Continuous heart rate monitoring for automatic detection of atrial fibrillation with novel bio-sensing technology

Aviram Hochstadt, M.D. [a],[*], Ehud Chorin, M.D., Ph.D. [a], Sami Viskin, M.D. [a], Arie Lorin Schwartz, M.D. [a], Natan Lubman, B.Sc [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, Northern Industrial Park, Caesarea, Israel

A B S T R A C T

Background: Asymptomatic atrial fibrillation [AF] is an important cause of fatal or disabling stroke. A continuous heart-rate monitoring device, comfortable enough to be worn continuously and reliable enough to detect AF, would allow for prompt initiation of anticoagulation therapy to prevent stroke.
Methods: We studied a new custom-made wearable photo-plethysmograph [PPG] wrist-watch sensor, specifically designed for continuous heart rate monitoring and incorporating contact and motion noise-filters. We tested its ability to automatically detect AF in patients undergoing elective cardioversion of AF, using simultaneously recorded electrocardiogram [ECG] as gold standard.
Results: A total of 18,608 consecutive R-R-interval measurements were recorded simultaneously with PPG and ECG in 20 patients, including 12,521 [67.3%] R-R-intervals during AF and 6087 [32.7%] R-R intervals during sinus rhythm. Scatter plots and Bland-Altman plots demonstrated that the PPG signals were highly correlated to the simultaneously recorded ECG [R = 0.980, p < 0.001], both during AF and during sinus rhythm. The automatic algorithm distinguished AF from sinus rhythm with a sensitivity of 100% and specificity of 93.1%.
Conclusions: This PPG-based wrist-watch sensor reliably detected AF in non-ambulatory patients.

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One third of all ischemic strokes, and an even higher percentage of lethal or disabling strokes are cardioembolic strokes caused by atrial fibrillation (AF) [1,2]. Moreover, the early phase, soon after the onset of AF, is a particularly high-risk period for the development of stroke [3]. It is therefore crucial to accurately detect *asymptomatic* AF, *as early as possible after its onset*, so that appropriate anticoagulation [the only drug therapy that significantly reduces the risk of stroke in patients with atrial fibrillation] [4], can be initiated for high-risk patients [2]. Therefore, there is a renewed interest in the early detection of AF [5,6] with the use of implanted [subcutaneous] long-term electrocardiogram [ECG] monitors [7,8], hand-held devices [9,10] or "smart" mobile-phones [11–14].

We studied a new portable photo-plethysmograph [PPG] "wrist-watch" sensor, specifically designed for continuous heart rate monitoring, and tested its ability to automatically detect AF. In contrast to recent studies on AF screening, which use either implanted devices [7,8] or non-invasive detection but only during very limited time periods [9–14], the device tested here allows for *continuous* long-term non-invasive monitoring and *automatic* detection of AF. To our knowledge, detection of AF using PPG has been attempted in only one study [15].

## Methods

Study design and patient selection

This is a single-center, prospective study assessing the effectiveness of novel bio-sensing technology for automatic detection of atrial fibrillation [CardiacSense]. The study cohort consisted of patients presenting to our department with atrial fibrillation, including patients electively scheduled for cardioversion, who

