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# Validity of the Pneumonitor for RR intervals acquisition for short-term heart rate variability analysis extended with respiratory data in pediatric cardiac patients

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**Validity of the Pneumonitor for RR intervals acquisition for short-term heart rate variability analysis extended with respiratory data in pediatric cardiac patients**

**Short title:** Validity of the Pneumonitor for heart rate variability in pediatrics

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**ABSTRACT**

**Background:** Breathing pattern alterations change the variability and the spectral content of the RR intervals (RRi) from electrocardiogram (ECG). However, actually there is no solution on how to record and control participant's breathing without influencing its natural rate and depth in heart rate variability (HRV) studies.

**Aim:** The aim of the study was to assess the validity of the Pneumonitor for acquisition of short-term (5 min) RRi in comparison to the reference ECG method for analysis of heart rate (HR) and HRV parameters in the group of pediatric patients with cardiac disease.

**Methods:** Nineteen patients of both sexes participated in the study. ECG and Pneumonitor were used to record RRi from 5 min static rest conditions, the latter also to measure the

relative tidal volume and respiratory rate. The validation comprised the Student's t-test, Bland-Altman analysis, Intraclass Correlation Coefficient and Lin's concordance correlation. The possible impact of the respiratory activity on the agreement between ECG and Pneumonitor was also assessed.

**Results:** Acceptable agreement for number of RRi, mean RR, HR and HRV measures calculated based on RRi acquired using ECG and Pneumonitor was presented. There was no association between breathing pattern and RRi agreement between devices.

**Conclusions:** Pneumonitor might be considered appropriate for cardiorespiratory studies in the group of pediatric cardiac patients in rest condition.

**Key words**: heart rate variability, impedance pneumography, Pneumonitor, RR intervals, validation

## WHAT'S NEW?

The paper describes the validity assessment of the research device — Pneumonitor — for the simultaneous acquisition of single-lead electrocardiogram (ECG) and impedance-based respiratory activity from the same set of electrodes. It enables to derive RR intervals (RRi) along with instantaneous frequency and depth of breathing. Importantly, the two latter signals can be directly measured as changes of trans-thoracic impedance, and not be solely derived from ECG or photoplethysmography. Both information can be utilized to perform heart rate variability (HRV) analysis supported not only by the assessment of RRi stationarity (requirement for the frequency domain calculations), but also by the assessment of respiratory stationarity and activity itself (e.g. HRV analysis can be distorted by too slow breathing pattern). The assessment is performed in the specific clinical context, within the group of pediatric cardiac patients and demonstrates the acceptable agreement of RRi and HRV with the reference device.

## INTRODUCTION

Heart rate variability (HRV), calculated based on consecutive RR intervals (RRi) between adjacent QRS complexes resulting from sinus node depolarizations [1], have been used to investigate the cardiac autonomic responsiveness in various populations [2]. Importantly, HRV is affected by respiratory parameters [3–5]. Classical interpretation of the high frequency (HF) component of HRV as the vagal influence on the heart rate (HR) is flawed in subjects with 3–9 breaths per minute (breaths/min) [6]. Respiratory rate (RespRate) below 6-7

breaths/min results in the respiration-related part of spectrum to be within (partly or totally) the low frequency (LF) band. Additionally, variability in respiratory period and mean tidal volume (TV) generates LF respiratory oscillations, even if the RespRate is within the HF band [7]. The highest value of root mean square of successive RRi differences (RMSSD) was obtained at 7 breaths/min [8]. On the other hand, in populations known to breath faster — more than 24 breaths/min — a wider than generally recommended [1] frequency bands for HF should be set [9, 10]. Despite the evidence that the respiratory alterations change the variability and the spectral content of the RRi, there is no optimal solution on how to record and control breathing without influencing its natural pattern in HRV studies [4, 11].

The electrocardiogram (ECG) is a gold standard method for collecting RRi [1] but can be also used to derive RespRate [12]. ECG-derived respiration might avoid potential influence of mask or belt on breathing parameters. However, the multi-lead ECG recorders' and Holter monitors' costs, limited portability, and limited stationarity of the signal acquisition during activities reduce their practical utility in real-world settings [13].

Last years, new convenient wearable devices have been developed to record parameters in cardiovascular populations more easily, quickly and frequently [14–16]. Pneumonitor is portable, academically developed device designed for environmental physiology and sports medicine analyses and offering synchronized recording of RRi (single-lead ECG) and respiratory mechanics using impedance pneumography (IP) technique with the same set of electrodes [17]. IP records changes of trans-thoracic impedance as the result of changes of the amount of air in lungs and thorax movements. It was shown the specific electrode configuration enables obtaining linear relationship between impedance and TV [18]. However, these relationships depend on subject's demographic parameters, e.g., sex and weight [19]. Therefore, to measure TV in liters, each participant should perform calibration before the main session, which is considered logistically challenging. However, this can be omitted, as the very high linear agreement between impedance and TV allows relying on relative volume changes (even divided into inspiratory- and expiratory-TV) [20]. On the other hand, detected respiratory onsets can be used to determine the RespRate series.

Before using a new tool or method of measurement in clinical practice, it is crucial to verify its agreement with the gold standard [21, 22]. Absence of measurement validation is among the barriers to the widespread use of wearable medical technologies in current practice [23]. Importantly, most wearable biosensors, have not been designed for children, despite numerous pediatric cardiac diseases that could benefit from this technology [16]. IP has been already applied in the pediatric population [24]. Addition of ECG registration, especially

using the same electrode configuration, does not affect the application. The main aim of this study was to assess the validity of the Pneumonitor for acquisition of short-term RRi in comparison to the reference ECG method in the group of pediatric cardiac patients for analysis of vagally-mediated HRV. Furthermore, this study aimed to extend the typically used setup with separate cardiac recording with simultaneous acquisition of respiration.

