PHILIPS

Clinical Evaluation Report (P&S Development)

ChARM

Clinical Evaluation Report for Product and Services Development

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APPROVAL

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1. INTRODUCTION

1.1. Purpose and scope

This report describes the results of the clinical evaluation for the following devices(s):

- Children's Respiration Monitor (ChARM) CHW and PHW

This report supports the safety and performance of the listed devices in the intended (clinical) environment, based on the assessment and analysis of clinical data, as required by European Council Directive 93/42/EEC.

1.2. Product lifecycle

This report is maintained and updated where applicable through the complete product life cycle. This report is updated when:

- There are post market clinical surveillance activities defined in the CER
- The intended use was changed
- New claims were intended
- New clinical data was assessed
- The product risk management file was updated and new risks were escalated to the clinical evaluation process.

1.3. References

Reference	Identification	Title / additional remarks
[REF-1]	DHF254275	Clinical Evaluation Plan ChARM
[REF-2]	DHF230134	User Needs Specifications
[REF-3]	DHF256700	Risk Management Matrix ChARM
[REF-4]	FDA database	MAUDE (Manufacturer and User Facility Device Experience Database) represents reports of serious adverse events involving medical devices since 1996. [Link to database]
[REF-5]	DHF258261	Literature Search Report ChARM
[REF-6]	DHF258244	ARIDA Target Product Profile from UNICEF
[REF-7]	DHF258477	Histogram based Respiration Measurement- Philips research report
[REF-8]	DHF256273	Report for Validation of Video Annotation Technique
[REF-9]	DHF259194	CIP_Research Data Collection Study Plan - Research document

2. DESCRIPTION OF THE DEVICE

2.1. Technical description

Pneumonia is a leading cause of child mortality under five, resulting in 1.1 million deaths annually (more than AIDS, malaria, and measles). 90% of deaths occur in low-resource settings in Asia and Africa, where poverty-related circumstances such as malnutrition and poor hygiene are contributing risk factors. A majority of deaths could be easily prevented through appropriate case management, specifically effective diagnosis and the rational provision of antibiotic treatment. However, this is hard to achieve in low-resource settings where diagnostics such as chest radiology and blood-tests are scarce.

The WHO 'Integrated Management of Childhood Illnesses (IMCI) and the Integrated Community Case Management (iCCM) guidelines' for diagnosing pneumonia by classifying breath-rates has proven to be challenging at the lowest levels of care. Therefore, the need for improved diagnostics has been recognized by UNICEF as an essential area of innovation to increase coverage of treatment and combat mortality from childhood pneumonia [REF-6]. We propose a cost-effective technology that will support health workers at the Base of the Pyramid (BoP) to accurately assess fast breathing rate in children under 5 years and support a better diagnosis of pneumonia: the Children's Automated Respiration Monitor (ChARM).
There are two versions(configurations) for the product:

- CHW ChARM : used by the community health worker in field settings
- PHW ChARM : used by the professional health worker in clinical settings

The monitoring device is small in size to be easily fixed to the child and carried by one hand. The size of the device exclusive of belt is smaller than 70 × 70 x 30 mm and weighs less than 75 grams. The sketch of the monitoring device and the belt shown below for reference.

Figure 1. Sketch of the Device with Attachment Mechanism (Belt)

2.2. Intended Use / Indications for Use

The ChARM device is intended to measure respiration rate in children under 5 years old and automatically classify fast breathing rate according to the IMCI guidelines as per the WHO. The device is to be used by health workers at the community level in low-resource settings and by clinical officers, nurses, midwives, clinicians (professional health workers) at primary or secondary care facilities.

This device is not intended to provide automated treatment decisions, nor is it to be used as a substitute for professional healthcare judgment. All patient medical diagnosis and treatment is to be performed under the supervision and oversight of an appropriate healthcare professional.

2.3. Specific claims

Philips intends to support the following claims with clinical data:

The device shall measure respiratory rate for children aged 0 (full term babies born after 37 weeks of gestation) to 5 years old with an accuracy of +/- 2 breaths per minute (root mean square error) when measured under calm (according to WHO guidelines) and moderate motion conditions.

3. PRODUCT RISK MANAGEMENT

The Risk Management Matrix [REF-3] documents the results of the safety risk management analysis.

The product risk management analysis showed that no significant risks remained after mitigation. As a result, there are no inputs from the product risk management process for this Clinical Evaluation.

4. CONTEXT AND CHOICE OF CLINICAL DATA TYPES

4.1. Developmental context

There are various vital signs and ways that can be used to measure the respiratory rate automatically e.g. using changes in the blood oxygen level (SpO2), breath motions from a video signal, breath sounds from a microphone, airflow through the noise and a band around the chest that measures volumetric change of the lounges, etc.

Then there is the 3D accelerometer that measures motion of the chest/belly. This method has many advantages over the other methods: It's minimally intrusive (can be worn over clothing), consumes little energy (batteries can last for years), it's easy to apply (suited for rural areas).

ChARM design uses a 3-axis accelerometer with advanced signal processing to measure breath rate in children under 5 years using breath motions captured by accelerometer data. The accelerometer data is sampled at 100 samples per second to be able to capture the the breathing rates on small children which can go as high as 150 breaths per minute or 2.5 breaths per second.

The technology of extracting breath rate by processing the motion signals from 3–axis accelerometer has been developed and released to market by Philips. This product known as Philips IntelliVue CL Respiration POD has been in market since Apr 2013 (K132320, K122223). This product apart from monitoring the respiratory rate of adult patients is also capable of giving approximate activity status and posture. The ChARM device however is only giving the respiratory rate and is specifically for children under 5 years of age. The technology used by ChARM for the breath rate measurement is substantially equivalent to the one used in Philips IntelliVue CL Respiration POD for breath rate measurement.

Figure 2. The Intellivue Cable-Less Respiration Pod.

The respiration measurement algorithm that is used by the above device formed the basis of the algorithm development for the ChARM project. This algorithm was originally developed for adults only and as such the initial efforts were concentrated into making adaptations such that it would also work with small children. The way a small child breaths is different than an adult: It's more irregular, unlike an adult, inhales and exhales have similar durations and a child moves a lot during the measurement.

Initially, in 2013 a study with 8 to 10 healthy children per each of the three age groups was conducted in the Netherlands, to collect respiration based data from different accelerometers placed on different parts of the child's chest and belly area, and in different postures. This helped in understanding the biomechanics of the children's breathing and the requirements for the algorithm development [REF-7].

Figure below gives a overview of how the Histogram Based Respiration Measurement algorithm works.

