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Novel Device for Measuring Lung Function using Oscillometry

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Abstract

The forced oscillation technique (FOT) is a non-invasive means of measuring lung mechanics. Broad-band oscillations in flow are delivered to the lungs while the resultant pressure oscillations are recorded. These signals are processed to yield the input impedance of the respiratory system (Z_{rs}), which encapsulates the mechanical properties of the lung over the frequency range spanned by the oscillations. Clinically, Z_{rs} can be used to assess pulmonary pathologies such as asthma and COPD. Standard methods of performing FOT are limited to the non-ambulatory clinical setting. Production of a light-weight device that operates without an external power source would allow real-time measurements of Z_{rs} in a wide variety of more natural settings. Breath-driven oscillators, such as the Smith's Medical Acapella and D R Burton vPEP, are currently used clinically to help cystic fibrosis patients clear mucus from their lungs by generating pressure oscillations that travel into the airways. We hypothesized that these oscillations could be used to determine Z_{rs}. We performed FOT on healthy individuals without history of lung disease using a calibrated piston oscillator (Flexivent) to determine reference Z_{rs} between 1 and 20 Hz. We then measured airway pressure and flow using the same sensors but with the oscillations produced by the Acapella and vPEP during tidal breathing. Respiratory resistance (R_{rs}), elastance (E_{rs}) and Inertance (I_{rs}) were determined by fitting the single-compartment model of the respiratory system to the time-domain signals from all three measurement devices. Correlation coefficients, Bland-Altman plots, and coefficients of variation were used to compare the results obtained with the three devices. We found bias values of 0.633857 [0.214382378, 1.053331908] $cmH_2O.s.L^{-1}$, 0.041333 [-0.38432604, 0.46699271] $cmH_2O.s.L^{-1}$ for R_{rs} comparing the Flexivent against the Acapella and vPEP, respectively. Coefficients of variation of 9.003%, 9.855%, and 9.643% were obtained for the Flexivent, Acapella, and vPEP, respectively. These results demonstrate that breath-driven oscillators are promising alternatives to conventional powered oscillators for the measurement of Z_{rs}.

Introduction

The forced oscillation technique (FOT) is a non-invasive means of measuring lung mechanics[1-3]. Controlled oscillations in flow (pressure) are delivered to the respiratory system while the resultant pressure (flow) is recorded. Assuming the respiratory system and its components behave like a linear dynamic system, information derived from these measurements is provided in the form of the input impedance of the respiratory system (Z_{rs}), which provides insight into the physiologic state of the lung over a range of oscillation frequencies. Prior studies have evaluated impedance over a wide range of frequencies from that of physiologic breathing to hundreds of hertz[4,5]. Z_{rs} is comprised of two parts. The real part is termed resistance and represents those components of the system that dissipate energy such as the flow of air through the airways. The imaginary part is termed reactance and represents the elastic and inertial components of the respiratory system.

Clinically, the use of FOT has expanded in recent years, and an increasing number of studies report its usefulness in evaluation of disease states such as COPD and asthma[1,2]. When used to explore healthy and diseased lungs, multiple frequencies imposed on one another allows Z_{rs} to be determined at multiple frequencies simultaneously. How the real and imaginary parts of Z_{rs} change with frequency helps differentiate between healthy and diseased lungs. Other modalities such as spirometry have also been used to evaluate pathology of the lung. Spirometry is a non-invasive means of gleaning useful information about the lung. However, it requires patient cooperation and effort, making it less suitable for older patients and young children. Thus, these populations might uniquely benefit from a modality such as FOT. Ideally, these modalities should be used together rather than in place of one another[1,2,5].

Standard methods of producing forced oscillations in flow include use of speakers and piston pumps[2,5]. These systems require a power source making them bulky and requiring the patient sit with the machine. This limits Z_{rs} measurements to the clinic setting. Production of a light-weight device that operates without an external power source to produce the forced oscillations, i.e. the patient's own

breathing, would allow real-time measurements of lung function in a wide variety of more natural settings including the home. Currently, there are FDA-approved oscillatory devices, such as the Smith's Medical Acapella, which produce pulses of air at various frequencies and are driven entirely by the air pressure from the subject's own breathing[8]. Clinically, these devices are used to clear airway mucus[6,7], but potentially could be used to perform the FOT by using the flows and pressures developed at the airway opening. This study aims to establish the efficacy of performing FOT with these oscillatory devices. As a proof of concept, this study could provide the framework for further development of patient-powered oscillatory devices for real-time measurement of lung function in a multitude of settings not limited to the clinic.

Methods

Participant selection

Healthy individuals age 18 to 65 with no prior history of pulmonary disease such as asthma or COPD were studied. Individuals were screened according to the following exclusion criteria. Individuals currently taking respiratory medications, greater than or equal to 10 pack-year history, currently smoking, or recent acute respiratory illness within the last four weeks were excluded. All screening was performed per participant report. This study was approved by the Institutional Review Board (IRB) of the University of Vermont, and subjects provided written informed consent.

Testing Devices

A total of three devices were tested including a piston-driven system based on the Flexivent small animal ventilator (Scireq, Montreal) which provided reference Z_{rs}, the Smith Medical Acapella, and the D R Burton vPEP. The device being tested was placed in series and downstream of a pneumotachometer (Hans Rudolph Inc.), which measured volumetric flow rate (L/s) through the system, and a pressure sensor (Scireq Inc.), which measured airway opening pressure (cmH_2O). During use of the Flexivent, a

stopper plug acting as an air flow resister was placed in the outlet valve of the system to allow for the participant to breath freely while keeping the system relatively closed allowing so that the imposed flow oscillations entered the subject's lungs rather than escaping through the outlet valve. A disposable mouthpiece and air filter separated the subject's mouth from the measuring equipment and was replaced for each subject. A schematic of the experimental setup is shown in figure 1.