## METHODS

### Population

The study group consisted of 19 (7 female) pediatric cardiac patients of both sexes. The inclusion criteria were: age between 7 and 18 years, absence of infection, and in case of constant pharmacological treatment – absence of change of medications in the last 3 months. The study was approved by the University Bioethical Committee (KB/70/2021) and followed the rules and principles of the Helsinki Declaration, all parents or legal guardians and patients 16 years and older gave their informed written consent.

### Procedures and measurement conditions

Patients and their parents/legal guardians were informed about the study objectives, measurement protocol, potential risks involved and its benefits by conversation. Recordings were performed in a hospital quiet, bright room, with stable, controlled temperature and humidity between 8:30 am and 2:00 pm. Patients were instructed to refrain from physical activity the day before and on the day of study, avoid junk food, sugar drinks, snacking, and use the toilet (if needed) on the day of study before examinations. The examination was carried out at least 1 hour after breakfast.

### RRi data acquisition using ECG and Pneumonitor

For ECG, 10 electrodes were placed on standard positions. For Pneumonitor, 5 electrodes were placed according to the scheme presented elsewhere [17]. Patients were placed in supine position for 5 min to stabilize HR. RRi were recorded simultaneously using ECG (Custo cardio 100 12-channel PC ECG system; sampling frequency fs = 1000 Hz, Custo med GmbH, Ottobrunn, Germany) and Pneumonitor in supine position for 6 min.

Pneumonitor measured single-lead ECG signals along with IP with the same set of electrodes (standard Holter-type, disposable ones), with fs = 250 Hz, considered sufficient for HRV analysis [1]. For Pneumonitor, ECG signal pre-processing comprised: (1) baseline alignment; (2) R peaks detection using Stationary Wavelet Transform [25]; (3) manual correction of

mistakenly detected R peaks (if applicable, based on the visual inspection) and (4) estimation of RRi between successive R peaks. The IP signal was measured with the tetrapolar method using specified electrode configuration [18]. RespRate were estimated as follows: (1) raw IP were smoothed (1 s window) to remove the cardiac component [26]; (2) respiratory onsets were found based on the differentiated, flow-related signal; (3) RespRate were estimated between successive respiratory onsets.

We did not transform impedance into volume in liters, assuming impedance changes reproduce the TV signal in terms of shape [20]. The first breath was hence assigned with the value of 1, and all next ones were related to this first. Inspiratory and expiratory phases were detected from the differentiated signal, and then, inspiratory- and expiratory-TV were estimated as the difference between the maximum after the inspiration and the minimum before the inspiration, and between the maximum before the expiration and the minimum after the expiration, respectively (Figure 1).

**Data synchronization, artifacts identification and correction**

Registered ECGs were inspected by a pediatric cardiologist for confirmation of sinus rhythm and identification of ectopic beats. The RRi were exported from the ECGs software and the analytical scripts prepared for Pneumonitor data, then imported into a single .xlsx spreadsheet file to carry out raw RRi time series synchronization, identify artifacts based on graphical presentation of raw RRi from both devices and implement manual editing according to recommendations [27]. Physiological artifacts (ectopic beats, premature atrial and/or ventricular beats) were replaced by interpolated RRi from adjacent RRi [28].

**Stationarity assessment**

Stationarity, requirement for spectral HRV indices [29], was verified before HRV analysis (Statistical analysis).

**HR and HRV**

The corrected RRi from both devices were imported into Kubios HRV Standard 3.4 software (University of Eastern Finland, Kuopio, Finland) [30] to calculate mean RR, mean HR (HR), time-domain (standard deviation of NN intervals — SDNN, RMSSD) and frequency-domain (low frequency — LF, HF, LF/HF) parameters based on 5 min recordings. Smoothness priors based on the detrending approach was applied (smoothing parameter, Lambda value = 500) [31], and then, RRi series were transformed to an evenly sampled time series using a cubic

spline interpolation followed by 4-Hz resampling. The detrended and interpolated RRi series were used to compute spectra by employing a fast-Fourier transform with Welch's periodogram method (300 s window, without overlap). The following bands for spectral components were set: LF (0.04–0.10 Hz) and HF (0.10–0.40 Hz). The power at both bands were estimated in absolute ($ms^2$). Natural log transformed (ln) absolute powers in the LF (lnLF) and HF (lnHF) bands were also presented.

**Statistical analysis**

All analyses were carried out in Python 3.9. The stationarity analyses were performed using Phillips–Perron test [32] for patients' RRi and RespRate series separately for ECG and Pneumonitor. Agreement of parameters between ECG and Pneumonitor was verified using a Bland–Altman plot with limits of agreement (LoA) [21, 33] and Intraclass Correlation Coefficient (ICC, model 3.1) with the a priori interpretation: 0–0.30 – small, 0.31–0.49 — moderate, 0.50–0.69 — large, 0.70–0.89 — very large, and 0.90–1.00 — nearly perfect [34]. Agreement sufficient for the interchangeable use of two methods is suggested when a lower 95% CI (confidence interval) value exceeded 0.75 [35]. To compare the values of parameters obtained using both devices, the Student t test was used. The smallest worthwhile change (SWC) was calculated by multiplying the between-subject ECG standard deviation values by 0.2 ($SWC_{0.2}$ small effect) and 0.6 ($SWC_{0.6}$ medium effect) and used to define the maximum allowed difference between methods presented in Bland–Altman plots. Two methods are considered in agreement if the LoA do not exceed the SWC between methods. Lin's concordance correlation coefficient (CCC) was also calculated [36]. To assess whether the agreement between ECG and Pneumonitor is affected by the respiratory depth and rate, Pearson's correlation tests were performed between standard deviations of relative TV and RespRate, and the difference between HRV parameters calculated using ECG and Pneumonitor. Descriptive data for quantitative features with normal distribution were presented as mean and standard deviation (SD). In all cases, the significance level was set at $\alpha = 0.05$.

