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Wireless Monitoring of Reconstructed 12-Lead ECG in Atrial Fibrillation Patients Enables Differential Diagnosis of Recurrent Arrhythmias

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Abstract — Differential diagnosis of symptomatic events in post-ablation atrial fibrillation (AF) patients (pts) is important; in particular, accurate, reliable detection of AF or atrial flutter (AFL) is essential. However, existing remote monitoring devices usually require attached leads and are not suitable for prolonged monitoring; moreover, most do not provide sufficient information to assess atrial activity, since they generally monitor only 1-3 ECG leads and rely on RR interval variability for AF diagnosis. A new hand-held, wireless, symptom-activated event monitor (CardioBip; CB) does not require attached leads and hence can be conveniently used for extended periods. Moreover, CB provides data that enables remote reconstruction of full 12-lead ECG data including atrial signal information. We hypothesized that these CB features would enable accurate remote differential diagnosis of symptomatic arrhythmias in post-ablation AF pts.

Methods: 21 pts who underwent catheter ablation for AF were instructed to make a CB transmission (TX) whenever palpitations, lightheadedness, or similar symptoms occurred, and at multiple times daily when asymptomatic, during a 60 day post-ablation time period. CB transmissions (TXs) were analyzed blindly by 2 expert readers, with differences adjudicated by consensus.

Results: 7 pts had no symptomatic episodes during the monitoring period. 14 of 21 pts had symptomatic events and made a total of 1699 TX, 164 of which were during symptoms. TX quality was acceptable for rhythm diagnosis and atrial activity in 96%. 118 TX from 10 symptomatic pts showed AF (96 TX from 10 pts) or AFL (22 TX from 3 pts), and 46 TX from 9 pts showed frequent PACs or PVCs. No other arrhythmias were detected. Five pts made symptomatic TX during AF/AFL and also during PACs/PVCs.

Conclusions: Use of CB during symptomatic episodes enabled detection and differential diagnosis of symptomatic arrhythmias. The ability of CB to provide accurate reconstruction of 12 L ECGs including atrial activity, combined with its ease of use, makes it suitable for long-term surveillance for recurrent AF in post-ablation patients.

Keywords — **Electrocardiography, Atrial Fibrillation, Remote, Wireless, Cardiac Monitoring.**

I. INTRODUCTION

Atrial fibrillation (AF) is the most common clinically significant arrhythmia, and is associated with increased morbidity and mortality, particularly from embolism and stroke [1]. Many patients with pacemakers and implantable cardioverter defibrillators ICDs have been shown to have AF, both symptomatic and asymptomatic, even when there is no prior history of atrial fibrillation at implant [2]. In addition, a high AF burden or AF episodes lasting > 5.5 h independently predict stroke and mortality risk [3].

Catheter ablation (CA) has emerged as an important therapeutic approach for patients with recurrent AF [4]. In patients undergoing CA, recurrent AF is common in the first 2-3 months post-procedure; hence CA patients are maintained on anticoagulant drugs during this time [1, 5] Subsequently, important decisions such as discontinuation of anticoagulation or antiarrhythmic drug therapy are presented to clinician and patient. Thus, reliable remote outpatient detection of recurrent AF represents an important objective that could improve clinical decision making and clinical outcomes. However, because of the low amplitude of atrial electrical activity and noise associated with use of remote monitoring, current systems predominantly rely on heart rate variability to detect AF. As a result, some patients may be misdiagnosed, especially in post-CA patients.

CardioBip, a wireless, handheld system for remote monitoring of patients with various forms of heart disease has the potential to improve outpatient assessment of patients with atrial fibrillation. At present, the primary method of monitoring such patients for recurrent AF include intermittent Holter and event monitoring, which may delay diagnosis of recurrent AF or delay key diagnostic decisions regarding the need for continued anticoagulation or antiarrhythmic drugs. CardioBip may address these problems by providing the clinician with an accurate, remote assessment of the patient's atrial activity, thereby improving diagnosis of recurrent AF.

We undertook this study to evaluate the accuracy of the CardioBip in remote monitoring of patients with AF, particularly to determine its ability to assess atrial activity in such patients.

