A novel application for the detection of an irregular pulse using an iPhone 4S in patients with atrial fibrillation

David D. McManus, MD,ScM,FACC,FHRS,[*†§] Jinseok Lee, PhD,[‡] Oscar Maitas, MD,[†] Nada Esa, MD,[*] Rahul Pidikiti, MD,[*] Alex Carlucci, BS,[*] Josephine Harrington, BS,[*] Eric Mick, PhD,[†] Ki H. Chon, PhD[§]

*From the *Cardiac Electrophysiology Section, Cardiovascular Medicine Division, Department of Medicine, University of Massachusetts Medical School, Worcester, Massachusetts, †Department of Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, Massachusetts, ‡Department of Biomedical Engineering, Wonkwang University School of Medicine, Iksan, Jeonbuk, Korea and §Department of Biomedical Engineering, Worcester Polytechnic Institute, Worcester, Massachusetts.*

BACKGROUND Atrial fibrillation (AF) is common and associated with adverse health outcomes. Timely detection of AF can be challenging using traditional diagnostic tools. Smartphone use is increasing and may provide an inexpensive and user-friendly means to diagnose AF.

OBJECTIVE To test the hypothesis that a smartphone-based application could detect an irregular pulse from AF.

METHODS Seventy-six adults with persistent AF were consented for participation in our study. We obtained pulsatile time series recordings before and after cardioversion using an iPhone 4S camera. A novel smartphone application conducted real-time pulse analysis using 2 statistical methods: root mean square of successive RR difference (RMSSD/mean) and Shannon entropy (ShE). We examined the sensitivity, specificity, and predictive accuracy of both algorithms using the 12-lead electrocardiogram as the gold standard.

RESULTS RMSDD/mean and ShE were higher in participants in AF than in those with sinus rhythm. The 2 methods were inversely related to AF in regression models adjusting for key factors including heart rate and blood pressure (beta coefficients per SD increment in RMSDD/mean and ShE were −0.20 and −0.35; $P < .001$). An algorithm combining the 2 statistical methods demonstrated excellent sensitivity (0.962), specificity (0.975), and accuracy (0.968) for beat-to-beat discrimination of an irregular pulse during AF from sinus rhythm.

CONCLUSIONS In a prospectively recruited cohort of 76 participants undergoing cardioversion for AF, we found that a novel algorithm analyzing signals recorded using an iPhone 4S accurately distinguished pulse recordings during AF from sinus rhythm. Data are needed to explore the performance and acceptability of smartphone-based applications for AF detection.

KEYWORDS: Atrial fibrillation; Smartphone; Detection; Technology

ABBREVIATIONS: AF = atrial fibrillation; **ECG** = electrocardiogram; **NSR** = normal sinus rhythm; **RMSSD** = root mean square of successive RR difference; **ShE** = Shannon entropy

(Heart Rhythm 2013;0:1–5)

Introduction

Atrial fibrillation (AF) is the most commonly diagnosed dysrhythmia, affecting approximately 3 million Americans.[1,2] AF negatively affects quality of life and survival, placing those with dysrhythmia at an increased risk for stroke and heart failure.[3,4] Although the 12-lead electrocardiogram (ECG) remains the gold-standard diagnostic test for AF,[5] a major challenge in the diagnosis of this arrhythmia is its paroxysmal nature, particularly in its early stages.[6] Recent studies have shown that more frequent monitoring can improve AF detection,[7] but contemporary monitoring technologies used for AF detection in clinical practice are costly and sometimes burdensome. Given these difficulties, a recent National Health, Heart, Lung, and Blood Institute expert panel has emphasized the pressing need to develop new methods for accurate AF detection and monitoring.[8]

On the basis of previously published data from our laboratory and elsewhere,[9–11] we hypothesized that an irregular pulse could be identified using recordings from an iPhone 4S camera combined with an accurate and real-time realizable AF detection algorithm.[12] In this original investigation, we report the beat-to-beat and overall detection capabilities of our novel algorithm running on an iPhone 4S in a prospectively recruited cohort of patients with persistent AF.

