

## Where to B in $dZ/dt$

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### Abstract

The B point on the impedance cardiograph waveform corresponds to the opening of the aortic valve and is an important parameter for calculating systolic time intervals, stroke volume, and cardiac output. Identifying the location of the B point is sometimes problematic because the characteristic upstroke that serves as a marker of this point is not always apparent. Here is presented a reliable method for B point identification, based on the consistent relationship between the R to B interval (RB) and the interval between the R-wave and the peak of the  $dZ/dt$  function (RZ). The polynomial function relating RB to RZ ( $RB = 1.233RZ - 0.0032RZ^2 - 31.59$ ) accounts for 90%–95% of the variance in the B point location across ages and gender and across baseline and stress conditions. This relation affords a rapid approximation to B point measurement that, in noisy or degraded signals, is superior to visual B point identification and to a derivative-based estimate.

**Descriptors:** B point, ECG, Impedance cardiography, LVET, PEP, Reliability, Validity

The B point on the  $dZ/dt$  waveform corresponds to the opening of the aortic valve, demarcating the onset of ventricular ejection. This time point is important in deriving the pre-ejection period (PEP), a reflection of myocardial contractility that is commonly used as an index of sympathetic cardiac control, as well as the left ventricular ejection time (LVET), which is a critical parameter in the Kubicek equation for stroke volume and cardiac output. Identifying the location of the B point is not always straightforward, however, as the characteristic notch and upstroke that constitutes the fiducial point on the rising slope of the  $dZ/dt$  function is not always present or may be indistinct. Moreover, some impedance devices (e.g., the Biopac EBI) derive the  $dZ/dt$  signal off-line from the digitized  $Z_0$  signal. Because of the large offset in  $Z_0$ , this approach can reduce resolution of the  $dZ/dt$  signal and may obscure the upstroke.

A number of approaches have been applied in such cases, including the inflection point of the second derivative or the peak of the third derivative of the  $dZ/dt$  signal (Debski, Zhang, Jennings, & Kamarck, 1993; Sherwood et al., 1990). These two approaches can give somewhat different values, can be sensitive to noise, and are not universally applicable. Debski et al. (1993) recommend the second derivative approach for signals with a

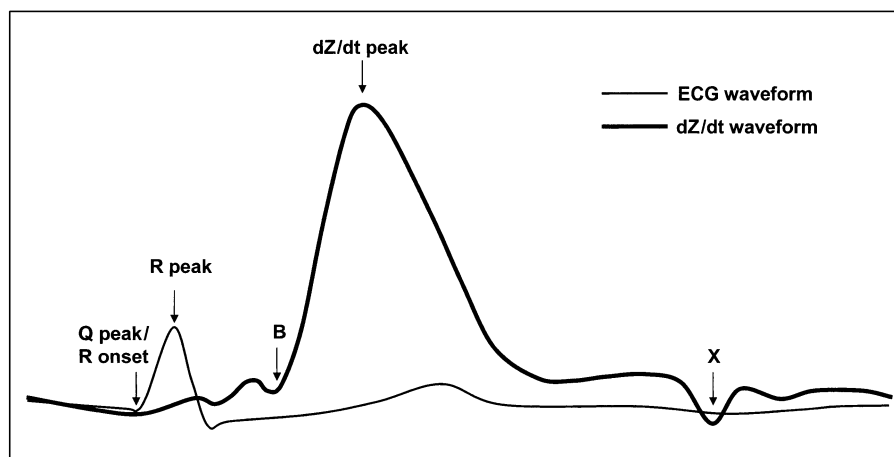
defined B notch/upstroke and the third derivative method in the absence of a notch/upstroke.

The biomechanics of the cardiac cycle suggest an alternative approach. The B point (and hence PEP) is influenced by myocardial contractility. An increase in contractility, such as that associated with increased sympathetic drive, is associated with a more rapid rise in ventricular pressure during myocardial contraction. Because of the more rapid rise in ventricular pressure during isovolumetric contraction, there is a shorter time (PEP) before the ventricular pressure exceeds the aortic pressure and the aortic valve opens (the B point). But changes in myocardial contractility that impact the opening of the aortic valve also impact peak aortic blood flow, which corresponds to the peak of the  $dZ/dt$  waveform ( $dZ/dt_{\max}$ ; Kubicek et al., 1974). In fact, it is the same ventricular pressure function (and ventricular/aortic pressure differential) that drives valve opening and shortly thereafter, peak ventricular ejection (see Noble, 1968; Noble, Trenchard, & Guz, 1966). Consequently, changes in the time to one of these events is associated with corresponding changes in the other. The simple subtraction of a constant from the peak  $dZ/dt$  would not suffice, however, as the time between valve opening and peak ventricular ejection is not fixed. Increases in slope of the ventricular pressure function that reduce the time to valve opening also reduce the time from valve opening to peak ventricular ejection (see Noble, 1968; Noble, Trenchard, & Guz, 1966; Figure 2). Nevertheless, as long as the relations are consistent, one should be able to estimate B from the peak of the  $dZ/dt$  function.

