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# New ambulatory impedance cardiograph validated against the Minnesota Impedance Cardiograph

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## Abstract

The validity and reliability of a new ambulatory impedance cardiograph (AZCG) was tested against the Minnesota Impedance Cardiograph (ZCG) during rest, orthostasis, and mental stress. Impedance cardiography allows noninvasive assessment of stroke volume, cardiac output, and systolic time intervals. A reliable ambulatory device would allow studies outside the lab. The devices were compared at two sites in healthy subjects. In both studies, the AZCG tracked changes across conditions closely with the ZCG (all Period × Device interactions were nonsignificant). Pearson *r*s, were .65 to .93, random intraclass correlation coefficients ranged from .80 to .98, indicating high degrees of shared measurement variance, and Cronbach's alpha indicated very good internal reliabilities (.91 to .99). Relative to the ZCG, the new AZCG appears to provide valid and reliable estimates of cardiac function at rest and during behavioral challenges in the lab.

**Descriptors:** Impedance cardiography, Ambulatory monitoring, Cardiac output, Validity, Reliability.

Impedance cardiography (ZCG) is a safe, noninvasive, and unobtrusive technique suitable for measuring cardiac function in psychophysiological studies (Wilson, Lovallo, & Pincomb, 1989). With this method, a high-frequency alternating current is passed along the thorax and recordings are made of impedance changes occurring in synchrony with respiration and ejection of blood into the aorta (Lamberts, Visser, & Zijlstra, 1984). These signals can be used to determine heart rate (HR) and systolic time intervals and, with a suitable algorithm, to estimate stroke volume (SV) and cardiac output (CO) (Kubicek et al., 1974).

The ZCG system most widely used in research is the Minnesota Impedance Cardiograph, Model 304B (Surcom, Inc., Minneapolis, MN). Although such units are useful in static applications, there is a need for a reliable and valid ambulatory impedance cardiograph (AZCG) that will permit research outside the laboratory. Advances in high-density data storage, rapid analogue-to-digital signal conversion, and amplifier miniaturization have made AZCG monitoring technically feasible. The authors have developed an AZCG and conducted two laboratory studies of its reliability and validity against the Minnesota ZCG for measurements of SV, CO, HR, and systolic time intervals.

## General Methods

Study 1 was conducted at the University of Oklahoma Health Sciences Center, and Study 2 was carried out at The Ohio State University. The goal of each was to assess reliability and external validity of the new AZCG against the standard Minnesota ZCG. We used postural adjustment, mental arithmetic, and public speaking as challenges because posture affects sympathetic outflow by eliciting cardiovascular reflexes (Dunlap & Pfeifer, 1989; Szabo, 1993), while mental arithmetic and public speaking typify psychological stressors frequently used in psychophysiology (e.g., al'Absi et al., 1997; Cacioppo et al., 1995). Because it is not possible to perform simultaneous ZCG measurements on a given subject, the units were tested successively with unit order counterbalanced across subjects. An alternative to successive tests would be to record parameters simultaneously via both units using the current imposed by one of them (e.g., Willemsen, De Geus, Klaver, Van Doornen, & Carroll, 1996). Because valid measurements depend critically on the ability of a unit to produce a reliably constant source current under a variety of conditions, the simultaneous

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method was considered a less stringent test than the successive method used here.

### Apparatus

Impedance measurements were made via disposable, self-adhesive, aluminum coated bands (Instrumentation for Medicine Inc., Greenwich, CT) placed according to published guidelines (Sherwood et al., 1990) using the four-electrode method of Kubicek et al. (1974).

*Minnesota ZCG.* The reference unit was a Minnesota Impedance Cardiograph, Model 304B (Surcom, Inc., Minneapolis, MN). This has a 4 mA constant current source with a 100 kHz oscillator and produces analog outputs for basal thoracic impedance ($Z_0$), cardiac and respiratory linked change in impedance ($\Delta Z$), and the first derivative of $\Delta Z$ ($dZ/dt$) (Kubicek et al., 1974).

*AZCG.* The AZCG is a wearable, untethered unit designed for noninvasive acquisition of physiological data during daily activity. It is 4.5 × 9.5 × 16 cm, weighing 400 gm with batteries. The analog subsystem comprises a three-lead ECG (bandwidth 0.05–100 Hz) and a four-lead electrical impedance system, which provides a constant current source (2 mA RMS at 50 kHz) to the outer electrodes (1 and 4) and records thoracic electrical impedance via the inner electrodes (2 and 3). The acquired analogue impedance signal is appropriately filtered and amplified and differentiated to produce signals for $Z_0$ (DC-100 Hz), $\Delta Z$ (DC-40 Hz), and $dZ/dt$ (DC-40 Hz). The ECG and ZCG each employ a digitally controlled, sampled-signal rebalance method for waveform stability. The digital subsystem provides A-D conversion of the above signals using a Motorola MC68332-based microcomputer with a 12-bit A-D converter and 256 kB RAM. Digitized signals are stored on a 20 MB Flash Card (PCMCIA), allowing 30 min of data acquisition at the 500 Hz A-D rate. Programming during set up, signal monitoring, and uploading of data are accomplished using standard communication software through digital input/output connectors and a serial interface to a microcomputer system.

Ambulatory data acquisition is controlled using an onboard programmable protocol manager. User selectable protocol parameters include A-D sampling rate (100–1000 Hz), analog channel selection, and timed or triggered initiation of recording epochs. Time between epochs and epoch durations may be set independently across acquisition periods according to the study protocol. Triggered epochs may be initiated by the subject using a push-button switch or controlled using an external device. For example, the AZCG system used in Study 1 was configured with a 50 Torr pressure-sense switch to allow simultaneous AZCG data acquisition initiated with inflation of an ambulatory blood pressure cuff.

