 issues or problems observed. A majority of these issues pertained to use of the iPhone and armband, with 8 problems with iPhone use and 3 instances of assistance required with the armband being recorded. Issues with the LungFIT system itself included 2 subjects that needed help to begin recording data, one subject required help to locate the 'exit' button on the application, and one subject struggled removing the finger probe input from the iPhone. This resulted in two navigation issues and one setup issue with the LungFIT system. There were no software issues with the LungFIT probe or application observed during all functionality assessments. Table 7 provides an overview of issues and problem observed during time-to-complete assessments.

The responses to the adapted Mobile Phone Usability Questionnaire overall indicated that 93% of responses were positive. The largest frequency of negative responses was reported in the 'Affective Aspect' and 'Multimedia Properties' sections of the questionnaire. The two questions that scored the worst had a total of 13 negative responses, and asked, "Do you feel excited when using LungFIT?" and "Would you miss LungFIT if you no longer had it?" Furthermore, 1 subject was frustrated using the LungFIT, 3 subjects found the system unattractive, two found picture quality and size unsatisfactory, and 3 subjects would not have been proud if they produced the LungFIT. All other sections of the questionnaire scored well with only 8 total questions having 1 to 2 negative responses. A complete summary of results from the MPUQ can be found in Table 8.

5.3 Weak Signal Quality Frequency

Each probe used in this study utilized different processing modules, thus the LungFIT application was capable of computing each module type. This also meant that each probe

measured different signal qualities for a given measurement time point. During data collection, instances in which a probe detected weak signal quality or a signal quality below 80%, resulted in no measurements displayed by the Nonin and Masimo probes and measurement recording exclusion by the LionsGate Technologies probe. In addition, an option for 'weak signal quality' on the data collection form was marked for the corresponding measurement point. During the cycle ergometer test in which a total of 135 measurements were recorded over 15 subjects, the Nonin probe had 13 missing values (9.63% of all measurements), the Masimo probe had 2 (1.48%), and the LionsGate Technologies probe had 10 (7.41%). Over 15 subjects undergoing the treadmill test, there were 3 missing values by the Nonin probe (2.22%), 4 by the Masimo probe (2.96%), and 6 by the LionsGate Technologies probe (4.44%). There were no missing values from gold standard measurements.

5.4 X-Y Plots for Oxygen Saturation and Heart Rate

All 12 X-Y plots displaying LungFIT measurements versus gold standard measurements of heart rate and oxygen saturation during both exercise tests are found in Figures 6-17. During the end of the second set of the cycle ergometer test, the HR detected by the LungFIT equipped with the Nonin and Masimo probes appear to have strong association with HR measurements by 12-lead ECG, while the LionsGate Technologies probe did not. For LungFIT measurements of SpO_2 during the cycle ergometer test representative of peak exercise during the study, compared to the Nonin 8500 pulse oximeter during the cycle ergometer test, the Nonin probe appeared to be have the strongest association. LungFIT HR measurement during end of exercise of the second set of the treadmill walking test compared to 12-lead ECG resulted in visually strong associations by all 3 probes. For SpO_2 measurements from the treadmill walking test, X-Y plots for all 3 probes displayed multiple measurements that were not well associated with

measurements made by the Nonin 8500 pulse oximeter. A basic summary of cumulative mean

and median SpO_2 and HR measurements over both exercise tests can be found in Table 9.

5.5 Bland-Altman Analyses of Oxygen Saturation and Heart Rate

5.5.1 Bland-Altman Analyses of Oxygen Saturation and Heart Rate: Nonin Probe

Bland-Altman analyses were used to determine mean differences or biases of each

LungFIT probe to the appropriate gold standard instrument for each measurement point during

both the cycle ergometer and treadmill walking tests. Bland-Altman plots displaying the

performance of each probe at each measurement point during each exercise test can be found in

Figures 6 to 41. Starting with the Nonin probe, biases, standard deviation of biases, and range of

95% level of agreement values for both SpO_2 and HR values during the cycle ergometer and

treadmill walking tests are in Table 10 and 11, respectively. Overall, all Nonin probe SpO_2

values during the cycle ergometer test were slightly underestimated by biases ranging from -0.15

to -1.31%, with bias SDs ranging from ±0.82 to $\pm1.97\%$. Thus, 95% of all SpO_2 s values were

within $\pm4\%$ of their respective bias. In addition to biases for each measurement point

individually, mean biases of each exercise test parameter according to measurement point were

also calculated. A summary of these result along with mean limits of agreement and 95%

confidence intervals are in Table 16. Over the 3 cycle ergometer test sets, the mean resting bias

of SpO_2 measurements by the Nonin probe was -0.40% and -0.64% during exercise. LoA were

below $\pm4\%$ during both measurement conditions at $\pm2.21\%$ ($\pm1.06\%$ CI) during rest and $\pm3.04\%$

($\pm1.46\%$ CI) during exercise. During the treadmill walking test, all SpO_2 were slightly

underestimated again as bias values ranged from -0.29 to -1.07%. When averaging biases, the

mean bias at rest was -0.93% and -0.65% during exercise sets. All LoA were within $\pm4\%$.

During the cycle ergometer test, HR biases were varied and ranged from 0.08 to -8.31 beats/min.

When biases were clustered according to measurement point, the mean bias at rest was -0.49 beats/min and -3.72 beats/min during exercise. However, LoA exceeded ±10 beats/min. Measurements at rest had LoA of ±16.61 (±7.98 CI) and ±23.39 (±11.24) during exercise. HR biases calculated from treadmill walking test HR values resulted in biases that generally slightly overestimated HR values. The smallest bias was 0.33 beats/min, while the greatest amplitude of bias was 4.64 beats/min. Mean biases over the 3 sets of treadmill walking resulted in a bias of -0.36 beats/min at rest and 3.66 beats/min at exercise. LoA were greater than ±10 beats/min in both cases.

5.5.2 Bland-Altman Analyses of Oxygen Saturation and Heart Rate: Masimo Probe

Data collected using the Masimo probe produced biases that slightly over estimated SpO_2 during both exercise tests. During the cycle ergometer test, biases ranged from 0.27 to 0.93%. The mean bias at rest and exercise were 0.67% and 0.73%, respectively. The treadmill walking test produced similar results with biases ranging from 0.13 to 1.00% with the mean bias at 0.18% at rest and 0.74% during exercise. Mean LoA for SpO_2 measurements during both exercise tests were all below ±4% with the highest mean LoA being ±2.79% (±1.34 CI) for SpO_2 measurements made during treadmill exercise. HR biases were much more varied with biases from 0.53 to -10.47 beats/min, with the smallest bias being -0.20 beats/min. During the cycle ergometer test, the mean bias at rest was -0.64 beats/min and -0.83 beats/min for exercise. However, LoA were ±16.99 beats/min (±8.17 beats/min CI) during rest and ±16.54 beats/min (±7.95 beats/min CI) during exercise. Biases for HR from the treadmill walking test were also varied, ranging from -2.07 to 9.47 beats/min, with -0.07 being the smallest bias value. At rest, the mean bias was -0.98 beats/min, while bias increased to 6.09 beats/min during exercise. Despite the difference between biases, both had LoA greater than ±10 beats/min (rest: ±12.89

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beats/min, ±6.20 beat/min CI; exercise: ±33.40 beats/min, ±16.06 beats/min CI). All individual

results from the Masimo probe can be found in Tables 12 and 13.

5.5.3 Bland-Altman Analyses of Oxygen Saturation and Heart Rate: LionsGate Technologies Probe

Overall, the LionsGate Technologies probe slightly overestimated SpO_2 values. Biases

during the cycle ergometer test ranged from -0.23 to 1.08%. When biases were grouped

according to measurement point, the bias at rest was 0.41% and similarly at 0.51% during

exercise. Data from the treadmill test resulted in biases from 0.07 to 1.25% with the mean bias

at rest at 0.48% and 0.88% during exercise. All SpO_2 mean biases had LoA within ±4% as they

ranged from ±3.24% (±1.56% CI) to ±3.78% (±1.82% CI). HR values from the LionsGate

Technologies probe greatly underestimated HR during exercise periods of the cycle ergometer

test. HR biases during the cycle ergometer test ranged from 0.20 to -17.25 beats/min. Mean

biases resulted in a bias of -1.61 beats/min at rest, then -16.44 beats/min during exercise. HR

values during the treadmill test were slightly more valid, but still consistently underestimated HR

with biases ranging from -0.64 to -7.50 beats/min. Calculations of mean biases resulted in a

mean bias of -5.45 beats/min at rest and -3.96 beats/min during exercise. Despite some mean

biases being within ±5 beat/min, all mean LoA were above ±10 beat/min, especially during the

cycle ergometer test. Bland-Altman calculations at each measurement point from the LionsGate

Technologies probe are in Tables 14 and 15.

5.6 Reliability of Oxygen Saturation and Heart Rate Measurements

A summary of ICC (3,3) values for each probe measuring both oxygen saturation and

heart rate over both exercise tests is in Table 17. All ICC values were statistically significant at

P<0.001. Overall, the Masimo probe was most reliable with all ICC values above 0.70. ICCs

during the cycle test and treadmill test were 0.87 and 0.82 for SpO_2 and 0.96 and 0.87 for heart rate, respectively. The Nonin probe was fairly reliable in all measurements as well with ICCs of 0.80 and 0.71 for SpO_2 and 0.95 and 0.97 for HR measurements during the cycle and treadmill tests respectively. Thus, SpO_2 measurements during the treadmill test were only modestly reliable. The LionsGate Technologies probe was modestly reliable in its SpO_2 measurements in both exercise test with an ICC of 0.65 from the cycle ergometer test and 0.68 from the treadmill test. HR measurements were reliable according to an ICC of 0.88 from the cycle test and 0.90 from the treadmill test.

5.7 Outdoor Walking Test

Means and SD values from the outdoor walking test were reported in Table 18. The cumulative mean distance measured by the LungFIT over all outdoor walk tests was 216.69 m (with a SD of ±55.09 m or 25.42% of the mean distance). This resulted in a mean difference of 152.66 m with a SD of the difference of ±28.19 m when compared to the reference value of 362 m. In order to distinguish consistency in measurements between test laps, mean distances, SDs and mean differences for each of the 3 laps were calculated separately as well. These results are also in Table 18. Lap 1 produced a mean distance of 218.79 m (SD of ±76.46 m), lap 2 had a mean distance of 207.77 m (SD of ±19.86 m), and the third lap had a mean distance of 209.06 m (SD of ±56.75 m). This resulted in mean differences of, 159.45 m (SD of ±24.08 m) for lap 1, 154.23 m (SD of ±19.86 m) for lap 2, and 155.83 m (SD of ±47.57 m) for lap 3.

6. Discussion

The key finding of this study is that the LungFIT system demonstrated modest to good validity and reliability in measuring oxygen saturation during low intensity exercise, but not heart rate and distance. Based on Bland-Altman and ICC analyses comparing Nonin 8500 pulse oximeter and 12-lead ECG accuracies to LungFIT probes tested, the Masimo probe was most valid and reliable in measuring oxygen saturation (SpO_2 mean bias $\leq 0.74\%$, LoA $\leq 2.79\%$, CI $\leq$ 1.34%, and ICC ≤ 0.82, $p < 0.001$, respectively) during rest and exercise, followed by the Nonin probe. Despite HR measurements during rest by the Nonin and Masimo probes being reliable (ICC ≤ 0.87, $p < 0.001$) and having mean biases less than ± 5 beats/min, limits of agreement greater than ± 10 beats/min placed the probes outside of the predetermined threshold for valid HR measurements.

6.1 Significance of Determining Accuracy of Oxygen Saturation Monitoring by the LungFIT

This study found that the LungFIT can accurately monitor oxygen saturation during rest and low intensity exercise using a smartphone platform. The strong agreement of LungFIT SpO_2 measurement by all 3 probes compared to the Nonin 8500 pulse oximeter agreed with the previous validation study of the Phone Oximeter measuring SpO_2 at resting conditions. The Phone Oximeter was originally validated by tests using a simulator of resting SpO_2 and HR across a systematic range of skin pigmentations. The Phone Oximeter had SpO_2 and HR Pearson's product moment correlation coefficient (r) values above 0.99 with biases ranging between -0.43 and 0.43%[97]. This study did not calculate r values due to this analysis only being capable of demonstrating linear association to gold standard measurements. Since HR during steady state exercise and SpO_2 in healthy adults were not expected to fluctuate much between

subjects or during exercise, an overall linear pattern was not expected. Especially in the case of SpO_2 analyses, in which values are expected to consistently stay within a 1 to 2 % range in healthy adults, small variations from a relatively horizontal gold standard linear relationship would have resulted in greatly affected r values. Thus, in this study, device agreement, as evaluated by Bland-Altman analyses, was a better determinant of validity. Based on biases, this study reconfirmed the accuracy of SpO_2 and HR monitoring by this technology at rest on actual human subjects, while further testing the capacity of the technology to accurately monitor these outcomes during low intensity exercise. Validity results also agreed with previous literature on pulse oximetry use for high intensity cycle ergometer exercise tests on elite athletes in which SpO_2 measurements were valid and unaffected by exercise[122].

The LionsGate Technology probe that utilized the audio input of the iPhone and designed to be a low-cost probe compared to other probes was the least reliable in monitoring SpO_2. The design of the probe and loose fit on participants' fourth fingers may have augmented motion artifacts during exercise. In addition, the prototype LionsGate Technologies probe tested was not implemented with a motion reduction function. This probe had the potential to be more feasible to use in PR interventions due to its low cost and simplification of processing resources required compared to the Nonin or the Masimo probes. However, despite its economic advantages, this study found the LionsGate Technologies probe tested to be unreliable for use during low-intensity exercise.

Monitoring oxygen saturation periodically during exercise for PR is imperative to ensuring patient safety in preventing oxygen desaturation and associated tissue damage from hypoxia[2, 47, 50]. COPD is characterized by a diminished pulmonary system resulting in symptoms

of hypoxia, increased work of breathing, and impaired gas exchange[2]. In addition, systemic symptoms of dyspnea, peripheral muscle dysfunction, and increased work of breathing, exercise tolerance and capacity are greatly reduced. Unless intervened upon by therapies like PR exercise, COPD patients face increased risks of mortality, hospitalizations, and decreased quality of life. PR programs delivered to COPD patients in which guidelines were followed to periodically monitor oxygen saturation, have shown significant improvements in mortality [58], exercise capacity [58, 59], health related quality of life[58, 59], and perceived dyspnea[69]. Therefore, determining accuracy of SpO_2 measurements by the LungFIT was a key step in developing an effective PR intervention tool for people with COPD.

6.2 Improvements Needed for LungFIT Measurements of Heart Rates During Exercise and Distance

Results from measurement points during exercise in heart rate measurements varied quite substantially in all 3 probes, and are thus all were below pre-determined validity thresholds in measuring heart rate during cycle ergometer and treadmill walking exercises. Despite validity thresholds not being met, HR measurements by all probes during both exercise tests had good reliable with ICC (3, 3) values no less than 0.87 (p<0.001). Potentially, the main reason for the inaccuracies observed in HR measurements may be attributed to motion artifacts from movement in hands during exercise tests. Thus, movements from exercise can easily create motion artifacts, interrupting or biasing measures of volume changes during each blood pulse within probes. HR accuracies may be improved by utilizing a finger probe that provides a more stable seal of the finger within it. Poor fitting within a finger probe may have been especially significant in the case of the LionsGate Technologies probe. While the Nonin and Masimo probes created a seal around a participant's finger with flexible and soft silicone, the interior of

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the LionsGate Technologies probe was designed with less flexible, hard, and smooth rubber. Thus, finger movements within this probe faced less resistance compared to the Nonin and Masimo probes. Furthermore, the LionsGate Technologies probe did not have a motion reduction application to compensate for the hand movements associated with exercise. SpO_2 measurements were less effected by motion artifact due to the Nonin 8500 pulse oximeter, Nonin probe and Masimo probe implementing algorithms that compensate for motion artifacts. Strategies behind these algorithms are increasing the signal averaging time or taking the highest SpO_2 measurement during the extended sampling time. This allows for SpO_2 measurements that are more representative of the true value and less biased by erroneous and poor quality measurements.

LungFIT HR measurements may also have been inaccurate during exercise due to poor detection of blood pulses from decreased perfusion in some subjects' fingertips during exercise. Blood flow during cycle ergometer and treadmill exercises can be shifted to increase blood flow to exercising muscles, leaving fingertips with decreased perfusion. However, this limitation was unlikely in the population tested, as subjects with known hypotension or low cardiac output would have been excluded from the study. HR measurements from pulse oximetry are prone to have greater inaccuracies than oxygen saturation measurements[98-100] and thus future interventions of the LungFIT monitoring patient home exercise should restrict heart rate measurements to resting points.

Distance measurements by the LungFIT during this study identified a significant area of concern that should be addressed in a future prototype. Great inaccuracy of distance measurements can be attributed to the use of an equation that factored in GPS detected latitude

and longitude coordinates to produce distances. The LungFIT application utilized the haversine

formula to determine distances travelled. This equation calculates distance along a sphere, like

the Earth, by comparing the differences between two spherical triangles made the radius of the

sphere and from changing latitudes and longitudes. By depending on accurate GPS detections of

latitude and longitude, inaccurate coordinates may have been a factor. GPS based measurements

may have been affected by outdoor walking tests being conducted on a relatively short, non-

linear course in an urban environment. GPS signals can be distorted by tall city buildings in an

urban setting interfering with signals[123]. Distance measurements could be improved in the next

LungFIT prototype by utilizing the manufacturer GPS[123] algorithm, rather than relying on

estimations from a non-manufacturer equation. However, obtaining licensing for the LungFIT

application to be allowed to use Apple Inc. manufacturer GPS distance measurements may be an

obstacle. Utilizing accelerometry from the smartphone in order to measure steps walked can be

another potential strategy to more accurately estimate distance travelled. In order to implement

this function, accelerometry thresholds indicating a step walked from a standardized smartphone

placement would need to be determined and integrated into an algorithm.

6.3 Functionality Assessment

In this study, the LungFIT was found to be easy to use, free of software issues like

unexpected shutdowns and other operating malfunctions, and with minimal navigation and setup

issues when used by a healthy, adult population with experience using a smartphone. Along with

the rise in smartphone use in Canada, the number of health applications available for download is

increasing despite a lack of quality control of these applications [124]. In order to confidently and

safely deliver TR to COPD patients, quality functionality and usability is required from the

LungFIT. Furthermore, research evaluating these factors was necessary as they can affect

adherence and clinical impact as complicated applications can deter use[125]. Users can have a wide range of familiarity with using smartphone applications and pulse oximeter probes, and thus, the LungFIT must be simple enough to use that those with lower smartphone dexterity will understand how to use it. The Phone Oximeter had MPUQ scores of 82% and 78% in medical personnel samples from Canada and Uganda[109]. The LungFIT scored just as well on the adapted MPUQ at 93%, thus, further development of a more sophisticated LungFIT that includes additional functions and options is justified. Furthermore, with the majority of negative responses on the MPUQ pertaining to the LungFIT's appearance and interface, the monitoring components of the LungFIT were deemed easy to understand and use.

The mean times and SDs for the time-to-complete test of the functionality assessment reinforce an overall ease of use of the LungFIT. Tasks 4 and 5 of the normal protocol had the most variation and time required as the majority of the LungFIT setup occurring during these tasks. However, participants underwent the time-to-complete assessment immediately after being introduced to the LungFIT and additional use of the iPhone and application should allow for learning effect to eliminate the setup and navigation issues observed. The advanced functionality assessment was conducted as after the first 10 subjects, it was noticed that there were no software problems with the LungFIT application, while many of the errors made were due to unfamiliarity with an iPhone. Thus, the advanced protocol for the time-to-complete test was implemented to focus tests more on identifying setup and navigation issues with the LungFIT. This aim was successful in better identifying these issues as 3 of the 4 navigation or setup issues observed occurred with subjects from the advanced protocol. A key reason for this observation can be attributed to a lack of learning effect as participants began the time-to-complete test just 10 to 15 minutes after being introduced to the LungFIT.

6.4 Comparison Between Study Sample and COPD Population

The study attempted to recruit and test 15 subjects that were age and sex matched to the

COPD population in Canada. Although successful in testing 15 subjects, the mean age of the

study sample was younger than Canada's COPD population. The study had a mean age of 47.2

years old with a SD of ±7.54 years and range of 35 to 60 years old. In comparison, about 91% of

Canadians with COPD are over the age of 45, with the majority of those Canadians being over

the age of 65 years old[126]. Thus, a limitation of this study was not age-matching the sample to

the COPD population , as 7 of the 15 subjects were 45 years old or younger. In addition, the

oldest subject was 60 years old, despite about 47% of Canadians with COPD being at least 65

years old[126].

The proportion of sexes in this study's sample was better matched to the COPD

population. In Canada, about 56% of those with COPD identify as females[126], this was

comparable to two thirds of the sample population being females. Inclusion of only one to two

additional male subjects would have created a closer representation.

The purpose of age matching the sample population was to produce a similar

representation of smartphone experience according to age cohorts. This study resulted in 13 out

of 15 subjects identifying as having at least an advanced knowledge of how to use a smartphone

from their daily use of one. Although this matched the prevalence rate of 78.4% of wireless

phone plans in Canada[127], this data may not have been the best representation of smartphone

experience by Canadians aged 60 and older. Furthermore, the oldest subject of 60 years was the

only subject to identify as being a novice smartphone user. Smartphone-experience and age

matching were additionally difficult in this study with the implementation of the advanced

functionality test protocol and from recruitment challenges. The advanced protocol used on the last five subjects required subjects to have previous experience using an iPhone, thus, these subjects were screened to be advanced or expert smartphone users. Recruiting subject over the age of 60 years old was difficult for this study due to those in older age cohorts often having co-morbidities and other health issues that excluded them from the study. In addition, this study recruited subjects within a hospital and university faculty largely consisting of middle-aged adults that have full time jobs. Thus, many found making a time commitment with no financial incentive challenging to rationalize. Those who did participate in the study had previous experience as researchers, were healthcare practitioners, or friends and family of laboratory staff.

The inclusion criteria for the study sought to recruit 'healthy' adults free of any limitation to exercise. Subject characteristic data suggested that the sample was relatively healthy for low intensity exercise. By analyzing the SDs for height and weight, subjects varied from each other, giving a good range of body types in the study. Overall, the mean BMI was $26.3 kg/m^2$, classifying the sample as slightly overweight. Mean resting heart rate and oxygen saturation values were within healthy limits, although there was a large SD in resting heart rates. Thus, in combination with varied BMIs, the sample provided a good diversity of subjects that allowed the LungFIT to be tested on a variety of subjects of varied physical fitness and anthropometrics.

6.5 Clinical Implications

With only 1.2% of Canadians with COPD having access to PR each year[72], significant healthcare, patient, and geographic barriers justify the need for increased TR interventions for PR [76, 77]. Patient identified barriers of inflexible PR program schedules[77] can also be addressed by the LungFIT by allowing users to exercise at their own convenience. The smartphone platform

used for the LungFIT potentially possess a significant contribution to reducing geographic barriers of PR program delivery. With distance from a PR program and transportation issues being large barriers to PR attendance[76, 78], the LungFIT has the potential to enable communication between a home-based COPD patient and an off-site PR practitioner. The ability to communicate PR program parameters and progress will allow for increased assess of PR along with providing integral social support and encouragement during a PR program. The smartphone platform of the LungFIT also eliminates the need for multiple telemonitoring devices by only using smartphone technology users will be more familiar and comfortable with[88] as the widespread use of cellular phones continues to grow in Canada[127].

The LungFIT can also help deliver effective maintenance PR programs. Maintenance programs after initial PR have been shown to sustain exercise capacity and quality of life increases from PR[79, 81, 82]. In addition, sustained, long-term physical activity is clinically effective in slowing the development of COPD severity[82]. By potentially reducing significant barriers to PR access and adherence, the LungFIT has the potential to monitor home-based exercise, thus improving the risk of mortality and exercise capacity of users.

Telemonitoring interventions on chronic lung diseases have proven to be feasible[85], well complied to[85], and effective in improving quality of life[86] and reducing hospitalizations by detecting changes in symptoms earlier[85, 86]. Continued development of the LungFIT's monitoring capabilities will advance the LungFIT to be able to deliver comprehensive PR programs to COPD patients without access to a conventional program simply though the use of a smartphone. Hayton et al[77] found that COPD patients have reported non-adherence to PR due to fears of exercise-induced breathlessness and dyspnea. The ability of the LungFIT to constantly monitor

SpO$_2$ accurately, even during exercise, may aid in self-efficacy and motivation to continue exercise and reduce sensations of perceived dyspnea. Future long-term studies assessing adherence and clinical effectiveness of the LungFIT delivering TR will better determine these psychophysical factors. Self-monitoring of SpO$_2$ should also allow patients to establish an exercise intensity that maintains their oxygen saturation at a safe level.

