In-house verification Study: Evaluating absolute lung volumes in healthy individuals using Vyntus™ ONE nitrogen Washout and Vyntus™ BODY body plethysmography

Authors: Margriet Kaldenbach, Manuel Pfeuffer, and Herman Groepenhoff, Ph.D.

Jaeger Medical

Introduction

Pulmonary function testing plays a vital role in the clinical assessment of respiratory disorders, both in adults and children. Accurate measurement of lung volumes helps in diagnosing and managing these conditions[1]. Traditional methods like body plethysmography and nitrogen washout have been widely used in clinical practice for this purpose[2,3].

Vyntus™ ONE and Vyntus™ BODY are two devices used to measure lung volumes: Vyntus™ BODY relies on body plethysmography, while Vyntus™ ONE uses the nitrogen washout technique. Both methods allow for the measurement of absolute lung volumes such as functional residual capacity (FRC), total lung capacity (TLC), and residual volume (RV). TLC is defined as the total volume of air after a maximal inhalation and is the sum of RV and vital capacity (VC)[2]. FRC represents the air remaining in the lungs after a normal exhalation and is the sum of RV and expiratory reserve volume (ERV). Finally, RV is defined as the amount of air remaining in the lungs after a full expiration. The absolute lung volumes and capacities are defined in Figure 1.

JAEGER™

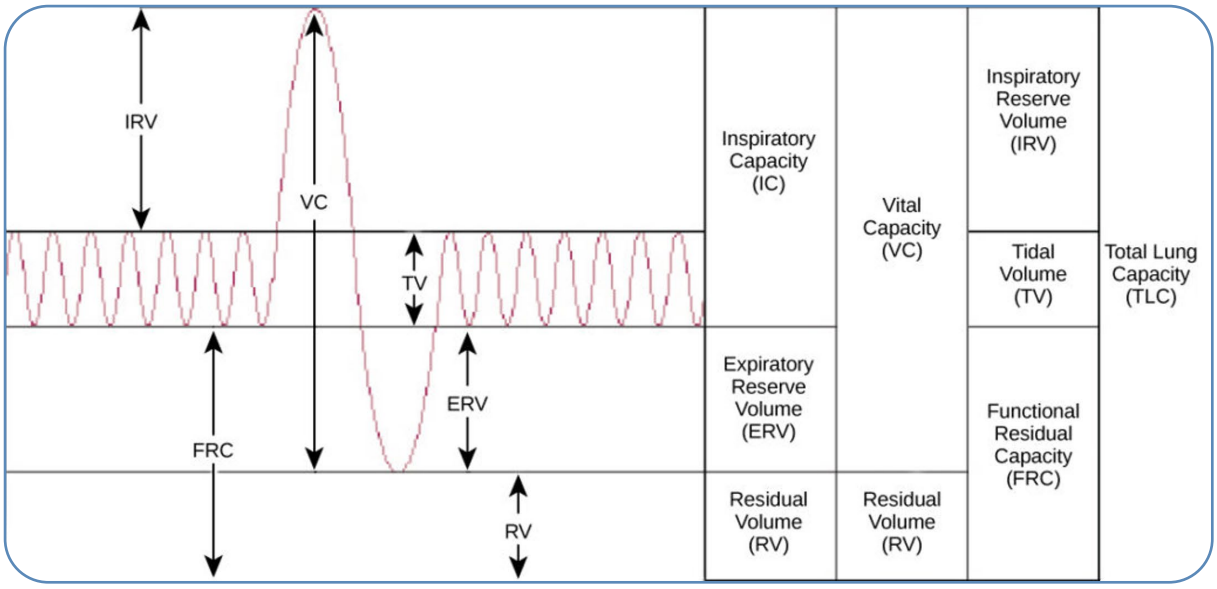


Figure 1. Definition absolute lung volumes and capacities.

It's important to remember that each method has its own advantages and disadvantages. Body plethysmography is less time consuming, measures thoracal gas volume (e.g., all the gas in the chest), whereas nitrogen washout requires more time and only measures the volume of the lungs accessible to the ambient air.[2] However, nitrogen washout has the advantage of measuring the lung clearance index (LCI), a noninvasive measurement of ventilatory inhomogeneity, which isn't possible with body plethysmography. When it comes to measuring absolute lung volumes (TLC, FRC and RV) in healthy subjects, we generally don't expect large differences between the two methods. However, when these tests are performed on patients with lung diseases, especially those involving ventilatory inhomogeneity, differences between the two methods become more apparent[5].

