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Committee Report

Methodological Guidelines for Impedance Cardiography

ANDREW SHERWOOD (CHAIR), *University of North Carolina;* MICHAEL T. ALLEN, *University of Southern Mississippi;* JOCHEN FAHRENBERG, *University of Freiburg, FRG;* ROBERT M. KELSEY, *State University of New York at Buffalo;* WILLIAM R. LOVALLO, *Oklahoma City Veterans Administration Medical Center and University of Oklahoma Health Sciences Center;* AND LORENZ J.P. VAN DOORNEN, *Free University of Amsterdam*

ABSTRACT

Impedance cardiography was introduced over 20 years ago as a noninvasive and unobtrusive technique for measuring systolic time intervals and cardiac output. Although our understanding of the physiological events reflected in the impedance cardiogram has become more refined, the technique's theoretical basis remains somewhat controversial and acceptance of its validity has relied heavily upon empirical validation. Largely as a consequence of this status, there have been inadequate grounds on which to develop sound methodological standardization. Currently, the methodological approaches that have been most frequently adopted may be viewed as representing the standard. The various aspects of impedance methodology are discussed, and alternative approaches described, with the objective of providing an informed basis for choosing among these methodological alternatives. It is recommended that studies utilizing impedance cardiography should be reported with clear and detailed methodological description. This should help clarify the extent to which methodological differences may underlie any discrepant research observations, as well as facilitate the emergence of improved methodological standards.

DESCRIPTORS: Impedance cardiography, Impedance plethysmography, Cardiac output, Stroke volume, Pre-ejection period, Left-ventricular ejection time, Heather Index.

Scope and Purpose

It is now more than ten years since the publication in *Psychophysiology* of Miller and Horvath's (1978) methodological critique of impedance cardiography. Since that time impedance cardiography has been used increasingly by psychophysiologists to monitor the mechanical functions of the heart. Many of the conclusions drawn by Miller and Horvath remain valid, because the fundamental principles underlying the technique remain essentially unchanged. Impedance methodology has, however, changed somewhat since 1978: a wider variety of impedance cardiographs has become commercially available, alternative recording-electrode configurations have been proposed, innovations in signal processing have been made, and new equations for the computation of cardiac function indices have been derived. As a result there is less standardization in the application of impedance cardiography at present than there was twelve years ago.

Lack of methodological standardization in impedance cardiography may contribute to discrepant research findings. The purpose of the present report is not to impose standardization by setting forth rules and regulations governing the use of impedance cardiography. Rather, it is to provide information regarding the various aspects of imped-

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Address requests for reprints to either: Andrew Sherwood, Department of Psychiatry, CB #7175, Medical Research Bldg A, University of North Carolina, Chapel Hill, NC 27599-7175, USA; or Jochen Fahrenberg, University of Freiburg, Forschungsgruppe Psychophysiologie, Belfortstrasse 20, Freiburg D-7800, FRG.

ance methodology that should be considered in utilizing the technique. Solid recommendations will be made only where there are sufficient logical or empirical grounds. Awareness of alternative approaches should emphasize the importance of reporting methodological detail in studies employing the impedance technique. This should help clarify those aspects of discrepant research findings that are likely to stem from methodological differences and perhaps, in the long-term, help permit future standardization.

Impedance cardiography is most widely recognized as a noninvasive technique for the measurement of cardiac output. Stroke volume is the actual parameter derived from measurements of thoracic electrical impedance changes, and cardiac output is computed as the product of heart rate and stroke volume. Other useful indices of cardiac function available from impedance measurement include systolic time intervals (pre-ejection period and left-ventricular ejection time) and a unique index of myocardial contractility, the Heather Index. Discussion of the methodological aspects of impedance cardiography relevant to the derivation of these flow, volume, and contractility indices forms the primary objective of this paper. Some evidence is available that ejection fraction, end-diastolic volume, and end-systolic volume can be derived from the impedance cardiogram (Judy, Hall, & Elliot, 1982; Gastfriend, Van De Water, Leonard, Macko, & Lynch, 1986), but these presently remain highly controversial measures and are therefore considered to be beyond the scope of this paper.

Impedance cardiography can be considered to fall under the more general category of impedance plethysmography, referring to the measurement of volume (and thereby flow) changes in the body, derived from changes in electrical impedance. Although thoracic blood volume changes are the specific concern of impedance cardiography, peripheral vascular blood volume and flow changes can also be measured using documented impedance plethysmographic techniques (see Jennings, Tahmoush, & Redmond, 1980). However, the present paper will focus exclusively on impedance cardiography, and thus events due to thoracic blood volume changes relating to myocardial performance.

Theoretical Overview of the Development of Impedance Cardiography

Many of the methodological problems to be addressed relate to the origin of the impedance cardiogram, so a brief overview of basic principles seems appropriate, especially for readers unfamiliar with the technique. However, it is recommended that for a thorough description of underlying theory, readers should consult texts by Nyboer (1959), Kubicek, Witsoe, Patterson, and From (1969), Mohapatra (1981), and Lamberts, Visser, and Zijlstra (1984). There are also a number of excellent review papers that are highly recommended (Miller & Horvath, 1978; Goldstein, Cannon, Zimlichman, & Keiser, 1986; Porter & Swain, 1987). These reference sources also provide comprehensive reviews of studies that have attempted to assess the validity of impedance cardiography as a noninvasive measurement of cardiac mechanical function, by comparison with simultaneous measurements utilizing more established invasive procedures.

As a measurement technique, impedance cardiography is generally viewed as a noninvasive methodology for measuring cardiac output. This objective is approached by the estimation of stroke volume based upon principles stemming from the relationship that exists between voltage and resistance in an electrical circuit:

$$V = I \cdot R$$

where R is resistance, V is voltage, and I is current. In a circuit with I held constant, V varies in direct proportion to R. Because blood is a conductor, each increase in thoracic blood volume following a heartbeat produces an interpretable change in thoracic resistance. Impedance cardiograph systems induce a constant magnitude, alternating current field along the thorax, measure impedance[1] (Z) changes occurring with each heartbeat (ΔZ), and provide an output voltage that can be interpreted as reflecting stroke volume.

After considerable development, building on the work of earlier investigators, Kubicek, Karnegis, Patterson, Witsoe, and Mattson (1966) proposed what has now become the most widely used formula for determining stroke volume:

$$SV = rho_b (L/Z_0)^2 \cdot LVET \cdot dZ/dt_{(max)}$$

where SV is stroke volume (ml), rho_b is the resistivity of blood (ohm·cm), L is the distance between the recording electrodes (cm), Z_0 is the baseline impedance between the recording electrodes (ohm), LVET is left-ventricular ejection time (seconds), and $dZ/dt_{(max)}$ is the absolute value of the maximum

[1]The term impedance applies to alternating current, whereas resistance applies to direct current. Although direct current presents a biological hazard, the 4 mA alternating current in the frequency range 20–100 kHz used in impedance cardiography does not. If no inductive or capacitive elements are contained in the system, impedance is equal to the resistance. Human tissue is known to be mainly resistive at 20–100 kHz (Mohapatra, 1981, p. 10).

rate of change (slope) in the impedance waveform on a given beat (ohm/second). The derivation of the Kubicek formula for stroke volume permits a description of the theory underlying impedance measurements. The interested reader is referred to the Appendix, where an overview of the historical development of the Kubicek equation is given.

Among early impedance cardiography researchers the question arose as to whether thoracic impedance varied as a function of left-ventricular ejection, right-ventricular ejection, or both. It is now known that the current lines produced by impedance recording systems are oriented along the length of the thorax. Decreases in impedance on each heartbeat reflect increased volume of the great vessels oriented along the current lines. The aorta is so oriented, and so impedance changes reflect aortic flow. The right ventricle empties into the pulmonary arteries, which are at right angles to the current field. Kubicek et al. (1967), using electromagnetic flowmeters in a dog preparation, demonstrated that aortic rather than pulmonary blood flow was responsible for the characteristic cardiac-related pulsatile changes in thoracic impedance. Lamberts et al. (1984, pp. 94–106) summarize studies addressing this point. It is concluded that ΔZ varies with blood flow from the left ventricle.

One limitation of the Kubicek equation concerns the assumed constancy of rho (resistivity of blood) over a cardiac cycle. In fact rho varies over a cardiac cycle because the aggregate resistive value for a group of red blood cells varies with their orientation. Red cells are randomly oriented when still but are aligned when flowing. Their orientation therefore varies as they undergo a pulsatile acceleration-deceleration on each heartbeat. Because rho varies, the right side of the Kubicek equation is affected to some degree by the unwanted influence of changing red cell orientation. Lamberts et al. (1984, pp. 76–94) have reported a series of studies of the effects of erythrocyte orientation on impedance changes using a rigid cylindrical tube model of an artery, as well as in vivo dog experiments. The results of their work indicated that ΔZ and thus dZ/dt in part reflect changes in red cell orientation and led these authors to conclude that it is incorrect to regard impedance cardiography as a plethysmographic method. This viewpoint illustrates the continuing controversy surrounding the theoretical basis of impedance cardiography.

An additional consideration in making impedance measurements of stroke volume and cardiac output is that the technique works well only for normal hearts. Persons with valve defects or cardiac shunts will yield impedance cardiograms that may not be amenable to interpretation using the equations described. Therefore, when stroke volume is to be measured, the technique is valid only for persons with structurally normal hearts.

Instrumentation

Impedance Cardiographs

The most widely used commercially-available impedance cardiograph is the Minnesota Impedance Cardiograph Model 304 B (Surcom Inc., Minneapolis, MN, USA; IFM Inc., Greenwich, CT, USA). This model utilizes a 4 mA constant current source with 100 kHz oscillator frequency and includes an LED display of basal thoracic impedance (Z_0), with electrical outputs of Z_0, ΔZ, and dZ/dt. The Minnesota Model 304 B also includes separate inputs for electrocardiogram (ECG) and phonocardiogram (heart sounds), with filtering and amplification of these signals prior to their output.

There are a number of other impedance cardiographs commercially available (e.g., the NCCOM-3 Cardiovascular Monitor, Medex Inc., Hilliard, OH, USA; the Tetrapolar High Resolution Impedance Meter (THRIM), UFI Inc., Morro Bay, CA, USA). As with the Minnesota instrument, most of these devices simply provide a means of recording the impedance waveforms, leaving derivation of cardiac function to some means of external signal processing. However, some impedance cardiographs may incorporate on-board microprocessors for real-time computation of cardiac function (e.g., the NCCOM-3). In the latter case it is important to consider whether automatic processing of the signal is appropriate for the intended application (e.g., adequate artifact rejection for monitoring during physical exercise) and whether electrical outputs of raw Z_0, ΔZ, and dZ/dt signals are available, should the option to perform external processing be required.

An alternative to commercially manufactured instruments is to develop and build an impedance monitoring system. Mohapatra (1981) has outlined basic considerations in the design of an impedance cardiograph; of these, safety aspects should be paramount. Regardless of whether a custom-built or commercially manufactured impedance cardiograph is used, the responsible investigator should make absolutely sure that the instrument satisfies the strictest safety standards. As well as obvious considerations such as subject isolation from any high voltage power supply and measures to prevent possible mix-up of the instrument's inputs and outputs, frequency and magnitude of excitation current are also critical. The recommended frequency range is 20–100 kHz at a current of 1–5 mA. High input impedance for the recording electrode

amplifier is also necessary. For a detailed example, Qu, Zhang, Webster, and Tompkins (1986) provide a description that includes the circuit diagram of their custom-built system. In reporting impedance-derived cardiovascular data, methodological description should include the make and model number (where appropriate), the excitation current and frequency, signal filtering characteristics, and the voltage electrode input impedance of the impedance cardiograph employed in the study.

Calibration of the impedance cardiograph is necessary for quantification of subjects' Z_0 (ohm) and dZ/dt (ohm/second) signals. The Minnesota Model 304 B, which is equipped with internal calibration circuitry, provides a good example of an appropriate means of instrument calibration: for Z_0, a 25.5 ohm precision resistor (1% tolerance, metal film) is used to provide a voltage output (as well as a front panel LED numerical display) corresponding to 25.5 ohm, and a zero ohm calibration level is produced from a 0 ohm resistance (shorted input). For dZ/dt, internal circuitry generates a pulsatile ΔZ calibration signal (also available as a separate 0.1 ohm ΔZ calibration output), which is characterized by an ascending voltage ramp that corresponds to a precise impedance change of 1 ohm/second. This signal is passed through the instrument's differentiation circuitry to generate the dZ/dt calibration signal (see Figure 2), in which the 0 ohm/second and 1 ohm/second calibration levels are clearly represented as plateaus. Precise instrument calibration sources of this kind, which are passed through the same amplification and processing circuitry as the subject signal, are essential requirements for an impedance cardiograph. The investigator is strongly advised to check the quality and design of the calibration functions on the impedance cardiograph to be used, and to consult with an engineer if necessary, to ensure acceptable consistency with the guidelines described above.