The present findings offer a simple and reliable method for B point identification, based on the consistent relationship between the R to B interval (RB) and the more salient and readily measured interval between the R-wave and the peak of the  $dZ/dt$

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**Figure 1.** Illustrative electroencephalograph (ECG) and impedance ( $dZ/dt$ ) waveforms, with arrows showing relevant reference points.

function (RZ). The polynomial (linear+quadratic) function relating RB interval to the RZ interval accounts for 90%–95% of the variance in the B point location across samples extending from adolescents to middle-age adults, across gender, across sitting and recumbent postures, and across baseline and stress conditions. This relation affords a rapid and reliable approximation to B point measurement that is comparable or superior to visual B point identification and to a derivative-based estimate, especially for noisy or degraded signals that do not have a clear B point upstroke.

## Methods

### Participants

For the primary analyses, 33 healthy college student participants were recruited at the Ohio State University (OSU). Because the development of a B point scoring method requires a clear criterion measure to assess validity, 7 subjects without a clear B point upstroke were excluded from the primary analysis, resulting in an  $N$  of 26 (13 men and 13 women; 17–24 years of age). A second OSU sample was comprised of older adults ( $N = 19$ ). Three of these subjects were excluded from the primary analysis because of an indistinct B point upstroke, and 1 because of an erratic and excessively noisy signal, leaving an  $N$  of 15 (7 men and 8 women,  $40.1 \pm 4.2$  ( $SD$ ) years). The 10 subjects who were excluded from the primary analysis because of the lack of a clear criterion, due to an indistinct B upstroke, were evaluated in a separate analysis based on the algorithm derived from the primary analysis.

A third group of adolescent asthmatic participants ( $N = 10$ ) was used to test the generality of the findings to younger subjects (University of Buffalo sample). One of these subjects was excluded due to an indistinct upstroke, leaving a final  $N$  of 9 (5 boys and 4 girls, 8–17 years of age).

### Apparatus

Electrocardiographic and impedance cardiographic measures were obtained using a Minnesota model 304B Impedance Cardiograph, with standard tetrapolar circumferential band electrodes (Sherwood et al., 1990) and internal EKG derivation. The  $Z_o$  and  $dZ/dt$  signals were digitized at 500 Hz (16 bit) and ana-

lyzed by the Mindware Cardiac Impedance software (Mindware Technologies, Gahanna, OH).

### Physiological Measures

All measures were derived from the ensemble averaged signals (Kelsey & Guethlein, 1990; Kelsey et al., 1998) over 1-min epochs. Measures included: (1) R peak; (2) Q peak/R onset; (3)  $dZ/dt$  peak amplitude; (4) RZ, or  $dZ/dt$  peak time; (5) X point; and (6) B point. Illustrative waveforms and scoring points are shown in Figure 1. The R wave peak (R) was automatically scored by the analysis software by means of a peak fitting algorithm of the Mindware system. Remaining time measures were all referenced to R. The Q wave was scored as the peak Q (R onset), as this has less variance than Q onset measures (Berntson, Lozano, Chen, & Cacioppo, 2004). The  $dZ/dt$  peak was taken as the maximum amplitude of this function, and the R to Z interval (RZ) was taken as the time between the R peak and the  $dZ/dt$  peak. Because the  $dZ/dt$  peak is not always sharp, noise could yield considerable errors of estimate. Preliminary analyses revealed that in extreme cases of wide plateaus, merely picking the first maxima could increase residual errors of estimate several-fold. Consequently, some peak finding or template matching algorithm needs to be employed. In the present study, we used a simple and easily implemented algorithm, which identified and set pointers to the maximum value in the  $dZ/dt$  data array. Data pointers then stepped progressively through the  $dZ/dt$  array from that point, in both directions, as long as the  $dZ/dt$  values pointed to were within 1 A/D unit of the maximum, which is the limit of amplitude resolution. Pointers continued stepping until the respective values decreased by 2 A/D units, and these points were defined as the start (left pointer) and end (right pointer) of the plateau. The  $dZ/dt$  peak (RZ) was taken as the midpoint of this interval, relative to the R peak.<sup>1</sup>

<sup>1</sup>A more comprehensive template matching approach that takes into account broader features of the  $dZ/dt$  waveform may be more accurate than the simple method used here. This is especially true if double peaked waveforms are seen, although none were observed in the present samples. In some cases, the latter may reflect the presence of distinct subperiods with different PEPs (and hence  $dZ/dt$  peaks) within the ensemble. One way to assess this would be to reduce the analytical epochs over which the ensemble is derived (e.g., from a single 5-min period to five 1-min epochs).

