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HYBRID COMPUTATION OF LEFT VENTRICULAR PERFORMANCE USING NONINV--ETC(U)
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HYBRID COMPUTATION OF LEFT VENTRICULAR PERFORMANCE USING NONINVASIVE TECHNIQS

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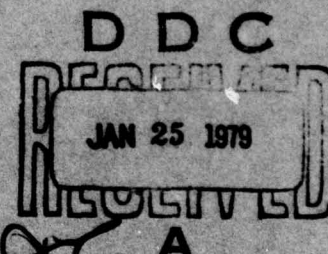
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USAF SCHOOL OF AEROSPACE MEDICINE
Aerospace Medical Division (AFSC)
Brooks Air Force Base, Texas 78235

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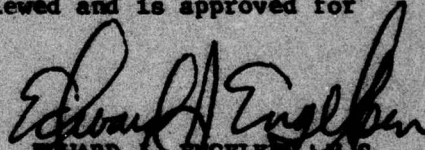
This final report was submitted by personnel of the Computer Systems Branch, Data Sciences Division and the Crew Environments Branch, Crew Technology Division, USAF School of Aerospace Medicine, Aerospace Medical Division, AFSC, Brooks Air Force Base, Texas, under job order 7930-11-10.

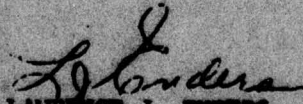
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This report has been reviewed by the Information Office (OI) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.


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HYBRID COMPUTATION OF LEFT VENTRICULAR PERFORMANCE USING NONINVASIVE TECHNIQS

INTRODUCTION

The relationship between left ventricular function and externally recorded cardiac cycle intervals (7, 17) has been appreciated for more than 50 years. The externally recorded signals include the phonocardiogram, electrocardiogram, and carotid pulse tracing. An explicit definition of the relationship between physiologic and left ventricular systolic intervals has been provided for both animal (1, 12, 13) and human (3, 14) subjects. Martin et al. (8) demonstrated a clear agreement between simultaneously recorded internal and external systolic time intervals (STI). A number of studies with human subjects and patients, as reviewed by Weissler and Garrard (15), have additionally related STI changes to various mechanical, physiologic, and pharmacologic interventions.

The application of STI analysis to physiologic investigations and clinical diagnosis has been relatively restricted because of inherent limitations in STI recording and interpretation. Lack of specificity, for instance, is illustrated by the observation that STI changes resulting from congestive heart failure (10) are markedly similar to those accompanying head-up tilt (16). Additionally, the standard methods of manually identifying and computing the intervals are very time consuming. Standard heart rate corrections in accordance with regression equations for group data (15) subsequently require even further computation, and the universal validity of such corrections for diverse conditions is suspect. The avoidance of beat-to-beat analysis in these standard technics may significantly reduce the information acquired, as evidenced in studies (5, 9) demonstrating identifiable instantaneous interval changes in atrial fibrillation. Additionally the latter study showed that the beat-to-beat changes conveyed information pertaining to severity of the mitral lesion. The need for automated STI analysis has subsequently been identified as a means of enhancing the reliability and accuracy of STI analysis.

Several digital computer programs (2, 4, 6, 11, 18) have been written in an attempt to reduce the computation time associated with STI analysis, but each of these programs has notable disadvantages. The computerized analysis is restricted to averaged data segments and thus fails to account for beat-to-beat variations (references 2 and 18 are exceptions). Furthermore, extremely clear signals are required for analysis, thereby prohibiting application to stress testing and other potential conditions wherein signal-to-noise ratios are reduced. Finally all existing programs (except reference 2, which requires a dedicated minicomputer) utilize small investigator-selected quantities of cardiac cycles, and this precludes continuous long-term analysis.

This paper describes a scheme for computerized analysis of STI that remedies some of the foregoing deficiencies. Externally recorded electrocardiogram, phonocardiogram, and carotid pulse signals are input to a unilateral hybrid system (analog computer, analog-digital converter, digital computer) to provide an automated printout of the standard left heart intervals on a beat-by-beat basis. The technic provides rapid analysis of large numbers of cardiovascular event complexes during periods of controlled rest or stress. The automatic nature of the pattern recognition process effectively removes observer bias and produces meaningful beat-to-beat information. This methodology thus enables the determination of both transient and long-term changes in left ventricular function that result from pathologic or physiologic stress.