6.6 Next Steps in LungFIT Development for Telerehabilitation

In addition to measuring distance to assess exercise intensity, the current prototype had the ability to record accelerometer data from the Smartphone itself. This accelerometer data will be used in conjunction with data collected from the Cosmed K4 b2 to create an algorithm for future prototypes to estimate energy expenditure. As well, future prototypes of the LungFIT will be able to screen patients for daily dyspnea levels using interactive Borg and RPE scales. Education and self-management modules will also be incorporated into the LungFIT application in order to meet all requirements of PR. Further development of the LungFIT interface to integrate these functions are currently being planned though the use of focus groups of COPD patients. This bottom-up approach will help identify the specific interface functions and appearance desired by COPD patients. Marshall et al[88] identified that requirements may include exercise reminders, visual and audible feedback of SpO$_2$ and HR, physiotherapist feedback, and adherence log to the program. Further testing of the LungFIT is also currently planned to further investigate validity and reliability of SpO$_2$ and HR measurements, but on a chronic lung disease population. This study will allow for evaluation of an updated distance measurement function as well as determine the accuracy of LungFIT probes in a population that is prone to oxygen desaturation, lower blood pressures, and decreased exercise capacities[2].

6.7 Current State on The Product Life Cycle

This study occurred in the product development stage of the LungFIT in its product life cycle[128]. Results from this study will be considered and used to further improve the LungFIT. Thus, further testing in the product development stage is still required. A final LungFIT model may be produced after interface improvements from LungFIT focus groups are implemented and tested for functionality and usability. Before the LungFIT can reach its market launch into PR practices in Canada, market testing on potential COPD and other chronic lung disease patients will be completed[128] through a TR, randomized controlled trial study of a comprehensive PR program of at least 4 weeks. If the intervention proves to be feasible, able to screen patients prior to exercise, free of adverse events during monitored sessions, and at least as effective as traditional PR in improving exercise capacity and health related quality of life, then market launch should be considered as the next step.

7. Conclusion

In conclusion, testing pulse oximeter finger probes by Nonin, Masimo, and LionsGate Technologies in a novel smartphone system called the LungFIT revealed that all three probes were valid in measuring oxygen saturation, but invalid in measuring heart rate during low intensity cycling and walking exercise. Probes ranged from moderate to good reliability in both oxygen saturation and heart rate measurements. Despite strong mean biases in measurements of resting heart rate, high limits of agreement classified probes as invalid in measuring heart rate during rest when compared to standards of medically used 12-lead electrocardiogram and pulse oximeter. Thus, motion artifacts during exercise were a considerable factor in biasing heart rate measurements. From the three probes tested, the Masimo probe proved to be the most valid and reliable overall and should be the probe to use with future LungFIT prototypes. Despite potentially being the most feasible probe for a TR intervention due to its low cost, the LionsGate Technologies prototype probe performed the worst overall.

Measurements of distance were a major limitation found with the LungFIT. With only about 60% of walked distances captured, the distance function of the application will be redesigned in the next LungFIT prototype. Utilizing a combination of GPS and smartphone accelerometer measurements instead of relying on an external equation using GPS coordinates should improve distance measurements.

Functionality assessment involving a time-to-complete assessments and the adapted Mobile Phone Usability Questionnaire demonstrated a general ease of use of the LungFIT with no software issues observed. The time-to-complete assessment found a number of setup and navigation issues that should be corrected by learning effects and improved instructions. In

addition, the MPUQ identified issues with the affect aspect and multimedia properties of the LungFIT. These issues will be solved through a bottom-up approach utilizing focus groups on COPD patients to create a user-friendly and attractive interface for the LungFIT.

This validation study of the current prototype of the LungFIT was able to determine the accuracies of oxygen saturation, heart rate, and distance measurements during low intensity exercise. Positive findings in measurements of oxygen saturation and ease of use were encouraging findings in the development of the LungFIT. Improving the LungFIT interface, and accuracy of heart rate and distance measurements will be key issues to address moving forward.

8. Tables, Figures, Illustrations, and Other Graphics

Table 1: GOLD Patient Categories (Adapted from Gruffydd-Jones, K, 2012)

Patient Category A **Low risk, Less symptoms** GOLD stage: 1-2 Exacerbations: 0-1/year mMRC: 0-1 CAT: <10	**Patient Category B** **Low risk, More symptoms** GOLD stage: 1-2 Exacerbations: 0-1/year mMRC: >2 CAT: >10
Patient Category C **High risk, Less symptoms** GOLD stage: 3-4 Exacerbations: >2/year mMRC: 0-1 CAT: <10	**Patient Category D** **High risk, More symptoms** GOLD stage: 3-4 Exacerbations: >2/year mMRC: >2 CAT: >10

CAT- Chronic Obstructive Pulmonary Disease Assessment Tool, GOLD- The Global Initiative for Chronic Obstructive Lung Disease, mMRC- Modified British Medical Research Council Dyspnoea Scale

Table 2: Summary of Systemic Effects and Influence During Exercise

Systemic Effect	Description	Effect on Exercise	Other Associated Symptoms
Dyspnea	-Discomfort from breathing -Breathlessness	-Exercise intolerance -Fatigue	-Contributes to exercise avoidance and inactivity -Decreased health related quality of life
Peripheral Muscle Dysfunction	-Physical inactivity, poor nutrition, and smoking contribute to deconditioning and decrease in muscle strength and endurance	-Muscular fatigue, especially in lower limb muscles	-Dyspnea -Further muscle weakening and deconditioning
Ventilation Constraints	-Increased ventilator requirement for a given workload -Lung hyperinflation -Impaired gas exchange and breathing mechanics	-Exercise-induced hypoxia -Increased work of breathing	-Lactic acidemia -Weakened inspiratory muscle function
Cardiac Dysfunction	-Pulmonary arterial hypertension -Increased right ventricular afterload	-Exercise intolerance -Exercise-induced hypoxia	-Hypoxia in peripheral muscles -Dyspnea
Lactic Acidosis	-Increased lactic acid production for a given workload	-Increased drive to breathe	-Dyspnea

Table 3: Summary of COPD Etiologies

Etiology	Description
Smoking	-Lifetime smoking increases risk of COPD by 30-40% -Accelerates lung function decline
Genetics	-Contribute to susceptibility to developing COPD - α1- antitrypsin deficiency increases damage to tissue from smoking -Future research will strengthen knowledge base
Pollution	-Excessive exposure to Pm10 leads to oxidative stress and damage -Increased concentration of air pollutants may negatively affect lung function -Domestic exposures to burning fuels is associated with increased COPD prevalence
Acute Exacerbations	-Events of prolonged and amplified symptoms which worsen disease severity, health related quality of life, and mortality risk -An increase in exacerbation frequency is positively associated with increased mortality -Further accelerate lung function decline and exercise intolerance symptoms

Table 4: Gold Standard Devices Used to Compare Against the LungFIT

Measure	LungFIT	Gold Standard
Heart Rate	Nonin (soft sensor)/Masimo (plastic finger clip)/LionsGate Technologies (plastic finger clip) Finger probes	12-Lead ECG
Oxygen Saturation	Nonin (soft sensor)/Masimo (plastic finger clip)/LionsGate Technologies (plastic finger clip) Finger probes	Nonin 8500 Pulse oximeter
Distance	Distance Calculator based on GPS Latitude and Longitude	Measured course (362 metres)

Table 5: Subject Characteristics

Characteristic	Value	Standard Deviation
Subjects (n)	15	
Mean Age	47.20	7.54
Sex	10 Female/5 Male	
Mean Height (cm)	167.33	9.96
Mean Weight (Kg)	73.66	16.25
Smoking Status	Never Smoker=8	
	Ex-Smoker=6	
	Active Smoker=1	
Mean Smoking History (pack years)	3.78	5.09
Smartphone Experience	Novice=1	
	Intermediate=1	
	Advanced=10	
	Expert=3	
Mean Resting Heart Rate (from Nonin 8500 Pulse Oximeter)	68.27	14.64
Mean Resting Oxygen Saturation (from Nonin 8500 Pulse Oximeter)	96.4	1.4

Table 6: Time-to-Complete Assessment

Original Protocol Tasks (n=10)	Mean Time-to-Complete (SD) (seconds)	Median Time-to-Complete (IQR) (seconds)
1. Get to iPhone's home screen and select the PC app	10.28 (±4.81)	9.60 (7.92 - 12.45)
2. Properly exit the application	2.95 (±0.70)	3.10 (2.30 - 3.62)
3. Assemble and connect probe to iPhone	18.68 (±3.41)	18.85 (15.48 - 21.35)
4. Insert iPhone into the armband and put armband on to arm.	20.04 (±7.96)	18.60 (13.50 - 27.60)
5. Put on probe, re-open PC app, and begin recording data.	13.16 (±6.26)	10.30 (8.50 - 16.80)
6. What is your oxygen saturation and heart rate?	6.81 (±3.97)	6.20 (4.85 - 7.05)
7. Take off probe and remove armband from arm.	9.94 (±4.31)	8.80 (7.70 - 10.70)
8. Remove iPhone from armband and stop recording data.	5.98 (±2.06)	6.70 (5.00 - 7.30)
9. Exit application and turn off iPhone.	10.32 (±5.37)	10.80 (4.20 - 14.60)
Original Protocol Total Time (n=10)	98.57 (±21.97)	93.80 (76.12 - 113.18)
Advanced Protocol Total Time (n=5)	167.38 (±41.12)	159.34 (135.22 - 196.37)

IQR-Interquartile Range, SD-Standard Deviation

Table 7: Issues and Problems Observed During Time-to-Complete Assessment

Identified Issue/Problem	Frequency	Type of Problem (iPhone, setup, navigation, software)
Pressed other applications by accident	5	iPhone
Trouble finding the 'power' button	3	iPhone
Frustration/assistance using the armband	3	Armband Setup
Help required to record data	2	Navigation
Help required to find 'exit' button on application	1	Navigation
Trouble removing probe from iPhone	1	Setup

Table 8: Adapted Mobile Phone Usability Questionnaire Responses

Questionnaire Section	Overall Score	Negative Responses (Question Theme)	Frequency of Negative Responses
Ease of Learning and Use	208/210 = 99%	Colour coding	1
		Armband use	1
Helpfulness and Problem-Solving Capabilities	27/30 =90%	Clarity of instruction manual	2
		Error correcting	1
Affective Aspect and Multimedia Properties	98/120 = 82%	Frustration of system use	1
		System attractiveness	3
		Picture quality and size	2
		Excited by use	6
		Miss the LungFIT if they no longer had it	7
		Proud of product	3
Commands and Minimal Memory Load	29/30 = 97%	Relevance of graphics and icons	1
Control and Efficiency	72/75 = 96%	LungFIT stopped unexpectedly	1
		Adequate information displayed	1
		Operation with one hand	1
Overall Score	434/465 = 93%		31

Table 9: Mean and Median Oxygen Saturations and Heart Rates During Cycle Ergometer and Treadmill Walking Exercise Tests

Measurement	Cumulative Mean	Cumulative Standard Deviation	Cumulative Median	Cumulative Interquartile Range
Nonin: Cycle Test HR	86.72 beats/min	17.12 beats/min	85.00 beats/min	75.00 - 97.75 beats/min
Masimo: Cycle Test HR	91.08 beats/min	20.59 beats/min	87.00 beats/min	78.00 - 102.00 beats/min
LionsGate Technologies: Cycle Test HR	81.42 beats/min	13.96 beats/min	82.00 beats/min	72.00 - 90.00 beats/min
Nonin: Cycle Test SpO$_2$	95.90%	1.52%	96.00%	95.00 - 97.00%
Masimo: Cycle Test SpO$_2$	97.11%	1.39%	97.00%	96.00 - 98.00%
LionsGate Technologies: Cycle Test SpO$_2$	96.93%	1.61%	97.00%	96.00 - 98.00%
Nonin: Treadmill Test HR	88.48 beats/min	15.15 beats/min	89.50 beats/min	77.00 - 99.25 beats/min
Masimo: Treadmill Test HR	90.05 beats/min	21.91 beats/min	87.00 beats/min	77.00 - 99.00 beats/min
LionsGate Technologies: Treadmill Test HR	82.18 beats/min	13.78 beats/min	82.00 beats/min	70.00 - 91.00 beats/min
Nonin: Treadmill Test SpO$_2$	95.25%	1.62%	95.00%	94.00 - 96.00%
Masimo: Treadmill Test SpO$_2$	96.58%	1.37%	97.00%	96.00 - 98.00%
LionsGate Technologies: Treadmill Test SpO$_2$	96.75%	1.35%	97.00%	96.00 - 98.00%

HR-Heart Rate, SpO$_2$-Oxygen Saturation

Table 10: Nonin Probe - Cycle Test Oxygen Saturation and Heart Rate Bland-Altman Calculations (n=15)

Nonin Cycle Test Measurement Points	SpO$_2$ MD (%)	SpO$_2$ SD (±%)	SpO$_2$ 95% LoA Range (%)	HR MD (beats/min)	HR SD (±beats/min)	HR 95% LoA Range (beats/min)
1	-0.67	0.82	3.26	-0.80	2.60	10.39
2	-0.79	1.97	7.87	-4.29	13.06	52.26
3	-1.31	1.70	6.81	-8.31	18.83	75.32
4	-0.15	1.21	4.86	0.23	2.62	10.48
5	-0.21	1.05	4.20	-2.86	5.23	20.92
6	-0.31	0.95	3.79	-2.15	6.20	24.81
7	-0.33	0.98	3.90	-0.80	3.32	13.28
8	-0.54	0.97	3.87	0.08	1.44	5.76
9	-0.58	1.16	4.66	-3.08	14.51	58.03

HR-Heart Rate, LoA-Limit of Agreement, MD-Mean Difference, SD-Standard Deviation, SpO$_2$-Oxygen Saturation

Table11: Nonin Probe - Treadmill Test Oxygen Saturation and Heart Rate Bland-Altman Calculations (n=15)

Nonin Treadmill Test Measurement Points	SpO$_2$ MD (%)	SpO$_2$ SD (±%)	SpO$_2$ 95% LoA Range (%)	HR MD (beats/min)	HR SD (±beats/min)	HR 95% LoA Range (beats/min)
1	-1.07	1.10	4.40	0.33	1.88	7.51
2	-0.73	1.16	4.65	3.53	12.00	48.00
3	-0.73	2.19	8.75	3.87	11.44	45.78
4	-1.00	0.85	3.38	-1.73	5.24	20.97
5	-0.29	1.38	5.53	4.64	9.56	38.22
6	-0.43	1.34	5.37	0.43	4.89	19.58
7	-0.73	0.96	3.84	0.33	3.35	13.41
8	-0.93	2.37	9.47	2.57	11.32	45.27
9	-0.80	2.68	10.71	4.20	12.68	50.71

HR-Heart Rate, LoA-Limit of Agreement, MD-Mean Difference, SD-Standard Deviation, SpO$_2$-Oxygen Saturation

Table 12: Masimo Probe - Cycle Test Oxygen Saturation and Heart Rate Bland-Altman Calculations (n=15)

Masimo Cycle Test Measurement Points	SpO$_2$ MD (%)	SpO$_2$ SD (±%)	SpO$_2$ 95% LoA Range (%)	HR MD (beats/min)	HR SD (±beats/min)	HR 95% LoA Range (beats/min)
1	0.80	1.01	4.06	-0.80	1.42	5.70
2	0.86	1.17	4.67	-10.47	32.51	130.04
3	0.86	1.17	4.67	-4.71	12.04	48.16
4	0.67	0.98	3.90	-0.20	2.46	9.82
5	0.93	0.88	3.53	0.47	1.96	7.84
6	0.87	1.13	4.50	0.27	1.53	6.13
7	0.53	0.83	3.33	-0.93	3.94	15.74
8	0.27	1.03	4.13	0.53	2.26	9.05
9	0.27	0.80	3.20	0.53	1.25	4.98

HR-Heart Rate, LoA-Limit of Agreement, MD-Mean Difference, SD-Standard Deviation, SpO$_2$-Oxygen Saturation

Table 13: Masimo Probe - Treadmill Test Oxygen Saturation and Heart Rate Bland-Altman Calculations (n=15)

Masimo Treadmill Test Measurement Points	SpO$_2$ MD (%)	SpO$_2$ SD (±%)	SpO$_2$ 95% LoA Range (%)	HR MD (beats/min)	HR SD (±beats/min)	HR 95% LoA Range (beats/min)
1	0.13	1.25	4.98	-0.07	2.02	8.07
2	0.20	1.26	5.06	9.47	18.22	72.86
3	0.93	1.59	6.37	6.64	18.17	72.67
4	0.20	1.32	5.28	-2.07	4.79	19.15
5	0.93	1.71	6.84	8.13	17.65	70.59
6	0.93	1.21	4.83	8.07	18.07	72.26
7	0.20	1.21	4.83	-0.80	3.59	14.36
8	0.64	1.28	5.11	0.57	12.72	50.88
9	1.00	1.24	4.96	4.00	11.22	44.90

HR-Heart Rate, LoA-Limit of Agreement, MD-Mean Difference, SD-Standard Deviation, SpO$_2$-Oxygen Saturation

Table 14: LionsGate Technologies Probe - Cycle Test Oxygen Saturation and Heart Rate Bland-Altman Calculations (n=15)

LionsGate Technologies Cycle Test Measurement Points	SpO$_2$ MD (%)	SpO$_2$ SD (±%)	SpO$_2$ 95% LoA Range (%)	HR MD (beats/min)	HR SD (±beats/min)	HR 95% LoA Range (beats/min)
1	0.27	1.75	7.00	0.20	3.45	13.79
2	1.08	1.19	4.75	-11.83	22.41	89.63
3	-0.23	2.83	11.33	-17.25	26.80	107.21
4	0.14	2.80	11.19	-1.50	5.17	20.68
5	0.64	1.78	7.12	-15.07	25.77	103.09
6	0.73	1.33	5.34	-16.20	25.93	103.74
7	0.80	0.94	3.76	-3.53	5.41	21.64
8	0.43	1.09	4.36	-11.21	20.02	80.08
9	0.64	1.08	4.33	-13.86	24.75	99.01

HR-Heart Rate, LoA-Limit of Agreement, MD-Mean Difference, SD-Standard Deviation, SpO$_2$-Oxygen Saturation

Table 15: LionsGate Technologies Probe - Treadmill Test Oxygen Saturation and Heart Rate Bland-Altman Calculations (n=15)

LionsGate Technologies Treadmill Test Measurement Points	SpO₂ MD (%)	SpO₂ SD (±%)	SpO₂ 95% LoA Range (%)	HR MD (beats/min)	HR SD (±beats/min)	HR 95% LoA Range (beats/min)
1	0.53	1.13	4.50	-3.60	6.96	27.83
2	0.93	1.38	5.54	-0.64	6.08	24.34
3	1.25	1.06	4.22	-3.25	10.38	41.50
4	0.86	0.77	3.08	-7.50	7.67	30.69
5	0.93	1.62	6.50	-5.20	7.95	31.79
6	1.07	1.44	5.75	-3.07	10.57	42.29
7	0.07	1.83	7.32	-5.40	6.23	24.92
8	0.29	2.73	10.92	-5.93	9.88	39.52
9	1.13	1.06	4.24	-4.47	8.03	32.14

HR-Heart Rate, LoA-Limit of Agreement, MD-Mean Difference, SD-Standard Deviation, SpO₂-Oxygen Saturation

Table 16: Mean Biases and Limits of Agreements for Oxygen Saturation and Heart Rate Measurements During Rest and Exercise

Test	Measurement Point	Nonin Probe	Masimo Probe	LionsGate Technologies Probe
Cycle Test - Oxygen Saturation (%)	Rest Bias	-0.40	0.67	0.41
	Rest LoA (95% CI)	±2.21 (±1.06)	±1.94 (±0.93)	±3.78 (±1.82)
	Exercise Bias	-0.64	0.73	0.51
	Exercise LoA (95% CI)	±3.04 (±1.46)	±2.33(±1.12)	±3.54 (±1.70)
Cycle Test - Heart Rate (beats/min)	Rest Bias	-0.49	-0.64	-1.61
	Rest LoA (95% CI)	±16.61 (±7.98)	±16.99 (±8.17)	±30.32 (±14.58)
	Exercise Bias	-3.72	-0.83	-16.44
	Exercise LoA (95% CI)	±23.39 (±11.24)	±16.54 (±7.95)	±50.22 (±24.14)
Treadmill Test – Oxygen Saturation (%)	Rest Bias	-0.93	0.18	0.48
	Rest LoA (95% CI)	±2.44 (±1.17)	±2.64 (±1.27)	±3.24 (±1.56)
	Exercise Bias	-0.65	0.74	0.88
	Exercise LoA (95% CI)	±3.71 (±1.78)	±2.79 (±1.34)	±3.26 (±1.57)
Treadmill Test - Heart Rate (beats/min)	Rest Bias	-0.36	-0.98	-5.45
	Rest LoA (95% CI)	±12.47 (±6.00)	±12.89 (±6.20)	±15.32 (±7.37)
	Exercise Bias	3.66	6.09	-3.96
	Exercise LoA (95% CI)	±23.69 (±11.39)	±33.40 (±16.06)	±18.72 (±9.00)

Table 17: LungFIT Intraclass Correlation Coefficients (ICC) of Reliability of Oxygen Saturation and Heart Rate

Test	Probe	ICC (3,3)	Statistical Significance (p<0.05)
Cycle Test - Oxygen Saturation (%)	Nonin	0.80	<0.001
	Masimo	0.87	<0.001
	LionsGate Technologies	0.65	<0.001
Cycle Test - Heart Rate (beats/min)	Nonin	0.95	<0.001
	Masimo	0.96	<0.001
	LionsGate Technologies	0.88	<0.001
Treadmill Test – Oxygen Saturation (%)	Nonin	0.71	<0.001
	Masimo	0.82	<0.001
	LionsGate Technologies	0.68	<0.001
Treadmill Test - Heart Rate (beats/min)	Nonin	0.97	<0.001
	Masimo	0.87	<0.001
	LionsGate Technologies	0.90	<0.001

