Journal of Electrocardiology 60 (2020) 138–141

Contents lists available at ScienceDirect

Journal of Electrocardiology

journal homepage: www.jecgonline.com

Continuous heart rhythm monitoring using mobile photoplethysmography in ambulatory patients

Aviram Hochstadt, M.D. [a,*,1], Ofer Havakuk, M.D. [a,1], Ehud Chorin, M.D., Ph.D. [a], Arie Lorin Schwartz, M.D. [a], Ilan Merdler, M.D., M.H.A. [a], Michal Laufer, M.D., M.H.A [a], Natan Lubman, B.Sc. [b], Eihab Ghantous, M.D. [a], Sami Viskin, M.D. [a,b], Raphael Rosso, M.D. [a]

[a] Department of Cardiology, Tel Aviv Sourasky Medical Center and Sackler School of Medicine, Tel Aviv University, Israel
[b] CardiacSense LTD., Caesarea, Israel

ARTICLE INFO

Available online xxxx

Keywords:
Photoplethysmography
Continuous monitoring
Atrial fibrillation
Wearable diagnostics

ABSTRACT

Background: Wearable devices using photo-plethysmography (PPG) can accurately detect heart beats and may be useful for heart rate measurement and diagnosis of arrhythmias such as atrial fibrillation (AF). A previous study of a new portable PPG sensor (CardiacSense) showed high accuracy in heart rate measurement and AF detection in resting patients. We report a trial done to test the same device in active ambulatory patients with diverse characteristics.
Methods: A cohort of 24 ambulatory volunteers, underwent simultaneous PPG recording and continuous electrocardiogram (ECG) recording under different environmental conditions and situations. Per study protocol, the subjects were diverse in age, BMI, hair density and skin tone. Four subjects had AF. Heart rate measurement using the PPG device was compared to measurements by ECG.
Results: Of 163,527 recorded ECG-detected beats in the trial, 86,929 (53.2%) were also recorded by the PPG device. Most undetected heart beats were due to motion induced noise. Correlation between ECG and PPG was high ($R = 0.94$, $p < 0.0001$), yet in subjects with AF correlation was lower ($R = 0.80$, $p < 0.0001$). A Bland-Altman analysis showed the mean difference between measurements was -0.7 ms (95% limit of agreement -93.8 to 92.2). A total of 86,217 (99.9%) of all RR measurements were reliably measured (RR difference within 100 ms). Reliability was sustained (>99.8%) in subjects of all groups including subjects with AF.
Conclusions: This study showed that, in the absence of movement-related noise, the CardiacSense PPG device can reliably detect HR in a variety of situations and subjects' characteristics.

A mobile watch-like device capable of measuring pulse rate was first made commercially available as early as 1701 by Sir John Floyer [1]. Wearable pulse-measuring technology has since advanced and a variety of commercially available devices, with varying degrees of accuracy, exists in the market today [2–6]. Photoplethysmography (PPG)-based wearable devices can accurately detect heart beats on a beat-to-beat basis and are not only useful for heart rate detection, but also for diagnosis of atrial fibrillation (AF) [7–11]. A significant amount of all ischemic strokes are caused by AF-related embolic events [12,13] and the early period after AF onset incurs a much higher incidence of stroke [14]. Therefore, early detection of asymptomatic AF is crucial for initiation of anticoagulation therapy [15].

We previously studied a new portable PPG "wrist-watch" sensor (CardiacSense), designed for continuous heart rhythm monitoring, and tested its ability to automatically detect AF. The study showed that the PPG signals were highly correlated to the simultaneously recorded ECG and that the automatic algorithm distinguished AF from sinus rhythm with a sensitivity of 100% and specificity of 93.1% [10]. A limitation of that study was that all measurements were done in resting subjects, thus precluding assessment of the device's ability to discern pulse waves from noise and motion artifacts. Here we report a trial designed to test the same PPG pulse detection system in ambulatory patients with diverse characteristics.

