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Caffeine and Airway Resistance

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by

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Dedication

I would like to dedicate this work to my wife, Alice, who has encouraged me, stood beside me and inspired me in these efforts.

Acknowledgements

I would like to thank Dr. Robert Haight for his assistance in this project. I would also like to thank Dr. Stuart Brooks for providing me encouragement and the opportunity to work on this project.

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ABSTRACT

This study investigated the effect of caffeine on airway resistance. The subjects were drawn from volunteers (18-90 years old) in good health, with no major cardiopulmonary conditions.

We found no association between the consumption of a single cup of the caffeinated beverage coffee and a decrease in airway resistance within one hour in a normal population of subjects as measured neither by impulse oscillometry nor with conventional spirometry. It appears that any possible bronchodilatory effect of the caffeine from a single cup of coffee in a normal population is below the limit of detection of spirometry and impulse oscillometry or is not sufficiently expressed in the one-hour time frame of the study.

The study did validate currently accepted methods of using the Jaeger impulse oscillometry (IOS) measurement for use at the University of South Florida (USF). The impulse oscillometry technique was found to be a useful adjunct to conventional pulmonary function testing. Conventional pulmonary function testing provides a useful measure of a person's ability to breathe yet is difficult to perform and only indirectly guides the physician to the diagnosis of the pathology behind the person's breathing

difficulties. The impulse oscillometry technique may help the physician to noninvasively determine the location of a pulmonary obstruction by measurement of the dynamics of sound wave travel through the airways of the lungs.

Introduction

Caffeine

Mankind has been drinking caffeinated beverages for almost 5000 years with the discovery of brewed tea attributed to the Second Emperor of China, Shen Nung, also known as the divine healer. Tea and coffee contain about 20-60 mg and 125-185 mg of caffeine respectively per cup and have been prized throughout their history as both stimulants and palliatives for respiratory disorders[1, 2]. The efficacy of caffeine in asthma has been evaluated in a recent evidence based medicine review of clinical trials which concludes "Caffeine appears to improve airways modestly in people with asthma for up to four hours"[3].

Yet, still much is not known both about the mechanisms of action of caffeine and the extent to which the general population, consciously or unconsciously uses caffeine to self-medicate respiratory ailments. Caffeine and its more active metabolic products, theophylline and theobromine have long demonstrated bronchodilator effects through relaxation of bronchial smooth muscle[4]. They are phosphodiesterase (PDE) inhibitors and decrease the rate at which the intracellular second messengers cAMP and cGMP are degraded. Phosphodiesterase inhibitors also increase diaphragmatic contractility and respiratory drive probably through adenosine receptor antagonism[5]. Recently, theophylline has been shown to exercise immunomodulatory and anti-inflammatory

properties even at sub-bronchodilator doses and plasma levels[6]. This has been confirmed by measurement of exhaled nitric oxide levels after caffeine consumption[7].

The discovery of tissue specific PDE isoenzymes in the 1970's has led to interest in the development of selective PDE inhibitors such as roflumilast and cilomilast[8, 9]. Selective PDE4 inhibitors are hoped to offer improved anti-inflammatory effects and improved safety over nonspecific PDE inhibitors such as theophylline. The PDE4 specific inhibitors cilomilast and roflumilast are now in clinical trials and appear promising[10-12].

Spirometry

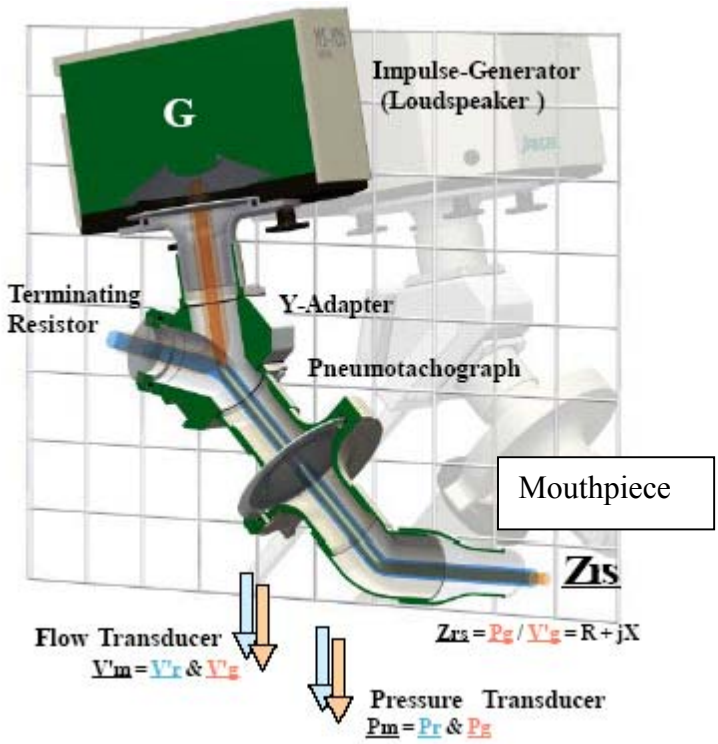
Spirometry has great utility for the diagnosis of respiratory disorders, monitoring of pulmonary disease progression, and assessment of treatment efficacy. It is a composite measure of lung function that reveals much about overall air exchange capability yet is less illuminating of the various factors contributing to obstructive and restrictive lung deficits. These factors may include body habitus, chest wall elasticity, lung compliance, airway resistance, cystic air trapping, respiratory muscle weakness and CNS impairment[13, 14]. Thus for obstructive lung disorders it has been desirable to directly measure airway resistance and many techniques have been developed to accomplish this[15]. Unfortunately these methods of airway resistance measurement such as plethysmography and the forced oscillation technique have previously been unsuitable for clinical application due to complexity and cost.

Impulse Oscillometry

Recently an application of the forced oscillation technique known as impulse

oscillometry (IOS) has become available in a compact package. This Jaeger Masterscreen IOS package is non-invasive and FDA approved for IOS and conventional spirometry measurements. A diagram of the typical equipment is shown in Figure 1[16].

Figure 1. Impulse Oscillometer



Impulse oscillometry uses the pressure-flow relationship of artificial impulse-shaped test signals produced by an external generator. These artificial signals are superimposed on the normal tidal breathing waveform of the subject while he is breathing ambient air. Fast Fourier Transform (FFT) and quotient calculation is performed to derive frequency versus impedance, resistance and reactance curves. This data can then be used to describe airflow characteristics of the subjects' lungs both in degree of and location of impairment[16]. Useful respiratory impedance parameters include R5, total

respiratory resistance; R20, proximal respiratory resistance; and X5, distal capacitive reactance (inversely related to the compliance of the lung).

Asthma

Asthma is the intermittent obstruction of lung airways in response to intrinsic or environmental provocation such as allergens, physiologic stress or infection. Asthma is thought to be under diagnosed both in the general population and the elderly. Many times there is a history of wheezing, especially after viral infections. Often childhood asthma enters remission in the second decade of life only to return in adulthood. Asthma may occur after decades of pulmonary insult from tobacco smoking, occasionally secondary to workplace exposures, and sometimes explosively with no prior history of asthma[17, 18].

Reports on the use of over-the-counter bronchodilator medications in asthmatics indicate not only are asthmatics under diagnosed, but medically diagnosed asthmatics who self-treat are less likely to receive and use anti-inflammatory therapy[19]. Modern anti-inflammatory therapy can both relieve the symptoms of and delay the progression of asthma. Further reports of other self and alternative medicine treatments for asthma include herbal products, coffee, black tea, reflexology, acupuncture, massage therapy, homeopathy, aromatherapy, and spinal manipulation[20-23]. Treatments, such as Chinese herbs, may have concerning safety profiles and unpredictable interactions with conventional medications[24]. Even if these alternative therapies are partially efficacious, it may only delay the diagnosis of asthma until an episode of respiratory failure places the patient in a hospital emergency department.

Asthma is not the only cause of obstructive pulmonary pathology. Other obstructive lung pathologies include chronic obstructive lung disease (chronic bronchitis or emphysema), bronchiectasis, cystic fibrosis, and bronchiolitis[25]. Recently it has been recognized that vocal cord dysfunction may present with asthma-like symptoms[26]. Each of these illnesses tends to obstruct different areas of the respiratory tree. Asthma tends to exercise a predominant effect on the bronchi (larger airways) while chronic obstructive lung disease tends to affect both large and small airways. In bronchiectasis, there is dilatation of the bronchi with obstruction of the smaller distal airways. Cystic fibrosis tends to initially affect the smaller airways with later evolution to bronchiectasis. In contrast, bronchiolitis tends to affect the bronchioles (smaller airways). Vocal cord dysfunction affects the flow of air through the larynx (voicebox).

Methods

The study was designed to investigate the question: "Is there a significant bronchodilator effect observed in a normal population with the consumption of a single cup of caffeinated coffee?" The hypotheses to be tested was: "A bronchodilator effect as measured as total respiratory resistance at 5 Hz by impulse oscillometry will be observed in a normal population with the consumption of a single cup of caffeinated coffee after one hour."

Study Subjects

Subjects by interview had no history of diagnosis of major cardiopulmonary conditions. The sample consisted of 20 subjects with an approximately equal distribution of gender in the group.

Subjects had to be of a certain age group to be eligible for the study: ages 18 to 90 years old (dates of birth 1914-1986). If the subjects were of this age group and decided to participate in this study, each reviewed the informed consent and discussed the study and possible participation with the study physician. If a subject was interested in participating, the informed consent was be signed before any study-related test or procedure was done. After signing the informed consent, screening tests were completed to determine if a subject met the requirements to be in the study.

Potential candidates were screened to determine whether they could be considered "normal". Screening tests include completing standard questionnaires, undergoing a physician's interview, submitting to a physical examination and completing spirometry measurements. The questionnaires are shown in Appendix A. The study physician investigator reviewed the questionnaire responses; interviewed the subjects and completed spirometry. All spirometry was performed according to American Thoracic Society specifications and predicted values were taken from Hankinson, Crapo and co-workers values[27]. In order to qualify, participants must have recorded a negative questionnaire response suggestive of heart problems such as chest pain, irregular heartbeats or uncontrolled high blood pressure. They also must not have been receiving any medical treatment for any pulmonary condition.

Data Collected

Data was collected about the airway resistance of subjects using the Jaeger impulse oscillometer and conventional pulmonary function tests. These tests were performed before and 60 minutes after coffee consumption and subjects were interviewed as to current and previous state of health, smoking history and current respiratory symptoms. Patients were interviewed before and after the test, filled out the questionnaires in Appendix A and asked to report any respiratory or sensory changes.

Pulmonary Measurement and Analysis

This study was performed in the respiratory investigations lab of the Occupational and Environmental Medicine Department at the College of Public Health at the University of South Florida, Tampa, FL. Over a two-week period, twenty subjects were

interviewed and tested during a single one to two hour visit. With the exception of the informed consent form, all documentation was only identified by subject number. They filled out a questionnaire screening for major medical conditions, underwent an interview and received a screening exam. They then filled out a pre-test symptom questionnaire, performed conventional spirometry and underwent impulse oscillometry. Spirometry and impulse oscillometry were perfomed in a seated position for safety. The subject was fitted with a nose clip and instructed in the performance of the forced expiratory maneuver. The use of the spirometry equipment is illustrated in Figure 2. Three acceptable maneuvers were obtained and the best was retained for comparison.

