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Cardio-Pulmonary Stethoscope: Clinical Validation with Heart Failure and Hemodialysis Patients

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Abstract

Objective—The purpose of this study is to evaluate the accuracy of a noninvasive radiofrequency-based device, the Cardio-Pulmonary Stethoscope (CPS), to monitor heart and respiration rates and detect changes in lung water content in human experiments and clinical trials.

Methods—Three human populations (healthy subjects (n=4), heart failure (n=12) and hemodialysis (n=13) patients) were enrolled in this study. The study was conducted at the University of Hawaii and The Queen's Medical Center in Honolulu, HI. Measurement of heart and respiration rates for all patients were compared with standard FDA - approved monitoring methods. For lung water measurements, CPS data were compared with simultaneous Pulmonary Capillary Wedge Pressure (PCWP) measurements for heart failure patients, and with change in weight of extracted fluid for hemodialysis patients.

Results—Statistical correlation methods (*Pearson*, mixed and intraclass) were used to compare the data and examine accuracy of CPS results. Results show that heart and respiration rates of all patients have excellent correlation factors, $r = 0.9$. Comparisons with fluid removed during hemodialysis treatment showed correlation factor of $r = 0.82$ to 1, while PCWP measurements of heart failure patients had correlation factor of $r = 0.52$ to 0.97.

Conclusion—These results suggest that CPS technology accurately quantifies heart and respiration rates and measure fluid changes in the lungs.

Significance—The CPS has the potential to accurately monitor lung fluid status noninvasively and continuously in a clinical and outpatient setting. Early and efficient management of lung fluid status is key in managing chronic conditions such heart failure, pulmonary hypertension, and acute respiration distress syndrome.

Index Terms

electromagnetic; lung water; cardiopulmonary; heart failure; hemodialysis; noninvasive; remote monitor

I. Introduction

Heart failure is the leading cause of hospitalization among adults >65 years old in the US, with over 1 million patients discharged with a diagnosis of heart failure annually, accounting for a total Medicare expenditure of >\$17 billion [1]. Despite dramatic improvements in outcomes with medical therapy, admission rates following heart failure hospitalizations remain high, with nearly 20% of the patients were readmitted within 30 days of discharge [2]. A cornerstone in the management of heart failure is the accurate assessment of a patient's fluid volume status, specifically in the lungs. Quantitative methods such as pulmonary artery catheterization [3] and implantable monitoring devices [4] are invasive and impractical for widespread use or have not been shown to be able to successfully guide clinical therapy [4]. Aside from measuring total body weight, many of these current methods are only available in clinical settings, require trained personnel, and may not be suitable for continuous out-patient monitoring of changes in lung water content. To overcome difficulties with presently available techniques for measuring changes in lung water content, we developed the Cardio-Pulmonary Stethoscope (CPS) system, a novel, non-invasive, "Chest Patch" radio frequency (RF) sensor based measurements [5].

The CPS technology is based on continuous monitoring of an RF signal to indicate changes in the dielectric properties of the lung tissue [6]. At RF frequencies, the dielectric properties of lung tissues are closely related to the amount of water content in the lungs, and hence, monitoring changes in transmitted RF signal is expected to provide indication of lung water content with high sensitivity. This method has the advantage of using highly penetrating RF signals and electromagnetic waves that are transmitted through the human thorax and provide at-depth tissue information including changes in lung water content. The RF technology developed in [6], is also utilized by others including the ReDS technology where they utilize a vest arrangement [7]. These transmission coefficient measurements across the thorax is different from the new "Chest patch" approach [5], used for the first time, in our clinical trials. The front-to-back measurement in our earlier work [6] and the ReDS vest technology, is cumbersome as it requires much alignment and adjustments. It also results in a highly-attenuated signal, which in some cases, not suitable large size patients. (See section S1 in the supplementary document).

The Cardio-Pulmonary Stethoscope (CPS) system described herein for simultaneous and noninvasive measurement of changes in lung water content, as well as heart and respiration rates, is a novel "Chest Patch" technology that has been clinically validated with heart failure and dialysis patients.