Accurate calibration is a fundamental determinant of the absolute magnitude of computed stroke volume and cardiac output measures. It is therefore of critical importance if these measures are to be compared from one session, or one subject, or one study to another, when different impedance cardiographs may be used. An ideal means of standardizing calibration would be through the use of some external calibration source, available to all investigators and applicable to all instruments. Using the instrument in its operate mode, a precision resistor of known value can be attached to the subject cables (in place of a subject) and Z_0 calibration accuracy thereby checked. Furthermore, by using a resistance decade box (e.g., Decade Resistor, General Radio Co., Concord, MA, USA) in this way, a series of precise resistance values can be applied and the linearity of Z_0 measurement evaluated. This procedure is recommended as a routine check because it provides an effective test of all components, including possible defects in the subject-electrode cables, which are not tested by internal Z_0 calibration. Unfortunately, such a simple procedure is not available for dZ/dt calibration, because the subject cables would need to be attached to a resistance that was known to fluctuate at a precise rate, preferably in the 1 ohm/second range. Construction of such a device would require ingenuity as well as technical competence and only the thorough methodologist may be inclined to undertake this task. All investigators are, however, again urged to ensure that calibration of their impedance cardiographs is accomplished as accurately as possible. Where custom-built, or relatively rare impedance cardiographs are utilized, it is recommended that calibration procedures should be clearly described in research reports.

Impedance Electrode Configurations

Band Electrodes. In introducing impedance cardiography Kubicek et al. (1966) described a tetrapolar band electrode system. This type of electrode configuration has since been adopted in the majority of studies utilizing the impedance technique for monitoring cardiovascular function. The outer two electrodes serve to introduce the high frequency excitation current, and are usually referred to as the current electrodes. The surface potential, which is proportional to impedance, is measured across the inner two voltage electrodes.

Commercially-manufactured Mylar band electrodes have been most often used in the acquisition of impedance signals (e.g., Electrode Tape No. M6001, Contact Products Inc., Dallas, TX, USA; also available from IFM Inc., Greenwich, CT, USA). These typically consist of disposable strips of adhesive tape, approximately 2.5 cm wide, which have a thin strip (approximately 0.6 cm wide) of aluminum-coated Mylar, forming the electrode along the center of the tape. Use of an electrode gel to facilitate skin contact conduction is optional, but may be advisable on subjects who have substantial body hair at the sites of contact. If a gel is to be used, it is recommended that either one intended for use with ECG electrodes or an ultrasonic transmission gel be used. It has previously been suggested that regardless of whether a gel is used, a 10-minute period should be allowed to lapse prior to the onset of impedance measurements for contact resistance to fall and stabilize (Mohapatra, 1981).

The placement of the four band electrodes most frequently reported in the literature is illustrated in

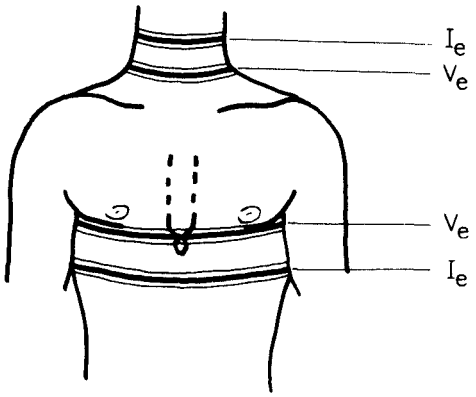

Figure 1. Band electrode placements most typically reported, with voltage electrodes (V_e) located around the base of the neck and around the chest at the level of the xiphisternal junction. Current electrodes (I_e) are located at least 3 cm distal to each voltage electrode.

Figure 1. The upper voltage electrode is placed around the base of the neck and the lower voltage electrode around the thorax at the level of the xiphisternal junction. These electrode sites are at easily identifiable anatomical landmarks and thereby provide a means of standardizing electrode placements across individuals. In studies involving repeated measurements over two or more experimental sessions, the voltage electrodes should be placed in the same location on each occasion, especially if stroke volume and cardiac output values are to be compared. The Kubicek stroke volume equation includes a constant (L) for the distance between voltage electrodes. L is usually computed as the mean distance (cm) between the inner edges of the voltage electrodes, measured at the front (over the sternum) and at the back (over the spine). Lamberts et al. (1984) observed that variation of the distance between voltage electrodes causes a substantial change in values of ΔZ and computed $dZ/dt_{(max)}$. They suggest that a standardized average distance of 22 cm should be used, whereby the distance may be 20 cm at the anterior side and 24 cm at the back, or the converse of this. However, this procedure will often interfere with the basic rule for positioning electrodes at the xiphisternal junction. In studies incorporating multiple testing sessions, replication of initial voltage electrode distances for a given subject is a useful means of checking placement consistency. An important assumption in the computation of stroke volume is that there should be a uniform distribution of excitation current density over the voltage electrodes. Mohapatra (1981, pp. 24–29) presents data showing that the outer current electrodes should be placed at locations where there is **at least** a 3 cm separation from the voltage electrodes in order to meet this assumption and thereby generate reproducible stroke volume values. Abiding by this rule, the usual placement of current electrode bands (as shown in Figure 1) is around the upper part of the neck and around the lower region of the rib-cage, in each case with approximately 3 cm separation from the adjacent voltage electrode.

All four band electrodes are normally placed circumferentially around the respective body segments, though successful use of half-band electrodes has been reported (Watanabe, Kamide, Torii, & Ochiai, 1981). Band electrodes should not be applied with too much tension, because this can lead to subjects experiencing distress associated with either a choking sensation or impairment of normal breathing. Subjects should be asked to inspire deeply, to fully expand the chest, during chest electrode application.

Deviations from the band electrode placements described above have been reported. In their original recommendation, Kubicek et al. (1966) suggested that the lower voltage electrode should be placed 2 cm below the xiphisternal junction. On many individuals this would approximate placement over the xiphoid process, an anatomical landmark that has been used for lower voltage electrode location in a number of studies (e.g., Edmunds, Godfrey, & Tooley, 1982; Miyamoto et al., 1983; Veigl & Judy, 1983; Ferrigno, Hickey, Liner, & Lundgren, 1986). Placement of the lower voltage electrode affects Z_0 and $dZ/dt_{(max)}$ as well as L (Boer, Roos, Geyskes, & Mees, 1979; Mohapatra, 1981, pp. 29–30). The effects on $dZ/dt_{(max)}$ are more pronounced for variations in placement of the lower voltage electrode above the xiphisternal junction than below, but generally, using the Kubicek equation, the lower the placement the greater will be the computed stroke volume. Because, as will be discussed later, relative changes in impedance derived volume and flow-rate measures are of greater validity than absolute levels, the preceding point primarily emphasizes the importance of consistent placement if reapplication of electrodes is necessary for repeated measurement sessions. However, in view of evidence that variations in surface impedance reflect variations in blood content of proximal organs and vessels (Sakamoto, Muto, Kanai, & Iizuka, 1979), placement of the lower voltage electrode over the xiphisternal junction may be preferable to lower placement if it is assumed that focus on the heart and aorta is the objective of impedance measurements pertaining to stroke volume calculation. For the current electrodes some investigators have reported placement of the upper electrode across the forehead, which can be very practical for subjects

with short necks. As long as the ***at least 3 cm*** rule is observed there are no solid grounds for a preferable placement recommendation and the consistency guideline alone is advised.

Spot Electrodes. As previously mentioned, band electrodes are sometimes experienced as being distressful or annoying. In addition to this problem, it is sometimes difficult to use band electrodes for clinical applications. For example, in patients with chest burns or patients with incisions and dressings following thoracic surgery, band electrodes would be inappropriate. For these reasons several investigators have explored the use of spot electrodes in impedance cardiography. Standard disposable ECG electrodes can be used, making the spot electrode approach inexpensive. Contact surface area is much smaller for spot electrodes than for band electrodes, so careful preparation of the site of application should be ensured. Cleansing the skin with an alcohol pad is recommended, followed by preparation of the electrode contact site with an abrasive ECG electrode gel. Where necessary, excessive body hair should be removed.

Penney, Patwardhan, and Wheeler (1985) described a four spot electrode configuration using pediatric ECG electrodes (#H8019-160350, Bard Biomedical, Lombard, IL). Two electrodes were placed at (and parallel to) the base of the neck, separated by 6 cm and centered about the prominence of the seventh cervical vertebra (C_7). The other two electrodes were placed on the left anteriolateral chest surface: one at the end of the ninth intercostal space, near the mid-clavicular line; and the other 8 cm from the first, in the tenth intercostal space, near the mid-axillary line. The current electrodes were on the right of the neck and over the ninth intercostal space, with the remaining two electrodes used as the voltage electrodes. Penney et al. (1985) recorded an impedance cardiogram from this spot electrode array while simultaneously recording the impedance cardiogram from subjects also instrumented with conventionally placed band electrodes (using a special two-channel impedance cardiograph). Good correspondence between the two techniques was found in terms of the general shapes and heights of recorded dZ/dt signals. However, stroke volumes computed using the Kubicek equation sometimes showed considerable discrepancy, and the authors concluded that although the relative change in stroke volumes may be equally reliable as for band electrodes, absolute stroke volume measures may be less accurate using spot electrodes.

Qu et al. (1986) proposed a new four-spot electrode array which they found to improve signal-to-noise ratio, thereby minimizing effects of motion artifact. In their configuration, using pregelled ECG electrodes (No. 047860, The Burdick Division of KONE Instruments Inc., Milton, WI, USA), one current electrode is placed on the back of the neck over the fourth cervical vertebra (C_4), and the other on the back over the ninth thoracic vertebra (T_9). One voltage electrode is placed on the front of the neck, 4 cm above the clavicle, and the other over the sternum at the fourth rib. In a study comparing cardiac output during treadmill exercise, the impedance derived values obtained using this spot electrode configuration showed a high correlation (r=.90, n=78) with those determined using the carbon dioxide (CO_2) rebreathing technique for measuring cardiac output (Zhang, Qu, Webster, Tompkins, Ward, & Bassett, 1986). Values derived from impedance signals recorded using the conventional band electrode configuration showed a slightly higher correlation (r=.96, n=76), although with modification in the $dZ/dt_{(max)}$ value (see later section on computation of stroke volume) entered into the Kubicek equation, the spot electrode cardiac output measures showed an improved correspondence with CO_2 rebreathing measures (r=.95, n=78).

A spot electrode configuration incorporating eight electrodes has been reported in studies that have utilized a commercially available cardiac output monitor based upon the impedance technique (NCCOM-3, Medex Inc., Hilliard, OH, USA). This configuration, which is recommended in the instructions accompanying the aforementioned instrument, is a tetrapolar arrangement that utilizes pairs of electrodes and bears a resemblance to the conventional band electrode configuration. One pair of voltage electrodes is placed as close as possible to the clavicles at the lateral aspect of the base of the neck. The lower pair of voltage electrodes is placed perpendicular to the longitudinal plane of the sternum, lateral to the xiphoid process in the mid-axillary line. The current electrodes are placed parallel to the voltage electrodes, with the upper pair 5 cm above the neck voltage electrodes and the lower pair 5 cm below the thoracic voltage electrodes. Using this electrode configuration in conjunction with the NCCOM-3, and computing stroke volume using the Sramek-Bernstein equation (Bernstein, 1986a; see section on computation of stroke volume), good correspondence with invasive cardiac output measures has been reported. For example, Bernstein (1986b) reported a significant correlation (r=.88, n=94) between impedance derived cardiac output values and those determined invasively using thermodilution in a group of 17 critically ill patients. Similar results were reported in another study of 16 critically ill patients where impedance and thermodilution cardiac outputs

were compared ($r=.83$, $n=391$), with the presence of cardiac function abnormalities in some of the patients leading the authors to consider the study as an evaluation of impedance cardiography in the worst possible situations (Appel, Kram, MacKabee, Fleming, & Shoemaker, 1986). These authors then repeated the statistical analysis after removal of the data from 5 patients with the poorest quality impedance signals, and found that the correlation between cardiac output measures rose to .90 ($n=285$) and that the average difference between absolute values was 11% ($\pm 8.9\%$).

The studies described above suggest that spot electrodes provide a viable alternative to band electrodes in impedance cardiography. In addition to the greater convenience of spot electrodes, there is evidence to suggest that when placed in certain anatomical locations, spot electrodes may permit recording of an impedance cardiogram that is less prone to problematic movement artifact (Qu et al., 1986). However, at the time of writing there is insufficient evidence to recommend which, if any, of the spot electrode recording techniques may be the best alternative to the band electrode approach. Also, given that the Kubicek stroke volume equation was arranged around a band electrode configuration, its application to signals recorded using spot electrodes (where Z_0 values are typically much lower and electrode-skin-resistance is more critical) may lead to diverse stroke volume values. Nevertheless, spot electrodes may provide equivalent accuracy for the measurement of systolic time intervals and relative changes in stroke volume. Future studies are required to resolve these issues. In the interim, it is stressed that when reporting studies using spot electrodes, precise anatomical locations for each electrode position should be described, particularly if a novel configuration is adopted. Similar descriptions and citation of appropriate references should be included in studies utilizing previously reported spot electrode configurations.

Electrocardiogram (ECG) and Phonocardiogram (PCG)

The ECG record serves two purposes in impedance cardiography. The first is for the measurement of heart rate, regarding which the reader is referred to an earlier publication guideline appearing in this journal (Jennings et al., 1981). The second is for the identification of the onset of electromechanical systole (see ECG Q-wave in Figure 2). Both purposes require primarily a clear recording of the QRS complex, which can usually be obtained using lead II or a precordial lead electrode configuration. An ECG can also be obtained from the electrodes used to record the impedance signals, with some commercially produced impedance cardiographs providing amplification and electrical output of the ECG obtained in this way. However, the quality of the QRS complex may not be adequate for all subjects using the latter approach, particularly with respect to the onset of the Q-wave. In general, it is recommended that following instrumentation, a display of the ECG should be obtained (e.g., using a polygraph or oscilloscope) and appropriate adjustments in recording electrodes should be made where necessary to obtain a good QRS complex.