This work was funded in part by the Office of Naval Research work unit N00014-12-1-0171. Dr McManus's time was funded by National Institutes of Health through grants 1U01HL105268-01 and KL2RR031981. Dr McManus, Dr Lee, and Dr Chon have ownership stake in DxMe, Inc. Dr Chon has a patent on the algorithm described in the article. **Address reprint requests and correspondence:** Dr David D. McManus, Cardiology Division, University of Massachusetts Medical School, Worcester, MA 01655. E-mail address: mcmanusd@ummhc.org.

The first 2 authors contributed equally to this article.

1547-5271/$-see front matter http://dx.doi.org/10.1016/j.hrthm.2012.12.001

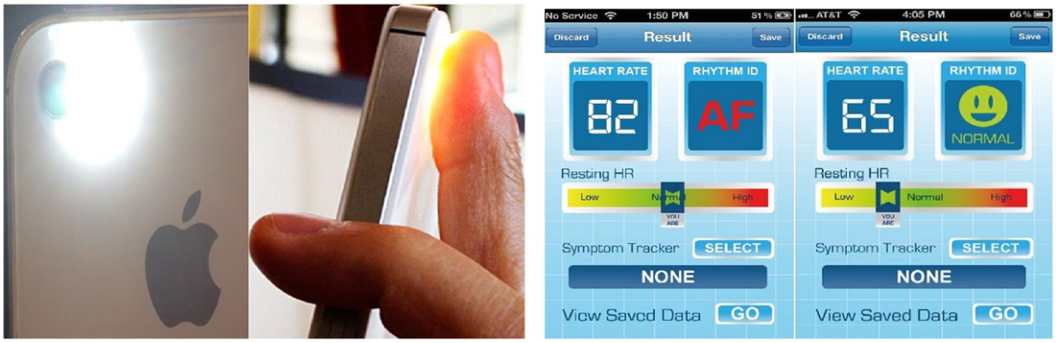

Figure 1 A prototype of the pulse waveform analysis application running on an iPhone 4S. From left to right: iPhone 4S camera; fingertip applied to iPhone 4S camera; a representative recording from a patient in atrial fibrillation; a representative recording from a patient in normal sinus rhythm.

Methods

Study sample

Seventy-six adults with AF were identified from a roster of patients scheduled to undergo elective cardioversion for AF at the University of Massachusetts Medical Center's Cardiac Electrophysiology Laboratory. After obtaining informed consent, baseline clinical, demographic, laboratory, and electrophysiologic variables, as well as postprocedure heart rate and blood pressure, were abstracted from participants' medical records by trained study staff. Subjects with AF on their preprocedure 12-lead ECG placed an iPhone 4S camera directly on their right index or second finger for 2 minutes while the AF detection application was run. After cardioversion, participants who were successfully converted to normal sinus rhythm (NSR) (based on postprocedure 12-lead ECG or telemetry recordings) had the iPhone 4S reapplied to their right index or second finger. Pulse signal recordings were obtained with patients while they were in a supine position and breathing spontaneously. Trained physicians reviewed all 12-lead ECG or telemetry data to determine heart rhythm using standard criteria.[5] In cases where reviewers disagreed about the electrocardiographic diagnosis, a third reader was consulted. This study was approved by the institutional review boards of the University of Massachusetts Medical School and Worcester Polytechnic Institute.

Signal processing

Our application acquired pulsatile signals by illuminating the fingertip using the standard iPhone lamp and recording video signal (30 frames/s) for 2 minutes (Figure 1). The signal was processed by averaging 50×50 green band pixels per frame.[12] We interpolated the pulsatile signal to 30 Hz using a cubic spline algorithm followed by peak detection. As described in prior work, we use a peak detection algorithm that uses a filter bank with estimates of heart rate, variable cutoff frequencies, rank-order nonlinear filters, and decision logic as well as motion noise correction.[13] The time required for computational processing on the iPhone 4S was approximately 25 ms per 64-beat segment.

