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#### **Highlights:**

- Respiratory inductive plethysmography was evaluated in high BMI subjects
- A non-negligible negative bias was linked with increased BMI values
- Vt values determined by RIP are slightly lowered by increase of ribcage perimeter
- Lowering of Vt values obtained by RIP is partially due to viscoelasticity of fat tissue

# Validity of thoracic respiratory inductive plethysmography in high body mass index subjects

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The authors declare that there is no conflict of interest.

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#### **Abstract**

We aim to evaluate thoracic Respiratory Inductive Plethysmography (RIP) in high body mass index (BMI) subjects with a pneumotachometer (PT) as a reference. We simultaneously evaluated spontaneous breathing by RIP and PT in 10 low and 10 high BMI subjects at rest and in moderate exercise. We then recorded RIP amplitude with different excursions mimicking respiratory thoracic deformation, with different sizes of RIP belts surrounding cylinders of different perimeters with or without deformable foam simulating adipose tissue. RIP responses correlated with PT values in low and high BMI groups for inspiratory time (r = 0.86 and r = 0.91, respectively), expiratory time (r = 0.96 and r = 0.91, respectively) and amplitude (r = 0.82 for both) but with a bias (-0.23 +/-0.25L) for high BMI subjects. ANOVA revealed the effects of perimeter and simulated adiposity (p<0.001 for both). We concluded that thoracic perimeter and deformity of adipose tissue are responsible for biases in RIP response in high BMI subjects.

**Keywords:** Respiratory inductive plethysmography, BMI, Exercise, Validation

#### 1. Introduction

Facing a worldwide epidemic of obesity, reduction of food intake and increased physical activity have been put forward as medical responses to limit and reverse obesity in high body mass index (BMI) subjects. However, this logical approach may underestimate difficulties in applying this concept in real life (Mauro et al., 2008). Obese populations are often affected by ventilatory discomfort and exhibit reduction in functional exercise capacity, limiting the extent to which exercise regimens may be applied (Frank et al., 2011; Hulens et al., 2003). This reduction of exercise capacity has been well evaluated by clinical tests such as the 6 minute walk test (6MWT) showing a decreased walk distance (6MWD) in high BMI subjects in comparison with control subjects (Bautista et al., 2011).

However, the 6MWT in its current design does not yield the ventilatory behavior or breathing pattern of subjects because it is classically not measured (ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002). Indeed, the reference device for ventilatory measurement, namely the pneumotachometer, is rarely used in this test because it did not depict spontaneous breathing by introducing bias (Rameckers et al., 2007). The alternative Respiratory Inductive Plethysmography (RIP) relies on the measurement of the current induced by an alternating magnetic field in coils, which is a function of the surface encircled by the coil (Gastinger et al., 2014), and has been industrialized and validated to evaluate tidal breathing during rest (Grossman et al., 2010; Zhang et al., 2012) and exercise (Witt et al., 2006). We aimed to use RIP during a 6MWT in obese populations, which lead us to develop a method to use RIP as a replacement of the pneumotachometer (PT) to avoid bias in measurement (Retory et al., 2016b), taking into account some concerns raised by Hollier et al. when using RIP in obese populations (Hollier et al., 2014). We thought to assess a one degree of freedom method independent of abdominal

motion because of the inaccuracy of the two degree of freedom model described by Konno and Mead is related to adiposity, which is particularly increased in the abdominal compartment in obese subjects (Avraam et al., 2016; Boudarham et al., 2013; Hollier et al., 2014; Konno and Mead, 1967). In a recent paper (Retory et al., 2016a), we proposed to enrich the 6MWT by using this method, and we described an increase in ventilatory response during the 6MWT in high BMI subjects. These results suggested that this increase could at least partly explain ventilatory discomfort. However, it seemed necessary to add unpublished data related to high BMI subjects regarding the previously validated method in low BMI subjects (Retory et al., 2016b).

Nevertheless, there are still some concerns regarding the reliability of RIP in obese populations. Indeed, as discussed in our previous study and by Hollier et al., there is doubt regarding adiposity's role in induction of artifacts and reduction of RIP response when measuring tidal volume in high BMI subjects (Hollier et al., 2014; Retory et al., 2016a). Moreover, this assumption remains questionable in part because they evaluated RIP in obese populations with no mention of artifact treatment resulting, as illustrated by the inability of the system to determine a valid breathing frequency, in poor reliability of RIP (Hollier et al., 2014). These considerations suggest that, particularly in obese populations, reduction of RIP response and tissue motion artifact need to be carefully taken into account when measuring tidal breathing. We aimed here to evaluate the calibrated RIP accuracy when using our custom-made artifact management algorithm in a population of high BMI subjects at rest and when performing physical activities stimulating ventilatory drive. Moreover, we developed a physical model with in vitro experiments to determine the respective role of the increased thoracic diameter in high BMI subjects and the deformity of adipose tissue.