The X point was identified by the Mindware system as the minima of the X wave. The criterion measure for the B point was derived from a visually guided, manually adjusted cursor set to coincide with the start of the upstroke or positive inflection, often at the end of a notch, on the rising dZ/dt function. For comparison, the peak of the third derivative was also determined, as an estimate of the B point as previously described (Debski et al., 1993; Sherwood et al., 1990). All measures were derived from minute by minute ensemble averages.

Derived estimates of cardiovascular parameters included (1) PEP, (2) left ventricular ejection time, (3) stroke volume, and (4) cardiac output. The PEP was quantified as the time from the R onset to the B point (termed PEPr; see Berntson et al., 2004). LVET was measured by the analysis software as the time from the B point to the X point. Stroke volume (SV) was derived from the equation  $SV = \rho(L/Z_0)^2 \cdot LVET \cdot dZ/dt \text{ max}$ , where  $Z_0$  is the basal impedance,  $\rho$  is the resistivity of blood (set at 135 ohm · cm; see Sherwood et al., 1990), and  $L$  is the distance between the recording electrodes. Cardiac output (CO) was derived by the analysis software using the equation  $CO = HR \cdot SV / 1000$ .

### Procedure

**Young adult sample.** Participants were informed of the study procedures, signed consent was obtained, electrodes were connected, and subjects sat quietly for 10 min of adaptation. Six minutes of baseline recording were then taken in a sitting position to ensure stable measures. At that point, 3 min of task baseline were recorded followed by 3 min of task, 3 additional minutes of sitting baseline, and a final 3 min of standing baseline. The tasks included mental arithmetic and speech preparation stress. For the mental arithmetic stress, a four-digit number was displayed on a computer screen and the participants were instructed to count backwards aloud, as quickly as possible, by serially subtracting seven from the displayed number. For the speech stress, the participants had been instructed prior to the task periods that they would be preparing a speech that they would be presenting later (they never did), which was to be a defense against an accusation of theft. Half of the subjects received one task and half the other. The tasks periods were merely intended to provide a psychological provocation, and preliminary analysis revealed comparable responses to the two stressors. Consequently, the subjects were pooled across tasks.

**Adolescent sample.** Five minutes of baseline and 5 min of stress measures were extracted from recordings in a broader study at the University of Buffalo. Recordings were taken while the participants watched the movie *ET*. The baseline period was the first 5 min of the movie and the stress period was the 5 min of the death scene.

**Older adult sample.** Five minutes of baseline and 5 min of stress were extracted from recordings from a broader study measuring the effects of psychological stress on the amino acid Homocysteine. The participants were reclined (30° from vertical) with legs elevated. There was a 10-min acclimatization period followed by 20 min of baseline (5 min were scored for the present study) succeeded by a 5-min speech stress where 4 min comprised preparation for a speech and the final minute was delivery of the speech.

### Data Analysis

Data was obtained over 1-min intervals in baseline and stress conditions, as described above, and then averaged across minutes within each condition. For the initial between-subjects analysis, baseline and stress values were averaged for each subject in the primary young adult sample. The relation between the criterion B measure (visually guided, manual scoring) and the RZ interval was evaluated by linear and quadratic curve fitting. These functions were then used to derive estimates of B, and the residual errors of estimate were derived as the mean absolute discrepancy of the predicted B from the criterion B measure. Because these estimates were based on the curves derived from these data, the residual error of estimate in this case is simply the mean deviation of the points from the fitted curve. For extrapolations to other populations, however, the residual error corresponds to the average absolute deviations of the predicted B of other participant samples from the regression functions of the primary sample. In addition to the overall residuals, separate residual errors of estimate were derived for males and for females, to evaluate generality of the functions across gender. Similarly, to examine generality across experimental conditions, separate residual errors were calculated for baseline and stress conditions.

To evaluate generality across participant samples, the linear and quadratic equations derived from the primary sample were then used to predict B values of the adolescent and the older adult samples, and residual errors of estimate were derived as described above.

An additional estimate of the B point was derived as the peak of the third derivative of dZ/dt. This estimate has been recommended for signals that lack a clear B notch/upstroke (Debski et al., 1993; Sherwood et al., 1990).