Recording of the phonocardiogram (PCG; first and second heart sounds; see Figure 2) can provide useful backup information for the measurement of systolic time intervals, particularly in individuals from whom poor quality impedance signals are obtained (see following section on waveform component identification). Illustrating the usefulness of the PCG in impedance cardiography, the Minnesota Model 304 B Impedance Cardiograph, for example, provides an input, amplification, and some electronic filtering for the PCG signal. The heart sounds microphone (e.g., Narco Biosystems 705-0016; Hewlett Packard 21050 A) should be placed over the upper part of the precordium in a position providing optimal recordings of the initial high frequency oscillations of the aortic component of the second heart sound (Weissler, 1977). The second heart sound is associated with closure of the aortic (semilunar) valves and is an accepted marker for the completion of left-ventricular ejection. However, the more prolonged first heart sound is generated by a number of cardiac systolic events and although onset of left-ventricular ejection is thought to be represented in its late phase, it is not widely viewed as providing a reliable marker of this event. For a more detailed description of their origin, as well as sites of auscultation of the various heart sounds, the reader is referred to Guyton (1981, Ch. 27) and Rushmer (1976, Ch. 11).

Analysis of the Impedance Cardiogram

Waveform Component Identification

An example of the waveforms normally requiring some form of graphical representation for the analysis of data acquired using impedance cardiography (ECG, dZ/dt, and PCG) is illustrated in Figure 2. It is normally not necessary to record ΔZ if the Kubicek stroke volume equation is to be adopted, because all the pertinent information required is available from the dZ/dt signal. The value of Z_0 during any given measurement period is required, but because this tends to show large intersubject variability and relatively little intrasubject variability it is difficult to display graphically a

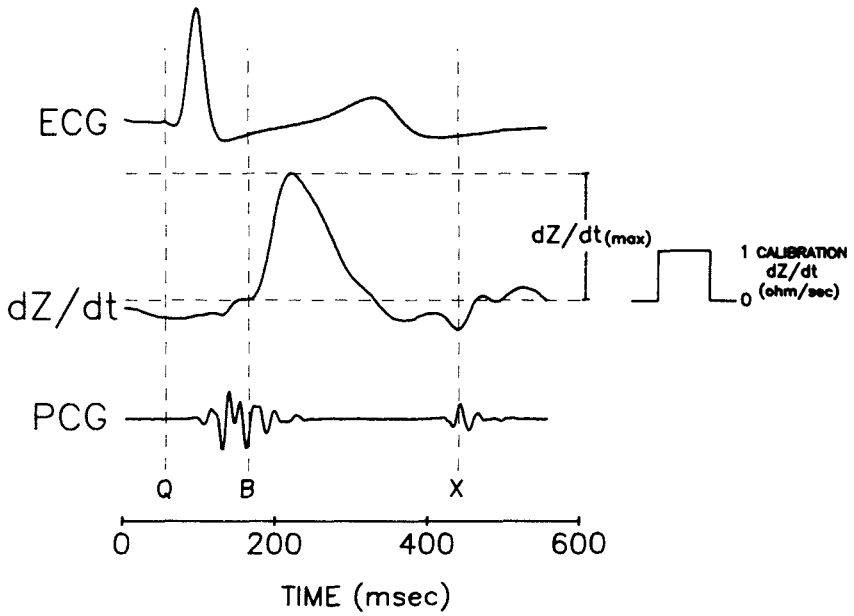

Figure 2. Electrocardiogram (ECG), first derivative of the pulsatile thoracic impedance signal (dZ/dt), and phonocardiogram (PCG) recorded during electromechanical systole of a cardiac cycle. Waveform components depicted are the ECG Q-wave (Q), dZ/dt B-point (B), and dZ/dt X-point (X). The $dZ/dt_{(max)}$ amplitude measure is also illustrated (Note: In this case the absolute magnitude of $dZ/dt_{(max)}$, relative to $dZ/dt=0$, also corresponds to its magnitude relative to the dZ/dt B-point).

meaningful record of Z_0. If computer processing of the impedance cardiograph signal outputs is not an option to the investigator, most impedance cardiographs provide a numeric display of Z_0 which can be recorded manually.

Figure 2 shows the points that are normally identified from the impedance cardiogram in order to derive the various indices of cardiac function. The impedance cardiogram shown in Figure 2 presents no difficulty for the identification of these various waveform components. However, the clarity of the impedance cardiogram for purposes of waveform analysis varies markedly across individuals (DeSouza & Panerai, 1981). As for most noninvasive physiological recording, signal quality tends to be poor in obese individuals. Also, because the dZ/dt signal is affected by both respiration and movement, signal quality may deteriorate with an increase in physical activity. The following guidelines are provided for identification of waveform components.

Q denotes the onset of the ECG Q-wave and represents the onset of electromechanical systole. Identification of this point normally presents little problem. However, even after trying several ECG electrode placements it may be difficult to identify a clearly defined Q-wave in some individuals. In such cases it may be necessary to focus upon the onset of the R-wave as an approximation of the onset of electromechanical systole.

B denotes the dZ/dt B-point that occurs at the onset of the rapid upslope of dZ/dt as it rises to its peak value ($dZ/dt_{(max)}$). The B-point is used to indicate the time of onset of left-ventricular ejection. Lababidi, Ehmke, Durnin, Leaverton, and Lauer (1970) originally reported that the B-point corresponded with the maximum deflection of the first heart sound, when recorded over the apex of the heart. This evidence would suggest that the B-point is proximally associated with the onset of isovolumic contraction, following closure of the atrioventricular (A-V) valves, an event that precedes the onset of left-ventricular ejection by an interval of .02 to .06 seconds. However, more recent and compelling evidence indicates temporal correspondence of the B-point with the onset of left-ventricular ejection, as shown from simultaneous recordings of the impedance cardiogram with echocardiography (Petrovick, Kizakevich, Stacy, & Haak, 1980; Stern, Wolf, & Belz, 1985) and carotid pulse tracings (Sheps, Petrovick, Kizakevich, Wolfe, & Craige, 1982). Most researchers involved with impedance cardiography now consider the B-point as the best approximation of the onset of left-ventricular ejection.

During breath-holding, or end-expiratory apnea, the B-point typically falls on the $dZ/dt=0$ axis.

This has led some investigators to use the dZ/dt = 0 crossing point prior to $dZ/dt_{(max)}$ to denote onset of left-ventricular ejection (e.g., Rasmussen, Sorensen, & Kahn, 1975). However, the B-point may consistently fall above dZ/dt = 0 in some individuals (Lamberts et al., 1984, pp. 115–116). Another criterion for identification of the onset of ejection, suggested by Kubicek, Patterson, and Witsoe (1970), is the point on the ascending limb of the dZ/dt as it reaches 15% of the $dZ/dt_{(max)}$ value. However, as Mohapatra (1981, p. 82) has illustrated, a fixed dZ/dt amplitude criterion does not take account of the fact that respiratory influences cause baseline shifts in the dZ/dt signal. Therefore, the dZ/dt = 0 and $.15(dZ/dt_{(max)})$ criteria may not provide reliable demarcation of the onset of left-ventricular ejection on all cardiac cycles, unless adjustments for baseline variations are made[2].

Identification of the B-point may present difficulty in some cases. Although it is often easily recognized as an incisura at the foot of the ascending limb of the $dZ/dt_{(max)}$ point, as shown in Figure 2, the B-point is not always so well defined. In the experience of the present authors, accurate identification of the onset of left-ventricular ejection from the dZ/dt waveform, due to ambiguity in the location of the B-point, presents the most frequent problem in analyzing the impedance cardiogram[3]. Siegel et al. (1970) have described how myocardial contractility changes can affect the form of the dZ/dt signal and the consequent appearance of the B-point. Using an experimental protocol that included intravenous administration of norepinephrine and isoproteronol in dogs, they found that when beta-adrenergic influences on the myocardium were low there were two detectable inflexion points, one of which was the B-point, near the dZ/dt upstroke. However, when beta-adrenergic influences were high there was a single inflexion point, corresponding to the B-point, which occurred lower on the dZ/dt curve. In either case, the point associated with the final rise of dZ/dt toward its peak corresponded

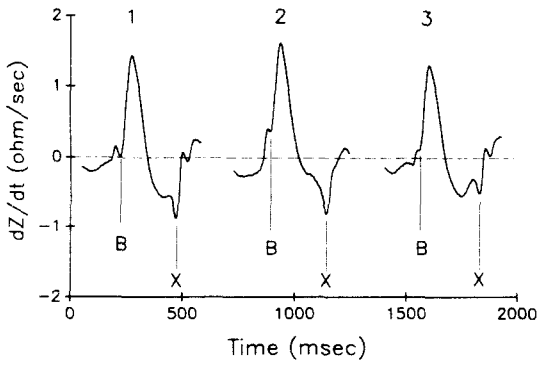

Figure 3. Three examples of variations in the morphology of the dZ/dt waveform, with the B-point and X-point identified in each case. In Example 1, the B-point takes the form of a well-defined incisura close to dZ/dt = 0 crossing. In Example 2, the B-point remains in the form of an incisura but occurs well above the dZ/dt = 0 baseline. In Example 3, the B-point is identified as a change in slope of the ascending limb of the dZ/dt waveform. In all three examples the B-point corresponds to the initiation of the rapid upslope of dZ/dt as it ascends toward $dZ/dt_{(max)}$.

to the onset of left-ventricular ejection. Therefore, as a general guideline, the B-point should be conceived as the initiation of the rapid upstroke of the dZ/dt signal as it rises toward $dZ/dt_{(max)}$. However, rather than appearing as a clear incisura, the B-point may sometimes take the form of a subtle inflexion and may vary considerably from beat to beat, emphasizing the need for a good visual record of the dZ/dt signal in order to identify it. Figure 3 illustrates some examples of variations in the ascending limb of the dZ/dt waveform which still provide a recognizable B-point, in each case corresponding to the initiation of the rapid change in dZ/dt as it rises toward $dZ/dt_{(max)}$. As a further guideline, the B-point, in whatever form, normally falls at, or close to, the dZ/dt = 0 axis, though it may occur somewhat above or slightly below it. Occasionally, there is simply no clearly identifiable point that can be chosen to fit the preceding description of the B-point. In such instances the point of dZ/dt = 0 crossing may be appropriate. Where there remains some ambiguity, reference to the maximum deflection of the first heart sound may be a helpful guide, remembering that this point corresponds most closely with closure of the A-V valves and therefore precedes aortic valve opening.

X denotes the lowest point in the dZ/dt waveform. It is usually seen as a sharp notch as shown in Figures 2 and 3, which corresponds with the second heart sound (S_2) and represents closure of the aortic valve at the end of left-ventricular ejection (Petrovick et al., 1980; Sheps et al., 1982). Most individuals exhibit a well defined X-point,

[2]Foerster, at the University of Freiburg, and a colleague of one of the present authors (Fahrenberg), has developed a computerized analysis strategy, which utilizes an interbeat-interval-dependent high-pass filtering to control for baseline variation with frequencies below the heart rate (e.g., respiration).

[3]One of the present authors (van Doornen) recommends using the second or third derivative of dZ/dt for identifying the onset of left-ventricular ejection. The purpose of this strategy is to permit accurate and objective identification of the point of strongest increase in acceleration of the rising limb of the dZ/dt waveform, which is then designated as the B-point.

with the lowest point easily recognized. Occasionally, however, in some individuals there may be two or more waveforms in close proximity, and this presents some difficulty in distinguishing the appropriate point associated with aortic valve closure. In other individuals there may be complete absence of a recognizable X-point. Such problems tend to arise in about 10% of individuals tested. In these cases the second heart sound of the phonocardiogram may be used to identify correctly the completion of left-ventricular ejection.

$dZ/dt_{(max)}$ represents the maximum rate of change occurring in the ΔZ waveform and is identified as the peak value in the dZ/dt signal, within a given cardiac cycle, following the QRS complex of the ECG. (Note: As discussed in the Appendix, $dZ/dt_{(max)}$ is actually the peak negative rate of change in ΔZ; hence the often used $dZ/dt_{(min)}$ notation.) Animal experiments have shown $dZ/dt_{(max)}$ to occur at approximately the same point in time as peak blood flow in the ascending aorta (Kubicek et al., 1974). Noise due to electrode movement or skeletal muscle activity that exceeds in amplitude the true $dZ/dt_{(max)}$ point is easily recognizable as such from visual examination. The $dZ/dt_{(max)}$ value is usually taken as the absolute value of $dZ/dt_{(max)}$, relative to the $dZ/dt=0$ baseline. However, it may be more appropriate, as Mohapatra (1981, p. 82) has suggested, to define the magnitude of $dZ/dt_{(max)}$ relative to the B-point, as illustrated in Figure 3. The rationale for this approach is to nullify the effects of extraneous factors on the dZ/dt signal and thereby isolate and measure the peak of the primary waveform (Doerr, Miles, & Bassett Frey, 1981). Nonetheless, the majority of studies evaluating impedance cardiography as a measure of cardiac output have incorporated the absolute value of $dZ/dt_{(max)}$ in the Kubicek stroke volume equation, so its measurement from the $dZ/dt=0$ baseline would be the more conservative standard approach.

The value of $dZ/dt_{(max)}$ has been found to be related in magnitude to peak aortic blood flow velocity (Witsoe, Patterson, From, & Kubicek, 1969; Kubicek et al., 1974). Corrected for basal thoracic impedance (i.e. $dZ/dt_{(max)}/Z_0$) it has been recommended as a useful index of blood ejection velocity which may be compared across individuals (Bernstein, 1986a). More studies are needed to provide empirical validation of the best definition of $dZ/dt_{(max)}$ for use in the computation of stroke volume. In the interim, it may be helpful for authors to describe their means of measuring $dZ/dt_{(max)}$ in the methodological description of studies utilizing impedance cardiography.