#### 2. Methods

#### 2.1. Subjects

Twenty volunteers (14 men and 6 women), participated in this study and were divided into two equal groups (n=10) depending on their BMI. Subjects with the highest BMI were free of comorbidities. Anthropometrics data are summarized in Table 1. They provided their informed written consent and the study was conducted in accordance with the principles of the Declaration of Helsinki. Approval for the study was obtained from the Institutional Review Board of the French Learned Society for Respiratory Medicine "Société de Pneumologie de Langue Française" (n° 2015-23).

#### 2.2. Recordings

Thoracic RIP signal was recorded at a sampling frequency of 20 Hz with a ventilatory polygraph (NOX T3 Sleep Monitor, NoxMedical, Reykjavík, Iceland). The median values calculated for 1 min of main ventilatory parameters (Vt, RR, Ti, and Te) were considered as reference variables in this study and were measured by a pulmonary function test machine distinct to the RIP device (Jaeger, Carefusion, Voisins-le-Bretonneux, France), including a pneumotachometer calibrated with a 3 L syringe. This machine allowed us to simultaneously measure volume changes with variations in thoracic perimeter with RIP. It should be emphasized that RIP was used with a thoracic belt ignoring the abdominal value (Fig. 1A). Further details are available in our previous paper (Retory et al., 2016b). Data from Nox T3 were exported in an .edf file and converted in ASCII file with EDFbrowser© software version 1.52 (GNU general public license). ASCII file was imported in Matlab software (Release 2015b; the MathWorks, Inc., Natick, MA, USA) for offline analysis.

#### 2.3. Calibration

Prior to and after recording the ventilation activity, RIP was calibrated by simultaneously measuring high and low levels of volume change by PT and thoracic perimeter change by RIP while the subject remained in a standing position. Once the voluntary calibration was initiated, subjects were not allowed to change their standing posture. A linear regression model was hypothesized to characterize the relationship between perimeter changes measured by RIP and volume measured by PT. Threshold for acceptance of calibration was set to a Spearman's correlation coefficient ≥0.85. Corresponding slope values were calculated offline to calculate volume changes from perimeter changes. Comparisons of these relative matched slopes from the two flanking calibrations (pre- and post-) were made to evaluate the effect of calibration drift or coil displacement induced by activity.

#### 2.4. Protocol

#### *In vivo* experiments

Recordings were performed in a quiet, warm lab room at rest and during submaximal exercise to stimulate ventilatory drive and generate tissue motion artifacts as previously described in our recent paper (Retory et al., 2016b). Exercise consisted of marching on the spot due to the non-portative aspect of our pneumotachometer, and knee-raising with swinging arms at various frequencies. These recordings were made between flanking calibration steps. Seven bouts of one-minute measurements were done for each subject. Each measurement resulted in calculation of the median for one minute of tidal volume (Vt), Respiratory rate (RR), inspiratory time (Ti) and expiratory time (Te). Data processing including filtering of artifacts was made by using a previously described algorithm (Retory et al., 2016b).

#### In vitro experiments

Evaluation of RIP response was made with variation of amplitude from RIP belts surrounding a flexible cardboard cylinder (Fig. 1B). The RIP response was determined as the peak-to-peak amplitude (consecutive minimum and maximum). We assessed 4 manual excursions with graduated support (5 mm, 10 mm, 15 mm and 20 mm). Compatible RIP belts were available in 3 sizes (small (S), medium (M) and large (L)); 3 perimeters of flexible cardboard cylinders were assessed (800 mm, 1000 mm and 1200 mm). All possible conditions (4 levels of excursions x 3 flexible cardboard perimeter x 3 belt sizes = 36) were assessed, but the 8 extremes possibility (the S belt size could not fit the 1200 mm cardboard cylinder and the L belt size was too large for the 800 mm cardboard cylinder). Each assessed condition consisted of a session of 10 repetitive excursions (Fig. 1C) for which amplitude (mV) related to variation of RIP was calculated. RIP response to adiposity was assessed with pieces of rigid cardboard and a deformable foam equivalent in dimension. RIP signal was bandpass filtered with cutoff frequencies of 0.1 and 5 Hz. RIP response to excursion was defined as the corresponding amplitude (in mV) represented by the difference between maximal and minimal peak values of the filtered signal.