Methods

Study design and patient selection

This is a single-center, prospective study assessing the accuracy of pulse detection using a novel bio-sensing pulse-sensing device

* Corresponding author at: Tel Aviv Sourasky Medical Center, Weizman 6, Tel-Aviv 64239, Israel.
E-mail address: aviramh@tlvmc.gov.il (A. Hochstadt).
[1] Contributed equally to this paper.

https://doi.org/10.1016/j.jelectrocard.2020.04.017
0022-0736/

(CardiacSense). The study cohort consisted of 24 ambulatory volunteers, who agreed to participate in this study and underwent simultaneous continuous PPG and ECG recording under different environmental and physical conditions. All participants provided written informed consent for participation in the study, which was approved by the institutional ethics committee. In order to show the device's accuracy in different conditions and different situations, the study protocol prespecified the inclusion of participants with the following characteristics: 4 subjects had high density of hair in the wrist area (where the watch is located), 2 were elderly (age > 65 years), 2 were young (age ≤ 30 years), 2 obese (BMI >30), 2 underweight (BMI < 18.5) and 4 subject had dark-toned skin (Fitzpatrick scale 5 and 6, equally represented). Finally, 4 patients had permanent AF.

The bio-sensing technology

CardiacSense is a wrist-worn device, similar in appearance to a watch, specifically designed to detect life-threatening arrhythmias and AF. The device is intended to record, store and transfer PPG signals. PPG is an optical technique that can be used to detect blood volume changes in the microvascular bed of tissues. Using this technology, it is possible to accurately detect pulse rate and pulse pressure. CardiacSense utilizes this technology to detect heart rate and cardiac arrhythmias on a beat-to-beat basis.

Detailed procedure

Each participant was connected to an ECG monitor and wore the PPG device for 90 min. All participants started the study period indoors in a 28 ± 3 °C room for 22.5 min and then walked into a 22 ± 3 °C room and remained there for further 22.5 min. Following these 45 min, all participants, barring four, walked outdoors for further 45 min. The remaining four participants were instructed to drive for 45 min, in a private car on city streets, under light traffic conditions. Excepting the driving period undertaken by these four subjects, all subjects in both groups, were instructed to sit for 10 min and then to walk in a normal pace for 1 min for every 10 min of sitting. This comprised a total of 8 min of walking time for the non-driving group and 4 min (plus variable walking time to the car) for the driving group.

For simplicity, the interval between two consecutive PPG signals is termed here as "G-G interval" (instead of PPG-PPG interval) in analogy to the R-R interval between two consecutive QRS complexes in the simultaneously recorded ECG. The G-G interval of every cardiac cycle, as recorded by PPG, was compared to its corresponding R-R interval, as recorded by ECG. Complexes recorded by ECG without a matched recorded PPG signal were considered as under-detected, PPG recorded beats without a matched ECG complex were considered as false-detection. Under-detected beats and false-detected beats were counted and are reported but were not included in accuracy analysis tests.

Statistical methods

The accuracy of R-R length of ECG-derived R-R values vs. PPG-derived G-G values was assessed by a Pearson's correlation, Bland-Altman Plots with multiple observations correction for limits of agreement, and measurements of the proportion of reliably detected measurements (PPG G-G measurements within 100 ms of ECG-RR measurements). Assessment of the influence of different participants' characteristics on the results was assessed using a linear regression model of the RR-difference between methods with all participant characteristics as covariates.

P values were considered significant p when $p < 0.05$. All results are shown as n(%), Mean ± Standard deviation or Median (IQR). All calculations were done using R version 3.5.0 from R Foundation for Statistical Computing, Vienna, Austria.

Results

Twenty-four subjects [41.2 ± 18.6 years old, 17 (70.8%) males] were enrolled in the study (Table 1). All 24 subjects completed the trial protocol as planned. One subject underwent the testing procedure twice due to a malfunction of the ECG Holter monitor (the results of his first test were ignored).

