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## Introduction

- Over 17 million people in the United States have coronary artery disease (CAD), with more than 7 million having chronic angina.<sup>1</sup> A similar high prevalence of CAD is present throughout the developed world.
- At present, there are no convenient and accurate means for outpatient, remote ECG monitoring of these patients. Some existing monitors provide full 12-lead ECG information, but their use is limited by the need for attached leads and wires, the relatively short duration that they may be left in place, and patient discomfort and inconvenience.<sup>2</sup>
- CardioBip is a wireless handheld system for remote monitoring and requires no attached leads or wires. It may improve outpatient assessment of CAD patients by providing full 12-lead ECG information, including accurate reconstruction of ST-segments and T-waves.
- In this study, we evaluate the accuracy of the CardioBip in remote monitoring of patients with myocardial ischemia. We chose exercise-induced ischemia as a general model of myocardial ischemia because: (1) in many advanced CAD patients, post-exercise extends well into the post-exercise period; (2) the patients would have 12-lead ECGs obtained throughout the study period, thereby enabling direct comparison of standard 12-lead ECGs to near-simultaneous CardioBip ECG data.
- The present study shows noninferiority of CardioBip ECG data to the standard 12-lead ECG for detection of post-ETT ischemia, and suggests that CardioBip may be a useful and convenient tool for ischemia monitoring in CAD patients.

## Methods

### CardioBip System for Remote 12-lead ECGs Monitoring

The CardioBip system has 2 major components: (1) a diagnostic and device calibration center, and (2) a mobile handheld device for ECG acquisition and transmission:

**(1) The diagnostic-calibration center** (Fig. 1, next column) is a PC and software connected to a wireless transceiver, and a calibration ECG device with 14 electrodes (10 conventional ECG electrodes and 4 integrated electrodes). The calibration device simultaneously records 12 standard ECG signals and 3 special leads from the same position as electrodes C, D, and E of the mobile device (as shown on Fig 2 ). The computer software calculates and stores an *individual transformation matrix for every patient*, enabling reconstruction of 12-lead ECG signals transmitted from the mobile ECG device .