To examine the utility of the predicted B value to estimate systolic time intervals, we compared PEP and LVET values derived from the criterion measured B and the estimated B. Similarly, stroke volume and cardiac output estimates based on the predicted B were compared to those based on the measured B.

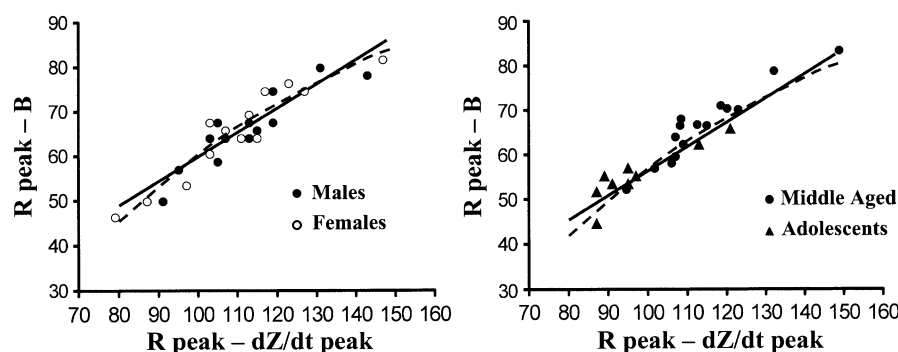
### Results

#### *Within- and Between-Scorer Reliabilities of the Criterion B Measure*

Two investigators separately scored the B point locations manually, and one scorer repeated the measures at least 1 week after the initial scoring. Intraclass correlation for within-scorer reliability was .98 ( $p < .001$ ) and between-scorer reliability was .88 ( $p < .001$ ). The absolute discrepancies were minimal for both the within-scorer ( $2.3 \pm 0.7$  ms) and between-scorer ( $2.5 \pm 0.6$  ms) differences, and approximated the minimum resolution (2 ms) of the 500-Hz sample rate or the recordings.

#### *RB Interval Is Closely Related to the RZ Interval across Subjects*

As illustrated in Figure 2(left), the interval between the R-wave peak and the peak of the dZ/dt wave (RZ) was a reliable predictor of the B point location (RB interval), averaged over baseline and stress conditions. The linear regression function ( $RB = 0.55RZ + 4.45$ ) accounted for 93% of the between-subjects variance in the measured B point ( $R = 0.96$ ,  $R^2 = .93$ ,  $p < .001$ ). There appeared to be some curvilinearity in the data, so a quadratic function was also obtained. The quadratic function ( $RB = 1.233RZ - .0032RZ^2 - 31.59$ ) was slightly but trivially better, accounting for 95% of the between-subjects variance ( $R = .98$ ,  $R^2 = .95$ ,  $p < .001$ ). As illustrated in Table 1, the abso-



**Figure 2.** Left: Aggregate best fit linear (solid lines) and quadratic (dashed lines) functions relating the RZ interval (R peak to dZ/dt peak) to the RB interval (R peak to B upstroke) in the young adult sample. Right: Data points from the adolescent sample and an older, middle-age sample superimposed on the linear and quadratic functions from the young adult sample. The latter functions provide a good fit to the data from the adolescent and middle-age samples.

lute residual errors of estimate were small (mean = 1.9 ms for the linear estimate and 1.7 ms for quadratic estimate). These residual errors were comparable to the reliability of within-scorer (mean absolute residual error = 2.3 ms) and between-scorer (mean = 2.5 ms) reliabilities of direct measures of the B point, and approximated the limits of temporal resolution of the signal (2 ms for the 500-Hz sample rate). As is apparent in Figure 2, the regression fit was comparable for males (mean absolute residual error =  $1.9 \pm 0.3$  SEM) and females (mean absolute residual error =  $1.8 \pm 0.3$  SEM).

As expected, the RB interval was also related to heart period or interbeat interval (IBI), although the correlation was low and nonsignificant ( $R = .22$ ,  $R^2 = .05$ ). This modest correlation was largely attributable to the weak association between IBI and the RZ interval, so that adding IBI to the regression did not increase the variance accounted for in RB (e.g.,  $R^2 = .933$  vs.  $.928$  for the linear function). Consequently, IBI was not further considered.

#### **The Regression Function Shows Considerable Generality across Participant Samples**

As illustrated in Figure 2 (right) and Table 2, the regression function derived above accurately describes the B point locations in a separate sample of adolescents ( $N = 9$ , ages 8–17) and a sample of older, middle-age adults ( $N = 15$ , ages 31–48). As illustrated in Table 2, B estimates for the adolescent and the older adult sample, derived from the quadratic equation defined above (based on the college student sample), closely approximated the

measured B values and were comparable to within- and between-scorer reliabilities of measurement and the temporal limits of resolution.