#### 2.5. Statistical method

Statistical analyses were performed by using GraphPad Prism version 5.01 for Windows (GraphPad Software, San Diego California USA, www.graphpad.com) and R software (R Core Team (2014). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, www.R-project.org). Data normality was first tested by using a Kolmogorov-Smirnov test. As most of the data were not normally distributed, correlations between RIP and PT values were evaluated by the Spearman coefficient calculation for each parameter recorded (Vt, Ti, Te). Slopes of these relationships

were determined by linear regression. Bland and Altman method was used to determine bias and limits of agreement for comparison of RIP and PT for all assessed parameters (Bland and Altman, 1986). Inter-group differences were assessed using a bilateral Mann Whitney comparison test except for sex ratio comparison, which was assessed using Fischer's exact test. Comparison of slope values from relationships between thoracic motion and airflow from flanking calibrations were realized with a two-way ANOVA after logarithmic transformation of the data. To identify factors implied in RIP response, we used a multiple linear regression model:

$$\Omega = a*X + b*Y + c*Z + \square$$

where  $\Omega$  represents individual amplitudes of RIP, X is the corresponding excursion (5, 10, 15 or 20mm), Y is the belt size (1, 2 or 3), and Z is the corresponding initial perimeter of the cardboard cylinder (800, 1000 or 1200 mm). The lower-case a, b, and c are the respective regression coefficients, whereas  $\square$  is the intercept. Factors that were found to be significant were then analyzed with two-way ANOVA. Two-way ANOVA was realized to firstly describe the effect of perimeter of the cardboard cylinder with one of the excursions on RIP amplitude and secondly to observe the effect of the deformity of the surface encircled by RIP belts with excursions. Sidak's multiple comparisons test was performed to analyze differences between excursions.

#### 3. Results

There was no significant difference between groups for anthropometrics data except for weight and BMI in accordance with the study design (Table 1). Our method showed highly significant correlation with PT values in both groups (r=0.82; p<0.0001 for Vt in high and low BMI subjects) (Fig. 2). Bland and Altman's analyses revealed a higher bias in high BMI subjects in comparison with their lower counterparts with comparable amplitude of limits of agreement (Table 2). In high BMI subjects, there was a bias of 0.23 +/- 0.50 L (equivalent to -

20.4% of RIP response), whereas in low BMI subjects, bias was 0.02 +/- 0.54L (equivalent to -5.3% of RIP response). Respiratory rate determinations by PT and RIP were strongly correlated in low and high BMI subjects (r=0.95; p < 0.0001 and r=0.94; p < 0.0001, respectively) (Fig. 2). Resultant biases and limits of agreements were -0.34 +/- 4.0 in low BMI subjects and -0.91+/- 3.8 in high BMI subjects. Regarding Ti determination, there was significant correlation in both groups (r=0.86; p<0.0001 for low BMI subjects and r=0.91; p<0.0001 for high BMI subjects). Moreover, corresponding biases and limits of agreements were in the same range in both groups (-0.03 +/- 0.30 s in low BMI group; 0.05 +/- 0.34 s in high BMI group) (Table 2). Te determination by our method and by PT was also significantly correlated in both groups (r=0.96; p<0.0001 for low BMI subjects and r=0.91; p<0.0001 for high BMI subjects). Biases and limits of agreements for Te determination were also in the same range (0.11 +/- 0.28 s in the low BMI group; 0.11 +/- 0.42 s in the high BMI group) (Table 2).

Mann-Whitney comparison test revealed that high BMI subjects had higher Vt values obtained with PT in comparison with low BMI subjects in a highly significant manner (Fig. 3).

Calibration drifts were represented by the confrontation of relative values of slopes of relationships between thoracic motion and airflow prior to and after measurement in both groups, ANOVA revealed no significant drift between pre- and post-calibration (Fig. 3). Determination of factors that may influence RIP response was made by multiple linear regression model with amplitude in explained values and belt sizes, initial value of the cardboard cylinder perimeter and excursion of the cylinder as potentially explicative values. A linear regression model (R-squared = 0.91) with multiple factors revealed that excursion is the major cause explaining RIP response with an estimate coefficient  $(1.1 \times 10^{-5} ; p < 0.0001)$  with more influence than initial cardboard cylinder perimeter  $(-7.6 \times 10^{-7} ; p < 0.05)$  and belt size (not

significant) (Table 3). Two-way ANOVA confirmed this finding showing that there was a significant effect of the initial cardboard cylinder perimeter value accounting for 7.2% of the total variation of amplitude and a significant effect of excursion accounting for 82.9% (Fig. 4). Multiple comparisons showed significant differences between initial perimeter of 1200 mm and 1000 mm for the 4 excursions tested representing 23.3% of reduction of global RIP response (4 excursions mixed). There were also significant differences between initial perimeter of 1200 mm and 800 mm for the 4 excursions tested, representing 20.9% of the reduction of global RIP response (4 excursions mixed). Finally, there was a significant reduction of RIP response regarding 800 mm initial perimeter value in comparison with the one of 1000 mm when the excursion was higher (20mm).

Considering effect of deformity of the surface encircled by belts, mimicking adiposity, there was a significant effect (p<0.001) of the viscoelasticity of the material revealed by the two-way ANOVA, accounting for 0.12% of total variation, whereas excursion effect (p<0.0001) accounted for 96.9% of total variance (Fig. 4). Multiple comparisons showed that this effect is greater for the lowest excursion (5 and 10 mm representing 14.7% and 8.4% of reduction of RIP response, respectively), and not significant for the others (15 and 20 mm).