**RESULTS**

**Participants characteristics**

Results of 3 patients out of 19 were excluded due to poor signal quality (n=2) and non-confirmed diagnosis (n = 1). Consequently, results of 16 (6 female) pediatric Polish Caucasian cardiac patients (congenital heart disease n=5, cardiac arrhythmia n = 4,

cardiomyopathy n = 7) from the following voivodeships of Poland: Mazowieckie (n = 11), Lubuskie (n = 1), Podlaskie (n = 1), Kujawsko-Pomorskie (n = 1), Podkarpackie (n = 1) and Świętokrzyskie (n = 1) were included in the analysis. The mean (SD) age, body mass, stature, body mass index (BMI) were: 12.6 years (3.4), 57.8 kg (25.3), 158.4 cm (18.1), 21.8 kg/m$^2$ (5.5).

**Number of RRi, synchronization, artifacts identification and correction, stationarity**

There were 5917 and 5813 RRi from ECG and Pneumonitor, respectively. Data from both devices required synchronization for 6 patients — from 5 to 11 RRi from the beginning of ECG signal was excluded. There were 27 technical artifacts notified in both ECG and Pneumonitor — 0.005% error rate. The most often detected type of error included short interval, followed by a long interval (n = 21) and missed interval(s) on the Pneumonitor, equivalent to 2 or 3 ECG RRi (n = 6). RRi series obtained using both devices appeared stationary for all patients.

**Agreement of HR and HRV parameters**

Results of agreement statistics for parameters calculated based on RRi obtained using ECG and Pneumonitor are presented in Table 1. There were no significant differences between parameters ($P$ >0.66 for all). Mean absolute percentage difference between parameters ranged from 1.5% to 15.8%. ICC and CCC ranged between 0.96 and 1.00.

The Bland–Altman plots are presented in Figure 2. $SWC_{0.2}$, $SWC_{0.6}$ and number of patients for whom LoA exceed the defined SWC (LoA > SWC) for selected parameters are presented in Table 2.

**Respiratory rate and its stationarity, TV relative changes**

The RespRate was between 8 and 25 breaths/min and was stationary for all patients with one exception (Figure 1). There was no statistically significant correlation between neither standard deviation of relative TV nor standard deviation of RespRate and the difference between parameters calculated using ECG and Pneumonitor (R between –0.36 and 0.38; $P$ >0.14 for all), suggesting lack of association between breathing pattern and RRi agreement between devices.

**DISCUSSION**

Number of RRi, mean RR, HR and HRV parameters calculated based on edited RRi acquired

during rest condition using ECG and Pneumonitor presented sufficient agreement in pediatric cardiac patients.

Widespread use of wearable devices in medical practice is hampered due to the lack of validation studies [23]. Polar chest strap seems to be the most popular wearable device used to register RRi, validated mostly in adults and rarely in children [37,38]. Nevertheless, breathing monitoring is not incorporated into such wearable sensors [39]. Like mentioned in plenty of previous studies, information on breathing is necessary to interpret HRV data accurately (see [4]), especially in populations with respiratory disturbances. Increased RespRate is a common symptom in children with congestive heart failure [40], integral to the diagnosis of acute lower respiratory infection [41].

Pneumonitor can be considered a wearable device allowing to record both cardiac and respiratory activity extending the possibilities to evaluate cardiorespiratory coupling and cardiorespiratory fitness [42] in various measurement conditions (also dynamic), still preserving the quantitativeness of the results. This enables assessing the flow between cardiac and respiratory systems within the causal domain (to identify of directionally and strength of cardiorespiratory coupling and interactions) [43]. It was studied both from the methodological and physiological perspective [44–46]. Procedures and tests developed to explore the coupling between time series in general (e.g., Granger causality) applied for cardiorespiratory data recorded during spontaneous and controlled activity showed ambiguous insights into causalities. Cardiorespiratory interaction has been regarded as primarily respiration-to-heart rate [47] heart rate-to-respiration [48], quasi-cyclical (TV through HR changes and rate to RespRate [45]) or bidirectional [49]. However, these differences probably depend on the different analytical technique employed [4], which could be studied further with the Pneumonitor, and applied specifically in pediatric cohort [50].

The following limitations can be pointed out: the exploratory character of the study, relatively small and heterogenic study size, no inclusion of the control group of healthy pediatric subjects, the differences in sampling frequencies between devices and the procedure assuming only the static conditions. An extension of the study could be to use the Lomb–Scargle periodogram — method that allows more efficient computation of a Fourier-like power spectrum estimator from unevenly sampled data.

Pneumonitor might be considered appropriate for cardiorespiratory studies in the group of pediatric cardiac patients in rest condition.

**Article information**

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## REFERENCES

1. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation. 1996; 93(5): 1043–1065, doi: 10.1161/01.CIR.93.5.1043, indexed in Pubmed: 8598068.
2. Malik M, Hnatkova K, Huikuri HV, et al. CrossTalk proposal: Heart rate variability is a valid measure of cardiac autonomic responsiveness. J Physiol. 2019; 597(10): 2595–2598, doi: 10.1113/JP277500, indexed in Pubmed: 31006862.
3. Gąsior JS, Sacha J, Jeleń PJ, et al. Heart Rate and Respiratory Rate Influence on Heart Rate Variability Repeatability: Effects of the Correction for the Prevailing Heart Rate. Front Physiol. 2016; 7: 356, doi: 10.3389/fphys.2016.00356, indexed in Pubmed: 27588006.
4. Quintana DS, Heathers JAJ. Considerations in the assessment of heart rate variability in biobehavioral research. Front Psychol. 2014; 5: 805, doi: 10.3389/fpsyg.2014.00805, indexed in Pubmed: 25101047.
5. Grossman P, Taylor EW. Toward understanding respiratory sinus arrhythmia: relations to cardiac vagal tone, evolution and biobehavioral functions. Biol Psychol. 2007; 74(2): 263–285, doi: 10.1016/j.biopsycho.2005.11.014, indexed in Pubmed: 17081672.
6. Hayano J, Yuda E. Pitfalls of assessment of autonomic function by heart rate variability. J Physiol Anthropol. 2019; 38(1): 3, doi: 10.1186/s40101-019-0193-2, indexed in Pubmed: 30867063.
7. Beda A, Simpson DM, Carvalho NC, et al. Low-frequency heart rate variability is related to the breath-to-breath variability in the respiratory pattern. Psychophysiology. 2014; 51(2): 197–205, doi: 10.1111/psyp.12163, indexed in Pubmed: 24423137.