#### **RB Interval Is Closely Related to the RZ Interval across Conditions within Subjects**

As illustrated in Figure 3(left), the overall quadratic regression function defined above was a good predictor of the B point for both baseline and stress conditions. Because derived indices such as PEP are employed as an index of stress and of sympathetic drive to the heart, for the regression-based estimate to be useful it would be important to document that stress does not alter the relationship between RB and RZ. As shown in Table 1, the residual errors of estimate of the B point, based on the overall regression function given above, were small and were not appreciably (or significantly) different from residual errors for individual regression functions from the separate baseline and stress conditions. The residual errors of estimate based on the overall regression function applied separately to the baseline, and stress conditions were comparable to within-scorer and between-scorer reliabilities of direct measures of B.

As illustrated in Figure 3 (right) and Table 2, the estimate based on the quadratic function from the young adult sample was also able to accurately predict the B point separately under baseline and stress conditions in the adolescent sample and in the older adult sample. Residual errors were again small, and approximated the limits of resolution of the measures and the

**Table 1.** Regression Estimates and Absolute Residual Errors of Estimate of the B Point Based on RZ Interval<sup>a</sup>

Condition	Measured B (criterion)	Estimated B <sup>c</sup>	Absolute residual errors <sup>b</sup>		
			Overall regression	Baseline regression	Stress regression
Linear function (RB = 0.55RZ+4.45)					
Overall	65.3 (1.7)	65.6 (1.5)	1.7 (0.3)	1.7 (0.3)	1.6 (0.3)
Baseline	67.7 (1.4)	67.6 (1.5)	1.5 (0.3)	1.5 (0.3)	1.5 (0.3)
Stress	62.9 (2.0)	63.5 (1.8)	2.1 (0.3)	2.2 (0.3)	2.1 (0.3)
Quadratic function (RB = 1.233RZ − 0.0032RZ <sup>2</sup> − 31.59)					
Overall	65.3 (1.7)	65.3 (1.4)	1.9 (0.3)	2.1 (0.3)	1.9 (0.3)
Baseline	67.7 (1.4)	67.2 (1.5)	2.0 (0.3)	1.9 (0.3)	2.2 (0.3)
Stress	62.9 (2.0)	63.4 (1.7)	2.2 (0.3)	2.5 (0.3)	2.2 (0.3)

<sup>a</sup>Means and SEM, in milliseconds.

<sup>b</sup>The B estimate is based on the regression function derived from the overall means (averaged across baseline and stress) and was applied to the overall data and also separately to the baseline and stress conditions.

<sup>c</sup>Columns illustrate the residual errors of estimate for the overall regression functions and for regression functions derived from the baseline and stress conditions separately.

**Table 2.** Mean B Point Estimates of Adolescent and Older Adult Samples, Based on the Overall Quadratic Function from the Young Adult Sample<sup>a</sup>

	Measured B (Criterion)	Regression estimate of B	Absolute residual error of estimate
Adolescent sample			
Overall	59.2 (2.2)	57.3 (2.3)	2.6 (.3)
Baseline	59.8 (2.2)	57.7 (2.1)	2.3 (.3)
Stress	58.6 (2.2)	56.9 (2.3)	3.1 (.3)
Older adult sample			
Overall	66.6 (2.1)	66.6 (1.6)	2.5 (.2)
Baseline	70.5 (1.8)	70.0 (1.3)	2.4 (.2)
Stress	62.6 (2.8)	62.6 (2.2)	2.9 (.2)

<sup>a</sup>Means and *SEM*, in milliseconds.

within- and between-scorer reliabilities of direct measures of the B point. Although the stress manipulation was not very effective for many of the adolescent subjects (at least as indexed by the B point and thus reflected in PEP), the 1-ms mean difference between the measured baseline and the stress conditions was also reflected in the regression estimates.

### ***RZ-Based Regression Estimate Is Superior to the Third Derivative Estimate of B***

The regression-based estimate is superior to the estimate of B based on the peak of the third derivative. For this analysis, the B estimate based on the quadratic function defined above (from the young adult sample) was compared to the derivative-based estimate. The most notable difference in the two estimates is the universal applicability of the regression estimate, because it is based on a broad and salient aspect of the signal (the  $dZ/dt$  peak). In contrast, the third derivative estimate is based on small, local signal changes and consequently is more susceptible to noise. In the present samples, the derivative-based estimate was not applicable to many of the subjects, as it gave widely disparate values (greater than 10 ms from the criterion B measure), which a competent scorer would declare invalid on visual examination. This was true for 8 (31%) of the 26 participants in the young adult sample, 1 of the 9 adolescents (11%), and 6 of the 15 (40%) participants in the older adult sample. Even for the remaining subjects, which were accurately scored by the third derivative approach, the regression-based estimates yielded comparable or