agreed to participate in this study and underwent continuous PPG recording during ECG recording, capturing sinus rhythm and AF in both recording modalities simultaneously. All participants provided written informed consent for participation in the study, which was approved by the institutional ethics committee. Reasons for exclusion in patients undergoing PPG recording were lack of appropriate synchronization with the ECG recording [making it impossible to use the ECG as the gold standard for determining the beat-to-beat heart rate and rhythm]. Only one patient was excluded because low peripheral perfusion precluded adequate PPG
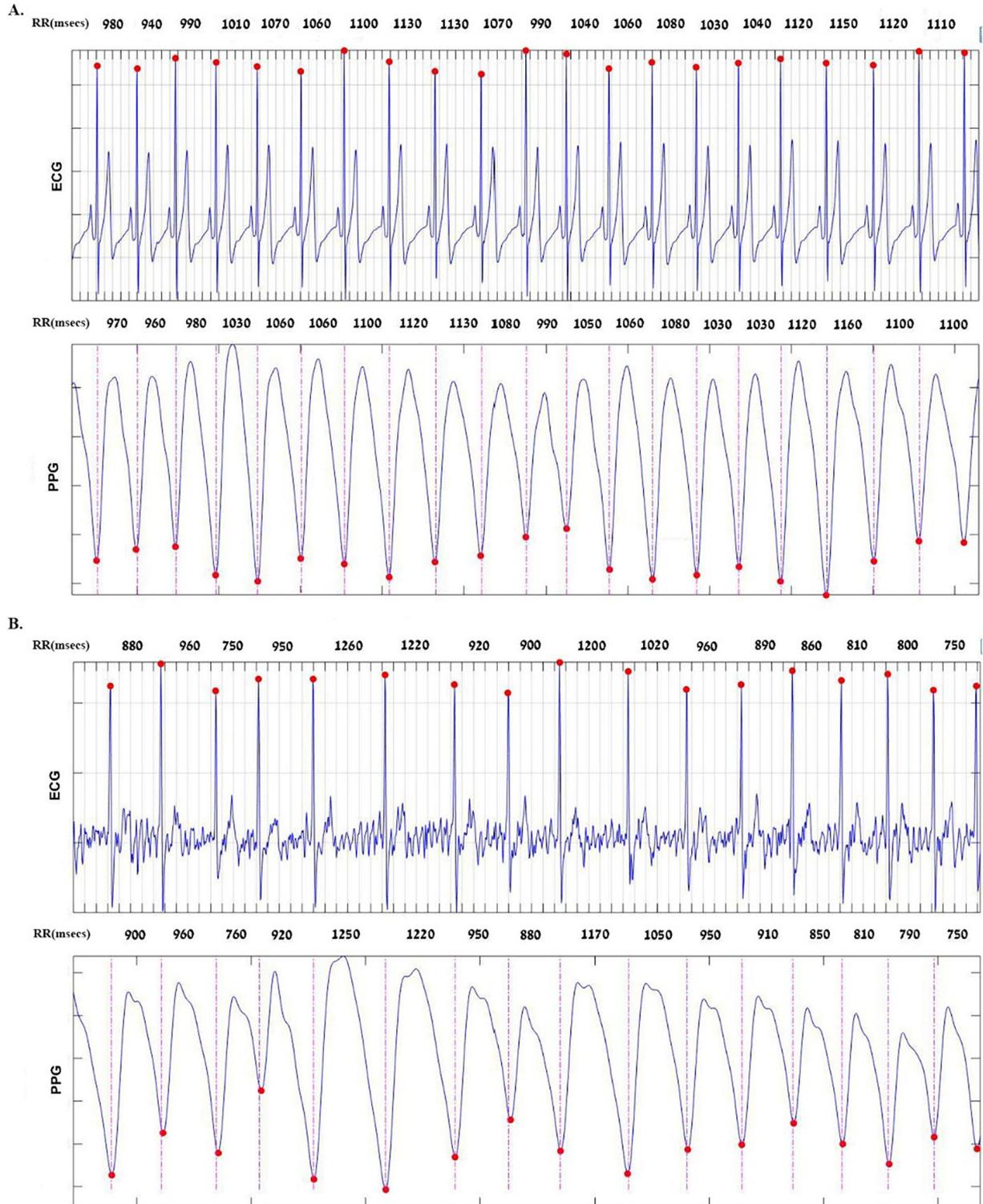
Fig. 1. Simultaneous recodings of ECG and PPG data for a patient with sinus rhythm [panel A] and atrial fibrillation [panel B]. The red dots are automatically annotated at the peak of the R-wave and the PPG signal and the R-R intervals are measured automatically between consecutive red dots. Note every PPG-wave peak corresponds fairly accurately to its corresponding R-wave peak on the ECG.

recordings whereas one was excluded because of incessant movement artifacts.