### Dependent Variables

The dependent variables were HR, SV, CO, preejection period (PEP), and left ventricular ejection time (LVET). HR (in beats per minute) was calculated from the time between successive QRS complexes of the ECG. PEP (in milliseconds) was measured as the interval from the initial upsweep of the QRS complex and the dZ/dt B-point (Sherwood et al., 1990). LVET (in milliseconds) was measured as the interval from the B-point to the X-point of the dZ/dt (Sherwood et al., 1990). SV (in milliliters per minute) was calculated using the Kubicek et al. (1974) equation:

$$\mathrm{SV} = \mathrm{rho}(\mathrm{L}/\mathrm{Z}_0)^2(\mathrm{LVET})(\mathrm{dZ}/\mathrm{dt})_{\max}$$

where rho (ohms centimeters) is set to a constant value of 135; L (in centimeters) is the distance between recording electrodes; $Z_0$ (in ohms) is basal thoracic impedance; LVET (in milliseconds) is the left ventricular ejection time; and $dZ/dt_{\max}$ is in ohm/second. CO (liters per minute) was calculated as $(\mathrm{HR} \cdot \mathrm{SV})/1{,}000$.

### External Validity and Reliability

External reliability of the AZCG was tested against the Minnesota ZCG using analysis of variance techniques comparing absolute differences between units as main effects of Unit and the ability of the AZCG to track changes across conditions as reflected in Unit × Period interactions. The linear relationship between units was tested using Pearson's $r$ across all test periods and at each separate period. The random effects intraclass correlation coefficient ($\rho$) was used to measure the shared variance between units across the six test periods independent of subject effects. Pearson's $r$ and $\rho$ can be interpreted as estimators of the between-unit effect size (Shrout & Fleiss, 1979). The intraclass correlation coefficient offers advantages over Pearson's $r$ because it provides a single index reflecting both rank order consistency and extent of agreement between units, thus providing a stringent evaluation of absolute reliability. Because SV is the unique cardiac parameter estimated from ZCG, multiple regression controlling for unit order and baseline HR was used to test the relationship between units on SV. Finally, internal reliability of each unit was assessed using Cronbach's coefficient $\alpha$ across test periods.

## STUDY 1

### Method

### Subjects

Participants were 10 healthy men recruited from the community who met the following criteria: ages 21 to 35 years, resting blood pressure (BP) $< 140/90$ mmHg, weight within 20% of Metropolitan Life Insurance Company norms for height, smoked $<10$ cigarettes per day, consumed $<2$ drinks of alcohol per day, had self-reported good health, used no prescription medications, and had no treatment for hypertension or other major illness. The final sample had: Age = 24.7 years ± 2.0, weight = 172 lbs ± 28.2., height = 70.6 in. ± 3.3, SBP = 118 mmHg ± 7.0, DBP = 64 mmHg ± 4.2 and HR = 62 bpm ± 8. Participants signed a consent form approved by the Institutional Review Board of the University of Oklahoma Health Sciences Center and the Oklahoma City Veterans Affairs Medical Center and were paid for participating.

### Procedure

All test sessions were held in the afternoon. Subjects abstained from food and caffeinated beverages for 2 hr, alcohol for 12 hr, and tobacco for 4 hr before entering the laboratory. The 50-min protocol, repeated for each unit, included: supine baseline (15 min), sitting upright (5 min), orthostasis (5 min), sitting recovery (5 min), mental arithmetic (5 min), and supine recovery (15 min).

*Tasks.* During orthostasis, the subject arose from his seated position and stood quietly with his arms relaxed by his side. Mental arithmetic calculations involved continuous subtraction as described elsewhere (al'Absi et al., 1997), with notification of errors by the experimenter.

### Apparatus

BP was measured using an automated oscillometric monitor (Dinamap$^{\mathrm{TM}}$, Critikon, Tampa, FL). Cardiac functions were measured by the Minnesota Impedance Cardiograph and the new AZCG, and signal quality was verified by oscilloscope. The same electrodes were used for both units. In attaching the cables, the ends of each adhesive band electrode were brought into contact and terminated using a disposable pregelled Ag/AgCl spot electrode (Cleartrace$^{TM}$, ConMed, Utica, NY). Snap leads were attached to the spot electrodes and connected to the unit's input cable (Ebert, Eckberg, Vetrovic, & Cowley, 1984; Wilson, Lovallo et al., 1989). The electrocardiogram (ECG) was recorded from Cleartrace electrodes in a three-lead configuration: left shoulder, right shoulder, and lower left abdomen.

### Signal Derivation and Scoring

Analogue $Z_0$ and $\Delta Z$ signals from the Minnesota ZCG and the source ECG were processed through an external interface (Worldwide Medical Data, Durham, NC), digitized at 500 Hz and stored on a microcomputer disk drive. $Z_0$, $\Delta Z$, and ECG signals from the AZCG were internally digitized at 500 Hz and stored until being uploaded to a computer using standard communication software.

Signal processing and scoring were accomplished off-line for both units with commercial software (Waveshell, Center for Biomedical Engineering, Research Triangle Institute, Research Triangle Park, NC). First, the $dZ/dt$ was derived from the digitized $\Delta Z$ signal using Waveshell.[1] Next, individual cardiac cycles were displayed and accepted or rejected by Waveshell according to qualification parameters based on an experimenter-chosen template of the subject's own waveform morphologies. The $dZ/dt$, $Z_0$, and ECG signals were then subjected to ensemble averaging in successive 1-min epochs across each period of the protocol. During averaging, successive ECG cardiac cycles were entrained to the Q wave of the ECG QRS complex. The software then displayed the ensemble average with cursors placed according to appropriate algorithms to denote the onset of electromechanical systole, the opening of the aortic valve, peak of $dZ/dt$, and aortic valve closure. Previous research supports the validity of ensemble averaging against manual scoring of waveforms (Everson, Lovallo, Pincomb, Kizakevich, & Wilson, 1991; Kelsey & Guethlein, 1990) and computer quality control against operator scoring (Kelsey et al., 1998).

