EP & Arrhythmia

Evaluation of the Accuracy of ECG Captured by CardioChip through Comparison of Lead I Recording to a Standard 12-Lead ECG Recording Device

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Background: Remote cardiac rhythm monitoring and recording, using hand-carried electrocardiogram (ECG) device had been widely used in telemedicine. The feasibility and accuracy analysis on the data recorded by a new miniature ECG system-on-chip (SoC) system has not been explored before.

Methods: This study evaluated the accuracy of the ECG recordings captured by CardioChip – a single-channeled, low-powered, miniature ECG SoC designed for mobile applications; comparing against Philips Pagewriter Trim III – a Food and Drug Administration certified, widely-used standard 12-lead ECG recording device, within Mackay Memorial Hospital in Taiwan.

Results: Total of 111 participants, age ranging from 39 to 87years old [mean age: 61.2 ± 13.4, 57 male (51.3%)] were enrolled. Two experienced cardiologists rated and scored the ECG morphology to be the same between the two devices, while CardioChip ECG was more sensitive to baseline noise. R-peak amplitudes measured both devices using single lead information (CardioChip ECG vs. Lead 1 in standard 12-lead ECG) showed statistical consistency. Offline analysis of signal correlation coefficients and coherence showed good correlation with both over 0.94 in average (0.94 ± 0.04 and 0.95 ± 0.04, respectively), high agreement between raters (94% agreement) for detecting abnormal cardiac rhythm with excellent R-peak amplitude (r = 0.98, p < 0.001) and PR interval (r = 0.91, p < 0.001) correlations, indicating excellent correlation between ECG recordings derived from two different modalities.

Conclusions: The results suggested that CardioChip ECG is comparable to medical industry standard ECG. The future implementation of wearable ECG device embedded with miniature ECG system-on-chip (SoC) system is ready for clinical use, which will potentially enhance efficacy on identifying subjects with suspected cardiac arrhythmias.

Key Words: Hand-carry electrocardiogram (ECG) device ● R-peak amplitude ● System-on-chip (SoC) system ● Telemedicine ● Wearable device

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INTRODUCTION

Electrocardiogram (ECG) is one of the most frequently used modality in medicine on clinical diagnosis and risk stratifications. However, standard 12-lead ECG has innate limitations that its tracing is less likely to be performed in a mobile or real-time manner in any symptomatic individual for timely data transmission. Portable or mobile ECG recordings are important to increase the power of detecting cardiac arrhythmia. Development of

the devices with good mobility is therefore a pillar of the future of telemedicine. NeuroSkyInc (San Jose, USA), a leading biosensor company, has developed a small-sized, low energy consumption biosignal system-on-chip (SoC) device, named CardioChip. It is a single chip solution designed to accurately measure, process and detect bioelectrical signal, such as ECG, by electrodes attached to the human skin surface.[1] The miniaturization of CardioChip, with a 3 mm × 3 mm × 0.6 mm footprint, makes embedding the chip into many mobile devices with ease possible, therefore makes it especially suitable to be used to develop low-cost and convenient mobile/portable ECG monitoring solution for health care industries.

While it has been proposed that certain ECG parameters may vary (such as wave amplitudes) by using modified or different ECG recording devices or systems,[2] data about the diagnostic yield and its comparison with standard 12-lead ECG for such newly developed system in daily clinical use remains unexplored. We sought to investigate these issues in our current study.

Study purposes

The aim of the study is to demonstrate that the CardioChip measured ECG, compared against the one by standard 12-lead ECG equipment, meets the clinical accuracy requirements on cardiac rhythm diagnosis. This is investigated by comparing Lead I ECG from CardioChip to Lead I ECG from a standard 12-lead device used in a clinical setting.

Environment of investigation

Prior to commencement of the investigation, the study was reviewed and approved by Human Research Institutional Review Board of MacKay Memorial Hospital (MMH), IRB No. 15CT001Ae. Dr. Hung Chung-Lieh, along with Dr. Lo, Chi-In and Dr. Chang, Sheng-Hsiung of Cardiovascular Medicine at MMH, were primary investigators, in compliance with MMH's policy requirement on human research study. NeuroSky's ECG was considered a noninvasive and safe measurement. Patients' private data was well encrypted in the study.