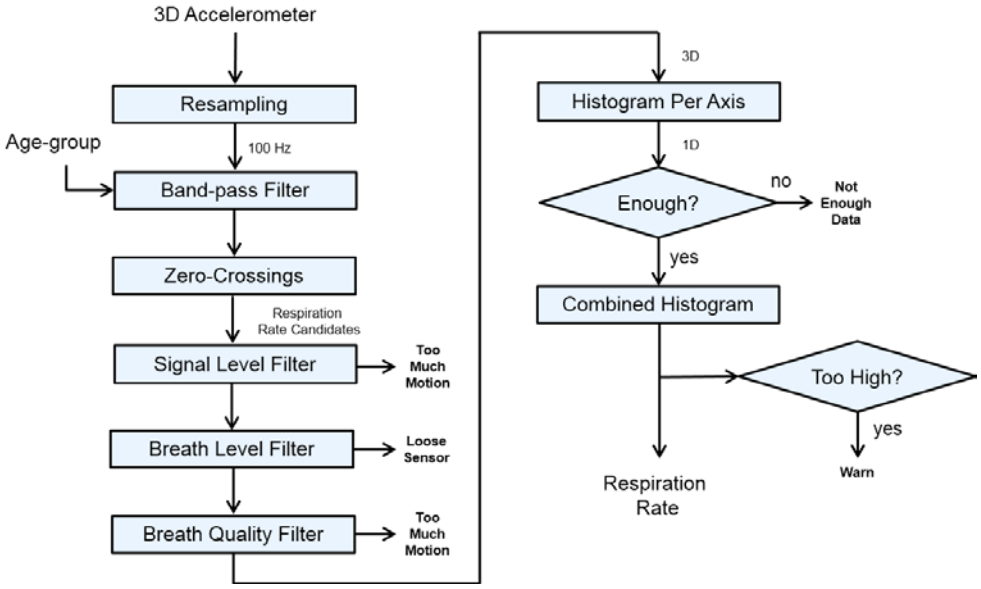
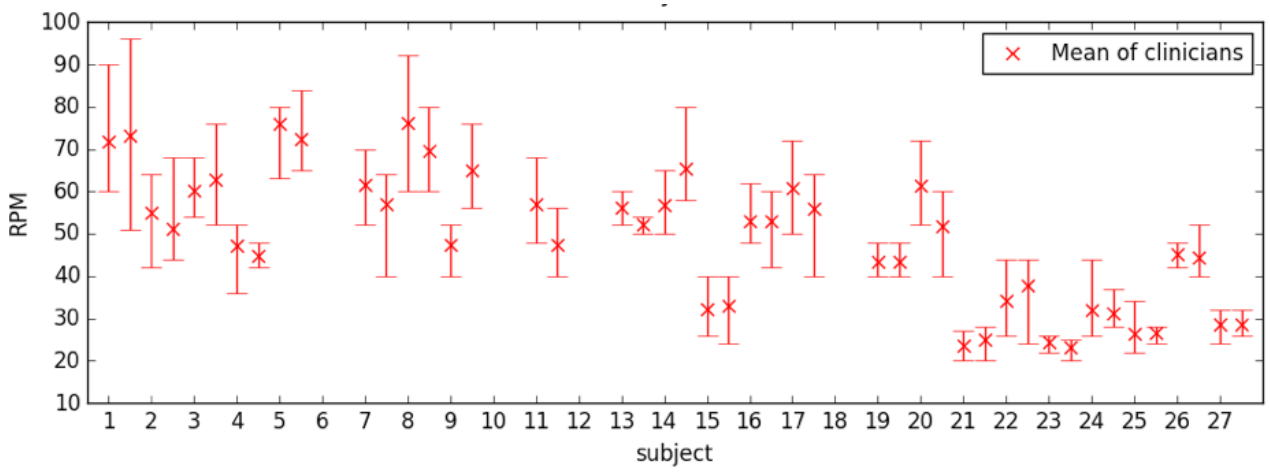


Figure 3. Histogram Based Respiration Measurement Algorithm.

First, the 3D accelerometer data (having X, Y and Z axes) is band-pass filtered to remove frequencies outside the valid respiration range (for a specific age-group).Then, in each filtered axis the zero-crossings are used to derive raw respiration rates.The raw respiration rate candidates goes through Signal Level filter to detect if excessive motion and then through Breath Level filter to detect Loose Belt (Sensor) and Finally agian a Breath Quality Filter to detect excessive motion. Next step is to form a histogram per axis by counting how often each respiration rate occurs. Counts below a certain threshold are removed. The valid data is checked if meets the minimum set threshold of duration to report a measureemnt result. Finally, the output respiration rate is calculated as the weighted mean center of the combined histogram [REF-7].

For years, the Global Health Community has used ‘expert counting’ as the ‘Golden Standard’ for respiratory rate measurements. At the same time, healthcare professionals acknowledge that counting breaths is difficult and that it is considered to be an inaccurate indicator. To measure the accuracy of the ‘expert count’ a clinician’s assessment study was carried out at the Maxima Hospital in Veldhoven, the Netherlands. Five clinicians from the Maxima Hospital were asked to do an assessment of the respiratory rate while watching video recordings of children’s chest and belly region. Every effort was made to make the test setup as realistic as possible, down to selection of camera angles that mimicked the position from which an observer would normally watch. The figure below shows their assessments. The red bars show the span between the lowest and highest assessment.



The WHO guideline for measuring respiratory rate is to count for a full minute, only when the child is calm, which rarely occurs. It turns out that clinicians use different strategies while counting the breaths, resulting in large differences between assessments. While some clinicians counted for a full minute, including uncalm

regions, others only counted during a calm period, stopped as soon as the child started moving and extrapolated (for example: count ten seconds and multiply by six). If two breaths are missed in those ten seconds, which is certainly not unthinkable, extrapolation would result in a significant error of as much as a dozen breaths per minute. On the other hand, when breaths are counted during motion, the resulting respiratory rate is often lower, as the breathing rate drops when children start moving. For these reasons, Philips decided to develop a new reference standard for measuring accuracy, to ensure test results and a resulting diagnostic aid are as useful as possible.

Manual Video Annotation - a new reference standard : Using the recorded videos, each breath is marked with a custom-built annotation tool. Also the sections where the child moved, cried, coughed, spoke or had a long breath pause are marked. Some breaths are marked as 'uncertain' if the breathing was too shallow or could be considered as part of a neighboring breath. The reference respiratory rate is calculated counting the annotated breaths while using the same measurement duration and starting point as the ChARM device. To cover different strategies of counting two values for the rate are derived: one where all breaths are counted (skipping uncertain ones) and one where only undistorted, calm regions are counted (including uncertain breaths). This gives us a lower and an upper limit for the respiratory rate. The area inbetween is the so-called 'Area of Uncertainty'. If this Area-of-Uncertainty is too wide (above 20 Rate Per Minute (RPM), i.e. breaths per minute, the measurement is skipped. The overall error is measured by first calculating the standard deviation (RMSE - Root Mean Square Error) for each child and then the standard deviation over all children [REF-7].

The video annotation technique is validated and the report for the same is available in [REF-8] DHF256273_Report for Validation of Video Annotation Technique..

4.2. Scope of the clinical evaluation

4.2.1. Safety

With respect to safety, no risk identified in the product risk management process requires escalation to the clinical evaluation. As a result, MDD essential requirements ER#1 (safety) and ER#6 (risk benefit) do not require clinical data.

4.2.2. Performance

With respect to performance (MDD essential requirement ER#3) the following device functionalities require support of clinical data:

1. Modified Algorithm for Children under 5 years measured from Abdomen site
2. Subject population: Children under 5 years
3. The device shall measure respiratory rate for children aged 0 (full term babies born after 37 weeks of gestation) to 5 years old with an accuracy of +/- 2 breaths per minute (root mean square error) when measured under calm (according to WHO guidelines) and moderate motion conditions

4.3. Clinical data types

The following clinical data types were used:

Main type	Description	Use?	Comments
Scientific Literature	Published articles	Yes	See [REF-5], literature search report
	Unpublished articles	Yes	Internal Study reports
Clinical experience	Complaint data on the device and equivalent Philips devices	Yes	Source: Trackwise or Equivalent tool used by PCMS Timeframe:12 Apr 2013 till now Filter: minimum severity level = Unacceptable,Unacceptable safety and Undesirable
	Adverse event reports (MAUDE) on the device and equivalent devices	Yes	Source: [MAUDE] Timeframe:12 Apr 2013 till now

Main type	Description	Use?	Comments
	Data from user evaluations with investigational devices	Yes	Inputs from Clinicians who were part of the investigation
	Data from validation testing	Yes	Inputs from Clinicians who were part of the investigation
Clinical Investigation	Clinical Investigation studies	Yes	For the change in population and the modified algorithm the clinical investigation studies already conducted by Research covering subjects of children under 5 years. The prototype used for data collection is considered equivalent to be able to use the data for analysis (refer Table 1 below). The data collected from these studies are used in clinical evaluation.

5. EQUIVALENT DEVICES

Considering the scope of this clinical evaluation as defined in 4.2 Scope of the Clinical Evaluation, the ChARM device is considered technologically equivalent to Philips IntelliVue CL Respiration POD and the modified Philips IntelliVue CL Respiration POD and equivalent in technology and algorithm to ChARM prototype.

The following table presents the comparison of the device with the equivalent devices. Information was sourced from publicly available sources (e.g. websites, manuals) / Philips internal sources (e.g. DHF's) / comparative testing.