### Data Reduction and Analysis

Parameters derived from ensemble averages were averaged within each of their six respective protocol periods. The primary analysis was a 2 Unit (Minnesota, AZCG) × 6 Period (supine, sitting, orthostasis, sitting, mental arithmetic, supine) split-plot repeated measures multivariate analysis of variance (MANOVA), where Unit is a between-subjects factor and Period is a within-subjects factor. A separate MANOVA was conducted on each dependent variable. The design allowed us to assess the main effects of Unit and Period and the Unit × Period interaction independent of the control variables. The effect of Unit was based on the omnibus $F$ test and the effect of Period and the Unit × Period interaction were based on the $F$ test corresponding to the Hotelling-Lawley trace statistic.

Because units were tested in succession, it was recognized that Unit effects could arise that were not due to a true unit difference. Preliminary analyses showed that AZCG HRs averaged 4 bpm higher across periods than the reference unit. We reasoned that this reflected measurement discrepancy, and for this reason, HR at seated baseline as well as unit order were entered as between-subjects control variables[2] in each MANOVA model, with the exception that baseline HR was not included as a covariate in the HR MANOVA model.

## Results

### Comparison of Units

Means and standard errors for the units at the 6 test periods are reported in Table 1. Relative to the Minnesota unit, the AZCG produced HRs that averaged 4 bpm higher across periods. After controlling for unit order, the main effect of Unit was nonsignificant for HR, $F(1,16) = 0.95$, $p = .35$ After controlling for unit order and baseline HR, there were no significant Unit main effects for SV, CO, PEP, or LVET, $Fs(1,15) < 0.28$, $ps > .60$.

On the other hand, the behavioral manipulations led to significant changes across periods measured by both units. The MANOVA revealed significant period effects for HR, $F(5,12) = 18.38$, $p < .0001$, and for SV, CO, and PEP, $Fs(5,11) > 3.77$, $ps < .03$, and a trend for LVET, $F(5,11) = 2.71$, $p = .07$. The units were substantially comparable in tracking changes across periods. The MANOVA revealed no significant Unit × Period interactions for HR, $F(5,12) = 0.55$, $p = .74$, or for SV, CO, PEP, and LVET, $Fs(5,11) < 1.88$, $ps > .18$.

### Crossinstrument Agreement

*Pearson's r.* Pearson's $r$ correlations revealed a significant linear relationship between units on HR, SV, CO, PEP, and LVET collapsing across all six periods (see Table 2). The correlations at each period were also significant and consistently high. For this analysis, Pearson's $r$ (which is equivalent to the standardized regression coefficient) can be considered the effect size estimator associated with the degree of relation between the two units.

*Intraclass correlation coefficient.* The intraclass correlation coefficients of agreement between units on each outcome measure across the 6 test periods were consistently high; $\rho s = .65$ to $.93$ (Table 2). The intraclass correlation estimates the effect size of the magnitude of the agreement between the two units.

*Multiple regression.* Multiple regression revealed that SV from the Minnesota ZCG had a significant positive relation to SV from the AZCG when unit test order and baseline HR were controlled,

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[1] In the case of both the Minnesota ZCG and the AZCG, the user has the option of scoring the $dZ/dt$ output signal itself or deriving $dZ/dt$ from $\Delta Z$ off-line. The internal $dZ/dt$ signal of the AZCG was designed for signal verification only and has an 11-ms phase delay due to filter design. When this internal $dZ/dt$ signal is used for analysis, the PEP will be artificially lengthened by 11 ms. Accordingly, PEP values should be corrected by that amount. No other parameters are affected. However, there is no phase delay with signal processing and scoring accomplished off-line with the Waveshell software (Waveshell, Center for Biomedical Engineering, Research Triangle Institute, Research Triangle Park, NC), as was used in Study 1. Because Study 2 used the AZCG internal $dZ/dt$, the 11-ms phase delay was present and corrected for in those data. Also, as noted, the signal quality of the internal $dZ/dt$ is lower than that of a signal derived off-line using appropriate software.

[2] A simple linear regression revealed a significant relation between baseline HR and SV, CO, and LVET, respectively, for both devices at each separate test period, $Fs(1,8) > 5.76$, $ps < .04$. No significant relationship was found, however, between baseline HR and PEP at any period, $Fs(1,8) < .97$, $ps > .35$ (although, given the sensitivity of PEP to ventricular loading effects, no such relationships were expected). This supports an assumption of linearity between HR and the physiologic outcome variables in the MANOVA models.