8. Soer R, Six Dijkstra MW, Bieleman HJ, et al. Influence of respiration frequency on heart rate variability parameters: A randomized cross-sectional study. J Back Musculoskelet Rehabil. 2021; 34(6): 1063–1068, doi: 10.3233/BMR-200190, indexed in Pubmed: 34024811.
9. Martín-Montero A, Gutiérrez-Tobal GC, Kheirandish-Gozal L, et al. Heart rate variability spectrum characteristics in children with sleep apnea. Pediatr Res. 2021; 89(7): 1771–1779, doi: 10.1038/s41390-020-01138-2, indexed in Pubmed: 32927472.
10. Gąsior JS, Sacha J, Pawłowski M, et al. Normative Values for Heart Rate Variability Parameters in School-Aged Children: Simple Approach Considering Differences in Average Heart Rate. Front Physiol. 2018; 9: 1495, doi: 10.3389/fphys.2018.01495, indexed in Pubmed: 30405445.
11. Plaza-Florido A, Sacha J, Alcantara J. Short-term heart rate variability in resting conditions: methodological considerations. Kardiol Pol. 2021; 79(7-8): 745–755, doi: 10.33963/KP.a2021.0054, indexed in Pubmed: 34227676.
12. Cysarz D, Zerm R, Bettermann H, et al. Comparison of respiratory rates derived from heart rate variability, ECG amplitude, and nasal/oral airflow. Ann Biomed Eng. 2008; 36(12): 2085–2094, doi: 10.1007/s10439-008-9580-2, indexed in Pubmed: 18855140.
13. Smulyan H. The Computerized ECG: Friend and Foe. Am J Med. 2019; 132(2): 153–160, doi: 10.1016/j.amjmed.2018.08.025, indexed in Pubmed: 30205084.
14. Bayoumy K, Gaber M, Elshafeey A, et al. Smart wearable devices in cardiovascular care: where we are and how to move forward. Nat Rev Cardiol. 2021; 18(8): 581–599, doi: 10.1038/s41569-021-00522-7, indexed in Pubmed: 33664502.
15. Sana F, Isselbacher EM, Singh JP, et al. Wearable Devices for Ambulatory Cardiac Monitoring: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020; 75(13): 1582–1592, doi: 10.1016/j.jacc.2020.01.046, indexed in Pubmed: 32241375.
16. Tandon A, de Ferranti SD. Wearable Biosensors in Pediatric Cardiovascular Disease. Circulation. 2019; 140(5): 350–352, doi: 10.1161/CIRCULATIONAHA.119.038483, indexed in Pubmed: 31356135.
17. , et al Młyńczak M, Niewiadomski W, Zylinski M, et al. Ambulatory devices measuring cardiorespiratory activity with motion. In Proceedings of the 10th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2017), Porto, Portugal, 21-23 February 2017; 91-97.

18. Seppä VP, Hyttinen J, Uitto M, et al. Novel electrode configuration for highly linear impedance pneumography. Biomed Tech (Berl). 2013; 58(1): 35–38, doi: 10.1515/bmt-2012-0068, indexed in Pubmed: 23348215.
19. Młyńczak M, Niewiadomski W, Żyliński M, et al. Assessment of calibration methods on impedance pneumography accuracy. Biomed Tech (Berl). 2016; 61(6): 587–593, doi: 10.1515/bmt-2015-0125, indexed in Pubmed: 26684348.
20. Młyńczak M, Krysztofiak H. Cardiorespiratory Temporal Causal Links and the Differences by Sport or Lack Thereof. Front Physiol. 2019; 10: 45, doi: 10.3389/fphys.2019.00045, indexed in Pubmed: 30804797.
21. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986; 1(8476): 307–310, indexed in Pubmed: 2868172.
22. Zaki R, Bulgiba A, Ismail R, et al. Statistical methods used to test for agreement of medical instruments measuring continuous variables in method comparison studies: a systematic review. PLoS One. 2012; 7(5): e37908, doi: 10.1371/journal.pone.0037908, indexed in Pubmed: 22662248.
23. Pevnick JM, Birkeland K, Zimmer R, et al. Wearable technology for cardiology: An update and framework for the future. Trends Cardiovasc Med. 2018; 28(2): 144–150, doi: 10.1016/j.tcm.2017.08.003, indexed in Pubmed: 28818431.
24. Milagro J, Gracia-Tabuenca J, Seppa VP, et al. Noninvasive Cardiorespiratory Signals Analysis for Asthma Evolution Monitoring in Preschool Children. IEEE Trans Biomed Eng. 2020; 67(7): 1863–1871, doi: 10.1109/TBME.2019.2949873, indexed in Pubmed: 31670660.
25. Kalidas V, Tamil L. Real-time QRS detector using stationary wavelet transform for automated ECG analysis. 2017 IEEE 17th International Conference on Bioinformatics and Bioengineering. 2017: 457–461, doi: 10.1109/BIBE.2017.00-12..
26. Młyńczak M, Cybulski G. Decomposition of the Cardiac and Respiratory Components from Impedance Pneumography Signals. Proceedings of the 10th International Joint Conference on Biomedical Engineering Systems and Technologies. 2017(4): 26–33, doi: 10.5220/0006107200260033.
27. Giles DA, Draper N. Heart Rate Variability During Exercise: A Comparison of Artefact Correction Methods. J Strength Cond Res. 2018; 32(3): 726–735, doi: 10.1519/JSC.0000000000001800, indexed in Pubmed: 29466273.