Testing Procedures

The order in which the three devices were tested was randomized using the Random app random number generator. Each device was assigned a number from one to three which was unchanged throughout the entirety of the experiment. The order in which the numbers were produced in the random number generator determined the device testing order for that participant. This was repeated for each participant.

Data were collected in triplicate using the Flexivent (reference device) and both the Acapella and vPEP devices. Measurements included pressure and flow during quiet breathing. Starting with the first device, participants were asked to breathe normally. After 1 to 2 breaths, a 16 second sample of the pressure and flow was recorded while the participant continued to breathe. Two subsequent samples were collected as the participant maintained tidal breathing. If needed, the participant could take a few breaths off the device between measurements. This procedure was repeated in accordance with the results of the randomization process until all three devices had been tested.

Data analysis

Impedance values were calculated by inputting flow and pressure measurements into custom software developed by Jason Bates, Ph.D. The signals were smoothed with a 1 s running mean and the oscillatory component isolated as the difference between the original and smoothed signals. The middle 1 s

segment of the oscillatory component of pressure (P), flow, volume and volume acceleration from each complete expiration were fit to the equation of the single-compartment linear model

$$P(t) = E_{rs}V(t) + R_{rs}\dot{V}(t) + I_{rs}\ddot{V}(t) \quad (1)$$

to provide values for R_{rs} (respiratory system resistance), E_{rs} (respiratory system elastance), and I_{rs} (respiratory system inertance). The mean and SD of each parameter from all three runs were determined for each subject for the Flexivent, Acapelle and Vpep. If any of R_{rs}, E_{rs}, or I_{rs} were negative then that breath was discarded.

Statistical analysis

Statistical analysis was performed in Origin (OriginLab Corporation) and Excel (Microsoft Corportation). Bland-Altman plots were used to assess the agreement between the established FO system (Flexivent) and the experimental devices (Acapella and vPEP) for R_{rs}, E_{rs}, and I_{rs}. Mean differences and limits of agreement (LOA) were evaluated for all devices and parameters. Correlation coefficients were also calculated using Excel to assess the relationship between R_{rs}, E_{rs}, and I_{rs} for the Flexivent and the two breath-driven oscillators. Coefficients of variation (CV) were determined for all three devices for all parameters to evaluate the variability of the devices.

Results

Mean R_{rs} values from the Flexivent ranged from 1.413 [1.27,1.55] $cmH_2O.s.L^{-1}$ to 3.365 [3.17,3.56] $cmH_2O.s.L^{-1}$, while values for the Acapella ranged from 1.448 [1.39,1.50] $cmH_2O.s.L^{-1}$ to 2.731 [2.53,2.93] $cmH_2O.s.L^{-1}$ and 1.707 [1.54,1.87] $cmH_2O.s.L^{-1}$ to 3.268 [3.07,3.46] $cmH_2O.s.L^{-1}$ for vPEP. Mean values of E_{rs} had more variability between devices with the Flexivent ranging from 17.162 [9.58,24.7] $cmH_2O.L^{-1}$ to 42.795 [31.0,54.6] $cmH_2O.L^{-1}$, while values ranged from 38.349 [20.6,56.0] $cmH_2O.L^{-1}$ to 161.781 [123.9,199.7] $cmH_2O.L^{-1}$ and 17.258 [8.39,26.1] $cmH_2O.L^{-1}$ to 55.639 [2.54,108.7] $cmH_2O.L^{-1}$ for Acapella

and vPEP, respectively. Similarly, mean values of I_{rs} had larger degrees of variability with values ranging from 0.002 [0.00102,0.00298] $cmH_2O.s^2.L^{-2}$ to 0.014 [0.0128,0.0152] $cmH_2O.s^2.L^{-2}$ for the Flexivent, 0.011 [0.00708,0.0149] $cmH_2O.s^2.L^{-2}$ to 0.028 [0.0227,0.0333] $cmH_2O.s^2.L^{-2}$ for Acapella, and 0.002 [-0.0091,0.0131] $cmH_2O.s^2.L^{-2}$ to 0.010 [0.00931,0.0107] $cmH_2O.s^2.L^{-2}$ for vPEP. The difference between mean R_{rs} values for the Flexivent and the Acapella were statistically significant for P02, P03, P05, and P06. Mean R_{rs} values were significantly different for P01 and P02 between the Flexivent and vPEP. Mean Ers values for Acapella were significantly different from the Flexivent only for P03, while no mean E_{rs} values were significantly different between the Flexivent and vPEP. Mean I_{rs} values were significantly different between the Flexivent and Acapella for P03, P06, and P07, while values for P01 were significantly different between Flexivent and vPEP (table 1, figure 1).

Bland-Altman plots comparing R_{rs} values for the Flexivent and Acapella show a mean difference of 0.633857 [0.214382378, 1.053331908] $cmH_2O.s.L^{-1}$, upper LOA of 1.743663 [0.800877938, 2.686447379] $cmH_2O.s.L^{-1}$, and lower LOA of -0.47595 [-1.41873309, 0.466836348] $cmH_2O.s.L^{-1}$. Analysis comparing R_{rs} values for the Flexivent to the vPEP showed a mean difference of 0.041333 [-0.38432604, 0.46699271] $cmH_2O.s.L^{-1}$, upper LOA of 1.083962 [0.069049324, 2.098875581] $cmH_2O.s.L^{-1}$, and a lower LOA of -1.0013 [-2.01620891, 0.013617343] $cmH_2O.s.L^{-1}$. Comparing E_{rs} values from the Flexivent and Acapella revealed a mean difference of -40.3354 [-74.9124234, -5.7584337] $cmH_2O.L^{-1}$, an upper LOA of 51.14502 [-26.5680278, 128.8580677] $cmH_2O.L^{-1}$, and a lower LOA of -131.816 [-209.528925, -54.1028293] $cmH_2O.L^{-1}$. Comparing E_{rs} values between the Flexivent and vPEP revealed there was a mean difference of -10.9158 [-17.2986764, -4.53299028] $cmH_2O.L^{-1}$, an upper LOA of 4.718588 [-10.5002268, 19.93740273] $cmH_2O.L^{-1}$, and a lower LOA of -26.5503 [-41.7690694, -11.3314399] $cmH_2O.L^{-1}$. I_{rs} values between the Flexivent and Acapella showed a mean difference of -0.006 [-0.01058665, -0.00141335] $cmH_2O.s^2.L^{-2}$, an upper LOA of 0.006135 [-0.00417375, 0.016443561] $cmH_2O.s^2.L^{-2}$, and a lower LOA of -0.01813 [-0.02844356, -0.00782625] $cmH_2O.s^2.L^{-2}$, and a mean