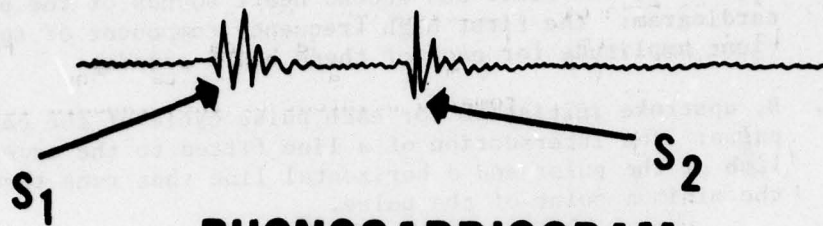
METHODS

Continuous recordings were made from ten human male subjects for baseline, centrifugal acceleration exposure, treadmill exercise exposure, and recovery periods. The following methodology was utilized at the USAF School of Aerospace Medicine in all cases.

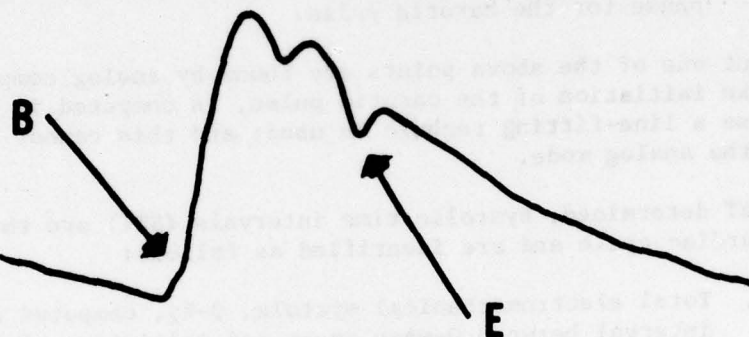
Bipolar ECG leads were placed on the subject. Signals were preamplified proximal to the subjects, displayed on a standard cathode-ray tube, and recorded on analog magnetic tape. The phonocardiogram was band-pass filtered in the preamplifier stage with lower corner frequency of 70 Hz. The upper corner frequency was set in accordance with characteristics of the individual to optimize the presentation of the aortic component of the second heart sound (S_2) and the first high-frequency component of the first heart sound (S_1). The microphone utilized a standard contact crystal which was acoustically insulated and positioned on the chest over the left sternal border. The carotid pulse was detected by an air-coupled diaphragm with the associated pressure transducer isolated from the subject. The carotid pulse diaphragm was strapped around the neck, with a minimum exposure area of the diaphragm positioned over the carotid artery. Voltage output was preamplified and band-pass filtered from 0.1 to 20 Hz. The phonocardiogram and carotid pulse signals were again filtered with the same band-pass range before display to develop a rolloff of 12 dB per octave.

The events identified by electronic processing for detection of systolic times (ST) are illustrated in Figure 1 and are defined as follows:

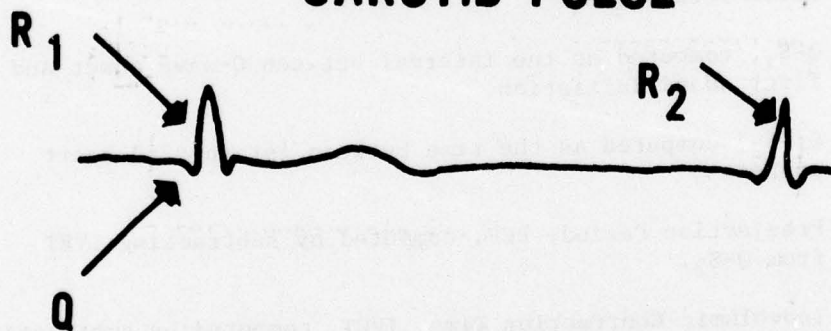
1. R_1 and R_2 , the R wave being the most dependable electrical event occurring during the cardiac cycle: the onsets of the R waves are used as fiducial points to bracket the cardiac cycle.
2. Q, the onset of electrical activity preceding ventricular contraction: the beginning of the Q wave if a Q wave is present, or the beginning of an R wave if no Q wave is detected.



PHONOCARDIOGRAM



CAROTID PULSE



ELECTROCARDIOGRAM

Figure 1. Simultaneous tracing of the electrocardiogram, phonocardiogram, and carotid arterial pulse illustrating the events necessary for detection of systolic times (ST). S_1 and S_2 : the first and second heart sounds. B : upstroke initiation for each cycle of the carotid pulse. E : end of the systolic phase of the cardiac cycle. R_1 and R_2 : R waves bracketing the cardiac cycle. Q : onset of electrical activity preceding ventricular contraction.