Sampling and Processing Strategies

The simplest approach to recording the impedance cardiogram is to use a chart recorder. To facilitate systolic time interval measurement, the ECG, dZ/dt, and PCG signals should be displayed on adjacent channels. The Z_0 value shows relatively little change (approximately 0.3 ohm) relative to its overall magnitude (typical range 15–35 ohm using band electrodes) and is less appropriate for chart display. However, the Z_0 value is required for entry in the Kubicek stroke volume equation, so it may be read from the impedance cardiograph LED display and manually noted on the chart record. As shown in Figure 1, a dZ/dt calibration signal of 1 ohm/second should be recorded to permit measurement of $dZ/dt_{(max)}$ amplitude on this channel. Using a paper-feed speed of 100 mm/second the waveform components described in the preceding section of this paper should be identifiable. The systolic time intervals, stroke volume, and other indices of cardiac function, as described in the next section, can be manually derived for each cardiac cycle from the chart records.

Because the dZ/dt signal is prone to respiratory and movement artifact, analysis of only artifact-free cardiac cycles as a basis for the derivation of cardiac function is one approach to waveform sampling. Cardiac cycles recorded during periods when the subject is relatively motionless can be selected to avoid the problem of movement artifact. The problem of respiratory artifact has been approached by requiring subjects to hold their breath, either at peak inspiration, or more usually at end expiration, while several cardiac cycles are recorded (e.g., Judy et al., 1969; Denniston et al., 1976; Hill & Merrifield, 1976; Kobayashi et al., 1978; Ebert, Eckberg, Vetrovec, & Cowley, 1984). Although this strategy circumvents the problem of respiratory artifact, it has been argued that cardiac function changes in association with the phases of respiration and selective sampling of one phase will not necessarily provide information representative of normal breathing (Pigott & Spodick, 1971; Andersen & Vik-Mo, 1984). Hence, DuQuesnay, Stoute, and Hughson (1987) found that during exercise, correlations of cardiac output with oxygen consumption were higher during normal breathing (.91) than for end-expiratory (.86) or end-inspiratory (.83) breath hold, and that absolute values for stroke volume were significantly lower for breath hold than for normal breathing. Furthermore, the breath-holding strategy may be distracting to subjects and thereby be unacceptable if measurements are required during performance on some attention demanding

task. The primary concern with respiratory artifact has been distortions of the dZ/dt signal in the amplitude domain, thereby confounding the absolute value of $dZ/dt_{(max)}$ and leading to error in computed stroke volumes. One solution suggested by Doerr et al. (1981) is to adopt the strategy of measuring $dZ/dt_{(max)}$ relative to the B-point (see section, present paper, on Waveform Component Identification) and averaging values over multiple cardiac cycles encompassing one or more respiratory cycles.

In view of the preceding considerations there is good reason to expect that increasing the sample size and averaging is likely to improve the reliability of measurements derived from the impedance cardiogram. With manual analysis, averaging cardiac cycles occurring over at least one full respiratory cycle is recommended as a minimum, with averaging over three or four preferable. DeSouza and Panerai (1981) recommend averaging approximately 60 cardiac cycles to produce a reliable averaged waveform. However, from a practical standpoint, the manual analysis of large numbers of cardiac cycles from chart records tends to be tedious, laborious, and time consuming. Computers can provide valuable assistance in this respect. Bassett Frey (1982) has reported one such approach which involves analysis of chart records using a computer peripheral "digitizer" which is manually moved over the relevant points on the impedance cardiogram. The temporal location and amplitude of waveform components are transmitted in this way to the computer which is programmed to subsequently derive the various indices of cardiac function. However, computers can also be used to replace entirely the need for chart records through on-line digitization and video display of waveforms, with operator controlled interactive graphics or automatic algorithms for the detection of waveform components (e.g., see Foerster, 1984).

A computer technique involving "ensemble averaging" of multiple cardiac cycles was first applied to impedance cardiography for the measurement of systolic time intervals, where its validity has been well documented (Kizakevich, Gollan, & McDermott, 1976; Gollan, Kizakevich, & McDermott, 1978; Petrovick et al., 1980; Sheps et al., 1982). Ensemble averaging of the impedance cardiogram involves detecting the peak of the R-wave of the electrocardiogram and using it as a reference point for averaging both the ECG and dZ/dt signals over a number of cardiac cycles. The R-wave is a consistent and easily detectable event (ventricular depolarization) occurring in the early part of systole and, in a healthy heart under steady-state conditions, other electrical and mechanical events in the cardiac cycle will tend to take place at the same relative temporal location with respect to it. Consequently, contributions to the dZ/dt signal originating from the heart will be superimposed on each other and become clearly defined in the waveform that is ensemble averaged in this way over multiple cardiac cycles. In contrast, respiratory influences, which are of lower frequency, and movement artifact, occurring randomly, will not be reinforced by ensemble averaging synchronized to the ECG R-wave, and will therefore be effectively filtered out. These artifact removal effects have made possible the recording of impedance signals of adequate fidelity for analysis during physical exercise.

Ensemble averaging of the impedance cardiogram has also been applied to the measurement of stroke volume and cardiac output during exercise as well as other active behavioral states (Miyamoto et al., 1981; Miyamoto et al., 1982; Miyamoto et al., 1983; Muzi et al., 1985; Muzi, Jeutter, & Smith, 1986; Sherwood, Allen, Obrist, & Langer, 1986). Computer software based on the ensemble averaging technique usually incorporates algorithms for automatic detection of relevant waveform components and equations for the automatic derivation of the various indices of cardiac function. However, reliance on such automatic processing is not recommended, because the overall form and quality of the impedance cardiogram shows substantial variability across individuals and automatic waveform component detection is unlikely to be reliable in all instances. One solution to this problem is to create or use existing software that permits inspection and interactive graphics editing facilities in order to confirm visually adequate signal quality. A computer-based system permitting interactive-graphics editing of individual cardiac cycles has been available commercially for a number of years (Impedance Cardiogram Microcomputer Model 7000, Surcom Inc., Minneapolis, MN, USA). More recently, IBM-PC compatible software, adopting the ensemble averaging technique, has become available commercially from at least two sources (e.g., HDC Company, Mesa, AZ, USA, and IFM Inc., Greenwich, CT, USA).

One criticism of the ensemble averaging approach is that cardiac cycles that may include large magnitude artifacts will be averaged into the ensemble averaged waveform, thereby introducing artifact into the averaged waveform used for analysis. This is primarily a problem for amplitude dependent measures such as $dZ/dt_{(max)}$, and some means of software-based artifact rejection may improve reliability. Despite these potential sources of

error, systolic time interval and cardiac output measures during exercise have been found to correspond well with standard techniques (Miyamoto et al., 1981; Sheps et al., 1982; Muzi et al., 1985). However, the steady-state conditions of controlled dynamic exercise may be particularly suited to impedance cardiogram processing by ensemble averaging. Under non-steady-state conditions there may be variations in beat-by-beat cardiac performance which may lead to some variability in the temporal location of waveform components relative to the R-wave over the cardiac cycles averaged. Variability in the temporal location of $dZ/dt_{(max)}$ would lead to an attenuated $dZ/dt_{(max)}$ representation in the ensemble averaged impedance cardiogram, and consequently an underestimation error would occur in the computation of stroke volume. For events used only for time interval derivation, such as the dZ/dt X-point, the presence of beat-by-beat temporal variability is less of a problem because the ensemble averaged representation of the temporal location of all waveform components will correspond to the average as represented by the modal time of occurrence. In view of these considerations it has been suggested that using the arithmetic mean of beat-by-beat determinations of $dZ/dt_{(max)}$ and ensemble averaging for the measurement of systolic time intervals may be the optimal approach to computer processing of the impedance cardiogram for reliable assessment of cardiac output under a wide range of behavioral states (Sherwood, Allen, Hutcheson, & Obrist, 1986). Ensemble averaging techniques could also be useful for analyzing the still largely unexplained late wave components that some authors have attempted to characterize in a very preliminary way (e.g., Lababidi et al., 1970; Sheps et al., 1982; Lamberts et al., 1984). However, for this purpose, such averaging should be done for each respiratory phase separately.

Indices of Cardiovascular Function and their Derivation

Systolic Time Intervals. Electromechanical systole is the time interval from the onset of electrical depolarization of the ventricles to the completion of ejection of blood from the left ventricle. Accordingly, it may be measured using impedance cardiography as the interval from the onset of the Q-wave of the ECG to the X-point of the dZ/dt waveform. Electromechanical systole may be subdivided into various component time intervals, including isovolumic contraction time, pre-ejection period (PEP), and left-ventricular ejection time (LVET). The latter two can be readily derived from the impedance cardiogram. PEP is the interval from the onset of the ECG Q-wave to the onset of left-ventricular ejection, as defined by the dZ/dt B-point. LVET is measured as the interval from the B-point to the X-point of the dZ/dt waveform.

Systolic time interval measures have attained prominence as indices of myocardial performance (Balasubramanian, Mathew, Behl, Tewari, & Hoon, 1978; Lewis, Rittgers, Forester, & Boudoulas, 1977), and impedance cardiographic techniques offer clear advantages over traditional noninvasive techniques for determining these measures. Traditional techniques employ ECG, peripheral pulse, and phonocardiographic signals, whereas impedance cardiographic techniques require only the dZ/dt signal and an ECG signal. In addition to its greater simplicity, the impedance method appears less vulnerable to the noise and movement artifacts that plague the traditional methods (Balasubramanian et al., 1978; Colin & Timbal, 1982; Gollan et al., 1978; Sheps et al., 1982). Furthermore, estimates of pre-ejection period (PEP) based on impedance cardiographic techniques should incorporate less measurement error than those based on traditional noninvasive techniques. Pre-ejection period is estimated indirectly with the traditional methods by subtracting left-ventricular ejection time (LVET) from electromechanical systole (EMS) (Lewis et al., 1977), thus combining the measurement error associated with the detection of four waveform points (the ECG Q-wave and the second heart sound for EMS, and the upstroke and dicrotic notch of a peripheral pulse wave for LVET). In contrast, the impedance method yields a more direct estimate of PEP which combines the measurement error associated with only two waveform points (the ECG Q-wave and dZ/dt B-point).

The measurement of PEP is particularly important in psychophysiological research because it is inversely related to myocardial contractility and is interpreted by many researchers as a sensitive index of beta-adrenergic influences on the heart (Ahmed, Levinson, Schwartz, & Ettinger, 1972; Cousineau, de Champlain, & Lapointe, 1978; Harris, Schoenfeld, & Weissler, 1967; Martin, Shaver, Thompson, Reddy, & Leonard, 1971; McCubbin, Richardson, Langer, Kizer, & Obrist, 1983; Newlin & Levenson, 1979; Obrist, Light, James, & Strogatz, 1987; Siegel et al.,1970), although evidence of parasympathetic innervation of the ventricles and possible vagal-sympathetic interactions influencing left-ventricular function should not be assumed as insignificant (see e.g., Stratton, Pfeifer, & Halter, 1987). PEP corresponds closely to isovolumic contraction time, the critical period associated with the generation of contractile force in the left ventricle (Harris et al., 1967; Martin et al., 1971; Siegel et al., 1970). Furthermore, the data relating isovolumic contraction

time to PEP suggest that an abbreviated PEP, calculated as the interval between the ECG R-wave and the dZ/dt B-point, may suffice as a measure of myocardial contractility. It is important, however, to consider the effects of preload and afterload when using PEP as an index of beta-adrenergic influences on the myocardium. Hence, increases in preload will lead to increased contractility via the heterometric autoregulatory mechanism of Starling's Law and produce decreases in PEP, independent of sympathetic influences, whereas increased peripheral vascular resistance will raise afterload and thereby tend to lengthen PEP. Although loading effects on PEP may not be especially significant under conditions commonly employed in psychophysiological research (Newlin & Levenson, 1979; Obrist et al., 1987), investigators should be alert to possible errors of interpretation due to potential loading effects and these effects should be assessed at least indirectly by evaluating PEP in the context of concurrent changes in (a) heart rate and blood pressure (see Obrist et al., 1987), or (b) electromechanical systole (see Lewis et al., 1977; McCubbin et al., 1983). Increased beta-adrenergic activation may be inferred tentatively when decreases in PEP are accompanied by increases in heart rate and blood pressure, or decreases in electromechanical systole, although precise statements concerning these relationships cannot be given at present. In line with these considerations the ratio of pre-ejection period to left-ventricular ejection time (PEP/LVET ratio) has been proposed as a sensitive index of left-ventricular function which is self-correcting for heart rate variations (Weissler, 1977; Weissler, Harris, & Schoenfeld, 1969). Moreover, a strong inverse relationship between the PEP/LVET ratio and ejection fraction has been demonstrated (Garrard, Weissler, & Dodge, 1970).