Figure 2. Use of Spirometry Equipment

The restrictor screen door (Figure 3a) on the impulse oscillometer was closed (Figure 3b) and the subject instructed on the IOS procedures. The device was zeroed and the subject was then instructed to begin breathing through the mouthpiece while supporting his cheeks with his hands (Figure 4). After thirty seconds of breathing

normally through the mouthpiece and acclimating to the device, thirty seconds of measurements were taken.

Figure 3. IOS Restrictor Screen Door

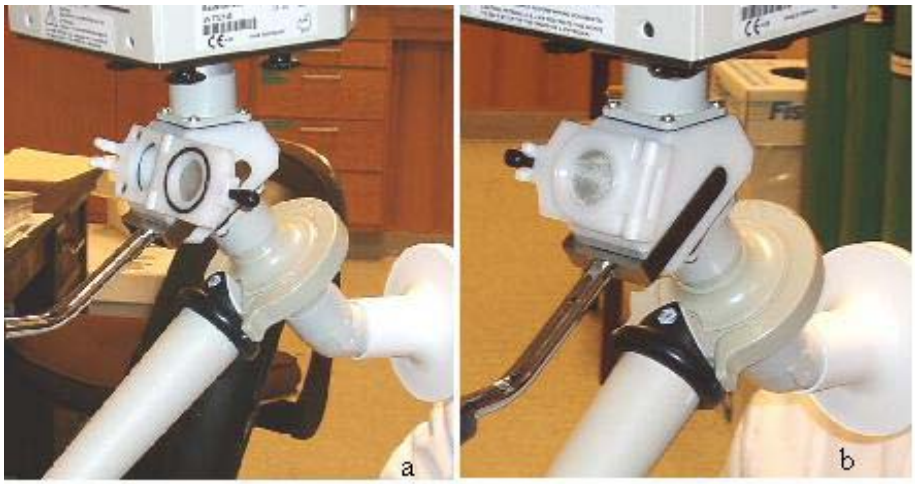


Figure 4. IOS Subject Hand Position

The subjects then received one eight ounce cup of premium caffeinated coffee and filled out a medical history questionnaire. The coffee was the brand name Starbucks Breakfast Blend and was prepared according to the instructions received with the package of coffee. One tablespoon (15 milliliters of dried ground coffee) per six ounces (180 milliliters) of water was prepared using a drip type coffee maker. One hour later the subjects again filled out a symptom questionnaire, performed conventional spirometry and underwent impulse oscillometry. These questionnaires are shown in Appendix A.

The investigator then interviewed the subject and performed a post-test auscultation of the subject's chest to conclude the subject's visit. Jaeger impulse oscillometry and conventional spirometry data were collected using the Jaeger LabManager software. It was then was integrated with medical history data in a Microsoft Excel spreadsheet and analyzed using the JMP 5.1 statistical program.

Results

Study Sample Characteristics

The study sample of twenty subjects was split approximately equally between male(11) and female(9) subjects. The age of the sample ranged from 26 to 68 years with a median age of 40 years. Seventeen of the subjects were Caucasian, two were US-Asian, and one was US-African. Sixteen of the twenty subjects reported no health problems. Health problems that were reported included mitral valve prolapse, migraine headaches, lower back pain, glaucoma, urinary stones, history of fractures, hypertension, and frequent urinary tract infections.

Pre and post coffee consumption symptoms were monitored by use of the questionnaires in Appendix A. Subjects were asked to describe symptoms of heavy or difficulty in breathing, phlegm production, runny or irritated nasal passages, throat irritation or burning, sensation of weight or tightness of the chest and feeling of chest burning. Each symptom was rated a numeric scale of none(1), very little(2), moderate amount(3) and very much(4). Descriptive statistics for the study sample are shown in Table 2 and Appendices E and F. Additional sample characterstics are detailed in Table 1 and Appendices B, C and D.

Table 1. Study Sample Characteristics

Gender	Female (9) 45% Male (11) 55%
Race / Ethnicity	Caucasian (17) 85% US African (1) 5% US Asian (2) 10%
Age	Range 26-68 years Median 40 years Mean 41.15 years Standard Deviation 9.76 years
Health Problems	None (16) 80%, Mitral valve prolapse (1) 5%, Migraine headaches (1) 5%, Lower back pain (1) 5%, Glaucoma (1) 5%, Urinary stones (1) 5%, History of fractures (1) 5%, Hypertension (1) 5%, Frequent urinary tract infections (1) 5%
Medications	None (10) 50%, Multivitamin (3) 15%, Calcium (1) 5%, Vitamin C (1) 5%, Saw palmetto (1) 5%, Lo Ovral (1) 5%, Tryoptic (1) 5%, Naprosyn (1) 5%, Premarin (1) 5%, OTC sinus medication (1) 5%, Yasmin (1) 5%, Spector (1) 5%, Paxil (1) 5%
Tobacco Smoker	No (15) 75% Yes (3) 15% Past (2) 10%

Table 2. Pre and Post Coffee Symptom Questionnaire Results

		Median	Mean	Standard Deviation
Breathing Difficulties	Pre Coffee	1.000	1.150	0.489
	Post Coffee	1.000	1.100	0.447
Phlegm Production	Pre Coffee	1.000	1.350	0.671
	Post Coffee	1.000	1.450	0.605
Nasal Problems	Pre Coffee	1.000	1.200	0.523
	Post Coffee	1.000	1.100	0.308
Throat Irritation	Pre Coffee	1.000	1.200	0.523
	Post Coffee	1.000	1.200	0.523
Chest Tightness	Pre Coffee	1.000	1.150	0.366
	Post Coffee	1.000	1.050	0.224
Chest Burning	Pre Coffee	1.000	1.000	0.000
	Post Coffee	1.000	1.000	0.000

Impulse Oscillometry Measurements

A significant trend could not be detected in impulse oscillometry measurements. The sample measurements appeared to be normally distributed and were analyzed using a matched pairs t-test. The results are summarized in Table 3 and detailed in Appendices G, I and J. Mean pre-coffee total respiratory resistance at 5 Hz (R5) was 4.125. Mean post-coffee R5 was 4.107. The t value was -0.15236 and the probability of obtaining this t value through chance alone when there is no difference is 0.4403. Therefore the null hypothesis failed to be rejected at alpha= 0.05. Wilcoxon Sign-Rank test results were similar.

Table 3. Impulse Oscillometry Measurements

	Median	Mean	Standard Deviation
Pre-coffee R5	4.000	4.125	1.095
Post-coffee R5	3.865	4.107	1.247

Spirometric Measurements

A significant trend could not be detected in conventional spirometry measurements of forced expiratory ventilation in one second (FEV1). The sample measurements did not appear to be normally distributed and therefore were analyzed using a matched pairs Wilcoxon Sign-Rank test. The results are summarized in Table 4 and detailed in Appendices H, I and J. Median pre-coffee FEV1 was 3.430. Median post-coffee FEV1 was 3.545. The Wilcoxon Sign-Rank test value was 7.000 and the probability of obtaining this value through chance alone when there is no difference is

0.387. Therefore this secondary measure also failed reach significance at alpha= 0.05. Matched pairs t-test results were similar.

Table 4. Spirometric Measurements

	Median	Mean	Standard Deviation
Pre-coffee FEV1	3.430	3.425	0.842
Post-coffee FEV1	3.545	3.454	0.832

Discussion

This study compared respiratory parameters in a sample of normal subjects before and one hour after consumption of one cup of the caffeinated beverage coffee. Although the study failed to show a significant difference in R5 before and after consumption of this beverage it did provide useful experience in the use of the Jaeger Impulse Oscillometer. Further, this study failed to confirm a bronchodilator effect in normal individuals from consumption of caffeine as measured by changes in FEV1. This stands in contrast to previous studies on asthmatics in which an increase in FEV1 was measured.

One possibility for the minimal changes observed in the study was that the study sample was too healthy. Previous studies that demonstrated a bronchodilator effect were performed on asthmatics. This study excluded known asthmatics.

Another explanation was that the interval of one hour between consumption of the coffee and measurement of lung parameters was too short to allow time for a significant bronchodilator effect to develop. Some studies in asthmatics demonstrated a larger effect in intervals of two to four hours. It is possible that there is a measurable effect in a normal population but it takes longer than one hour to develop.

It is also possible that the dose of caffeine delivered by this coffee was less than that delivered by other brands or types of coffee. No attempt was made to quantify the caffeine content of this coffee. Although Starbucks Breakfast Blend Coffee was

presumed to have between 125 and 185 mg of caffeine per cup the actual caffeine content of this blend is unknown to this researcher. Caffeine has complex pharmacodynamics and remains in the body for more than one day. Thus in a habitual coffee drinker the effect may be masked by the previous days consumption of coffee.

There may simply be too much intra-subject and inter-subject variability in the in the amount of bronchodilation and bronchoconstriction existing even in normal subjects in response to environmental stimuli and personal characteristics from day to day and hour to hour. This "noise" would tend to mask small effects.

This study could be repeated on asthmatic subjects to characterize their response to caffeine using the IOS. The caffeine dose given could be exactly determined and subjects could be asked to abstain from caffeine for more than just overnight. Finally the study could be performed over a longer period of time on normal subjects to determine when a bronchodilatory effect occurs in normal subjects.

The study could be repeated with a greater attempt to control subjects activity and confounding exposures in the interval between the pre and post caffeine pulmonary measurements. The subjects were allowed to leave the lab area in the interval between being given the coffee and the post coffee respiratory measurements. By requiring the test subjects to remain in the lab area during the entire duration of the study the activities of the subjects can be monitored and external exposures could be controlled.

Conclusions

There was no evidence of bronchodilation induced one hour after consumption of a single cup of caffeinated coffee in normal individuals neither as measured by impulse oscillometry nor by conventional spirometry.

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Appendices

Appendix A: Questionnaires

Subject number:_____

Caffeine and Airway Resistance Study Pre-Coffee Questionnaire

Today's Date _____

People who are pregnant or have heart problems such as chest pain, irregular heartbeats or uncontrolled high blood pressure should not drink caffeinated beverages such as coffee.

Do you have any health problems that would prevent you from drinking coffee or have you been told by a doctor, nurse or other healthcare provider that you should avoid caffeinated beverages such as coffee?

Please circle "yes" or "no".

YES or NO

Do you take any medications from a doctor or other healthcare provider for your lungs?

Please circle "yes" or "no".

YES or NO

SUBJECT NUMBER:

_____

Pre-Coffee Consumption Symptom Questionnaire

"At this point in time, to what degree do you note the following symptoms?"

(1) Heavy or difficulty in your breathing

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

(2) Phlegm production

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

(3) Runny or irritated nose or nasal passages

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

(4) Throat irritation or burning sensation

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

(5) Sensation of a "weight" or tightness of the chest

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

(6) Feeling of chest burning

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

SUBJECT NUMBER:

_____

Post-Coffee Consumption Symptom Questionnaire

"At this point in time, to what degree do you note the following symptoms?"