28. Cilhoroz B, Giles D, Zaleski A, et al. Validation of the Polar V800 heart rate monitor and comparison of artifact correction methods among adults with hypertension. PLoS One. 2020; 15(10): e0240220, doi: 10.1371/journal.pone.0240220, indexed in Pubmed: 33031480.
29. Seely AJE, Macklem PT. Complex systems and the technology of variability analysis. Crit Care. 2004; 8(6): R367–R384, doi: 10.1186/cc2948, indexed in Pubmed: 15566580.
30. Tarvainen MP, Niskanen JP, Lipponen JA, et al. Kubios HRV: heart rate variability analysis software. Comput Methods Programs Biomed. 2014; 113(1): 210–220, doi: 10.1016/j.cmpb.2013.07.024, indexed in Pubmed: 24054542.
31. Tarvainen MP, Ranta-Aho PO, Karjalainen PA. An advanced detrending method with application to HRV analysis. IEEE Trans Biomed Eng. 2002; 49(2): 172–175, doi: 10.1109/10.979357, indexed in Pubmed: 12066885.
32. Phillips P, Perron P. Testing for a unit root in time series regression. Biometrika. 1988; 75(2): 335–346, doi: 10.1093/biomet/75.2.335.
33. Abu-Arafeh A, Jordan H, Drummond G. Reporting of method comparison studies: a review of advice, an assessment of current practice, and specific suggestions for future reports. Br J Anaesth. 2016; 117(5): 569–575, doi: 10.1093/bja/aew320, indexed in Pubmed: 27799171.
34. Hopkins WG, Marshall SW, Batterham AM, et al. Progressive statistics for studies in sports medicine and exercise science. Med Sci Sports Exerc. 2009; 41(1): 3–13, doi: 10.1249/MSS.0b013e31818cb278, indexed in Pubmed: 19092709.
35. Lee J, Koh D, Ong CN. Statistical evaluation of agreement between two methods for measuring a quantitative variable. Comput Biol Med. 1989; 19(1): 61–70, doi: 10.1016/0010-4825(89)90036-x, indexed in Pubmed: 2917462.
36. Lin LK. A concordance correlation coefficient to evaluate reproducibility. Biometrics. 1989; 45(1): 255, doi: 10.2307/2532051.
37. Gamelin FX, Baquet G, Berthoin S, et al. Validity of the polar S810 to measure R-R intervals in children. Int J Sports Med. 2008; 29(2): 134–138, doi: 10.1055/s-2007-964995, indexed in Pubmed: 17614016.
38. Speer KE, Semple S, Naumovski N, et al. Measuring Heart Rate Variability Using Commercially Available Devices in Healthy Children: A Validity and Reliability Study. Eur J Investig Health Psychol Educ. 2020; 10(1): 390–404, doi: 10.3390/ejihpe10010029, indexed in Pubmed: 34542492.

39. Charlton PH, Bonnici T, Tarassenko L, et al. An assessment of algorithms to estimate respiratory rate from the electrocardiogram and photoplethysmogram. Physiol Meas. 2016; 37(4): 610–626, doi: 10.1088/0967-3334/37/4/610, indexed in Pubmed: 27027672.
40. Kay JD, Colan SD, Graham TP. Congestive heart failure in pediatric patients. Am Heart J. 2001; 142(5): 923–928, doi: 10.1067/mhj.2001.119423, indexed in Pubmed: 11685182.
41. Smyth RL. Lessons from normal heart and respiratory rates in children. Lancet. 2011; 377(9770): 974–975, doi: 10.1016/S0140-6736(11)60102-5, indexed in Pubmed: 21411135.
42. Muntaner-Mas A, Martinez-Nicolas A, Lavie CJ, et al. A Systematic Review of Fitness Apps and Their Potential Clinical and Sports Utility for Objective and Remote Assessment of Cardiorespiratory Fitness. Sports Med. 2019; 49(4): 587–600, doi: 10.1007/s40279-019-01084-y, indexed in Pubmed: 30825094.
43. Acampa M, Voss A, Bojić T. Editorial: Cardiorespiratory Coupling-Novel Insights for Integrative Biomedicine. Front Neurosci. 2021; 15: 671900, doi: 10.3389/fnins.2021.671900, indexed in Pubmed: 33897367.
44. Rosoł M, Młyńczak M, Cybulski G. Granger causality test with nonlinear neural-network-based methods: Python package and simulation study. Comput Methods Programs Biomed. 2022; 216: 106669, doi: 10.1016/j.cmpb.2022.106669, indexed in Pubmed: 35151111.
45. Młyńczak M, Krysztofiak H. Discovery of Causal Paths in Cardiorespiratory Parameters: A Time-Independent Approach in Elite Athletes. Front Physiol. 2018; 9: 1455, doi: 10.3389/fphys.2018.01455, indexed in Pubmed: 30425645.
46. Nuzzi D, Stramaglia S, Javorka M, et al. Extending the spectral decomposition of Granger causality to include instantaneous influences: application to the control mechanisms of heart rate variability. Philos Trans A Math Phys Eng Sci. 2021; 379(2212): 20200263, doi: 10.1098/rsta.2020.0263, indexed in Pubmed: 34689615.
47. Zhu Y, Hsieh YH, Dhingra RR, et al. Quantifying interactions between real oscillators with information theory and phase models: application to cardiorespiratory coupling. Phys Rev E Stat Nonlin Soft Matter Phys. 2013; 87(2): 022709, doi: 10.1103/PhysRevE.87.022709, indexed in Pubmed: 23496550.

48. Tzeng YC, Larsen PD, Galletly DC. Cardioventilatory coupling in resting human subjects. Exp Physiol. 2003; 88(6): 775–782, doi: 10.1113/eph8802606, indexed in Pubmed: 14603377.
49. Porta A, Castiglioni P, Di Rienzo M, et al. Cardiovascular control and time domain Granger causality: insights from selective autonomic blockade. Philos Trans A Math Phys Eng Sci. 2013; 371(1997): 20120161, doi: 10.1098/rsta.2012.0161, indexed in Pubmed: 23858489.
50. Joshi R, Kommers D, Long Xi, et al. Cardiorespiratory coupling in preterm infants. J Appl Physiol (1985). 2019; 126(1): 202–213, doi: 10.1152/japplphysiol.00722.2018, indexed in Pubmed: 30382810.