3. S_1 and S_2 , the first and second heart sounds of the phonocardiogram: the first high frequency component of sufficient amplitude for each of these heart sounds.
4. B, upstroke initiation for each pulse cycle of the carotid pulse: the intersection of a line fitted to the ascending limb of the pulse and a horizontal line that runs through the minimum point of the pulse.
5. E, onset of incisura: the fastest negative moving portion of the dicrotic notch, marking the end of the systolic phase for the carotid pulse.

All but one of the above points are found by analog computer: B, the upstroke initiation of the carotid pulse, is computed in digital mode because a line-fitting technic is used; and this cannot be performed in the analog mode.

With ST determined, systolic time intervals (STI) are then computed for each cardiac cycle and are identified as follows:

1. Total electromechanical systole, $Q-S_2$, computed as the interval between Q-wave onset and initiation of the second heart sound.
2. Left ventricular ejection time, LVET, computed as the interval between carotid upstroke initiation and dicrotic notch occurrence.
3. $Q-S_1$, computed as the interval between Q-wave onset and first sound initiation.
4. S_1-S_2 , computed as the time between 1st and 2nd heart sounds.
5. Preejection Period, PEP, computed by subtracting LVET from $Q-S_2$.
6. Isovolumic Contraction Time, IVCT, computed by subtracting LVET from S_1-S_2 .

The unilateral analog/digital technic utilized to locate the cardiac events is diagrammed in Figure 2. Heart sounds, EKG, and the carotid pulse analog signals are reproduced from magnetic tape (Ampex 2000A) at double the recording speed (7.5 IPS) to reduce analog processing time. The analog signals are then low-pass filtered to remove tape noise and trunked to the analog computer (EAI 680). Heart sound signals are scaled and squared to achieve the proper amplitude necessary for event detection and simultaneously attenuate nonusable signals (see Fig. 3).

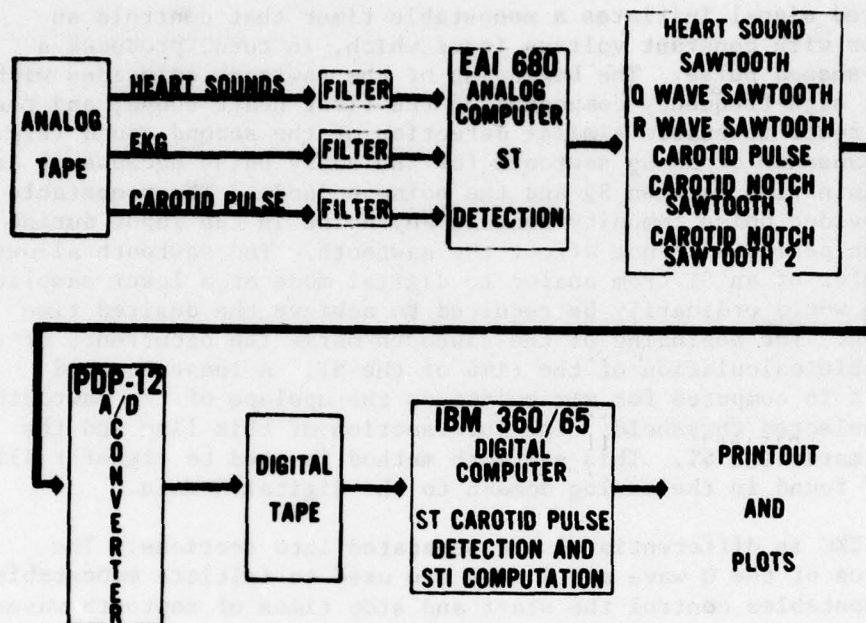


Figure 2. Block diagram of unilateral analog/digital technic.