The bio-sensing technology

CardiacSense is a wrist-worn device, in appearance similar to a watch, specifically designed to detect life-threatening arrhythmias and atrial fibrillation. The device is intended to record, store and transfer photoplethysmographic [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 the pulse rate and the pulse pressure. CardiacSense utilizes this technology to detect heart rate and cardiac arrhythmias on a beat-to-beat basis.

Automatic diagnosis of atrial fibrillation was performed using a Lorentz plot. This is a scatter plot showing every R-R interval as a function of its previous R-R. The device automatically drawn Lorentz plots for varying numbers of beats and by using a proprietary algorithm that utilizes graph dispersion radius and angular trends, determined the rhythm to be "atrial fibrillation" or "sinus rhythm." During the pilot phase of the study, it was determined that with the current algorithm, it was possible to declare AF with diagnostic certainty following up to 250 consecutive ventricular beats during AF and to declare sinus rhythm following 30 beats of sinus rhythm [even in the presence of sinus arrhythmia]. In this study, interim beats, that is, all beats between the start of "rhythm change" [from sinus rhythm to AF or vice versa] and the final definition by the algorithm, were considered to be beats of the final rhythm diagnosed by the algorithm.

Detailed procedure

Each participant was connected to an ECG monitor and wore the PPG device for about 30 min of the study period. All the simultaneous
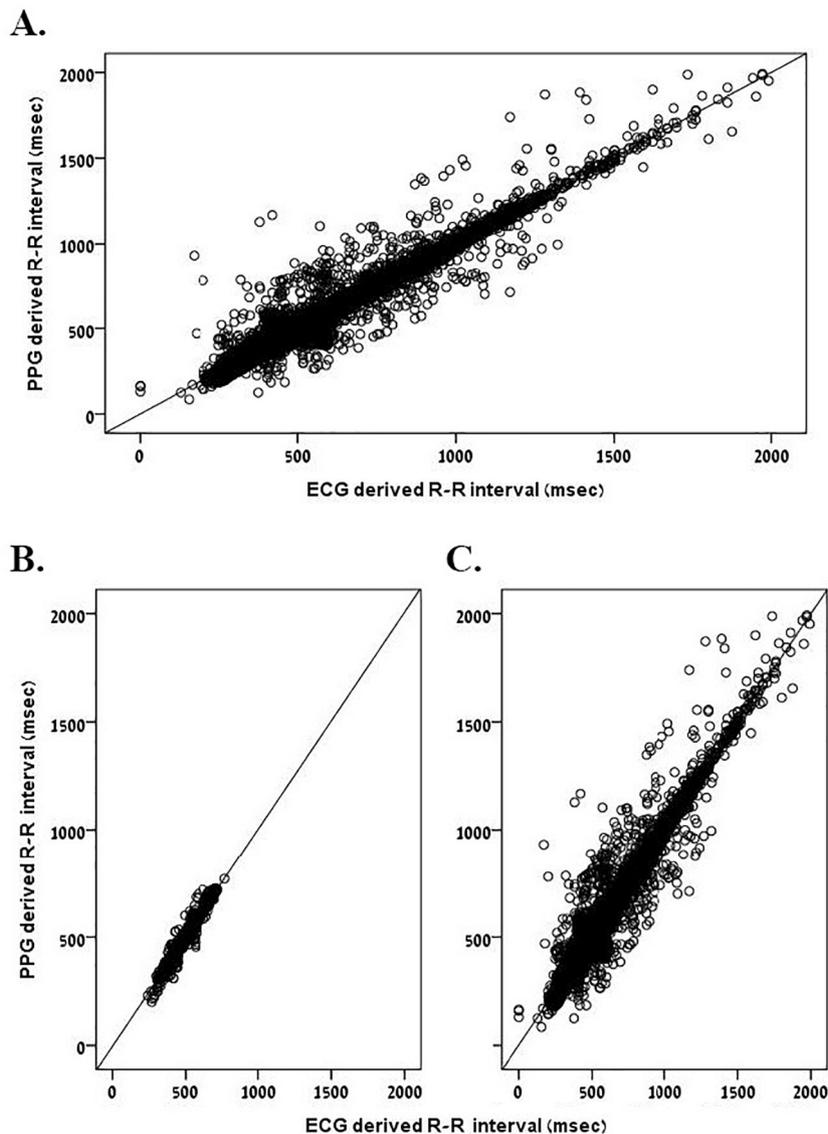
Fig. 2. Scatter plots of R-R intervals, as recorded by PPG [Y-axis] vs. ECG [X-axis] for: [panel A] All 18,608 intervals recorded in 20 patients; [panel B] for all 12,521 ventricular beats recorded during atrial fibrillation and [panel C] for 6087 ventricular beats recorded during sinus rhythm. Note the excellent correlation between R-R intervals recorded by both modalities, and the higher dispersion of the scatter in the beats recorded during atrial fibrillation.