Table 1: Table of Comparison with equivalent devices

	ChARM	**ChARM prototype**	**IntelliVue CL Respiration POD**	**Modified IntelliVue CL Respiration POD**
Intended use				
Intended purpose	See 2.2	Same as ChARM	Comparable with additional parameters of posture and activity	Comparable with additional parameters of posture and activity
Measurement Type	Single, Non-continuous	Single, Non-continuous	Monitoring, Continuous	Monitoring, Continuous
Application site / body part	Abdomen	Abdomen	Chest	Chest
Patient population	Children Under 5 years	Children Under 5 years	Adults	Adults
Technical characteristics				
Technology	3 axis accelerometer based	3 axis accelerometer based	3 axis accelerometer based	3 axis accelerometer based
Algorithm	use band-pass filtering of the accelerometer data, and try to measure periodicity in the collected data The histogram based approach is used. Motion segments not completely discarded but tries to use as much data as possible	use band-pass filtering of the accelerometer data, and try to measure periodicity in the collected data The histogram based approach is used. Motion segments not completely discarded but tries to use as much data as possible	use band-pass filtering of the accelerometer data, and try to measure periodicity in the collected data. Measures the angular change in a 2D plane by normalizing the direction of motion. has motion detection and motion skipping.	use band-pass filtering of the accelerometer data, and try to measure periodicity in the collected data. Measures the angular change in a 2D plane by normalizing the direction of motion. has motion detection and motion skipping.
Sensor used	Digital 3 axis accelerometer	Digital 3 axis accelerometer	Analog 3 axis accelerometer	Analog 3 axis accelerometer
Processing	Runs on the stand alone device	Runs on the stand alone device	The functionality of data processing happens on the monitor instead of on the device. Conceptually it is similar	The functionality of data processing happens on the monitor instead of on the device. Conceptually it is similar
Measurement Display	Single measurement Shown as single Breath rate value on the display of device for the measurement duration of <2 mins.	Single measurement Shown as single Breath rate value on the display of device for the measurement duration of <2 mins.	Continuous Measurement Shown as a running RR rate on the separate monitor	Shown as a running RR rate on the separate monitor

Attachment	Fixed with Velcro based Belt	Fixed with Velcro based Belt	Fixed with an Adhesive Patch	Fixed with an Adhesive Patch

Major similarities of ChARM with Philips Intellivue CL Respiration POD :

- measures respiratory rate in Breaths per minute
- uses 3-axis accelerometer to measure respiratory rate
- attaches to the body on the torso near abdomen in case of CHARM and on torso near chest in case of CL Respiration POD

Basic differences of CHARM with Philips Intellivue CL Respiration POD :

- ChARM used for children and CL Respiration POD used on adult
- Measurement Algorithm on ChARM is for breath patterns of children and that on CL Respiration POD is for breath pattern of adult

Major similarities of ChARM with ChARM prototype:

- measures respiratory rate in Breaths per minute
- uses 3-axis accelerometer to measure respiratory rate
- attaches to the body on the torso near abdomen
- used for children under age of 5 years
- Measurement Algorithm on ChARM is for breath patterns of children

Basic differences of CHARM with ChARM prototype:

- NIL

Conclusion: ChARM has sufficient Clinical equivalence in the intended use of respiratory measurement and have biological equivalence due to the devices attached to the similar body parts and technical equivalence is the use of 3-axis accelerometer based signals to measure the breathing rate with Philips Intellivue CL Respiration POD. The clinical data related to Philips IntelliVue CL Respiration POD and the modified Philips IntelliVue CL Respiration POD may be used in the analysis to support the safety and/ or performance of ChARM.

ChARM has clinical, biological and technical equivalence with the ChARM prototype. The clinical data related to ChARM prototype may be used in the analysis to support the safety and performance of ChARM.

6. SUMMARY CLINICAL DATA

The below section covers the summary of the analysis using clinical data by means of literature and by means of clinical experience.

6.1. Literature

The literature search is used to identify published clinical data that may assist to demonstrate clinical safety and performance.

The literature search is documented in the Literature Search Report [REF-5]. Suitable articles are listed in the table below. For each article, a summary of the key results is presented together with any specific safety or performance claim.

No.	Authors / title / journal / year / PubMed-ID	Quality	Type of study	Key results summary, describe relation to safety, performance and claims
1	Chan AM, Selvaraj N, Ferdosi N, Narasimhan R. Wireless patch sensor for remote monitoring of heart rate, respiration, activity, and falls. Conf Proc IEEE Eng Med Biol Soc. 2013;2013:6115-8. doi: 10.1109/EMBC.2013.6610948. PMID:24111135	D1 O1 A2 S2 C1	Controlled	This paper contains validation results of a wireless Bluetooth Low Energy (BLE) patch sensor consisting of two electrocardiography (ECG) electrodes, a microcontroller, a tri-axialaccelerometer, and a BLE transceiver. The sensor measures heart rate, heart rate variability (HRV), respiratory rate, posture, steps, and falls and was evaluated on a total of 25 adult participants who performed breathing exercises, activities of daily living (ADLs), various stretches, stationary cycling, walking/running, and simulated falls. Compared to reference devices, the heart rate measurement had a mean absolute error (MAE) of less than 2 bpm, time-domain HRV measurements had an RMS error of less than 15 ms, respiratory rate had an MAE of 1.1 breaths per minute during metronome breathing, posture detection had an accuracy of over 95% in two of the three patch locations, steps were counted with an absolute error of less than 5%, and falls were detected with a sensitivity of 95.2% and specificity of 100%.
2	Chan AM, Ferdosi N, Narasimhan R. Ambulatory respiratory rate detection using ECG and a triaxial accelerometer. Conf Proc IEEE Eng Med Biol Soc. 2013;2013:4058-61. doi: 10.1109/EMBC.2013.6610436. PMID:24110623	D1 O1 A2 S2 C1	Controlled	In this paper, an algorithm is described with low computational complexity for combining multiple respiratory measurements to estimate breathing rate from an unobtrusive chest patch sensor. Respiratory rates derived from the respiratory sinus arrhythmia (RSA) and modulation of the QRS amplitude of electrocardiography (ECG) are combined with a respiratory rate derived from tri-axialaccelerometer data. The three respiration rates are combined by a weighted average using weights based on quality metrics for each signal. The algorithm was evaluated on 15 elderly subjects who performed spontaneous and metronome breathing as well as a variety of activities of daily living (ADLs). When compared to a reference device, the mean absolute error was 1.02 breaths per minute (BrPM) during metronome breathing, 1.67 BrPM during spontaneous breathing, and 2.03 BrPM during ADLs.
3	Drummond GB, Bates A, Mann J, Arvind DK. Characterization of breathing patterns during patient-controlled opioid analgesia. Br J Anaesth. 2013 Dec;111(6):971-8. doi: 10.1093/bja/aet259. Epub 2013 Aug 21. PMID:23970443	D1 O1 A2 S2 C1	Controlled	Here investigated respiratory patterns in patients receiving postoperative morphine analgesia to assess the capacity of the device to detect abnormalities. Respiratory movement signals were transmitted wirelessly to a recorder from two encapsulated tri-axial accelerometer (RESpeck) sensors. The signals analysed using two different sensor placements, each for 30 min. The nasal cannula signal was used to classify breathing

				patterns as obstructive or non-obstructed. 20 patients studied for a mean duration of 49 min each. Breathing patterns were very variable, between and within patients. The median breathing rates ranged from 6.4 to 19.5 bpm. Breathing was partly obstructed in 10 patients, and six patients had repeated cycles of obstruction and transient recovery. In these patients, a consistent and statistically significant pattern of changes in chest wall movement found, with increased abdominal and decreased rib cage movement during obstruction. In patients with slow respiratory rates, breath-to-breath times were highly variable.
4	Drummond GB, Bates A, Mann J, Arvind DK. Validation of a new non-invasive automatic monitor of respiratory rate for postoperative subjects. Br J Anaesth. 2011 Sep;107(3):462-9. doi: 10.1093/bja/aer153. Epub 2011 Jun 16. PMID:21685112	D1 O1 A2 S2 C1	Controlled	Respiratory movement was detected with an encapsulated tri-axial accelerometer (Orient speck) and the data transmitted wirelessly to a computer for analysis. Subjects were studied after gynaecological surgery who received opioid analgesia, and compared the derived signal with a signal from nasal cannula using directly matched breaths and within the same 5 min epoch. The signals were analysed for 5 min epochs over a 15 h recording period. For matched breath analysis, the instantaneous respiratory rates matched within 2 bpm on 86% of occasions. A similar match was found between epoch averages of the respiratory rate. The mean absolute difference between the respiratory rate measured by nasal cannula and Orient speck was 0.6 bpm. The Orient speck generated reliable measures of respiratory rate every 5 min in 95.4% of epochs.
5	Jin A, Yin B, Morren G, Duric H, Aarts RM. Performance evaluation of a tri-axial accelerometry-based respiration monitoring for ambient assisted living. Conf Proc IEEE Eng Med Biol Soc. 2009;2009:5677-80. doi: 10.1109/IEMBS.2009.5333116. PMID:19964139	D1 O1 A2 S2 C1	Investigational non-controlled	This paper proposes a home respiration monitoring system using a tri-axial accelerometer. Three different methods to extract a single respiratory signal from the tri-axial data are proposed and analyzed. The performance of the methods is evaluated for various possible respiration conditions, defined by the sensor orientation and respiration-induced abdomen movement. The method based on Principal Component Analysis (PCA) performs better than selecting the best axis. The analytical approach called Full Angle shows worse results than the best axis when the gravity vector is close to one of the sensor's axes (<15 degrees). Hybrid-PCA, which is a combination of both methods, performs comparable to PCA. The system is evaluated using simulated data from the most common postures, such as lying and sitting, as well as real data collected from five subjects. The results show that the system can successfully reconstruct the respiration-induced movement, which is necessary to determine the respiratory rate accurately.
6	Fekr AR, Janidarmian M, Radecka K, Zilic Z. A medical cloud-based platform for respiration rate measurement and hierarchical classification of breath disorders. Sensors (Basel). 2014 Jun 24;14(6):11204-24. doi: 10.3390/s140611204. PMID:24961214	D1 O1 A2 S2 C1	Controlled	In this work, presented a real-time cloud-based platform for both monitoring the respiration rate and breath pattern classification, remotely. The proposed system is designed particularly for patients with breathing problems (e.g., respiratory complications after surgery) or sleep disorders. The system includes calibrated accelerometer sensor, Bluetooth Low Energy (BLE) and cloud-computing model. A procedure to improve the accuracy of respiration rate for patients at rest positions was also suggestted. The overall error in the respiration rate calculation is obtained 0.53%