II. METHODS

1. CardioBip System for remote monitoring of 12-lead ECGs. The CardioBip system has 2 major components: (1) a diagnostic and device calibration center, and (2) a mobile, handheld ECG device for ECG data acquisition and wireless transmission (Fig. 1):

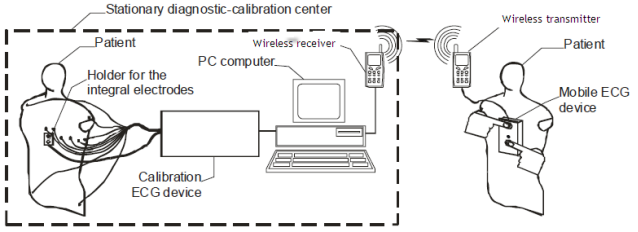

Fig. 1. Schematic of CardioBip remote monitoring system.

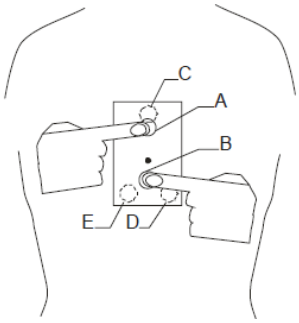

Fig. 2. Recording position of the mobile ECG device [6].

The mobile ECG device is a pocket sized, battery powered device with integrated electrodes connected to amplifiers, digital control and communication unit [6]. The basic technical specifications are: +/- 2.5 mV measuring range, 10 bit A/D conversion, 300 Hz sampling rate, 0.05-75 Hz pass band and 1 MΩ input impedance. It has 5 integrated electrodes, with 2 (A and B in Fig. 2) placed on the top of the device, to be contacted by the patient's left and right index fingers. The other 3 (C, D and E) are on the bottom of the device to contact specific points on the patient's precordium. One of the electrodes (E) is passive (ground). The potential difference between electrodes A and B corresponds to the Lead I of the standard ECG. The position of active electrodes C and D are chosen to compose, together with the electrodes A and B, a lead system that is as close to orthogonal as possible. The electrodes A, B, C, D and E are connected to the system of amplifiers (Fig. 3) and to the digital data processing and control unit. Electrode E is ground, Electrode B is the common reference, and the potentials of A, C and E with respect to the reference electrode define three base leads. The digital data processing and control unit provides several functions: (1) A/D conversion of the amplified signals, (2) control of the recording process, (3) storage of the recorded signals, (3) data transmission and control of the data transfer, (4) control of light and sound indicators and power supply.

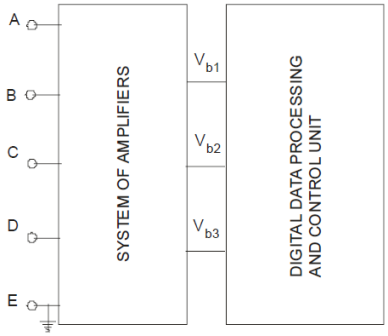

Fig. 3. Mobile ECG device electrical interconnections.

The data collected by the handheld device are transmitted via Bluetooth to a smartphone. From the smartphone, data are sent via the Internet to the diagnostic center. The stationary diagnostic-calibration center (Fig. 1) comprises a PC computer and software connected to a wireless transceiver, and a calibration ECG device with 14 electrodes (10 conventional ECG electrodes with cables and 4 integrated electrodes). The calibration device simultaneously records 12 standard ECG signals 3 special leads obtained from the same position as electrodes C, D, and E of the mobile device. Using information from the 3 special leads and Leads I and II, the computer software calculates an individual transformation matrix for every patient. This matrix is stored in the computer memory and enables reconstruction of 12-lead ECG signals from patient information transmitted from the mobile ECG device.

Reconstruction of AF 12-lead ECG from CardioBip input signals and the individualized transformation matrix has been previously described [7]. The conventional 12-lead ECG is calculated from the measured signals using matrix multiplication:

$$V_{12L} = \mathbf{T_i} * V_{CBip}$$

where conventional 12 ECG leads are represented with the vector:

$$V_{12L} = (\text{I, II, III, aVR, aVL, aVF, } V_1, V_2, V_3, V_4, V_5, V_6)$$

And

$$V_{CBip} = (V_{b1}, V_{b2}, V_{b3})$$

The transformation matrices, $\mathbf{T_i}$, i = 1, 2, 3, are patient-specific and computed using least-square error algorithms during the patient calibration step. T_1 is used to reconstruct the atrial depolarization segment of the cardiac cycle. T_2 reconstructs the ventricular depolarization segment, while T_3 covers the ventricular repolarization segment of cycle.