(1) Heavy or difficulty in your breathing

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

(2) Phlegm production

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

(3) Runny or irritated nose or nasal passages

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

(4) Throat irritation or burning sensation

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

(5) Sensation of a "weight" or tightness of the chest

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

(6) Feeling of chest burning

1. ❒ NONE 2. ❒ VERY LITTLE 3. ❒ MODERATE AMOUNT 4. ❒ VERY MUCH

Subject number:_____

Caffeine and Airway Resistance Study Questionnaire

Today's Date _____

Gender: Male Female (circle one)

1) How old are you? _____years
2) Do you have any health problems that you see a physician for? Please list them below.

1._____

2. _____

3. _____

4. _____

5._____

3) Are you taking any medications? If so please list them below. (Including over the counter medications)

1._____

2. _____

3. _____

4. _____

5._____

4) If you have ever smoked, answer the following.

How many packs per day did you smoke? _____

For how many years did you smoke? _____

When did you stop smoking? _____

5) On what date were you last ill? _____

6) What illness did you have? _____

7) What is your occupation? _____

8) Are you exposed to second hand smoke at home or at work? Please circle "yes" or "no".

YES or NO

9) Were you or are you exposed to any gases, dusts, or fumes at your job?

YES or NO

If so, please explain: _____

_____

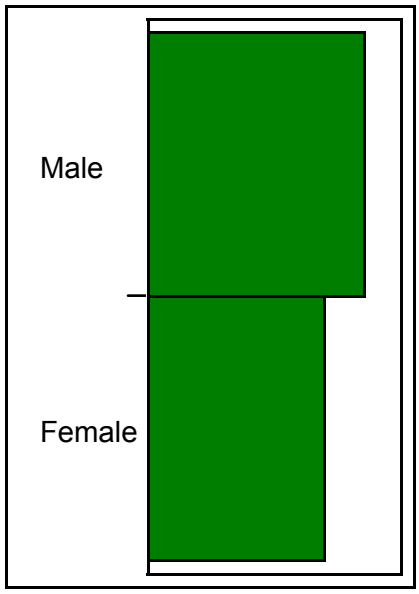
10) Do you ever wheeze or become short of breath? Please circle "yes" or "no".

YES or NO

Appendix B: Study Sample Characteristics

Gender	Ethnicity	Age	Health Problems	Medications	Smoker	Pack-years
Male	Caucasian	36	None	None	Past	1
Female	US-Asian	37	None	MVI, calcium	No	0
Female	Caucasian	26	None	MVI	No	0
Female	US-Asian	35	None	None	No	0
Male	Caucasian	39	None	None	No	0
Female	Caucasian	48	None	MVI, vitamin C	No	0
Male	Caucasian	35	None	None	No	0
Male	Caucasian	36	None	Saw palmetto	No	0
Female	Caucasian	40	MVP, migraine, LBP	Lo Ovral	Yes	15
Male	Caucasian	42	None	None	Yes	0.1
Female	Caucasian	42	None	None	No	0
Male	Caucasian	42	Glaucoma, stones, fx	Tryoptic, naprosyn	No	0
Female	Caucasian	54	None	Premarin, OTC sinus	No	0
Male	Caucasian	45	None	None	No	0
Female	Caucasian	26	None	Yasmin	Past	0.5
Male	Caucasian	68	None	Spector	No	0
Male	Caucasian	32	None	None	No	0
Male	Caucasian	52	Hypertension	None	No	0
Female	Caucasian	48	Frequent UTIs	Paxil	Yes	8
Male	US-African	40	None	None	No	0

Distributions
Gender

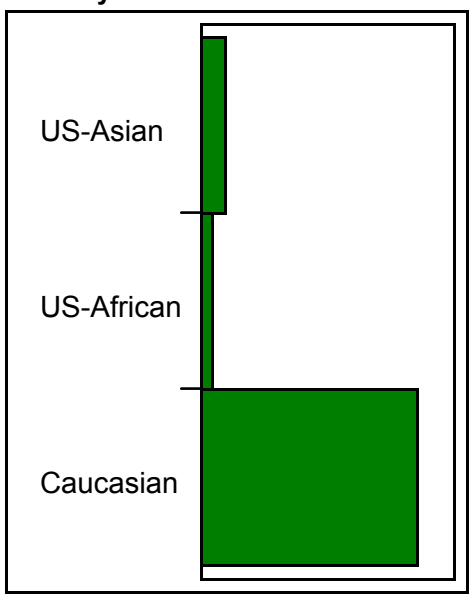


Frequencies

Level	Count	Prob
Female	9	0.45000
Male	11	0.55000
Total	20	1.00000

N Missing
0
2 Levels

Ethnicity

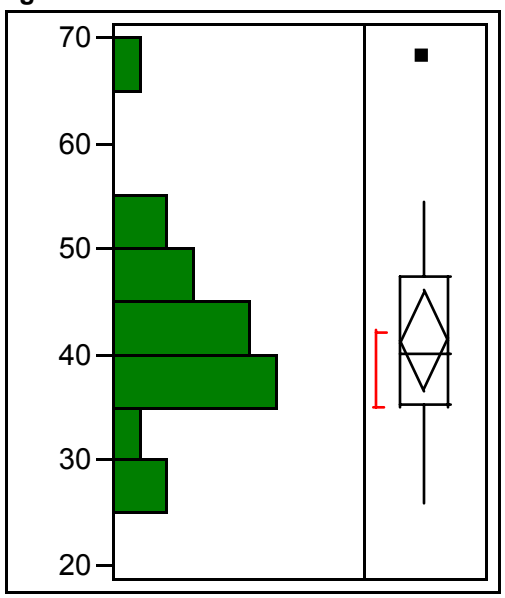


Frequencies

Level	Count	Prob
Caucasian	17	0.85000
US-African	1	0.05000
US-Asian	2	0.10000
Total	20	1.00000

N Missing
0
3 Levels

Age



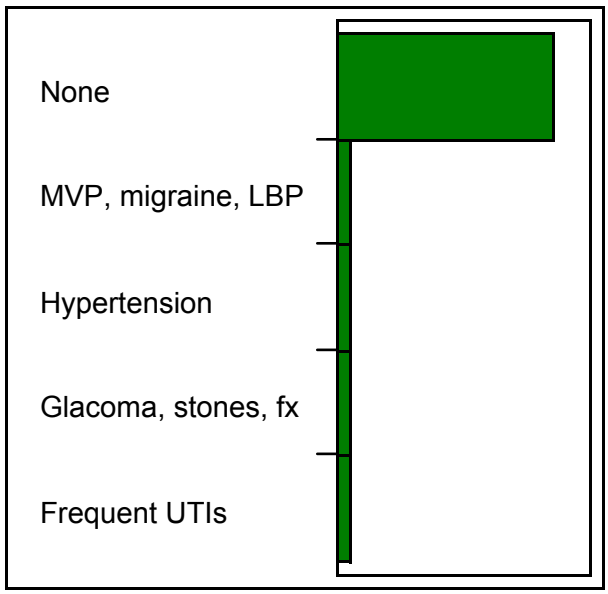
Quantiles

100.0%	maximum	68.000
99.5%		68.000
97.5%		68.000
90.0%		53.800
75.0%	quartile	47.250
50.0%	median	40.000
25.0%	quartile	35.250
10.0%		26.600
2.5%		26.000
0.5%		26.000
0.0%	minimum	26.000

Moments

Mean	41.15
Std Dev	9.7617675
Std Err Mean	2.1827976
upper 95% Mean	45.718648
lower 95% Mean	36.581352
N	20

Health Problems

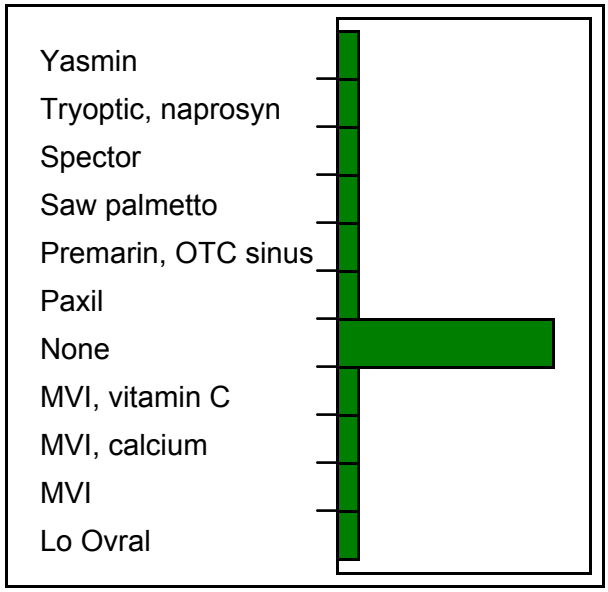


Frequencies

Level	Count	Prob
Frequent UTIs	1	0.05000
Glacoma, stones, fx	1	0.05000
Hypertension	1	0.05000
MVP, migraine, LBP	1	0.05000
None	16	0.80000
Total	20	1.00000

N Missing
0
5 Levels

Medications

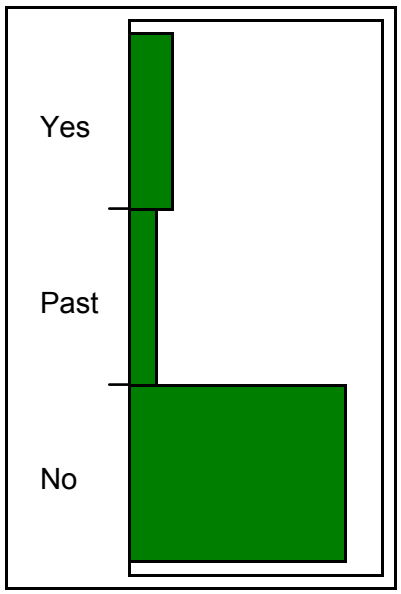


Frequencies

Level	Count	Prob
Lo Ovral	1	0.05000
MVI	1	0.05000
MVI, calcium	1	0.05000
MVI, vitamin C	1	0.05000
None	10	0.50000
Paxil	1	0.05000
Premarin, OTC sinus	1	0.05000
Saw palmetto	1	0.05000
Spector	1	0.05000
Tryoptic, naprosyn	1	0.05000
Yasmin	1	0.05000
Total	20	1.00000