Ability to detect pulse

Altogether, 163,527 ECG beats were recorded: 86,301 (52.6%) of them were also recorded by the PPG device. The reason for under-detection of ECG beats by PPG was a high signal to-noise ratio. A total of 628 (0.7%) of PPG recorded beats could not be matched to ECG recorded beats and are considered false-detected. The proportion of heart beats correctly recorded by both methods did not differ substantially across values of age and BMI or between the different subject-groups, and varied between 51.4% and 55.5% (supplementary Table-s1).

To assess whether the number of beats not detected by PPG was lengthy, we calculated how many consecutive beats were undetected by PPG and found that the median number of beats undetected was 11 [IQR 8-22] heart beats, with 95% of all bulks shorter than 147 consecutive beats.

Accuracy of R-R estimation

The R-R interval of the 86,301 beats acquired by both ECG and PPG was compared by means of Pearson correlation and Bland-Altman plots. Correlation between ECG and PPG was high ($R = 0.994$, $p < 0.0001$) (Fig. 1). The correlation remained high (between 0.981 and 0.996, $p < 0.0001$) for all subgroups of tested individuals.

A Bland-Altman plot of the entire cohort was constructed (Fig. 2A) and the mean difference between measurements was -0.1 ms with a 95% limit of agreement (LoA) of -29.2 to 29 ms. Bland-Altman plot for subgroups of patients with or without AF showed better results for patients without AF, which had a mean difference of -0.1 with a 95% LoA of -23.4 to 23.3 ms versus a mean difference of -0.2 with a 95% LoA of -49.3 to 48.9 ms for patients with AF (Fig. 2B and Fig. 2C).

A total of 86,217 (99.9% with 95% CI 99.9 to 1) of all R-R measurements were reliably measured (i.e. PPG-GG was within 100 ms of ECG-RR). This proportion remained very high (>99.8%) for all subgroups of patients.

Linear regression

A linear model was built to assess the independent influence of the different factors on the accuracy of R-R measurements, with absolute measurement differences as the independent variable and patients' characteristics as covariates. Model intercept was statistically significant, yet of small magnitude (-8.62 ms) (95% CI 8.29 to 8.96, $p < 0.001$) with the only significant (b-value >1 ms and $p < 0.05$) predictor being atrial fibrillation (11.7 ms for AF patients, 95% CI of 11.5 to 12.0, $p < 0.001$) (Table 2).

Table 1
Demographic data for subjects enrolled.

n	24
Male Gender (%)	17 (70.8)
Age [years] (mean ± SD)	41.25 ± 18.63
Height [cm] (mean ± SD)	171.58 ± 9.12
Weight [kg] (mean ± SD)	78.76 ± 24.64
BMI [kg/m^2] (mean ± SD)	26.41 ± 6.57
Systolic BP [mmHg] (mean ± SD)	125.62 ± 13.98
Diastolic BP [mmHg] (mean ± SD)	76.29 ± 13.00

Table legend: BMI - Body mass index; BP - Blood pressure.

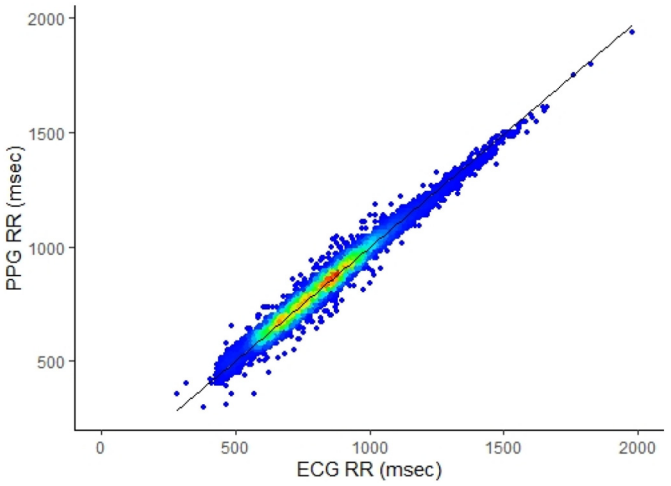

Fig. 1. Heat map scatterplot of PPG-GG values as function of ECG-RR values. Each dot shows one measurement dot color indicates relative density of dots (Dense areas are shown in warmer colors).