The data collection was completed over the period of June 25-July 15, 2015 at MMH by clinical staffs. All patients who were undertaking scheduled or unscheduled 12-lead ECGs required for medical diagnosis or treatment at MMH were considered to be eligible to participate in the study. Totally 111 patients were enrolled in the study. Participant were volunteered to participate and they signed written consent forms before the study.

METHODS

Study devices

This study was designed to evaluate the accuracy of ECG recordings captured by CardioChip, using a mobile prototype device named Starter Kit developed by NeuroSky. Starter Kit is a handheld device with a CardioChip BMD101 biosensor, two dry Ag/Ag Cl electrodes (10 mm diameter), a Bluetooth transmitter, and embedded battery (Figure 1). Through a wireless Bluetooth connection, Lead I ECG was recorded and processed by customized software running on personal computer (PC). Filtered ECG, frequency range between 0.5 Hz to 40 Hz, was displayed real-time on computer, and 10-second filtered ECG trace was saved in a PDF file in the medical standard format of 25 mm/s at 10 mm/mV. In the meantime of ECG recording, unfiltered raw ECG captured by CardioChip also was saved in a text file, for offline analysis.
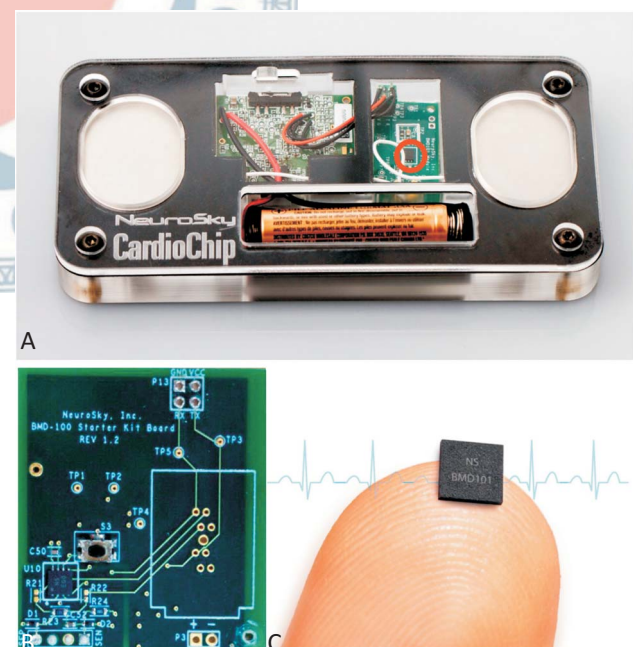

Figure 1. *Handholding Starter Kit (A), including two electrodes for fingers on the other side and the red cycle indicates the embedded CardioChip BMD101 and the IC board (B). The mini size of CardioChip BMD101 biosensor of NeuroSky used in current device (C) illustrated.*

A Food and Drug Administration (FDA) cleared, standard 12-lead ECG device, Philips Pagewriter Trim III by Philips Medical Systems,[3] was chosen for the study. A printed copy of 12-lead ECG, under a 0.5 Hz-40 Hz filter, along with a printed copy of simultaneous Lead I ECG recording from Starter Kit, were sent to two cardiovascular doctors who performed back to back ECG morphology comparisons. Digitized ECG recording from Philips Pagewriter Trim III was also saved in an XML format, which was used to compare against CardioChip ECG in offline analysis.

Subjects enrollment and population

Patients who were older than 18 years old and who were undertaking scheduled or unscheduled 12-lead ECGs required for medical diagnosis or treatment at MMH were eligible to participate in the study. Exclusion criteria included patients < 18 years of age and patients had difficulty to steadily hold mobile device.

A total of 111 patients consented to participate in the study. The basic character of them is shown in Table 1. However, lead II instead of lead I signal was recorded in initial 40 subjects because of incorrect setting of filter range. Of the remaining 71 subjects, one patient's ECG was discarded because he was less than 18 years old. Ten patients could not keep holding Starter Kit still enough during ECG recording, involving hands tremor and shivering causing baseline instability or drift, therefore their ECGs were discarded. So total 60 patients' ECG remained, with ages from 39 to 87 years old (mean = 62.7, std = 11.9), including 24 female and 36 male. This study had been approved by local ethical committee (IRB No. 15CT001Ae).