#### 4. Discussion

Few data are available regarding the validity of RIP in obese populations, especially during exercise. Hollier et al. (2014) found poor agreement between RIP and PT for Obesity Hypoventilation Syndrome subjects and raised some possible factors causing inaccuracy (Hollier et al., 2014). In our previous studies (Retory et al., 2016a, 2016b), we developed a method for the use of RIP, taking into account these possible reasons for imprecision and successfully applied it in a high BMI population. The choice of only a thoracic RIP was supported by the Banzett calibration, which satisfactorily attributes a thoracic contribution

two-fold more than the abdominal one (Banzett et al., 1995). Moreover, in the Sackner method used in a study by Avraam et al. the relative contribution of thorax compared to abdomen was greater in obese than in normal weight subjects (Avraam et al., 2016; Sackner et al., 1989). The major limit of this method is related to the lack of abdominal information, but our results demonstrate that some useful ventilatory information, which is unreachable in obese subjects with conventional RIP method can be provided by the thoracic RIP. Nevertheless, validation of this method directly in a high BMI population remained to be established. Thus, the aim of the present study was firstly to evaluate the behavior of our RIP method in high BMI subjects in comparison with low BMI controls. Since this comparison showed some differences in RIP accuracy for high BMI subjects, the second aim was to determine, with *in vitro* experiments, factors that might influence RIP method accuracy.

First of all, results exhibited in this study show that correlation coefficients, bias and limits of agreements are in the same range as those found in the literature in low BMI subjects (Clarenbach et al., 2005; Witt et al., 2006). Indeed, basic ventilatory parameters obtained with thoracic RIP only, such as Vt, and RR are well correlated with those obtained by PT and with acceptable limits of agreements. Furthermore, it should be highlighted that results exhibited in the literature regarding validity of RIP especially during exercise have been performed in lean subjects without any influence of weight or adiposity. By contrast, results from Bland and Altman demonstrated a non-negligible bias (0.230 L) accounting for 20% of underestimation in high BMI subjects, which was not seen in low BMI controls. This finding underlines the fact that Vt obtained by RIP should be interpreted carefully. As discussed previously by Hollier et al., and in our previous paper alteration of RIP values may be found in high BMI subjects (Hollier et al., 2014; Retory et al., 2016a).

We agree with Hollier et al., who brings out several possibilities explaining this inaccuracy: artifacts in RIP signal, deformity of adipose tissue, calibration issues (drift,

displacement of belts, discrepancy in range of Vt during calibration and measurement, position of the body), and asynchrony between thorax and abdomen. However respective roles of these factors remain unknown. Consequently, we designed this study to quantify the relative role of these factors potentially responsible for inaccuracy in addition to the role of torso perimeter and belt size.

#### **Artifacts**

Quality of signal is a major concern when evaluating ventilatory parameters from RIP signals. During walking, tissue motion artifacts induced by vibration of tissue related to heel strike, can easily contaminate RIP signal. This is especially true in obese populations for whom adipose tissue may represent a major source of tissue vibration. There are some methods for filtering in frequency domain, but this implies to specifically know the frequency content of the signal and determine the most appropriate cutoff frequency. More complex adaptive filtering methods can be used when available, as described by Liu to bypass this difficult choice (Liu et al., 2013). When artifacts are falsely considered as respiratory signals, the dependent parameter will be altered in both amplitude (Vt) and time (Ti, Te or Respiratory Rate (RR)). This is well illustrated in the Hollier et al. study, which did not apply any filter in OHS and did not find any agreement in RR values obtained with PT and RIP (Hollier et al., 2014). On our side, we obtained good agreement for time parameters in high BMI subjects likely due to artifact management. Finally, we conclude that rejection of artifacts is necessary when using RIP in high BMI subjects.

Even though our amplitude parameter is less in agreement in high than in low BMI subjects, it could not be argued that this weaker performance is attributable to artifact

contamination because if it were the case, both time and amplitude parameters should be altered. The remaining explanations that could explain this decreased performance of thoracic RIP in high BMI subjects would rely on mechanical properties of belts and the ribcage.