II. CP–Stethoscope System

In its present form, the Cardio-Pulmonary Stethoscope system as shown in Fig. 1, consists of "Chest Patch", microprocessor unit (MPU) and a mobile app. The "Chest Patch" consists of copper based sensors with redesigned feed system to improve impedance matching to the chest and hence, improve RF signal coupling to the patient's body. The scattering parameters are measured at 915 MHz, and multiple vital signs are derived from the single

CPS measurement (at 40 samples per second) using developed digital signal processing (DSP) algorithms [8]. Various DSP techniques such as spectral analysis was examined and compared to improve the accuracy of results. With the new CPS app, real time reading of changes in lung water content is now available. (See section S2 in the supplementary document).

While our earlier work included validation with animal and isolated lung experiments [6], as well as stationary healthy volunteers [8–11], none of our earlier work included the clinical trial methods, results with dialysis and heart failure patients, and the statistical analysis that are presented in this paper. The objective of this study is to clinically evaluate the accuracy of the CP-Stethoscope for monitoring heart and respiration rates and changes in lung water content. More specifically:

1. Accuracy of the CPS heart and respiration rate measurements are validated on healthy participants during a stress test on a treadmill.
2. Heart and respiration rates are also clinically validated on all heart and hemodialysis patients.
3. For monitoring changes in lung water content, CPS data are compared with clinical data from pulmonary capillary wedge pressure measurements from heart failure patients and weight of total fluid removed from hemodialysis patients.

Methods and results for healthy participants will be discussed in Section III, and in Section IV results from clinical trials with heart failure and hemodialysis patients. All studies that are mentioned in this paper were approved by an Institutional Review Board.

III. Measurement Methods for Healthy Participants

To evaluate the accuracy of the CPS in monitoring human vital signs, a stress test based on a modified *Bruce* Protocol [12] was conducted to vary the heart and respiration rate of the healthy participants.

A. Study Participants

Measurements were conducted on four adult male participants with an average age of 25.75 ± 2.06 years. Average height and weight were 175.28 ± 3.58 cm and 150.5 ± 10.38 lbs., respectively. All healthy participants met the healthy condition criteria based on a medical questionnaire that was prepared by a medical doctor and completed all exercise without difficulty.

B. Study Design

Heart and respiration rate measurements were compared with a 3-lead electrocardiogram (EKG or ECG) [13] and respiration belt [14], respectively.

The air-filled respiration belt consisted of an air pressure sensor to determine the end of the inspiration and expiration of the respiration cycle. Figure 2 shows the experimental setup which includes a photo of the study participant on a treadmill and screenshot of the mobile app.

Measured heart and respiration rates were recorded simultaneously from all three devices throughout the experiments for all the participants. The study protocol started with breathing exercises (normal breathing and breath holds) while the patients were standing on the treadmill, followed by the modified *Bruce* Protocol which included warm up period of walking, exercise (jog and run), and cool down. Speed and incline level of the treadmill was varied for each stage. The test was concluded with a 1-min normal breathing cycle while the patient was standing on the treadmill.

C. Healthy Participants - Results and Analysis

Sample results of the calculated heart and respiration rate from the CPS and benchmark devices are included in Fig. 3. Measured heart and respiration rates from the CPS system increased and decreased with the changed in the speed and incline of the treadmill as shown in Fig 3.

Statistical analysis based on *Pearson* Correlation method, was used to assess the strength of the association between the CPS and benchmark devices. For heart rate, the CPS and ECG data had a correlation factor of $r = 0.912$, while for respiration rate, the CPS and respiration belt data had a correlation factor of $r = 0.965$. Correlation between the CPS and the benchmark devices are further illustrated using *Bland – Altman* analysis as shown in Fig. 4. The plot shows that most values are within the limits of agreement.

These results from healthy participants, with variable heart and respiration rates, clearly validates the accuracy and versatility of the CPS technology.