The discussion of PEP/LVET ratio and, generally, the standardization of systolic time intervals (STI's) to "correct" for heart rate dependencies occupies much space in the STI literature (e.g., List, Gravenstein, & Spodick, 1980). There have been various suggestions as to how to obtain optimal transformations, acknowledging various contributing factors such as ranges of heart rate and sex of subject, but such statistical adjustments have failed in cross-validation studies (Kesteloot, 1980; Mantysaari, Antila, & Peltonen, 1984). The rationale for such corrections remains very questionable on hemodynamic as well as statistical grounds, so the use of uncorrected PEP and LVET scores is sometimes recommended. Depending on the given research question, relations between STI's and heart rate (as well as other relevant parameters) should be dealt with in a physiologically and conceptually explicit manner; furthermore, the incremental contributions or redundancy of each parameter in empirical predictions (as, for example, in discriminating experimental conditions or groups) should be evaluated, thus avoiding standard, but possibly irrelevant, "correction formulas."

A further index of myocardial contractility that is unique to impedance cardiography was suggested by Heather (1969). The Heather Index (HI) is defined as $dZ/dt_{(max)}$ divided by the time interval between the ECG Q-wave and the occurrence of $dZ/dt_{(max)}$. Its postulated sensitivity to changes in contractility is based upon the strategy of combining the estimate of peak ejection velocity ($dZ/dt_{(max)}$) with the electromechanical time interval (Q–Z interval) for its accomplishment. However, as previously noted, it has been suggested that $dZ/dt_{(max)}$ should be corrected for Z_0 to provide accurate information about ejection velocity (Bernstein, 1986a; Djordjevich & Sadove, 1981). Accordingly, it has been suggested that this correction should be extended to the Heather Index, producing a revised contractility index calculated as the ratio of $dZ/dt_{(max)}$ to Z_0, divided by the Q–Z interval (Kelsey, Guethlein, Eichler, Blascovich, & Katkin, 1987).

Stroke Volume and Cardiac Output. As described in the theoretical overview of impedance cardiography, the most widely used equation for estimating left-ventricular stroke volume is that originally suggested by Kubicek et al. (1966):

$$SV = rho \cdot (L/Z_0)^2 \cdot LVET \cdot dZ/dt_{(max)}$$

All of the elements in this equation, with the exception of rho, have been defined in earlier sections of the present paper. In their original description of the above equation, Kubicek et al. (1966) recommended using a fixed value for rho of 150 ohm·cm, the average electrical resistivity of blood at 100 kHz. It has been argued, however, that because the computed stroke volume will be directly proportional to the value of rho used in the Kubicek equation, serious error may be introduced through the use of inappropriate rho values. The relationship between blood resistivity and hematocrit (Hct) has been evaluated by bench experiments measuring the resistivity of blood samples of varying hematocrits (Geddes & Sadler, 1973; Hill & Thompson, 1975; Mohapatra & Hill, 1975; Mohapatra, Costeloe, & Hill, 1977). From the results of these studies several equations are available for estimating the appropriate rho value based upon hematocrit, which can be determined by centrifuging a small blood sample. The general finding was that blood resistivity varies as a curvilinear function of hematocrit, with resistivity increasing as hematocrit rises. Mohapatra (1981, pp. 97–99) concluded

that individual blood resistivity estimates computed by an appropriate equation (e.g., rho (ohm·cm) = 67.919 exp(0.0247 Hct)) should improve the accuracy of stroke volumes derived using the Kubicek equation.

In a more recent study the relationship of hematocrit to resistivity was evaluated in vivo (Quail, Traugott, Porges, & White, 1981). This was accomplished by recording the impedance cardiogram in conscious dogs (N=7) in which electromagnetic flow probes had been surgically implanted around the aortic root. Blood hematocrit was experimentally manipulated between 26% and 66% and resistivity was derived by rearranging the Kubicek equation to make rho the subject of the equation and entering the stroke volume values measured from the electromagnetic flow probes. The results of this compelling study were in contrast to those reported by the bench experiments, with rho remaining relatively constant at an average value of 135 ohm·cm across the entire range of hematocrits tested. The authors suggested that changes in blood flow velocity in addition to volume changes in the thorax probably contribute to impedance changes, accounting for the discrepancy with the assumptions of the Kubicek equation in view of the rho-hematocrit relationship established by the bench experiments (see Lamberts et al. (1984) for further evidence regarding flow velocity, blood cell orientation, and electrical impedance). These findings, which have been replicated in other animals including man (Traugott, Quail, & White, 1981), indicate that a constant for rho of 135 ohm·cm may be assumed for use in the Kubicek equation when there are no grounds on which to expect the subject's hematocrit to be abnormal.

The study described above illustrates the empirical nature of impedance cardiography as a technique for estimating stroke volume and cardiac output. In other words, unlike traditional invasive techniques, which are based on better understood theoretical principles, the impedance technique has relied heavily on cross-validation studies with these traditional techniques in gaining credibility. For an overview of the numerous validation studies that have been reported, the reader is referred to Kubicek et al. (1969), Mohapatra (1981), Lamberts et al. (1984), Miller and Horvath (1978), Goldstein et al. (1986), and Porter and Swain (1987).

The criteria by which validity is judged may vary with the application to which the method is put. Validity for a diagnostic measurement may require a small absolute error in individual cases because each person's data may determine the individual's diagnosis and course of treatment. For research involving group comparisons, the standard for validation may be based on an acceptably low percent error for an entire group. In this case validity is judged according to the technique's ability to permit accurate inferences based on grouped data. Ultimately, the validity of impedance measurement of stroke volume rests on the extent of agreement obtained between impedance measurements and those obtained by another (reference) method. In considering a reference method for determining cardiac output it must be borne in mind that each method, however well grounded on a physical model, has its own problems in specific application. The primary traditional methods for determining cardiac output are direct and indirect application of the Fick method, indicator dilution methods (e.g., thermal or dye dilution), echocardiography, and nuclear ventriculography. A recent review of 23 studies reporting comparison of impedance measurement of stroke volume or cardiac output against one of the reference methods is summarized in Table 1. Approximately half of these (11 of 23) found impedance to correlate very well with a reference method, yielding r values $>.90$. As expected, the correlations are better for Fick than for indicator dilutions, suggesting that the more precise the reference method, the stronger the correlation. This degree of agreement between impedance and other methods compares favorably with that found when the reference methods are compared with each other. A recent study (Christie, Sheldahl, Tristani, Sagar, Ptacin, & Wann, 1987) found that cardiac output by thermal dilution correlated significantly with Doppler and two-dimensional echocardiography (r's = .78 and .88, respectively). Similar correlations were found between the Fick method and echocardiography (r's = .81 and .90, respectively).

Most validation studies have judged impedance cardiography against the standards applied to clinical measurements. These standards require that

Table 1

Impedance cardiography compared with other methods

Correlations by Subsets of Studies Reviewed			Correlations for Each Reference Method		
Subsets by r range	N	Avg. r	Method	N	Avg. r
.49–.97	23	.79	Fick	5	.89
.90–.97	11	.93	Dilution	16	.81
.80–.89	6	.84	Flow Probe	1	.92
.49–.79	6	.65	NVG	1	.82

Note. Fick refers to direct (n=3) or indirect (n=2) application of the Fick principle. Dilution refers to dye dilution (n=13), thermal dilution (n=2), or I131 dilution (n=1). NVG refers to nuclear ventriculography. Data are limited to studies on humans having hearts without shunts or valvular defects.

the method be accurate against a standard and that large errors occur only in an acceptably small number of individual cases. Using these standards, most authors have concluded that impedance cardiographic measurements accurately follow changes in stroke volume or cardiac output, but that they produce unacceptably high (>10%) errors in individual cases. In most research applications data are treated as representing a mean of a group of observations and inferences are made about groups, not individuals. For grouped comparisons impedance measurements of stroke volume have generally been found to approximate the reference standards very well (error ranges 0–9%), although the general finding has been that impedance cardiography tends to overestimate stroke volume. In view of the continuing controversy surrounding the validity of absolute measures for stroke volume and cardiac output, it may be appropriate to refer to these measures as "estimates" or "equivalents." Relative change measures for stroke volume and cardiac output are, as Miller and Horvath (1978) concluded, still viewed as being more reliable than absolute values. It is recommended to use within-subject designs and methods of analysis appropriate for repeated measurements data (Huitema, 1980; Plewis, 1985; Rogosa, Brandt, & Zimowski, 1982; Stemmler & Fahrenberg, in press) whenever research hypotheses allow for this approach.

Cardiac output and stroke volume measurements are often reported in the scientific and clinical literature as cardiac index (CI) and stroke volume index (SVI) respectively. Conversion to these indices is accomplished by simply dividing individual cardiac output and stroke volume measures by body surface area (BSA), which can be estimated on the basis of height and weight (e.g., BSA (m^2) = Weight (kg)$^{0.425}$ · Height (cm)$^{0.725}$ · 0.007184), yielding units of liter/min/m^2 for cardiac index and ml/m^2 for stroke volume index. These conversions serve to standardize the measurements for variations in body size, because cardiac output and stroke volume increase approximately in proportion to body surface area. Therefore, computation of cardiac index and stroke volume index is especially appropriate where comparisons of absolute values for cardiac output and stroke volume are to be made across individuals, or groups of individuals, who may differ in body size. These standardized indices may be computed for impedance cardiographic data. However, as mentioned earlier, the comparison across individuals of relative changes, rather than absolute values, is the recommended strategy for analyzing cardiac output and stroke volume measures derived using impedance cardiography.

One issue that has been addressed regarding stroke volume index determined by impedance cardiography is the possibility that sex differences may emerge due to differences in the impedance measures entered in the Kubicek stroke volume equation. Females have been shown to exhibit generally higher values for transthoracic basal impedance (Z_0), possibly associated with differences in muscle/fat ratio due to the presence of breast tissue (Frey, Doerr, & Miles, 1982). Because Z_0 is a squared denominator in the Kubicek equation, this raised some concern regarding possible underestimation of stroke volume in women. However, in a subsequent study, which replicated the observation of higher Z_0 values in women, it was also found that women showed generally higher $dZ/dt_{(max)}$ values, which are incorporated as a numerator in the equation (McKinney, Buell, & Elliot, 1984). As a result, it was shown in the latter study that calculated stroke volume index did not differ across the sexes.

Alternatives to the Kubicek Equation for Computing Stroke Volume. In view of the general acceptance of impedance cardiography as a reliable means of tracking relative changes in stroke volume, it would seem feasible that a modified equation may make possible some improvement in the reliability of absolute stroke volume measures. Bernstein (1986a) has provided a detailed description, which includes the underlying theoretical rationale, of one such equation, originally conceived by Sramek (Sramek, 1981; Sramek, Rose, & Miyamoto, 1983). Unlike the Kubicek equation, which uses a cylindrical model of the thorax, the Sramek-Bernstein approach views the thorax as a volume conductor that is geometrically similar to a frustum, or truncated cone. Secondly, based upon results, including those of Quail et al. (1981) noted earlier, which suggest that blood resistivity is not a significant independent variable in the derivation of stroke volume, the rho value is eliminated. Thirdly, rather than incorporate the distance between electrodes as an intersubject variable contributing to the absolute stroke volume values derived, the Sramek equation uses a percentage of body height (17%) mathematically adjusted to estimate ideal body weight, which is normally directly proportional to cardiac output. These changes lead to the replacement of rho and L in the Kubicek equation by (0.17 · Height)^3/4.2 in the modified equation, which Bernstein (1986a) has argued should provide a more accurate estimate of the volume of electrically participating thoracic tissue in a given individual. Finally, Bernstein (1986a) has suggested the inclusion of a body habitus correction factor, delta, which is computed on the basis of the ratio of observed to ideal body weight multiplied by the

"relative blood volume index," which adjusts for blood volume variations associated with deviations from ideal body weight. Hence, the complete Sramek-Bernstein stroke volume equation is:

$$SV = \text{delta} \cdot (0.17\ \text{Height})^3/4.2 \cdot \text{LVET} \cdot dZ/dt_{(max)}/Z_0$$

As an alternative to the computation of delta in the above equation, which requires reference to an estimate of blood volume based upon studies by Feldschuh and Enson (1977) and Messerli, Christie, and DeCarvaiho (1981), a nomogram for determining a corrected L value based on height and weight has been published by Bernstein (1986a).

There has been some encouraging empirical support for the Sramek-Bernstein equation, but of limited quantity (see section on Spot Electrodes, this paper, for a summary of results reported by Bernstein (1986b) and Appel et al. (1986), who compared cardiac outputs in critically ill patients measured simultaneously by impedance cardiography using the Sramek-Bernstein equation and by thermodilution). Less favorable findings were recently reported by De Mey and Enterling (1988) who found that the Kubicek and Sramek equations did not show agreement in the magnitude of stroke volume responses to upright tilt. In addition, the Sramek equation was found to overestimate absolute stroke volume values to an even greater extent than the Kubicek equation, so the latter authors were unable to conclude that the Sramek equation represents an improvement over the Kubicek equation. However, at this point in time, whether the Sramek-Bernstein equation will provide a new and more accurate standard in impedance cardiography will be determined only by the availability of more validation data. In contrast, the sizeable literature on the experimental and clinical evaluation of the Kubicek stroke volume equation, already in existence, provides a clearer definition of its strengths and limitations.

Total Peripheral Resistance of the Systemic Vasculature (TPR). Blood pressure is the product of cardiac output and total peripheral resistance (BP = CO×TPR, where BP is mean arterial pressure, which may be estimated as diastolic pressure plus one third pulse pressure). Hence, a change in blood pressure may reflect a change in cardiac output, total peripheral resistance, or both. The determination of cardiac output using impedance cardiography, with simultaneous measurement of blood pressure, permits the derivation of total peripheral resistance (TPR = BP/CO) and therefore provides access to the hemodynamic basis of blood pressure changes.