## Methods (continued)

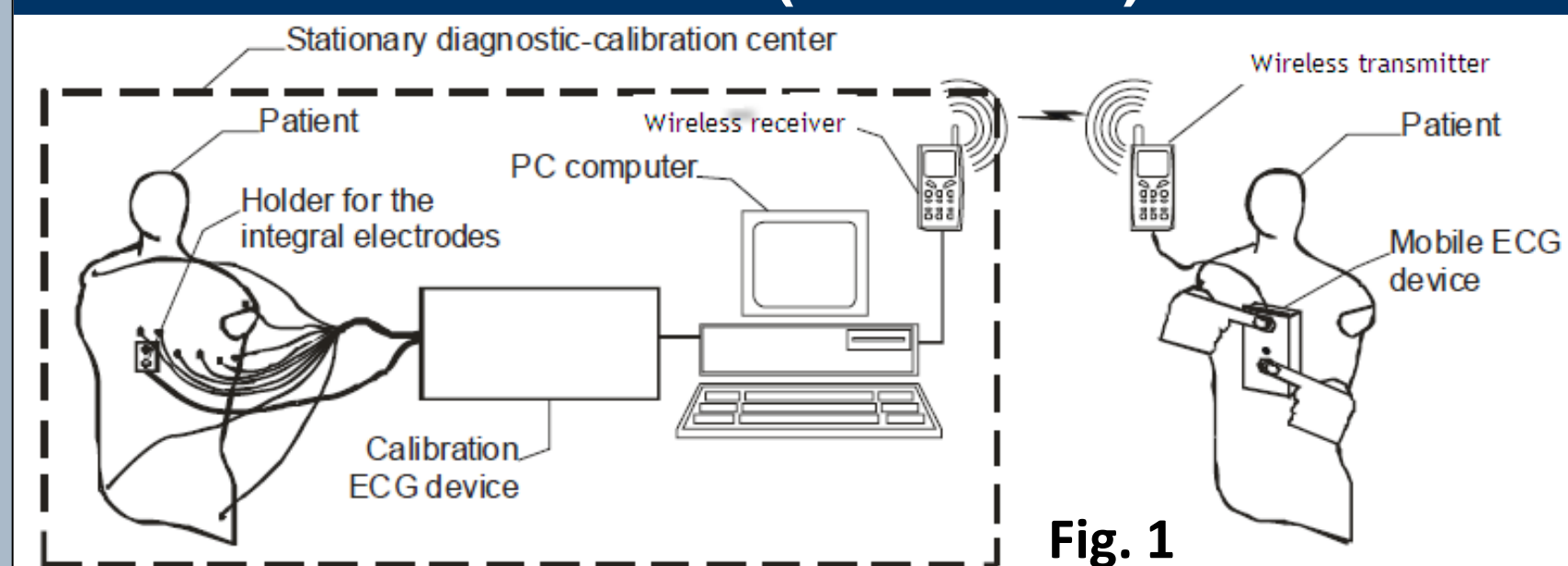


Fig. 1

**(2) The mobile ECG device** (Fig. 2) is a pocket sized, battery powered device with 5 integrated electrodes, 2 on the device top (A and B), which are contacted by the patient's index fingers, and 3 (C, D and E in Fig. 2) on the device bottom which are precordial electrodes.



Fig. 2

### Clinical Study Design

Study entry criteria were: age  $\geq 18$ , documented CAD by angiography ( $\geq 70\%$  occlusion in  $\geq 1$  coronary artery), at least 1 episode of angina in the preceding month, and undergoing exercise treadmill testing (ETT) for clinically indicated reasons.

All 47 enrolled patients had a standard 12-lead ECG (12L) and a CardioBip recording (12CB) immediately before ETT, and at 3 times up to 8 min after ETT. 12-lead ECG (12L) and CardioBip recordings (12CB) were made within 10s of each other.

All 12L and 12CB recordings were analyzed by 2 fully-blinded cardiologist expert readers. Each reviewed the 12L and 12CB independently, with patients in random order, and without knowledge of other readings in the study.

The cardiologist ECG readers determined: (1) whether or not the ETT was positive for ischemia; (2) the total number of abnormal leads, and (3) the identity of the lead with the largest abnormality. Primary endpoint was the number of patients with ETT judged positive by 12L and 12CB; secondary endpoint was the number of leads judged positive. The study tested the noninferiority hypothesis that 12CB was equivalent to 12L for the endpoint. Statistical comparisons were made using McNemar's test with continuity correction.

## Results



**Fig. 3.** Representative comparisons of 12-lead ECGs (12L) and CardioBip transmissions with reconstructed 12-lead ECGs (12CB) before and immediately after ETT. Left 2 columns, 12L and 12CB results from Patient No. 28, a few minutes prior to exercise treadmill testing (ETT). Right 2 columns, 12L and 12CB results about 2 min after ETT. In each instance, 12L and 12CB were obtained within 10 sec of each other.

**Table 1. Comparison of 12L and 12CB in ETT (next column).** Summary of ETT results by 12L and 12CB. Only data from the 1-3 min post-ETT window is shown due to space constraints.

The overall ETT result was scored as positive (Pos) if the patient had at least 1 lead with ST-segment depression during at least 1 of the 3 post-ETT time windows; otherwise it was scored as negative (Neg). The number of leads with ST-segment depression in the 1-3 min post-ETT window is listed (No. Abn leads), along with the most abnormal lead identified (Most Abn).