**Table 1**. Results of agreement statistics for HRV parameters

| **Parameter** | **Mean (SD) ECG** | **Mean (SD) Pneumonitor** | **Mean difference (95% CI)** | **LoA** | **95% CI for lower; upper LoA** | **ICC (95% CI)** | **CCC** |
|---|---|---|---|---|---|---|---|
| RRi, n | 348.7 (55.3) | 342.6 (54.0) | 6.1 (5.3–7.0) | 3.1; 9.1 | (1.7–4.5); (7.7–10.6) | 1.00 (1.00–1.00) | 0.99 |
| Mean RR, ms | 881.4 (124.8) | 896.9 (126.6) | –15.5 (–17.0 to –14.0) | –20.7; –10.3 | (–23.2 to –18.2); (–12.8 to –7.9) | 1.00 (1.00–1.00) | 0.99 |
| HR, bpm | 69.7 (10.9) | 68.5 (10.8) | 1.2 (1.0–1.4) | 0.4; 2.0 | (0.1–0.8); (1.6–2.3) | 1.00 (1.00–1.00) | 0.99 |
| SDNN, ms | 45.8 (17.4) | 48.2 (16.9) | –2.4 (–3.6 to –1.2) | –6.7; 1.9 | (–8.7 to –4.7); (–0.2–3.9) | 0.99 (0.98–1.00) | 0.98 |
| RMSSD, ms | 52.2 (22.7) | 55.7 (21.6) | –3.5 (–5.7 to –1.4) | –11.1; 3.9 | (–14.6 to –7.5); (0.4–7.5) | 0.99 (0.96–0.99) | 0.97 |
| LF, $ms^2$ | 433.6 (298.5) | 479.6 (324.4) | –46.0 (–76.7 to –15.3) | –155.3; 63.3 | (–207.2 to –103.4); (11.4–115.2) | 0.98 (0.95–0.99) | 0.97 |
| lnLF | 5.8 (0.8) | 5.9 (0.8) | –0.1 (–0.2–0.0) | –0.5; 0.3 | (–0.7 to –0.3); (0.1–0.4) | 0.97 (0.91–0.99) | 0.96 |
| HF, $ms^2$ | 1529.3 (1141.8) | 1601.9 (1105.4) | –72.6 (–137.5 to –7.8) | –303.6; 158.3 | (–413.2 to –193.9); (48.7–267.9) | 0.99 (0.98–1.00) | 0.99 |
| lnHF | 6.9 (1.1) | 7.0 (1.0) | –0.1 (–0.1–0.0) | –0.3; 0.1 | (–0.4 to –0.2); (0.0–0.2) | 1.00 (0.99–1.00) | 0.99 |
| LF/HF | 0.42 (0.28) | 0.42 (0.25) | 0.00 (–0.03 – 0.04) | –0.12; 0.13 | (–0.18 – –0.06); (0.07–0.18) | 0.97 (0.92–0.99) | 0.97 |

Data for quantitative features with normal distribution were presented as mean and standard deviation (SD)

Abbreviations: CI, confidence interval; LoA, limits of agreement; ICC, Intraclass Correlation Coefficient; CCC, concordance correlation coefficient; RR, time elapsed between two successive R waves of the QRS signal on the electrocardiogram; RRi, RR intervals; ms, milliseconds; $ms^2$, milliseconds squared; HR, heart rate; bpm, beats per minute; SDNN, standard deviation of NN intervals; RMSSD, root mean square of successive RRi differences; LF, low frequency; HF, high frequency; ln, natural log transformed;

**Table 2**. Smallest worthwhile change (SWC) and number of patients for whom LoA exceeded the defined SWC

| | Mean RR, ms | HR, bpm | SDNN, ms | RMSSD, ms | LF, $ms^2$ | lnLF | HF, $ms^2$ | lnHF | LF/HF |
|---|---|---|---|---|---|---|---|---|---|
| $SWC_{0.2}$ | 11.4 | 2.3 | 3.6 | 4.7 | 61.7 | 0.16 | 236 | 0.2 | 0.06 |
| LoA $>SWC_{0.2}$ | None | None | 4 | 4 | 4 | 1 | 2 | 2 | 2 |
| $SWC_{0.6}$ | 34.3 | 6.8 | 10.8 | 14.1 | 185.0 | 0.48 | 708 | 0.7 | 0.18 |
| LoA $>WC_{0.6}$ | None | None | None | None | None | 1 | None | None | 1 |

RR, time elapsed between two successive R waves of the QRS signal on the electrocardiogram; ms, milliseconds; $ms^2$, milliseconds squared; HR, heart rate; bpm, beats per minute; SDNN, standard deviation of NN intervals; RMSSD, root mean square of successive RRi differences; LF, low frequency; HF, high frequency; ln, natural log transformed; SWC, smallest worthwhile change; LoA, limits of agreement