2. Clinical Study design. Twenty-one patients underwent catheter ablation (CA) for AF and who gave informed consent for post-ablation cardiac monitoring with CardioBip were enrolled in the study. Digital data from the 12L and the CardioBip recording were used to construct an individualized transformation matrix for each patient. In subsequent CardioBip recordings and transmissions, the individualized transformation matrix was used to transform the CardioBip input data into a reconstructed 12-lead ECG (12CB). Each enrolled patient was requested to make up to 3 transmissions per day when asymptomatic, and whenever symptoms such as palpitations or lightheadedness developed. All 12L and 12CB were read by 2 expert blinded readers.

III. RESULTS

Patients enrolled in the study ranged from 31 to 69 yrs in age, with an average age of 50.0 +/- 13.8 yrs. On average, there were 53.3 days of follow-up during the post-ablation monitoring period (range 41-68 days), and made an average of 2.07 transmissions per day. A total of 2324 transmissions were made, or which 2237 (96%) were judged by blinded expert cardiologist readers to be of adequate quality to allow diagnosis of rhythm and assessment of atrial activity.

	CardioBip Transmissions								Holter Recordings					
	Asymptomatic				Symptomatic				Holter No. 1			Holter No. 2		
Pt. No.	total	Neg for AF/AFL	AF pos	AFL pos	Neg for AF/AFL	AF pos	AFL pos	Symptom Correlation	AF pos	AFL pos	other	AF pos	AFL pos	other
1	124	108	0	0	16	0	0	Freq PVCs	no	no	Freq PVCs	no	no	Freq PVCs
2	126	125	1	0	0	0	0		no	no		no	no	
3	133	107	2	0	1	10	13	AF/AFL, PACs	no	yes		no	yes	
4	115	113	0	0	2	0	0	Freq PVCs	no	no	NSAT	no	no	
5	166	151	0	0	0	15	0	AF	yes	no	NSVT	no	no	NSAT
6	78	77	1	0	0	0	0		no	no		no	no	NSAT
7	117	115	0	0	0	2	0	AF	no	no		no	no	
8	185	183	1	0	1	0	0	Freq PACs	no	no	NSAT	no	no	NSAT
9	107	94	5	0	8	0	0	Freq PACs	no	no		no	no	
10	125	119	1	0	0	5	0	AF	no	no	NSAT	no	no	NSAT
11	90	88	0	0	0	2	0	AF	no	no		no	no	
12	113	84	0	0	7	18	4	AF/AFL, PACs	yes	no	Freq PVCs	yes	no	Freq PACs
13	108	77	6	0	5	15	5	AF/AFL, PACs	yes	no		yes	no	
14	125	117	0	0	5	3	0	AF, PACs	no	no		no	no	NSAT
15	61	26	35	0	0	0	0		no	no		no	yes	
16	85	83	2	0	0	0	0		no	no		no	no	
17	155	152	3	0	0	0	0		no	no		no	no	
18	63	36	27	0	0	0	0		no	no	NSAT	no	no	NSAT, NSVT
19	96	70	23	0	1	2	0	AF, PACs	no	no		no	no	
20	57	48	9	0	0	0	0		no	no		no	no	NSAT
21	95	5	66	0	0	24	0	AF	yes	no		yes	no	
Total	2324	1978	182	0	46	96	22							

Table 1. Results of CardioBip and Holter Monitoring in 21 Post-Ablation AF Patients. PACs = frequent premature atrial complexes; PVCs = frequent premature ventricular complexes; NSAT = nonsustained atrial tachycardia; NSVT = nonsustained ventricular tachycardia.

Detection of Recurrent AF and AFL with CardioBip. A total of 359 transmissions (15.4% of total transmissions) showed either AF or AFL. Recurrent atrial fibrillation was detected by CardioBip in 274 transmissions (11.8% of total transmissions), and was observed at some point follow-up period in 19/21 patients. In the 19 patients in whom recurrent AF was detected by CardioBip, an average of 13.7 transmissions showed AF (range, 1-90). Recurrent AFL was detected in 85 transmissions from 6 patients, an average of 14.2 AFL transmissions (range, 1-36) per patient. All 6 AFL patients also had transmissions positive for AF during follow-up.