difference of 0.001833 [-0.00033845, 0.004005114] $cmH_2O.s^2.L^{-2}$, an upper LOA of 0.007153 [0.001974745, 0.012331235] $cmH_2O.s^2.L^{-2}$, and a lower LOA of -0.00349 [-0.00866457, 0.001691922] $cmH_2O.s^2.L^{-2}$ between the Flexivent and vPEP. These values can be referenced in table 2.

Correlation coefficients (r) were calculated to compare values of R_{rs}, E_{rs}, and I_{rs} between the Flexivent and the Acapella and vPEP. Correlation analysis between the Flexivent and Acapella showed r values of 0.5584, -0.311, and 0.3221 (Table 3, row 1) for R_{rs}, E_{rs}, and I_{rs}, respectively. Analysis comparing the Flexivent with the vPEP revealed r values of 0.7043, 0.906, and 0.766 (table 3, row 2) for R_{rs}, E_{rs}, and I_{rs}, respectively.

To evaluate the relative variability of these devices in measuring R_{rs}, E_{rs}, and I_{rs}, CV's were calculated for all three devices (Table 4). For the Flexivent, the values were 9.003%, 34.764%, and 17.391% for R_{rs}, E_{rs}, and I_{rs}, respectively. For the Acapella, the values were 9.855%, 56.289%, and 33.010% for R_{rs}, E_{rs}, and I_{rs}, respectively. For the vPEP, the values were 9.643%, 50.221%, and 44.444% for R_{rs}, E_{rs}, and I_{rs}, respectively.

Discussion

The forced oscillation technique (FOT) is a non-invasive means of obtaining meaningful information about lung mechanics[1-3]. Physiologic information obtained from this method comes in the form of impedance, which can be further broken into its real and imaginary components. The real component is termed resistance and represents components of the system that dissipate energy such as the flow of air through the airways. The imaginary component is termed the reactance which represents the elastic and inertial components of the respiratory system. FOT's clinical use is expanding as a useful way of understanding disease states such as asthma and COPD in different clinical settings such as the pediatric population and mechanical ventilation[1,2,9]. Alternate ways of performing FOT would allow for further integration of this method into clinical practice.

Analysis of the impedance values between the three devices showed similar values for mean R_{rs} across the devices with good consistency between each participant for each device (table 1, row 1, row 8, and row 15). While the absolute values between devices was promising, there were statistical differences between the means when comparing the Flexivent to both the Acapella and vPEP. For the Acapella, four of the seven subjects had statistically different mean R_{rs} values (Table 1, row 8), while the vPEP had only two of the six which were statistically different (table 1, row 15). This variation between the devices could due to the single frequency at which these devices operate. Conversely, the Flexivent uses multi-frequency oscillatory impulses. There is inherent heterogeneity in the respiratory system and values of R_{rs} and E_{rs} are thus heterogeneous. These values change throughout the respiratory system dependent on the frequency applied[9] implying that multi-frequency oscillatory inputs would have an inherent stability over single frequency oscillatory inputs. This could explain the differences in R_{rs} seen between the multi-frequency Flexivent and single frequency devices.

Although there was relative stability of the means of R_{rs} across the three devices, the means of E_{rs} and Irs had much larger fluctuations between devices and individual participants (table 1, figure 2). Despite the larger variations between means of E_{rs} and I_{rs}, only one out of seven means of E_{rs} was statistically different than the Flexivent for the Acapella, while none of the means of E_{rs} were different for the vPEP. Similarly, three out of the seven means from the Acapella were statistically different from those of the Flexivent, while one out of six was different for the vPEP. This increased spread seen for E_{rs} and I_{rs} between the Flexivent and the other oscillatory devices is likely due to the values being driven by a single oscillatory frequency rather than multiple frequencies as in the Flexivent. At a single frequency, the single-compartment model is not able to robustly determine the values of E_{rs} and I_{rs}. In this model, reactance is dependent on both E_{rs} and I_{rs}, thus co-variations in both may result in a relatively small change in the overall reactance produced by the model while large variations occur for E_{rs} and I_{rs}. If it were possible to include multiple frequencies for the Acapella and vPEP devices, this would likely

improve the single-compartment model's ability to accurately determine E_{rs} and I_{rs}. The lack of significant difference between the means of the vPEP and Acapella compared to the Flexivent is likely due to the relatively small sample size in this study. A large sample size would likely show a more significant difference between the Flexivent and the single-frequency oscillatory devices for E_{rs} and I_{rs}.