Approaches to pulse waveform analysis

The rapid and disorganized electrical activity that characterizes AF generates a random sequence of heart beat intervals with increased beat-to-beat variability. Our approach to irregular pulse detection combines 2 statistical techniques to exploit these characteristics (Figure 2). A root mean square of successive difference (RMSSD) of RR intervals is used to quantify RR variability, and Shannon entropy (ShE) is used to characterize its complexity.[14] In order to adjust for the effect of heart rate on RR variability, we normalized RMSSD to the mean RR time series value.

$$\text{Normalized RMSSD} = \sqrt{\frac{1}{l-1}\sum_{j=1}^{l-1}[a(j+1)-a(j)]^2}\,\frac{1}{\sum_{j=1}^{l} a(j)}$$

where l is the length of RR intervals and $a(j)$ is the jth RR interval in the segment with length l, where $j = 1, 2, \ldots, l$. The normalized RMSSD is expected to be higher in a segment recorded from a patient with an irregular pulse due to AF since AF is associated with higher variability of

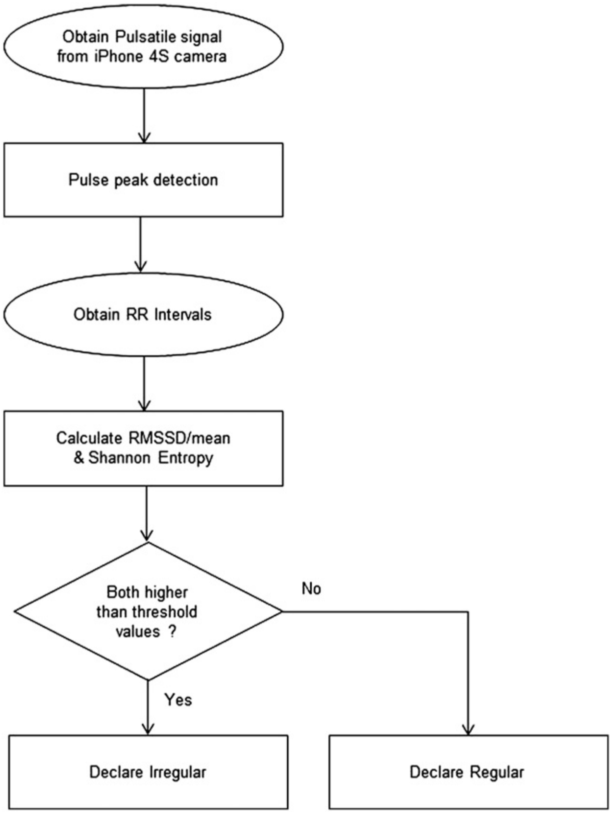

Figure 2 A flowchart of the pulse waveform analysis algorithm. RMSSD/mean = root mean square of successive RR difference.