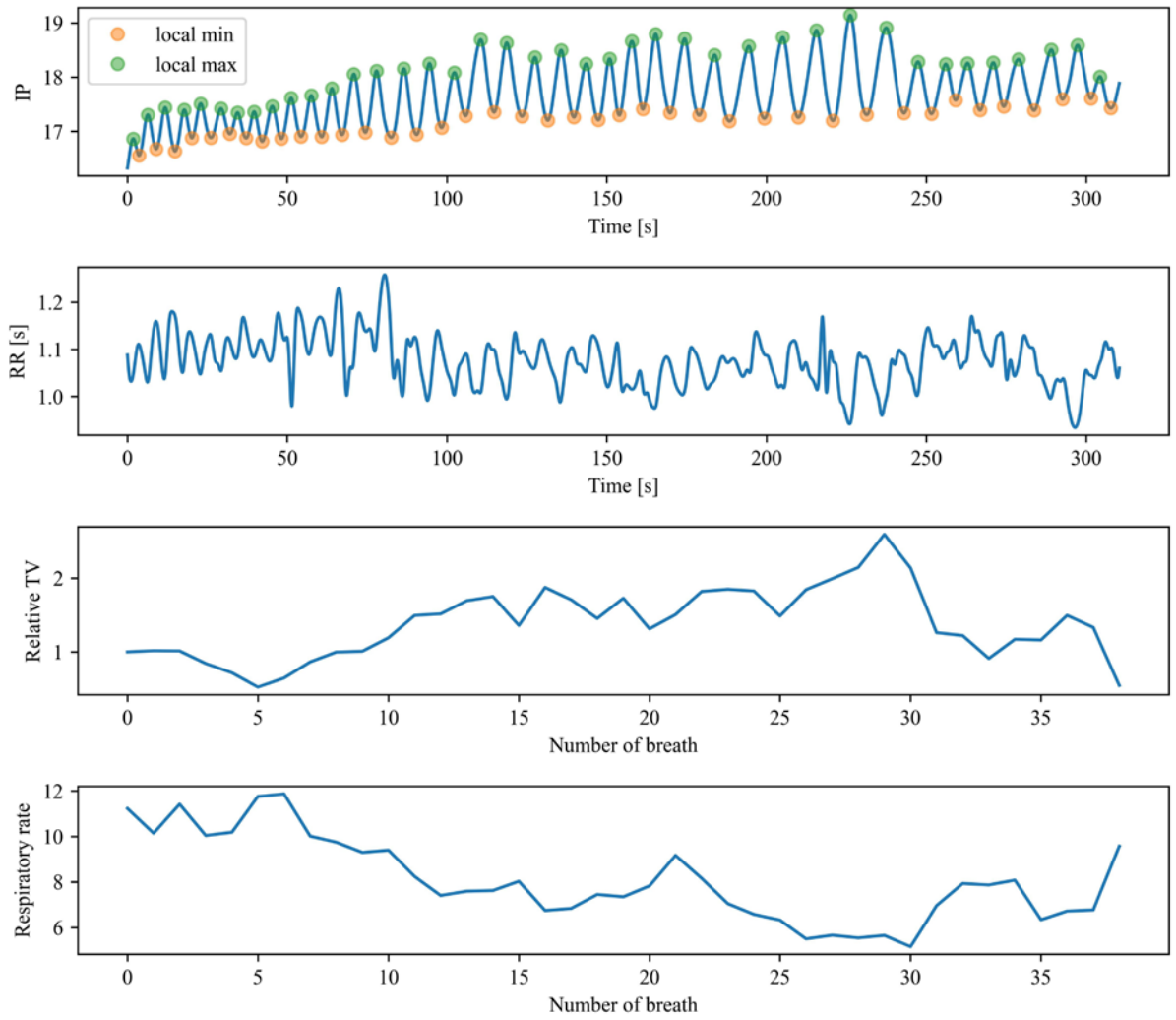


**Figure 1**. The sample series of IP signal (top) with marked local minima and maxima enabling to calculate respiratory rate (bottom) and the course of relative TV (second from the bottom), along with the interpolated RR intervals (second from the top); the only example with nonstationary (decreasing) respiratory rate

Abbreviations: IP, impedance pneumography; s, seconds; RR, time elapsed between two successive R waves of the QRS signal on the electrocardiogram; TV, tidal volume