When comparing measuring techniques, it is important to evaluate the agreement of the methods rather than simply looking at the correlation coefficients to evaluate how well methods compare[10]. Bland-Altman plots for R_{rs} (figure 3) showed bias values of 0.634 $cmH_2O.s.L^{-1}$ and 0.0413 $cmH_2O.s.L^{-1}$ for the Acapella and vPEP, respectively. This represents the average difference between the values obtained by the Flexivent and Acapella for a given participant[11]. When measured against the absolute values of these measurements, the bias seen is small. This contrasts with the 95 percent upper and lower LOA seen in these same plots. For the Acapella (figure 3, top) and vPEP (figure 3, bottom), the upper and lower LOA's are sufficiently wide making it difficult to conclude the Acapella and vPEP are equal are greater at performing FOT for R_{rs} values. Although, this is, in part, due to the limited sample size available for this study and is very plausible that the LOA would be appropriately small with a greater sample size. The Bland-Altman plots evaluating E_{rs} (figure 4) and I_{rs} (Figure 5) show much larger values of bias when compared to their absolute values. Bias values for E_{rs} were -40.34 $cmH_2O.L^{-1}$ and -10.92 $cmH_2O.L^{-1}$ for the Acapella and vPEP, respectively. Bias values for I_{rs} were -0.006 $cmH_2O.s^2.L^{-2}$ and 0.00183 $cmH_2O.s^2.L^{-2}$ for the Acapella and vPEP, respectively. In the case of E_{rs} and I_{rs}, bias values were sufficiently large to suggest poor agreement between the Flexivent and the alternate devices for measuring of these parameters. Similarly to that of R_{rs}, the upper and lower LOA for E_{rs} (figure 4) and Irs (figure 5) are sufficiently large to suggest poor agreement between the Flexivent and the alternate devices for these measurements. This is likely contributed to by the small sample size of the current study, but more importantly, this highlights the deficiency of the Acapella and vPEP devices to produce

robust values of E_{rs} and I_{rs} with only a single frequency. Alterations in these devices to produce multiple frequencies would likely improve the agreement of all three parameters.

When evaluating the ability of these devices to perform these measurements, it is also important to establish repeatability between individual measurements. This was done by calculating the CV for each parameter and each device, using ≤ 10% as the current standard[9], although this standard is classically applied to the values of impedance rather than the constituents of impedance. For all three devices, the CV of R_{rs} was below this threshold suggesting sufficiently artifact-free samples for all three devices. Conversely, for both E_{rs} and I_{rs}, none of the devices were below this 10% threshold. Despite none of the devices meeting the standard, we noticed that CV's for the Acapella and vPEP were about 1.5-2.5 times higher than those of the Flexivent. This suggests the repeatability of the Flexivent is superior to that of the Acapella and vPEP for both E_{rs} and I_{rs}, which is supported by our earlier findings.

Conclusion

Agreement between the Flexivent and alternate devices is promising despite the relatively poor agreement of E_{rs} and I_{rs}. Repeatability of measurements for the devices also shows adequate variability for values of R_{rs}, while the larger variability of E_{rs} and I_{rs} would be greatly improved with multiple frequency oscillations. Results of this study are limited due to the sample size. Further work to develop a multi-frequency oscillatory device is warranted. The ability to perform FOT using alternate oscillatory devices shows promise.

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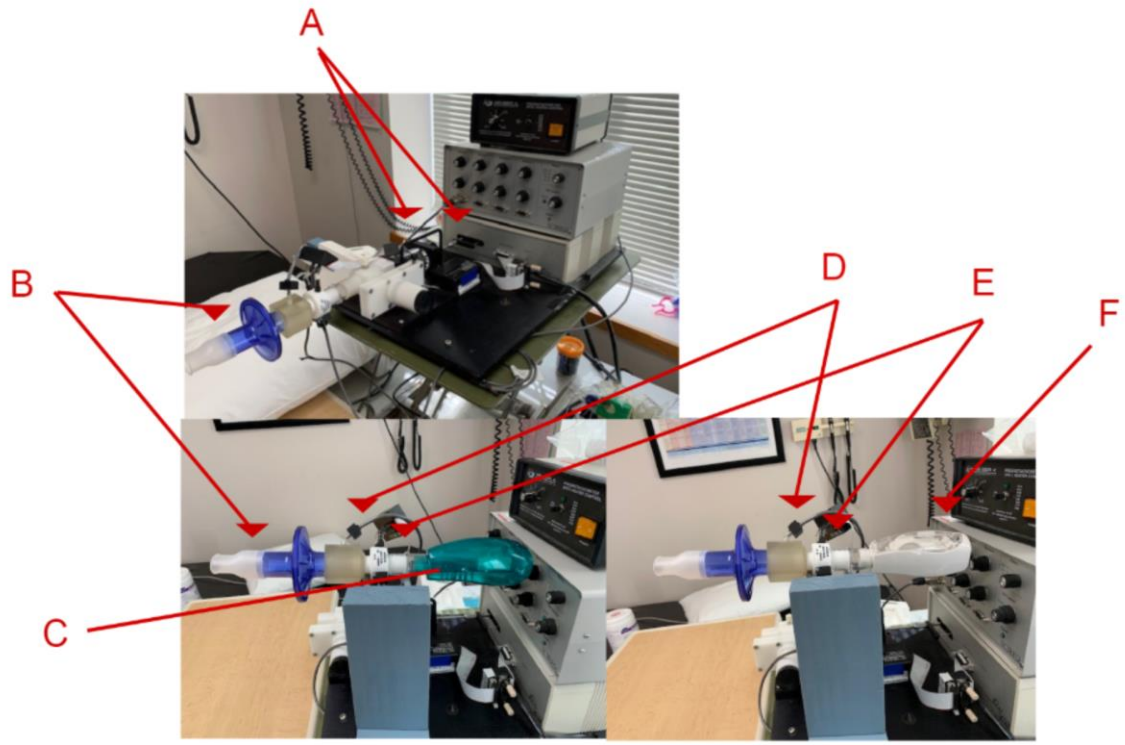

Figure 1: Testing setup for all three devices. (A) Flexivent drive system with piston cylinder. (B) Mouthpiece and air filter. (C) Smith's Medical Acapella Device. (D) Pressure transducer. (E) Pneumotachograph. (F) D R Burton vPEP device.