IV. Methods for Clinical Trials

The second objective of the study was to clinically evaluate the accuracy of the CPS to detect changes in lung water content in human clinical trials. Two patient population were included in this study, heart failure and hemodialysis patients. For lung water measurements, changes in the trend of the CPS signals were compared with the trend in the PCWP measurements, a catheterization procedure, for the heart failure patients and trend of the fluid removed during hemodialysis treatment. Detailed study protocols are presented in the proceeding section and these studies were approved by a joint IRB between the University of Hawaii and Queen's Medical Center. These protocols included specific guidelines for patient eligibility, measurement methods, and data collection and management.

A. Patients

Two adult patient populations were eligible for this study, patients with pulmonary artery catheter and patients undergoing hemodialysis treatment at The Queen's Medical Center. Exclusion criteria included patients with intra-aortic balloon pump, automatic implantable cardioverter-defibrillator or pacemaker, patients with open chest, those who had a scheduled procedure during the study period, patients who were unstable where setting up or obtaining data from the CPS would interfere with patient care, and pregnant women. All patients or their surrogate provided written informed consent. In this study, twenty-five patients were enrolled (heart failure ($n=12$), hemodialysis ($n=13$)). Average age and body mass index (BMI) of the patients that were enrolled were 56.72 ± 13.6 and 32.29 ± 8.88 , respectively.

B. Study Design

Patients with pulmonary catheter—Measurements including CPS measurements were conducted over a 1-hr monitoring period. For CPS measurements, data were recorded continuously throughout the 1-hr period. For the wedge pressure measurements, data points were collected every 15-minutes, for a total of four measurements. Heart and respiration rates from standard bedside monitoring methods were also recorded every five minutes. However due to the short duration of the monitoring period, data points were limited and observed changes in the measurements were minimal (within the limits of standard deviation). Additional IRB approval was obtained to allow for extended monitoring for patients with pulmonary artery catheters for several days and patients undergoing hemodialysis treatment.

Patients undergoing hemodialysis treatment—CPS measurements were conducted throughout the dialysis treatment (3–4 hr. monitoring period). CPS lung water trend was compared with total fluid removed throughout the hemodialysis treatment. Heart and respiration rates from standard bedside monitoring methods were also recorded every five minutes.

Standard FDA-approved heart and respiration rate monitors such as ECG leads were used as reference measurement, while in limited number of hemodialysis patients, visual observations were used. These values are labeled “Reference RR” in column 3 of Table I. (See section S3 in the supplementary document).

Unlike the healthy human measurements, the modified Bruce protocol or any exercise protocols were not used in the clinical trials with heart failure and dialysis patients. Measurements conducted in these studies followed the IRB-approved study protocol and were supervised by qualified medical personnel.

C. Statistical Analysis

Pearson correlation and correlation by mixed model approach were used to assess the strength of association and concordance correlation (see justification in section S4 of the supplementary document) and intraclass correlation coefficient (ICC) were used to measure agreement between ECG and CPS data. To ensure that sample data meet “normality” criterion when using mixed model for calculating correlation factors [15], histograms of residuals were calculated and found to be close to symmetric. Of the 25 enrolled patients, 7 heart failure and 11 hemodialysis patients completed the study. Incomplete studies (n=7) were due to unexpected deterioration in the subject’s clinical status and/or unplanned procedures that interfered with data collection.

D. Clinical Trial Results

Statistical analysis of the completed experiments showed good correlation values over 0.978 for HR and 0.951 for RR measurements as shown in Table II.

Bland-Altman and regression line analysis of the heart and respiration rates are also included in Fig. 5. and 6, respectively. For the heart failure patients, statistical correlation analysis

between the measured lung water trend from the CPS and PCWP were between 0.52 to 0.97. (See section S5 in the supplementary document).

Example results from a heart failure patient taken in three 1-hour periods over three days are included in Fig. 7. The correlation factors between the measured lung water trend from the CPS with the fluid removed during hemodialysis treatment were between 0.82 to 1.00. Sample results of the lung water trend compared with the fluid removed during a hemodialysis treatment is included in Fig. 8.

The correlation between the CPS and the PCWP data for the HF patients are lower than the HD patients. This is attributed to: (a) the limited data available (3 to 4 data points within the 1-hr measurement session), and (b) the lack of statistically significant changes in the PCWP data during this limited period. Overall, the wedge pressure measurements and the fluid removed correlated well with the trend of the CPS signal that indicated changes in lung water content.