N Missing
0
11 Levels

Smoker

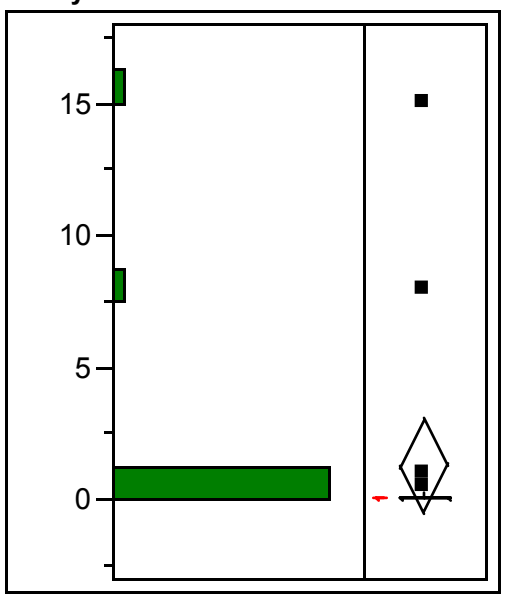


Frequencies

Level	Count	Prob
No	15	0.75000
Past	2	0.10000
Yes	3	0.15000
Total	20	1.00000

N Missing
0
3 Levels

Pack-years



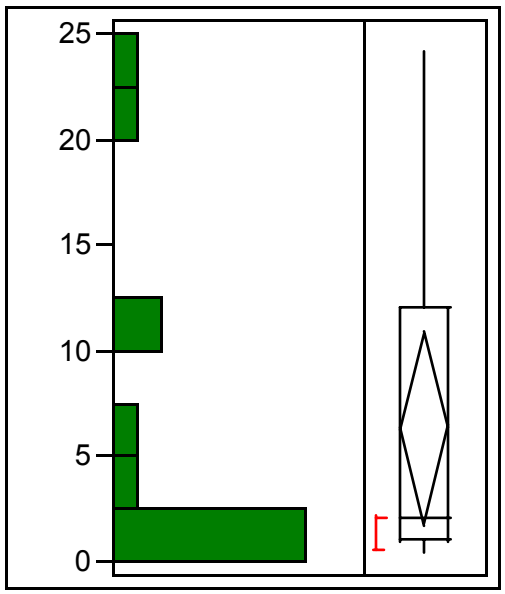
Quantiles

100.0%	maximum	15.000
99.5%		15.000
97.5%		15.000
90.0%		7.300
75.0%	quartile	0.075
50.0%	median	0.000
25.0%	quartile	0.000
10.0%		0.000
2.5%		0.000
0.5%		0.000
0.0%	minimum	0.000

Moments

Mean	1.23
Std Dev	3.6992318
Std Err Mean	0.8271734
upper 95% Mean	2.9612938
lower 95% Mean	-0.501294
N	20

Months Since Sick



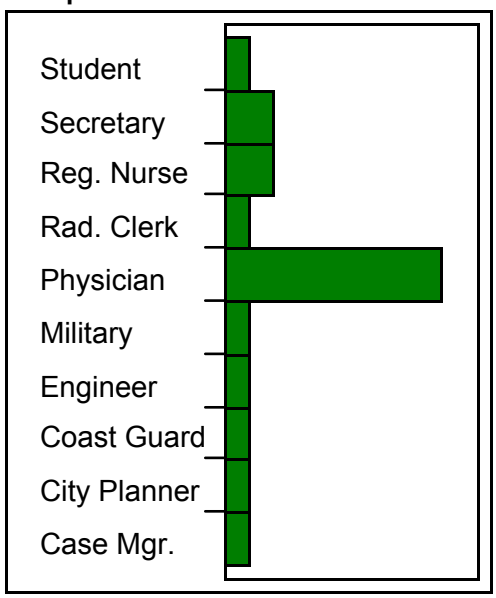
Quantiles

100.0%	maximum	24.000
99.5%		24.000
97.5%		24.000
90.0%		22.000
75.0%	quartile	12.000
50.0%	median	2.000
25.0%	quartile	1.000
10.0%		0.750
2.5%		0.500
0.5%		0.500
0.0%	minimum	0.500

Moments

Mean	6.25
Std Dev	7.7577505
Std Err Mean	2.073346
upper 95% Mean	10.729192
lower 95% Mean	1.7708082
N	14

Occupation

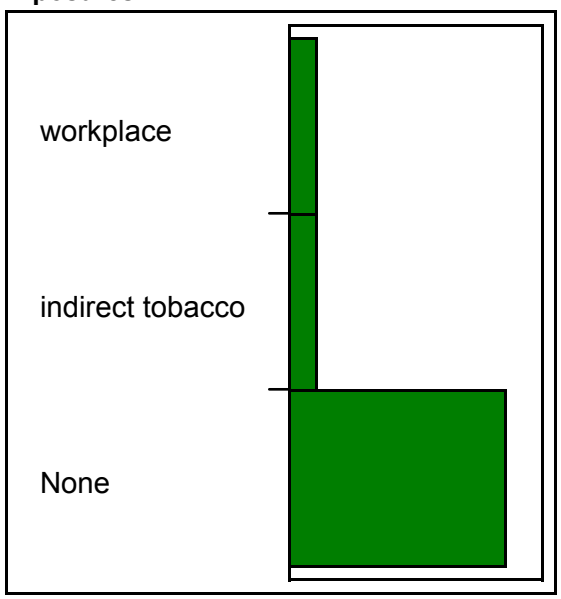


Frequencies

Level	Count	Prob
Case Mgr.	1	0.05000
City Planner	1	0.05000
Coast Guard	1	0.05000
Engineer	1	0.05000
Military	1	0.05000
Physician	9	0.45000
Rad. Clerk	1	0.05000
Reg. Nurse	2	0.10000
Secretary	2	0.10000
Student	1	0.05000
Total	20	1.00000

N Missing
0
10 Levels

Exposures

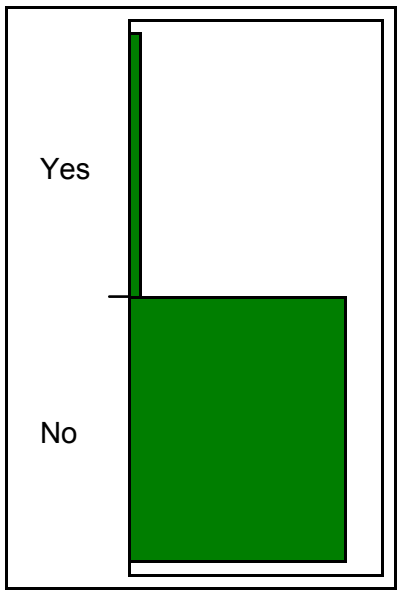


Frequencies

Level	Count	Prob
None	16	0.80000
indirect tobacco	2	0.10000
workplace	2	0.10000
Total	20	1.00000

N Missing
0
3 Levels

Wheeze/SOB



Frequencies

Level	Count	Prob
No	19	0.95000
Yes	1	0.05000
Total	20	1.00000

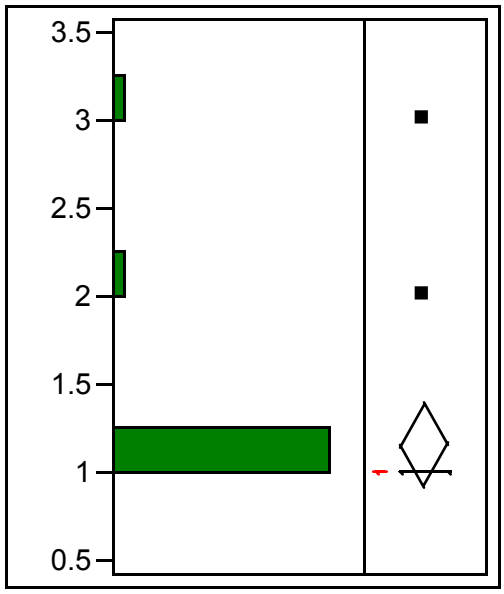
N Missing
0
2 Levels

Appendix E: Pre and Post Coffee Symptom Questionnaire Results

Pre Breathing	Post Breathing	Pre Phlegm	Post Phlegm	Pre Nose	Post Nose
1	1	1	2	1	1
1	1	1	2	1	1
1	1	1	2	1	1
1	1	3	2	1	1
1	1	1	2	1	1
3	3	3	3	2	2
1	1	2	1	3	2
1	1	1	1	1	1
2	1	1	2	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	2	2	2	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	2	1	1	1
1	1	1	1	1	1

Pre Throat	Post Throat	Pre Tightness	Post Tightness	Pre Burning	Post Burning
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
3	3	2	2	1	1
2	2	2	1	1	1
1	1	1	1	1	1
1	1	2	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
2	2	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1
1	1	1	1	1	1

Distributions
Pre Breathing



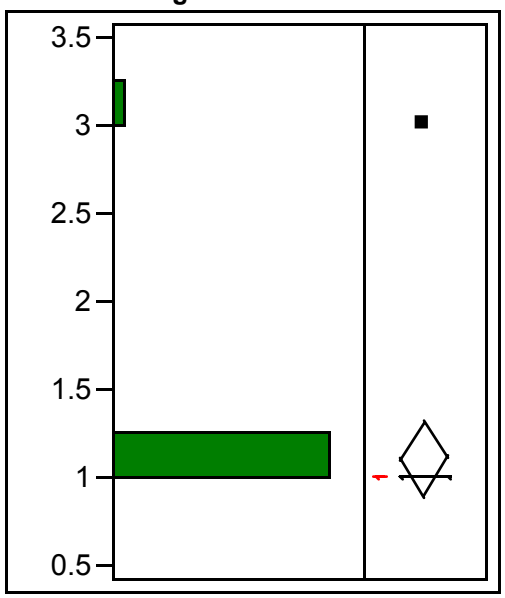
Quantiles

100.0%	maximum	3.0000
99.5%		3.0000
97.5%		3.0000
90.0%		1.9000
75.0%	quartile	1.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1.15
Std Dev	0.4893605
Std Err Mean	0.1094243
upper 95% Mean	1.3790278
lower 95% Mean	0.9209722
N	20

Post Breathing



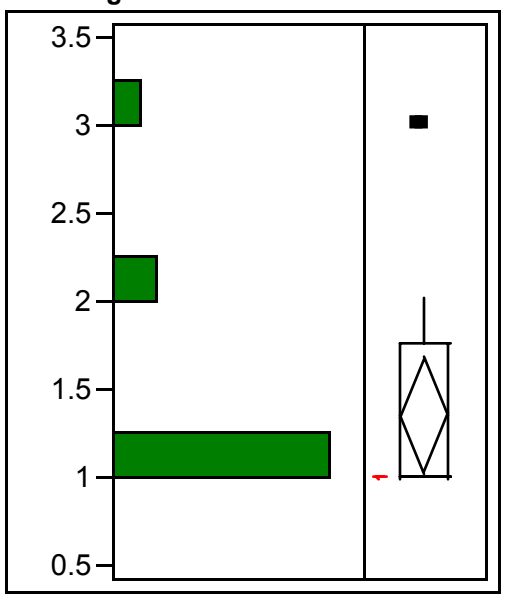
Quantiles

100.0%	maximum	3.0000
99.5%		3.0000
97.5%		3.0000
90.0%		1.0000
75.0%	quartile	1.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1.1
Std Dev	0.4472136
Std Err Mean	0.1
upper 95% Mean	1.3093024
lower 95% Mean	0.8906976
N	20

Pre Phlegm



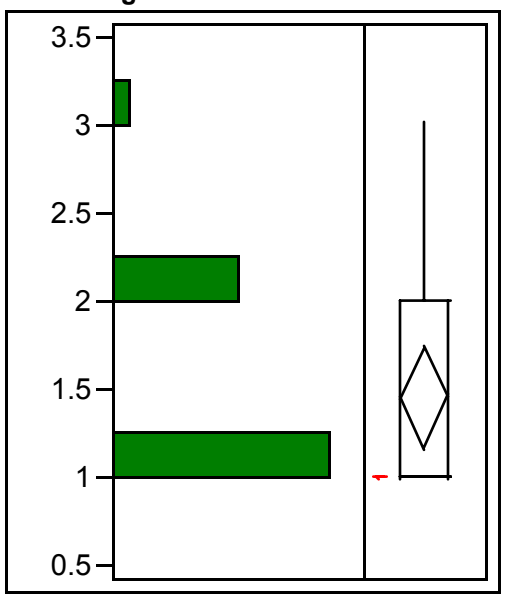
Quantiles

100.0%	maximum	3.0000
99.5%		3.0000
97.5%		3.0000
90.0%		2.9000
75.0%	quartile	1.7500
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1.35
Std Dev	0.6708204
Std Err Mean	0.15
upper 95% Mean	1.6639536
lower 95% Mean	1.0360464
N	20