Table 2
Linear regression results for absolute ECG-PPG difference.

Parameter	Coefficient [95% CI]	*P*-value
Intercept	8.63 [8.29 to 8.96]	<0.001
Female gender	0.81 [0.57 to 1.05]	<0.001
Age (for 10 y increments)	-0.13 [0.18 to -0.07]	<0.001
AF	11.73 [11.5 to 11.96]	<0.001
Increased hair	0.27 [0.05 to 0.5]	0.018
High BMI	-0.32 [-0.61 to -0.03]	0.032
Driving	-0.31 [-0.56 to -0.05]	0.018
Dark skin	0.98 [0.71 to 1.25]	<0.001
Low BMI	-0.15 [-0.47 to 0.17]	0.347

AF- Atrial Fibrillation; BMI- Body mass index.

Discussion

Continuous and accurate pulse detection is fundamental for creating a pulse watch. Ideally, detection should be accurate not only at rest but also during motion. Once this is achieved, such a pulse watch could be used to detect the pulse rate during sports activity, to calculate heart rate variability, which is significant in assessing autonomic nervous system effects on cardiac health [16], and more importantly, to detect life-threatening arrhythmias [17] and asymptomatic AF. Specifically, detection of AF, before it leads to a stroke, is important because highly-effective treatment with anticoagulation could then be timely initiated [12,15]. This study attempts to define the accuracy of pulse detection by PPG in ambulatory individuals with different predefined subject characteristics.

Present study

We studied a custom-made wristwatch that uses PPG technology for continuous heart rate monitoring and tested its accuracy in detecting heart beats during day-to-day activities amongst individuals with varying characteristics, using simultaneously recorded ECG as gold standard. We found that although PPG signal was able to detect a relatively small portion of the ECG recorded heart beats (53.2%), the median number of consecutive missing beats was only 11 and substantial under-sensing of the pulse occurred for short periods at each time. False detection rate was also small (0.7%), meaning *the vast amount of recorded PPG beats have corresponding ECG complexes*. Amongst the beats recorded by both ECG and PPG, PPG-derived G-G intervals correlated well with ECG-derived R-R intervals with a correlation coefficient of 0.99 and a Bland-Altman plot derived mean difference of 0.1 ms with a 95% limit of agreement of -29.2 to 29 ms, and 99% of measurements being within 100 ms. These results were comparable across all subpopulations except for patients with AF, in whom clinically acceptable, yet lesser agreement was shown between both methods. Explanations for the difference between measuring methods were primarily the effect of motion noise and local factors affecting the PPG signal. Additionally, the coupling of electrically-based ECG signal with the mechanically-based PPG signal, can be interrupted between a short-cycled beat and a long-cycled beat, such as in a premature contraction or in AF, and thus disrupt the accuracy of R-R interval measurements. These results, together with a previous report of the CardiacSense device ability to distinguish AF in resting patients [10], show promise.

Limitations

The subjects participating in our trial were studied in a variety of situations including driving, staying indoors and outdoors, and in varied temperatures. Yet, because participants were active in only a part of the trial period, we cannot verify the accuracy of measurements done specifically during activity. Nevertheless, assuming measurement's reliability only at rest would not preclude its value for detecting asymptomatic AF, as a substantial percentage of such events begins during night sleep [18,19]. A second limitation is that, although the CardiacSense PPG technology has shown promise in AF detection at rest, the present trial did not address the rhythm question directly and therefore cannot conclude regarding the PPG device ability to detect AF in ambulatory patients. Further studies are currently being performed to address this question.

In conclusion, the CardiacSense PPG device can accurately detect pulse in a variety of situations and patient's characteristics in an ambulatory setting. Noise suppression during activity remains a challenge. Until complete noise-suppression is achieved, the use of PPG-based devices for detecting arrhythmias will involve accepting the presence of “blanking periods” during the continuous recording.