In this study, our primary objective was to assess the accuracy of nitrogen washout absolute lung volume measurements in comparison to body plethysmography in healthy subjects in terms of the standard error of the mean (SEM). Moreover, we aimed to determine whether any systematic differences in key lung volume parameters such as TLC, FRC, and RV between the two methods fall within clinically acceptable thresholds. Lastly, our study aimed to validate the LCI against a predefined acceptability range and identify any systematic differences across the two Vyntus™ ONE devices.

Methods

This study utilized a randomized crossover design and involved four devices, consisting of two Vyntus™ ONE and two Vyntus™ BODY devices. Measurements obtained through nitrogen washout with the two Vyntus™ ONE devices were labeled as VONE1 and VONE2. While those obtained through body plethysmography, using the two Vyntus™ BODY devices, were labeled as VBODY7 and VBODY10. All devices were equipped with SentrySuite™ software (version SES 3.20.6.32091).

According to ERS/ATS guidelines[2], it is recommended to conduct multiple trials when measuring absolute lung volumes (see table 1). For body plethysmography, three repeated FRC trials are advised, with differences between them not exceeding 5%. Meanwhile, for N2 washout, a minimum of two repeated FRC trials are required, with differences between them not exceeding 10%, to ensure accurate mean outcomes.

Volume	Number of trials	Acceptability criteria	
FRC N2	^{3}2	Mean	< 10%
TGV slope	0.5-1 Hz (2-3 seconds)	± 1 kPa	
FRC pleth	^{3}3	Mean	< 5%
FRC pleth	^{3}3	(Highest - lowest) /mean	≤ 0.05
VC	^{3}3	Difference between two largest	≤ 150 ml

Table 1. Summary of ERS/ATS acceptability criteria for lung volumes *(Where: N2= nitrogen; FRC = functional residual capacity; TGV = thoracic gas volume; Pleth = plethysmography; VC = vital capacity).*

Initially, nineteen healthy subjects were recruited for the study. However, only fourteen participants, ten males and four females, fulfilled all inclusion criteria (see Table 2) and completed all required measurements according to the guidelines (see Table 1). Among these fourteen individuals, the mean age and standard deviation (SD) were 44 (12) years, the mean height and SD were 177 (7) cm, and the mean weight and SD were 79 (10) kg.

Table Inclusion and Exclusion Criteria Subjects
Inclusion Criteria
• Healthy subjects with no known pulmonary and/or cardio-vascular condition
• >=18 years of age
• Subjects capable of giving their consent
Exclusion Criteria
• Subjects with a known pulmonary and/or cardio-vascular condition
• <18 years of age
• Pregnant women
• Subjects unable to give their consent

Table 2. Inclusion and Exclusion Criteria subjects for study.

Each participant underwent one testing session with each device, all within a single day. Each testing session included two N2 washout measurements using Vyntus™ ONE device and three body plethysmography measurements using Vyntus™ BODY device, following international guidelines.[2,3] The testing period extended over three days, and participants were randomly assigned to different testing sequences. Before participating, all subjects provided a written, signed informed consent.

Results

Figure 1 illustrates the mean values along with the standard error of the mean (SEM) for TLC, FRC, RV, VC, ERV, and IC of all 14 participants on all four devices individually. In summary, the comparison between the Vyntus™ ONE and Vyntus™ BODY devices revealed no significant differences in TLC, FRC, RV, VC, and ERV. The only notable distinction was a small but statistically significant difference in IC between Vyntus™ ONE1 and Vyntus™ BODY7. When comparing within the Vyntus™ ONE device family, a small but significant difference was observed in TLC and RV between the two devices. However, there were no significant differences in TLC, FRC, VC, ERV, and IC between the two Vyntus™ ONE devices. Within the Vyntus™ BODY device family, no significant differences were found in any of the tested parameters.