Post Phlegm



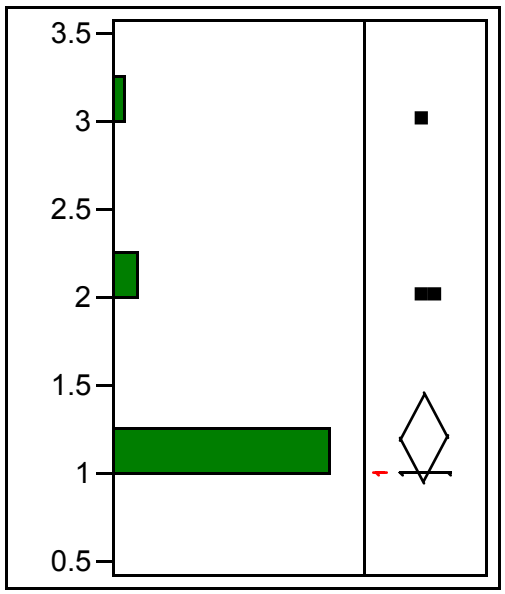
Quantiles

100.0%	maximum	3.0000
99.5%		3.0000
97.5%		3.0000
90.0%		2.0000
75.0%	quartile	2.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1.45
Std Dev	0.6048053
Std Err Mean	0.1352386
upper 95% Mean	1.7330576
lower 95% Mean	1.1669424
N	20

Pre Nose



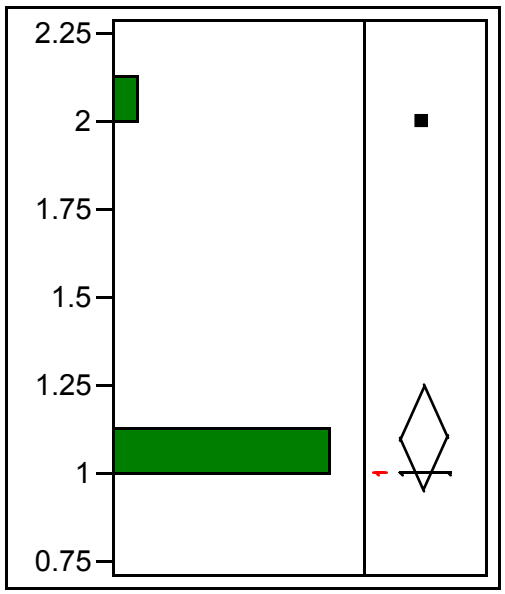
Quantiles

100.0%	maximum	3.0000
99.5%		3.0000
97.5%		3.0000
90.0%		2.0000
75.0%	quartile	1.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1.2
Std Dev	0.5231484
Std Err Mean	0.1169795
upper 95% Mean	1.444841
lower 95% Mean	0.955159
N	20

Post Nose



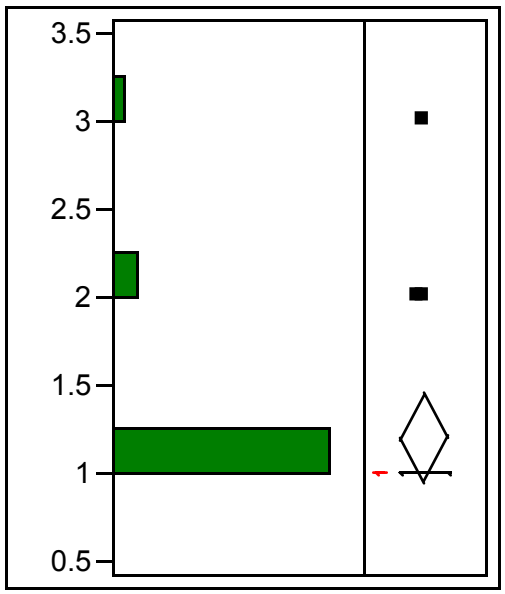
Quantiles

100.0%	maximum	2.0000
99.5%		2.0000
97.5%		2.0000
90.0%		1.9000
75.0%	quartile	1.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1.1
Std Dev	0.3077935
Std Err Mean	0.0688247
upper 95% Mean	1.2440518
lower 95% Mean	0.9559482
N	20

Pre Throat



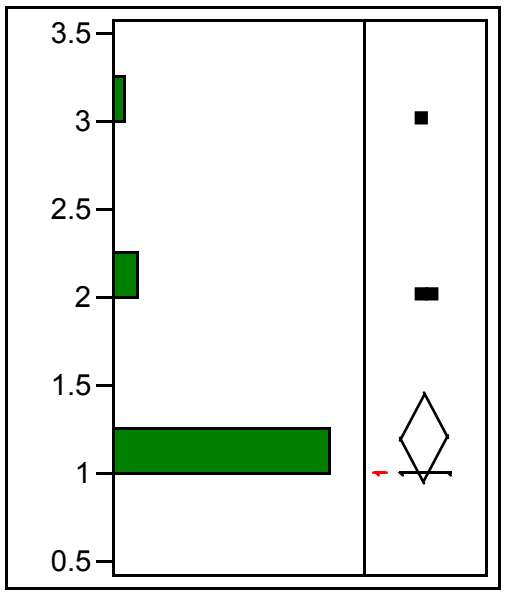
Quantiles

100.0%	maximum	3.0000
99.5%		3.0000
97.5%		3.0000
90.0%		2.0000
75.0%	quartile	1.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1.2
Std Dev	0.5231484
Std Err Mean	0.1169795
upper 95% Mean	1.444841
lower 95% Mean	0.955159
N	20

Post Throat



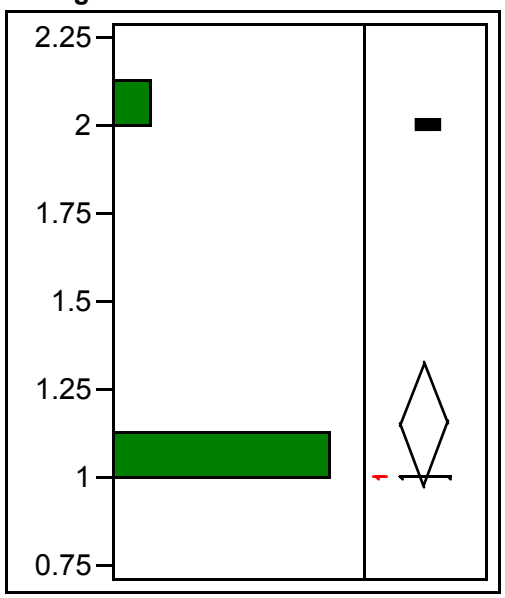
Quantiles

100.0%	maximum	3.0000
99.5%		3.0000
97.5%		3.0000
90.0%		2.0000
75.0%	quartile	1.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1.2
Std Dev	0.5231484
Std Err Mean	0.1169795
upper 95% Mean	1.444841
lower 95% Mean	0.955159
N	20

Pre Tightness



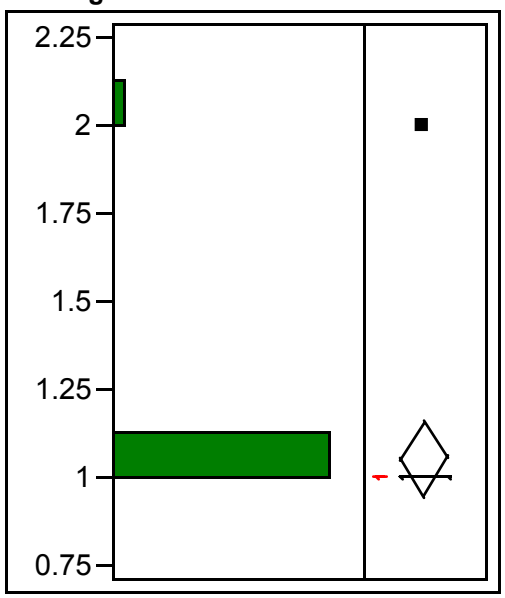
Quantiles

100.0%	maximum	2.0000
99.5%		2.0000
97.5%		2.0000
90.0%		2.0000
75.0%	quartile	1.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1.15
Std Dev	0.3663475
Std Err Mean	0.0819178
upper 95% Mean	1.3214559
lower 95% Mean	0.9785441
N	20

Post Tightness



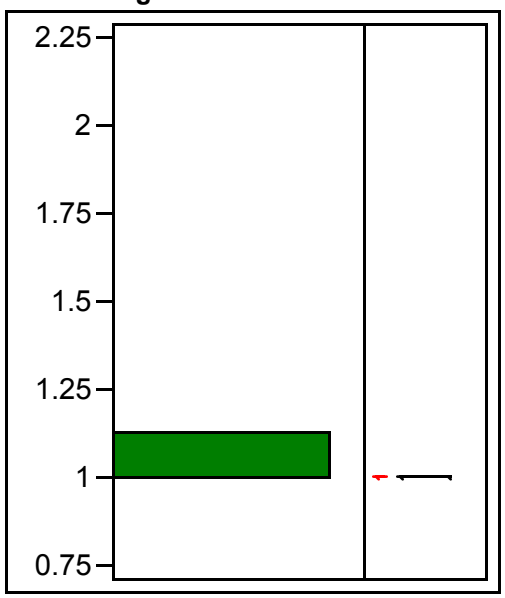
Quantiles

100.0%	maximum	2.0000
99.5%		2.0000
97.5%		2.0000
90.0%		1.0000
75.0%	quartile	1.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1.05
Std Dev	0.2236068
Std Err Mean	0.05
upper 95% Mean	1.1546512
lower 95% Mean	0.9453488
N	20

Pre Burning



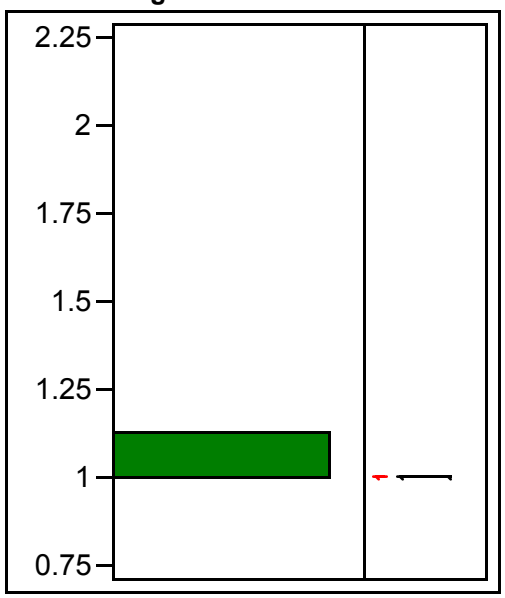
Quantiles

100.0%	maximum	1.0000
99.5%		1.0000
97.5%		1.0000
90.0%		1.0000
75.0%	quartile	1.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1
Std Dev	0
Std Err Mean	0
upper 95% Mean	1
lower 95% Mean	1
N	20