Study procedures

MMH clinical personnel took responsibility to enroll subjects who were undertaking scheduled or unscheduled 12-lead ECG recordings and to obtain their signed consent forms. MMH clinical personnel also took the responsibility to guide or train participants on how to use the Starter Kit. There was no patient contactor interference from NeuroSky during the entire study. NeuroSky only provided backend technical support and training to clinical personnel on Starter Kit and associated software.

During the study, each participant was assigned a 20-digit study ID, among which encrypted patient's private information such as sex and age. From the study ID, it was impossible to identify the patient. The ID was used to label all printed copies of the participant's ECG and to link electronic copies of the ECG from two devices.

During his/her 12-lead medical ECG recording, the participant was provided a Starter Kit and held it between two hands (Figure 1), with index fingers contacting with two dry electrodes. The participant was in a supine position, holding the Starter kit above the chest or abdomen, keeping it as steady as possible. Lead I electrodes of Philips Pagewriter Trim III were glued onto both arms between wrists and elbows, following medical ECG protocol.

The study personnel simultaneously clicked the "start" button on the screen of Starter Kit software and the "start" button on Philips Pagewriter Trim III to synchronize the ECG recording. The synchronized 10-second Lead I ECG from Starter Kit was recorded into a PDF file in medical standard format for print and was simultaneously saved in a text file for off-line analysis; the 10-second standard 12-lead ECG from Philips Pagewriter Trim III was printed out directly by the machine, and meanwhile an XML file was generated with digitized and compressed ECG data.

Once all data collection was completed, paper copies of ECG from the Starter Kit and Philips Pagewriter Trim III were sent to two experienced cardiologists to perform independent and double blind test on both sets of the 10-second ECG data. They compared the simultaneously recorded ECG from both devices and judged if they had clinical relevance, to the best of their expert knowledge. The basic judging criteria was to determine

Table 1. Basic characteristics of the initial 111 enrolled study subjects in this study

Patient character	Total (n = 111)
Age, mean $\pm$ SD	61.2 $\pm$ 13.4
Male, n (%)	57 (51.3%)
Body weight, cm	67.6 $\pm$ 13.0
Body height, kg	161.0 $\pm$ 9.2
Body mass index (kg/m^2), mean $\pm$ SD	25.9 $\pm$ 4.0
Hypertension, n (%)	86 (77.5%)
Diabetes, n (%)	26 (23.4%)
Hyplipidemia, n (%)	69 (62.2%)
Coronary artery disease, n (%)	31 (27.9%)
Stroke, n (%)	6 (5.4%)

SD, standard deviation.

if the inflection points of QRS complex and the apex of P and T waves were able to overlay to the unaided eye. Occasional baseline wander caused by unstable hand holding of the device during recording, affecting one or two beats among the 10-second ECG, was neglected as long as there were still enough good beats remained to make good judgement. Rhythm disorder (cardiac arrhythmias) were defined by the presence of tachycardia of any form (heart rate > 100/minute), bradycardia of any form (heart rate < 60/minute), notable and obvious cardiac rhythm abnormalities (defined by having atrial fibrillation, atrial premature contraction, or ventricular premature contraction), or conduction disorders (presence of various degree of AV block) confirmed by 10-second standard 12-lead ECG. Potentially abnormal ECG reading includes notable widened QRS (such as bundle branch block), abnormal ST-T segment indicating possible ischemia.

Data analysis

R-peak amplitudes and PR interval comparison

The mean and standard deviation of R-wave amplitudes for the two devices from single lead comparisons between CardioChip derived ECG R-peak amplitudes/PR intervals and Lead 1 R-peak amplitudes/PR intervals from standard 12-lead ECG (by Philips Pagewriter Trim III) were calculated and evaluated for significant difference using a paired t-test and a Pearson linear correlation analysis. Bland-Altman difference plot was used to assess the agreement of single lead R-peak amplitudes between these two methods. Heart rates analyses between these 2 modalities were compared by analyzing the R-peak numbers derived from the middle 8-second data of 10-second recordings of study participants. Part of the information has been published as conference paper in 2016 IEEE 25th International Symposium on Industrial Electronics (ISIE).