Detection of Recurrent AF/AFL with 24 Hour Holter Monitoring. All patients had a 12-lead, 24-hour Holter at approximately 30 and 60 days after ablation. In contrast to the 19 patients with recurrent AF/AFL detected by CardioBip monitoring, only 6 patients had recurrent AF/AFL detected by Holter monitoring (4 AF, 2 AFL). Other arrhythmias observed on Holters included runs of atrial tachycardia (9 patients), and nonsustained ventricular tachycardia (2 patients). All 6 patients who had recurrent AF/AFL detected by Holter had previously been identified by CardioBip monitoring. Detection of recurrent AF/AFL by Holter occurred an average of 24.5 days after first detection by CardioBip.

Detection of Recurrent AF/AFL by CardioBip During Asymptomatic Periods. A total of 2160 transmissions were made while the patient was asymptomatic (92.9% of the total transmissions), and were received from all 21 study patients. A total of 182 transmissions from asymptomatic patients showed AF/AFL (7.8% of the total transmissions, and 66.4% of all transmissions showing AF/AFL) and came from 14/21 patients, 4 of which also had transmissions during symptoms that showed AF/AFL, and 7 of which had no symptoms during all AF/AFL transmissions.

Detection of Recurrent AF/AFL and Distinction from Other Arrhythmias by CardioBip During Symptoms. Fourteen patients had symptomatic episodes, and made a total of 164 transmissions during symptoms in the follow up period. AF/AFL was present in 118 symptomatic transmissions originating from 10 patients (72.0% of total symptomatic transmissions). Frequent premature atrial complexes were present in 28 symptomatic transmissions from 7 patients (17.1% of symptomatic transmissions), and frequent premature ventricular complexes were present in 18 symptomatic transmissions from 2 patients (11.0% of symptomatic transmissions). No other symptomatic arrhythmias were observed. Four patients made multiple symptomatic transmissions.

IV. Discussion and Conclusions

Catheter ablation (CA) is a rapidly emerging option for long-term treatment of AF, with an estimated 15% year-after-year annual growth rate [4]. Initial success rates (defined as freedom from AF) range from 50-75% depending on the clinical characteristics of the treated population [4, 5]. However, AF recurrences are not uncommon after CA [4, 5]. Accordingly, the American College of Cardiology/American Heart Association/Heart Rhythm Society AF guidelines recommend monitoring for recurrent AF for up to 2 years after CA [5]. Similarly, alternative AF treatment approaches – for example antiarrhythmic drugs and heart rate control – also require periodic outpatient monitoring to assess therapeutic efficacy.

The data from this study suggest that long-term intermittent cardiac monitoring with CardioBip is a viable approach to recurrent arrhythmia detection in post-ablation AF patients. All patients were able to provide high quality transmissions and showed good compliance with the study protocol. In symptomatic patients, CardioBip distinguished AF and AFL from other causes of symptoms, such as frequent premature beats. Moreover, CardioBip frequently detected recurrent AF in the absence of symptoms – an important result because asymptomatic AF recurrences carry the same risk of stroke or other embolic events. It is also noteworthy that CardioBip was more sensitive and timely in detecting recurrent AF/AFL than periodic Holter monitoring.

Current monitoring approaches for recurrent AF include periodic Holter monitoring, patient-activated event monitors, and continuous monitoring from implantable devices, such as implantable loop recorders, pacemakers and cardioverter-defibrillators (ICD) [5, 8]. Each of these has significant limitations for AF surveillance:

- Both Holters and event monitors require attached skin electrodes and wires, which may be uncomfortable and difficult to tolerate for extended periods, and may have low sensitivity for recurrent AF detection, particularly asymptomatic episodes [9].
- Implantable devices provide continuous monitoring, but require an invasive procedure and are suitable only for a subset of AF patients.
- All current devices monitor a limited number of leads (typically 1-3) and accordingly cannot accurately reconstruct atrial activity. Thus, diagnosis of recurrent arrhythmias relies largely on detecting variability of the RR interval, which does not allow for differential diagnosis between the various atrial and ventricular rhythm disturbances that occur in this population.

Frequent, intermittent remote monitoring with CardioBip addresses many of the limitations of existing devices. CardioBip is a convenient, hand-held device with integrated electrodes and does not require attached leads or wires. Thus, the device can be used at various times of the day whether symptoms are present or not, and can be used for extended time periods. Moreover, the device provides sufficient information about cardiac electrical activity to allow remote reconstruction of a full 12-lead ECG. This enables accurate assessment of atrial activity, including PACs, flutter and fibrillatory waves, and consequently, accurate differential diagnosis of arrhythmias.

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