Post Burning



Quantiles

100.0%	maximum	1.0000
99.5%		1.0000
97.5%		1.0000
90.0%		1.0000
75.0%	quartile	1.0000
50.0%	median	1.0000
25.0%	quartile	1.0000
10.0%		1.0000
2.5%		1.0000
0.5%		1.0000
0.0%	minimum	1.0000

Moments

Mean	1
Std Dev	0
Std Err Mean	0
upper 95% Mean	1
lower 95% Mean	1
N	20

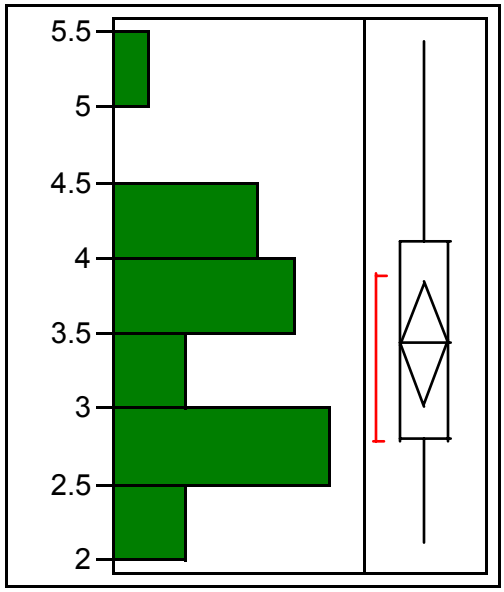
Appendix G: Impulse Oscillometry Measurements

Pre R5	Pre R5 %ile	Post R5	Post R5 %ile	R5 Change	R5 %ile Chg
3.85	138.3	3.57	128.2	-0.28	-10.1
3.43	94.3	2.72	74.9	-0.71	-19.4
5.04	146.2	4.78	138.7	-0.26	-7.5
5.99	166.4	7.29	202.5	1.3	36.1
4.44	157.5	4.01	142.1	-0.43	-15.4
3.18	83.3	3.26	85.2	0.08	1.9
4.25	153.4	4.49	161.9	0.24	8.5
6.94	249.1	6.21	223	-0.73	-26.1
3.29	89.2	3.07	83.4	-0.22	-5.8
2.64	92.6	2.9	101.6	0.26	9
4.05	109	3.55	95.4	-0.5	-13.6
3.2	112.3	3.3	115.9	0.1	3.6
4.17	106.3	4.37	111.3	0.2	5
3.45	119.6	4.51	156.2	1.06	36.6
5.25	152.4	5.28	153.3	0.03	0.9
4.44	141.3	4.54	144.7	0.1	3.4
2.64	96.4	2.44	89.1	-0.2	-7.3
4.91	165.6	5.34	180.2	0.43	14.6
3.95	103.5	3.72	97.4	-0.23	-6.1
3.39	119.6	2.79	98.5	-0.6	-21.1

Appendix H: Spirometric Measurements

Pre FEV1	Pre FEV1 %ile	Post FEV1	Post FEV1 %ile	FEV1 Change	FEV1 %ile Chg
4.17	102	4.26	104.3	0.09	2.3
2.54	88.2	2.36	82	-0.18	-6.2
3.53	103.4	3.48	102.2	-0.05	-1.2
2.12	74.6	2.02	71.1	-0.1	-3.5
3.03	82.8	3.67	100.3	0.64	17.5
2.64	99.7	2.95	111.2	0.31	11.5
3.65	73.5	3.65	73.6	0	0.1
4.42	117.8	4.2	111.9	-0.22	-5.9
2.78	98.9	2.9	103.1	0.12	4.2
4.27	93.1	4.28	93.2	0.01	0.1
2.89	107.3	2.59	95.9	-0.3	-11.4
3.75	81.7	3.8	82.7	0.05	1
2.34	79.9	2.33	79.7	-0.01	-0.2
4.42	110.6	4.37	109.3	-0.05	-1.3
2.83	91.4	3.05	98.5	0.22	7.1
2.84	81.2	2.98	85.3	0.14	4.1
5.41	103.7	5.41	103.6	0	-0.1
3.67	92.6	3.61	91.2	-0.06	-1.4
3.33	115.3	3.35	116	0.02	0.7
3.87	80.3	3.83	79.5	-0.04	-0.8

Pre FEV1



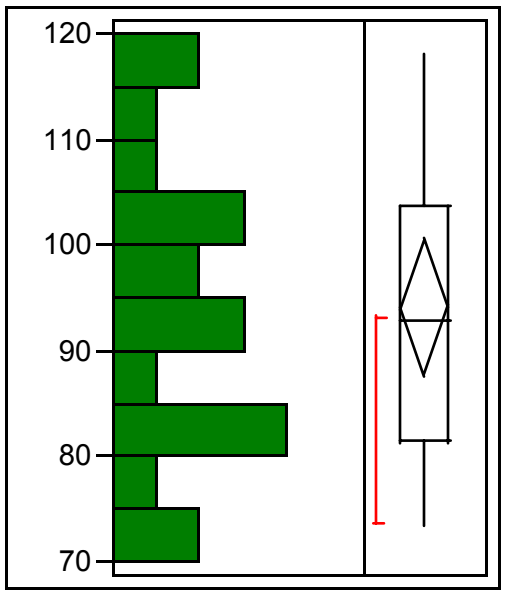
Quantiles

100.0%	maximum	5.4100
99.5%		5.4100
97.5%		5.4100
90.0%		4.4200
75.0%	quartile	4.0950
50.0%	median	3.4300
25.0%	quartile	2.7925
10.0%		2.3600
2.5%		2.1200
0.5%		2.1200
0.0%	minimum	2.1200

Moments

Mean	3.425
Std Dev	0.8416119
Std Err Mean	0.1881901
upper 95% Mean	3.8188865
lower 95% Mean	3.0311135
N	20

Pre FEV1 %ile



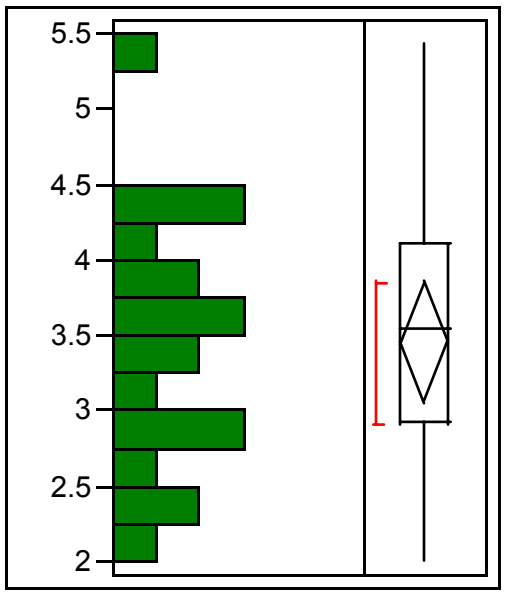
Quantiles

100.0%	maximum	117.80
99.5%		117.80
97.5%		117.80
90.0%		114.83
75.0%	quartile	103.63
50.0%	median	92.85
25.0%	quartile	81.33
10.0%		75.13
2.5%		73.50
0.5%		73.50
0.0%	minimum	73.50

Moments

Mean	93.9
Std Dev	13.459843
Std Err Mean	3.0097123
upper 95% Mean	100.1994
lower 95% Mean	87.6006
N	20

Post FEV1



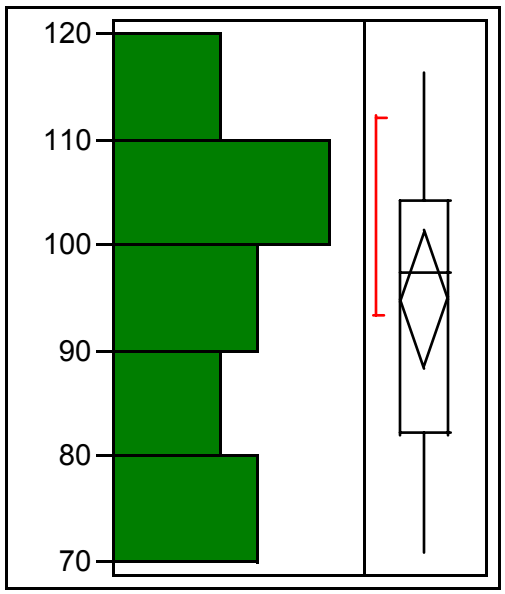
Quantiles

100.0%	maximum	5.4100
99.5%		5.4100
97.5%		5.4100
90.0%		4.3610
75.0%	quartile	4.1075
50.0%	median	3.5450
25.0%	quartile	2.9125
10.0%		2.3330
2.5%		2.0200
0.5%		2.0200
0.0%	minimum	2.0200

Moments

Mean	3.4545
Std Dev	0.8318431
Std Err Mean	0.1860058
upper 95% Mean	3.8438145
lower 95% Mean	3.0651855
N	20

Post FEV1 %ile



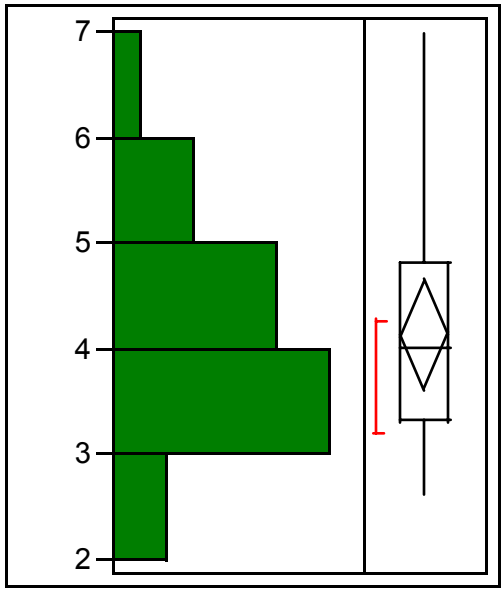
Quantiles

100.0%	maximum	116.00
99.5%		116.00
97.5%		116.00
90.0%		111.83
75.0%	quartile	104.13
50.0%	median	97.20
25.0%	quartile	82.17
10.0%		74.19
2.5%		71.10
0.5%		71.10
0.0%	minimum	71.10

Moments

Mean	94.73
Std Dev	13.468681
Std Err Mean	3.0116886
upper 95% Mean	101.03354
lower 95% Mean	88.426463
N	20

Pre R5



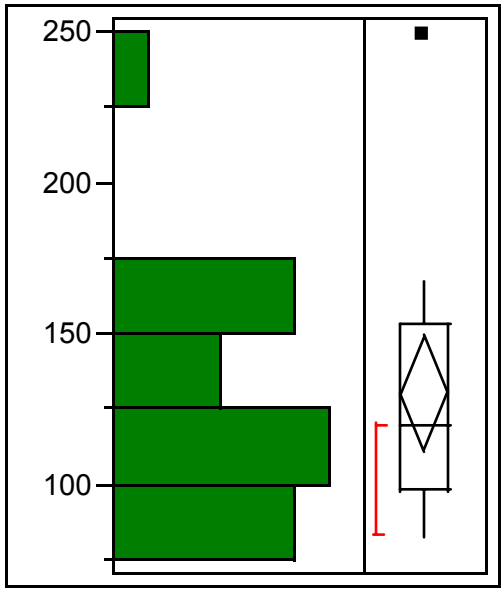
Quantiles

100.0%	maximum	6.9400
99.5%		6.9400
97.5%		6.9400
90.0%		5.9160
75.0%	quartile	4.7925
50.0%	median	4.0000
25.0%	quartile	3.3150
10.0%		2.6940
2.5%		2.6400
0.5%		2.6400
0.0%	minimum	2.6400