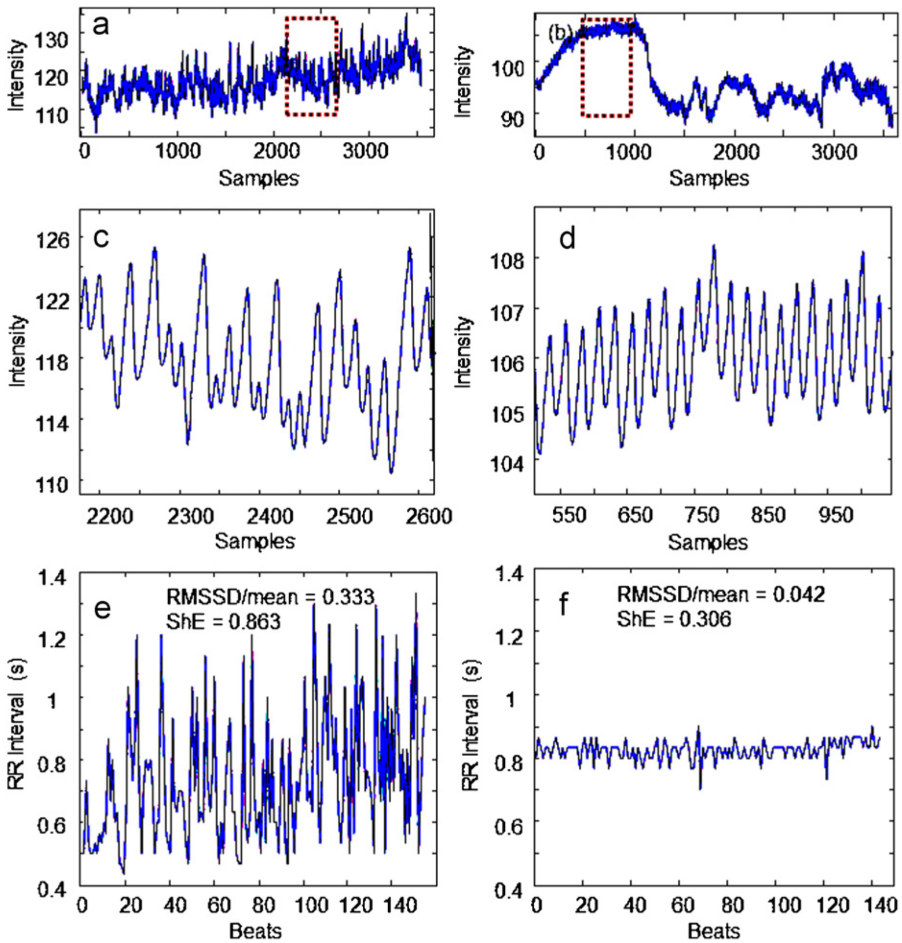

Figure 3 Representative pulse recordings, RR intervals, and resultant statistical values, obtained using an iPhone 4S from a patient in atrial fibrillation **(A, C, E)** and normal sinus rhythm **(B, D, F)**. RMSSD/mean = root mean square of successive RR difference; ShE = Shannon entropy.

RR intervals than is NSR. ShE provides a quantitative measure of uncertainty for a random variable in the following:

$$SE = -\sum_{i=1}^{N} p(i)\frac{\log(p(i))}{\log\left(\frac{1}{N}\right)}, \quad p(i) = \frac{N(i)}{l}$$

where N is the number of bins and $N(i)$ is the number of beats in the i-th bin. We used $N = 16$, which provided the best accuracy.[14,15] ShE provides a quantitative measure of uncertainty for a random variable.[9] Specifically, ShE quantifies the likelihood that runs of patterns exhibiting regularity over some duration of data also exhibit similar regular patterns over the next incremental duration of data. ShE is therefore expected to be higher in the setting of AF since patients with AF have pulses that exhibit greater RR interval irregularity when compared with pulse waveforms recorded from patients in NSR.

Based on the 2 statistical techniques, the classification of the RR interval segment of length $l = 64$ is given by a simple logical AND condition in the following:

$$\begin{gathered}\text{If(Normalized RMSSD} > \mathrm{TH_{RMSDD}}\text{) AND (ShE} > \mathrm{TH_{ShE}}\text{),}\\ \text{then classify the segment as IRREGULAR,}\\ \text{else classify the statement as REGULAR.}\end{gathered}$$

where $\mathrm{TH_{RMSSD}}$ and $\mathrm{TH_{ShE}}$ are the threshold values of RMSSD/mean and ShE, respectively (Figure 3).

To derive threshold values of RMSSD/mean and ShE, we used the MIT-BIH AF and MIT-BIH NSR databases.[14] The MIT-BIH AF database contains approximately 500,000 AF beats, and the number of NSR is approximately 700,000 and 1,700,000 beats from MIT-BIH AF and MIT-BIH NSR databases, respectively. We downsampled the MIT-BIH AF and NSR RR time series to 30 Hz to match the sampling rate of an iPhone 4S. Each ECG recording is approximately 10 hours in duration. The MIT-BIH NSR database contains 18 ECG recordings, and the duration of each ECG data is approximately 24 hours. We found the threshold values of 0.115 for RMSSD/mean and 0.55 for ShE, as these values corresponded to the largest area under receiver operating characteristic curves.[14]

Data analysis

We compared the characteristics of participants by AF status (precardioversion AF and postcardioversion NSR) using analysis of variance or relevant nonparametric test for continuous variables and χ^2 tests for categorical variables. We calculated the test characteristics for the automated smartphone-based AF detection algorithms (RMSSD/mean and ShE) individually and in combination when compared with the expert reviewer diagnosis (criterion standard) of NSR and AF based on 12-lead ECG, using 0.115 and 0.55 as the threshold values of RMSSD/mean and ShE, respectively.