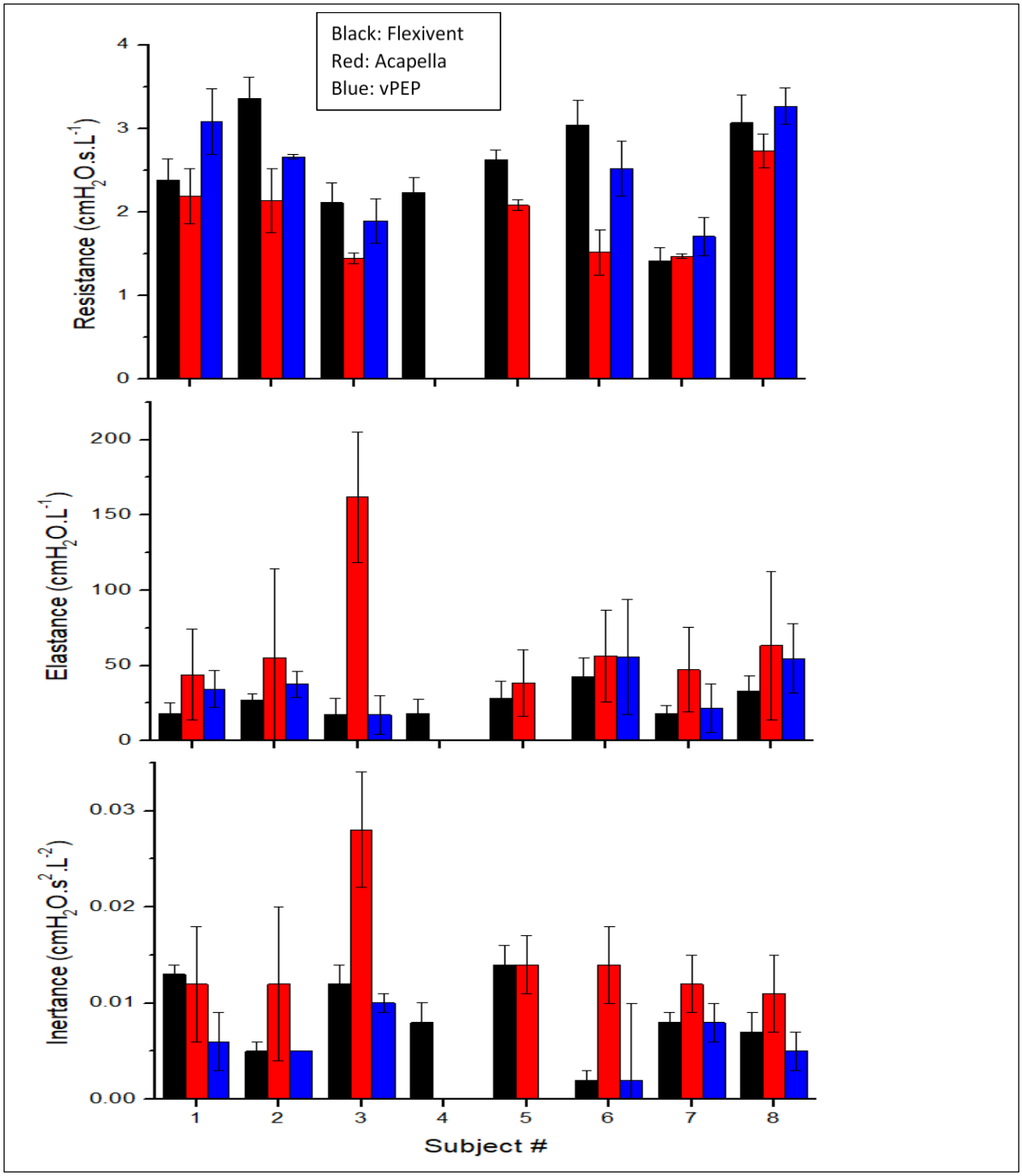

Figure 2: Mean values of R_{rs}, E_{rs} and I_{rs} from the fitting of the single-compartment linear model. These values represent the mean of each parameter over all three runs for each subject for the Flexivent, Acapella, and vPEP. Values of R_{rs}, E_{rs}, or I_{rs} that were negative were excluded.