Validation of CardioChip ECG signal quality

Lead I ECG of each participant from NeuroSky Starter Kit and Philips Pagewriter Trim III were also saved for offline analysis. Philips ECG were first re-sampled from 500 Hz to match the sampling rate of CardioChip at 512 Hz, then two ECGs were preprocessed to remove noises or artifacts which contaminated the ECG raw signal,

such as power line interference, EMG noise, and baseline wander, using NeuroSky's custom algorithms. After the preprocessing, the ECG data were converted to voltage range. The correlation coefficient, power spectral density, and the magnitude squared spectral coherence were calculated.

RESULTS

Of the 60 subjects, two cardiovascular doctors found that the morphology of QRS complex, P wave, and T wave to be the same between two devices' ECG recordings, though CardioChip ECG had more baseline noise than Philips ECG did, as illustrated in the two examples shown in Figure 2(A). Both agreed that CardioChip ECG was accurate for ECG assessment and ECG arrhythmias could be accurately diagnosed by CardioChip Lead I ECG tracings.

A variety of ECG arrhythmias were found among 60 subjects, as listed in Table 2. Among them, 27/60 (45%) subjects were detected having potentially abnormal ECG, and 16/60 (26.7%) subjects were detected more than one kind of rhythm disorders (cardiac arrhythmia). The concordance of cardiac arrhythmia detection by two blinded cardiologists were high (94% agreement, with only 1 detection error). The intra-class correlation coefficients (ICC) in R-peak amplitude and PR interval analysis were 0.98, 0.95 (R-peak amplitude) and 0.96, 0.95 (PR interval) for intra- and inter-observer reliability among 40 random samples, respectively.

Clinical cases

Several exemplary clinical cases demonstrated that Lead I CardioChip ECG enabled detecting significant ECG abnormalities (Figure 2). The first case was sinus bradycardia with right bundle branch block (RBBB), manifesting slow heart rate = 49, broad QRS > 120 ms, and wide, slurred S wave (Figure 2B). The second case was atrial fibrillation associated with a premature ventricular contraction (PVC), characterized by varied heart rate and one premature ventricular beat (Figure 2C). The third case shows sinus tachycardia, with heart rate > 110 (Figure 2D).

Validation of CardioChip ECG signal quality

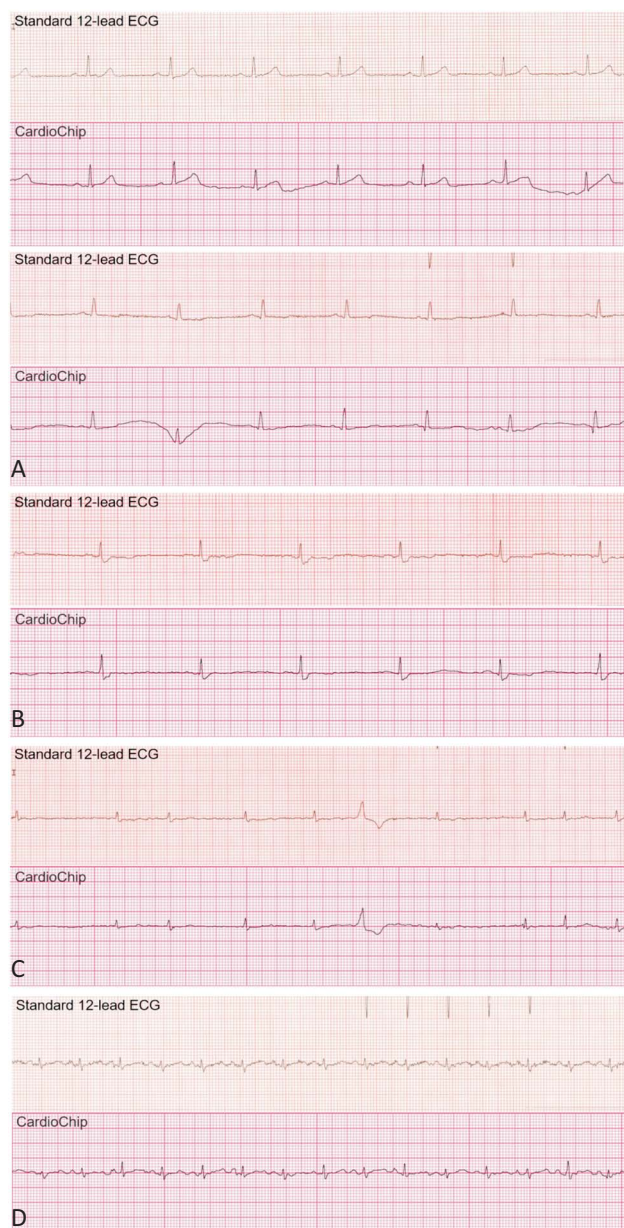Offline analysis was applied to validate the similarity