Table 1 Baseline characteristics of the study sample

Baseline characteristics	Total (N = 76)
Age (y) mean (SD)	65.3 (11.6)
Male, n (%)	59 (77)
White, n (%)	73 (96)
Body mass index (kg/m^2), mean (SD)	31.0 (8.3)
Medical characteristics, n (%)	
Hypertension	54 (71)
Hyperlipidemia	47 (62)
Current smoking	6 (8)
Diabetes mellitus	21 (28)
Coronary artery disease	22 (29)
Congestive heart failure	16 (21)
Sleep apnea	12 (16)
Coronary artery bypass	8 (11)
Prior cardioversion	20 (27)
Stroke	9 (12)
Treatment characteristics, n (%)	
Beta-blocker	47 (62)
Calcium channel blocker	15 (20)
Statin	42 (56)
Antiarrhythmic drug	19 (31)
Class I	5 (7)
Class III	18 (24)
Digoxin	4 (5)
Procedural characteristics, mean (SD)	
Number of shock	1.1 (0.4)
Joules delivered, mean (SD)	226 (86)

Exact binomial 95% confidence intervals were calculated for sensitivity, specificity, and accuracy for each method.

Since we were also interested in improving the detection algorithms by investigating clinical and demographic factors related to potential misclassification, we conducted regression modeling to examine the relation between key factors such as age, sex, heart rate, systolic blood pressure, and beta-blocker and calcium-channel blocker use with the 2 algorithms used in our application, RMSSD/mean and ShE. All analyses were conducted using Stata 11.0 (StataCorp LP, College Station, TX).

Results

The baseline characteristics of the 76 participants with AF included in our prospective clinical investigation are shown in Table 1. The mean age of the cohort was 65 years of age, and 35% were women. There was a high burden of cardiovascular morbidity at study entry in the cohort.

Table 2 Clinical and pulse recording characteristics before and after electrical cardioversion (AF, no AF)

Clinical and pulse recording characteristics	Mean (SD)		
	AF	No AF	P
Systolic blood pressure (mm Hg)	131 (18)	112 (18)	<.001
Diastolic blood pressure (mm Hg)	81 (14)	68 (12)	<.001
Heart rate (beats/min)	91 (22)	70 (16)	<.001
Respiration rate (breaths/min)	19 (3)	16 (4)	<.001
RMSSD/mean*	0.29 (0.09)	0.08 (0.08)	<.001
Shannon entropy	0.80 (0.09)	0.45 (0.13)	<.001

AF = atrial fibrillation.
*RMSSD/mean = root mean square of successive RR difference.

Table 3 Beta coefficients for statistical approaches in relation to atrial fibrillation

Pulse recording characteristics	Adjusted beta coefficient*	95% confidence interval
RMSSD/mean†	−0.20	−0.23 to −0.16
Shannon entropy	−0.38	−0.43 to −0.33

*Adjusted for age, sex, heart rate, respiratory rate, systolic blood pressure, and receipt of beta-blocker and calcium channel blocker.
†RMSSD/mean = root mean square of successive RR difference.

Participants in AF had significantly higher heart rates, respiratory rates, and systolic and diastolic blood pressures before cardioversion than they did after their successful cardioversion (Table 2). RMSSD/mean and ShE values were significantly higher when participants were in AF than they were in NSR. In multivariate regression models adjusting for age, sex, heart rate, systolic blood pressure, respiratory rate, and receipt of beta or calcium-channel blockers, RMSSD/mean and ShE values remained associated with the presence of AF (Table 3).

Using the established threshold values of 0.115 for RMSSD/mean and 0.55 for ShE,[14] we observed that RMSDD/mean, ShE, and the combination of RMSSD/mean and ShE exhibited excellent sensitivity, specificity, and diagnostic accuracy for the beat-to-beat detection of an irregular pulse in patients with AF (Table 4) when compared to the gold-standard diagnosis of AF by 12-lead ECG. A 2-step algorithm requiring that both threshold values of RMSDD/mean and ShE be exceeded had the best specificity and diagnostic accuracy. The algorithm combining RMSDD/mean and ShE was 100% and 96.05% accurate for identifying (as irregular or regular) pulse recordings obtained from participants in AF and NSR, respectively.