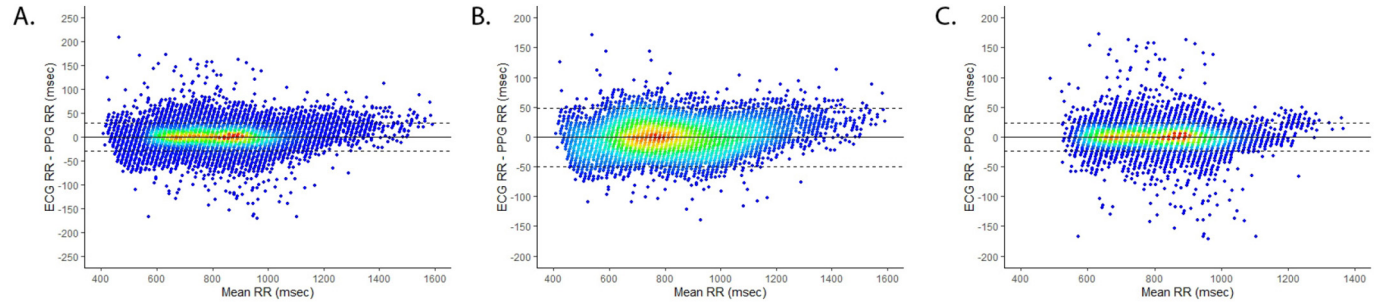

Fig. 2. Heat map of the Bland-Altman plot of PPG-ECG RR difference as a function of mean PPG-ECG RR values for (A) all patients; (B) patients with AF and (C) patients without AF. Each dot shows one measurement, dot color indicates relative density of dots (Dense areas are shown in warmer colors). Note that there is no noticeable change in accuracy for higher or lower RR values.

Funding

This research was funded by CardiacSense Ltd., Caesarea, Israel as part of an application of a new medical device to the FDA.

CRediT authorship contribution statement

Aviram Hochstadt: Conceptualization, Formal analysis, Writing - original draft. **Ofer Havakuk:** Conceptualization, Project administration, Writing - original draft. **Ehud Chorin:** Project administration, Writing - review & editing. **Arie Lorin Schwartz:** Project administration, Writing - review & editing. **Ilan Merdler:** Formal analysis, Visualization. **Michal Laufer:** Conceptualization, Writing - review & editing. **Natan Lubman:** Methodology, Software. **Eihab Ghantous:** Formal analysis, Visualization. **Sami Viskin:** Conceptualization, Methodology, Writing - review & editing. **Raphael Rosso:** Conceptualization, Supervision, Writing - review & editing.

Declaration of competing interest

Natan Lubman designed the atrial fibrillation detection algorithm for CardiacSense. Sami Viskin is Chief Medical Officer for the cardiac arrhythmia section at CardiacSense. The funders designed the study and collected the data according to guidance from the FDA for a new medical device application. Analyses, interpretation of data; the writing of the manuscript, and the decision to publish the results were done by the manuscript writers alone.