V. Conclusion

Presented in this study is the clinical validation of the Cardio-Pulmonary Stethoscope (CPS) system for noninvasive and continuous monitoring of heart and respiration rate and changes in lung water content. The clinical studies included three patient populations, healthy, heart failure and hemodialysis patients. total of 29 patients were enrolled in the study. Heart and respiration rates were compared with standard clinical methods such as an ECG. Results from statistical analysis shows excellent correlation for all patients. Stress test with patients on a treadmill also demonstrated the accuracy of the CPS system for ambulatory applications such as homecare use. Validations of monitoring changes in lung water content also shows good correlation between the CPS and wedge pressure measurements in heart failure patients and fluid removed during hemodialysis treatment.

Results from this study shows that the CPS system has the potential to monitor lung fluid status noninvasively and continuously in a clinical and outpatient setting. This is significant for early and efficient management of lung fluid status which is key in managing chronic conditions such heart failure and lung disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Schematic of the Cardio-Pulmonary Stethoscope system which includes RF sensors, MPU, and mobile app for real-time and remote monitoring. Also shown is a typical waveform signal from a single CP-Stethoscope measurement. Low frequency cycles correspond to respiration rate while high frequency cycles correspond to heartbeat and the change in the signal baseline indicates change in lung water content.

Fig. 2.
Setup of the stress test study. (a) Photo of a study participant running on a treadmill with the CPS system, ECG leads, and respiration belt.

Fig. 3. Sample results of heart and respiration rate from one of the healthy participants during the stress test on the treadmill.

Fig. 4.

Bland – Altman analysis of heart and respiration rates from ECG and CPS.

Fig. 5.

Bland – Altman analysis to illustrate the differences between the measured heart rate and respiration rate from the CPS and the ECG from the HF and HD patients.

Fig. 6.

Regression analysis of the heart and respiration rates of HF and HD patients.

Fig. 7. Sample clinical results of wedge-pressure measurements compared with changes in the CPS signal trend of a heart-failure patient. Measurements were taken in three 1-hr periods over three days.

Fig. 8.
Results from a hemodialysis patient comparing fluid removed and trend of the CPS signal.

TABLE I

Study Design Summary

Patient	Measurement	Device	Frequency
Healthy	HR	ECG Monitor ¹	once every 5-min in a 30 min. period
	RR	ECG Monitor ¹ Respiration Belt ²	
	HR and RR	CPS	
Heart Failure	HR	ECG Monitor ³	once every 5-min in a 60 min. period
	RR	Reference RR ⁶	
	HR and RR	CPS	once every 15-min in a 60 min. period
	PCWP	PA Catheter ⁴	
	Signal Trend	CPS	
Hemo-dialysis	HR	BP-Cuff	once every 5-min in a 3–4 hr. period
	RR	Reference RR ⁶	
	HR and RR	CPS	once every 5-min in a 3–4 hr. period
	Fluid Removed	HD Machine ⁵	
	Signal Trend	CPS	

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³Phillips IntelliVue MX 800 Monitor

⁴Edwards' Swan-Ganz Catheter

⁵Phoenix® Hemodialysis System

⁶ECG (Phillips IntelliVue MX 800) or visual observation of the chest (1 breath = complete rise and fall of the chest)

HR: Heart Rate

RR: Respiration Rate

PCWP: Pulmonary Capillary Wedge Pressure

PA: Pulmonary Artery

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TABLE II
Heart and Respiration Rate Statistical Analysis from Heart Failure (HF) and Hemodialysis (HD) Patients

Patient Type	Variable	Pearson	Concordance	Mixed	ICC
<i>HF</i>	HR	0.977	0.978	0.981	0.990
	RR	0.975	0.973	0.974	0.994
<i>HD</i>	HR	0.974	0.972	0.970	0.996
	RR	0.934	0.931	0.926	0.991
<i>HF & HD</i>	HR	0.978	0.978	0.981	0.995
	RR	0.951	0.950	0.956	0.991