**Table 3.** Regression-Based B Estimates and Residual Errors of Estimate in Different Samples<sup>a</sup>

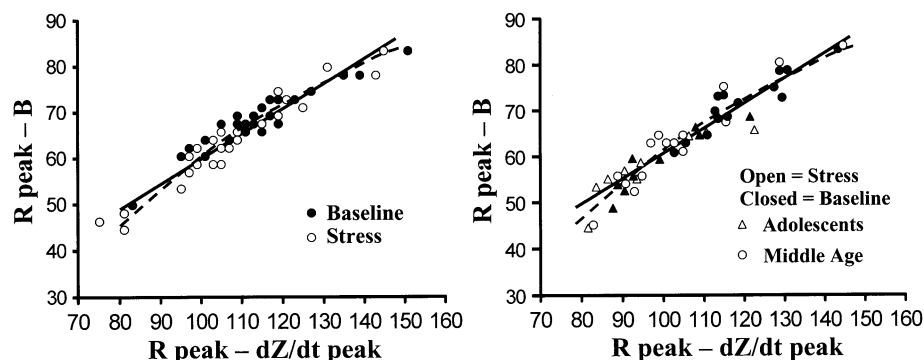
B	Absolute difference from measured B	Absolute residual error of estimate
College sample		
Measured B (criterion)		
$N = 26$	65.3 (1.7)	
$N = 18^b$	65.2 (1.9)	
Regression estimate		
$N = 26$	65.6 (1.5)	0.3
$N = 18^b$	65.5 (1.4)	0.3
Derivative estimate		
$N = 18^b$	67.1 (1.6)	1.9
Adolescent sample		
Measured B		
$N = 9$	59.2 (2.2)	
$N = 8^b$	58.3 (2.2)	
Regression estimate		
$N = 9$	57.3 (2.3)	1.9
$N = 8^b$	57.4 (2.5)	0.9
Derivative estimate		
$N = 8^b$	59.1 (1.9)	0.8
Older adult sample		
Measured B		
$N = 15$	66.6 (2.1)	
$N = 9^b$	67.1 (2.7)	
Regression estimate		
$N = 15$	66.6 (1.6)	0
$N = 9^b$	66.7 (2.5)	0.4
Derivative estimate		
$N = 9^b$	68.4 (2.3)	1.3

<sup>a</sup>Means and *SEM*, in milliseconds.<sup>b</sup>Subsets that were scored accurately by the third derivative method.<sup>c</sup>Smaller than derivative-based estimate ( $t = 2.5$ ,  $p < .01$ ); other comparisons are nonsignificant.

significantly smaller (young adult sample) residual errors for all participant samples (see Table 3).

### ***RZ Can Be Used to Reliably Estimate the B Point When a Notch/Upstroke Is Not Apparent***

The regression function derived above reliably estimates the criterion B point in low-resolution impedance signals that do not include clear upstrokes and was superior to manual scoring and to the estimate based on the third derivative. For this evaluation,



**Figure 3.** Left: Aggregate best fit linear (solid line) and quadratic (dashed line) functions relating the RZ interval (R peak to  $dZ/dt$  peak) to the RB interval (R peak to B upstroke) in the young adult sample. Functions show a good fit to values under both baseline and stress conditions. Right: Data points from the adolescent and middle-age samples, under baseline and stress conditions, superimposed on the linear and quadratic functions from the young adult sample. The latter functions provide a good fit to baseline and stress data for both the adolescent and middle-age samples.

**Table 4.** Estimates and Residual Errors of Estimate for Derived (Degraded)  $dZ/dt$  Signal in the Young Adult Sample<sup>a</sup>

B	Absolute difference from measured B	Mean residual error of estimate
Criterion B (from directly recorded $dZ/dt$ )		
N = 26	65.3 (1.7)	
N = 22 <sup>b</sup>	66.2 (1.7)	
Regression estimate		
N = 26	65.8 (1.6)	2.1 (0.3) <sup>c</sup>
N = 22	65.9 (1.6)	2.1 (0.3) <sup>c</sup>
Manual scoring		
N = 26	57.2 (2.8)	8.7 (1.1)
N = 22	56.9 (9.4)	9.1 (1.0)
Third derivative		
N = 26	52.7 (10.2)	12.6 (1.6)
N = 22	56.7 (9.2)	10.1 (0.8)