recordings were performed in patients at rest, either supine at the electrophysiologic laboratory or in the supine or seating position in the hospital ward. Nine patients who underwent cardioversion were connected to a continuous ECG recorder and to the PPG device ≥30 min before a scheduled cardioversion and stayed connected to the monitoring devices for ≥10 min after the procedure was performed. For simplicity, the interval between two consecutive PPG signals is termed here as "R-R interval" [instead of PPG-PPG interval] in analogy to the R-R interval between two consecutive QRS complexes in the simultaneously recorded ECG. The R-R interval of every cardiac cycle, as recorded by PPG was compared to its simultaneous R-R as recorded by ECG. The gold standard for defining the presence of sinus rhythm and the presence of AF was the ECG, which was analyzed by one cardiologist [EC]. All complexes assigned as being "atrial fibrillation rhythm" by both PPG and ECG were considered true positives; all complexes assigned correct diagnosis as being of sinus rhythm by both techniques were considered true negatives. Out of these results sensitivity [true positive rate], specificity [true negative rate], and positive and negative predictive values were calculated.

Statistics

The accuracy of R-R length measurements was assessed by a Bland-Altman Plot, pairwise *t*-test and a Pearson correlation test of ECG derived R-R values vs. PPG derived R-R values. Comparison of R values was done using the Fisher R to Z transformation. Agreement between rhythm assessments was calculated using an unweighted Cohen's kappa. Significant p values were considered when p < 0.05, all figures are shown as Mean ± Standard deviation. All calculations were done using SPSS v.24 from IBM, Armonk, Virginia and R version 3.3.2 from R Foundation for Statistical Computing, Vienna, Austria.

Results

There were 18,608 R-R measurements done during simultaneous recordings of ECG and PPG in 20 patients, including 12,521 [67.3%] measurements during atrial fibrillation rhythm and 6087 [32.7%] measurements during sinus rhythm. Out of the 20 patients that were eventually included 15 [75%] were male and 5 [25%] were female, the average age was 74.1 ± 8.7 years. Nine of the participants had an elective cardioversion performed, one participant had an unsuccessful cardioversion and stayed in atrial fibrillation while the others converted successfully to sinus rhythm.

R-R measurements by PPG and ECG were highly correlated [R = 0.980 [p < 0.001], Figs. 1–2]. This correlation was minimally lower [albeit reaching statistical significance] for R-R intervals recorded during atrial fibrillation [R = 0.978, p < 0.001] compared to R-R intervals recorded during sinus rhythm measurements [R = 0.993, p < 0.001, p < 0.001 for the difference between correlation coefficients; Fig. 2B and C]. Correlation between R-R measurements by PPG and ECG remained high for measurements within the high [>120] or low [<60] pulse rates [R = 0.882 and R = 0.929 accordingly, p < 0.001 for both].