**Table 1.** *Study 1: Means and Standard Errors of the Means of Cardiovascular Variables and MANOVA Results*

| | Supine | | Sitting | | Standing | | Recovery | | MA | | Recovery | | $F(p)$ from MANOVA | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variable | ZCG | AZCG | ZCG | AZCG | ZCG | AZCG | ZCG | AZCG | ZCG | AZCG | ZCG | AZCG | Unit | Per | U × P |
| HR (bpm) | 63 | 65 | 65 | 67 | 77 | 83 | 62 | 65 | 69 | 73 | 62 | 67 | 0.95 | 18.38 | 0.55 |
| | 2.7 | 3.0 | 2.5 | 2.8 | 2.5 | 3.1 | 2.4 | 2.6 | 2.8 | 2.9 | 2.8 | 2.5 | (.35) | (.001) | (.74) |
| SV (mL) | 102 | 96 | 92 | 90 | 70 | 61 | 97 | 93 | 86 | 81 | 97 | 90 | 0.28 | 10.85 | 0.22 |
| | 7.2 | 7.2 | 7.5 | 7.5 | 6.5 | 6.6 | 8.5 | 8.5 | 7.7 | 7.7 | 7.4 | 7.4 | (.60) | (.001) | (.94) |
| CO (L/min) | 6.27 | 5.83 | 5.84 | 5.68 | 5.29 | 4.91 | 5.92 | 5.70 | 5.78 | 5.72 | 5.91 | 5.81 | 0.16 | 3.77 | 1.88 |
| | 0.38 | 0.39 | 0.42 | 0.42 | 0.43 | 0.43 | 0.44 | 0.44 | 0.40 | 0.40 | 0.38 | 0.38 | (.69) | (.03) | (.17) |
| PEP (ms) | 114 | 113 | 115 | 115 | 124 | 128 | 118 | 114 | 121 | 114 | 116 | 115 | 0.05 | 3.91 | 1.28 |
| | 6.8 | 6.8 | 6.4 | 6.4 | 5.9 | 5.9 | 5.6 | 5.7 | 5.6 | 5.7 | 6.4 | 6.4 | (.83) | (.02) | (.33) |
| LVET (ms) | 286 | 288 | 275 | 281 | 248 | 237 | 279 | 286 | 270 | 274 | 287 | 290 | 0.08 | 2.71 | 0.48 |
| | 6.3 | 6.4 | 5.7 | 5.8 | 9.0 | 9.0 | 4.4 | 4.4 | 6.3 | 6.4 | 7.7 | 7.8 | (.78) | (.07) | (.78) |

*Note:* M = least squares means adjusted for baseline heart rate and unit test order (HR means adjusted only for unit order); ZCG = the Minnesota Impedance Cardiograph Model 304B; AZCG = Ambulatory Impedance Cardiograph. HR = heart rate; SV = stroke volume; CO = cardiac output; PEP = preejection period; LVET = left ventricular ejection time. Unit = main effect of ambulatory versus bedside unit collapsing across periods; Per = main effect of period; U × P = Unit × Period interaction.

$R^2 = .96$, $\beta = .979$, $t(16) = 11.32$, $p < .0001$. A scatter plot is shown in Figure 1.

### *Internal Reliability*

Internal reliability estimates using Cronbach's coefficient $\alpha$ were very high and comparable for both units; $\alpha$s = .91 to .99 for the Minnesota unit and from .93 to .99 for the AZCG (see Table 3).

## STUDY 2

### Method

### *Subjects*

Participants were 12 healthy undergraduates, 6 men and 6 women (mean age = 20.0 years, *SEM* = 0.52 years, range 18–24 years) who participated for course credit under the Introductory Psychology Research Experience Program at The Ohio State University. Inclusion criteria were: no self-reported current acute illness or history of chronic illness, low to moderate alcohol consumption, no needle, math, or speech phobias, body weight within 20% of ideal, and no current or chronic use of medicinal or recreational drugs, excluding birth control pills. In addition to course credit, participants received a sack dinner following participation. All participants signed an informed consent form approved by the Institutional Review Board of the Ohio State University.

### *Procedure*

Participants fasted for 4 hr prior to arrival at the General Clinical Research Center in The Ohio State University Hospital. The protocol included: adaptation (10 min) and orthostasis (11 min) followed by nonsocial speech (8 min), social speech (8 min), standard speech (4 min), and verbal mental arithmetic tasks (4 min) in a random order for each participant, each preceded by 5 min of

**Table 2.** *Study 1: Pearson and Intraclass Correlation Coefficients Between ZCG and AZCG*

| | | | | | | | All conditions | |
|---|---|---|---|---|---|---|---|---|
| Variable | Supine | Sitting | Standing | Recovery | MA | Supine | $r$ | $\rho$ |
| HR | .85<br>(.002) | .81<br>(.004) | .62<br>(.05) | .89<br>(.0006) | .83<br>(.003) | .80<br>(.005) | .88<br>(.0008) | .73 |
| SV | .98<br>(.0001) | .98<br>(.0001) | .97<br>(.0001) | .99<br>(.0001) | .97<br>(.0001) | .88<br>(.0007) | .98<br>(.0001) | .90 |
| CO | .94<br>(.0001) | .91<br>(.0002) | .94<br>(.0001) | .95<br>(.0001) | .90<br>(.0004) | .87<br>(.0009) | .94<br>(.0001) | .93 |
| PEP | .84<br>(.002) | .91<br>(.0003) | .88<br>(.0008) | .83<br>(.003) | .80<br>(.005) | .89<br>(.0006) | .90<br>(.0003) | .82 |
| LVET | .70<br>(.02) | .68<br>(.03) | .59<br>(.07) | .92<br>(.0002) | .75<br>(.01) | .52<br>(.13) | .80<br>(.005) | .65 |

*Note:* Entries show Pearson's $r$ and ($p$ value). Right column gives intraclass correlation coefficient ($\rho$). ZCG = the Minnesota Impedance Cardiograph Model 304B; AZCG = Ambulatory Impedance Cardiograph. MA = mental arithmetic; $r$ = Pearson's $r$; $\rho$ = Intraclass Correlation Coefficient; HR = heart rate (bpm); SV = stroke volume (mL); CO = cardiac output (L/min); PEP = preejection period (ms); LVET = left ventricular ejection time (ms).