				considering SPR-BTA spirometer as the reference. Five types of respiration disorders, Bradapnea, Tachypnea, Cheyn-stokes, Kaussmal, and Biot's breathing are classified based on hierarchical Support Vector Machine (SVM) with seven different features. The performance of the proposed classification have been evaluated while it is individualized to every subject (case 1) as well as considering all subjects (case 2). Since the selection of kernel function is a key factor to decide SVM's performance, in this paper three different kernel functions are evaluated. The experiments are conducted with 11 subjects and the average accuracy of 94.52% for case 1 and the accuracy of 81.29% for case 2 are achieved based on Radial Basis Function (RBF). Finally, a performance evaluation has been done for normal and impaired subjects considering sensitivity, specificity and G-mean parameters of different kernel functions.
7	Pandia K, Inan OT, Kovacs GT, Giovangrandi L. Extracting respiratory information from seismocardiogram signals acquired on the chest using a miniature accelerometer. Physiol Meas. 2012 Oct;33(10):1643-60. Epub 2012 Sep 18. PMID:22986375	D1 O1 A2 S1 C1	Controlled	Seismocardiography (SCG) is a non-invasive measurement of the vibrations of the chest caused by the heartbeat. SCG signals can be measured using a miniature accelerometer attached to the chest, and are thus well-suited for unobtrusive and long-term patient monitoring. Additionally, SCG contains information relating to both cardiovascular and respiratory systems. In this work, algorithms were developed for extracting three respiration-dependent features of the SCG signal: intensity modulation, timing interval changes within each heartbeat, and timing interval changes between successive heartbeats. Simultaneously with a reference respiration belt, SCG signals were measured from 20 healthy subjects and a respiration rate was estimated using each of the three SCG features and the reference signal. The agreement between each of the three accelerometer-derived respiration rate measurements was computed with respect to the respiration rate derived from the reference respiration belt. The respiration rate obtained from the intensity modulation in the SCG signal was found to be in closest agreement with the respiration rate obtained from the reference respiration belt: the bias was found to be 0.06 breaths per minute with a 95% confidence interval of -0.99 to 1.11 breaths per minute. The limits of agreement between the respiration rates estimated using SCG (intensity modulation) and the reference were within the clinically relevant ranges given in existing literature, demonstrating that SCG could be used for both cardiovascular and respiratory monitoring. Furthermore, phases of each of the three SCG parameters were investigated at four instances of a respiration cycle-start inspiration, peak inspiration, start expiration, and peak expiration-and during breath hold (apnea). The phases of the three SCG parameters observed during the respiration cycle were congruent with existing literature and physiologically expected trends.
8	Estrada L, Torres A, Sarlabous L, Jané R Respiratory signal derived from the smartphone built-in accelerometer during a Respiratory Load Protocol. Conf	D1 O1 A2 S1 C1	Controlled	The scope of our work focuses on investigating the potential use of the built-in accelerometer of the smartphones for the recording of the respiratory activity and deriving the respiratory rate. Five healthy subjects performed an

	Proc IEEE Eng Med Biol Soc. 2015;2015:6768-71. doi:10.1109/EMBC.2015.7319947. PMID:26737847			inspiratory load protocol. The excursion of the right chest was recorded using the built-in triaxial accelerometer of a smartphone along the x, y and z axes and with an external uniaxial accelerometer. Simultaneously, the respiratory airflow and the inspiratory mouth pressure were recorded, as reference respiratory signals. The chest acceleration signal recorded in the z axis with the smartphone was denoised using a scheme based on the ensemble empirical mode decomposition, a noise data assisted method which decomposes nonstationary and nonlinear signals into intrinsic mode functions. To distinguish noisy oscillatory modes from the relevant modes the detrended fluctuation analysis was used. A very strong correlation reported between the acceleration of the z axis of the smartphone and the reference accelerometer across the inspiratory load protocol (from 0.80 to 0.97). Furthermore, the evaluation of the respiratory rate showed a very strong correlation (0.98). A good agreement was observed between the respiratory rate estimated with the chest acceleration signal from the z axis of the smartphone and with the respiratory airflow signal: Bland-Altman limits of agreement between -1.44 and 1.46 breaths per minute with a mean bias of -0.01 breaths per minute. This preliminary study provides a valuable insight into the use of the smartphone and its built-in accelerometer for respiratory monitoring.
9	Hubner P, Schober A, Sterz F, Stratil P, Wallmueller C, Testori C, Grassmann D, Lebl N, Ohrenberger I, Herkner H, Weiser C. Surveillance of Patients in the Waiting Area of the Department of Emergency Medicine. Medicine (Baltimore). 2015 Dec;94(51):e2322. doi: 10.1097/MD.0000000000002322. PMID:26705221	D1 O1 A2 S2 C1	Investigational Observational	Many patients visiting an emergency department are in reduced general condition of health and at risk of suffering further deterioration during their stay. We wanted to test the feasibility of a new monitoring system in a waiting area of an emergency department.In an observational cross-sectional single-center study, patients with acute cardiac or pulmonary symptoms or in potentially life-threatening conditions were enrolled. Monitoring devices providing vital signs via short range radio (SRR) at certain time points and compliance evaluation forms were used. The monitoring devices tested together with the Philips IntelliVue Guardian Solution consisted of cableless measurement devices that provided blood oxygen saturation (SpO2), pulse, respiratory rate, and noninvasive oscillometric blood pressure measurements via short-range radio (SRR) technology to the IntelliVueCableless Hotspot while not having the patient directly connected to a conventional patient monitor (Philips IntelliVue Guardian Software, Philips IntelliVue MP5SC spot check monitor, Philips IntelliVue CL SpO2, Philips IntelliVue CLNBP, Philips IntelliVue CL respiration pod and Philips IntelliVue CL infrastructure). Out of 230 patients, 4 wanted to terminate their participation prematurely. No data was lost due to technical difficulties. Over a median monitoring period of 178 (118-258) min per patient, 684 h of vital sign data were collected and used to assist managing those patients. Linear regression analysis between clinical symptom category groups of patients showed significant differences in the respiratory rate and noninvasive blood pressure courses. Feedback from patients and users via

				questionnaires showed overall very good acceptance and patients felt that they were given better care.To assist medical staff of an emergency department waiting area to rapidly response to potentially life-threatening situations of its patients, a new monitoring system proved to be feasible and safe.