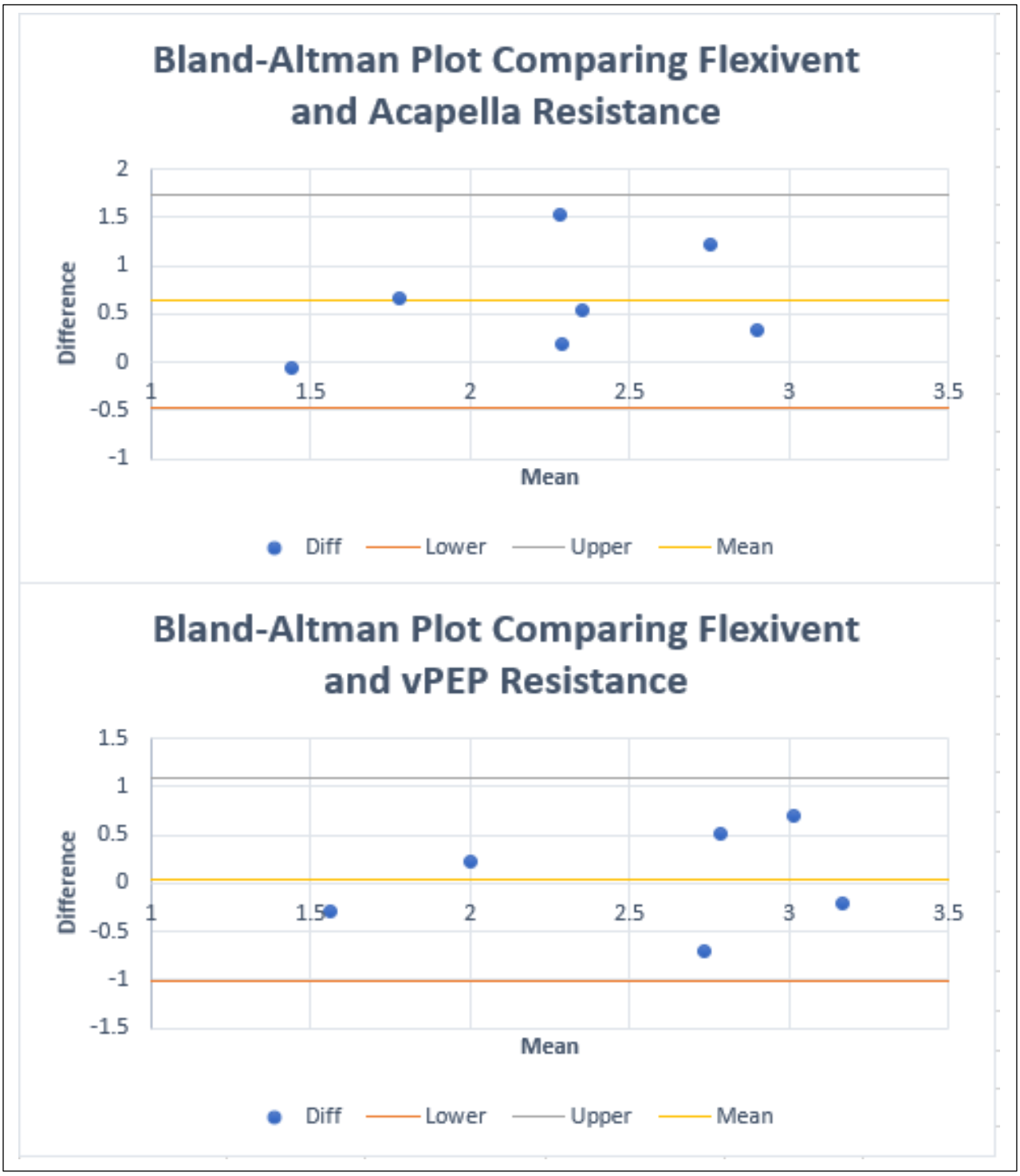

Figure 3: Bland-Altman plots looking at the measurements of R_{rs} ($cmH_2O.s.L^{-1}$) for the Flexivent compared to the Acapella and vPEP. The mean (X axis) is the average of the R_{rs} measurements for the two devices (either Flexivent and Acapella or Flexivent and vPEP) for each participant. The difference (Y axis) is the difference between the R_{rs} measurement for the two devices. Only includes data points participants that had positive values of $R_{rs}$for both devices being compared.

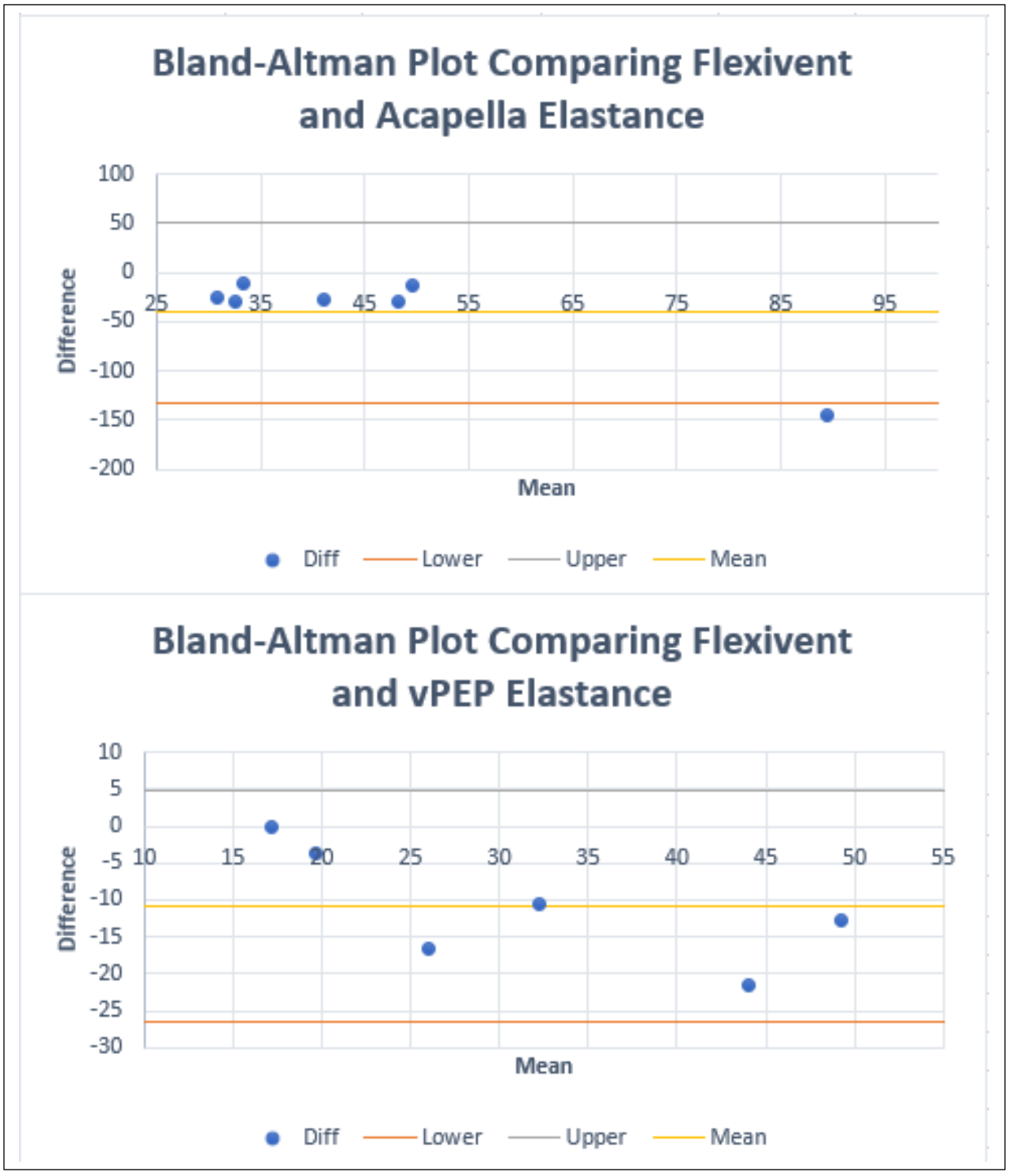

Figure 4: Bland-Altman plots looking at the measurements of E_{rs} ($cmH_2O.L^{-1}$) for the Flexivent compared to the Acapella and vPEP. The mean (X axis) is the average of the E_{rs} measurements for the two devices (either Flexivent and Acapella or Flexivent and vPEP) for each participant. The difference (Y axis) is the difference between the E_{rs} measurement for the two devices. Only includes data points for participants that had positive values of E_{rs} for both devices being compared.