Table 18: LungFIT Distance Measurements and Mean Difference/Bias

| Measure	Lap 1	Lap 2	Lap 3
Mean Distance (m)	218.79	207.77	209.06
Median Distance (m)	205.00	206.30	203.10
Mean Distance Standard Deviation (m)	76.46	19.86	56.75
Mean Difference (m)	159.45	154.23	155.83
Median Difference (m)	157.00	155.70	158.90
Mean Difference Standard Deviation(m)	24.08	19.86	47.57
Interquartile Range (m)	21.00	29.20	23.35
Cumulative Mean Distance (m)	216.69		
Cumulative Median Distance (m)	205.00		
Cumulative Mean Distance Standard Deviation (m)	55.09		
Cumulative Mean Difference (m)	152.66		
Cumulative Median Difference (m)	157.00		
Cumulative Mean Difference Standard Deviation(m)	28.19		
Cumulative Interquartile Range (m)	193.70 – 219.00		
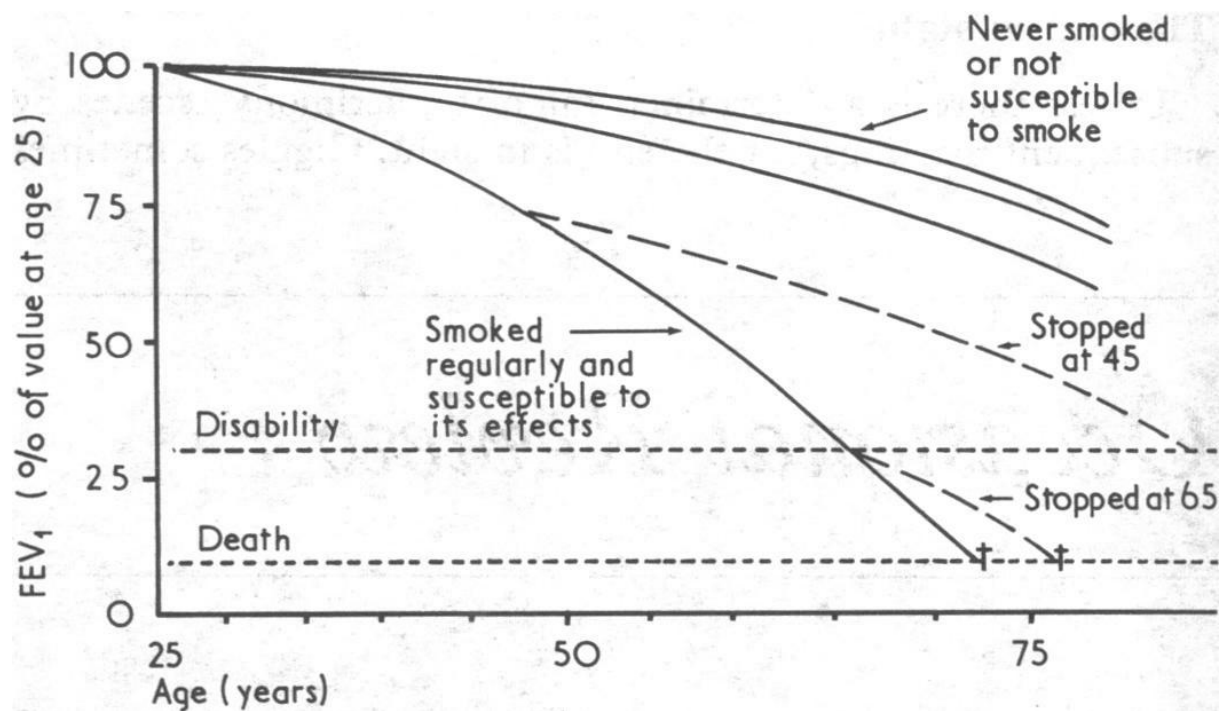
Figure 1: Risks for various men if they smoke: differences between these lines illustrate effects that smoking, and stopping smoking, can have on FEV1 of man who is liable to develop chronic obstructive lung disease if he smokes. t =Death, the underlying cause of which is irreversible chronic obstructive lung disease, whether the immediate cause of death is respiratory failure, pneumonia, cor pulmonale, or aggravation of other heart disease by respiratory insufficiency. Although this shows rate of loss of FEV, for one particular susceptible smoker, other susceptible smokers will have different rates of loss, thus reaching "disability" at different ages. (Fletcher and Peto, 1977) (Used with permission from the British Medical Journal)
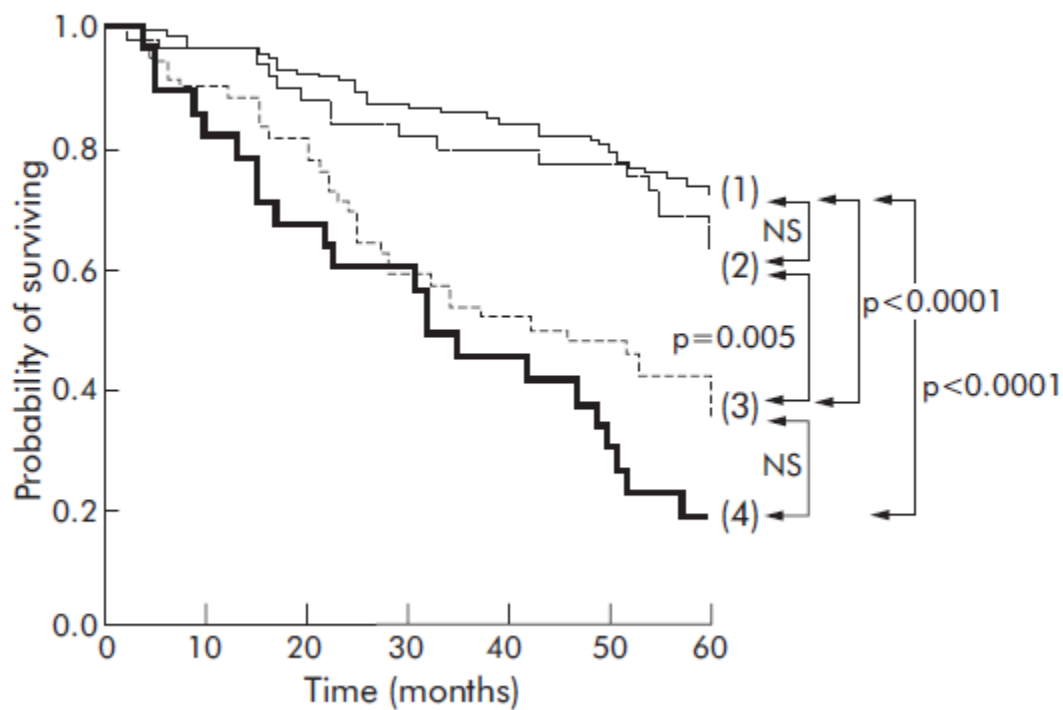
Figure 2: Kaplan-Meier survival curves by severity of exacerbations in patients with COPD: (1) no acute exacerbations of COPD; (2) patients with acute exacerbations of COPD requiring emergency service visits without admission; (3) patients with acute exacerbations of COPD requiring one hospital admission; (4) patients with readmission. (Soler-Cataluna, et al, 2005) (Used with permission from the British Medical Journal)
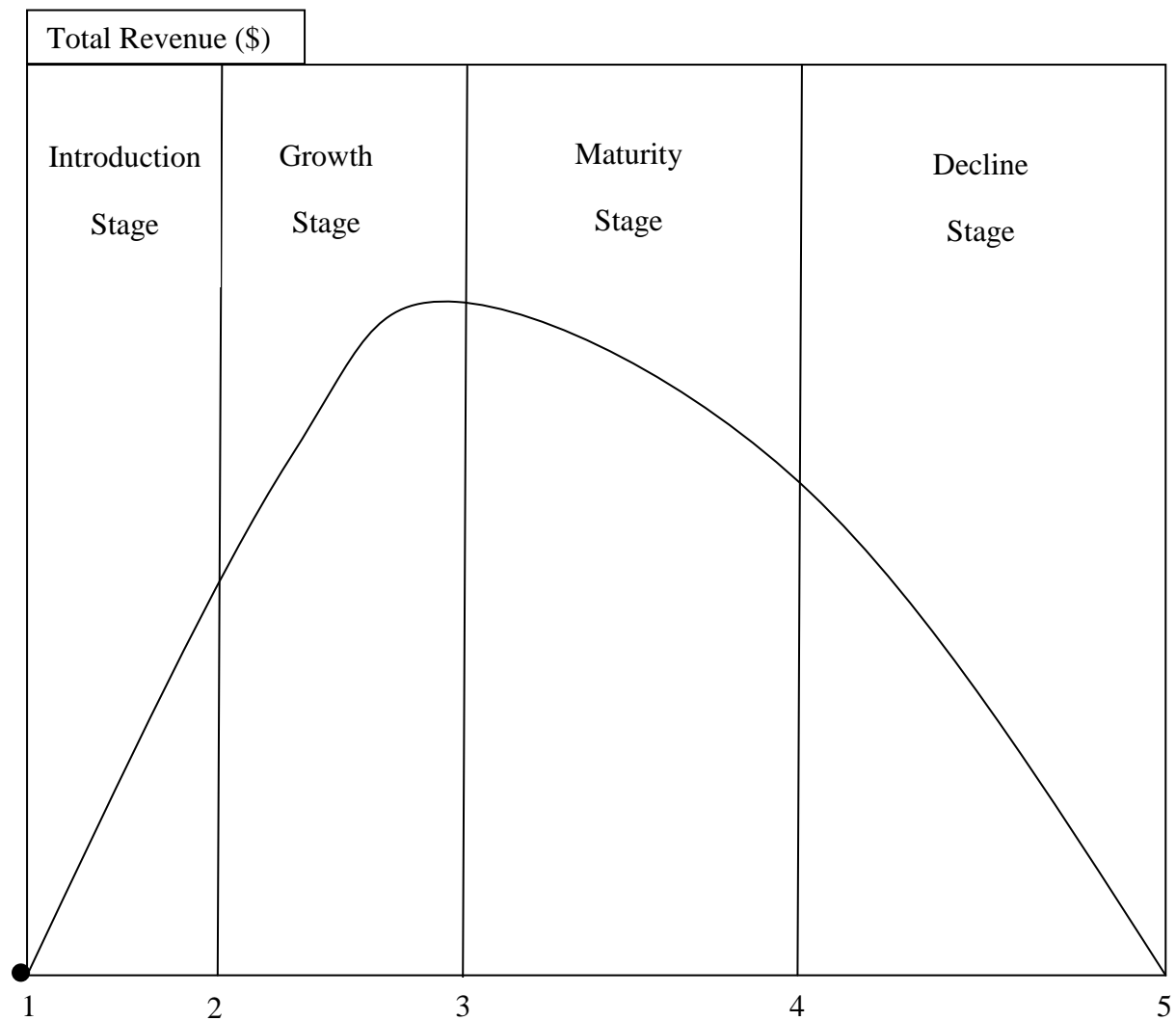
Figure 3: The Product Life Cycle (Adapted from Cox, W, 1967)
1 = Catalogue Birth
2 = Commercial Birth
3 = Maximum Monthly Revenue
4 = Commercial Death
5 = Catalogue Death
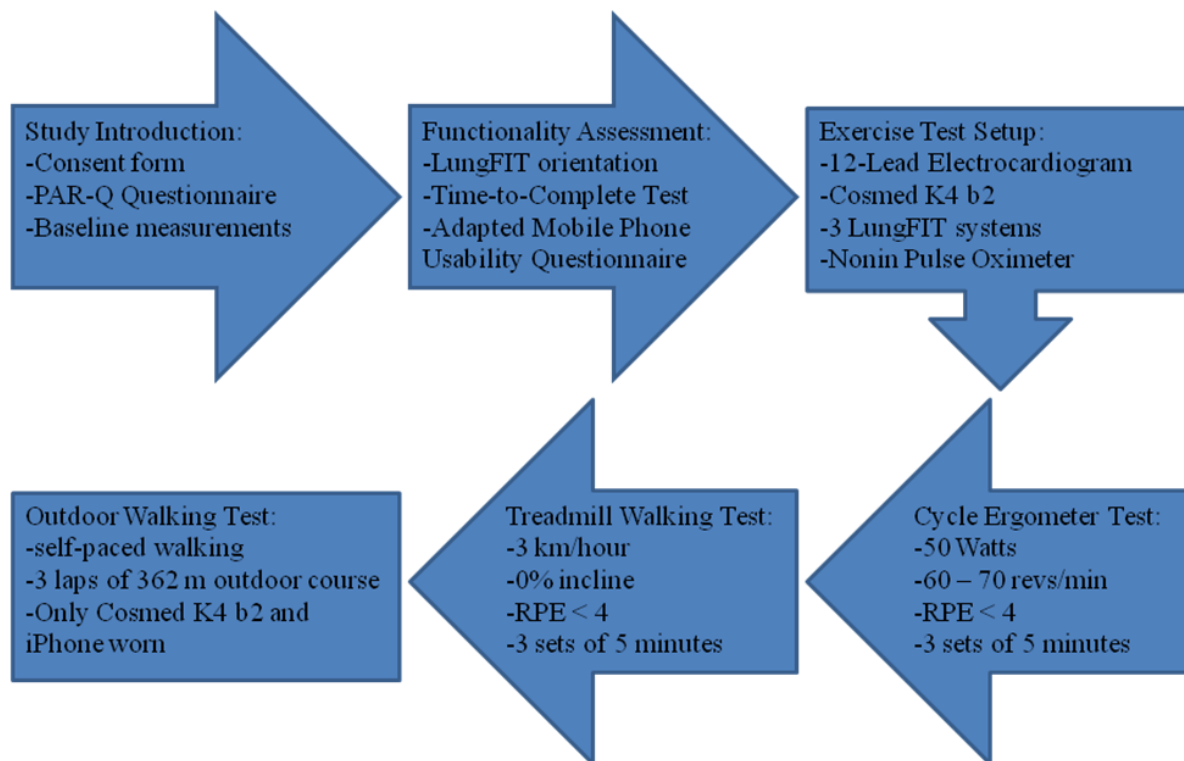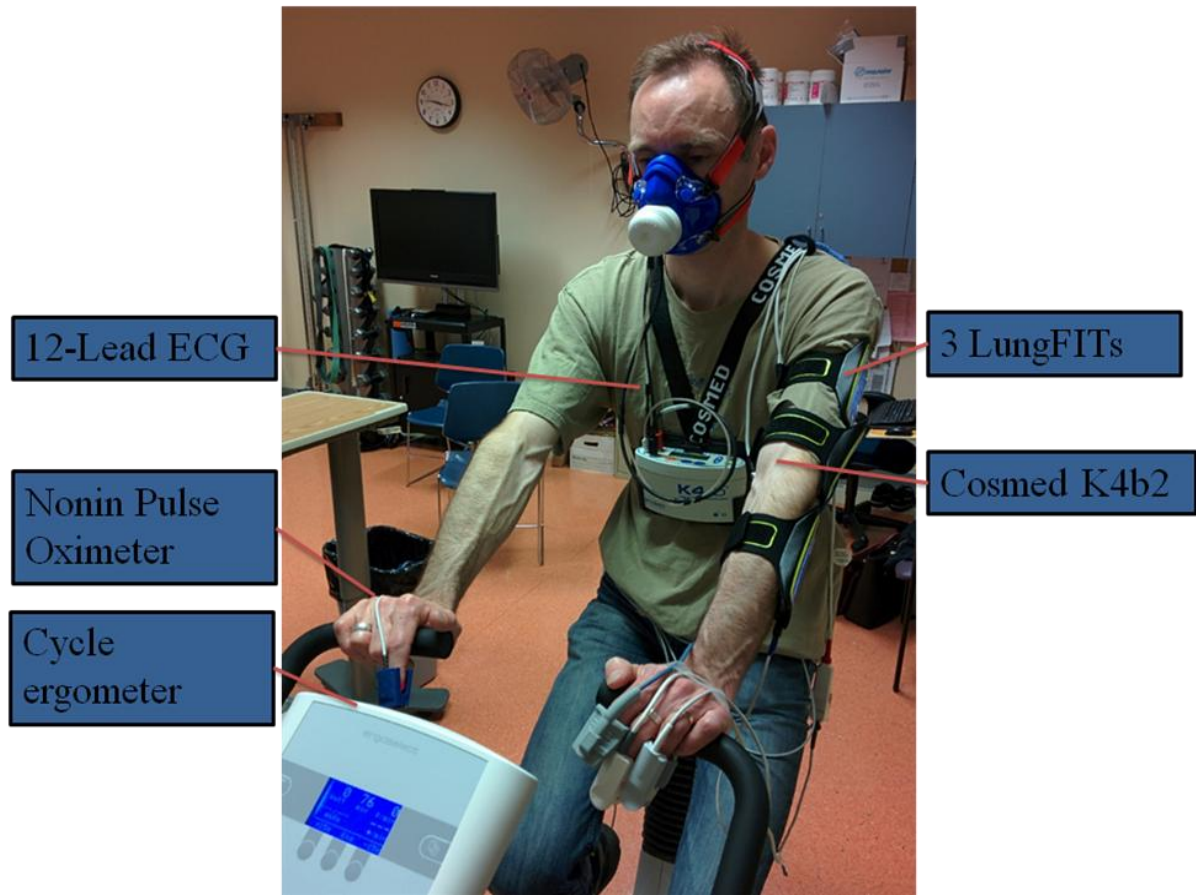●= Current location of the LungFIT on the Product Life Cycle

Study Introduction:
-Consent form
-PAR-Q Questionnaire
-Baseline measurements

Functionality Assessment:
-LungFIT orientation
-Time-to-Complete Test
-Adapted Mobile Phone
Usability Questionnaire

Exercise Test Setup:
-12-Lead Electrocardiogram
-Cosmed K4 b2
-3 LungFIT systems
-Nonin Pulse Oximeter

Cycle Ergometer Test:
-50 Watts
-60 – 70 revs/min
-RPE < 4
-3 sets of 5 minutes

Treadmill Walking Test:
-3 km/hour
-0% incline
-RPE < 4
-3 sets of 5 minutes

Outdoor Walking Test:
-self-paced walking
-3 laps of 362 m outdoor course
-Only Cosmed K4 b2 and
iPhone worn

Figure 4: Flow Diagram of Study Methodology

Figure 5: Equipment Setup for Heart Rate and Oxygen Saturation Measurements
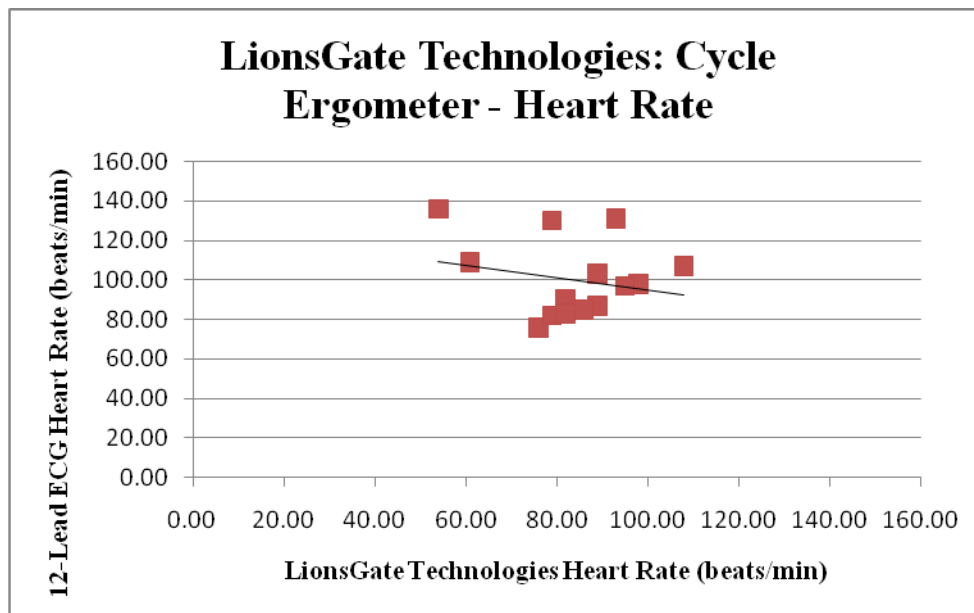
Nonin: Cycle Ergometer - Heart Rate
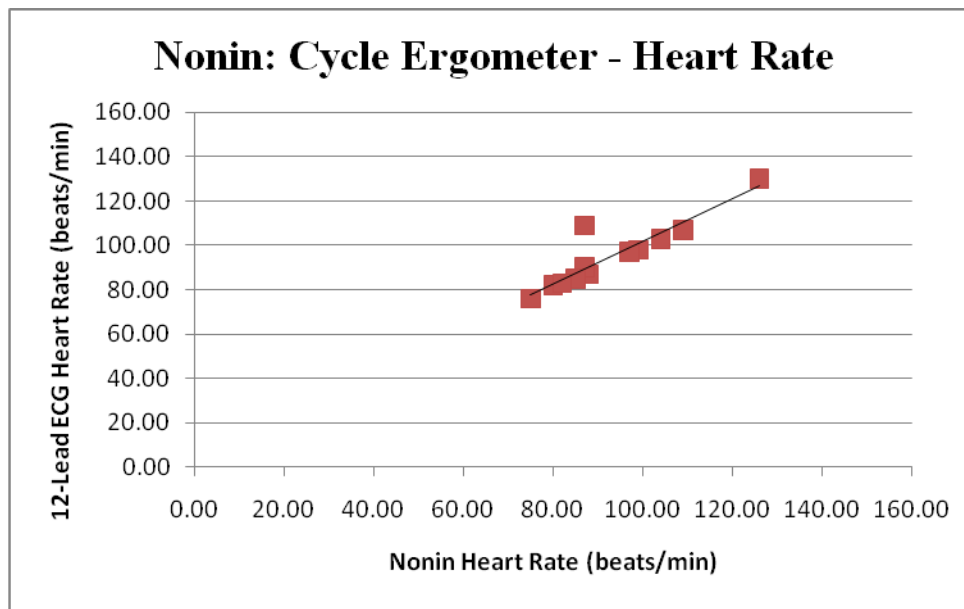
ECG-Electrocardiogram

Figure 6: Nonin probe versus 12-lead electrocardiogram at the end of exercise during the second set of the cycle ergometer test. N=13, 2 missing values. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the Nonin probe and the gold standard.

Masimo: Cycle Ergometer - Heart Rate
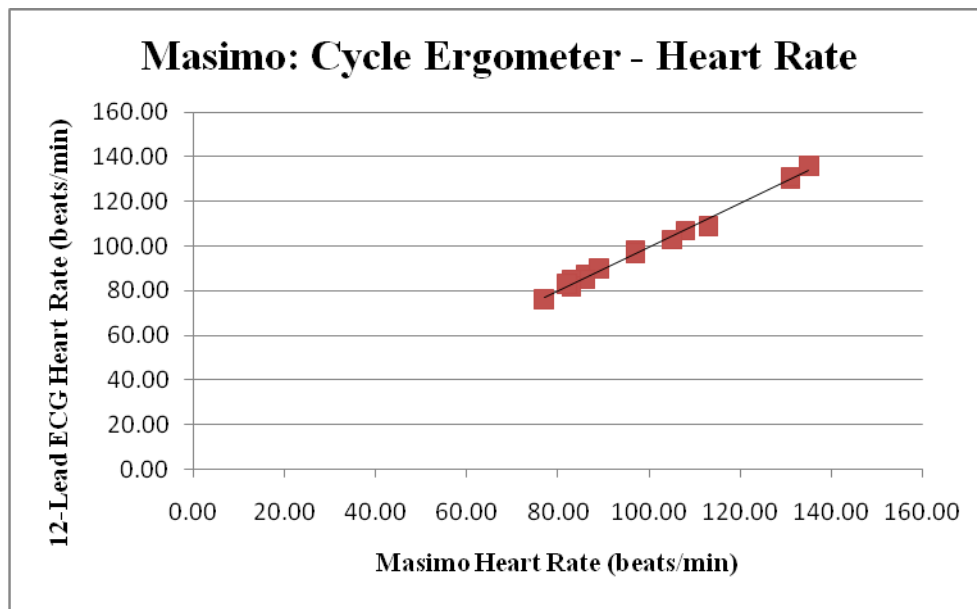
ECG-Electrocardiogram

Figure 7: Masimo probe versus 12-lead electrocardiogram at the end of exercise during the second set of the cycle ergometer test. N=15. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the Masimo probe and the gold standard.