Discussion

Several prior investigations have described the use of a smartphone to detect an irregular pulse during AF.[9,11,14,16,17] In contradistinction to previously described systems, our application does not require additional hardware, instead rely on the iPhone 4S camera and lamp to obtain pulse recordings, and is not bedeviled by motion and noise artifacts.[15–19] Two prior investigations from our group introduced the concept of using a camera to extract RR intervals and established threshold values for RMSDD/mean and ShE in a developmental cohort.[9,11] In this larger clinical study involving a distinct and

Table 4 Test characteristics* for the detection of an irregular pulse in a sample of 76 patients with atrial fibrillation

Algorithm	Sensitivity	Specificity	Accuracy
RMSSD/mean	0.9818	0.9150	0.9533
Shannon entropy	0.9750	0.8218	0.9097
RMSSD/mean + Shannon entropy	0.9619	0.9752	0.9676

*Test characteristics of statistical methods established using the threshold values of RMSSD/mean = 0.115 and Shannon entropy = 0.55. RMSSD = root mean square of successive RR difference.

better phenotyped cohort with AF, we report the sensitivity, specificity, and accuracy of a novel 2-phase real-time algorithm and show that the associations between RMSDD/mean and ShE with recordings obtained from patients in AF persist after adjustment for demographic and clinical characteristics.

Traditional methods of AF detection, such as office-based electrocardiograpy and continuous ambulatory electrocardiographic monitoring, are confounded by the often paroxysmal and minimally symptomatic nature of the arrhythmia. Since AF is associated with increased morbidity and reduced survival, there is a great need for sensitive and accessible AF screening instruments. Although monitors with automated detection capabilities (eg, Medtronic REVEAL XT) are used to screen for AF, the cost, inconvenience, and technical limitations of these monitors have limited their widespread use.[20,21] The ideal AF detection instrument would provide real-time realizable and accurate detection of AF in a sensitive and specific manner. Furthermore, the ideal screening instrument would be inexpensive, accessible, and easy to use for patients with, or at risk for, this serious arrhythmia.

Eighty percent of Americans who are older than 65 years currently use a mobile phone.[22] Based on current trends, the penetration of smartphones is expected to surge to 67.1% by 2015.[22] In light of the increasing accessibility of smartphones, a smartphone-based application for pulse analysis provides patients with, or at-risk for, AF with ready access to an inexpensive instrument for AF monitoring. Importantly, a large percentage of older individuals have reported a willingness to use their mobile phones for health management.[22,23]

Conclusions

In our moderately sized prospective cohort study involving 76 patients with AF undergoing cardioversion, we observed that 2 statistical methods (RMSDD/mean and ShE) were strongly related to AF and that a novel arrhythmia detection application combining these 2 statistical methods reliably distinguished an irregular pulse from AF from pulse waveforms obtained during NSR. Since our application is accurate and real-time realizable using hardware that already exists within a standard smartphone, we believe that this software could be effectively and inexpensively used to improve AF detection in the general population. Further data are needed to explore the acceptability and feasibility of smartphone-based applications for pulse waveform analysis in older, at-risk populations and in out-of-hospital settings.

Strengths and limitations

We anticipate that some participants with very large, or very small, or calloused fingertips may have difficulty transilluminating their fingers sufficiently so as to allow for successful heart rhythm analysis. We conducted our study in a hospitalized and largely white cohort examined in a standardized, temperature, and light-controlled environment. It is possible that exposure to extreme temperatures or bright ambient light might affect the performance characteristics of our iPhone-based AF detection application. It is possible that patients with a high burden of premature beats and/or atrial tachyarrhythmias with variable ventricular responses may be falsely detected as AF. We are developing an algorithm for testing in patients with a broader spectrum of arrhythmias and using a wider array of smartphones. Further testing of the performance and acceptability of our pulse waveform analysis application in large and ethnically diverse cohorts and in real-world scenarios is necessary.