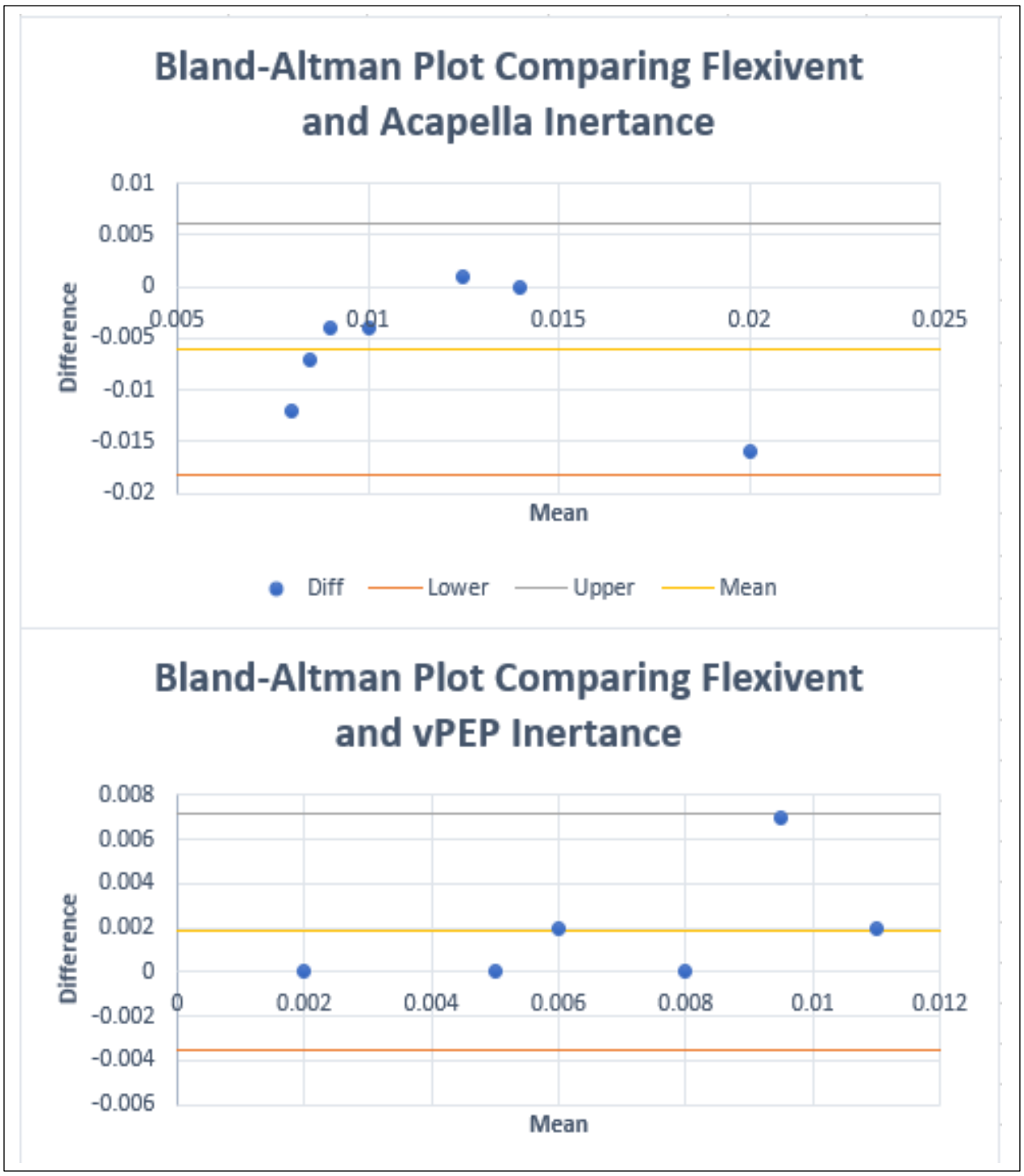

Figure 5: Bland-Altman plots looking at the measurements of I_{rs} ($cmH_2O.s^2.L^{-2}$) for the Flexivent compared to the Acapella and vPEP. The mean (X axis) is the average of the I_{rs} measurements for the two devices (either Flexivent and Acapella or Flexivent and vPEP) for each participant. The difference (Y axis) is the difference between the I_{rs} measurement for the two devices. Only includes data points for participants that had positive values of I_{rs} for both devices being compared.