LionsGate Technologies: Cycle Ergometer - Heart Rate

ECG-Electrocardiogram

Figure 8: LionsGate Technologies probe versus 12-lead electrocardiogram at the end of exercise during the second set of the cycle ergometer test. N=15. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the LionsGate Technologies probe and the gold standard.
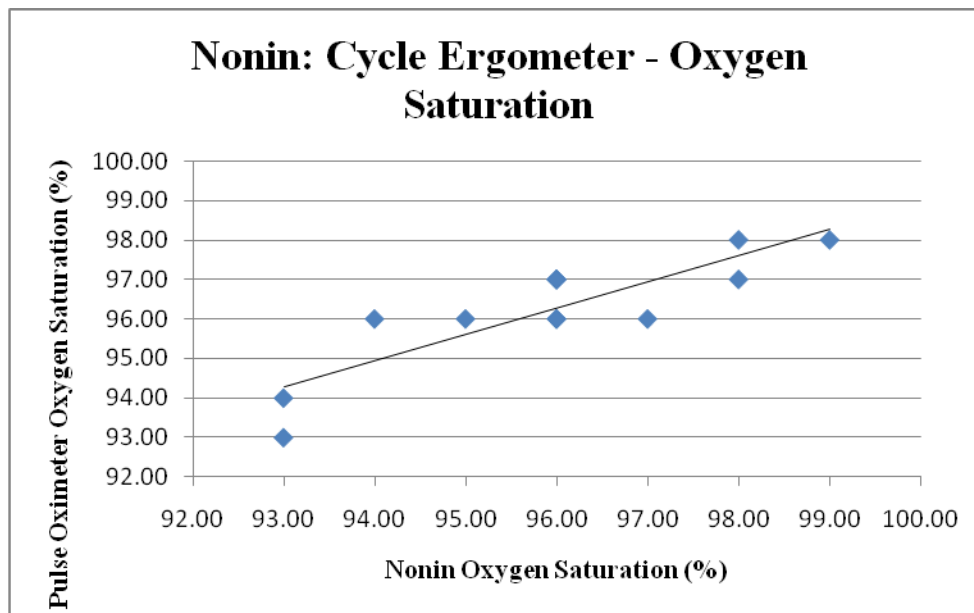
Figure 9: Nonin probe versus the Nonin 8500 pulse oximeter at the end of exercise during the second set of the cycle ergometer test. N=13, 2 missing value. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the Nonin probe and the gold standard.
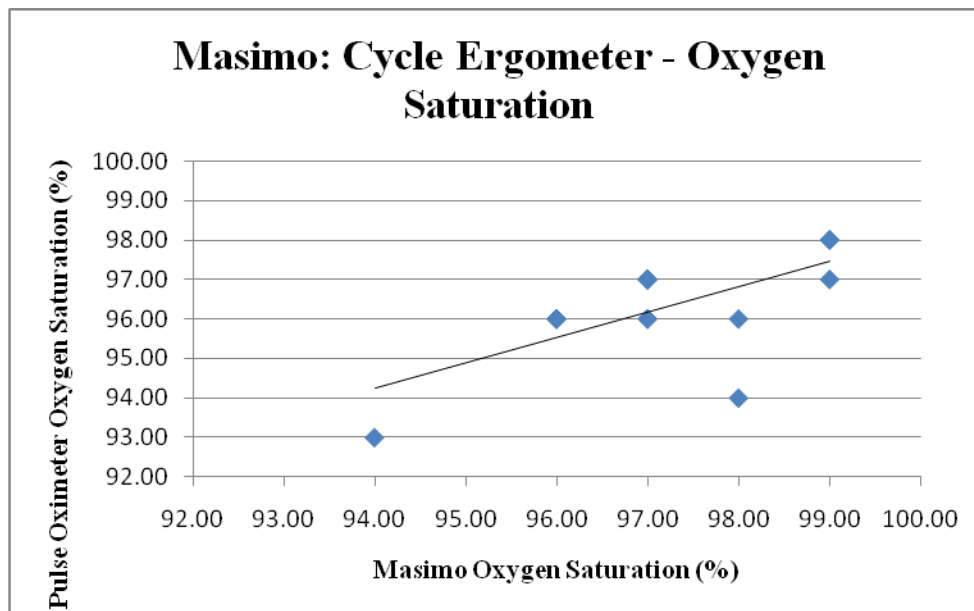
Figure 10:Masimo probe versus the Nonin 8500 pulse oximeter at the end of exercise during the second set of the cycle ergometer test. N=15. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the Masimo probe and the gold standard.
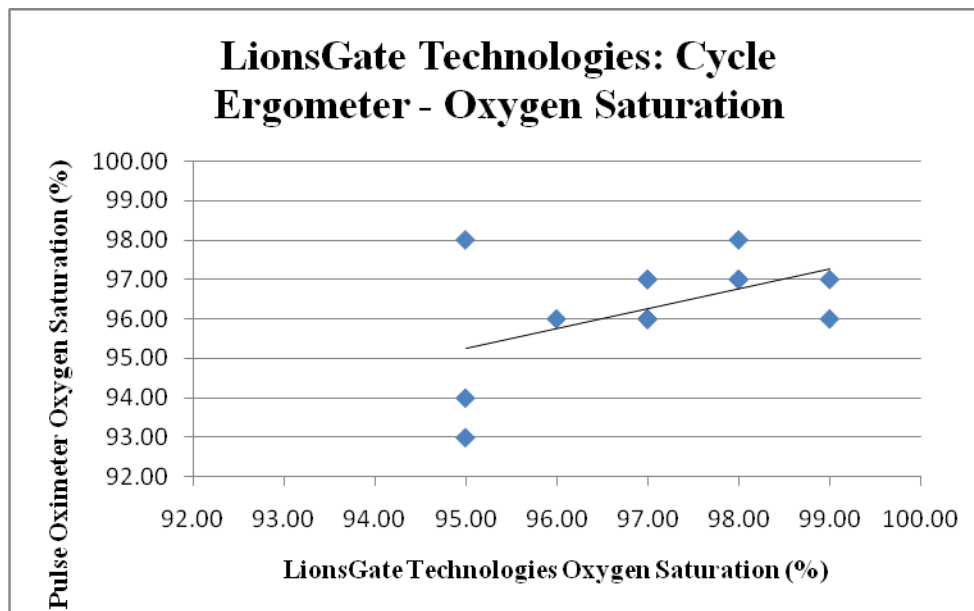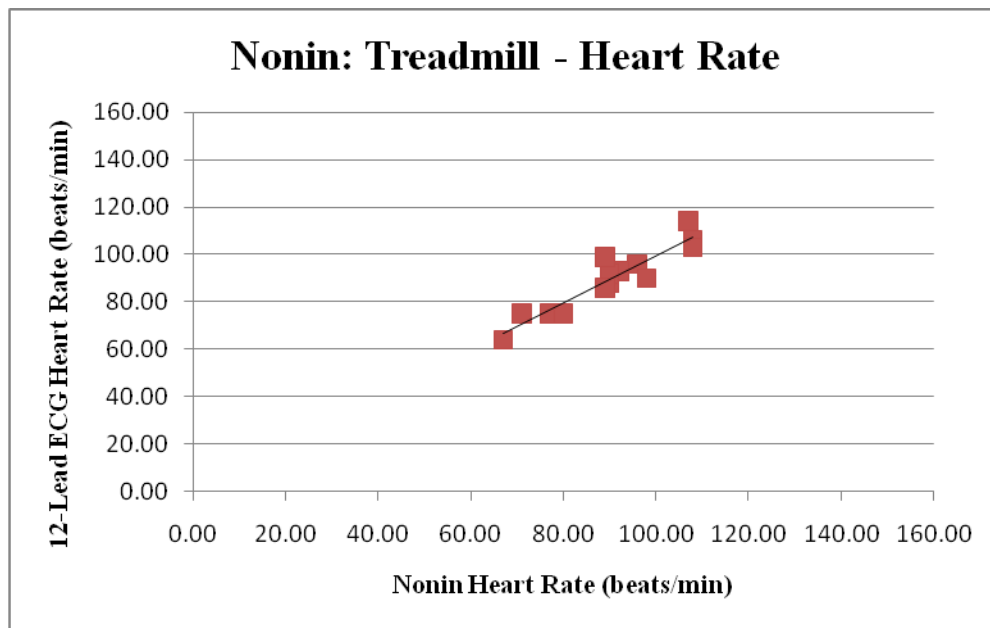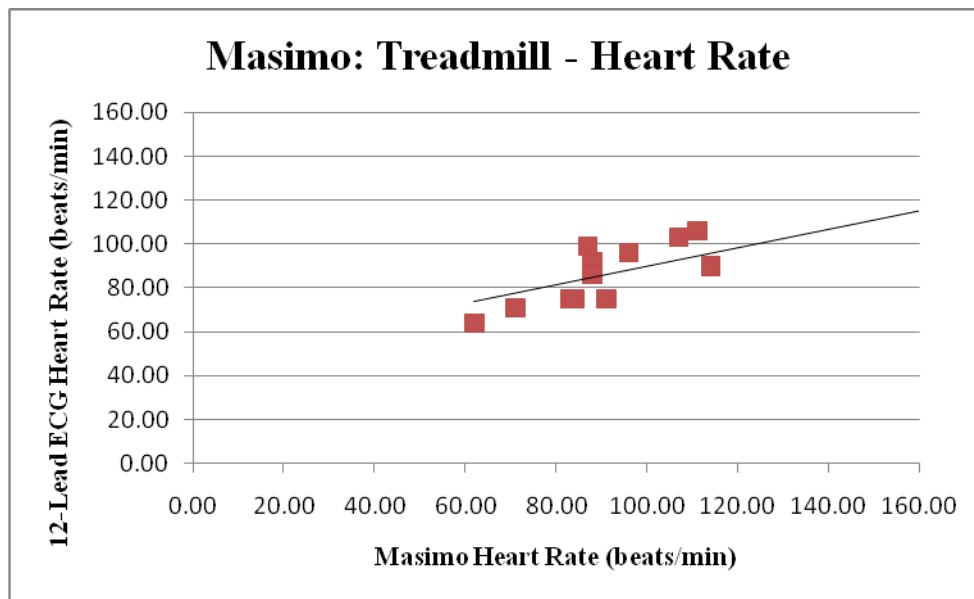
Figure 11: LionsGate Technologies probe versus the Nonin 8500 pulse oximeter at the end of exercise during the second set of the cycle ergometer test. N=15. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the LionsGate Technologies probe and the gold standard.

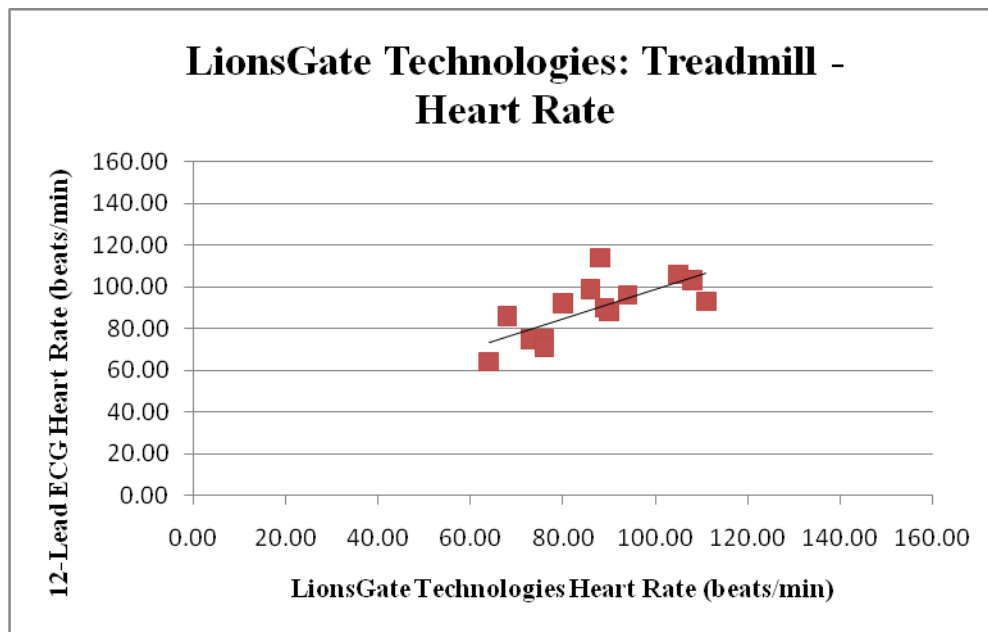**Nonin: Treadmill - Heart Rate**

ECG-Electrocardiogram

Figure 12: Nonin probe versus 12-lead electrocardiogram at the end of exercise during the second set of the treadmill walking test. N=14, 1 missing values. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the Nonin probe and the gold standard.

Figure 13: Masimo probe versus 12-lead electrocardiogram at the end of exercise during the second set of the treadmill walking test. N=14, 1 missing values. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the Masimo probe and the gold standard.

LionsGate Technologies: Treadmill – Heart Rate

ECG-Electrocardiogram

Figure 14: LionsGate Technologies probe versus 12-lead electrocardiogram at the end of exercise during the second set of the treadmill walking test. N=15. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the LionsGate Technologies probe and the gold standard.
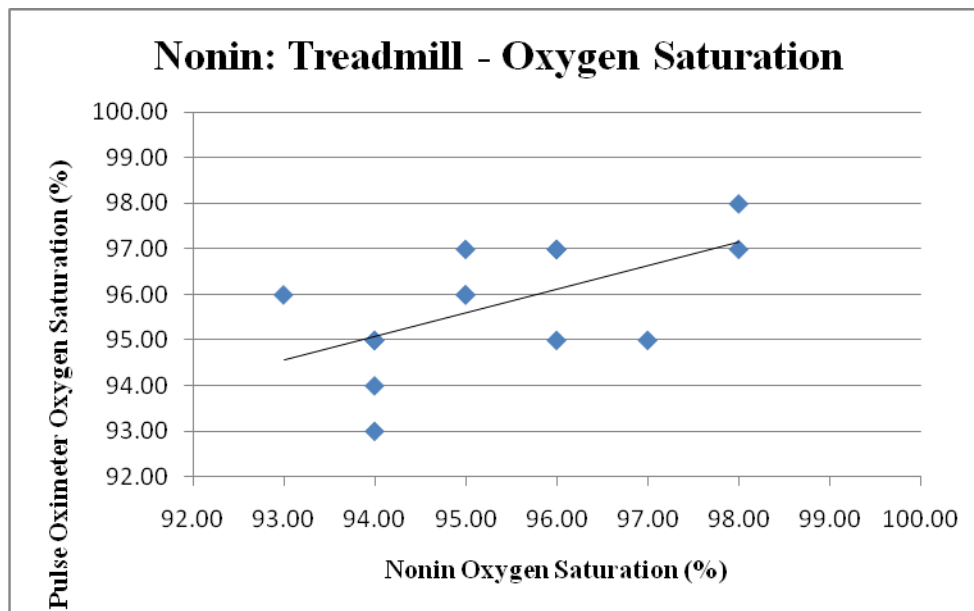
Figure 15: Nonin probe versus the Nonin 8500 pulse oximeter at the end of exercise during the second set of the treadmill walking test. N=14, 1 missing values. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the Nonin probe and the gold standard.
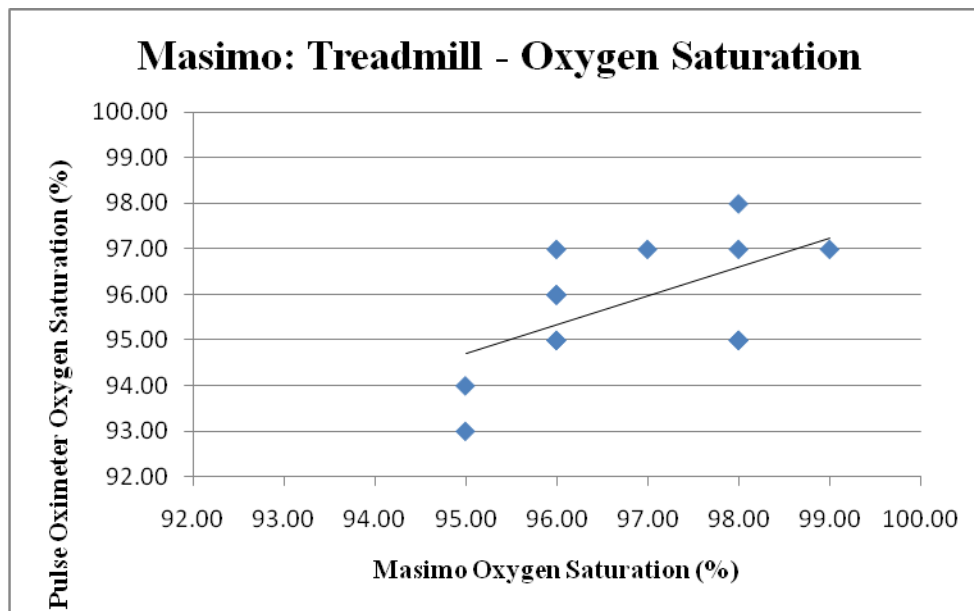
Figure 16: Masimo probe versus the Nonin 8500 pulse oximeter at the end of exercise during the second set of the treadmill walking test. N=14, 1 missing values. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the Masimo probe and the gold standard.

Figure 17: LionsGate Technologies probe versus the Nonin 8500 pulse oximeter at the end of exercise during the second set of the treadmill walking test. N=15. The further away a data points from the linear relationship line, the greater the mismatch between the measurment by the LionsGate Technologies probe and the gold standard.
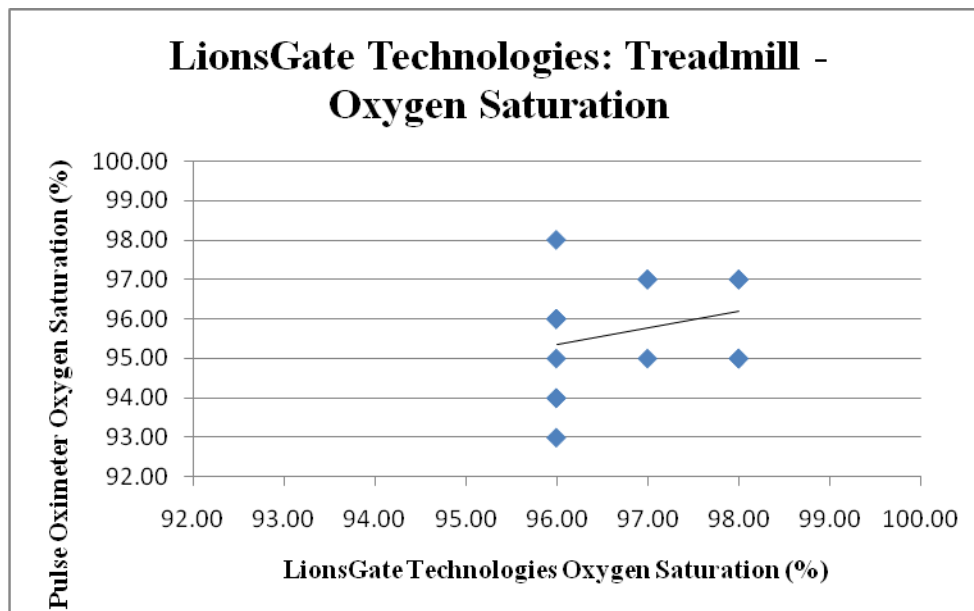
Bland-Altman Plot: Oxygen Saturation - Cycle Ergometer Test - Nonin - Rest
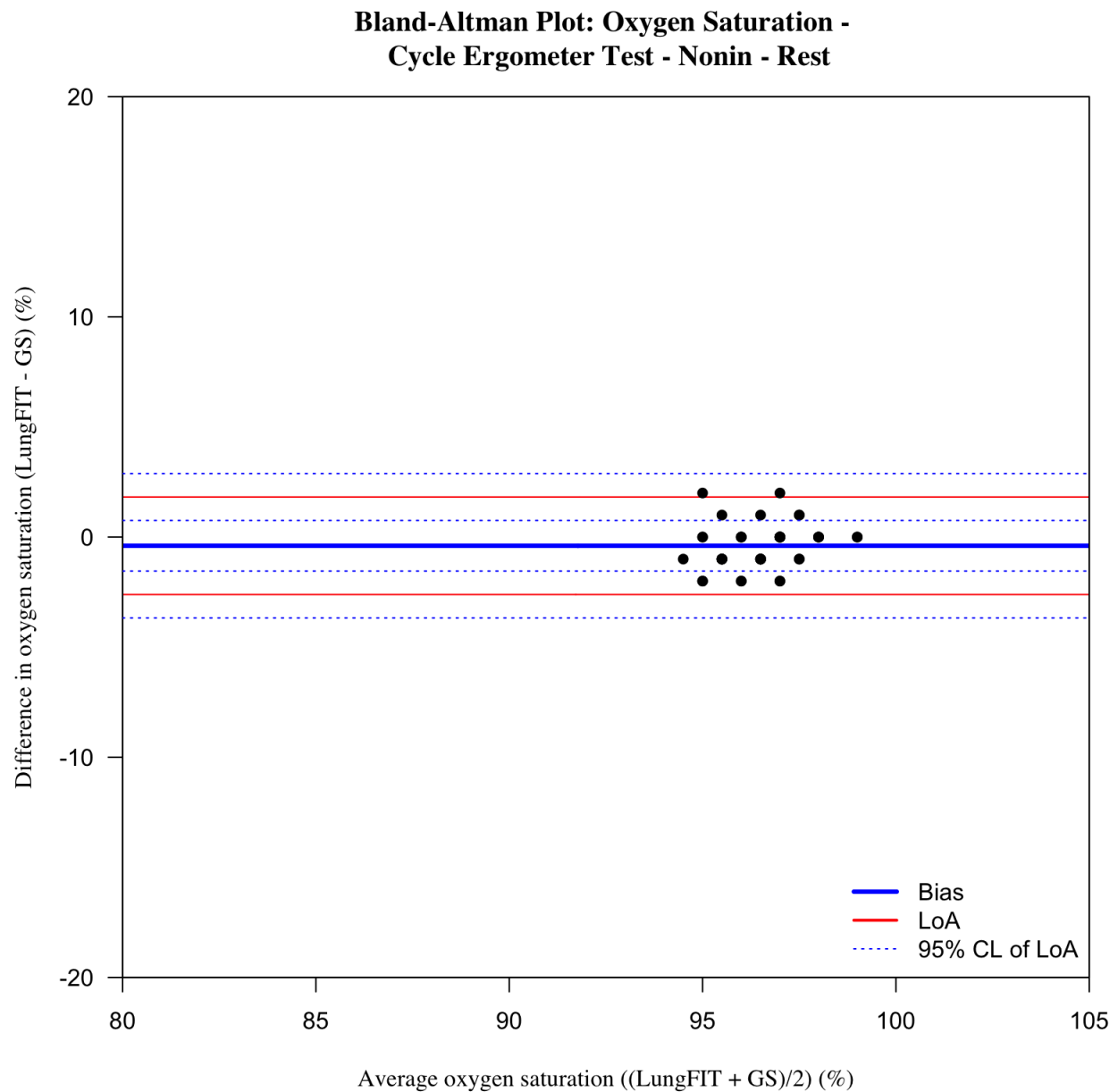
LoA-Limit of Agreement, GS-Gold Standard

Figure 18: Bland-Altman Plot: Oxygen Saturation – Cycle Ergometer Test – Nonin – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was `≤ ±2% and limits of agreement were ≤ ±4%.

**Bland-Altman Plot: Oxygen Saturation -
Cycle Ergometer Test - Nonin - Exercise**
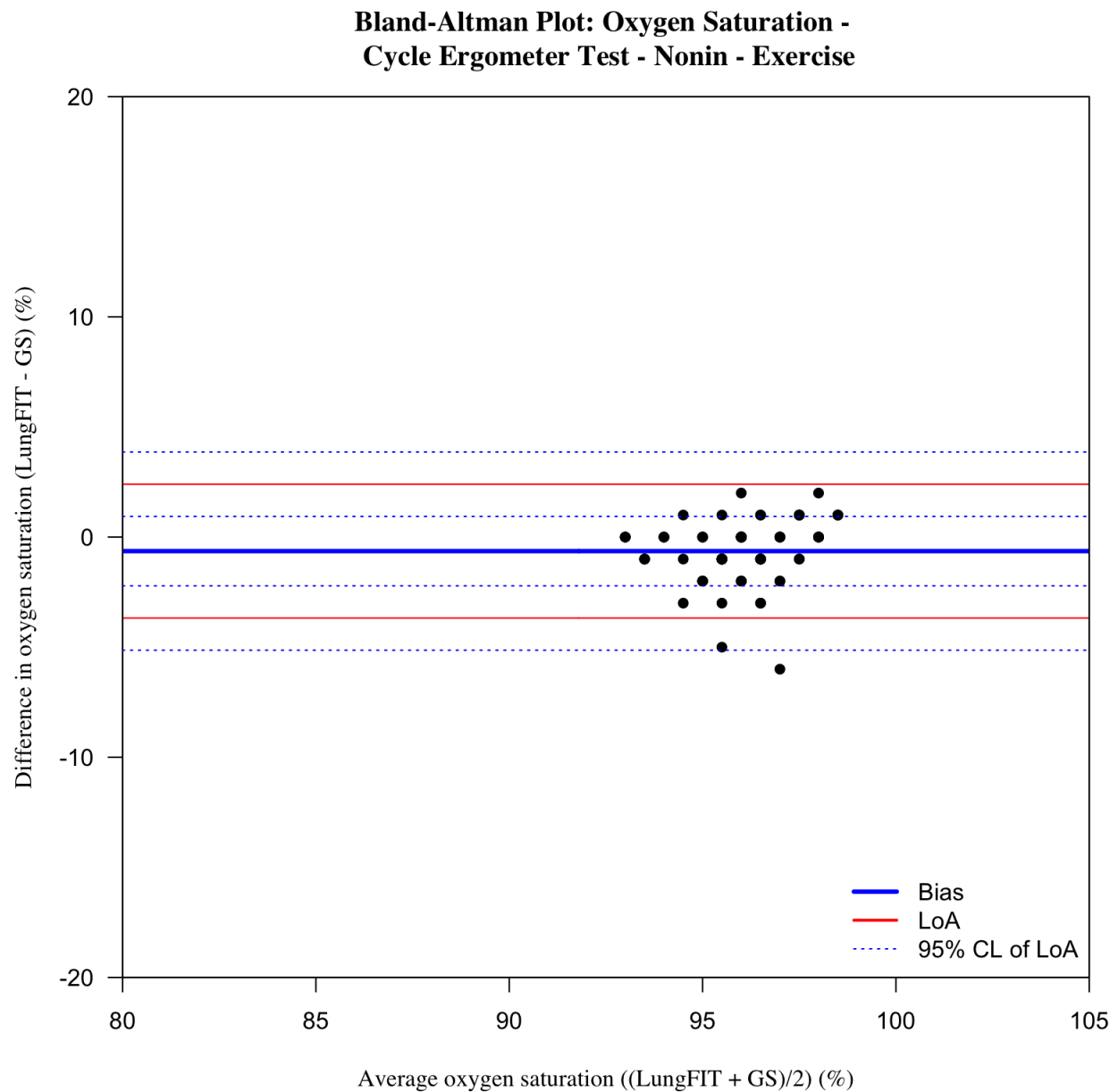
LoA-Limit of Agreement, GS-Gold Standard

Figure 19: Bland-Altman Plot: Oxygen Saturation – Cycle Ergometer Test – Nonin – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq$ $\pm2\%$ and limits of agreement were $\leq \pm4\%$.