The R-R intervals recorded with PPG were slightly longer than those simultaneously recorded with ECG [mean R-R = 540.4 ± 221.7 msec for PPG vs. 539.1 ± 217.2 msec for ECG]; this very small absolute difference reached statistical significance in view of the very large number of measurements [p < 0.001].

A Bland Altman plot for the above data showed high agreement between ECG and PPG with a mean difference of 1.3 msec between R-R measurements with a 95% CI of 0.6 to 1.9 msec [Fig. 3].

Measuring the accuracy of the atrial fibrillation PPG detection algorithm

Analyzing the above 12,521 atrial fibrillation beats, there was a 100% sensitivity for detection of AF by the PPG algorithm.
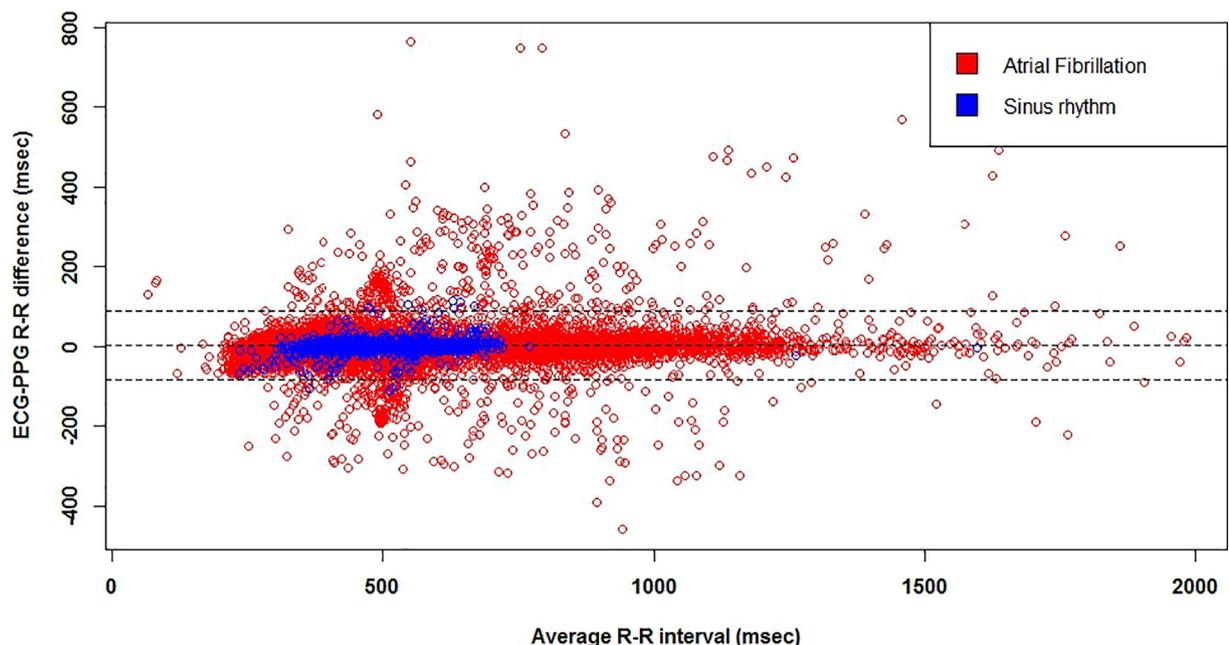

Fig. 3. Bland-Altman plot of R-R interval between ECG and PPG for atrial fibrillation [Red] or sinus rhythm [blue]. Note similar agreement across the range of R-R intervals and that agreement is higher for beats recorded during sinus rhythm.