Figure 2. *Demonstration of simultaneous ECG signal acquired by using conventional 12-leads body surface ECG (lead 1) and ECG recordings captured by mobile CardioChip. Effect of baseline noise demonstrated (A). ECG of sinus bradycardia with right bundle branch block (RBBB) (B). ECG of atrial fibrillation combined with premature ventricular contraction (PVC) (C). ECG of sinus tachycardia (D).*

of ECGs from both devices, in both time and frequency domain. The middle 8-second data in the 10-second recording were used to calculate correlation coefficient, power spectral, and coherence. Coherence was calculated by the mean value between 5 Hz and 25 Hz which contains the major frequency components of ECG sig-

Table 2. Abnormal ECG findings from the ECG analyzed

Detected abnormal ECG	Number of subjects
Atrial fibrillation	2
RBBB	9
LBBB	1
PVC	1
Sinus bradycardia	11
Sinus tachycardia	1
1st degree AV block	1
T wave inversion	3

LBBB, left bundle branch block; PVC, premature ventricular contraction; RBBB, right bundle branch block.

nal. Figure 3 took one subject's plots of ECG waveforms, power spectral, and coherence as an example. Figure 4 displayed all subjects' calculated correlation coefficients and coherence. The mean value of correlation coefficients for all subjects was 0.942, as shown in Figure 4. Among total 60 subjects, 52 subjects (87%) had correlation coefficient over 0.9, 5 subjects (8%) between 0.85 and 0.9, and 3 subjects (5%) less than 0.85 but greater than 0.8. Examining the ECG waveforms of those having low correlation coefficients found that baseline noise contaminating CardioChip ECG was a major reason. Presumably, dry electrodes of Starter Kit are more sensitive to change of skin-electrode impedance than gel-based electrodes used by medical devices. The mean value of coherence for all 60 subjects was 0.945, 55 subjects (92%) above 0.9, 5 subjects (8%) below 0.9, as shown in Figure 4(A & B). Offline analysis indicated high correlation between the two ECGs.

R-peak amplitudes and PR interval comparison

For each subject's printed copies of both CardioChip Lead I and Philips Pagewriter Trim III single Lead I ECG, R-peak amplitudes (n = 60) and PR intervals (n = 58) were measured to the nearest tenth of a millimeter on the corresponding pairs of QRS complexes and the initiation of P waves, result shown in Figure 4. Owing to the absence of P wave in 2 participants with atrial fibrillation, PR intervals were available in 58 study subjects. The mean and standard deviation of R-peak amplitudes for CardioChip and Philips ECG recordings were 0.72/ 0.24 mV and 0.71/0.24 mV, and 165.2/23.5 ms and 168.6/28.4 ms, respectively. Of the 60 subjects, 8 subjects' R-peak amplitude of CardioChip were different to
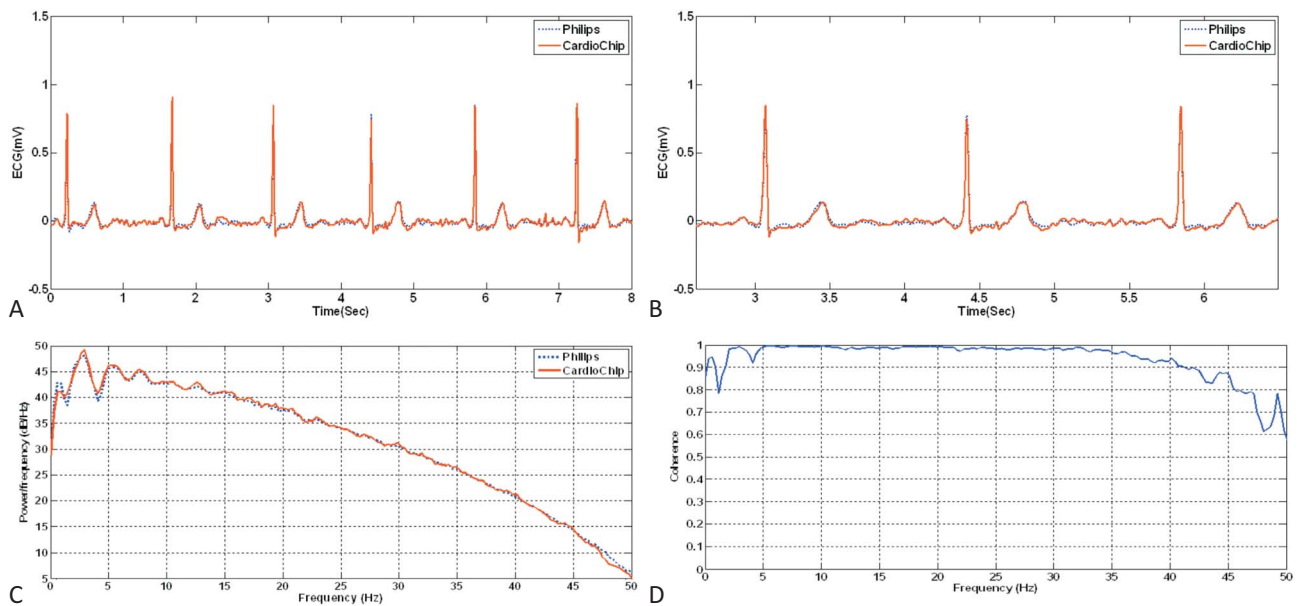
Figure 3. *Preprocessed CardioChip ECG (A, red, solid) and Philips ECG (blue, dashed), and zoomed view (B). Power spectral of CardioChip ECG (red, solid) and Philips ECG (C, blue, dashed) and Coherence function between CardioChip ECG and Philips ECG (D).*