References

1. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention. The anticoagulation and risk factors in atrial fibrillation (ATRIA) study. JAMA 2001;285:2370–2375.
2. Magnani JW, Rienstra M, Lin H, et al. Atrial fibrillation: current knowledge and future directions in epidemiology and genomics. Circulation 2011;124:1982–1993.
3. Wang TJ, Larson MG, Levy D, et al. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study. Circulation 2003;107:2920–2925.
4. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The Framingham Study. Stroke 1991;22:983–988.
5. Fuster V, Ryden LE, Asinger RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association task force on practice guidelines and the European Society of Cardiology committee for practice guidelines and policy conferences (committee to develop guidelines for the management of patients with atrial fibrillation) developed in collaboration with the North American Society of Pacing and Electrophysiology. Eur Heart J 2001;22:1852–1923.
6. Humphries KH, Kerr CR, Connolly SJ, et al. New-onset atrial fibrillation: sex differences in presentation, treatment, and outcome. Circulation 2001;103:2365–2370.
7. Defaye P, Dournaux F, Mouton E. Prevalence of supraventricular arrhythmias from the automated analysis of data stored in the ddd pacemakers of 617 patients: the AIDA study. The AIDA Multicenter Study Group. Automatic interpretation for diagnosis assistance. Pacing Clin Electrophysiol 1998;21:250–255.
8. Benjamin EJ, Chen PS, Bild DE, et al. Prevention of atrial fibrillation: report from a National Heart, Lung, and Blood Institute workshop. Circulation 2009;119:606–618.
9. Lee J, McManus D, Chon K. Atrial fibrillation detection using time-varying coherence function and Shannon entropy. Conf Proc IEEE Eng Med Biol Soc 2011;2011:4685–4688.
10. Lee J, McManus DD, Merchant S, Chon KH. Automatic motion and noise artifact detection in Holter ECG data using empirical mode decomposition and statistical approaches. IEEE Trans Biomed Eng 2012; 59:1499–1506.
11. Lee J, Reyes BA, McManus D, Maitas O, Chon KH. Atrial fibrillation detection using an iphone 4s. IEEE Trans Biomed Eng 2012: epub ahead of print.
12. Scully CG, Lee J, Meyer J, et al. Physiological parameter monitoring from optical recordings with a mobile phone. IEEE Trans Biomed Eng 2012; 59: 303–306.
13. Aboy M, McNames J, Thong T, Tsunami D, Ellenby MS, Goldstein B. An automatic beat detection algorithm for pressure signals. IEEE Trans Biomed Eng 2005;52:1662–1670.
14. Dash S, Chon KH, Lu S, Raeder EA. Automatic real time detection of atrial fibrillation. Ann Biomed Eng 2009;37:1701–1709.
15. Sankari Z, Adeli H. Heartsaver: a mobile cardiac monitoring system for auto-detection of atrial fibrillation, myocardial infarction, and atrio-ventricular block. Comput Biol Med 2011;41:211–220.
16. Gregoski MJ, Mueller M, Vertegel A, et al. Development and validation of a smartphone heart rate acquisition application for health promotion and wellness telehealth applications. Int J Telemed Appl 2012:1–7.
17. Tateno K, Glass L. Automatic detection of atrial fibrillation using the coefficient of variation and density histograms of RR and deltaRR intervals. Med Biol Eng Comput 2001;39:664–671.
18. Pawar T, Chaudhuri S, Duttagupta SP. Body movement activity recognition for ambulatory cardiac monitoring. IEEE Trans Biomed Eng 2007;54:874–882.
19. Petterson MT, Begnoche VL, Graybeal JM. The effect of motion on pulse oximetry and its clinical significance. Anesth Analg 2007;105:S78–S84.
20. Sarkar S, Ritscher D, Mehra R. A detector for a chronic implantable atrial tachyarrhythmia monitor. IEEE Trans Biomed Eng 2008;55:1219–1224.
21. Barthelemy JC, Feasson-Gerard S, Garnier P, et al. Automatic cardiac event recorders reveal paroxysmal atrial fibrillation after unexplained strokes or transient ischemic attacks. Ann Noninvasive Electrocardiol 2003;8:194–199.
22. Barrett L. Health and caregiving among the 50+: ownership, use and interest in mobile technology. AARP Research and Strategy Analysis 2011.
23. Mobile healthcare opportunities, monitoring applications and mhealth strategies 2010–2014. Juniper Research 2011.