Analyzing the above 6087 sinus beats, there was a 93.1% specificity for sinus rhythm detection by the PPG algorithm. Calculating Cohen's Kappa for agreement between the cardiologist's diagnosis of rhythm and the PPG algorithm's showed a high agreement rate with $\kappa = 0.948$ [95% CI 0.942–0.952].

Discussion

Detecting asymptomatic AF, *before* it leads to a devastating embolic stroke, remains an important goal so highly-effective preventive therapy with anticoagulation can be timely initiated [5,6]. By remaining unrecognized and untreated, *asymptomatic* AF more than doubles the annual risk of stroke [5]. Conversely, initiation of anticoagulation therapy, following the incidental detection of asymptomatic AF, is associated with a significant reduction in the risk of stroke [from 4% to 1%] and death [from 7% to 4%] within only 1.5 years of the initiation of therapy [5]. Screening for AF is particularly important for *asymptomatic* patients with high $CHA_2DS_2\text{-}VAS_c$ because these risk factors not only increase the risk of stroke in the event of AF, but also increase the risk of asymptomatic AF [16].

Present study

We studied a custom-made wristwatch that uses PPG technology for continuous heartrate monitoring and tested its ability to automatically detect AF, using simultaneously recorded ECG as a gold standard. We found that PPG and ECG measurements of R-R intervals were highly correlated [$R = 0.980$ [$p < 0.001$], Fig. 1]. Moreover, we found that the Lorenz-plot based algorithm automatically detected AF with a sensitivity >99%. These results are comparable to those reported with hand-held devices and mobile phones [17] with the following advantage: Hand-held devices and mobile-phones require active and intentional recordings that are performed either in response to symptoms or during very short sampling periods. In contrast, wrist-watch based PPG technology can be used for continuous, long-term heartrate monitoring and allows for automatic detection of AF in truly asymptomatic patients.

Recently, Nemati et al. [15] also tested PPG technology within a different wrist worn monitoring device [the Samsung Simband] to detect AF and showed similar accuracy. However, the device described here has several advantages: the device does not require a training session, uses only one PPG channel and does not use accelerometers. These differences allow for a much lower energy consumption and thus a longer time between charges which allows for truly long-term continuous monitoring of heart rate and rhythm.

Of note, the algorithm requires 250 consecutive irregular beats to diagnose AF. This implies that for AF episodes with an averaged ventricular rate of 100 beats/min, automatic recognition of AF would require approximately 2.5 min of ongoing arrhythmia. AF episodes shorter than this value would remain undiagnosed. Importantly, previous studies looking at the correlation between the *duration* of AF episodes and the risk of stroke in patients with implanted devices that have long-term ECG recording capabilities, differ in their definition of the minimal duration of AF that is associated with an increased stroke risk [5]. Single AF episodes <3 min would not be considered "potentially thrombogenic" by any of those studies [5]. However, a very high number of short episodes of AF leading to a high AF burden could still impose risk and be missed.

Limitations

All the patients participating in our study were purposely resting [supine or seating] when the simultaneous PPG and ECG recordings were made. Obviously, the technological challenges needed for reliable detection of atrial fibrillation in active, ambulatory patients, are formidable and it remains to be seen if the present device will reliably detect AF in ambulatory patients. Nevertheless, even if PPG technology is ultimately used only for heart rate monitoring at rest, it would still be of value for detecting asymptomatic AF because a substantial percentage of such events begin during sleep at night [18,19]. Another possible limitation is over-detection of irregular rhythms other than AF. The algorithm used in arrhythmia detection should be robust enough to discern multiple atrial or ventricular premature beats and marked sinus arrhythmia from AF except in the most extreme cases. However, we did not test the device in a patient population with a high burden of these irregular rhythms and hence cannot quantify their effect on specificity. Further studies are currently being planned to be performed in "real life" situations and their result will address the above limitations.

Conflicts of interest

Natan Lubman designed the atrial fibrillation detection algorithm for CardiacSense. Sami Viskin is Chief Medical Officer for the cardiac arrhythmia section at CardiacSense.

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