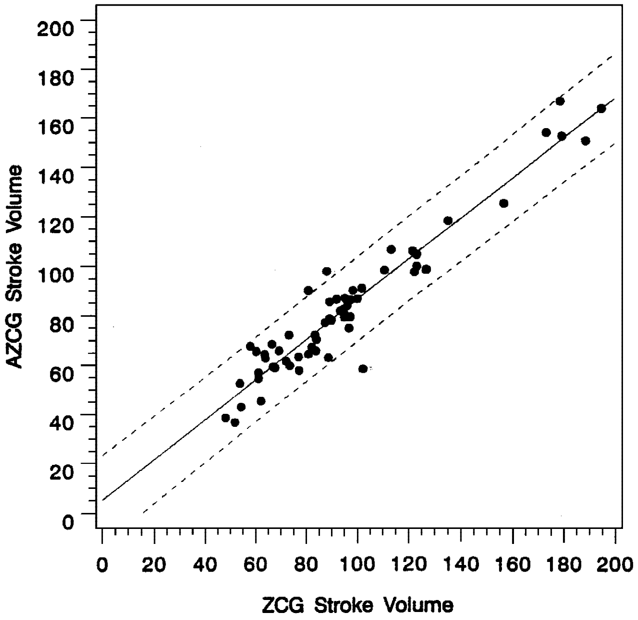

**Figure 1.** Scatter plot with 95% confidence limits of 60 estimates of stroke volume by the Minnesota ZCG and the ambulatory AZCG, recorded from 10 subjects tested under six conditions of rest and behavioral challenge following adjustment for baseline heart rate and device order.

seated rest. Afterward, subjects were debriefed, thanked for their participation, and given a sack dinner.

### Tasks

*Orthostasis.* After sitting quietly for 3 min, participants stood for 5 min and then sat for an additional 3 min. Cardiovascular measures were collected continuously during the last 2 min, 4 min, and 2 min of the respective periods.

*Nonsocial speech.* Participants prepared (2 min) and gave (2 min) speeches on two nonsocial topics: “What I saw on my way to my first class of the week” and “Demographic information about myself,” while imagining that they were talking on the telephone. For all speech tasks, participants were told that their speeches were being audiotaped for further evaluation.

**Table 3.** *Study 1: Cronbach’s Coefficient Alphas for ZCG and AZCG Units on Each Cardiovascular Variable Across Test Periods*

| Variable | ZCG | AZCG |
|---|---|---|
| HR | .94 | .94 |
| SV | .98 | .98 |
| CO | .99 | .99 |
| PEP | .95 | .97 |
| LVET | .91 | .93 |

*Note:* A higher Cronbach’s coefficient $\alpha$ indicates greater internal reliability across test periods. ZCG = the Minnesota Impedance Cardiograph Model 304B; AZCG = Ambulatory Impedance Cardiograph. HR = heart rate; SV = stroke volume; CO = cardiac output; PEP = preejection period; LVET = left ventricular ejection time.

*Social speech.* Participants prepared (2 min) and delivered (2 min) two speeches on social topics: “Why I am a good friend” and “Telephoning someone for a first date,” again imagining that they were talking on the telephone.

*Standard speech.* Participants prepared (2 min) and gave (2 min) a speech imagining that they were falsely accused of stealing a belt in a department store and were defending themselves to the store manager (Saab, Matthews, Stoney, & McDonald, 1989).

*Mental arithmetic.* Mental arithmetic (4 min) consisted of serial subtractions from a three-digit number by steps of three as described elsewhere (Cacioppo et al., 1995).

### Apparatus

The ECG was collected by the Colin Vital Signs Monitor (model BP-508) for all minutes using the lead II configuration with three disposable Ag/AgCl electrodes (Protrace 9113) and by the AZCG using an additional three disposable Ag/AgCl electrodes arranged, also, in the lead II configuration. Cardiac functions were measured by the Minnesota Impedance Cardiograph and the new AZCG.

### Signal Derivation and Scoring

Data were recorded during the last 4 min of each rest period and during each minute of each task. Each unit was used to record half the minutes in each recording epoch with unit order counterbalanced across subjects. This called for a single set of electrodes with two sets of leads and electrode cables that were alternately unplugged and plugged back in to their respective units. Signals from both units were acquired, extracted, and digitized using software developed by The Ohio State University Social Neuroscience Laboratory (The ANS Suite, version 5.2.1), (see footnote 1) yielding measures of SV, CO, PEP, LVET, HR (Litvack, Lozano, Ernst, Berntson, & Cacioppo, 1999). During extraction, the ECG and dZ/dt signals were decimated to 500 Hz, whereas the $Z_0$ signal was decimated at 250 Hz.

Waveforms were edited for artifacts, beat-to-beat ensemble averages were formed based on the R-wave of the ECG, and these were averaged over 1-min epochs (Kelsey & Guethlein, 1990). Determination of systolic time intervals was done automatically by detection algorithms in the scoring program followed by visual inspection and adjustment when necessary.

A heart period time series was created from the interbeat interval series using a weighted beat algorithm described elsewhere (Berntson, Quigley, Jang, & Boysen, 1990). Sharp transitions in the time series reflecting artifacts were detected using an algorithm and removed by smoothing (Litvack, Oberlander, Carney, & Saul, 1995). It was found that the filters in the AZCG prototype, for Study 2, introduced a phase lag between the ECG and dZ/dt, but not the $\Delta Z$, analog outputs (see footnote 1). The phase shift artificially lengthened AZCG estimates of PEP by approximately 11 ms relative to the Minnesota ZCG. Therefore, in Study 2, the PEP from the AZCG was corrected by subtracting 11 ms.