The quality criteria listed are defined in the table below:

Quality criteria	Description	Grading System	
Study Design	Was the design of the study appropriate?	D1	Yes
		D2	No
Outcome of study	Does the outcome of the study reflect the intended performance of the device?	O1	Yes
		O2	No
Adverse effects	Are adverse effects considered in the outcome of the study?	A1	Yes
		A2	No
Statistical significance	Has a statistical analysis of the data been provided and is it appropriate?	S1	Yes
		S2	No
Clinical significance	Was the effect observed clinically significant?	C1	Yes
		C2	No

6.2. Clinical Experience

6.2.1. Complaint data on equivalent Philips devices

In total, 19 complaints were listed in the internal tracking tool related to the Philips IntelliVue CL Respiration POD (Refer Appendix 10.2). All the complaints were of service requests type and none were reported as malfunctions. There were none that were reported as malfunctions and hence none that reported as adverse events. So there are no reported complaint identified as relevant based on the filter criteria as defined in 4.3 Clinical experience.

From the complaint data list and since there are no reported malfunctions or adverse events, there were no indications of any risks that were not yet addressed in the risk management matrix [REF-3].

6.2.2. Adverse event reports (MAUDE) and recall data on equivalent devices

The MAUDE database from US FDA searched for adverse events reported for Philips Intellivue CL respiration pod from April 2013 to 6th April 2016, however no complaints were found to be registered yet. Similarly US FDA recall database was searched for any recalls of Philips Intellivue CL respiration pod from April 2013 to 6th April 2016 and no recall was found in the database.

Since there were no adverse events reported, there were no indications of any risks that were not yet addressed in the risk management matrix [REF-3].

6.2.3. Data from evaluations with study devices

The following studies were available related to the ChARM prototype (an equivalent device). The data collected from the below data collection studies are used in the clinical evaluation for the performance claim. Refer section 7.2 for the detailed analysis.

Study ref	Title, author	Key results summary & links
ICBE-2-1572 First Study in [REF-7]	Dx Solutions for Low Resource Settings: Second data collection for respiration rate in children, Project Leader - Pavan Dadlani	Accelerometer data collected with video annotation for about 6 minutes at two postures; lying and sitting with video annotation reference from 29 subjects below 5 year old.
ICBE-2-6535 [REF-9]	Clinical Investigation Plan; Clinical evaluation of ChARM prototype Project Leader -Pavan Dadlani	Accelerometer data with video annotation reference from 78 (60 + 18) subjects covering 26 each in three age groups. There is equal mix of normal and respiratory distress subjects in all 3 age groups.

7. CLINICAL DATA ANALYSIS

7.1. Safety

Till date no adverse events are registered in MAUDE database and no recall record for the Philips Intellivue CL respiration pod device found in US FDA recall database. With respect to safety, no risk identified in the product risk management process required clinical data to assess risk or risk benefit.

7.2. Performance

The analysis presented below is based on the data collected using ChARM prototype from the subjects aged 0 (full term) to 5 years old with spread of the samples in all the three age groups and with device attached on abdomen/ belly as expected for ChARM. The analysis presented here is the respiratory rate measured by ChARM algorithm compared against the reference respiratory rate measured by the reference technique of manual video annotation[REF-8].

Clinical Performance Analysis :

The analysis uses data from the two studies (study 1: 29 subjects + study 2: 78 subjects) as indicated in section 6.2.3 resulting in a total of 107 subject data.

The study 1 used a higher sampling rate of 125 samples/sec for data collection and hence the raw data from the first study is re-sampled to generate data at 100 samples/sec and a representative noise reference is added in each of the 3 axis. This is done to make the data from study1 equivalent to that from ChARM device.

The study 2 data has two sets of data:

- First set of 60 subjects (study2_set1)
- Second set of 18 subjects(study2_set2)

The algorithm parameters were optimised using data from first study of 29 subjects(study1_set1) and the first set of 60 subjects from the second study (study2_set1). Optimisation reduces the error but has the danger of overfitting when there are many parameters to tune and a limited data set. The algorithm then becomes tailored for a specific data set and might not have a good performance for a new data set. To avoid this bias the following analysis was carried out. The algorithm parameters is first optimised using only the data of first study(study1_set1). When the algorithm is optimized using only the first study data (study1_set1), the overall error for both data sets is: 0.82 and 1.72 breaths per minute for respectively the first and the second set.

When the algorithm is optimised using the second study data(study2_set1), the overall error for both data sets is: 1.12 and 1.27 breaths per minute for respectively the first and the second data set. So in both cases the error remains below 2 breaths per minute [REF-7]. Also the variation in error for any particular data set based on the optimization method is not more than 0.45 breaths per minute . The above analysis shows that the bias caused due to the optimisation is low.

Additional 18 subject data is collected as part of study 2 to have independent data available for analysis [REF-9]. Hence the last 18 subject data collected as part of the second set(study2_set2) is used as a completely unbiased data(as shown in Table for last 18 subjects) used only for analysis and reporting.

The analysis is hence reported in three forms:

A. Consolidated results of all 107 subjects
B. Results from 78 subjects from study 2 only
C. Results from second set of 18 subjects from study 2 only (study2_set2)

In all the cases the manual video annotation is used to generate the reference breath rate measurement and the ChARM algorithm code is used to generate the device measurement. The primary analysis looks at the comparison of the initial measurement result given by ChARM and by video annotation. This is reported as "Initial measurements".

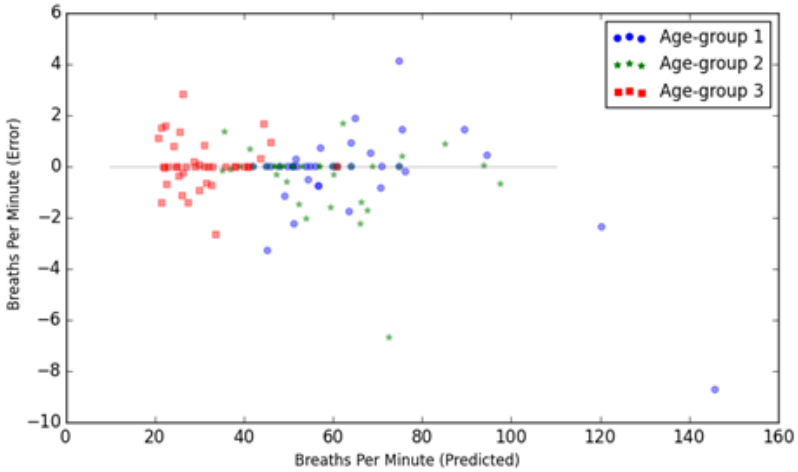
Also an extended analysis is done with the data from each recording session, where multiple measures are made by delaying the start time at steps of 10 seconds. The duration of the recordings is 2 minutes for each session for the first study and 3 minutes for the second study. With the delayed start the duration of the remaining data will become shorter until there is not enough data to do a measurement at which point the measurement series will end. This is reported as "Repeated measurements" and is covered in Appendix 10.1

As indicated in section 4.2.2 the performance target is to "measure respiratory rate for children aged 0 (full term babies born after 37 weeks of gestation) to 5 years old with an accuracy of +/- 2 breaths per minute (root mean square error) when measured under calm (according to WHO guidelines) and moderate motion conditions". The performance target is achieved and the same is demonstrated in below analysis. The RMSE Error in all the cases for the initial measurements is below 2 breaths per minute.

A. Consolidated results of all 107 subjects

Initial measurements: The first result given by the ChARM device

- Results completed for 96 subjects (11 of the 107 subjects skipped because of no reading due to excessive motion)
- RMSE Error: 1.46 BREATHS PER MINUTE
- Mean Duration: 79.29 seconds
- 91 % below 2 BREATHS PER MINUTE

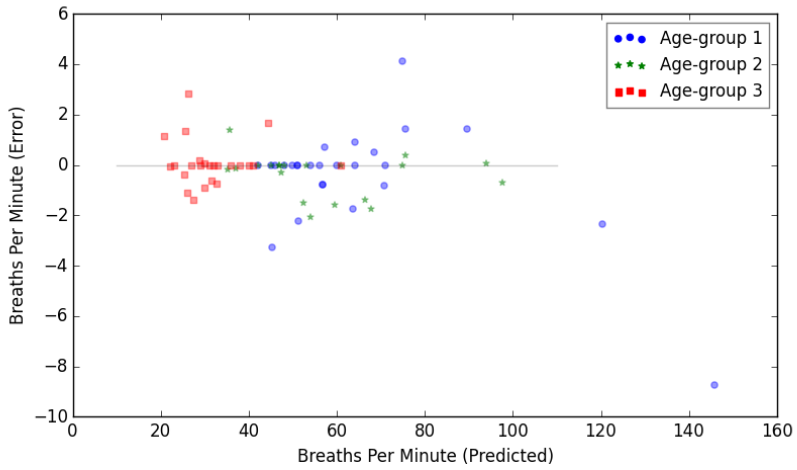


B. Results from 78 subjects from study 2 only

Initial measurements:

- Results completed for 70 subjects (8 of the 78 subjects skipped because of no reading due to excessive motion)
- RMSE Error: 1.52 BREATHS PER MINUTE
- Mean Duration: 77.00 seconds

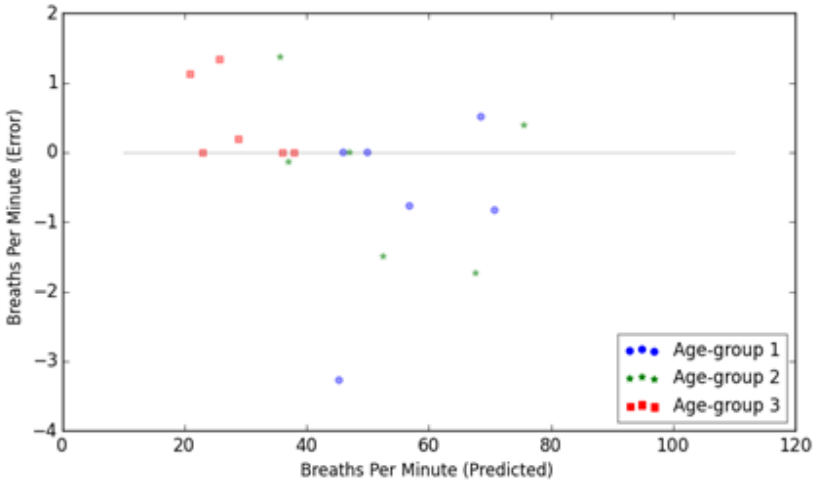
- 90 % below 2 BREATHS PER MINUTE



C. Results from second set of 18 subjects from study 2 (study2_set2)

Initial measurements:

- Results completed for all 18 subjects
- RMSE Error: 1.12 BREATHS PER MINUTE
- Mean Duration: 77.39 seconds
- 94% below 2 BREATHS PER MINUTE



8. CONCLUSIONS

With respect to safety of the device, there were no risks from the risk analysis that required clinical data for the purpose of evaluation or risk benefit analysis. Furthermore, reviewed clinical data did not identify any risk specific to the device that was not already assessed in the risk analysis. Therefore, this clinical evaluation concludes that the device will not compromise the clinical condition or the safety of patients, or the safety and health of users and other persons.

With respect to performance of the device, the analysis as documented in 7.2 indicates that the performances as claimed in the intended use have been established. Furthermore, the analysis links all specific clinical claims to the clinical data and concludes that all claims have been sufficiently substantiated.

Final conclusion:

1. The clinical safety and performance of the device was demonstrated with this clinical evaluation
2. No (further) clinical investigations are required

3. Conformity with the relevant essential requirements is demonstrated

With respect to post market clinical follow up following specific device features or other aspects were identified that require special attention during the post market phase;

- The extent of the data that could be gathered in the pre-market phase did not enable us to detect all rare complications. Monitoring for wide-spread or long term use of the device is necessary for the accuracy of fast breathing classification in all possible cases.

- The residual risk of community health workers not able to identify preterm babies and hence use the device on preterm babies also needs to be monitored in post-market phase

Post market surveillance monitoring activities (i.e., conducting a search in the literature and clinical experience databases) related to the use of the device in the market are planned to conform our internal processes.

9. ABOUT THE AUTHORS

Dr. Shrutin Ulman completed his MBBS from Goa Medical College. He has a Diploma in Occupational Health and Industrial Medicine from Goa Medical College. He did his Master of Technology in Biomedical Engineering from IIT Bombay. Dr. Shrutin has a PhD in VLSI and also has completed M B A from Symbiosis Institute of Business Studies. He is presently working as Leader Clinical Affairs and Outside-In Innovation in Philips India Research. His area of specialization in recent years has been on Mother and Child Care Research.

Dr. Kishor Bapu Londhe completed his MBBS from B J Medical College, Pune. He did his Master of Technology in Biomedical Engineering from IIT Bombay. Dr. Kishor has a PhD in Molecular Medicine (Oncology) and also has completed MBA (EPMBD) from IIM Calcutta. He is presently working as Clinical Analyst in Philips Healthcare Innovation Center, India. He has certifications for Biostatistics and Bio-safety. His recent areas of research are respiratory diseases (Lung carcinoma, Lung dysplasia) and medical/literature Big Data databases.

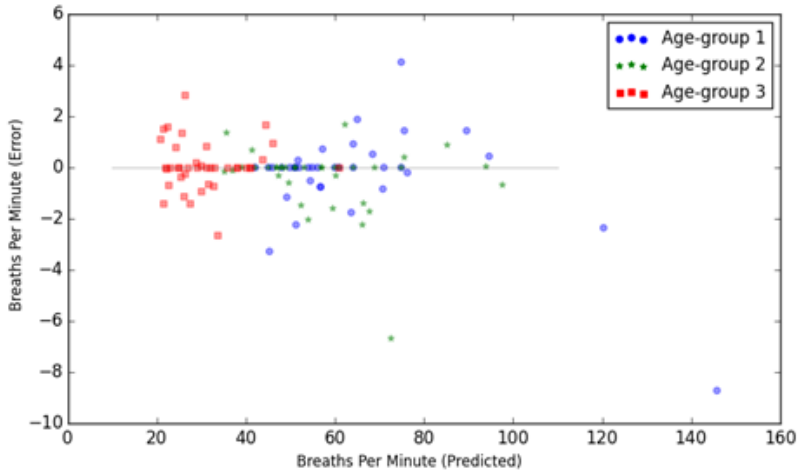
10. APPENDIX

10.1. Detailed Analysis of Accuracy of measurements based on data collected

A. Consolidated results of all 107 subjects

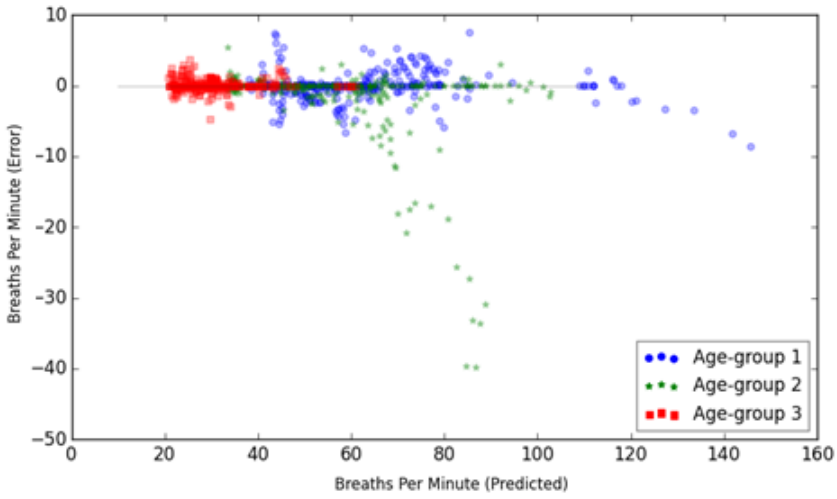
Initial measurements: The first result given by the ChARM device

- Results completed for 96 subjects (11 of the 107 subjects skipped because of no reading due to excessive motion)
- RMSE Error: 1.46 BREATHS PER MINUTE
- Mean Duration: 79.29 seconds
- 91 % below 2 BREATHS PER MINUTE



Repeated measurements:

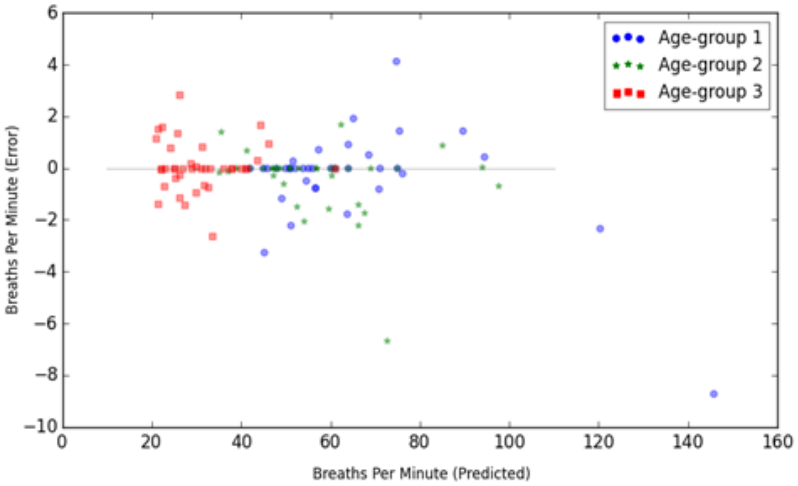
- Results completed for 100 subjects (7 of the 107 subjects skipped because of no reading due to excessive motion)
- RMSE Error: 3.25 BREATHS PER MINUTE (One outlier of subject 65 pushing the overall results – see results below for without the outlier)
- Mean Duration: 78.34 seconds
- 84% below 2 BREATHS PER MINUTE



Without outlier subject 65:

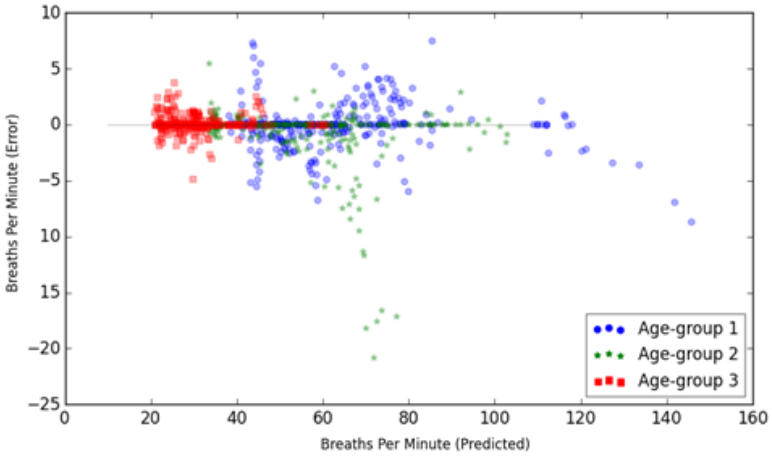
Initial measurements:

- Results completed for 95 subjects (11 of the 106 subjects skipped because of no reading due to excessive motion)
- RMSE Error: 1.46 BREATHS PER MINUTE
- Mean Duration: 79.34 seconds
- 90% below 2 BREATHS PER MINUTE



Repeated measurements:

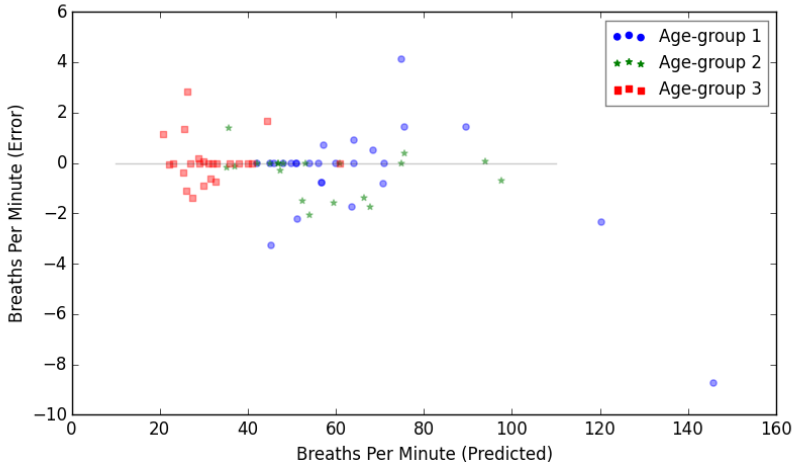
- Results completed for 99 subjects (7 of the 106 subjects skipped because of no reading due to excessive motion)
- RMSE Error: 1.87 BREATHS PER MINUTE
- Mean Duration: 78.33 seconds
- 85% below 2 BREATHS PER MINUTE



B. Results from 78 subjects from study 2 only

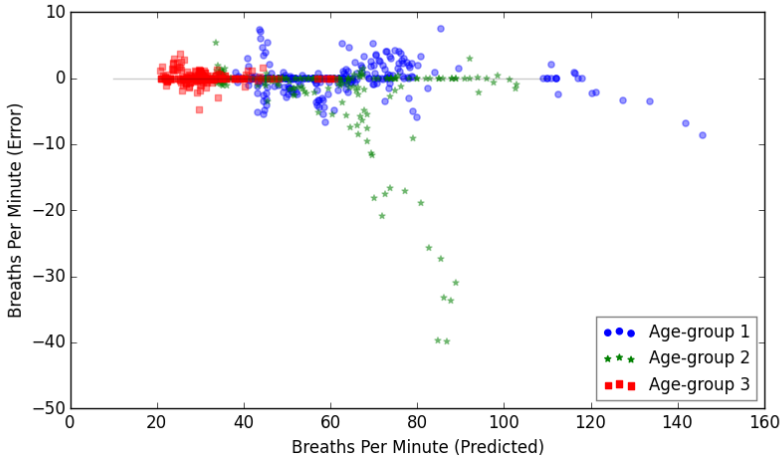
Initial measurements:

- Results completed for 70 subjects (8 of the 78 subjects skipped because of no reading due to excessive motion)
- RMSE Error: 1.52 BREATHS PER MINUTE
- Mean Duration: 77.00 seconds
- 90 % below 2 BREATHS PER MINUTE



Repeated measurements:

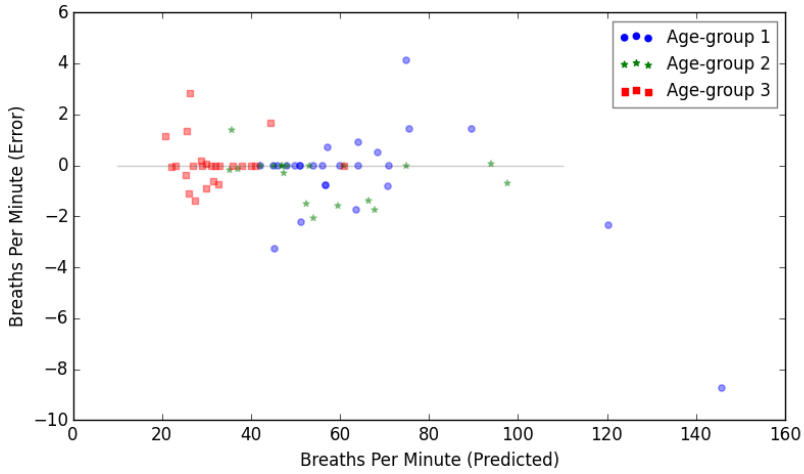
- Results completed for 74 subjects (4 of the 78 subjects skipped because of no reading due to excessive motion)
- RMSE Error: 4.0 BREATHS PER MINUTE
- Mean Duration: 76.98 seconds
- 82 % below 2 BREATHS PER MINUTE



Without outlier 65:

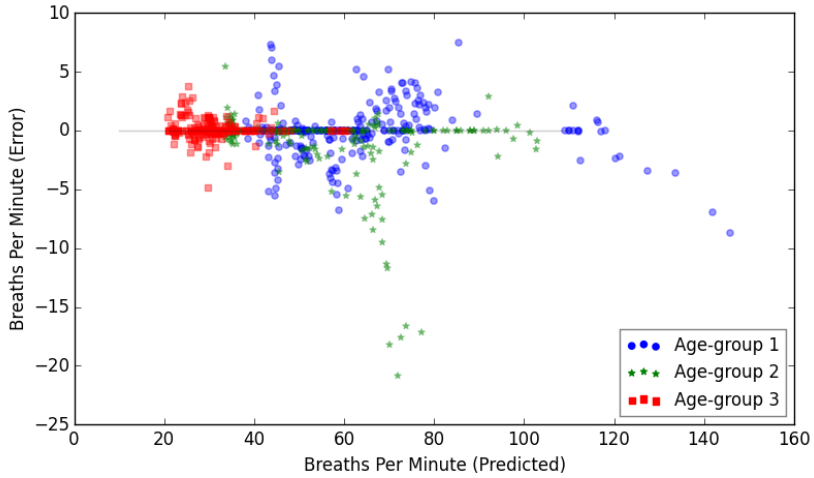
Initial measurements:

- Results completed for 69 subjects (8 of the 77 subjects skipped because of no reading due to excessive motion)
- RMSE Error: 1.53 BREATHS PER MINUTE
- Mean Duration: 77.12 seconds
- 89 % below 2 BREATHS PER MINUTE



Repeated measurements:

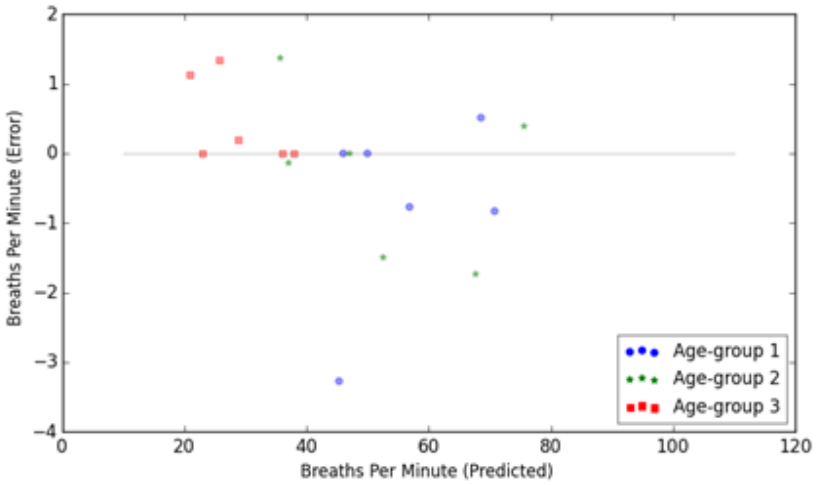
- Results completed for 73 subjects (4 of the 77 subjects skipped because of no reading due to excessive motion)
- RMSE Error: 2.21 BREATHS PER MINUTE
- Mean Duration: 76.95 seconds
- 83 % below 2 BREATHS PER MINUTE



C. Results from the data collected of 18 subjects (study2_set2)

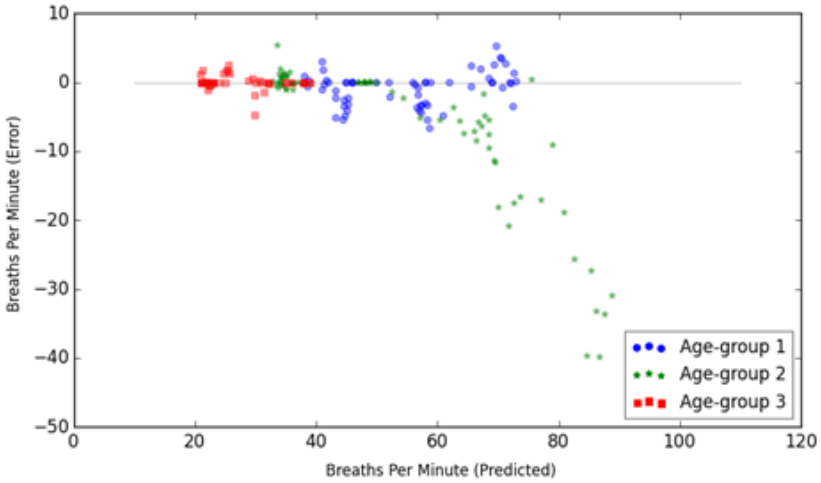
Using initial measurements:

- Results completed for all 18 subjects
- RMSE Error: 1.12 BREATHS PER MINUTE
- Mean Duration: 77.39 seconds
- 94% below 2 BREATHS PER MINUTE



Repeated measurements:

- Results completed for 18 subjects
- RMSE Error: 7.80 BREATHS PER MINUTE (outlier case 65 is pushing the results out)
- Mean Duration: 78.24 seconds
- 65% below 2 BREATHS PER MINUTE



Without outlier 65:

Initial measurements:

- Results completed for 17 subjects
- RMSE Error: 1.15 BREATHS PER MINUTE
- Mean Duration: 77.88 seconds
- 94% below 2 BREATHS PER MINUTE

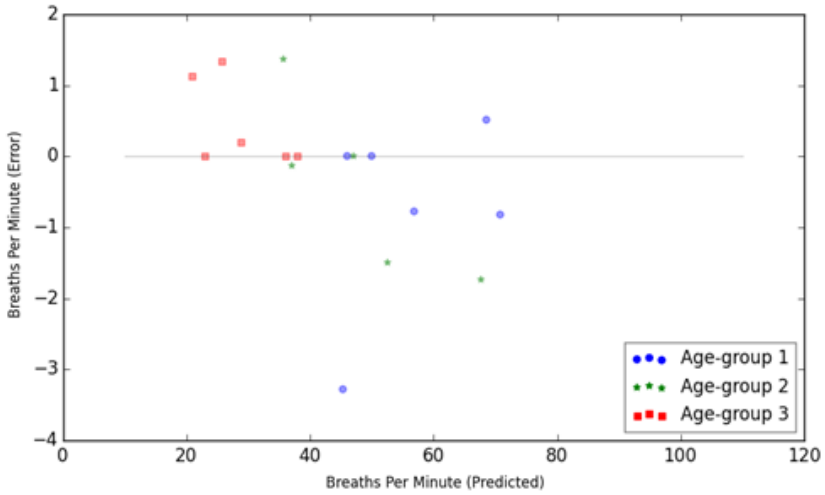


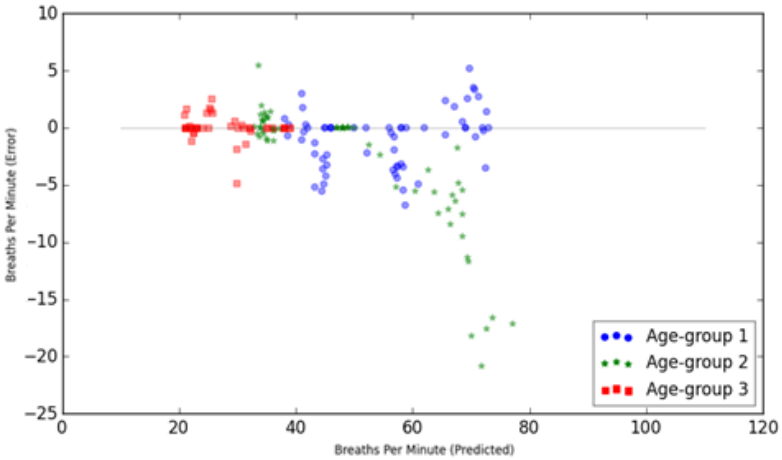
Table of initial values for the 18 subjects(study2_set2):

Subject	Age-Gr	Rate	Ref-1	Ref-2	ERROR	Condition
76:	1	69	64.57	68.48	0.52	RD
85:	1	42	45.28	52.63	3.28	RD
66:	1	50	47.05	51.89	0.00	
67:	1	70	70.83	73.24	0.83	
68:	1	46	36.74	49.73	0.00	
77:	1	56	56.78	56.78	0.78	RD
86:	2	51	52.49	68.28	1.49	
65:	2	76	74.01	75.61	0.39	RD
70:	2	37	37.13	37.13	0.13	
80:	2	66	67.73	76.74	1.73	RD
74:	2	37	34.80	35.62	1.38	
84:	2	47	46.28	47.02	0.00	RD
73:	3	38	36.97	41.94	0.00	RD
83:	3	36	34.29	36.13	0.00	
82:	3	29	25.56	28.80	0.20	RD
71:	3	23	22.53	23.12	0.00	
75:	3	27	22.46	25.65	1.35	
78:	3	22	19.61	20.87	1.13	RD

Rate is the predicted rate in breaths per minute , Ref-1 and Ref-2 are the lower and the upper reference rates. The error is the shortest distance to the reference.

Repeated measurements:

- Results completed for 17 subjects
- RMSE Error: 4.01 BREATHS PER MINUTE
- Mean Duration: 78.16 seconds
- 68% below 2 BREATHS PER MINUTE



10.2. List of complaints from complaint tracking tool for Philips Intellivue CL Respiration POD

query_export_results_
865218_Philips IntelliV

Total number of complaints: 19
Total number of malfunctions: NIL
Total number of adverse events: NIL
PR ID : 5231133 indicated as “failure to measure” is a service order and did not get converted into a compliant as per records.

11. REFERENCES:

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