	PO1 (95%CI)	PO2 (95%CI)	PO3 (95%CI)	PO4 (95%CI)	PO5 (95%CI)	PO6 (95%CI)	PO7 (95%CI)	PO8 (95%CI)
FlexiV								
R mean	2.383 (2.09-2.67)	3.365 (3.17-3.56)	2.111 (1.95-2.27)	2.235 (2.09-2.38)	2.626 (2.55-2.70)	3.045 (2.76-3.33)	1.413 (1.27-1.55)	3.071 (2.82-3.32)
R SD	0.258	0.249	0.235	0.181	0.119	0.288	0.16	0.333
E mean	17.782 (9.34-26.2)	26.958 (23.5-30.4)	17.162 (9.58-24.7)	18.307 (11.2-25.4)	28.311 (21.4-35.3)	42.795 (31-54.6)	17.802 (12.8-22.8)	33.173 (26.0-40.3)
E SD	7.458	4.338	10.943	8.925	11.228	12.058	5.721	9.653
I mean	0.013 (0.0119-0.0141)	0.005 (0.0042-0.0058)	0.012 (0.0106-0.0134)	0.008 (0.0064-0.0096)	0.014 (0.0128-0.0152)	0.002 (0.00102-0.00298)	0.008 (0.0071-0.0089)	0.007 (0.00552-
I SD	0.001	0.001	0.002	0.002	0.002	0.001	0.001	0.002
n	3	6	8	6	10	4	5	7
Acapella								
R mean	2.192 (1.87-2.51)	2.136 (1.76-2.51)	1.448 (1.39-1.5)	-	2.082 (2.03-2.13)	1.517 (1.25-1.78)	1.471 (1.44-1.50)	2.731 (2.53-2.93)
R SD	0.327	0.381	0.061	-	0.064	0.272	0.029	0.204
E mean	43.994 (14.5-73.5)	55.139 (-2.76-113)	161.781 (123.9-199.7)	-	38.349 (20.6-56)	56.521 (26.6-86.4)	47.239 (15.3-79.1	63.308 (15-112)
E SD	30.093	59.083	43.187	-	22.164	30.529	28.158	49.278
I mean	0.012 (0.0061-0.0179)	0.012 (0.00416-0.0198)	0.028 (0.0227-0.0333)	-	0.014 (0.0116-0.0164)	0.014 (0.0101-0.0179)	0.012 (0.0086-0.0154)	0.011 (0.00708-
I SD	0.006	0.008	0.006	-	0.003	0.004	0.003	0.004
n	4	4	5	0	6	4	3	4
vPEP								
R mean	3.083 (2.77-3.39)	2.664 (2.63-2.70)	1.894 (1.71-2.08)	-	-	2.524 (2.06-2.98)	1.707 (1.54-1.87)	3.268 (3.07-3.46)
R SD	0.389	0.028	0.266	-	-	0.331	0.225	0.221
E mean	34.326 (24.4-44.2)	37.61 (25.5-49.7)	17.258 (8.39-26.1)	-	-	55.639 (2.54-108.7)	21.554 (9.55-33.6)	54.78 (34.9-74.7)
E SD	12.347	8.72	12.807	-	-	38.299	16.154	22.747
I mean	0.006 (0.0036-0.0084)	0.005 (0.005-0.005)	0.010 (0.00931-	-	-	0.002 (-0.0091-0.0131)	0.008 (0.00652-	0.005 (0.00325-
I SD	0.003	0	0.001	-	-	0.008	0.002	0.002
n	6	2	8	0	0	2	7	5

Table 1: Results from fitting pressure, flow, volume and acceleration data to the single-compartment linear model to provide mean and SD values for R_{rs} ($cmH_2O.s.L^{-1}$), E_{rs} ($cmH_2O.L^{-1}$), and I_{rs} ($cmH_2O.s^2.L^{-2}$). The mean and SD of each parameter from all three runs were determined for each subject for the Flexivent, Acapelle and vPEP. If any of R_{rs}, E_{rs} or I_{rs} were negative then that breath was discarded. Values of R_{rs}, E_{rs} or I_{rs} for the Acapella or vPEP device that are statistically different than those of the Flexivent are shaded in gray.

Parameter	Value	Upper 95% CI	Lower 95% CI	SE
Flexivent and Acapella-Resistance				
Mean Diff	0.6338571	1.053331908	0.214382378	0.2140177
95% Lower LOA	-0.475948	0.466836348	-1.418733094	1.9341521
95% Upper LOA	1.7436627	2.686447379	0.800877938	1.9341521
Flexivent and vPEP-Resistance				
Mean Diff	0.0413333	0.46699271	-0.384326044	0.2171732
95% Lower LOA	-1.001296	0.013617343	-2.016208915	1.6628147
95% Upper LOA	1.0839625	2.098875581	0.069049324	1.6628147
Flexivent and Acapella-Elastance				
Mean Diff	-40.33543	-5.758433704	-74.91242344	17.641324
95% Lower LOA	-131.8159	-54.1028293	-209.5289248	159.43073
95% Upper LOA	51.14502	128.8580677	-26.56802785	159.43073
Flexivent and vPEP-Elastance				
Mean Diff	-10.91583	-4.53299028	-17.29867639	3.2565526
95% Lower LOA	-26.55025	-11.33143987	-41.76906939	24.934222
95% Upper LOA	4.718588	19.93740273	-10.5002268	24.934222
Flexivent and Acapella-Inertance				
Mean Diff	-0.006	-0.001413353	-0.010586647	0.0023401
95% Lower LOA	-0.018135	-0.007826249	-0.028443561	0.0211485
95% Upper LOA	0.0061349	0.016443561	-0.004173751	0.0211485
Flexivent and vPEP-Inertance				
Mean Diff	0.0018333	0.004005114	-0.000338447	0.0011081
95% Lower LOA	-0.003486	0.001691922	-0.008664569	0.0084839
95% Upper LOA	0.007153	0.012331235	0.001974745	0.0084839

Table 2: Results of the Bland-Altman analysis of the Flexivent compared to the Acapella and vPEP for R_{rs}, E_{rs}, and I_{rs}. Mean difference, 95 percent limits of agreement (LOA), 95 percent confidence intervals for LOA, and standard errors were evaluated for all parameters.

	Correlation Coefficients		
	Rrs	Ers	Irs
Flexivent and Acapella	0.558408	-0.311	0.3221
Flexivent and vPEP	0.7043139	0.90626	0.766

Table 3: Results of the correlation coefficients comparing the values of R_{rs}, E_{rs}, and I_{rs} obtained by the Flexivent (gold standard) to those values obtained by the Acapella and vPEP devices.

Parameter	CV (%)
Flexivent	
Resistance	9.002913724
Elastance	34.76395274
Inertance	17.39130435
Acapella	
Resistance	9.854901672
Elastance	56.28877342
Inertance	33.00970874
vPEP	
Resistance	9.64332893
Elastance	50.22177811
Inertance	44.44444444

Table 4: Correlation coefficients for the parameters R_{rs}, E_{rs}, and I_{rs} for each of the three oscillatory devices.