Total peripheral resistance is normally presented in units of dyne-seconds·cm^{-5} which is computed by multiplying BP/CO by 80; i.e.

$$\text{TPR (dyne-seconds·cm}^{-5}) = [\text{mean BP (mmHg)} / \text{CO (liters/min)}] \cdot 80$$

Alternatively, peripheral resistance units (see Guyton, 1981, p. 212) may be computed according to the formula:

$$\text{TPR (pru)} = \text{mean BP (mmHg)} / \text{CO (liters/min)} / 16.67$$

Because total peripheral resistance is derived from the cardiac output measurement, the same reservations regarding validity of absolute values and statistical approach to data analyses should be followed as recommended for the impedance stroke volume and cardiac output measures.

Test-retest Reliability of Measures derived using Impedance Cardiography. Reliability of a measurement device or method refers to its ability to obtain the same values when measurements are repeated under similar conditions. A number of studies have presented evidence supportive of satisfactory reliability for impedance measures. In one study, in which stroke volume was measured in 15 healthy young men, a coefficient of reliability of .96 (using the Spearman-Brown prophecy formula) was obtained based on 15–20 resting measurements on each of three separate days, indicating very good measurement reliability (Pincomb et al., 1985). Examining consistency of stroke volume measures in 11 healthy men, as determined using computer ensemble averaging of 30-s continuous samples, Sherwood et al. (1986) found high correlations for a 90-min test-retest interval, when recording electrodes were not removed (r=.994), as well as one week later, using re-applied electrodes (r=.983). The latter values compared very favorably with the corresponding correlations for heart rate (r = .946 and .817 respectively), where little or no measurement error is involved. Findings from another study, based on assessments with intervals of three weeks, three months, and one year under various experimental task conditions found that a generalizability coefficient for left-ventricular ejection time was of the order of those for heart rate and respiration, whereas that for stroke volume index was somewhat lower (Fahrenberg, Foerster, Schneider, Muller, & Myrtek, 1986). A number of other investigators have utilized a variety of statistical approaches to evaluate reproducibility of impedance-derived myocardial performance indices over intervals ranging from days to weeks (Boer et al., 1979; Colin & Timbal, 1982; Fahrenberg, Schneider, &

Safian, 1987; Myrtek, 1985; Stick & Buchsel, 1978; Veigl & Judy, 1983; Venitz & Lucker, 1984). Overall, the results of studies examining reproducibility indicate that a high test-retest reliability for impedance cardiographic measures can be obtained, when the circumstances of repeated measurement are comparable. Care taken during the instrumentation procedure to ensure consistent electrode placement, and the application of consistent signal processing and analysis strategies are likely to represent the most crucial factors for ensuring good measurement reliability.

Experimental Design and Statistical Analysis

The statistical analysis of impedance cardiography data presents some additional complexities beyond those associated with the analysis of most psychophysiological data in general. These complexities arise from the controversy regarding the interpretation of absolute values of impedance-derived volume measures (stroke volume and cardiac output). A number of researchers (e.g., Miller & Horvath, 1978; Mohapatra, 1981; Sherwood et al., 1986) have questioned the validity of inter-subject comparisons on both theoretical and empirical grounds. There are often large ranges in the resting levels of impedance-derived stroke volume and cardiac output, but these differences often do not covary with other measures such as body size that should be closely related. It is apparent that many factors discussed earlier, such as thoracic density, erythrocyte orientation, and electrode placement, may influence the absolute volume values in ways that are unpredictable and unrelated to the actual amount of blood expelled from the left ventricle on a given beat. Thus, many researchers would be reluctant to say that Subject A truly has a higher level of cardiac output than Subject B based upon absolute impedance-derived values. As pointed out earlier, the validity of absolute values of time-based impedance measures such as systolic time intervals is much more widely accepted.

In contrast to lack of confidence in individual absolute volume measures by many researchers, the applicability of relative changes in these measures within individuals has generally been accepted. Miller and Horvath (1978) have suggested that the factors that may influence absolute volume measures in unpredictable ways remain relatively constant within subjects, "justifying the use of the ZCG as a reliable method for the continuous monitoring of intra-subject levels of stroke output" (p. 89). If one accepts the usefulness and validity of making within-subject comparisons, a study that simply seeks to compare the cardiac output and/or stroke volume responses of a single group of individuals during different conditions may reasonably compare mean levels of the volume variables in a meaningful way. Again, the assumption is that the sources of "error" that make one wary of absolute values are a constant across the conditions, making these within-subject comparisons valid.

Problems arise when the design of the study addresses differences among groups. In the case of a completely randomized analysis of variance (ANOVA) design or independent groups t-test, it is possible that true random assignment of subjects to groups could yield a "cancelling out" of the sources of variability of absolute values. With increasing numbers of subjects in each group, it is quite possible that baseline mean values of stroke volume and cardiac output for the groups would not be significantly different. Repeated measurements on subjects could then be analyzed without concern for the nonequivalence of groups.

If the research design does not involve the completely random assignment of subjects to groups, the questionable validity of the volume absolute values raises statistical and interpretative issues. For instance, suppose an experimenter wishes to compare physiological reactivity in male versus female subjects. This type of research question involves the comparison of nonequivalent groups. Even with a measure such as heart rate with which one has confidence in the meaningfulness of baseline levels, a group difference in means at baseline between males and females forces decisions to be made on the appropriate ways to evaluate levels in other conditions. Indeed, a researcher may hope that the groups do not differ on a dependent measure at baseline to make analysis and interpretation of responses to other conditions easier. When one analyzes impedance-derived volume measures with nonequivalent groups, it can be argued that interpretation problems arise even if the baseline values are not statistically different. If assignment of subjects to groups has not been completely random, one cannot be certain that group means that appear similar are actually reflecting "true" cardiac output or stroke volume levels because of the possibility of systematic bias in the factors such as thoracic composition, electrode placement, etc. The actual analysis of repeated conditions is made simpler if baseline levels are not different among groups, but one should be cautious about asserting the equivalence of basal levels in the groups.

Due to the wider acceptance of the validity of within-subject changes in the volume measures, researchers have often focused their attention on mean change from baseline to condition(s). Both

raw change (condition level minus baseline level) and percentage change from baseline have been reported in the literature. To date, it is not clear which of these choices is preferable with impedance data. The choice ultimately reflects the degree to which the researcher believes that the change scores are influenced by baseline levels. Some unpublished calculations concerning this issue have been conducted by two of the present authors with two different data sets, but results were not generally supportive of either method being preferable.

The use of change or gain scores in general has been questioned by a number of investigators (e.g., Cronbach & Furby, 1970). Alternative methods such as the use of "residualized" gain scores using regression techniques have been proposed by a number of writers (Cronbach & Furby, 1970; Dubois, 1957; Lord, 1956) and have been utilized in some psychophysiological research (e.g., Pittner & Houston, 1980; Smith, Houston, & Zurawski, 1984). The rationale for these procedures is grounded in logical statistical principles, but many researchers have not utilized them perhaps due to the added calculations and/or the fact that these scores are a form of statistical transformation and therefore removed from the actual observations. Analysis of covariance (ANCOVA) procedures have also been utilized to attempt to remove the effect of baseline differences from subsequent measures. The relative merits of covariance procedures have also been a source of controversy in the statistical literature (Lord, 1967; Snedecor & Cochran, 1967). The appropriate application of covariance techniques also requires a number of assumptions that can be relatively restrictive.

The above brief listing of the procedures often used with nonequivalent groups is not to recommend the use of one over the other. The appropriate technique is dependent on the data set and whether it meets the assumptions of the various procedures. It is beyond the space limitations of this paper to examine these procedures in detail. The reader is referred to Reichardt (1979) or similar articles to find detailed descriptions of the pros and cons of each technique. The important point to be made is that the researcher who seeks to examine group mean differences in volume measures among nonequivalent groups will almost certainly need to consider one of the above procedures.

Finally, researchers analyzing impedance-derived measures, in addition to being sensitive to the above concerns, should also be aware of the problems inherent in the use of repeated measures ANOVA designs with psychophysiological data. Readers are directed to a statement of editorial policy by *Psychophysiology* on the analysis of repeated measures ANOVAs (Jennings, Cohen, Ruchkin, & Fridlund, 1987).

Summary and Conclusions

Controversy over the biophysical basis of impedance measures has restricted the development of methodological standardization. Consequently, many methodological aspects of the application of impedance cardiography are open to either subtle or substantial variation. This may partially account for the inconsistent results from validation studies comparing impedance and reference measures of cardiac output. Nonetheless, general acceptance of the validity of impedance cardiography has relied predominantly upon such validation studies. Unfortunately, as discussed in this paper, these studies have themselves been subject to various sources of error. Thus, impedance cardiography remains a methodology that has yet to gain widespread acceptance in the scientific and medical communities.

The available evidence indicates that although absolute values for systolic time intervals can be relied upon, stroke volume and cardiac output measures derived from the impedance cardiogram should be viewed more prudently, with relative changes rather than absolute values being more reliable. Although essentially the same conclusion was drawn more than ten years ago (Miller & Horvath, 1978), in the interim there have been attempts to elucidate the nature of cardiac contributions to impedance changes. These efforts have led to suggestions for alterations in methodology, ranging from new recording electrode configurations to revised equations for deriving stroke volume. Implementation of revised methodology holds the potential of bringing impedance cardiography to a renewed and improved status of scientific acceptance. However, the technique currently remains accepted for its empirical validity, which is based upon the most widely adopted methodology as a standard. The relatively limited empirical support for suggested methodological revisions therefore places the researcher interested in using impedance cardiography in something of a dilemma: choices must be made between using less controversial, established methodological standards, and purportedly improved, but relatively untested new methodologies. Increased utilization of new methodologies should ultimately lead to the generation of a sufficient database for new methodological standards to become established. The careful description of impedance methodology in published studies should expedite this process, as well as permit appropriate scientific replication.

REFERENCES

Ahmed, S.S., Levinson, G.E., Schwartz, C.J., & Ettinger, P.O. (1972). Systolic time intervals as measures of the contractile state of the left ventricular myocardium in man. *Circulation, 46*, 559–571.

Andersen, K., & Vik-Mo, H. (1984). Effects of spontaneous respiration on left ventricular function assessed by echocardiography. *Circulation, 69*, 874–879.

Appel, P.L., Kram, H.B., MacKabee, J., Fleming, A.W., & Shoemaker, W.C. (1986). Comparison of measurements of cardiac output by bioimpedance and thermodilution in severely ill surgical patients. *Critical Care Medicine, 14*, 933–935.

Balasubramanian, V., Mathew, O.P., Behl, A., Tewari, S.C., & Hoon, R.S (1978). Electrical impedance cardiogram in derivation of systolic time intervals. *British Heart Journal, 40*, 268–275.

Bassett Frey, M.A. (1982). Computer-assisted method for performing impedance cardiography calculations. *Journal of Applied Physiology, 52*, 274–277.

Bernstein, D.P. (1986a). A new stroke volume equation for thoracic electrical bioimpedance: Theory and rationale. *Critical Care Medicine, 14*, 904–909.

Bernstein, D.P. (1986b) Continuous noninvasive real-time monitoring of stroke volume and cardiac output by thoracic electrical bioimpedance. *Critical Care Medicine, 14*, 898–901.

Boer, P., Roos, J.C., Geyskes, G.G., & Mees, E.J. (1979). Measurement of cardiac output by impedance cardiography under various conditions. *American Journal of Physiology, 237*, H491–H496.

Bonjer, F.H., Van Den Berg, J.W., & Dirken, M.N.J. (1952). The origin of the variations of body impedance occurring during the cardiac cycle. *Circulation, 6*, 415–420.

Christie, J., Sheldahl, L.M., Tristani, F.E., Sagar, K.B., Ptacin, M.J., & Wann, S. (1987). Determination of stroke volume and cardiac output during exercise: Comparison of two-dimensional and Doppler echocardiography, and Fick oximetry, and thermodilution. *Circulation, 76*, 539–547.

Colin, J., & Timbal, J. (1982). Measurement of systolic time intervals by electrical plethysmography: Validation with invasive and noninvasive methods. *Aviation, Space, and Environmental Medicine, 53*, 62–68.

Cousineau, D., de Champlain, J., & Lapointe, L. (1978). Circulating catecholamines and systolic time intervals in labile and sustained hypertension. *Clinical Science and Molecular Medicine, 55*, 65s–68s.

Cronbach, L.J., & Furby, L. (1970). How should we measure "change" or should we? *Psychological Bulletin, 74*, 68–80.

De Mey, C., & Enterling, D. (1988). Noninvasive assessment of cardiac performance by impedance cardiography: Disagreement between two equations to estimate stroke volume. *Aviation, Space, and Environmental Medicine, 59*, 57–62.

Denniston, J.C., Maher, J.T., Reeves, J.T., Cruz, J.C., Cymerman, A., & Grover, R.F. (1976). Measurement of cardiac output by electrical impedance at rest and during exercise. *Journal of Applied Physiology, 40*, 91–95.

DeSouza, W.M., & Panerai, R.B. (1981). Variability of thoracic impedance cardiograms in man. *Medical and Biological Engineering and Computing, 19*, 411–415.

Djordjevich, L., & Sadove, M.S. (1981). Experimental study of the relationship between the base impedance and its time derivative in impedance plethysmography. *Medical Physics, 8*, 76–78.

Doerr, B.M., Miles, D.S., & Bassett Frey, M.A. (1981). Influence of respiration on stroke volume determined by impedance cardiography. *Aviation, Space and Environmental Medicine, 52*, 394–398.

DuBois, P.H. (1957). *Multivariate correlational analysis.* New York: Harper.