that of Philips, 6 subjects' 0.1 mV CardioChip higher than Philips, 1 subject's 0.2 mV CardioChip higher than Philips, and 1 subject's 0.1 mV CardioChip lower than Philips. Pearson's linear correlation coefficient and Bland-Altman difference plot further suggested the similarity in R-peak amplitudes and PR intervals from two devices (r = 0.98 and r = 0.91 for R-peak amplitudes and PR intervals, both p < 0.0001) [Figure 4(C, D and E)]. The correlation of heart rate (mean: 75.6 ± 16.4 beats/min) based on 8-second counting from R-peak recognition and numbers calculation was 1.0 (100% accuracy) between CardioChip and Philips Trim III for those 60 subjects enrolled for final ECG parameters analysis.

DISCUSSION

To date, ECG is one of the most highly used modality in Cardiology and ECG abnormalities are associated with increased cardiovascular risks and mortality, therefore early detection is clinically important.[4-7] However, standard 12-lead ECG may have congenital limitations that its tracing may be of limited value on a highly mobile subject with outdoor activity, leading to inadequate power to detect inconsistent abnormalities, such as cardiac arrhythmias, in a timely fashion. Therefore, porta-

ble or mobile ECG devices are established and becoming more prevalent recently to overcome the shortcoming of standard ECG. Tele-monitoring health industry is developing handheld devices that can aid in disclosing ECG abnormalities and cardiac arrhythmias.[8] Mobile electrocardiac monitoring can be used to disclose the events in competitions or high-risk activities.[9,10] Moreover, ECG telemedicine pre-hospital system can improve patient's access to primary percutaneous coronary intervention.[11-14] ECG consultation through telemedicine can also lead to significant changes in patient management in distance.[8,15]

However, the developmental efforts mentioned above depend on the technologic advancement of these monitoring devices. Many kinds of technologies are currently involved, such as ECG signal acquisition analysis and transmission. The size of them is one of the most important factors making these devices convenient. Some devices can acquire the ECG tracing and then transmitted to smartphone or elsewhere in distance. Moreover, ECG signals can also be recorded directly by smartphones with special smartphone case or smartphone connected electrodes.[16]