<sup>a</sup>Means and SEM, in milliseconds.<sup>b</sup>Subgroup excluding 4 subjects for which the third derivative method gave widely divergent estimates.<sup>c</sup>Significantly less than manually scored or derivative based estimates ( $t > 5.0$ ,  $p < .001$ ); the latter did not differ from each other.

the  $dZ/dt$  signal was derived off-line from the Zo output signal of the Minnesota device, rather than from the direct recording of the  $dZ/dt$  output channel. As discussed in the Methods, this derivation often obscures the notch and upstroke because of the reduced sensitivity associated with the large Zo offset. The criterion B values were again based on the manual measurements of the visually identified B point in the directly recorded  $dZ/dt$  output channel, whereas all estimates were obtained from the degraded signal derived from Zo. As illustrated in Table 4, estimates of B derived from the quadratic regression function were more accurate than manually scored data or those based on the third derivative. The degraded signals of 4 of the 26 participants (15%) could not be meaningfully scored with the third derivative method (which gave widely disparate, unrealistic values), but were accurately scored by the regression model. Even for the remaining participants, the regression method yielded more accurate estimates of the group mean and significantly smaller residual errors of estimate for individuals than did visual scoring or the derivative-based approach.

The regression function also can identify the B point in the subjects who were excluded from the primary analysis because of absent or indistinct B point upstrokes. As illustrated in Table 5, the regression method was able to reliably estimate the measured B, with residual errors of estimate that were comparable to the within-scorer reliability of the measured values (average residual error of within-scorer repeated measures =  $4.7 \text{ ms} \pm 1 \text{ SEM}$ ). This represents a rather conservative analysis, as the criterion measured values would be expected to be more variable in view of

**Table 5.** Regression-Based Estimates for 10 Subjects with Indistinct B Notches/Upstrokes<sup>a</sup>

	Measured B	Estimated B	Absolute residual error of estimate
Overall	67.7 (2.4)	67.0 (2.3)	2.8 (0.6)
Baseline	69.1 (2.5)	68.2 (2.3)	3.2 (0.7)
Stress	66.2 (2.6)	65.7 (2.6)	3.0 (0.6)

<sup>a</sup>Means and SEM, in milliseconds.**Table 6.** Systolic Time Intervals and Volumetric Measures<sup>a</sup>

	PEP (ms)	LVET (ms)	SV (ml)	CO (l/min)
Young adult sample				
Measured B	92.6 (2.5)	262.3 (3.3)	70.9 (4.9)	5.59 (0.48)
Estimated B	92.7 (2.3)	262.2 (3.2)	70.1 (5.0)	5.60 (0.38)
Adolescent sample				
Measured B	103.4 (0.9)	248.3 (7.7)	89.6 (5.0)	6.74 (0.36)
Estimated B	102.5 (0.8)	249.2 (7.6)	89.5 (4.9)	6.77 (0.36)
Older adult sample				
Measured B	107.8 (2.3)	287.4 (6.6)	71.4 (4.7)	5.75 (0.50)
Estimated B	107.8 (2.0)	287.4 (6.3)	72.7 (4.6)	5.84 (0.49)

<sup>a</sup>Means and SEM.

the absence of a distinct upstroke. This is consistent with the fact that the within-scorer reliability was significantly higher than the corresponding within-scorer consistency for the subjects with clear upstrokes. The mean residual error for the 10 subjects without a clear B upstroke was  $4.7 \pm 1.0$  versus  $2.3 \pm 0.7$  ms for the remaining subjects ( $t = 2.61$ ,  $p = .02$ ). In any event, it is clear that the regression function can approximate the performance of a highly skilled scorer and can do so for the most problematic subjects.

### The Regression Method Yields Accurate Derived Measures of Cardiac Function

By virtue of its ability to accurately estimate the B point, the regression method also provides for accurate estimates of systolic time intervals and volumetric measures from degraded signals. As shown in Table 6, PEP, LVET, SV, and CO derived by the regression method from the degraded signals yielded estimates of these parameters that were highly comparable to those based on direct measures from the corresponding nondegraded  $dZ/dt$  signals.

### Posture Needs to Be Controlled or Accounted For

The older adult participants were reclined (approximately  $30^\circ$  from the vertical), whereas the young adult participants were sitting upright. The fact that the regression function from the young adult sample could accurately predict the B points in the older adult sample indicates that the regression approach is not highly sensitive to moderate variations in posture. Standing, however, does introduce a bias. For the standing condition available for the young adult subjects, the slope of the regression function was comparable, but there was a larger offset, so that the regression function derived from the sitting posture underestimated the true value of B by  $4.5 (\pm 1.7)$  ms. As illustrated in Table 7, if this offset is added as a correction factor, the regression function accurately estimates B under the standing condition, with small residual errors.