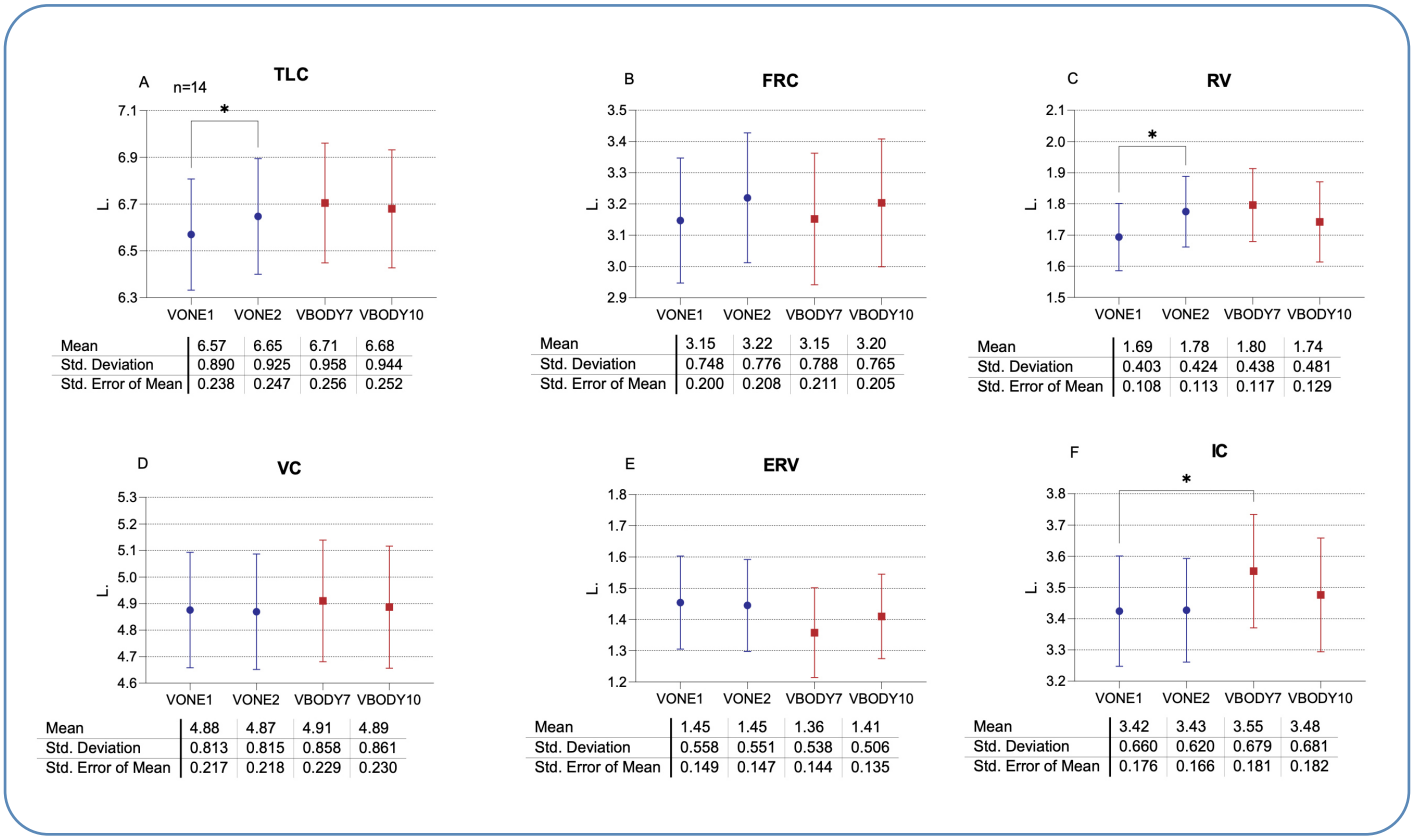


Figure 1. A, B, C, D, E, F Mean ± standard error of mean (SEM) of TLC, FRC, RV, VC, ERV, and IC from all 14 subjects as measured by the four devices. Two Vyntus™ One devices labeled as" VONE1" and "VONE2", two Vyntus™ BODY devices labeled as "VBODY7" and "VBODY10". *: p <0.05.

Figure 2 illustrates the mean absolute overall differences along with the 95% confidence interval for TLC, FRC, RV, VC, ERV, and IC across all measurements taken with both Vyntus™ ONE devices in comparison to both Vyntus™ BODY devices across all 14 participants. The red shadowed area represents the clinically acceptable difference range. As shown in Figure 2, there were no clinically significant differences observed between the Vyntus™ ONE and Vyntus™ BODY devices.