Moments

Mean	4.125
Std Dev	1.0950775
Std Err Mean	0.2448668
upper 95% Mean	4.637512
lower 95% Mean	3.612488
N	20

Pre R5 %ile



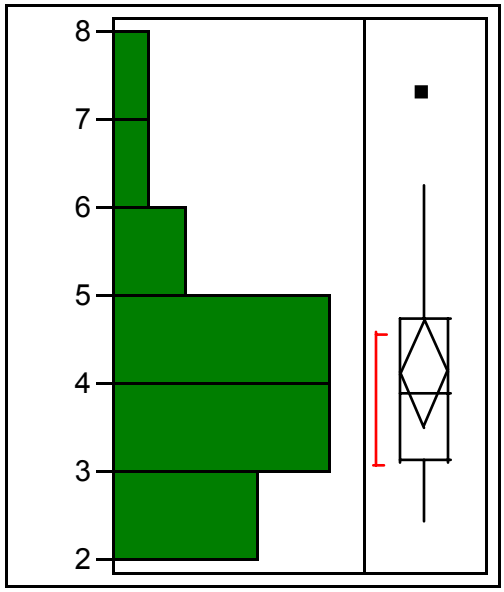
Quantiles

100.0%	maximum	249.10
99.5%		249.10
97.5%		249.10
90.0%		166.32
75.0%	quartile	153.15
50.0%	median	119.60
25.0%	quartile	98.18
10.0%		89.54
2.5%		83.30
0.5%		83.30
0.0%	minimum	83.30

Moments

Mean	129.815
Std Dev	39.016411
Std Err Mean	8.7243346
upper 95% Mean	148.07524
lower 95% Mean	111.55476
N	20

Post R5



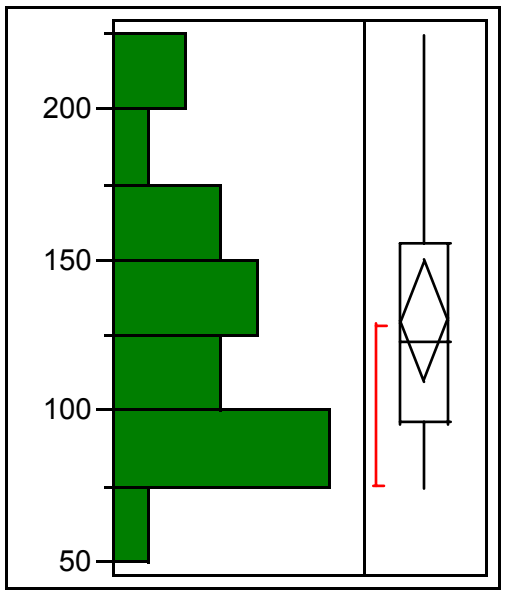
Quantiles

100.0%	maximum	7.2900
99.5%		7.2900
97.5%		7.2900
90.0%		6.1230
75.0%	quartile	4.7200
50.0%	median	3.8650
25.0%	quartile	3.1175
10.0%		2.7270
2.5%		2.4400
0.5%		2.4400
0.0%	minimum	2.4400

Moments

Mean	4.107
Std Dev	1.2474146
Std Err Mean	0.2789304
upper 95% Mean	4.690808
lower 95% Mean	3.523192
N	20

Post R5 %ile



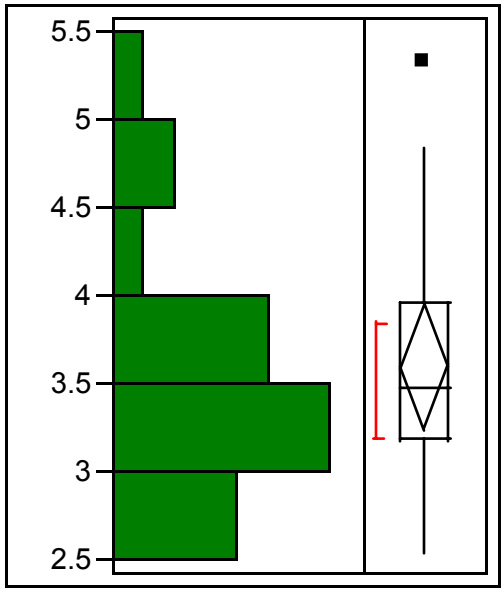
Quantiles

100.0%	maximum	223.00
99.5%		223.00
97.5%		223.00
90.0%		200.27
75.0%	quartile	155.47
50.0%	median	122.05
25.0%	quartile	95.90
10.0%		83.58
2.5%		74.90
0.5%		74.90
0.0%	minimum	74.90

Moments

Mean	129.175
Std Dev	41.41872
Std Err Mean	9.2615074
upper 95% Mean	148.55956
lower 95% Mean	109.79044
N	20

Pre R20



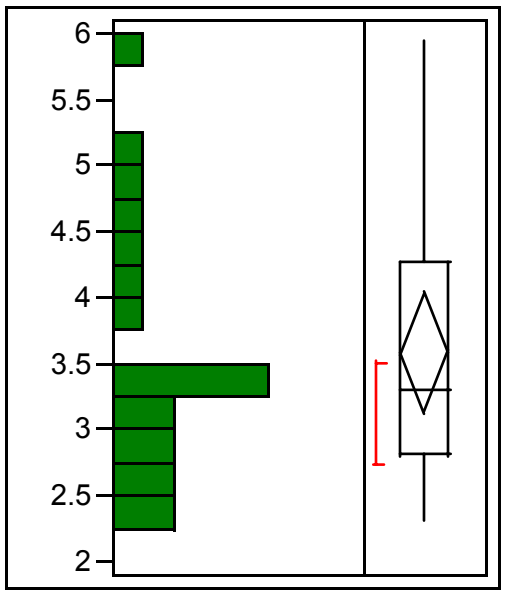
Quantiles

100.0%	maximum	5.3200
99.5%		5.3200
97.5%		5.3200
90.0%		4.8010
75.0%	quartile	3.9500
50.0%	median	3.4650
25.0%	quartile	3.1825
10.0%		2.6470
2.5%		2.5500
0.5%		2.5500
0.0%	minimum	2.5500

Moments

Mean	3.595
Std Dev	0.7431901
Std Err Mean	0.1661824
upper 95% Mean	3.9428237
lower 95% Mean	3.2471763
N	20

Post R20



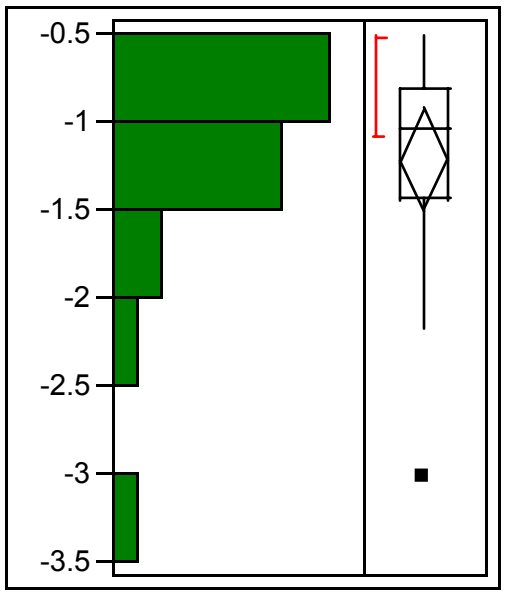
Quantiles

100.0%	maximum	5.9200
99.5%		5.9200
97.5%		5.9200
90.0%		5.1760
75.0%	quartile	4.2725
50.0%	median	3.2900
25.0%	quartile	2.8175
10.0%		2.4950
2.5%		2.3200
0.5%		2.3200
0.0%	minimum	2.3200

Moments

Mean	3.5795
Std Dev	0.9626579
Std Err Mean	0.2152569
upper 95% Mean	4.0300378
lower 95% Mean	3.1289622
N	20

Pre X5



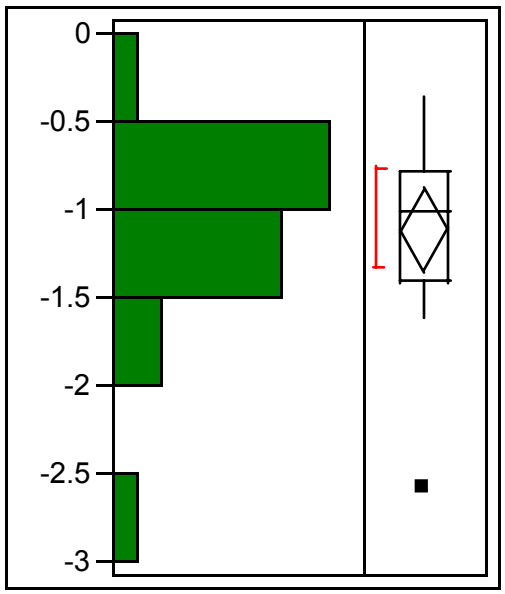
Quantiles

100.0%	maximum	-0.530
99.5%		-0.530
97.5%		-0.530
90.0%		-0.635
75.0%	quartile	-0.818
50.0%	median	-1.050
25.0%	quartile	-1.432
10.0%		-2.115
2.5%		-3.020
0.5%		-3.020
0.0%	minimum	-3.020

Moments

Mean	-1.223
Std Dev	0.5911283
Std Err Mean	0.1321803
upper 95% Mean	-0.946343
lower 95% Mean	-1.499657
N	20

Post X5



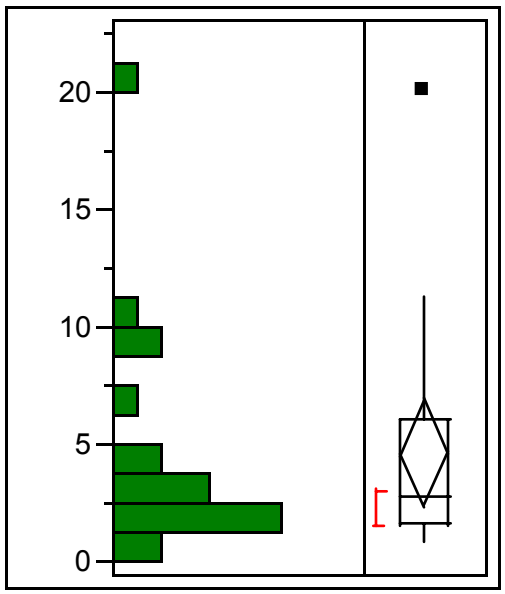
Quantiles

100.0%	maximum	-0.380
99.5%		-0.380
97.5%		-0.380
90.0%		-0.598
75.0%	quartile	-0.785
50.0%	median	-1.010
25.0%	quartile	-1.408
10.0%		-1.594
2.5%		-2.580
0.5%		-2.580
0.0%	minimum	-2.580