**Bland-Altman Plot: Oxygen Saturation -
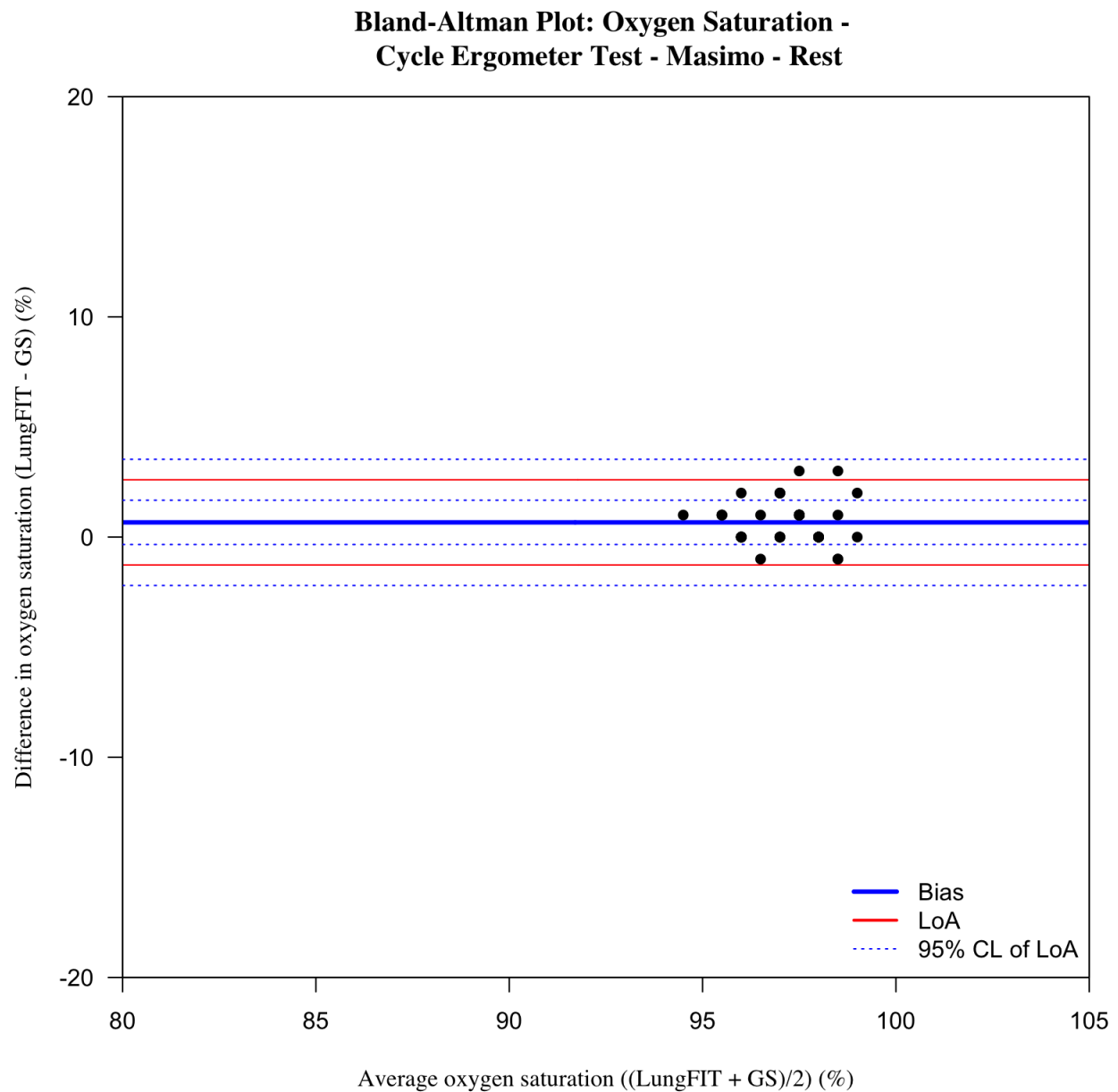Cycle Ergometer Test - Masimo - Rest**

LoA-Limit of Agreement, GS-Gold Standard

Figure 20: Bland-Altman Plot: Oxygen Saturation – Cycle Ergometer Test – Masimo – Rest.
The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent
limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for
each limit of agreement. Each black data point represents a subject's measurement difference
between the LungFIT probe and gold standard. Validity was determined if mean bias was ≤
±2% and limits of agreement were ≤ ±4%.

**Bland-Altman Plot: Oxygen Saturation -
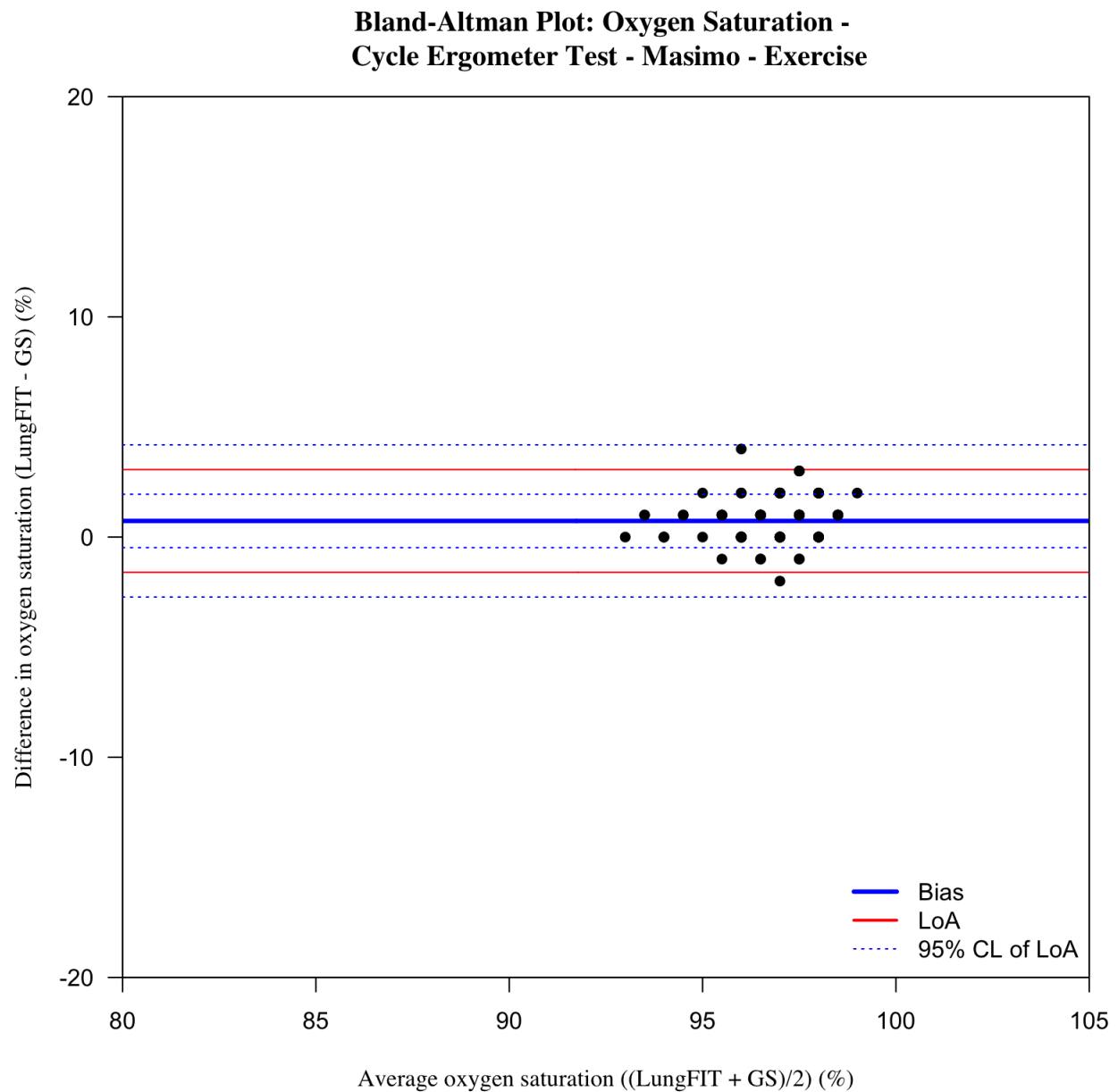Cycle Ergometer Test - Masimo - Exercise**

LoA-Limit of Agreement, GS-Gold Standard

Figure 21: Bland-Altman Plot: Oxygen Saturation – Cycle Ergometer Test – Masimo – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was ≤ ±2% and limits of agreement were ≤ ±4%.

**Bland-Altman Plot: Oxygen Saturation -
Cycle Ergometer Test - LGT - Rest**

LGT-LionsGate Technologies, LoA-Limit of Agreement, GS-Gold Standard

Figure 22: Bland-Altman Plot: Oxygen Saturation – Cycle Ergometer Test – LionsGate Technologies – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was ≤ ±2% and limits of agreement were ≤ ±4%.
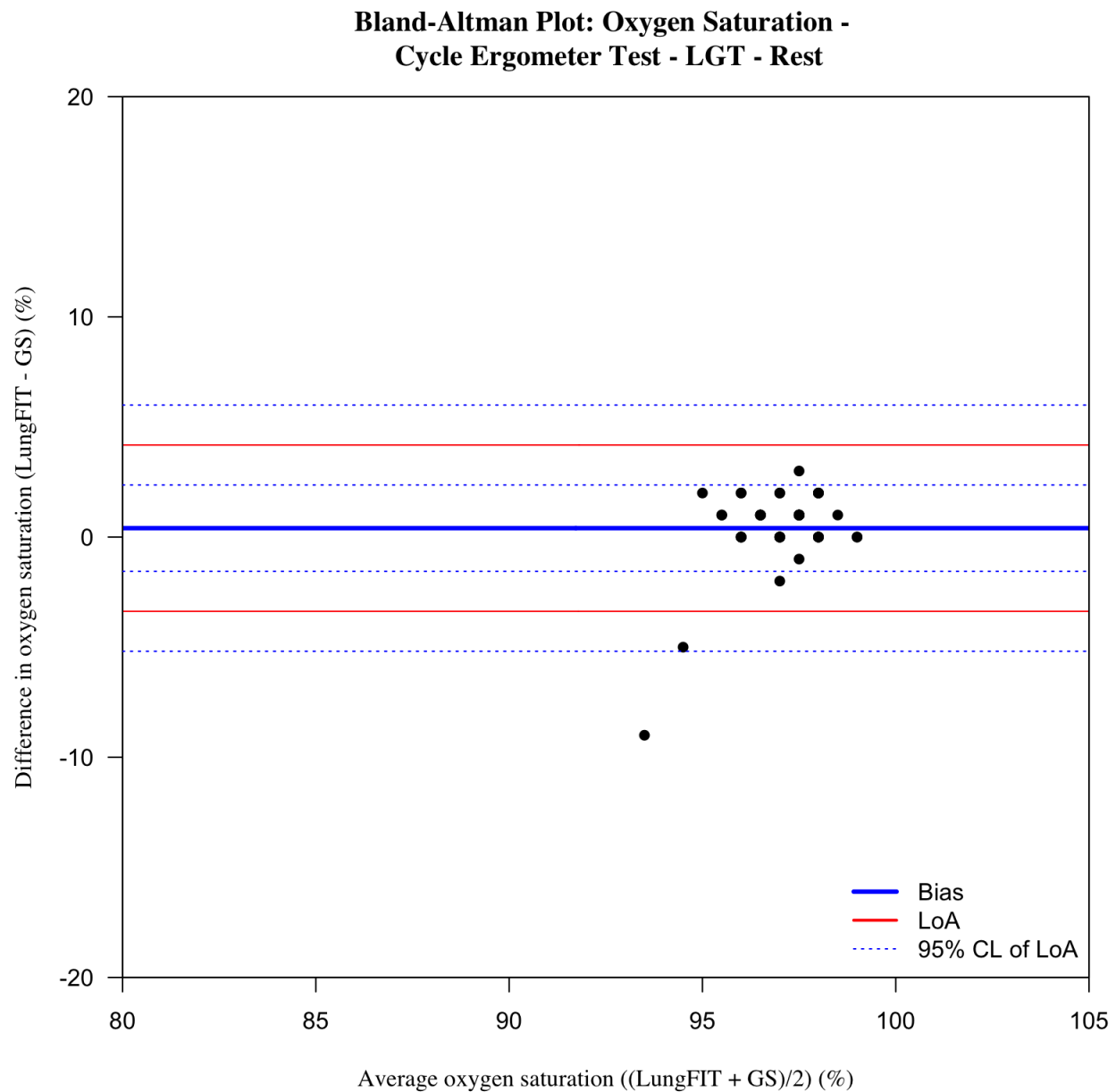
**Bland-Altman Plot: Oxygen Saturation -
Cycle Ergometer Test - LGT - Exercise**

LGT-LionsGate Technologies, LoA-Limit of Agreement, GS-Gold Standard

Figure 23: Bland-Altman Plot: Oxygen Saturation – Cycle Ergometer Test – LionsGate Technologies –Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 2\%$ and limits of agreement were $\leq \pm 4\%$.
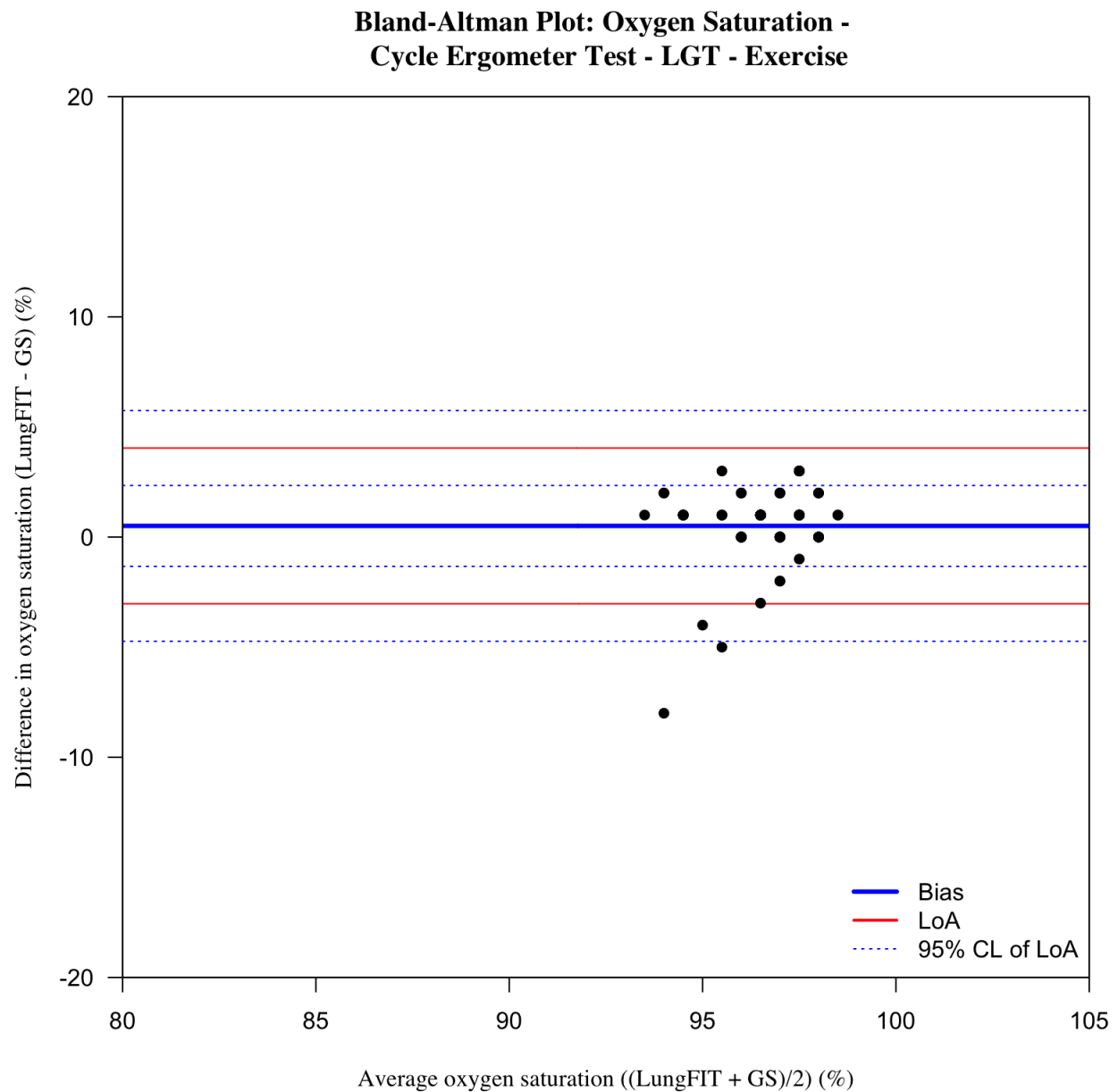
**Bland-Altman Plot: Heart Rate -
Cycle Ergometer Test - Nonin - Rest**

LoA-Limit of Agreement, GS-Gold Standard
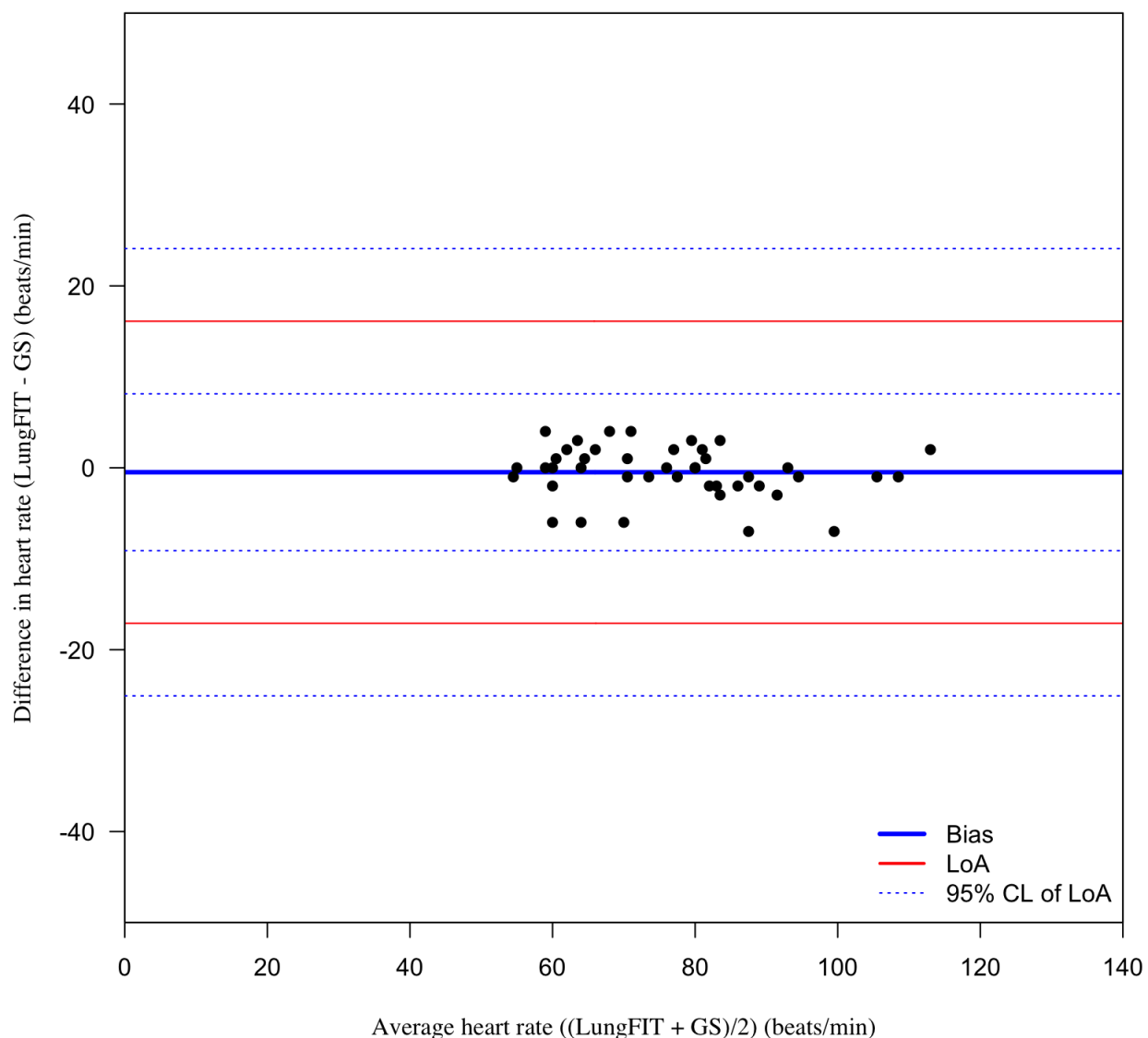
Figure 24: Bland-Altman Plot: Heart Rate – Cycle Ergometer Test – Nonin – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was ≤ ±5 beats/min and limits of agreement were ≤ ±10 beats/min.

**Bland-Altman Plot: Heart Rate -
Cycle Ergometer Test - Nonin - Exercise**

LoA-Limit of Agreement, GS-Gold Standard

Figure 25: Bland-Altman Plot: Heart Rate – Cycle Ergometer Test – Nonin – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 5$ beats/min and limits of agreement were $\leq \pm 10$ beats/min.
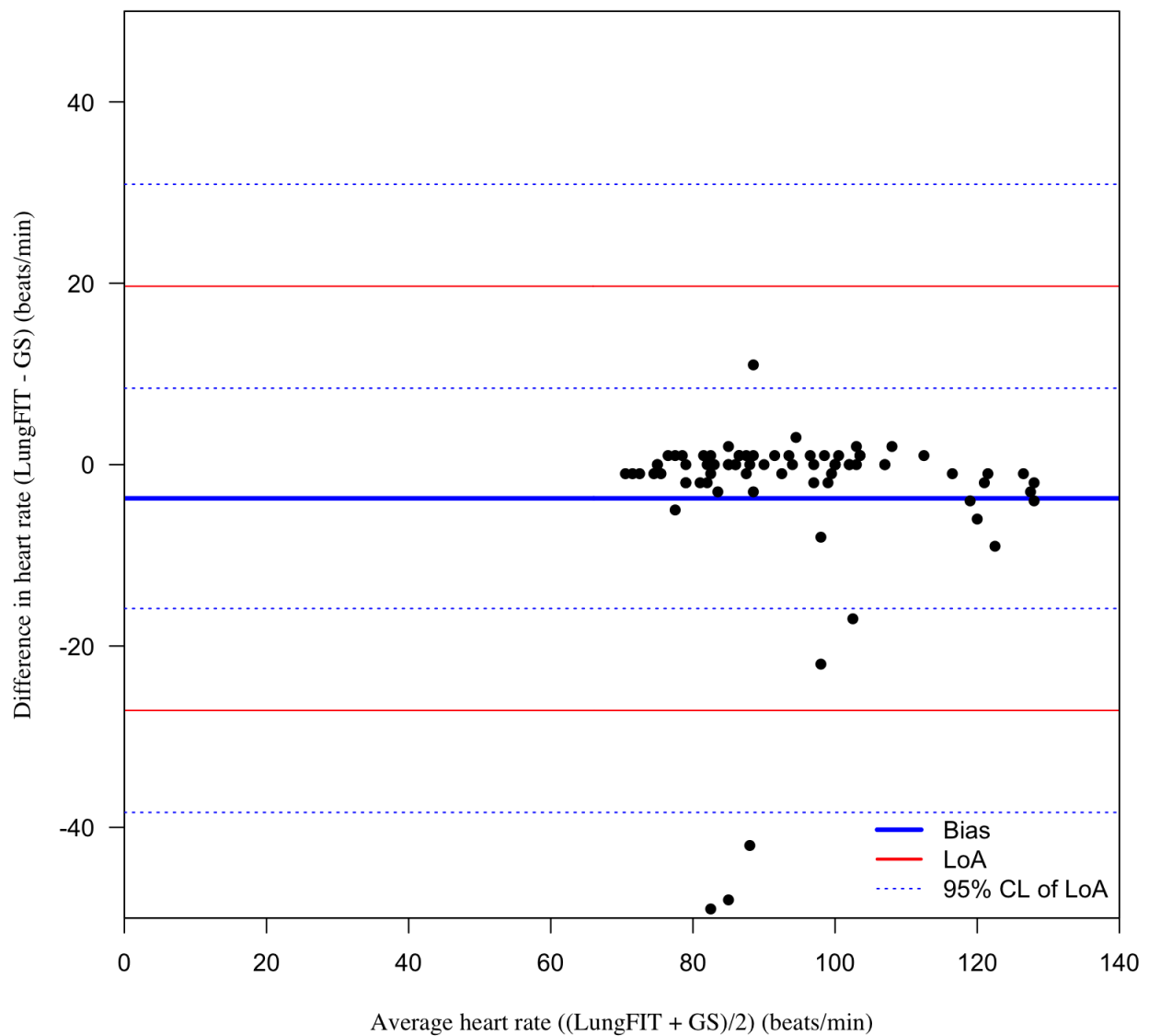
Bland-Altman Plot: Heart Rate - Cycle Ergometer Test - Masimo - Rest

LoA-Limit of Agreement, GS-Gold Standard

Figure 26: Bland-Altman Plot: Heart Rate – Cycle Ergometer Test – Masimo – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 5$ beats/min and limits of agreement were $\leq \pm 10$ beats/min.