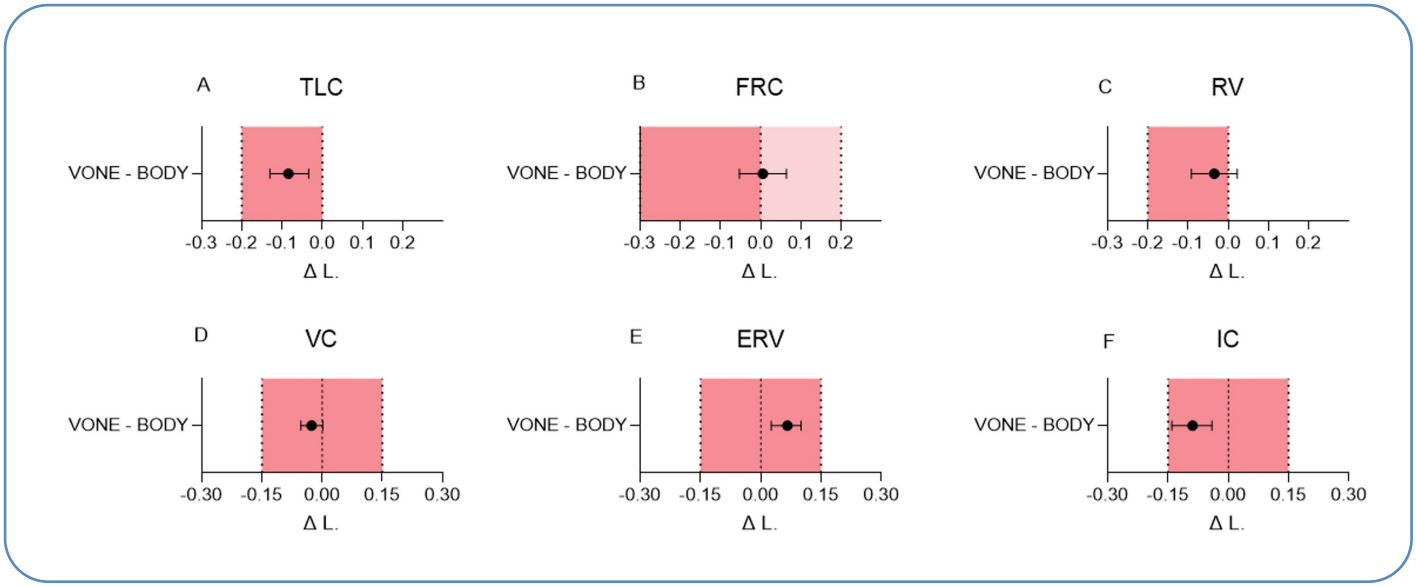
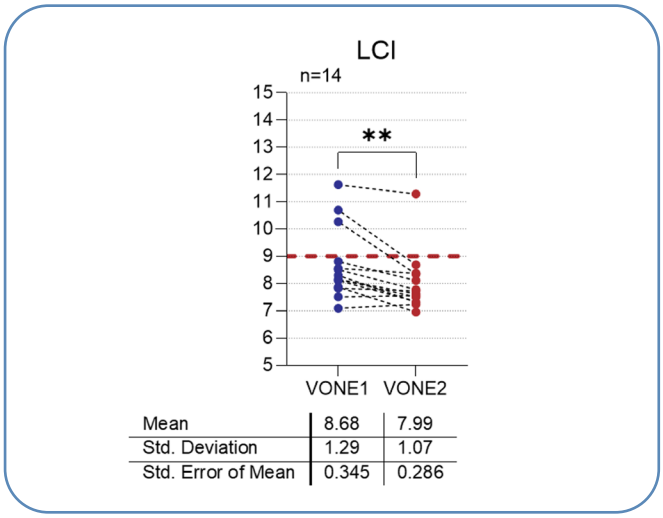


Figure 2. A, B, C, D, E, F Mean absolute overall differences ± 95% confidence interval between both Vyntus™ ONE devices and both Vyntus™ BODY devices for TLC, FRC, RV, VC, ERV, and IC obtained from all 14 participants. Clinically acceptable difference range is indicated by the red shadowed area.

Figure 3 illustrates the mean values along with the standard error of mean (SEM) for LCI across all 14 participants individually tested on each Vyntus™ ONE device. The red dashed lines represent the predefined acceptable tolerance limits, set below nine based on pediatric standards due to the absence of adult reference values[6,7]. In summary, the mean LCI fell below the established tolerance threshold for both devices Furthermore, the comparison between both Vyntus™ ONE devices revealed a small but significant difference in LCI of 0.69.