DuQuesnay, M.C., Stoute, G.J., & Hughson, R.L. (1987). Cardiac output in exercise by impedance cardiography during breath holding and normal breathing. *Journal of Applied Physiology, 62*, 101–107.

Ebert, T.J., Eckberg, D.L., Vetrovec, G.M., & Cowley, M.J. (1984). Impedance cardiograms reliably estimate beat-by-beat changes of left ventricular stroke volume in humans. *Cardiovascular Research, 18*, 354–360.

Edmunds, A.T., Godfrey, S., & Tooley, M. (1982). Cardiac output measured by transthoracic impedance cardiography at rest, during exercise and various lung volumes. *Clinical Science, 63*, 107–113.

Fahrenberg, J., Schneider, H.J., & Safian, P. (1987). Psychophysiological assessments in a repeated-measurement design extending over a one-year interval: Trends and stability. *Biological Psychology, 24*, 49–66.

Fahrenberg, J., Foerster, F., Schneider, H.J., Muller, W., & Myrtek, M. (1986). Predictability of individual differences in activation processes in a field setting based on laboratory measures. *Psychophysiology, 23*, 323–333.

Feldschuh, J., & Enson, Y. (1977). Prediction of the normal blood volume: Relation of blood volume to body habitus. *Circulation, 56*, 605.

Ferrigno, M., Hickey, D.D., Liner, M.H., & Lundgren, C.E. (1986). Cardiac performance in humans during breath holding. *Journal of Applied Physiology, 60*, 1871–1877.

Foerster, F. (1984). *Computerprogramme zur Biosignalanalyse.* Berlin: Springer.

Frey, M.A.B., Doerr, B.M., & Miles, D.S. (1982). Transthoracic impedance: Differences between men and women with implications for impedance cardiography. *Aviation, Space, and Environmental Medicine, 53*, 1190–1192.

Garrard, C.L., Jr., Weissler, A.M., & Dodge, H.T. (1970). The relationship of alterations in systolic time intervals to ejection fraction in patients with cardiac disease. *Circulation, 42*, 455–462.

Gastfriend, R.J., Van De Water, J.M., Leonard, M.L., Macko, P., & Lynch,P.R. (1986). Impedance cardiography: Current status and clinical applications. *The American Surgeon, 52*, 636–640.

Geddes, L.A. & Sadler, C. (1973). The specific resistance of blood at body temperature. *Medical and Biological Engineering, 11*, 335–339.

Goldstein, D.S., Cannon, R.O., Zimlichman, R., & Keiser, H.R. (1986). Clinical evaluation of impedance cardiog-

raphy. *Clinical Physiology, 6*, 235–251.

Gollan, F., Kizakevich, P.N., & McDermott, J. (1978). Continuous electrode monitoring of systolic time intervals during exercise. *British Heart Journal, 40*, 1390–1396.

Guyton, A.C. (1981). *Textbook of medical physiology*. Philadelphia: W.B. Saunders Co.

Harris, W.S., Schoenfeld, C.D., & Weissler, A.M. (1967). Effects of adrenergic receptor activation and blockade of the systolic pre-ejection period, heart rate, and arterial pressure in man. *The Journal of Clinical Investigation, 46*, 1704–1714.

Heather, L.W. (1969). A comparison of cardiac output values by the impedance cardiograph and dye dilution techniques in cardiac patients. In W.G. Kubicek, D.A. Witsoe, R.P. Patterson, & A.H.L. From (Eds.), *Development and evaluation of an impedance cardiographic system to measure cardiac output and other cardiac parameters* (pp. 247–258). (NASA-CR-101965) Houston: National Aeronautics and Space Administration.

Hill, D.W. & Merrifield, A.J. (1976). Left ventricular ejection and the Heather index measured by noninvasive methods during postural changes in man. *Acta Anaesthesiologica Scandinavica, 20*, 313–320.

Hill, D.W., & Thompson, F.D. (1975). The importance of blood resistivity in the measurement of cardiac output by the thoracic impedance method. *Medical and Biological Engineering, 13*, 187–191.

Huitema, B.E. (1980). *The analysis of covariance and alternatives*. New York: Wiley.

Jennings, J.R., Berg, W.K., Hutcheson, J.S., Obrist, P.A., Porges, S., & Turpin, G. (1981). Publication guidelines for heart rate studies in man. *Psychophysiology, 18*, 226–231.

Jennings, J.R., Cohen, M.J., Ruchkin, D.S., & Fridlund, A.J. (1987). Editorial policy on analyses of variance with repeated measures. *Psychophysiology, 24*, 474–478.

Jennings, J.R., Tahmoush, A.J., & Redmond, D.P. (1980). Noninvasive measurement of peripheral vascular activity. In I. Martin & P.H. Venables (Eds.), *Techniques in psychophysiology* (pp. 69–137). Chichester: Wiley & Sons.

Judy W.V., Hall J.H., & Elliot W.C. (1982). Ejection fraction index calculated from the impedance cardiographic signal. *Proceedings of the AAMI, 17*, 56.

Judy, W.V., Langley, F.M., McCowen, K.D., Stinnett, D.M., Baker, L.E., & Johnson, P.C. (1969). Comparative evaluation of the thoracic impedance and isotope dilution methods for measuring cardiac output. In W.G. Kubicek, D.A. Witsoe, R.P. Patterson, & A.H.L. From (Eds.), *Development and evaluation of an impedance cardiographic system to measure cardiac output and other cardiac parameters* (pp. 296–300). (NASA-CR-101965) Houston: National Aeronautics and Space Administration.

Kelsey, R.M., Guethlein, W., Eichler, S., Blascovich, J.J., & Katkin, E.S. (1987). An evaluation of ensemble-averaged impedance cardiographic measures of myocardial performance [Abstract]. *Psychophysiology, 24*, 595.

Kesteloot, H. (1980). Limitations of systolic time intervals for evaluation of cardiac function. In W.F. List, J.S. Gravenstein, & D.S. Spodick (Eds.), *Systolic time intervals* (pp. 30–35). Berlin: Springer.

Kizakevich, P.N., Gollan, F., & McDermott, J. (1976). An automated system for systolic time interval analysis. *Proceedings of the Digital Equipment Users Society, 2*, 795–798.

Kobayashi, Y., Andoh, Y., Fujinami, T., Nakayama, K., Takada, K., Takeuchi, T., & Okamoto, M. (1978). Impedance cardiography for estimating cardiac output during submaximal and maximal work. *Journal of Applied Physiology, 45*, 459–462.

Kubicek, W.G., Karnegis, J.N., Patterson, R.P., Witsoe, D.A., & Mattson, R.H. (1966). Development and evaluation of an impedance cardiograph system. *Aerospace Medicine, 37*, 1208–1212.

Kubicek, W.G., Kottke, F.J., Ramos, M.U., Patterson, R.P., Witsoe, D.A., Labree, J.W., Remole, W., Layman, T.E., Schoening, H., & Garamella, J.T. (1974). The Minnesota impedance cardiograph—theory and applications. *Biomedical Engineering, 9*, 410–416.

Kubicek, W.G., Patterson, R.P., & Witsoe, D.A. (1970). Impedance cardiography as a noninvasive method of monitoring cardiac function and other parameters of the cardiovascular system. *Annals of the New York Academy of Science, 170*, 724–732.

Kubicek, W.G., Witsoe, D.A., Patterson, R.P., & From, A.H.L. (Eds.) (1969). *Development and evaluation of an impedance cardiographic system to measure cardiac output and other cardiac parameters*. (NASA-CR-101965) Houston: National Aeronautics and Space Administration.

Kubicek, W.G., Witsoe, D.A., Patterson, R.P., Mosharrata, M.A., Karnegis, J.N., & From, A.H.L. (1967). *Development and evaluation of an impedance cardiographic system to measure cardiac output and development of an oxygen consumption rate computing system utilizing a quadrapole mass spectrometer*. (NASA-CR-92220) Houston: National Aeronautics and Space Administration.

Lababidi, Z., Ehmke, D.A., Durnin, R.E., Leaverton, P.E., & Lauer, R.M. (1970). The first derivative thoracic impedance cardiogram. *Circulation, 41*, 651–658.

Lamberts, R., Visser, K.R., & Zijlstra, W.G. (1984). *Impedance cardiography*. Assen, The Netherlands: Van Gorcum.

Lewis, R.P., Rittgers, S.E., Forester, W.F., & Boudoulas, H. (1977). A critical review of the systolic time intervals. *Circulation, 56*, 146–158.

List, W.F., Gravenstein, J.S., & Spodick, D.H. (Eds.) (1980). *Systolic time intervals*. Berlin: Springer.

Lord, F.M. (1956). The measurement of growth. *Educational and Psychological Measurement, 16*, 421–437.

Lord, F.M. (1967). A paradox in the interpretation of group comparisons. *Psychological Bulletin, 68*, 304–305.

Mantysaari, M., Antila, K., & Peltonen, T. (1984). Relationship between systolic time intervals and heart rate during four circulatory stress tests. *European Journal of Applied Physiology, 52*, 282–286.

Martin, C.E., Shaver, J.A., Thompson, M.E., Reddy, P.S., & Leonard, J.J. (1971). Direct correlation of external systolic time intervals with internal indices of left ventricular function in man. *Circulation, 44*, 419–431.

Messerli, F.H., Christie, B., & DeCarvaiho, J.G.R. (1981). Obesity and essential hypertension: Hemodynamics, intravascular volume, sodium excretion and plasma renin activity. *Archives of Internal Medicine, 141*, 81.

McCubbin, J.A., Richardson, J.E., Langer, A.W., Kizer, J.S., & Obrist, P.A. (1983). Sympathetic neuronal function and left ventricular performance during behavioral stress in humans: The relationship between plasma catecholamines and systolic time intervals. *Psychophysiology, 20*, 102–110.

McKinney, M.E., Buell, J.C., & Elliot, R.S. (1984). Sex differences in transthoracic impedance: Evaluation of effects on calculated stroke volume index. *Aviation, Space, and Environmental Medicine, 55*, 893–895.

Miller, J.C., & Horvath, S.M. (1978). Impedance cardiography. *Psychophysiology, 15*, 80–91.

Miyamoto, Y., Higuchi, J., Abe, Y., Hiura, T., Nakazono, Y., & Mikami, T. (1983). Dynamics of cardiac output and systolic time intervals in supine and upright exercise. *Journal of Applied Physiology, 55*, 1674–1681.

Miyamoto, Y., Takahashi, M., Tamura, T., Nakamura, T., Hiura, T., & Mikami, M. (1981). Continuous determination of cardiac output during exercise by the use of impedance plethysmography. *Medical and Biological Engineering and Computing, 19*, 638–644.

Miyamoto, Y., Tamura, T., Hiura, T., Nakamura, T., Higuchi, J., & Mikami, T. (1982). The dynamic response of the cardiopulmonary parameters to passive head-up tilt. *Japanese Journal of Physiology, 32*, 245–258.

Mohapatra, S.N. (1981). *Non-invasive cardiovascular monitoring by electrical impedance technique.* London: Pittman Medical Ltd.

Mohapatra, S.N., Costeloe, K.L., & Hill, D.W. (1977). Blood resistivity and its implications for the calculation of cardiac output by the thoracic electrical impedance technique. *Intensive Care Medicine, 3*, 63–67.

Mohapatra, S.N., & Hill, D.W. (1975). The changes in blood resistivity with hematocrit and temperature. *European Journal of Intensive Care Medicine, 1*, 153–162.

Muzi, M., Ebert, T.J., Tristani, F.E., Jeutter, D.C., Barney, J.A., & Smith, J.J. (1985). Determination of cardiac output using ensemble-averaged impedance cardiograms. *Journal of Applied Physiology, 58*, 200–205.

Muzi, M., Jeutter, D.C., & Smith, J.J. (1986). Computer-automated impedance-derived cardiac indexes. *IEEE Transactions on Biomedical Engineering, BME-33*, 42–47.

Myrtek, M. (1985). Adaptation effects and the stability of physiological responses to repeated testing. In A. Steptoe, H. Ruddel, & H. Neus (Eds.), *Clinical and methodological issues in cardiovascular psychophysiology* (pp. 93–106). Heidelberg: Springer.

Newlin, D.B., & Levenson, R.W. (1979). Pre-ejection period: Measuring beta-adrenergic influences upon the heart. *Psychophysiology, 16*, 546–553.

Nyboer, J. (1959). *Electrical impedance plethysmography.* Springfield, IL: Thomas Publishers.

Obrist, P.A., Light, K.C., James, S.A., & Strogatz, D.S. (1987). Cardiovascular responses to stress: I. Measures of myocardial response and relationships to high resting systolic pressure and parental hypertension. *Psychophysiology, 24*, 65–78.

Patterson, R.P. (1965). *Cardiac output determinations using impedance plethysmography.* Unpublished doctoral dissertation, University of Minnesota, Minneapolis.

Penney, B.C., Patwardhan, N.A., & Wheeler, H.B. (1985). Simplified electrode array for impedance cardiography. *Medical and Biological Engineering and Computing, 23*, 1–7.

Petrovick, M.L., Kizakevich, P.N., Stacy, R.W., & Haak, E.D. (1980). A comprehensive cardiac exercise stress processor for environmental health effects studies. *Journal of Medical Systems, 4*, 137–150.

Pigott, V.M., & Spodick, D.H. (1971). Effects of normal breathing and expiratory apnea on duration of the phases of cardiac systole. *American Heart Journal, 82*, 786–793.