In our current work, we demonstrated that hand-carry Lead I recording ECG by using CardioChip device is capable of accurate signal acquisition and data recording. ECG data quality and R-peak counting for cardiac
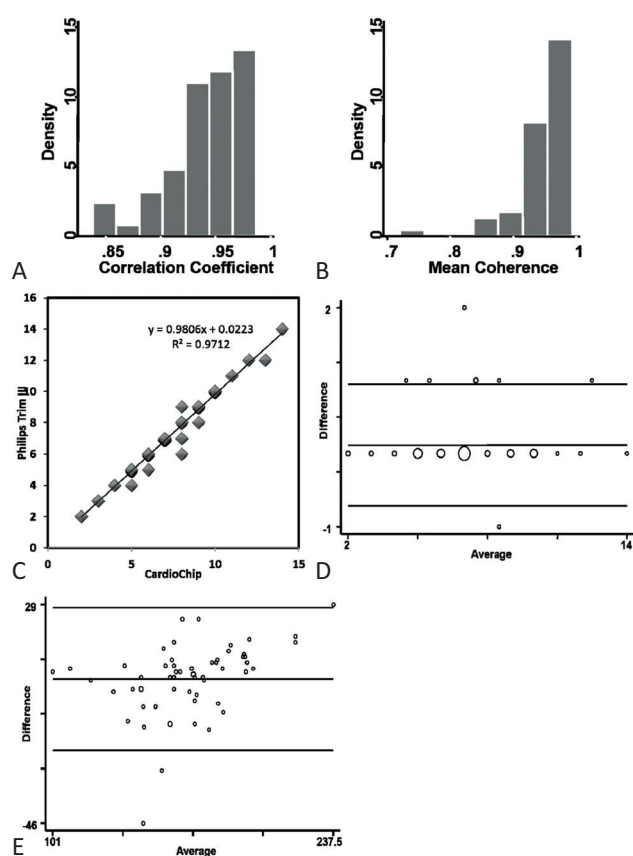
Figure 4. *Correlation coefficient data from 60 final enrolled study participants (A, mean: 0.94 ± 0.04, min: 0.838, max: 0.989) and the coherence data (B, mean: 0.945, min: 0.721, max: 0.993). The Pearson's linear correlation coefficient for CardioChip and Philips Pagewriter Trim III, together with Bland-Altman difference plot for R-peak amplitudes/PR intervals were also displayed (C-E).*

rhythm evaluations from this device can be comparable in quality medically to current facility used in daily clinical practice. We also showed high agreement between these two methods in several aspects, including signal quality, R-wave amplitude, cycle length variability and recognition of certain arrhythmias. Of note, we showed that PR interval assessment may be feasible with good correlations for data derived from hand-carry Lead I ECG (CardioChip) when compared to traditional standard 12-lead ECG in current work ($r = 0.91$, $p < 0.001$). While atrial activities have been shown to play a key role in identifying rhythm disorders,[17-21] our data suggested with the possibility of implementing an ECG device in highly mobilized fashion, along with more future works in characterizing atrial activities (P wave parameters), may be of substantial clinical benefit in identifying patterns or types of supra-ventricular arrhythmias.

The advantage of CardioChip is its miniature 3 mm × 3 mm × 0.6 mm footprint and excellent quality in ECG tracing comparable to traditional ECG device. Its tiny size makes it possible to be integrated into future new designs of smaller wearable or mobile devices for ECG monitoring in healthy or selected patient population.

In addition to CardioChip device, a well validated and customized algorithms is used to remove artifacts created during the ECG recording. ECG is a small electrical signal (in millivolt scale) and can be significantly affected by noise, Including baseline wandering, 50/60 Hz power line noise, electromyogram (EMG), and body movement artifacts. In this study, baseline wandering was detected due to hand tremor or breathing when subjects hold the device. Though the ECG quality is not affected, more mechanism to detect and remove noise in order to obtain good quality ECG for further diagnosis are expected especially for handheld devices in the future.

CONCLUSIONS

Philips Pagewriter Trim III has been FDA approved and widely used for years in medical care environments as a valid ECG recording tool for cardiac conditions diagnosis. Comparing ECG recorded by this device against the one from the NeuroSky's CardioChip produced no significant difference both clinically and statistically. The high similarity and correlation of the two recordings were reaffirmed by offline analysis. Therefore, a mobile device with embedded CardioChip will accurately measure ECG and allow users to learn about and characterize their heart rate and rhythms.[22-24] Wide spread use of the technology could improve public awareness of heart health and identify unknown cardiac conditions at early stage.[25-28]

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