#### From RIP excursions to Vt

Calibration is a major concern when using RIP (Augousti and Radosz, 2011; Lo and Huang, 2016; Raoufy et al., 2013), especially in obese populations (Hollier et al., 2014) and is naturally a target when searching for Vt error estimation. There is evidence that imprecision occurs when switching posture between calibration and measurement (Augousti and Radosz, 2011; Hollier et al., 2014; Konno and Mead, 1967). In this study, this issue cannot be put forward because we kept subjects in a standing position during the whole session to maintain assumptions made during calibrations steps. Drift or belt slipping can also be incriminated because these elements could lead to altered slope of relationship between ribcage movement and airflow. We kept this concern in mind by flanking measurement by calibration phases and calculated these slopes relying on the two corresponding data arrays to reduce these effects. This is not a satisfying explanation for observed bias in high BMI subjects because ANOVA did not shown any effect of BMI or time on variation of slopes. Unpredictable thoracoabdominal asynchrony could lead to misinterpretation of RIP excursion, but this is not a concern because we used the thoracic belt only (Raoufy et al., 2013). The range of Vt in both calibration and measurement periods should ideally be the same. Indeed, if the range of Vt during calibration is far away from the one of the measurement period, this could induce major extrapolation leading to aberrant values. We limited this issue by asking subjects to breathe at low and high levels of Vt during calibration phases to border measurement range. Because we took the same great precaution in both groups to contain error due to calibration,

inaccuracy for Vt determination encountered only in high BMI subjects cannot be assumed by calibration itself.

Vt values, obtained with PT, of our high BMI population are higher than those of low BMI subjects. This may have an impact because deep breathing may increase Vt level in vital capacity range and because it is known that breathing at high volumes may change the relationship between ribcage and airflow (Lo and Huang, 2016) and may weaken the assumption made in the Konno and Mead model (Konno and Mead, 1967). Moreover, higher Vt values imply higher excursion range of RIP belts. To maintain RIP accuracy, sensitivity of belts needs to be constant along the whole measurement span. This assumption is true for small excursions and weaker for large ones. Thus, higher Vt values and corresponding higher excursions in high BMI subjects could play a role in diminishing RIP belt sensitivity. However, this is not a satisfying explanation for bias regarding Vt determination because even if there is a statistical difference for Vt values, they remain in the same range for both groups. Imprecision related to small differences in excursions and overstretching of belts were toned down because high BMI subjects were equipped with larger belts than their counterparts and because our results have shown that there was no influence of belt size in all 28 in vitro experimental conditions. Nevertheless, we choose in these in vitro experiments to avoid under- or overstretching of belts because such effects in these conditions may prove rather an effect of poorly fitting belts rather than an effect of belt size.

Among all possible causes of errors as discussed previously, we have to also examine specific characteristics of high BMI subjects—namely, the greater thoracic perimeter and the mechanical properties of adipose tissue.

In our study, effect of torso perimeter has been assessed by in vitro simulation with cardboard cylinders of various sizes. Even though it was not an exact replica of a ribcage, it allowed us to observe effects on RIP response of equivalent ranges of excursion from different perimeters representing different starting points. Three cardboard perimeters were selected with 800 mm representing the lower limit of thoracic perimeter in healthy populations, 1000 mm representing the medium range, and 1200 mm representing the higher limit (Heyde et al., 2014). Linear regression with multiple factors and two-way ANOVA indicate that thoracic perimeter plays a non-negligible role in RIP response representing 20.9% and 23.28% reduction of RIP response for the comparison of 1200 mm vs. 800mm and 1200 mm cylinder vs. 1000mm, respectively. This is especially true for the higher excursion range (20 mm). Applying these results to humans would mean that high BMI subjects could have 20% of their ribcage movement could truly be achieved but not detected. Somehow, it is compatible with the hypothesis of a decrease of RIP resolution because intergroup difference in Vt was lower than the one of thoracic perimeter but was measured with a technology that depends on thoracic variation over thoracic perimeter ratio, which is much smaller in high BMI subjects. This information is interesting because the range of reduction of RIP response is compatible with a 20% error in determination of Vt obtained in high BMI subjects. Thus, difference in torso perimeters could be an explicative factor for RIP error in determining Vt, especially for higher values.

The hypothesis that deformity of adipose tissue could have a reducing effect on RIP response has been tested by using a simulation with soft foam. In a certain way, simulation may not precisely represent thoracic adiposity, but we exhibited a real visco-elasticity behavior. Thus, results showed here suggest that viscoelasticity has a reduction effect on RIP response, especially for the lowest excursions. Thus, we cannot rule out a specific role of adiposity in the determination of Vt, especially to the lowest values corresponding to the

lowest excursions in subjects with high body fat values. Nevertheless, this is a qualitative and simple approach without direct measurement of deformity effect on RIP response and physical assessment would more precisely complete these results.

#### 5. Conclusion

RIP was accurate enough to detect respiratory signals in both high and low BMI populations, which is demonstrated by agreement with PT for respiratory rate. Nevertheless, Vt determination was skewed with a greater bias in high BMI populations, which could be explained by the reduction of resolution coming with increasing thoracic perimeter and by the reduction due to deformity of adipose tissue. Although all these technical considerations of our recently published results demonstrated higher range of Vt for high BMI subjects during a 6MWT, It may be underlined that those differences are likely to be underestimated taking into account results of the present study. Future research could be done to determine corrective equations taking in account adiposity and thoracic perimeter when determining Vt in high BMI populations. This thoracic RIP method could be helpful to evaluate ventilatory adaptation of obese subjects during the worldwide used 6MWT.