### Discussion

The present results indicate that the B point of the impedance cardiograph signal, corresponding to the opening of the aortic valve, is highly related to the time to peak of the  $dZ/dt$  function (RZ), at least over the range of variation typically seen for healthy subjects and across conditions typical of laboratory studies. This relationship offers an automated estimate of the B point by identifying a fiducial point (the  $dZ/dt$  peak) on a large and consistent feature of the impedance waveform. Estimates derived from the regression equation were within the range of

**Table 7.** B Estimates under Standing Conditions<sup>a</sup>

	B	Mean residual error of estimate
Measured B (criterion)	73.1 (1.5)	
Estimate (+4.5) <sup>b</sup>	73.2 (1.4)	1.9 (.2)

<sup>a</sup>Means and SEM, in milliseconds.

<sup>b</sup>Regression estimate based on sitting condition +4.5 ms standing-posture offset.

between- and within-scorer reliabilities and approximated the temporal resolution of the sampling time of the recorded signals (2 ms). Systolic time intervals and volumetric cardiovascular parameters derived from the B point were also accurately estimated. Although this was not intended as a validation study, the outlined algorithm can accurately identify the dZ/dt upstroke that serves as the fiducial point in manual scoring.

Despite its accuracy, application of the regression approach does not preclude the need for visual examination of the scoring. This should always be included as an important component of data analysis, to identify artifacts, inappropriate placements related to unusual signal morphology, or other possible anomalies. The regression-based estimate can dramatically reduce manual processing time, however, and that is its primary application. A significant advantage of the approach is its broad applicability, as it is not dependent on small, local features of the dZ/dt waveform. It is especially useful in the absence of a B

notch or clear upstroke or with low-resolution or degraded impedance signals in which the upstroke is indistinct. In these cases, the regression estimate may be superior to either manual scoring or the use of the third derivative. This was clear from the analysis of degraded signals as well as the analysis of subjects lacking a distinct B upstroke, although the lack of a clear criterion in the latter analysis constrains conclusions somewhat in this subgroup. Even in these subjects, however, it remains the case that the regression estimates closely approximate those of a skilled scorer.

Although the algorithm appears to have considerable generality across ages, its application to younger or older participants needs to be validated. All subjects in the present study were generally healthy, although the younger group suffered from asthma, and there may be additional limits of generality in clinical populations. An addition caveat relates to the effect of posture or other condition that may alter preload or afterload or change the shape of the dZ/dt peak. Although most laboratory studies entail a sitting posture, this is not always the case, and a constant may need to be added for standing. Although the approach appears applicable over moderate degrees of recline, we did not examine a supine position, so it is unclear if the regression function would apply to this postural state. We also did not examine the effects of physical exercise. For many psychophysiological studies on healthy adults, however, the regression-based B point estimate can improve accuracy and facilitate data processing.

## REFERENCES

- Berntson, G. G., Lozano, D. L., Chen, Y.-J., & Cacioppo, J. T. (2004). Where to Q in PEP. *Psychophysiology*, 41, 333–337.
- Debski, T. T., Zhang, Y., Jennings, J. R., & Kamarck, T. W. (1993). Stability of cardiac impedance measures: Aortic opening (B point) detection and scoring. *Biological Psychology*, 36, 63–74.
- Kelsey, R. M., & Guethlein, W. (1990). An evaluation of the ensemble averaged impedance cardiogram. *Psychophysiology*, 27, 24–33.
- Kelsey, R. M., Reiff, S., Wiens, S., Schneider, T. R., Mezzacappa, E. S., & Guethlein, W. (1998). The ensemble-averaged impedance cardiogram: An evaluation of scoring methods and interrater reliability. *Psychophysiology*, 35, 337–340.
- Kubicek, W. G., Kottke, J., Ramos, M. U., Patterson, R. P., Witsoe, D. A., Labree, J. W., Remole, W., Layman, T. E., Schoening, H., & Garamela, J. T. (1974). The Minnesota impedance cardiograph—Theory and applications. *Biomedical Engineering*, 9, 410–416.
- Noble, M. I. (1968). The contribution of blood momentum to left ventricular ejection in the dog. *Circulation Research*, 23, 663–670.
- Noble, M. I., Trenchard, D., & Guz, A. (1966). Left ventricular ejection in conscious dogs. Measurement and significance of the maximum acceleration of blood from the left ventricle. *Circulation Research*, 19, 139–147.
- Sherwood, A., Allen, M. T., Fahrenberg, J., Kelsey, R. M., Lovallo, W. R., & van Doornen, L. J. (1990). Methodological guidelines for impedance cardiography. *Psychophysiology*, 27, 1–23.

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