**Bland-Altman Plot: Heart Rate -
Cycle Ergometer Test - Masimo - Exercise**

LoA-Limit of Agreement, GS-Gold Standard

Figure 27: Bland-Altman Plot: Heart Rate – Cycle Ergometer Test – Masimo – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 5$ beats/min and limits of agreement were $\leq \pm 10$ beats/min.
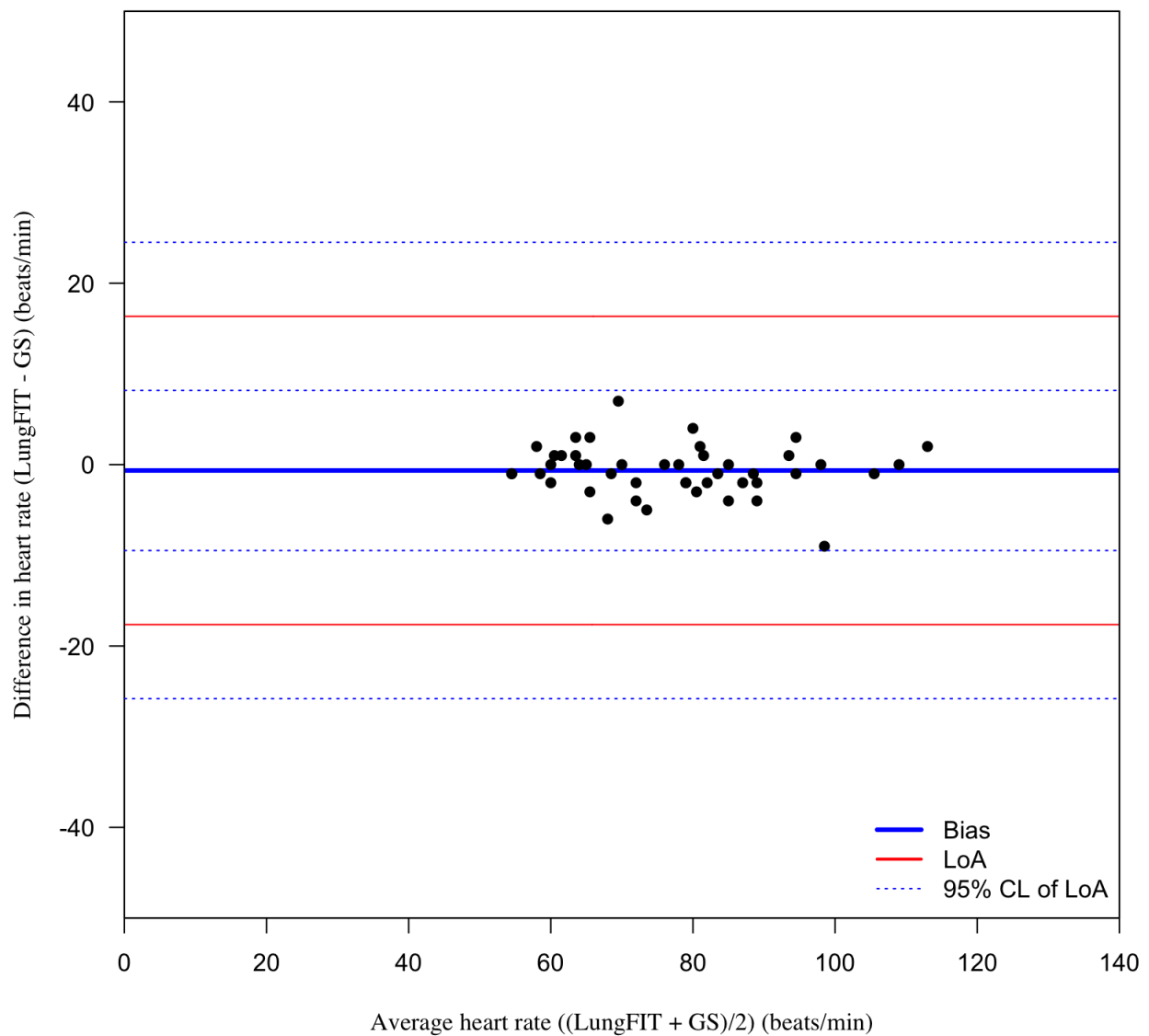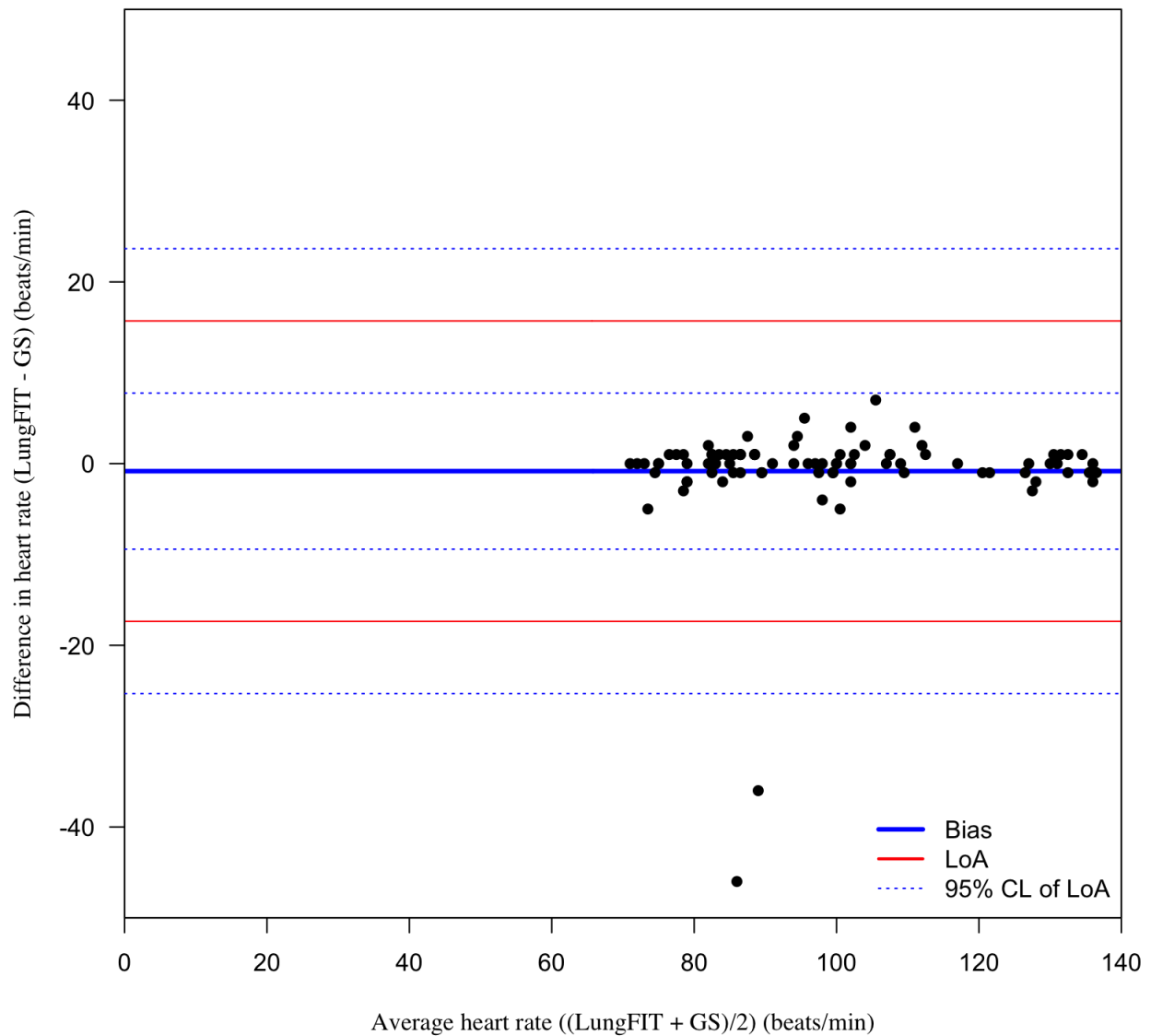
Bland-Altman Plot: Heart Rate -
Cycle Ergometer Test - LGT - Rest
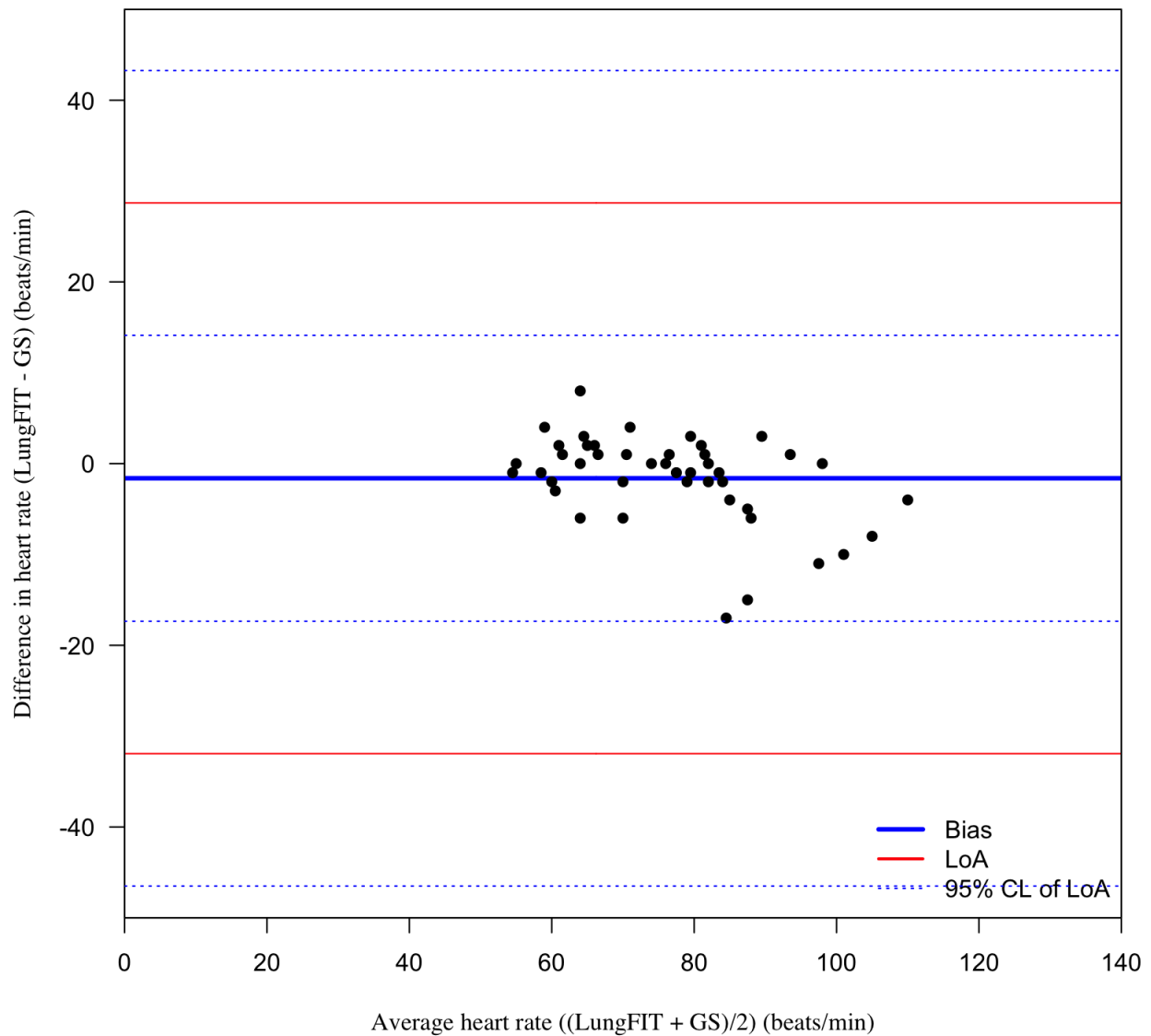
LGT-LionsGate Technologies, LoA-Limit of Agreement, GS-Gold Standard

Figure 28: Bland-Altman Plot: Heart Rate – Cycle Ergometer Test – LionsGate Technologies – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was ≤ ±5 beats/min and limits of agreement were ≤ ±10 beats/min.

Bland-Altman Plot: Heart Rate -
Cycle Ergometer Test - LGT - Exercise
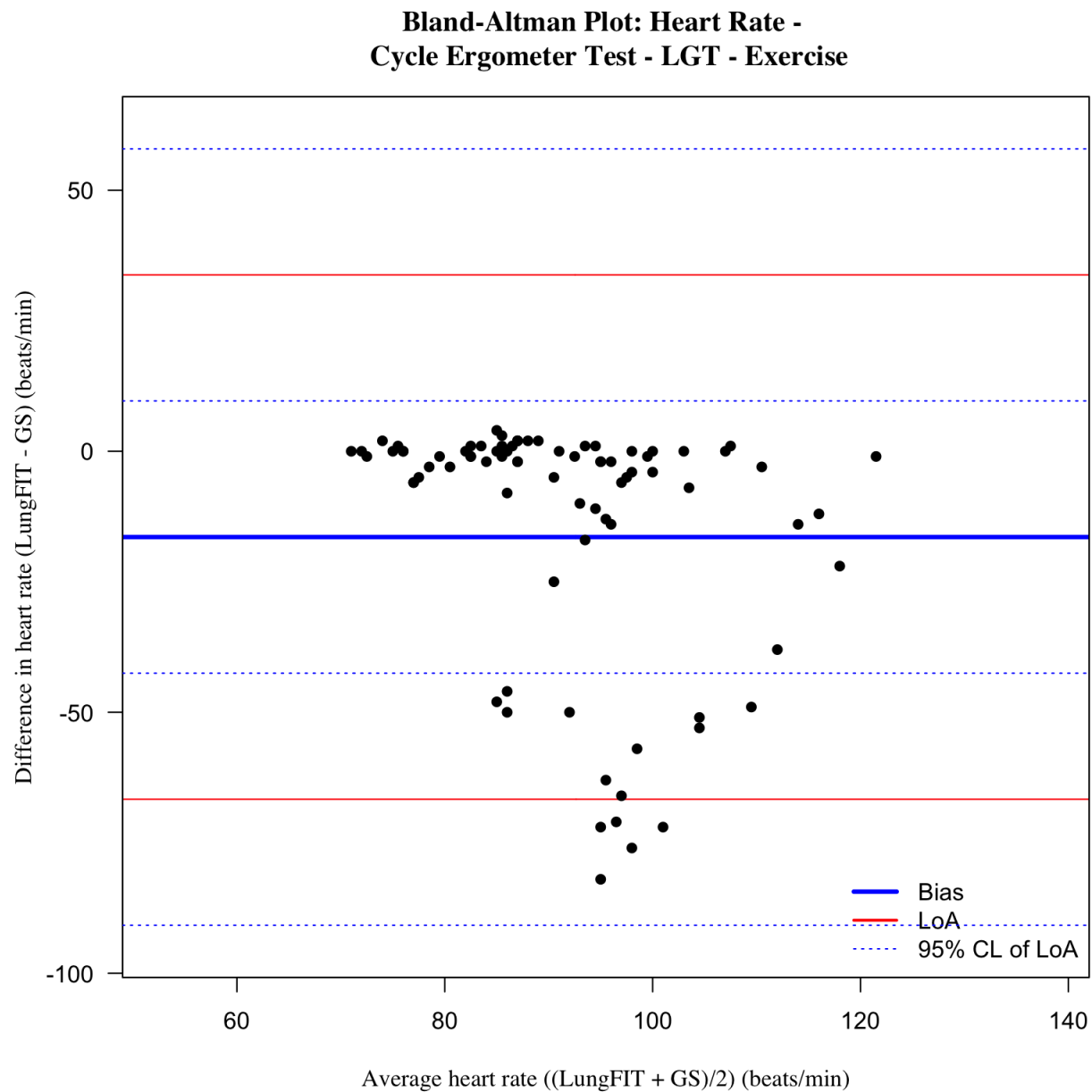
LGT-LionsGate Technologies, LoA-Limit of Agreement, GS-Gold Standard

Figure 29: Bland-Altman Plot: Heart Rate – Cycle Ergometer Test – LionsGate Technologies – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was ≤ ±5 beats/min and limits of agreement were ≤ ±10 beats/min.

**Bland-Altman Plot: Oxygen Saturation -
Treadmill Test - Nonin - Rest**
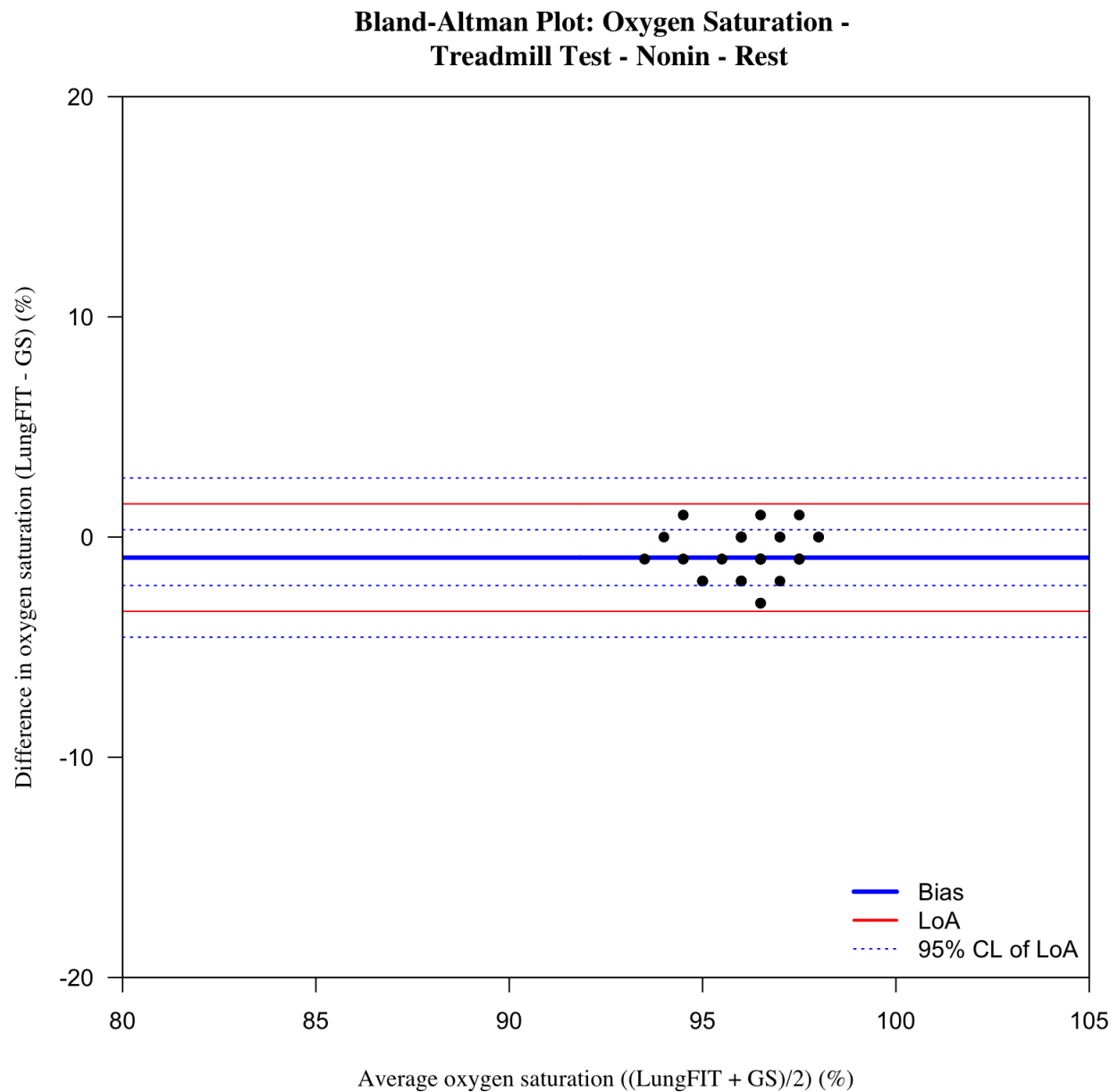
LoA-Limit of Agreement, GS-Gold Standard

Figure 30: Bland-Altman Plot: Oxygen Saturation – Treadmill Test – Nonin – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 2\%$ and limits of agreement were $\leq \pm 4\%$.

**Bland-Altman Plot: Oxygen Saturation -
Treadmill Test - Nonin - Exercise**

LoA-Limit of Agreement, GS-Gold Standard

Figure 31: Bland-Altman Plot: Oxygen Saturation – Treadmill Test – Nonin – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was ≤ ±2% and limits of agreement were ≤ ±4%.

Bland-Altman Plot: Oxygen Saturation - Treadmill Test - Masimo - Rest

LoA-Limit of Agreement, GS-Gold Standard

Figure 32: Bland-Altman Plot: Oxygen Saturation – Treadmill Test – Masimo – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 2\%$ and limits of agreement were $\leq \pm 4\%$.

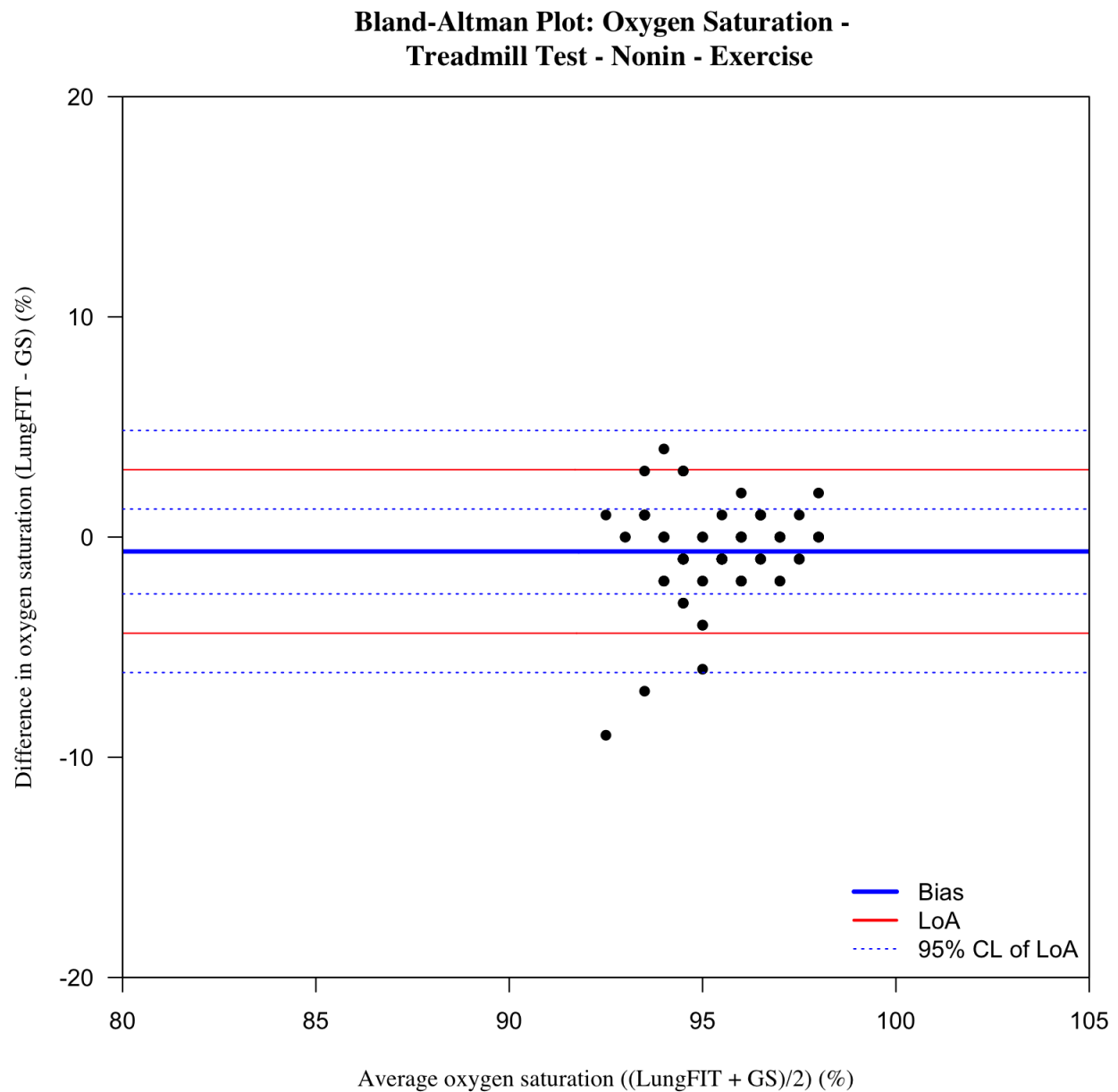**Bland-Altman Plot: Oxygen Saturation -
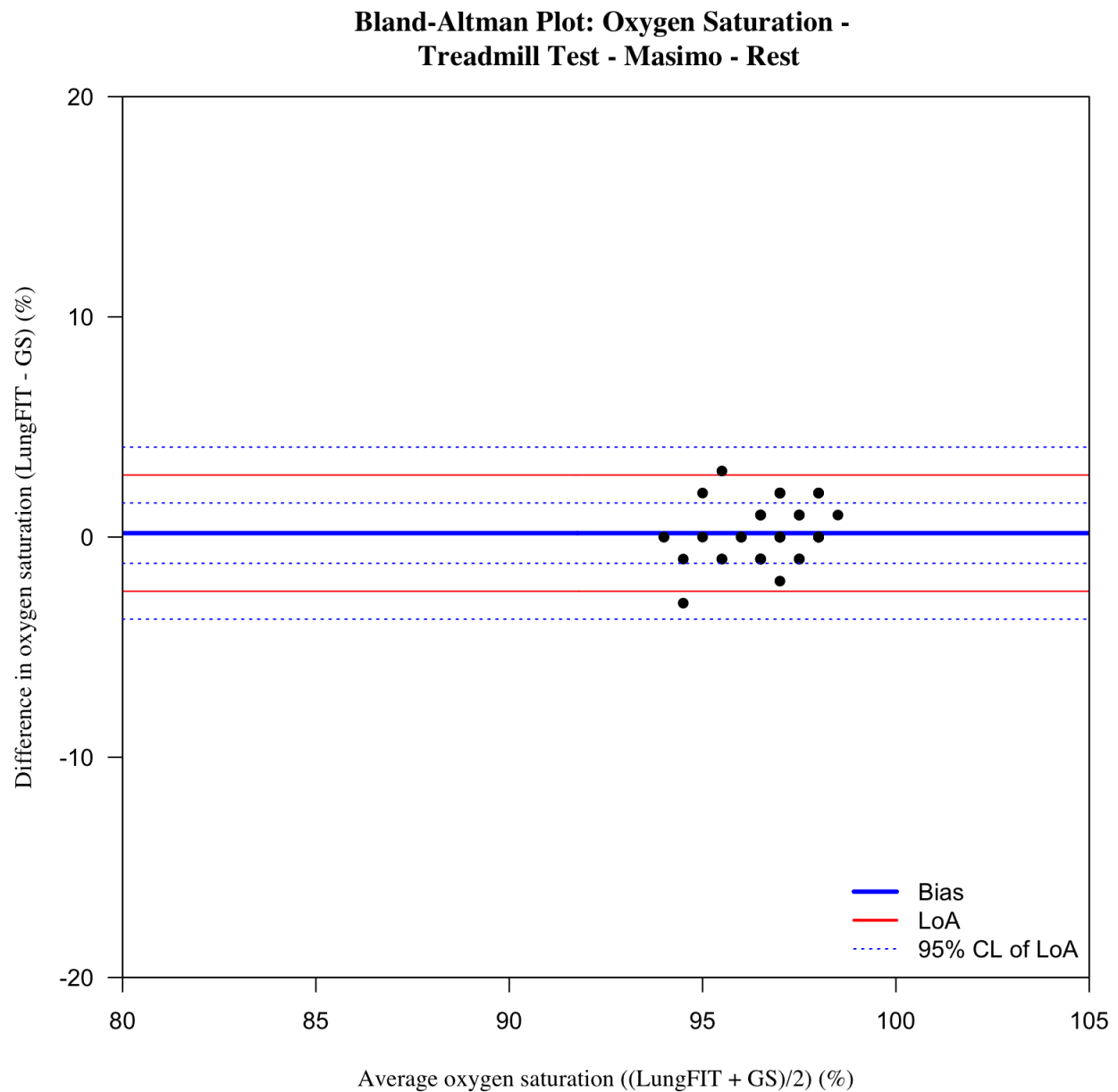Treadmill Test - Masimo - Exercise**

LoA-Limit of Agreement, GS-Gold Standard

Figure 33: Bland-Altman Plot: Oxygen Saturation – Treadmill Test – Masimo – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq$ $\pm 2\%$ and limits of agreement were $\leq \pm 4\%$.