References

[1] Floyer J, Atkinson J. The physician's pulse-watch: or, an essay to explain the old art of feeling the pulse, and to improve it by the help of a pulse-watch: in three part London: Printed for Sam. Smith and Benj. Walford; 1707.
[2] Laukkanen RMT, Virtanen PK. Heart rate monitors: state of the art. J Sports Sci 1998; 16:3–7. https://doi.org/10.1080/026404198366920.
[3] Terbizan DJ, Dolezal BA, Albano C. Validity of seven commercially available heart rate monitors. Measurement in Physical Education and Exercise Science 2002;6:243–7. https://doi.org/10.1207/S15327841MPEE0604_3.
[4] El-Amrawy F, Nounou MI. Are currently available wearable devices for activity tracking and heart rate monitoring accurate, precise, and medically beneficial? Healthcare Informatics Research 2015;21:315–20. https://doi.org/10.4258/hir.2015.21.4.315.
[5] Patel MS, Asch DA, Volpp KG. Wearable devices as facilitators, not drivers, of health behavior change. JAMA 2015;313:459–60. https://doi.org/10.1001/jama.2014.14781.
[6] Wang R, Blackburn G, Desai M, Phelan D, Gillinov L, Houghtaling P, et al. Accuracy of wrist-worn heart rate monitors. JAMA Cardiol 2017;2:104–6. https://doi.org/10.1001/jamacardio.2016.3340.
[7] Bonomi AG, Schipper F, Eerikäinen LM, Margarito J, Aarts RM, Babaeizadeh S, et al. Atrial fibrillation detection using photo-plethysmography and acceleration data at the wrist. Computing in Cardiology Conference (Cin C) 2016;2016:277–80.
[8] Bonomi AG, Schipper F, Eerikäinen LM, Margarito J, van Dinther R, Muesch G, et al. Atrial fibrillation detection using a novel cardiac ambulatory monitor based on photo-plethysmography at the wrist. J Am Heart Assoc 2018;7(15):e009351. https://doi.org/10.1161/JAHA.118.009351.
[9] Tison GH, Sanchez JM, Ballinger B, Singh A, Olgin JE, Pletcher MJ, et al. Passive detection of atrial fibrillation using a commercially available Smartwatch. JAMA Cardiol 2018;3:409–16. https://doi.org/10.1001/jamacardio.2018.0136.
[10] Hochstadt A, Chorin E, Viskin S, Schwartz AL, Lubman N, Rosso R. Continuous heart rate monitoring for automatic detection of atrial fibrillation with novel bio-sensing technology. J Electrocardiol 2019;52:23–7. https://doi.org/10.1016/j.jelectrocard.2018.10.096.
[11] Dörr M, Nohturfft V, Brasier N, Bosshard E, Djurdjevic A, Gross S, et al. The WATCH AF trial: smart WATCHes for detection of atrial fibrillation. JACC: Clinical Electrophysiology 2019;5:199–208. https://doi.org/10.1016/j.jacep.2018.10.006.
[12] Freedman SB, Lowres N. Asymptomatic atrial fibrillation: the case for screening to prevent stroke. JAMA 2015;314:1911–2. https://doi.org/10.1001/jama.2015.9846.
[13] Friberg Leif, Rosenqvist Mårten, Lindgren Arne, Terént Andreas, Norrving Bo, Asplund Kjell. High prevalence of atrial fibrillation among patients with ischemic stroke. Stroke 2014;45:2599–605. https://doi.org/10.1161/STROKEAHA.114.006070.
[14] Procter NEK, Stewart S, Horowitz JD. New-onset atrial fibrillation and thromboembolic risk: cardiovascular syzygy? Heart Rhythm 2016;13:1355–61. https://doi.org/10.1016/j.hrthm.2015.12.010.
[15] Freedman B, Potpara TS, Lip GYH. Stroke prevention in atrial fibrillation. The Lancet 2016;388:806–17. https://doi.org/10.1016/S0140-6736(16)31257-0.
[16] Rajendra Acharya U, Paul Joseph K, Kannathal N, Lim CM, Suri JS. Heart rate variability: a review. Med Bio Eng Comput 2006;44:1031–51. https://doi.org/10.1007/s11517-006-0119-0.
[17] Rickard J, Ahmed S, Baruch M, Klocman B, Martin DO, Menon V. Utility of a novel watch-based pulse detection system to detect pulselessness in human subjects. Heart Rhythm 2011;8:1895–9. https://doi.org/10.1016/j.hrthm.2011.07.030.
[18] Viskin S, Golovner M, Malov N, Fish R, Alroy I, Vila Y, et al. Circadian variation of symptomatic paroxysmal atrial fibrillation. Data from almost 10000 episodes. Eur Heart J 1999;20:1429–34. https://doi.org/10.1053/euhj.1999.1632.
[19] Mitchell ARJ, Spurrell PAR, Sulke N. Circadian variation of arrhythmia onset patterns in patients with persistent atrial fibrillation. Am Heart J 2003;146:902–7. https://doi.org/10.1016/S0002-8703(03)00405-8.