### Data Reduction and Analysis

Parameters were derived for every minute of each task and rest period and then averaged. Simple change scores (task minus rest) were computed for each minute of each period, with paired minutes used to represent each unit. HR, measured by the Colin Vital Signs Monitor, was used to eliminate paired minutes from the ZCG units that differed by 10 bpm or more in order to minimize arbitrary minute-

**Table 4.** *Study 2: Cardiovascular Variables across AZCG and ZCG*

| | Orthostatic domain | | | | Psychological domain | | | |
|---|---|---|---|---|---|---|---|---|
| | Sit | | Stand | | Rest | | Task | |
| Variable | AZCG | ZCG | AZCG | ZCG | AZCG | ZCG | AZCG | ZCG |
| HR | 70<br>(3.3) | 70<br>(3.5) | 85<br>(3.0) | 84<br>(3.3) | 71<br>(3.5) | 71<br>(3.7) | 80<br>(3.6) | 79<br>(3.6) |
| PEP | 134<br>(4.5) | 133<br>(4.2) | 143<br>(4.4) | 141<br>(4.4) | 129<br>(4.1) | 127<br>(4.1) | 123<br>(4.4) | 122<br>(3.9) |
| LVET | 253<br>(5.4) | 255<br>(5.8) | 215<br>(4.3) | 217<br>(4.2) | 259<br>(6.8) | 262<br>(7.3) | 253<br>(6.4) | 254<br>(6.4) |
| SV | 100<br>(9.8) | 108<br>(11.0) | 68<br>(6.1) | 70<br>(5.8) | 104<br>(10.6) | 111<br>(11.3) | 99<br>(10.5) | 102<br>(10.1) |
| CO | 6.73<br>(0.40) | 6.89<br>(0.38) | 5.58<br>(0.36) | 5.72<br>(0.29) | 7.06<br>(0.45) | 7.41<br>(0.47) | 7.53<br>(0.51) | 7.73<br>(0.52) |
| $Z_0$ | 25.14<br>(1.29) | 24.46<br>(1.27) | 26.82<br>(1.30) | 26.06<br>(1.27) | 25.00<br>(1.29) | 24.32<br>(1.28) | 24.91<br>(1.28) | 24.22<br>(1.24) |

*Note:* Entries show mean (*SEM*). ZCG = Minnesota Impedance Cardiograph; AZCG = Ambulatory Impedance Cardiograph; HR = heart rate (bpm); PEP = preejection period; LVET = left-ventricular ejection time (ms); SV = stroke volume (mL); CO = cardiac output (L/min); $Z_0$ = basal thoracic impedance (ohms).

to-minute error inherent in the test design. This eliminated 7.3% of the total minutes.

To determine whether measurements were similar for the AZCG and ZCG, a 2 Device (AZCG, ZCG) × 2 Period (rest, task) repeated measures MANOVA was used. A separate MANOVA was conducted for the orthostatic and psychological stressors on each measure. This design allowed us to assess the main effects of Device and Period and the Device × Period interaction. Pearson's $r$ and $\rho$ were computed between devices at each rest period, task period, and change score and internal reliabilities were assessed using Cronbach's $\alpha$ for the orthostatic stressor and the psychological stressors.

## Results

### *Orthostatic Stressor*

*Comparison of Devices*

Data from Study 2 are shown in Table 4. Orthostasis led to the expected changes, including increased HR, PEP, and $Z_0$, $Fs(1,11) \geq 31.48$, $ps < .001$; and decreased LVET, SV, and CO, $Fs(1,11) = 42.32$, $ps < .001$.

The devices were not different in their estimates of SV, CO, or HR, $Fs(1,11) \leq 3.62$, $ps > .09$. However, the AZCG gave larger values for PEP and $Z_0$ than the Minnesota ZCG, whereas LVET was smaller, $Fs(1,11) = 7.93$ to 9.01, $ps \leq .02$. The MANOVA revealed no significant Device × Period interactions for $Z_0$, SV, CO, PEP, LVET, or HR, $Fs(1,11) < 1.85$, $ps > .20$.

*Crossinstrument Agreement*

*Pearson's r.* Correlations between devices were consistently large during both sitting and standing, as were correlations for the change scores (Table 5).

*Intraclass correlation coefficient.* Intraclass correlations were also large for sitting and standing ($\rho s > .94$, $ps < .005$), as well as for change scores ($\rho = .67$ to .96, $ps < .05$) (Table 5).

*Internal Reliability*

Cronbach's coefficient $\alpha$ revealed high internal consistency in the orthostatic domain for both devices; $\alpha s = .91$ to .99 for the Minnesota ZCG and .96 to .99 for the AZCG (Table 6).

## Results

### *Psychological Stressors*

*Comparison of Devices*

Cell means and standard errors for the MANOVA are given in Table 4. The psychological stressors resulted in increased HR, $F(1,11) = 36.98$, $p < .001$, and CO, $F(1,11) = 7.52$, $p = .019$, with decreases in PEP, $F(1,11) = 17.21$, $p = .002$, LVET, $F(1,11) = 29.05$, $p < .001$, SV, $F(1,11) = 18.87$, $p = .001$, and $Z_0$, $F(1,11) = 5.84$, $p = .034$.