	VONE1	VONE2
Mean	8.68	7.99
Std. Deviation	1.29	1.07
Std. Error of Mean	0.345	0.286

Figure 3. Mean lung clearance index (LCI) as estimated by both Vyntus™ ONE devices **: p <0.01

Discussion

This in-house, in vivo verification study provides a comprehensive analysis, comparing absolute lung volumes measured by N2 washout technique (using the Vyntus™ ONE) and body plethysmography (using the Vyntus™ BODY) in a group of healthy individuals. The results highlight the accuracy of N2 washout in measuring lung volumes, by the small differences found compared to body plethysmography, where lung volumes are falling well within clinically acceptable limits.

The minor differences observed in absolute lung volumes between the devices can be attributed to inherent methodological differences. For example, the nitrogen washout method only measures the volume of the lungs accessible to the gas, whereas body plethysmography captures all the gas in the chest. These fundamental distinctions underscore the significance of comprehending each method's principle to accurately interpret the results.

Furthermore, the LCI results, although indicating a slight yet statistically significant difference between the two Vyntus™ ONE devices, remained within the predetermined acceptability range. This observation holds clinical significance, underscoring the LCI's potential as a sensitive indicator of ventilation distribution abnormalities, especially in conditions where traditional spirometry may fail to detect early lung function impairment.

Despite the robustness of the findings, it's important to acknowledge its limitations. The study solely focused on healthy individuals, which may limit the generalizability of the results to populations with pulmonary disorders. Future research should aim to validate these outcomes among patients with diverse respiratory disorders. Such investigations will provide a comprehensive understanding of the clinical utility of Vyntus™ ONE nitrogen washout and Vyntus™ BODY plethysmography across a wider spectrum of pulmonary diseases.

Conclusion

In conclusion, the comparison between nitrogen washout (measured with Vyntus™ ONE) and body plethysmography (measured with Vyntus™ BODY) demonstrates their ability to provide lung volume measurements in healthy subjects. The minimal differences observed between these two methods fall well within clinically acceptable limits for healthy subjects, supporting their use in clinical practice.

Although stringent criteria were used in this in-house verification study, any small differences observed in absolute lung volumes, specifically for TLC and RV, within the Vyntus™ ONE device family, remained within the acceptable range expected for healthy subjects. These differences may partially arise from individual subject variations. Despite this inherent variability, the reduced absolute lung volumes measured by nitrogen washout compared to body plethysmography remain within the expected range for healthy subjects. This variance can be explained by the differences in testing methodologies[5].

References

1. S. Stanojevic et al., "ERS/ATS Technical Standard on Interpretive Strategies for Routine Lung Function Tests," Eur. Respir. J., vol. In Press, 2021.
2. N. R. Bhakta et al., "European Respiratory Society/American Thoracic Society Technical Standard on Standardisation of the Measurement of Lung Volumes - 2023 Update," Eur. Respir. J., no. May, p. 2201519, 2023, doi: 10.1183/13993003.01519-2022.
3. P. D. Robinson et al., "Consensus statement for inert gas washout measurement using multiple- and singlebreath tests," Eur. Respir. J., vol. 41, no. 3, pp. 507–522, 2013, doi: 10.1183/09031936.00069712.
4. C. Tantucci, D. Bottone, A. Borghesi, M. Guerini, F. Quadri, and L. Pini, "Methods for Measuring Lung Volumes: Is There a Better One?," Respiration, vol. 91, no. 4, pp. 273–280, 2016, doi: 10.1159/000444418.
5. I. J. Cliff, A. H. Evans, C. F. Pantin, and D. R. Baldwin, "Comparison of two new methods for the measurement of lung volumes with two gold standard methods," Thorax, vol. 52, no. SUPPL. 6, pp. 329–333, 1997.
6. A. M. Zwitserloot et al., "Differences in lung clearance index and functional residual capacity between two commercial multiple-breath nitrogen washout devices in healthy children and adults," ERJ Open Res., vol. 6, no. 2, pp. 00247–02019, 2020, doi:10.1183/23120541.00247-2019.
7. M. Stahl, C. Joachim, M. O. Wielpütz, and M. A. Mall, "Comparison of lung clearance index determined by washout of N2 and SF6 in infants and preschool children with cystic fibrosis," J. Cyst. Fibros., vol. 18, no. 3, pp. 399–406, 2019, doi: 10.1016/j.jcf.2018.11.001.

This document is intended for health care professionals for educational purposes only.

JAEGER™

Jaeger Medical GmbH
Leibnizstrasse 7
97204 Hoechberg
Germany

Jaeger Medical America, Inc.
14050 Rebecca St, Bldg 4
Moreno Valley, CA 92553
USA

CE 0123

For global distribution.