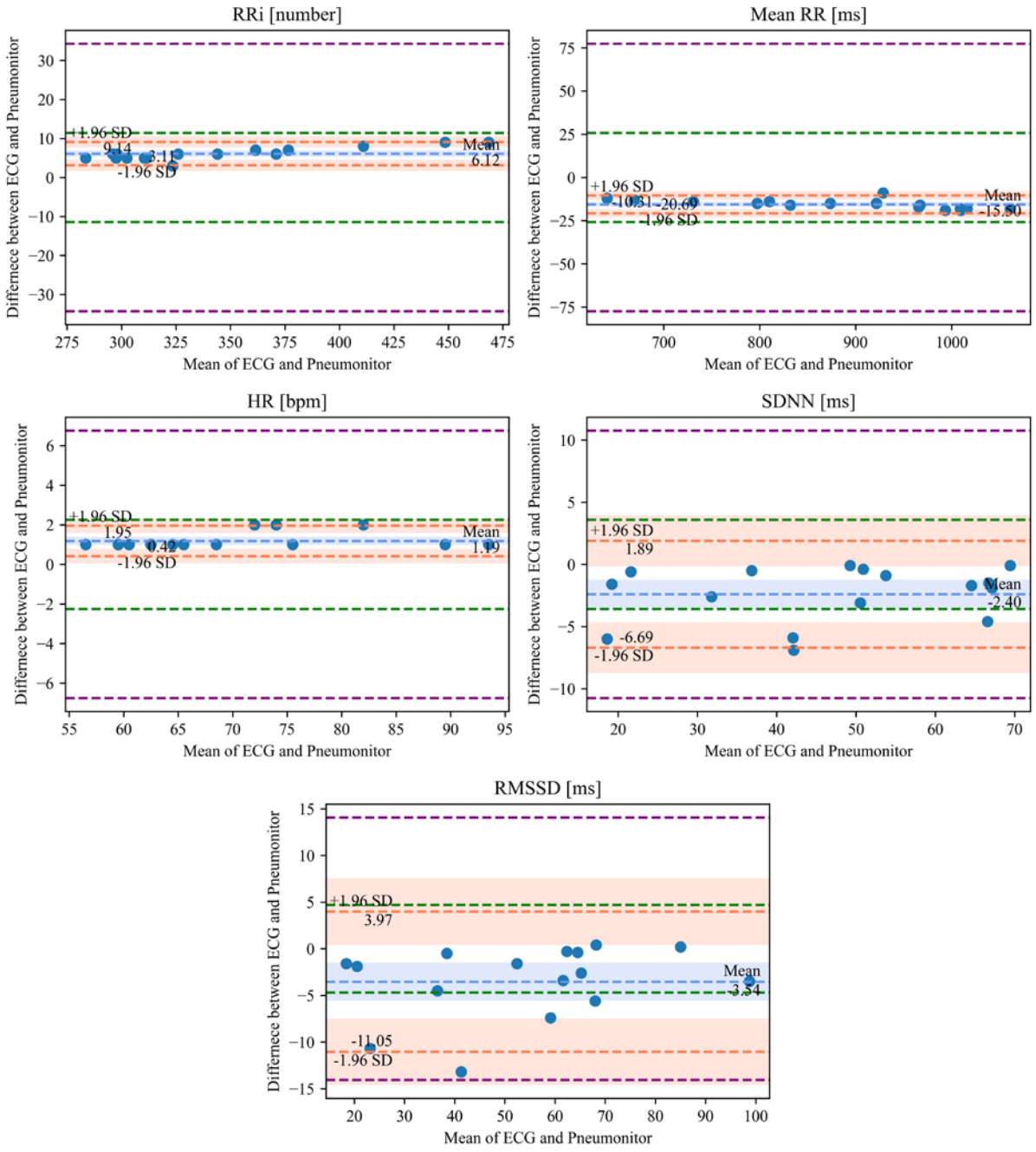


**Figure 2**. Bland-Altman plots for number of RRi, mean RR, HR and time-domain HRV calculated based on RRi obtained using ECG and Pneumonitor. Dashed blue line presents mean difference, dashed orange lines represent LoA. The blue and orange areas highlight the confidence intervals for the mean and LoA, respectively. The dashed green and purple lines shows the $SWC_{0.2}$ and $SWC_{0.6}$

Abbreviations: RRi, RR intervals; ms, milliseconds; HR, heart rate; bpm, beats per minute; RMSSD, root mean square of successive RRi differences; SDNN, standard deviation of NN intervals; other — see Figure 1

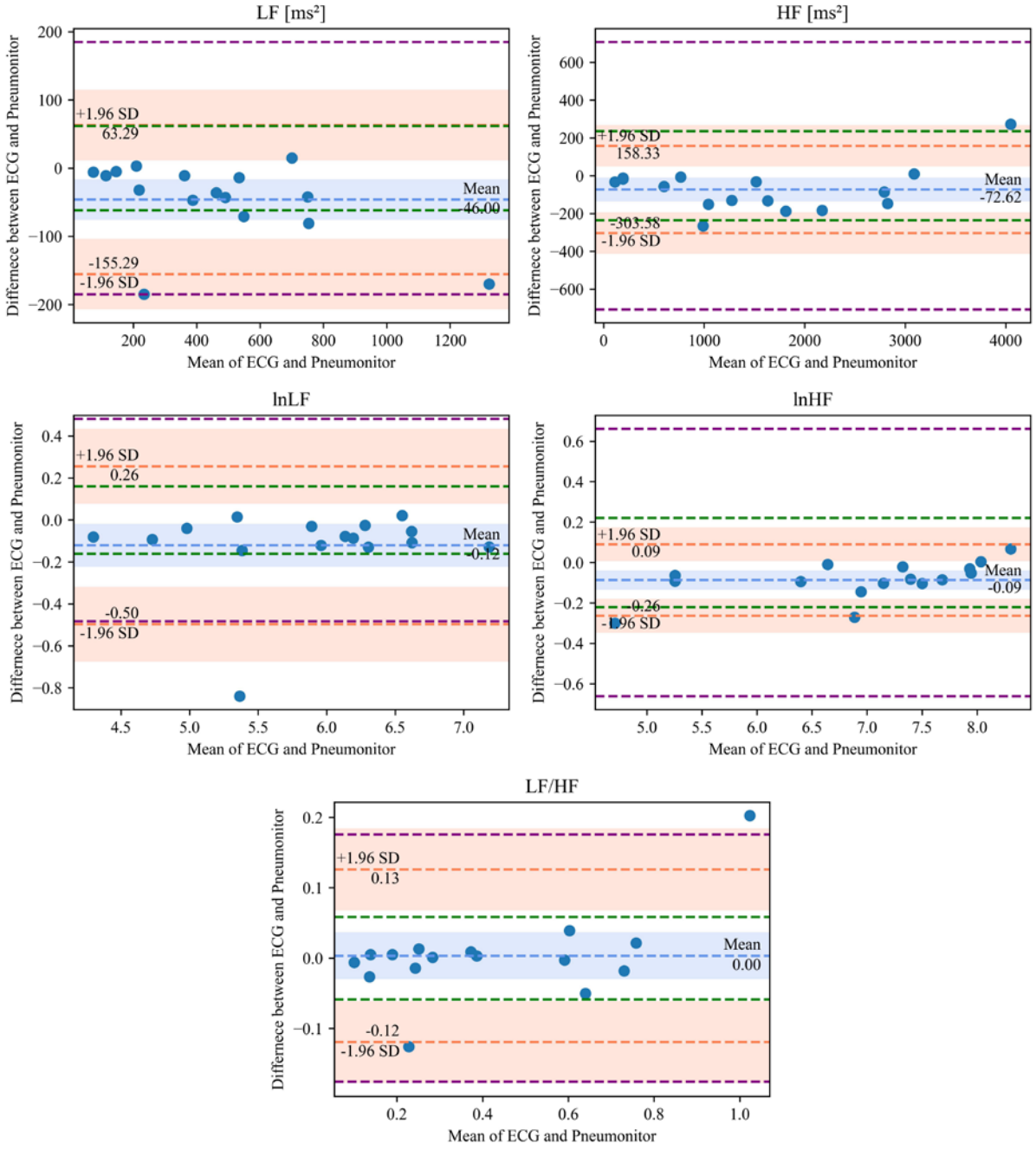


**Figure 3**. Bland-Altman plots for number of RRi, mean RR, HR and time-domain HRV calculated based on RRi obtained using ECG and Pneumonitor. Dashed blue line presents mean difference, dashed orange lines represent LoA. The blue and orange areas highlight the confidence intervals for the mean and LoA, respectively. The dashed green and purple lines shows the $SWC_{0.2}$ and $SWC_{0.6}$

Abbreviations: LF, low frequency; HF, high frequency; $ms^2$, milliseconds squared; ln, natural log transformed