Pincomb, G.A., Lovallo, W.R., Passey, R.L., Whitsett, T.L., Silverstein, S.M., & Wilson, M.F. (1985). Effects of caffeine on vascular resistance, cardiac output, and myocardial contractility in young men. *American Journal of Cardiology, 56*, 119–122.

Pittner, M.S., & Houston, B.K. (1980). Response to stress, cognitive coping strategies, and the Type A behavior pattern. *Journal of Personality and Social Psychology, 39*, 147–157.

Plewis, I. (1985). *Analyzing change.* New York: Wiley.

Porter, J.M., & Swain, I.D. (1987). Measurement of cardiac output by electrical impedance plethysmography. *Journal of Biomedical Engineering, 9*, 222–231.

Qu, M., Zhang, Y., Webster, J.G., & Tompkins, W.J. (1986). Motion artifact from spot and band electrodes during impedance cardiography. *IEEE Transactions on Biomedical Engineering, BME-33*, 1029–1036.

Quail, A.W., Traugott, F.M., Porges, W.L., & White, S.W. (1981). Thoracic resistivity for stroke volume calculation in impedance cardiography. *Journal of Applied Physiology, 50*, 191–195.

Rasmussen, J.P., Sorensen, B., & Kahn, T. (1975). Evaluation of impedance cardiography as a non-invasive means of measuring systolic time intervals and cardiac output. *Acta Anaesthesiologica Scandinavica, 19*, 210–218.

Reichardt, C.S. (1979). The statistical analysis of data from nonequivalent group designs. In T.D. Cook & D.T. Campbell (Eds.), *Quasi-experimentation: Design and analysis issues for field settings* (pp. 147–205). Chicago: Rand McNally.

Rogosa, D.R., Brandt, D. & Zimowski, M. (1982). A growth curve approach to the measurement of change. *Psychological Bulletin, 92*, 726–748.

Rushmer, R.F. (1976). *Cardiovascular dynamics.* Philadelphia; W.B. Saunders Co.

Sakamoto, K., Muto, K., Kanai, H., & Iizuka, M. (1979). Problems of impedance cardiography. *Medical and*

Biological Engineering and Computing, 17, 697–709.

Sheps, D.S., Petrovick, M.L., Kizakevich, P.N., Wolfe, C., & Craige, E. (1982). Continuous noninvasive monitoring of left ventricular function during exercise by thoracic impedance cardiography-automated derivation of systolic time intervals. *American Heart Journal, 103*, 519–524.

Sherwood, A., Allen, M.T., Hutcheson, J.S., & Obrist, P.A. (1986). Ensemble averaging of the impedance cardiogram [Abstract]. *Psychophysiology, 23*, 461.

Sherwood, A., Allen, M.T., Obrist, P.A., & Langer, A.W. (1986). Evaluation of beta-adrenergic influences on cardiovascular and metabolic adjustments to physical and psychological stress. *Psychophysiology, 23*, 89–104.

Siegel, J.H., Fabian, M., Lankau, C., Levine, M., Cole, A., & Nahmad, M. (1970). Clinical and experimental use of thoracic impedance plethysmography in quantifying myocardial contractility. *Surgery, 67*, 907–917.

Smith, T.W., Houston, B.K., & Zurawski, R.M. (1984). Finger pulse volume as a measure of anxiety in response to evaluative threat. *Psychophysiology, 21*, 260–264.

Snedecor, G.W., & Cochran, W.G. (1967). *Statistical methods.* Ames, Iowa: Iowa State University Press.

Sramek, B.B. (1981). *Noninvasive technique for measurement of cardiac output by means of electrical impedance.* Paper presented at the Fifth International Conference on Electrical Bioimpedance, Tokyo, Japan.

Sramek, B.B., Rose, D.M., & Miyamoto, A. (1983). *Stroke volume equation with a linear base impedance model and its accuracy as compared to thermodilution and magnetic flowmeter techniques in humans and animals.* Paper presented at the Sixth International Conference on Electrical Bioimpedance, Zadar, Yugoslavia.

Stern, H.C., Wolf, G.K., & Belz, G.G. (1985). Comparative measurements of left ventricular ejection time by mechano-, echo- and electrical impedance cardiography. *Drug Research, 35*, 1582–1586.

Stemmler, G., & Fahrenberg, J. (in press). Psychophysiological assessment: Conceptual, psychometric, and statistical issues. In G. Turpin (Ed.), *Handbook of clinical psychophysiology.* Chichester: Wiley.

Stick, C., & Buchsel, R. (1978). Impedance cardiography: The reproducibility of stroke volume measurements under conditions of mass examination. *Basic Research in Cardiology, 73*, 627–638.

Stratton, J., Pfeifer, M.A., & Halter, J.B. (1987). The hemodynamic effects of sympathetic stimulation combined with parasympathetic blockade in man. *Circulation, 75*, 922–929.

Traugott, F.M., Quail, A.W., & White, S.W. (1981). Evaluation of blood resistivity in vivo for impedance cardiography in man, dog and rabbit. *Medical and Biological Engineering and Computing, 19*, 547–552.

Veigl, V.L., & Judy, W.V. (1983). Reproducibility of hemodynamic measurements by impedance cardiography. *Cardiovascular Research, 17*, 728–734.

Venitz, J., & Lucker, P.W. (1984). Impedance cardiography—a reliable method for measuring cardiac function noninvasively. *Methods and Findings in Experimental Clinical Pharmacology, 6*, 339–346.

Watanabe, T., Kamide, T., Torii, Y., & Ochiai, M. (1981). A convenient measurement of cardiac output by half-taped impedance cardiography. *Japanese Journal of Medical Electronics and Biological Engineering, 19*, 30–34.

Weissler, A.M. (1977). Current concepts in cardiology: Systolic-time intervals. *The New England Journal of Medicine, 296*, 321–324.

Weissler, A.M., Harris, W.S., & Schoenfeld, C.D. (1969). Bedside techniques for the evaluation of ventricular function in man. *The American Journal of Cardiology, 23*, 577–583.

Witsoe, D.A., Patterson, R.P., From, A.H.L., & Kubicek, W.G. (1969). Evaluation of impedance cardiographic techniques for measuring relative changes in cardiac output by simultaneous comparison with indicator dilution and electromagnetic flowmeter. In W.G. Kubicek, D.A. Witsoe, R.P. Patterson, & A.H.L. From (Eds.), *Development and evaluation of an impedance cardiographic system to measure cardiac output and other cardiac parameters* (pp. 330–355). (NASA-CR-101965) Houston: National Aeronautics and Space Administration.

Zhang, Y., Qu, M., Webster, J.G., Tompkins, W.J., Ward, B.A., & Bassett, D.R. (1986). Cardiac output monitoring by impedance cardiography during treadmill exercise. *IEEE Transactions on Biomedical Engineering, BME-33*, 1037–1042.

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Appendix

Development of the Kubicek Stroke Volume Equation

The vast majority of studies to date using impedance cardiography have reported stroke volume (SV) estimates derived using the Kubicek SV equation, originally described by Kubicek et al. (1966):

$$SV = rho_b(L/Z_0)^2 \cdot LVET \cdot dZ/dt_{(max)} \quad (1)$$

where SV is stroke volume (ml), rho_b is the resistivity of blood (ohm·cm), L is the distance between the recording electrodes (cm), Z_0 is impedance between the recording electrodes (ohm), LVET is left-ventricular ejection time (seconds), and $dZ/dt_{(max)}$ is the absolute value of the maximum rate of change (slope) in the impedance waveform on a given beat (ohm/second).

Bonjer (Bonjer, Vandenberg, & Dirken, 1952) demonstrated the relationship between blood volume and resistance (R_b) in an artery:

$$R_b = rho_b \cdot L/S \quad (2)$$

where S is the cross-sectional area of the artery and L is the length of the arterial segment. The volume (V_b) of a section of artery with length (L) and cross section (S) is:

$$V_b = L \cdot S \text{ and } S = V_b/L$$

Substituting for S in Formula 2:

$$R_b = rho_b \cdot L/V_b/L$$
$$= rho_b \cdot L^2/V_b$$

Given that rho and L are constants, this demonstrates that resistance decreases as the volume of conductor (blood) in the artery increases. By solving for volume, it can be seen that resistance in an arterial segment can be interpreted as reflecting a given volume of blood in that segment:

$$V_b = rho_b \cdot L^2/R_b \quad (3)$$

Similarly, *changes* in resistance can be shown to reflect *changes* in volume. It can be established that for small changes (Δ) in volume:

$$\Delta V_b/V_b = -\Delta R_b/R_b$$
$$\Delta V_b = -V_b \cdot \Delta R_b/R_b$$

substituting the formula for V_b from equation 3, we have:

$$\Delta V_b = -rho_b \cdot L^2/R_b \cdot \Delta R_b/R_b$$
$$= -rho_b \cdot L^2/R^2 \cdot \Delta R_b \quad (4)$$

which indicates that when the base resistance (R) of an arterial segment is known, changes about that resistance (ΔR) are interpretable as volume changes (ΔV), making Formula 4 useful for determining stroke volume.

Impedance cardiographic measurements of cardiac stroke volume generally assume that the thorax can be viewed as a cylinder similar to an arterial segment and that changes in resistance are primarily a function of changes in volume of blood entering the thorax from the heart. Equation 4 forms the basis for modern impedance measurements of stroke volume with two modifications.

First, besides the biological hazard posed by direct current, resistance measurements along the thorax are difficult to make using direct current circuits. Patterson (1965) demonstrated that impedance (Z, opposition to current flow within an alternating current circuit) could be usefully substituted for resistance measurements, allowing the advantages of AC circuitry to be employed. Substituting Z for R_b in Equation 4, and using the above assumptions, left-ventricular stroke volume may be approximated by:

$$SV = -rho_b \cdot L^2/Z_0^2 \cdot \Delta Z \quad (5)$$

where Z_0 is baseline impedance along the thorax and ΔZ is the change in impedance with each heartbeat.

The second modification is made necessary by the fact that the ΔZ curve recorded over a cardiac cycle is a joint function of blood entering the thorax from the heart and of blood leaving the thorax via the large arteries. Therefore, the height of the ΔZ waveform underestimates the impedance drop due to ejection of blood from the heart. This difficulty is overcome by extrapolating a line along the maximum slope of the ΔZ waveform until the extrapolated line intersects a second line extending vertically across the point at which ejection ends. By measuring the height of this line (in ohms) starting at Z_0 the extrapolated value of ΔZ due solely to stroke volume (blood entering the thorax) may be determined.

The above forward extrapolation procedure is cumbersome. Kubicek et al. (1966) adopted a related approach. For a given left-ventricular ejection time (LVET), the height of the vertical ΔZ line is strictly a function of the slope of the line extrapolated along the maximum slope of ΔZ (steeper slopes would yield larger ΔZ values). The numerical value of the maximum slope of the ΔZ curve is expressed as $dZ/dt_{(max)}$, or the maximum value of the change in Z over a given change in time. Because $dZ/dt_{(max)}$ is a slope, multiplying that slope by LVET essentially extrapolates that slope over the time of ejection, as was done manually on the ΔZ waveform, to yield the forward extrapolated value for ΔZ. Therefore:

$$\text{Hypothetical maximum } \Delta Z = LVET \cdot dZ/dt_{(max)}$$

Substituting for ΔZ in Equation 5 we have:

$$SV = -rho_b \cdot L^2/Z_0^2 \cdot LVET \cdot dZ/dt_{(max)} \quad (6)$$

which gives left-ventricular stroke volume. It is of note that impedance decreases with ejection of blood from the heart, so ΔZ and also dZ/dt have negative values during the initial phase of ejection. Hence, $dZ/dt_{(max)}$ (recommended notation as adopted by Mohapatra, 1981) is actually the maximum rate of negative change in ΔZ and is therefore sometimes referred to as $dZ/dt_{(min)}$ or $-dZ/dt_{(max)}$. In Equation (6) the value of the right side of the equation becomes positive, yielding a positive value for stroke volume. In practice it is common to ignore the negative value of $dZ/dt_{(max)}$ and to eliminate the negative sign next to rho as shown in Equation (1).

Announcements

Fifth International Conference of Psychophysiology

From July 9th through 14th, 1990, the Fifth International Conference of Psychophysiology will be held in Budapest, Hungary. The conference will focus on integrative aspects of psychophysiology, and will include symposia, open paper sessions, and poster sessions on a range of topics related to psychophysiology mechanisms and models, and human adaptations and maladaptation. Further information may be obtained from: I.O.P. Conference Secretariat, PX Ltd, H—1051 Budapest, Arany J.U.6—8, H—1361 Budapest, 501. PO BOX: 1, Hungary.

Psychophysiological Aspects of Cerebral Dominances: A Symposium

The International Society on Cerebral Dominances is organizing a one-day symposium on the Psychophysiological Aspects of Cerebral Dominances, in connection with the Fifth International Conference of Psychophysiology, to be held in Budapest, Hungary, from July 9th through 14th, 1990. The official language of the symposium will be English. Abstracts (one typed page) of papers to be presented at the symposium should be submitted before April 30, 1990, to: C.H. Bick, M.D., International Society on Cerebral Dominances, Schloss-Strasse 8, D-6783 Dahn, West Germany. The abstracts and some selected papers will be published in the *International Journal of Neuroscience.*

The provisional program and final registration forms for the Fifth International Conference of Psychophysiology can be obtained from: I.O.P. Conference Secretariat, PX LTD, H-1051 Budapest, Arany J.U.6-8, H-1361 Budapest, 501.PO BOX:1, Hungary.