Moments

Mean	-1.116
Std Dev	0.4880078
Std Err Mean	0.1091219
upper 95% Mean	-0.887605
lower 95% Mean	-1.344395
N	20

Pre AX



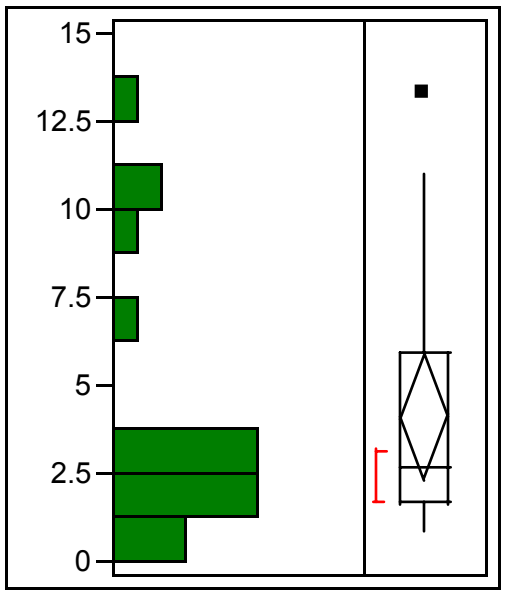
Quantiles

100.0%	maximum	20.040
99.5%		20.040
97.5%		20.040
90.0%		10.975
75.0%	quartile	5.977
50.0%	median	2.680
25.0%	quartile	1.648
10.0%		1.099
2.5%		0.960
0.5%		0.960
0.0%	minimum	0.960

Moments

Mean	4.578
Std Dev	4.7440984
Std Err Mean	1.0608126
upper 95% Mean	6.7983064
lower 95% Mean	2.3576936
N	20

Post AX



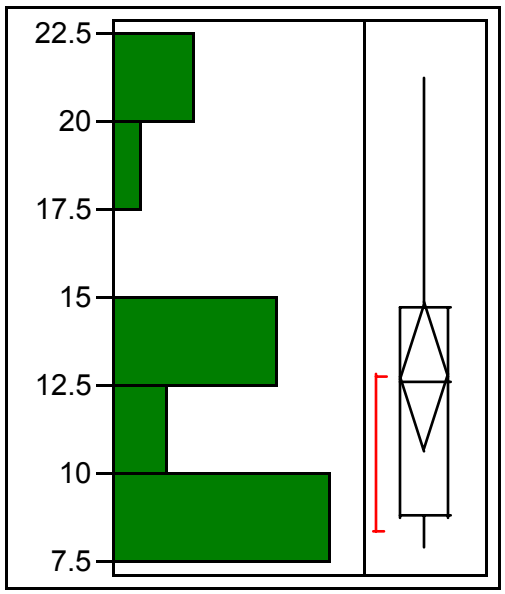
Quantiles

100.0%	maximum	13.260
99.5%		13.260
97.5%		13.260
90.0%		10.840
75.0%	quartile	5.918
50.0%	median	2.650
25.0%	quartile	1.680
10.0%		0.979
2.5%		0.920
0.5%		0.920
0.0%	minimum	0.920

Moments

Mean	4.1095
Std Dev	3.7563048
Std Err Mean	0.8399353
upper 95% Mean	5.8675048
lower 95% Mean	2.3514952
N	20

Pre Fres



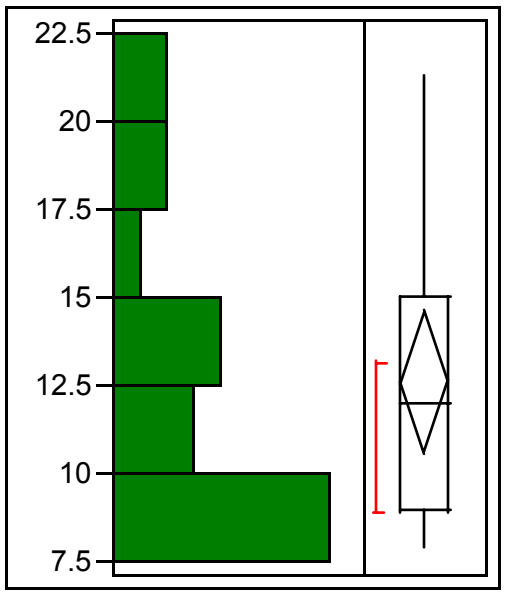
Quantiles

100.0%	maximum	21.100
99.5%		21.100
97.5%		21.100
90.0%		20.509
75.0%	quartile	14.698
50.0%	median	12.555
25.0%	quartile	8.777
10.0%		8.383
2.5%		7.980
0.5%		7.980
0.0%	minimum	7.980

Moments

Mean	12.7465
Std Dev	4.3390616
Std Err Mean	0.9702437
upper 95% Mean	14.777243
lower 95% Mean	10.715757
N	20

Post Fres



Quantiles

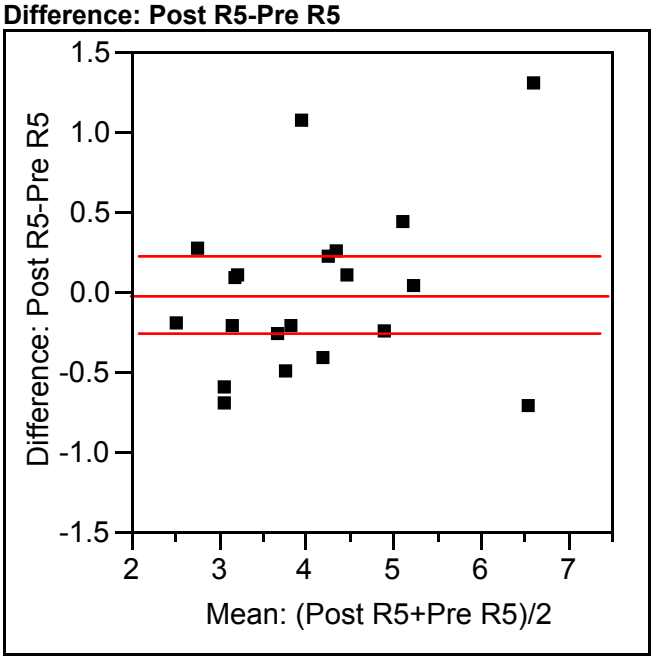
100.0%	maximum	21.200
99.5%		21.200
97.5%		21.200
90.0%		20.611
75.0%	quartile	15.015
50.0%	median	11.940
25.0%	quartile	8.957
10.0%		8.281
2.5%		7.920
0.5%		7.920
0.0%	minimum	7.920

Moments

Mean	12.589
Std Dev	4.2574367
Std Err Mean	0.9519918
upper 95% Mean	14.581542
lower 95% Mean	10.596458
N	20

Appendix J: Analysis of Post-test vs Pre-test Differences in R5, R20 and FEV1

Matched Pairs
Difference: Post R5-Pre R5

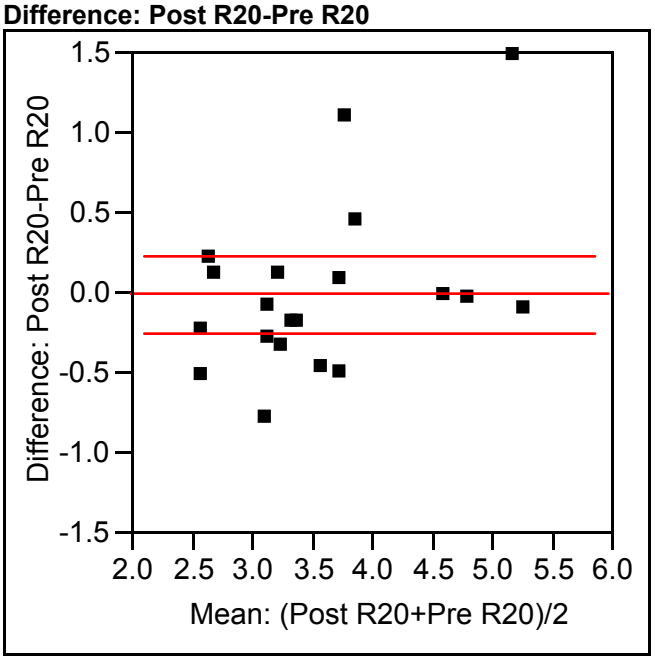


Post R5	4.107	t-Ratio	-0.15236
Pre R5	4.125	DF	19
Mean Difference	-0.018	Prob > |t|	0.8805
Std Error	0.11814	Prob > t	0.5597
Upper95%	0.22927	Prob < t	0.4403
Lower95%	-0.2653		
N	20		
Correlation	0.90632		

Wilcoxon Sign-Rank

	Post R5-Pre R5
Test Statistic	-18.000
Prob > |z|	0.516
Prob > z	0.742
Prob < z	0.258

Matched Pairs
Difference: Post R20-Pre R20

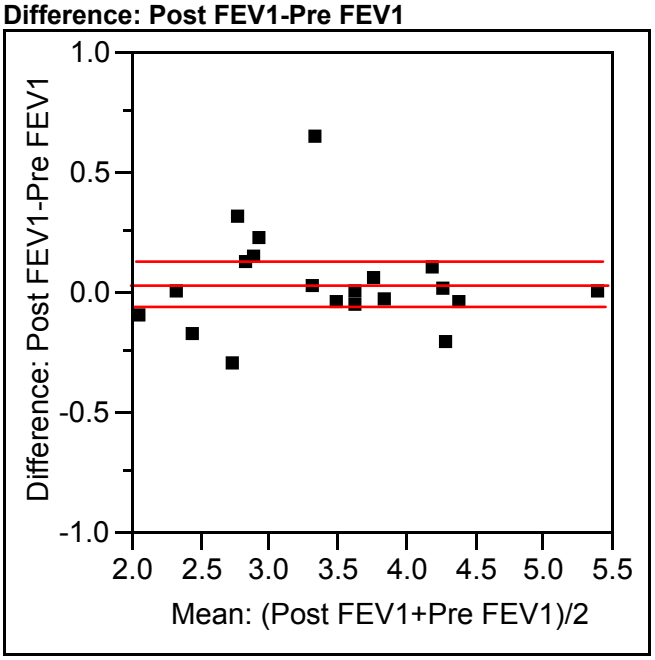


Post R20	3.5795	t-Ratio	-0.13075
Pre R20	3.595	DF	19
Mean Difference	-0.0155	Prob > |t|	0.8973
Std Error	0.11855	Prob > t	0.5513
Upper95%	0.23262	Prob < t	0.4487
Lower95%	-0.2636		
N	20		
Correlation	0.83723		

Wilcoxon Sign-Rank

	Post R20-Pre R20
Test Statistic	-27.000
Prob > |z|	0.330
Prob > z	0.835
Prob < z	0.165

Matched Pairs
Difference: Post FEV1-Pre FEV1



Post FEV1	3.4545	t-Ratio	0.654114
Pre FEV1	3.425	DF	19
Mean Difference	0.0295	Prob > |t|	0.5209
Std Error	0.0451	Prob > t	0.2604
Upper95%	0.12389	Prob < t	0.7396
Lower95%	-0.0649		
N	20		
Correlation	0.97102		

Wilcoxon Sign-Rank

	Post FEV1-Pre FEV1
Test Statistic	7.000
Prob > |z|	0.775
Prob > z	0.387
Prob < z	0.613