## Results (continued)

Pt	12L			Pt	12CB		
	ETT Result	No. Abn Leads	Most Abn.		ETT Result	No. Abn Leads	Most Abn.
1	Neg	0		1	Neg	0	
2	Pos	6	V4	2	Pos	3	V4
3	Neg	0		3	Neg	0	
4	Neg	0		4	Neg	0	
5	Pos	2	V4	5	Pos	2	V4
6	Pos	2	V4	6	Pos	2	II
7	Neg	0		7	Neg	0	
8	Neg	0		8	Pos	2	V5
9	Pos	5	V5	9	Pos	2	I
10	Pos	5	V5	10	Pos	5	I
11	Pos	2	V6	11	Pos	3	V4
12	Pos	2	V5	12	Pos	2	V5
13	Pos	1	I	13	Pos	1	I
14	Neg	0		14	Neg	0	
15	Neg	0		15	Neg	0	
16	Neg	0		16	Neg	0	
17	Neg	0		17	Neg	0	
18	Neg	0		18	Neg	0	
19	Neg	0		19	Neg	0	
20	Neg	0		20	Neg	0	
21	Pos	3	V4	21	Pos	3	V4
22	Neg	0		22	Neg	0	
23	Pos	2	V4	23	Neg	0	
24	Pos	3	V5	24	Pos	3	V5
25	Pos	1	V4	25	Neg	0	
26	Neg	0		26	Neg	0	
27	Neg	0		27	Neg	0	
28	Pos	3	V4	28	Pos	5	V4
29	Pos	1	V5	29	Neg	0	
30	Pos	2	V4	30	Pos	1	V5
31	Pos	2	V4	31	Neg	0	
32	Neg	0		32	Pos	0	
33	Pos	4	V5	33	Pos	5	V4
34	Neg	0		34	Neg	0	
35	Neg	0		35	Neg	0	
36	Pos	3	V5	36	Pos	1	V5
37	Pos	2	V5	37	Pos	1	V5
38	Pos	3	V4	38	Pos	2	V4
39	Pos	2	V4	39	Pos	6	V4
40	Neg	0		40	Neg	0	
41	Neg	0		41	Neg	0	
42	Neg	0		42	Neg	0	
43	Pos	2	V4	43	Pos	3	V4
44	Pos	2	V4	44	Pos	2	V4
45	Neg	0		45	Pos	0	
46	Neg	0		46	Neg	0	
47	Pos	1	V4	47	Pos	1	V4

**Primary Endpoint – Number of Positive ETT (Table 2, next column).** By 12L, 24 of 47 subjects had positive ETT results, whereas by 12CB, 22 subjects were positive.

Of the 22 positive 12CB results, and taking 12L to be the “gold standard”, 20 were true positive (TP), and 2 were false positive (FP). Correspondingly, 23 of 47 subjects had negative ETT results by 12L, and 25 of 47 subjects had negative results by 12CB (21 true negative [TN], 4 false negative [FN]).

There was no significant difference in the results between 12L and 12CB ( $p=1.00$ , McNemar's test with continuity correction). Thus, the primary endpoint was met.

**Secondary Endpoint – Number of Positive and Negative Leads (Table 3, next column).** In each patient, 6 leads (I, II, aVF and V4-V6) were analyzed by the blinded expert readers; thus, a total of 846 leads were evaluated.

## Results (continued)

	Overall ETT Results			Total Positive and Negative Leads		
	Pos ETT 12L	Neg ETT 12L	Total	No. Pos Leads by 12L	No. Neg Leads by 12L	Total
Pos ETT 12CB	20	2	22	80	11	91
Neg ETT 12CB	4	21	25	18	737	755
<b>Total</b>	<b>24</b>	<b>23</b>	<b>47</b>	<b>98</b>	<b>748</b>	<b>846</b>

**Table 2.** Two-by-two table comparing overall ETT test results obtained with 12L and 12CB.

**Table 3.** Two-by-two table comparing total positive and negative leads with 12L and 12CB.

**Secondary Endpoint – Number of Positive and Negative Leads (continued from previous column).** By 12L, 98 of 846 leads were positive, whereas by 12CB, 91 of 846 were positive. Of 91 positive leads by 12CB, 80 were TP (concordant with 12L results) and 11 were FP. For leads scored negative, there were 748 scored negative by 12L, and 755 by 12CB (737 TN, 18 FN).

There was no significant difference in the results between 12L and 12CB ( $p=0.26$ , McNemar's test with continuity correction). Thus, the secondary endpoint was met.

## Conclusions and Implications

- CardioBip, a mobile, handheld device that records and wirelessly transmits ECG data, enables accurate assessment of cardiac electrical activity, including accurate ST-segment analysis.
- The data shows by a variety of measures that the transmitted and reconstructed CardioBip 12-lead ECGs were equivalent to the standard 12-lead ECG in detecting exercise-induced myocardial ischemia.
- The data show that CardioBip is useful for remotely acquiring ECG information, transmitting it, and accurately reconstructing a patient's full 12-lead ECG, in a remote setting such as a call center or physician's office. This has the potential to provide better diagnostic, prognostic and treatment information to the clinician. This may lead to improved clinical outcomes for CAD patients.
- The system requires no attached leads or wires, which lessens patient discomfort and may improve long-term compliance.
- The patient can carry the CardioBip with them and use it to transmit accurate 12-lead ECGs at physician prescribed intervals of time, during ordinary daily activity or when symptoms develop.