#### 6. References

- ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002. ATS statement: guidelines for the six-minute walk test. Am. J. Respir. Crit. Care Med. 166, 111–117. doi:10.1164/ajrccm.166.1.at1102
- Augousti, A.T., Radosz, A., 2011. Comparative analysis of the isovolume calibration method for non-invasive respiratory monitoring techniques based on area transduction versus circumference transduction using the connected cylinders model. Physiol. Meas. 32, 1265–1274. doi:10.1088/0967-3334/32/8/016
- Avraam, J., Bourke, R., Trinder, J., Nicholas, C.L., Brazzale, D., O'Donoghue, F.J., Rochford, P.D., Jordan, A.S., 2016. The effect of body mass and sex on the accuracy of respiratory magnetometers for measurement of end-expiratory lung volumes. J. Appl. Physiol. 121, 1169–1177. doi:10.1152/japplphysiol.00571.2016
- Banzett, R.B., Mahan, S.T., Garner, D.M., Brughera, A., Loring, S.H., 1995. A simple and reliable method to calibrate respiratory magnetometers and Respitrace. J. Appl. Physiol. Bethesda Md 1985 79, 2169–2176.
- Bautista, J., Ehsan, M., Normandin, E., Zuwallack, R., Lahiri, B., 2011. Physiologic responses during the six minute walk test in obese and non-obese COPD patients. Respir. Med. 105, 1189–1194. doi:10.1016/j.rmed.2011.02.019
- Bland, J.M., Altman, D.G., 1986. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1, 307–310.
- Boudarham, J., Pradon, D., Prigent, H., Vaugier, I., Barbot, F., Letilly, N., Falaize, L., Orlikowski, D., Petitjean, M., Lofaso, F., 2013. Optoelectronic vital capacity measurement for restrictive diseases. Respir. Care 58, 633–638. doi:10.4187/respcare.01916
- Clarenbach, C.F., Senn, O., Brack, T., Kohler, M., Bloch, K.E., 2005. Monitoring of ventilation during exercise by a portable respiratory inductive plethysmograph. Chest 128, 1282–1290. doi:10.1378/chest.128.3.1282
- Frank, I., Briggs, R., Spengler, C.M., 2011. Respiratory muscles, exercise performance, and health in overweight and obese subjects. Med. Sci. Sports Exerc. 43, 714–727. doi:10.1249/MSS.0b013e3181f81ca2
- Gastinger, S., Donnelly, A., Dumond, R., Prioux, J., 2014. A review of the evidence for the use of ventilation as a surrogate measure of energy expenditure. JPEN J. Parenter. Enteral Nutr. 38, 926–938. doi:10.1177/0148607114530432
- Grossman, P., Wilhelm, F.H., Brutsche, M., 2010. Accuracy of ventilatory measurement employing ambulatory inductive plethysmography during tasks of everyday life. Biol. Psychol. 84, 121–128. doi:10.1016/j.biopsycho.2010.02.008
- Heyde, C., Leutheuser, H., Eskofier, B., Roecker, K., Gollhofer, A., 2014. Respiratory Inductance Plethysmography—A Rationale for Validity during Exercise: Med. Sci. Sports Exerc. 46, 488–495. doi:10.1249/MSS.000000000000130
- Hollier, C.A., Harmer, A.R., Maxwell, L.J., Menadue, C., Willson, G.N., Black, D.A., Piper, A.J., 2014. Validation of respiratory inductive plethysmography (LifeShirt) in obesity hypoventilation syndrome. Respir. Physiol. Neurobiol. 194, 15–22. doi:10.1016/j.resp.2014.01.014
- Hulens, M., Vansant, G., Claessens, A.L., Lysens, R., Muls, E., 2003. Predictors of 6-minute walk test results in lean, obese and morbidly obese women. Scand. J. Med. Sci. Sports 13, 98–105.
- Konno, K., Mead, J., 1967. Measurement of the separate volume changes of rib cage and abdomen during breathing. J. Appl. Physiol. 22, 407–422.
- Liu, S., Gao, R.X., John, D., Staudenmayer, J., Freedson, P., 2013. Tissue artifact removal from respiratory signals based on empirical mode decomposition. Ann. Biomed. Eng. 41, 1003– 1015. doi:10.1007/s10439-013-0742-5