Bland-Altman Plot: Oxygen Saturation - Treadmill Test - LGT - Rest

LGT-LionsGate Technologies, LoA-Limit of Agreement, GS-Gold Standard

Figure 34: Bland-Altman Plot: Oxygen Saturation – Treadmill Test – LionsGate Technologies – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 2\%$ and limits of agreement were $\leq \pm 4\%$.
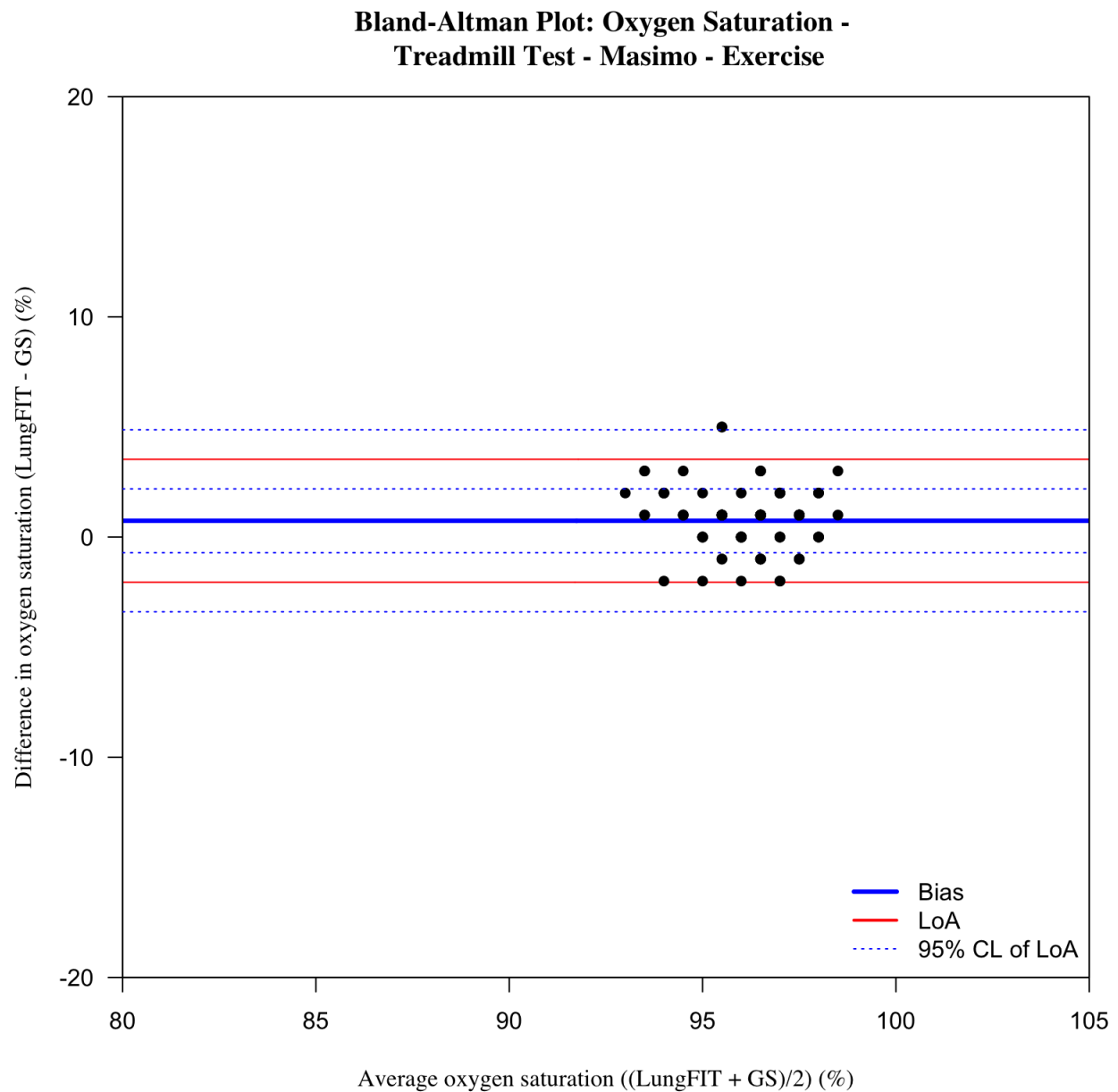
Bland-Altman Plot: Oxygen Saturation - Treadmill Test - LGT - Exercise

LGT-LionsGate Technologies, LoA-Limit of Agreement, GS-Gold Standard

Figure 35: Bland-Altman Plot: Oxygen Saturation – Treadmill Test – LionsGate Technologies – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 2\%$ and limits of agreement were $\leq \pm 4\%$.
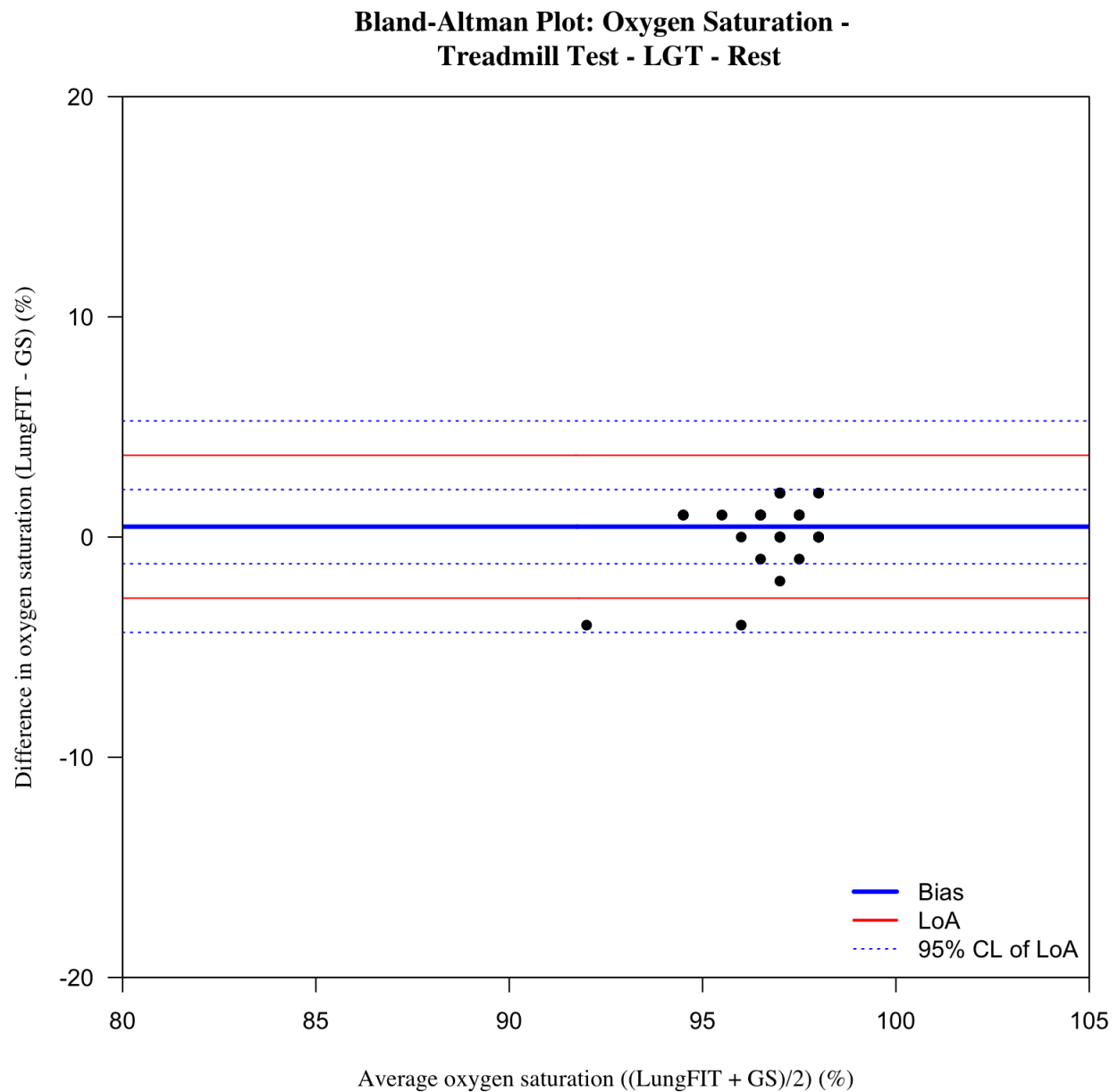
**Bland-Altman Plot: Heart Rate -
Treadmill Test - Nonin - Rest**

LoA-Limit of Agreement, GS-Gold Standard

Figure 36: Bland-Altman Plot: Heart Rate – Treadmill Test – Nonin – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 5$ beats/min and limits of agreement were $\leq \pm 10$ beats/min.
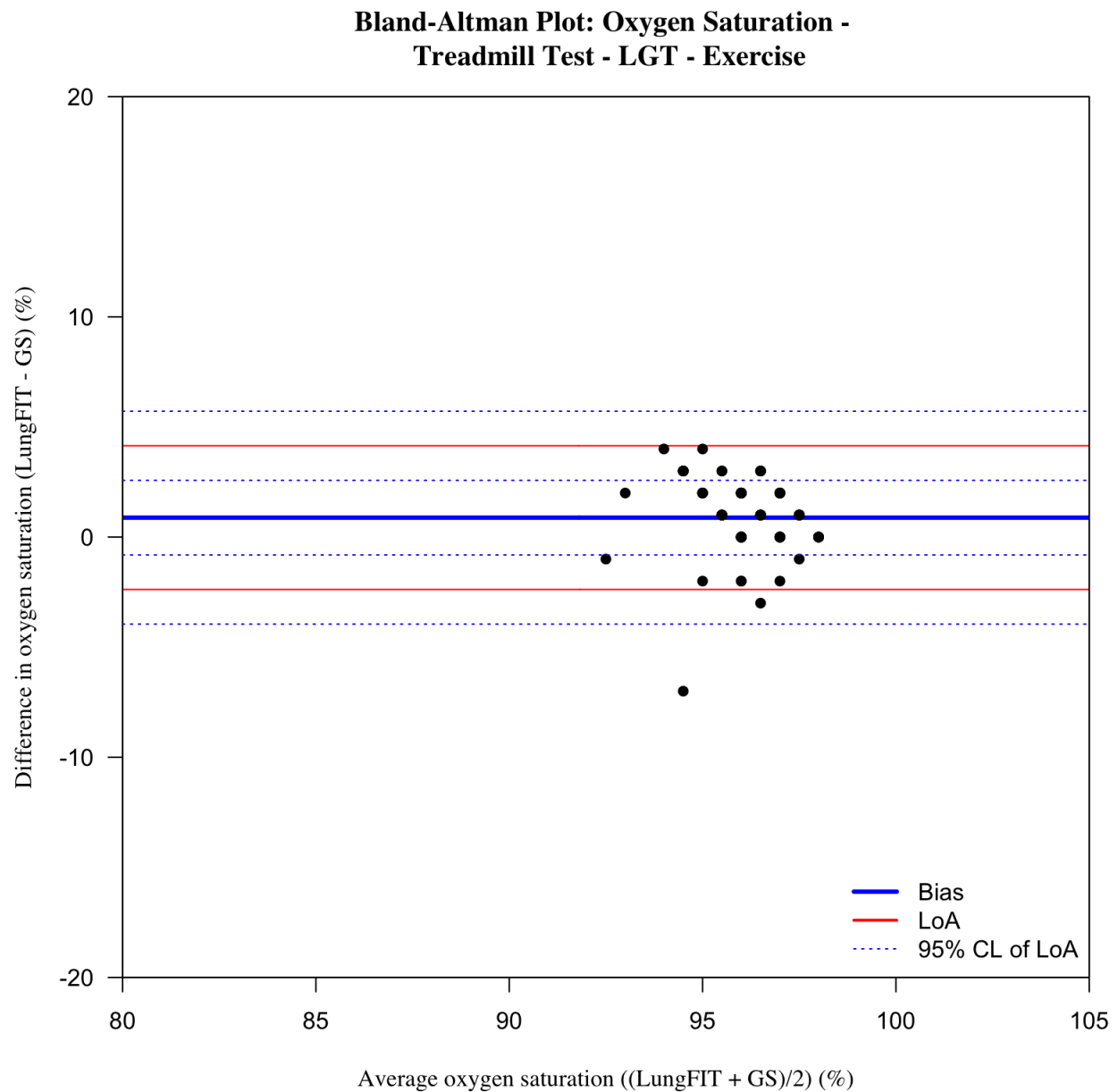
**Bland-Altman Plot: Heart Rate -
Treadmill Test - Nonin - Exercise**

LoA-Limit of Agreement, GS-Gold Standard

Figure 37: Bland-Altman Plot: Heart Rate – Treadmill Test – Nonin – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 5$ beats/min and limits of agreement were $\leq \pm 10$ beats/min.

**Bland-Altman Plot: Heart Rate -
Treadmill Test - Masimo - Rest**

LoA-Limit of Agreement, GS-Gold Standard
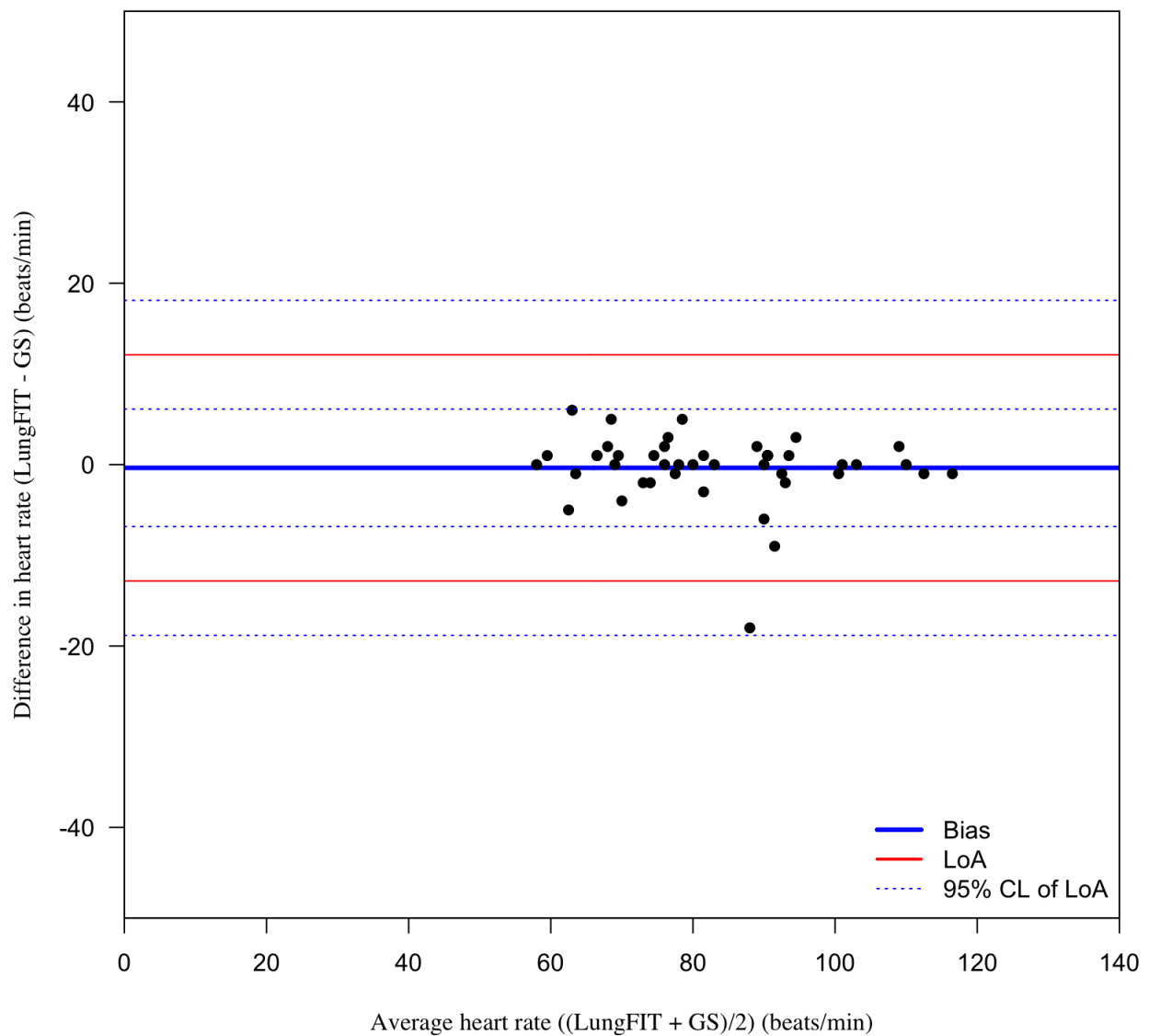
Figure 38: Bland-Altman Plot: Heart Rate – Treadmill Test – Masimo – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 5$ beats/min and limits of agreement were $\leq \pm 10$ beats/min.

**Bland-Altman Plot: Heart Rate -
Treadmill Test - Masimo - Exercise**
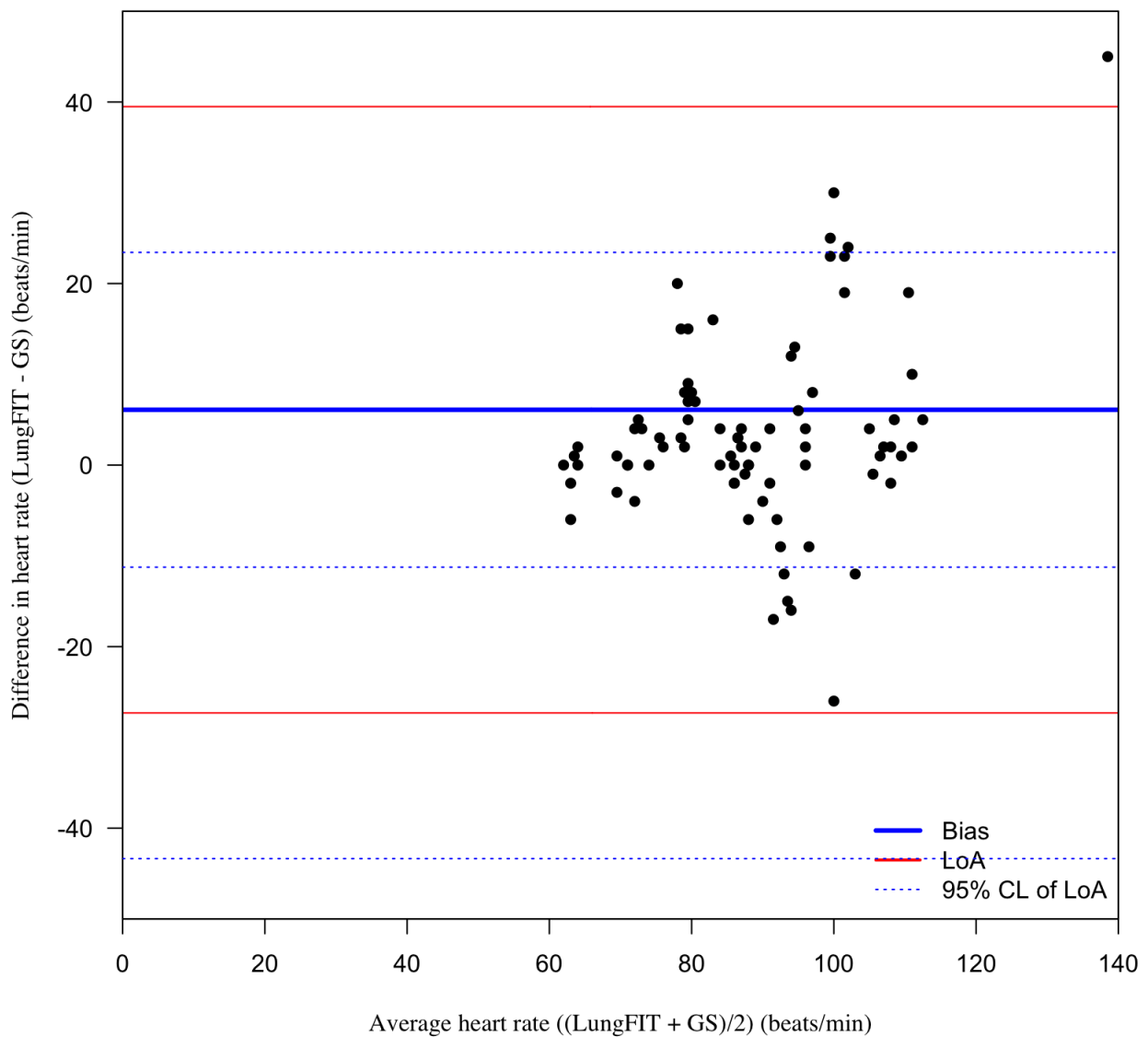
LoA-Limit of Agreement, GS-Gold Standard

Figure 39: Bland-Altman Plot: Heart Rate – Treadmill Test – Masimo – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 5$ beats/min and limits of agreement were $\leq \pm 10$ beats/min.