Comparison of the devices revealed significant Device main effects for LVET, SV, CO, and $Z_0$, $Fs(1,11) \geq 7.90$, $ps < .02$. $Z_0$

**Table 5.** *Study 2: Pearson's and Intraclass Correlation Coefficients between AZCG and ZCG for Orthostatic and Psychological Domains*

| Domains | HR | PEP | LVET | SV | CO | $Z_0$ |
|---|---|---|---|---|---|---|
| Orthostatic Domain | | | | | | |
| Pearson *r* | | | | | | |
| Sit | .99** | .99** | .99** | .98** | .97** | .99** |
| Stand | .98** | .99** | .97** | .99** | .99** | .99** |
| Change | .88** | .94** | .95** | .94** | .86** | .93** |
| Intraclass correlations | | | | | | |
| Sit | .99** | .99** | .99** | .94** | .97** | .99** |
| Stand | .99** | .99** | .98** | .99** | .97** | .98** |
| Change | .93** | .91** | .96** | .83** | .67* | .96** |
| Psychological Domain | | | | | | |
| Pearson *r* | | | | | | |
| Rest | .98** | .98** | .98** | .99** | .99** | .99** |
| Task | .95** | .96** | .98** | .99** | .98** | .99** |
| Change | .80** | .84** | .62* | .51* | .73** | .64* |
| Intraclass correlations | | | | | | |
| Rest | .99** | .99** | .99** | .99** | .98** | .99** |
| Task | .99** | .98** | .99** | .99** | .98** | .98** |
| Change | .90** | .85** | .66* | .58* | .77* | .75* |

*Note:* ZCG = Minnesota Impedance Cardiograph; AZCG = Ambulatory Impedance Cardiograph; HR = heart rate; PEP = preejection period; LVET = left-ventricular ejection time; SV = stroke volume; CO = cardiac output; $Z_0$ = basal thoracic impedance.
*p < .05, one-tailed. ** p < .01, one-tailed.

**Table 6.** *Study 2: Cronbach's Coefficient Alphas for AZCG and ZCG on Each Cardiovascular Variable*

| | AZCG | | ZCG | |
|---|---|---|---|---|
| Variable | Ortho | Psychol | Ortho | Psychol |
| HR | .98 | .97 | .99 | .98 |
| PEP | .98 | .95 | .98 | .94 |
| LVET | .96 | .99 | .95 | .99 |
| SV | .97 | .99 | .91 | .99 |
| CO | .99 | .99 | .98 | .99 |
| $Z_0$ | .99 | .99 | .99 | .99 |

*Note:* Ortho = Orthostatic stress; Psychol = Psychological stress; AZCG = Ambulatory Impedance Cardiograph; ZCG = Minnesota Impedance Cardiograph; HR = heart rate; PEP = preejection period; LVET = left-ventricular ejection time; SV = stroke volume; CO = cardiac output; $Z_0$ = basal thoracic impedance.

values were larger for the AZCG than for the Minnesota ZCG, whereas values for LVET, SV, and CO were smaller. The devices did not differ for HR, $F(1,11) = 3.8$, $p = .08$, or PEP, $F(1,11) = 1.97$, $p = .19$. The MANOVA, however, revealed no significant Device × Period interactions for SV, $F(1,11) = 3.73$, $p = .08$, or for CO, $Z_0$, PEP, LVET, or HR, $Fs(1,11) \leq 1.63$, $ps > .22$.

*Crossinstrument Agreement*

*Pearson's r.* The correlations were high and statistically significant for all six measures during rest and task periods (Table 5). For the change scores, correlations for were high for HR, PEP, and CO and moderate for LVET, SV, and $Z_0$.

*Intraclass correlation coefficient.* The intraclass correlation coefficients were high, $\rho s > .98$, $ps < .005$, for all measures during both rest and tasks (Table 5). Change scores had moderate-to-large values, $\rho s = .58$ to $.90$, $ps < .05$.

*Internal Reliability*

Cronbach's $\alpha$s revealed very high internal reliability during the psychological tasks for both devices; $\alpha s = .94$ to $.99$ for the Minnesota ZCG and .95 to .99 for the AZCG (Table 6).

## General Discussion

The two studies examined reliability and validity of a new AZCG against the Minnesota ZCG for the measurements of SV, CO, HR, PEP, LVET, and $Z_0$. We examined the validity of the AZCG by performing successive measurements with both devices, using the Minnesota ZCG as the reference device. In Study 1, estimates of cardiac function generated using the AZCG were nearly identical to those produced by the Minnesota ZCG after controlling for device test order and baseline HR. The AZCG and Minnesota ZCG tracked changes nearly identically across behavioral conditions, suggesting that measurements of HR, SV, CO, PEP, and LVET using the AZCG are valid as referenced to the Minnesota ZCG.

Study 2 obtained similar results with minor between-device differences. The AZCG values were similar to those of the Minnesota ZCG for HR, SV, and CO during orthostasis, and of PEP and HR during the psychological tasks. However, the devices differed during orthostasis in PEP, LVET, and $Z_0$ and during psychological tasks in SV, CO, LVET, and $Z_0$. The internal dZ/dt signal from the AZCG used in Study 2 was noisier than the comparable Minnesota ZCG signal, affecting the resolution of variables depending on landmarks taken from this signal. The device difference in PEP orthostasis, although significant, reflects a difference of less than one pixel in the placement of the B-point using our detection algorithm, and probably reflects the difficulty in detecting the proper point in the AZCG dZ/dt signal. The same problem would be expected in placing the X-point, and this was the case for LVET during both orthostasis and psychological tasks. The magnitude of these effects was quite small, however, and did not interact with conditions. Thus, although some variables differed in absolute levels, the AZCG faithfully tracked changes across conditions.

Additionally, Study 2 found a greater $Z_0$ of about 0.7 ohms for the AZCG during both stressors, suggesting a small calibration difference. The greater $Z_0$, in turn, produced smaller stress values for SV and CO. Correction of this calibration difference should mitigate these differences in SV and CO. Again, the absence of Period × Device interactions suggests little discrepancy in the ability of the AZCG to track across conditions relative to the Minnesota ZCG.