- Lo, W.L.A., Huang, D.F., 2016. Assessment of an alternative calibration technique to record breathing pattern and its variability with respiratory inductive plethysmography. J. Clin. Monit. Comput. doi:10.1007/s10877-016-9894-9
- Mauro, M., Taylor, V., Wharton, S., Sharma, A.M., 2008. Barriers to obesity treatment. Eur. J. Intern. Med. 19, 173–180. doi:10.1016/j.ejim.2007.09.011
- Rameckers, H., Kohl, J., Boutellier, U., 2007. The influence of a mouthpiece and noseclip on breathing pattern at rest is reduced at high altitude. Respir. Physiol. Neurobiol. 156, 165–170. doi:10.1016/j.resp.2006.09.001
- Raoufy, M.R., Hajizadeh, S., Gharibzadeh, S., Mani, A.R., Eftekhari, P., Masjedi, M.R., 2013. Nonlinear model for estimating respiratory volume based on thoracoabdominal breathing movements: Nonlinear model for RIP calibration. Respirology 18, 108–116. doi:10.1111/j.1440-1843.2012.02251.x
- Retory, Y., de Picciotto, C., Niedzialkowski, P., Petitjean, M., Bonay, M., 2016a. Body Mass Index-Dependent Ventilatory Parameters From Respiratory Inductive Plethysmography During 6-Minute Walk Test. Respir. Care. doi:10.4187/respcare.04426
- Retory, Y., Niedzialkowski, P., de Picciotto, C., Bonay, M., Petitjean, M., 2016b. New Respiratory Inductive Plethysmography (RIP) Method for Evaluating Ventilatory Adaptation during Mild Physical Activities. PloS One 11, e0151983. doi:10.1371/journal.pone.0151983
- Sackner, M.A., Watson, H., Belsito, A.S., Feinerman, D., Suarez, M., Gonzalez, G., Bizousky, F., Krieger, B., 1989. Calibration of respiratory inductive plethysmograph during natural breathing. J. Appl. Physiol. Bethesda Md 1985 66, 410–420.
- Witt, J.D., Fisher, J.R.K.O., Guenette, J.A., Cheong, K.A., Wilson, B.J., Sheel, A.W., 2006. Measurement of exercise ventilation by a portable respiratory inductive plethysmograph. Respir. Physiol. Neurobiol. 154, 389–395. doi:10.1016/j.resp.2006.01.010
- Zhang, Z., Zheng, J., Wu, H., Wang, W., Wang, B., Liu, H., 2012. Development of a respiratory inductive plethysmography module supporting multiple sensors for wearable systems. Sensors 12, 13167–13184. doi:10.3390/s121013167

#### Figure legends

**Fig 1A**: Illustration of the thoracic RIP setup. **Fig 1B**: Illustration of in vitro experimentations. Excursions (5, 10, 15 or 20 mm) of cylinder of several perimeters (800, 1000 or 1200 mm) were done (10 times each) with several RIP belt sizes (S, M or L) with or without rigid cardboard pieces or soft foam. **Fig 1C**: Representative processing of in vitro experiments with 5, 10, 15 and 20 mm excursion. RIP signal bandpass ([0.1 - 5] Hz) filtered. Calculation of amplitude is the difference between consecutive maximal and minimal peaks.

**Fig 2**: Evaluation of Vt, and RR by RIP signals processed by the custom-made algorithm in low (upper panel) and high (bottom panel) BMI groups. Bland and Altman diagrams and linear relationships (solid line) between parameters (Vt and RR) determined by PT, and the same parameters determined by RIP plus the algorithm. Identity line is represented as a dotted line; r =Spearman correlation coefficient; n =number of values.

**Fig 3:** Upper panel: Comparison with Mann Whitney test of Vt values obtained by PT from low (black) and high (grey) BMI subjects. \*\*\*: p value < 0.001. Bottom panel: ANOVA of slope values with two factors (BMI and Time)

**Fig 4:** Upper panel: ANOVA with 2 factors influencing RIP amplitude (excursion (5, 10, 15 and 20 mm) x cylinder perimeter (800, 1000 and 1200 mm)). Excursion effect: p<0.001 explaining 82.9 % of total variation. Cylinder perimeter effect: p<0.001, explaining 7.2% of total variation. \*\*: p<0.01, \*\*\*: p<0.001. Bottom panel: ANOVA with 2 factors influencing RIP amplitude (Excursion (5, 10, 15 and 20 mm) x Deformity (rigid, soft)). Excursion effect: p<0.001 explaining 96.88 % of total variation. Deformity effect: p<0.001 explaining 0.1% of total variation. \*\*: p<0.01, \*\*\*: p<0.001.