Bland-Altman Plot: Heart Rate - Treadmill Test - LGT - Rest
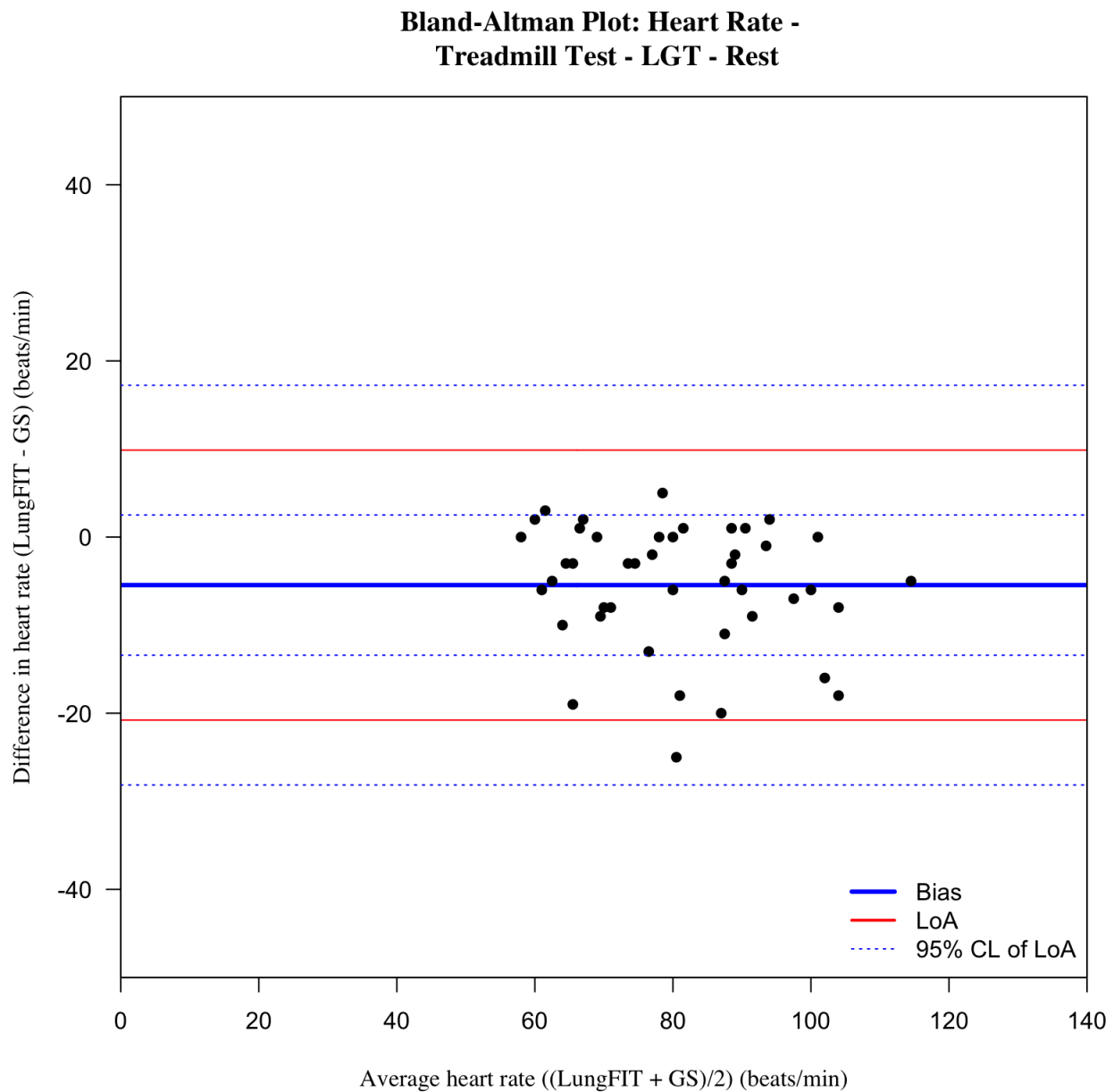
LGT-LionsGate Technologies, LoA-Limit of Agreement, GS-Gold Standard

Figure 40: Bland-Altman Plot: Heart Rate – Treadmill Test – LionsGate Technologies – Rest. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was $\leq \pm 5$ beats/min and limits of agreement were $\leq \pm 10$ beats/min.
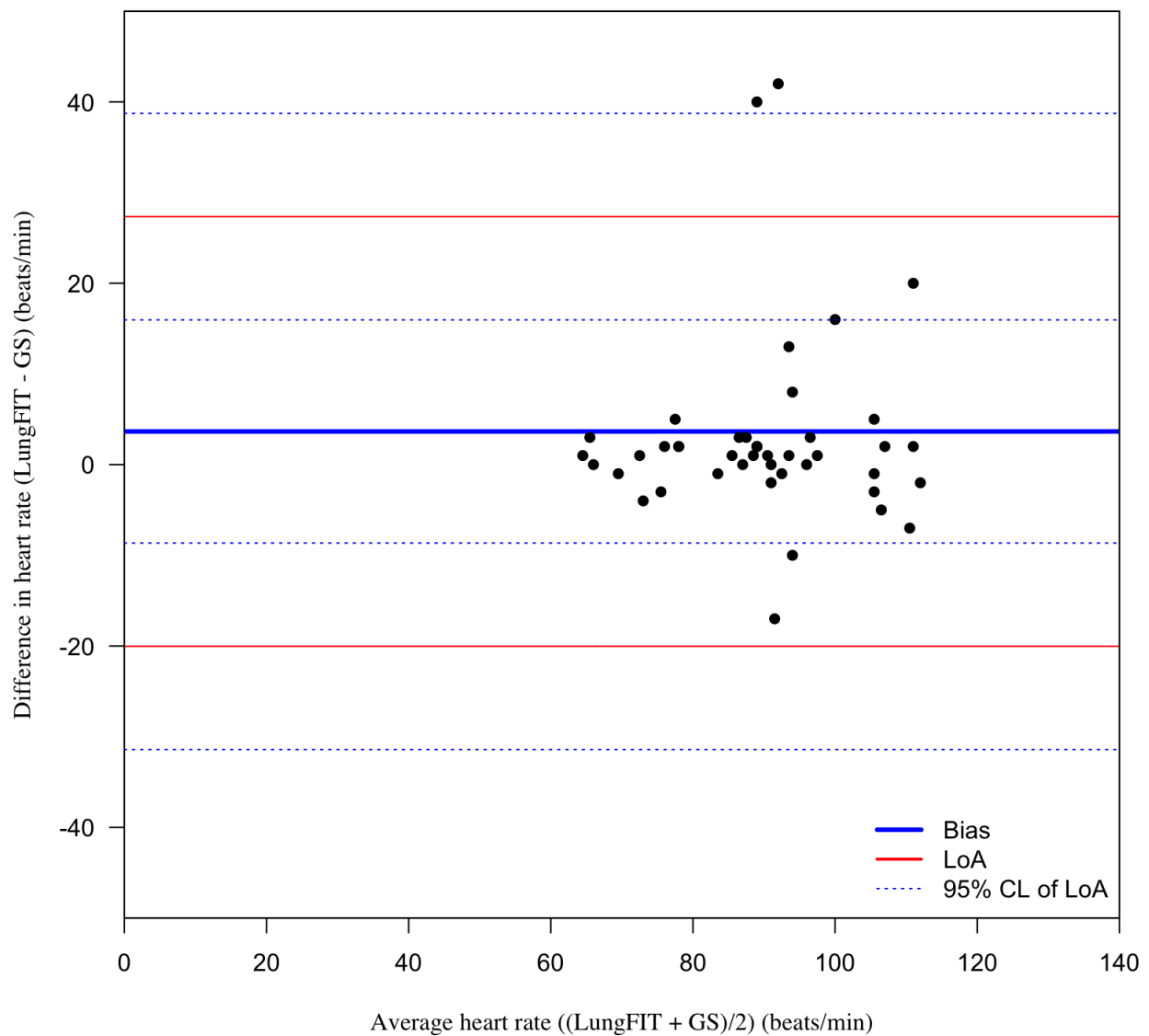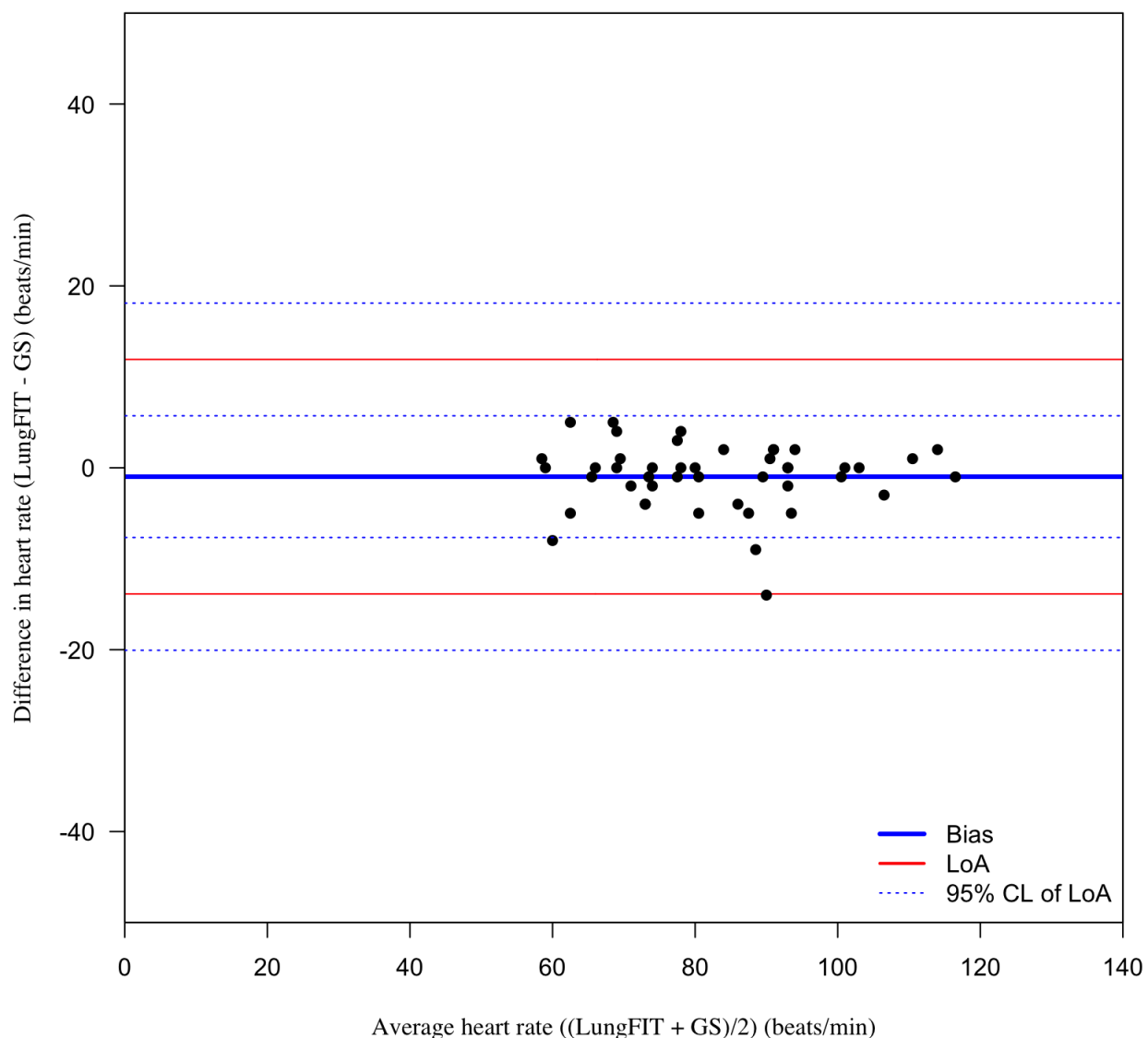
**Bland-Altman Plot: Heart Rate -
Treadmill Test - LGT - Exercise**
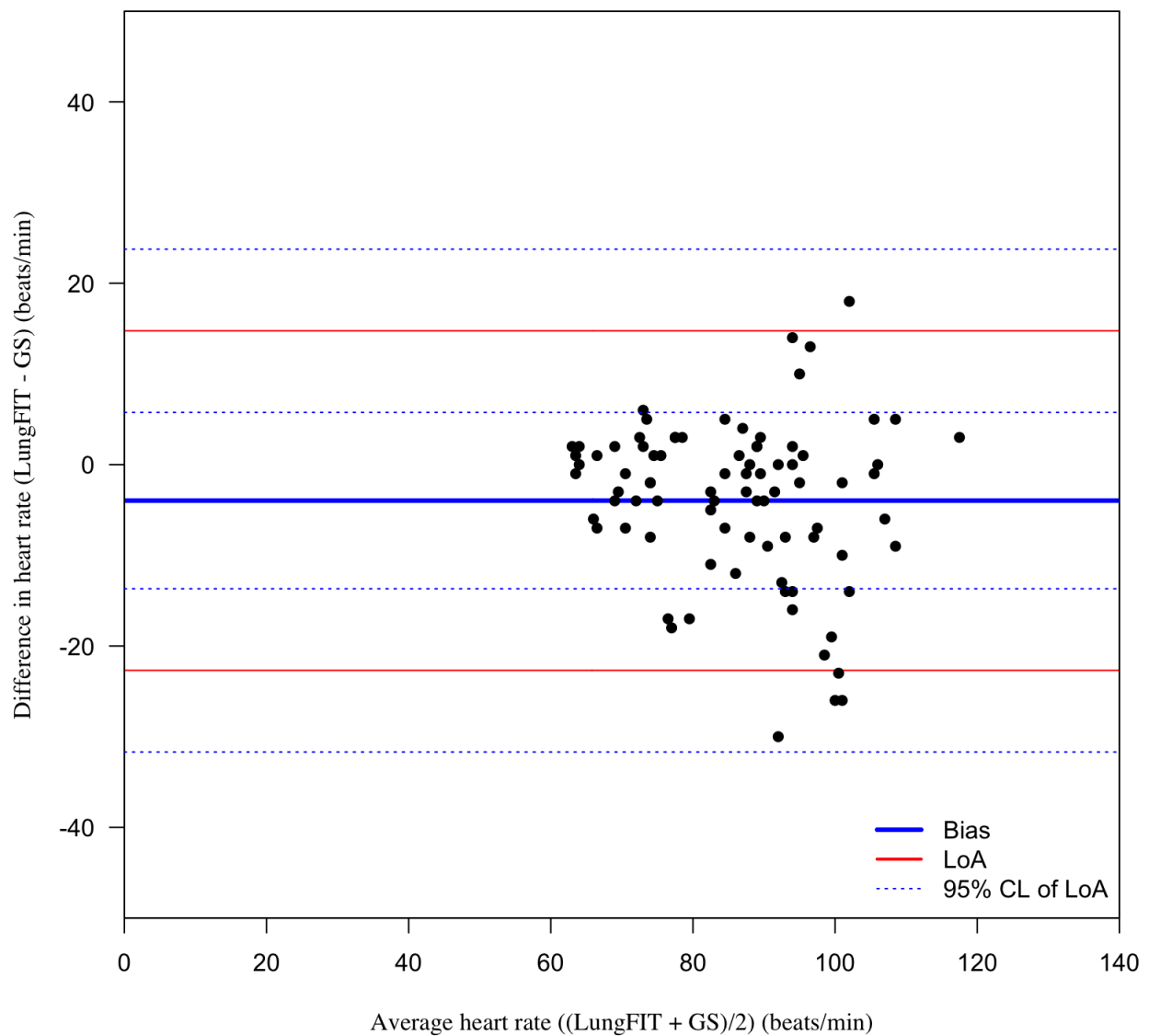
LGT-LionsGate Technologies, LoA-Limit of Agreement, GS-Gold Standard

Figure 41: Bland-Altman Plot: Heart Rate – Treadmill Test – LionsGate Technologies – Exercise. The solid blue line represents the mean difference or bias over 3 trials. Solid red lines represent limits of agreement over three trials. Blue, dashed lines are the 95% confidence intervals for each limit of agreement. Each black data point represents a subject's measurement difference between the LungFIT probe and gold standard. Validity was determined if mean bias was ≤ ±5 beats/min and limits of agreement were ≤ ±10 beats/min.

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Appendices

Appendix A: Exercise Test Instructions Script

Instructions to the subject will be as follows: "There are 3 different tests you will be performing today. You will start with exercising on a stationary bike. You will be cycling 3 times for 5 minutes at 60-70 RPM with a 3 minute break after each set. The intensity will be set at a level that you consider moderate to somewhat hard. For this test, we ask that you rest your hands in a relaxed state on the handle bars in front of you while cycling. I will be taking measurement periodically from the LungFITs on your arm. You will then walk on a treadmill 3 times for 5 minutes each time at a 3 km/hr which is a low and comfortable speed. For this test, we ask that you keep your arms to your sides in a normal swinging fashion, but you may touch the handlebars if you need to for balance. You will be given 3 minutes to rest after each set. Finally, you will walk outside around the park at Thurlow Street and Comox Street. You will walk around a standardized course 3 times with a 3 minute break in between each lap. For this test, we will ask you to pause at 3 locations in order to record data off the iPhone. You will be wearing an oximeter on one hand, the LungFIT system on 3 other fingers, and the Cosmed K4b2 Metabolic System. The Cosmed device involves wearing a face mask that measures every breath you take. We will be recording your heart rate and oxygen saturation during the last 30 seconds of each set while you exercise and at the end of each of your rest breaks. We will be with you throughout all your exercise in case you need to stop and rest or need help with anything. You will be allowed to rest or stop during any point of the experiment if you feel fatigued, uncomfortable, light-headed or ill. If you need a break from the mask you will be permitted to remove it in between the 3 different tests. Do you have any questions or concerns so far?"

Appendix B: LungFIT Study: Data Collection Form

PATIENT CHARACTERISTICS

Patient ID#	LGF_sub_			
Age				
Sex				
Height (cm)				
Weight (kg)				
Smoking Status (circle one)	Active smoker	Ex-Smoker	Never-Smoker	
Smoking History (pack years) 20/pack	= (packs smoked per day) x (years as a smoker) =			
Smartphone Experience	Novice (never used)	Intermediate (used before)	Advanced (use daily)	Expert (refined use)
Resting Heart Rate (beats/min)	Pulse Oximeter			
Resting Oxygen Saturation (%)	Pulse Oximeter			
LungFIT arm	Left			Right
Other Medical History				

LungFIT Orientation Test

	Time to Complete (seconds, 1 decimal place)	Comments / Observations
1. Get to iPhone's home screen and select the PC app		
2. Properly exit the application		
3. Assemble and connect probe to iPhone		
4. Insert iPhone into the armband and put armband on to arm.		
5. Put on probe re-open PC app, and begin recording data.		
6. What is your oxygen saturation and heart rate?		
7. Take off probe and remove armband from arm.		
8. Remove iPhone from armband and stop recording data.		
9. Exit application and turn off iPhone.		

LungFIT Advanced Orientation Test

	Time to Complete (seconds, 1 decimal place)	Comments / Observations
Field Test Setup the LungFIT system on your arm. Determine your heart rate and oxygen saturation. Disassemble and turn off the LungFIT		

LungFIT Usability Questionnaire

Adapted from Ryu YS, Smith-Jackson TL. Reliability and validity of the Mobile Phone Usability Questionnaire (MPUQ). Journal of Usability studies 2006; 2:39-53.

		Yes	No
	Ease of Learning and Use		
1.	Is it easy to learn to operate the LungFIT system?		
2.	Is the operation of this system simple and uncomplicated?		
3.	Is it easy to access the information you need from the system?		
4.	Is the organization of information on the screen clear?		
5.	Does the system have all the functions and capabilities you would expect it to have?		
6.	Are the colour coding and data display compatible with typical smartphones?		
7.	It is easy for you to remember how to perform tasks with this system?		
8.	Is the system clear and understandable?		
9.	Are the characters on the screen easy to read?		

		Yes	No
10	Does using the LungFIT system require a lot of mental effort?		
11	Is it easy to set up the LungFIT system?		
12	Is inputting the probe into the smartphone easy?		
13	Are you able to identify when readings from the probe are strong and stable?		
14	Can you insert the smartphone into an armband easily?		
	Helpfulness and Problem-Solving Capabilities		
15	Are the documentation and instructions for LungFIT clear and understandable?		
16	Is it easy to take corrective actions once an error has been recognized?		
	Affective Aspect and Multimedia Properties		
17	Is the smartphone size convenient for wearing or storage?		
18	Is using the system frustrating?		
19	Is the LungFIT system attractive?		
20	Do you feel confident using LungFIT?		

		Yes	No
21	Are pictures on the screen of satisfactory quality and size?		
22	Do you feel excited when using LungFIT?		
23	Would you miss LungFIT if you no longer had it?		
24	Would you be proud of this product?		
	Commands and Minimal Memory Load		
25	Is the design of the graphic symbols, icons and labels on the icons sufficiently relevant?		
26	Are the home and menu buttons sufficiently easy to locate for all operations?		
	Control and Efficiency		
27	Are the response time and information display fast enough?		
28	Has the LungFIT system at some time stopped unexpectedly?		
29	Is the amount of information displayed on the screen adequate?		
30	Is the data display consistent?		
31	Is it easy to operate keys with one hand?		

Cycle Test

Cycle Test	Time Point	Time Recorded	LungFIT HR (beats/min)			LungFIT SpO2 (%O2)			LungFIT Reading Strength (X=weak)		
			Nonin	Masimo	Aux	Nonin	Masimo	Aux	Nonin	Masimo	Aux
Trial #1	(mark) Rest										
	2 min										
	End (mark)										
Trial #2	(mark) Rest										
	2 min										
	End (mark)										
Trail #3	(mark) Rest										
	2 min										
	End (mark)										

Treadmill Test

Treadmill Test	Time Point	Time Recorded	LungFIT HR (beats/min)			LungFIT SpO2 (%O2)			LungFIT Reading Strength (X=weak)		
			Nonin	Masimo	Aux	Nonin	Masimo	Aux	Nonin	Masimo	Aux
Trial #1	(mark) Rest										
	2 min										
	End (mark)										
Trial #2	(mark) Rest										
	2 min										
	End (mark)										
Trail #3	(mark) Rest										
	2 min										
	End (mark)										

Outside Walking Test

Outside Walking Test	LungFIT Distance (coordinates)					Difference to 362m	Cosmed (kcal)
	Start point	1st pylon	2nd pylon	3rd pylon	End point Total Distance		
Trial #1 (mark)							
Trial #2 (mark)							
Trail #3 (mark)							

Cycle Test

Cycle Test	Time Point	Time Recorded	ECG HR (beats/min)	Pulse Oximeter (%02)	Cosmed EE (kcal)
Trial #1	Rest				
	2 min				
	End				
Trial #2	Rest				
	2 min				
	End				
Trail #3	Rest				
	2 min				
	End				

Treadmill Test

Treadmill Test	Time Point	Time Recorded	ECG HR (beats/min)	Pulse Oximeter (%02)	Cosmed EE (kcal)
Trial #1	Rest				
	2 min				
	End				
Trial #2	Rest				
	2 min				
	End				
Trail #3	Rest				
	2 min				
	End				

Appendix C: Bland-Altman Analysis of: Heart Rate – Cycle Test – Nonin Probe – Rest

Nonin probe: Cycle Ergometer Test - Heart Rate	12-Lead ECG	Difference (y-axis)	Average (X-axis)
Set 1	Set 1		
55.00	55.00	0.00	55.00
67.00	65.00	2.00	66.00
81.00	83.00	-2.00	82.00
57.00	63.00	-6.00	60.00
73.00	74.00	-1.00	73.50
77.00	78.00	-1.00	77.50
73.00	69.00	4.00	71.00
88.00	90.00	-2.00	89.00
93.00	93.00	0.00	93.00
60.00	60.00	0.00	60.00
82.00	81.00	1.00	81.50
76.00	76.00	0.00	76.00
67.00	73.00	-6.00	70.00
80.00	80.00	0.00	80.00
54.00	55.00	-1.00	54.50
	Mean Difference (beats/min)	-0.8	
	Standard Deviation (+/- beats/min)	2.6	
	Upper limits of agreement (beats/min)	4.39	
	Lower limits of agreement (beats/min)	-5.99	
Set 2	Set 2	Difference (y-axis)	Average (X-axis)
61.00	57.00	4.00	59.00
65.00	64.00	1.00	64.50
	89.00		89.00
61.00	67.00	-6.00	64.00
80.00	80.00	0.00	80.00
78.00	76.00	2.00	77.00
81.00	78.00	3.00	79.50
	98.00		98.00
108.00	109.00	-1.00	108.50
61.00	60.00	1.00	60.50
82.00	84.00	-2.00	83.00
94.00	95.00	-1.00	94.50
65.00	62.00	3.00	63.50

Nonin probe: Cycle Ergometer Test - Heart Rate	12-Lead ECG	Difference (y-axis)	Average (X-axis)
87.00	88.00	-1.00	87.50
59.00	59.00	0.00	59.00
	Mean Difference (beats/min)	0.23	
	Standard Deviation (+/- beats/min)	2.62	
	Upper limits of agreement (beats/min)	5.47	
	Lower limits of agreement (beats/min)	-5.01	
Set 3	Set 3	Difference (y-axis)	Average (X-axis)
63.00	61.00	2.00	62.00
71.00	70.00	1.00	70.50
96.00	103.00	-7.00	99.50
70.00	71.00	-1.00	70.50
90.00	93.00	-3.00	91.50
82.00	85.00	-3.00	83.50
82.00	80.00	2.00	81.00
105.00	106.00	-1.00	105.50
114.00	112.00	2.00	113.00
64.00	64.00	0.00	64.00
85.00	87.00	-2.00	86.00
84.00	91.00	-7.00	87.50
70.00	66.00	4.00	68.00
85.00	82.00	3.00	83.50
59.00	61.00	-2.00	60.00
	Mean Difference (beats/min)	-0.8	
	Standard Deviation (+/- beats/min)	3.32	
	Upper limits of agreement (beats/min)	5.84	
	Lower limits of agreement (beats/min)	-7.44	
	Cumulative Mean Difference (beats/min)	-0.49	

R code to determine mean limits of agreement and 95% confidence intervals:

#convert to a Meth object

dataname <- Meth(dataname)

calculates the estimate values

est <- BA.est(dataname, linked=FALSE)

#number of participants/subjects

n<-15

#t-alpha one sided for n-1=14 df, alpha=0.05 = 1.76; for two-sided=2.15 (from t-table)

t.alpha <- 2.15

#se is the square root of 3 times the sd-squared, divided by n

se <- sqrt(((((est$LoA[1,4])^2)*3)/n)

#use this se estimate to calculate confidence intervals

lowerLoA_lowerCL <- (est$LoA[1,2]-t.alpha*se)

lowerLoA_upperCL <- (est$LoA[1,2]+t.alpha*se)

upperLoA_lowerCL <- (est$LoA[1,3]-t.alpha*se)

upperLoA_upperCL <- (est$LoA[1,3]+t.alpha*se)