Reliability refers to measurement error reflected in variation over replications of the same operations (Cliff, 1993). Internal reliability of the AZCG was estimated using Cronbach's coefficient $\alpha$, and crossinstrument reliability was estimated by Pearson's $r$ (Shrout & Fleiss, 1979). Cronbach's $\alpha$s were very high in both studies for both devices, with the internal reliability of the AZCG being equal to or greater than that of the Minnesota ZCG. The Pearson $r$s as well as the intraclass correlations indicate a high degree of crossinstrument reliability. The similarity of results from both laboratories is noteworthy given differences in subject samples, experimental protocols, and signal processing procedures. Together, the results of both studies indicate that crossinstrument reliability of the AZCG is excellent relative to the Minnesota ZCG.

The present data may be contrasted with those reported using another ambulatory ZCG device, the VU-AMD (Willemsen et al., 1996). The VU-AMD was compared with a Nihon Koden bedside monitor across several behavioral conditions with signals derived simultaneously from a four-spot electrode system using the current source from the bedside device. Although crossinstrument Pearson $r$ values were acceptably high (.75–.86 for SV), the absolute values for SV and CO from the VU-AMD differed significantly. The VU-AMD device used an A-D conversion rate of 250 Hz and the dZ/dt signal was generated directly from the raw $\Delta Z$ signal. In the present study, signals were digitized off-line at 500 Hz. The use of band electrodes with the new ambulatory device needs to be evaluated for esthetic acceptability in the ambulatory environment, as the upper band electrode is difficult to cover with normal clothing.

The validity and reliability of the AZCG is only as good as its reference method. The validity and reliability of the Minnesota device has been established previously by comparing its estimates of SV, CO, and systolic time intervals with those obtained by invasive and noninvasive reference methods (e.g., Ebert et al., 1984; Muzi et al., 1985; Wilson, Sung, Pincomb, & Lovallo, 1989). The reliability of the Minnesota ZCG to track cardiac function within and between sessions is considered excellent (Pincomb et al., 1985; Sherwood et al., 1990). A 1998 Medline search of papers that addressed the validity of impedance cardiography yielded 44 articles, and of these, 26 concluded that ZCG correlated well with the SV and/or CO measurements obtained by indicator dilution, echocardiography, or the Fick method (Pearson $r$s often exceeding .82). Nevertheless, ZCG estimates of SV and CO are considered by some to be poor in research or clinical practice (Jensen, Yakimets, & Teo, 1995). In contrast to this view, a meta-analysis found ZCG estimates of CO to be moderately good in healthy persons or in patients not in intensive care, with Pearson *r*s of .82, .83, and .80 for thermodilution, dye dilution, and Fick, respectively (Fuller, 1992). In general, such evaluations have found greater agreement between ZCG estimates and an external standard when group data are being compared, and have found lower levels of agreement when individual data are the device of analysis. This suggests that ZCG is presently better suited to research applications on grouped data than to clinical applications where absolute values for individual patients may be desired.

The use of successive comparisons between devices may provide some insight into the performance of the AZCG. Because we tested the devices successively rather than simultaneously, we recognized that an inevitable degree of measurement error may have occurred that was not due to a true difference between devices. Using HR as the benchmark for correcting this source of error in Study 1, we found that the devices agreed well in absolute estimates of the cardiovascular parameters of interest and tracked comparably across conditions. Although successive measurements may have allowed the participants to become less anxious with repetition of the protocol, the data indicate very similar responses across repetitions.

Our use of small samples in both studies could call into question our conclusion that the devices are comparable, because the likelihood of making an incorrect no-difference conclusion (Type II error) increases when sample size and $\alpha$ are both small (Cook & Campbell, 1979). To address this concern, we carried out a power analysis using the Pearson-Hartley power charts (Pearson & Hartley, 1951). With an $\alpha$ of .05, 10 subjects per cell, and a medium-to-large effect size of at least .75, statistical power of the design for Study 1 was at least .96 (Cohen, 1988). When the effect size estimate was reduced to .60, statistical power of the Study 1 design was .85. Power analyses for Study 2 yielded comparable estimates. This power evaluation, therefore, mitigates concern about false data of a Type II error. Although the small sample sizes may leave lingering concerns about statistical power, the comparable findings of the two studies lend further credence to our conclusion that the new AZCG performs the same as the standard Minnesota device.

The exclusive use of males in the sample for Study 1 may decrease the generalizability of the results. Men and women differ in cardiovascular reactivity to short-term behavioral stressors (e.g., Girdler, Turner, Sherwood, & Light, 1990; Lash, Gillespie, Eisler, & Southard, 1991; Lawler, Wilcox, & Anderson, 1995; Saab, 1989), and the sample used in Study 1 may not be adequate to draw conclusions regarding women. Although Study 2 used both male and female subjects, additional work needs to be done to replicate and extend the generalizability of the results, especially to the elderly and children. In addition, application of ZCG is generally less complex in healthy, nonobese males and females that constituted the present samples. Therefore, the present results should not be generalized to other groups without further tests. Additional studies employing more heterogeneous subject samples as well as other tasks that elicit differing patterns of hemodynamic reactivity (e.g., movement tasks) would strengthen the generalizability of the current findings for the AZCG.

The ultimate use of the AZCG is to obtain cardiac activity data outside the laboratory. The present laboratory-based test was a necessary first step in the validation process. Future studies will be needed to establish the AZCG's limits in a truly ambulatory environment.

In conclusion, the AZCG seems to be valid and reliable for measuring stroke volume, cardiac output, heart rate, and systolic time intervals at rest and during behavioral challenge. The findings from the current studies indicate that in the laboratory, the AZCG performs as well as the standard Minnesota Impedance Cardiograph Model 304B. Additional studies are needed to establish how well the AZCG performs in the field. This new ambulatory thoracic impedance monitor could permit psychophysiological research outside the laboratory in real-life settings.

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