	BMI < 25 kg,m <sup>-2</sup> n=10	BMI >30 kg,m <sup>-2</sup> n=10	P value
Age (years)	40,8 +/- 12,6	46 +/- 11,2	0.310
Height (cm)	165,5 +/- 6,7	173,1+/-11,0	0.071
Weight (kg)	65,4 +/- 12,8	122,8 +/- 16,7	< 0.001
BMI (kg.m <sup>-2</sup> )	23,7 +/- 3,0	41,2 +/- 5,9	< 0.001
Gender (M/F)	7/3	7/3	>0.999

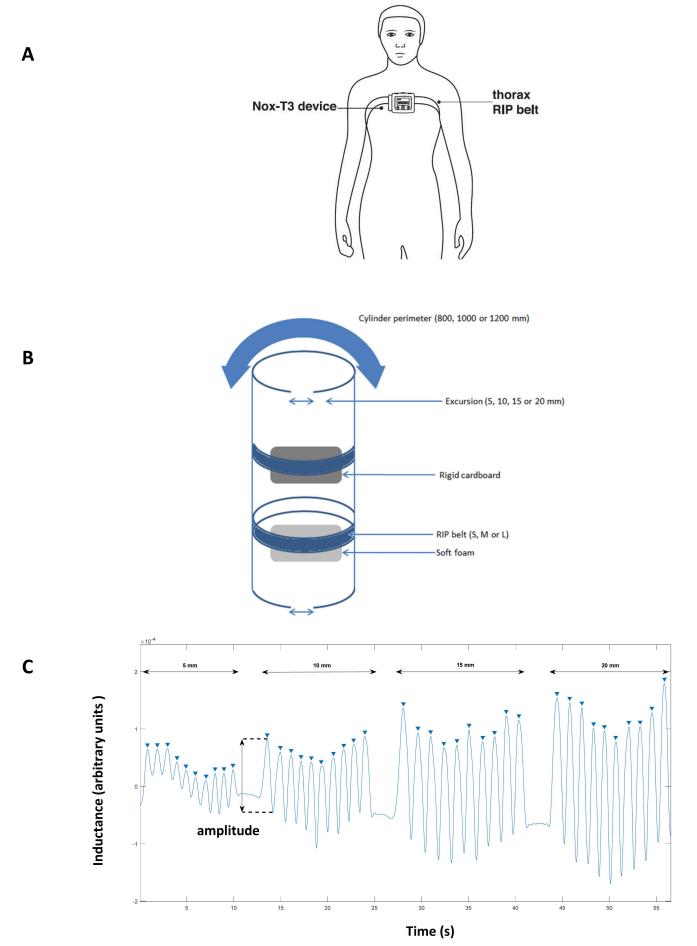
**Table 1**. Anthropometric data expressed as mean +/- SD. P value: significance level from Mann-Whitney test and Fischer exact test.

		BMI < 25 kg,m <sup>-2</sup> n=10; 62 paired values	BMI >30 kg,m <sup>-2</sup> n=10; 59 paired values
Vt	Bias (L)	0,02	0,23
	Bias (%)	5,3	20,4
	Limits of Agreement(L)	[-0,52 0,56]	[-0,27 0,73]
	Limits of Agreement(%)	[-37,1 47,7]	[-17,6 58,4]
RR	Bias (cycles/min)	-0,34	-0,91
	Bias (%)	-2,1	-4,75
	Limits of Agreement (cycles/min)	[-4,34 3,66]	[-4,71 2,89]
	Limits of Agreement (%)	[-17,3 13,1]	[-22,4 12,9]
Ti	Bias (s)	-0,03	0,05
	Bias (%)	-2,3	3,2
	Limits of Agreement (s)	[-0,33 0,27]	[-0,29 0,39]
	Limits of Agreement (%)	[-24,3 19,7]	[-18,8 25,2]
Te	Bias (s)	0,11	0,11
	Bias (%)	6,2	5,9
	Limits of Agreement(s)	[-0,17 0,39]	[-0,31 0,53]
	Limits of Agreement (%)	[-12 24,4]	[-17,3 29,1]

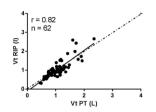
**Table 2:** Comparison of PT and RIP measurements with Bland and Altman method. SD: standard deviation. Vt: tidal volume, RR: Respiratory rate Ti: inspiratory time, Te: Expiratory time.

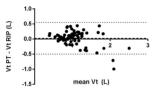
	Coefficients	Std. Error	t value	p value	
Model 1 Multiple R-squared	0.9101			1.079e-12	
(Intercept)	1.087e-04	2.867e-05	3.792	0.00089	***
Excursion	1.102e-05	7.230e-07	15.243	7.65e-14	***
Size of belt	-3.729e-06	6.174e-06	-0.604	0.55148	
Perimeter of cylinder	-7.596e-07	3.087e-07	-2.461	0.02144	*

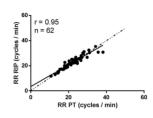
**Table 3:** Linear regression model with 3 explicative factors (Excursion, size of belt and perimeter of cylinder) for RIP amplitude variation \*\*\*: p<0.001, \*\*: p<0.1

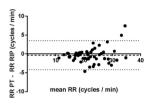


# $BMI < 25 \text{ kg.m}^{-2}$









# $BMI > 30 \text{ kg.m}^{-2}$