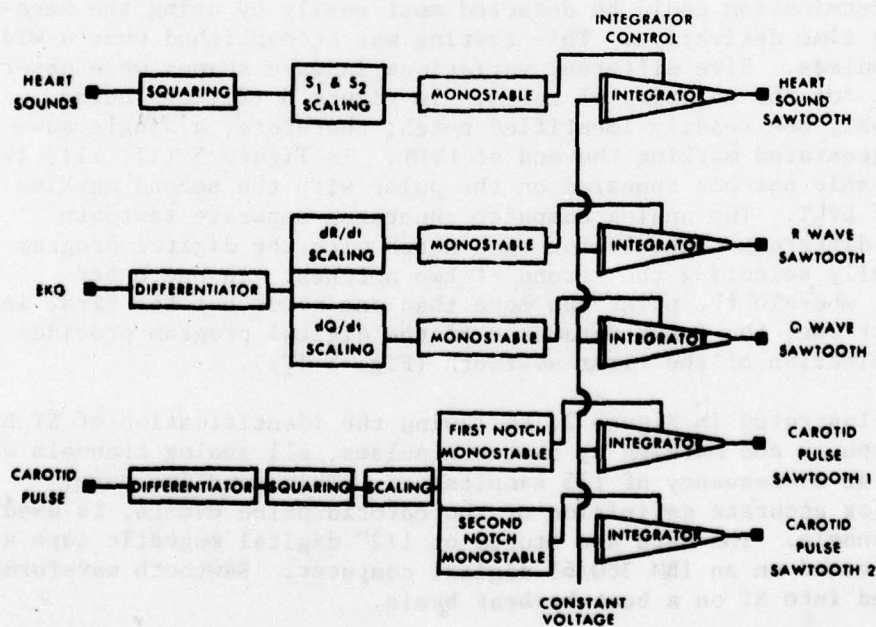


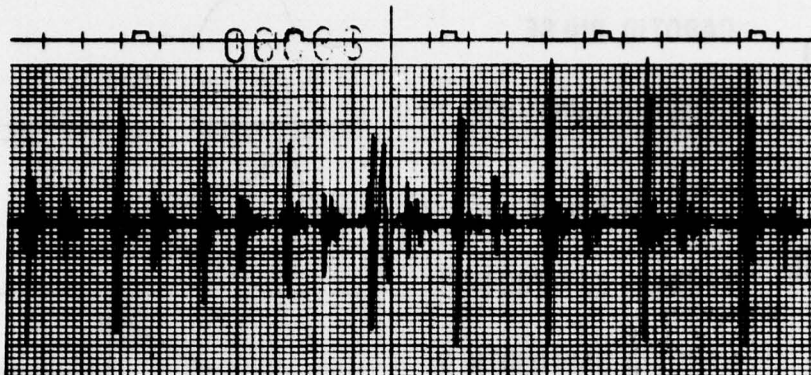
Figure 3. Block diagram of 680 analog computer program. Sawtooth pulses are generated marking the occurrence of systolic times (ST).

The squared signal initiates a monostable timer that controls an integrator with constant voltage input which, in turn, produces a sawtooth-shaped pulse. The beginning of the sawtooth coincides with the first high-frequency component of the first heart sound, and the pulse is reset to enable similar detection of the second sound (Fig. 4). Note the absence of an S₂ sawtooth for the noisy pulse because of lack of discrimination between S₂ and the noise episode. The monostable timer provides noise immunity because any noise in the input during the timer's on period will not affect the sawtooth. The sawtooth allows the transfer of an ST from analog to digital mode at a lower sampling rate than would ordinarily be required to achieve the desired time resolution. The beginning of the sawtooth marks the occurrence of the ST to enable calculation of the time of the ST. A least-squared linear fit is computed for six points on the upslope of the sawtooth above a selected threshold. The intersection of this line and the baseline marks the ST. This sawtooth method is used to transfer all of the ST found in the analog domain to the digital domain.

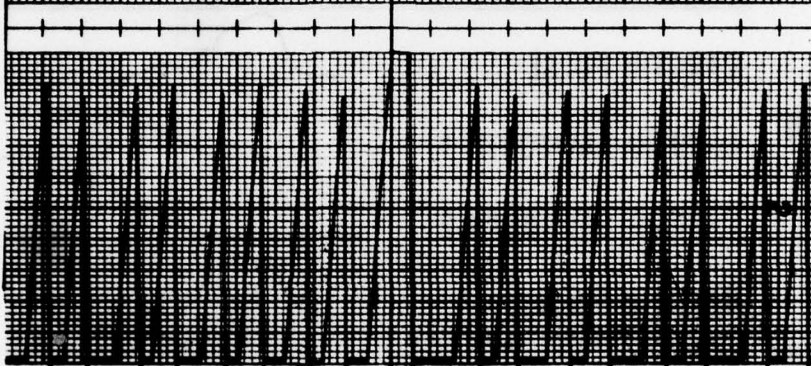
The EKG is differentiated and separated into sections. The derivatives of the Q wave and R wave are used to initiate monostables; these monostables control the start and stop times of sawtooth waves that mark the occurrence of the Q and R waves. Analog technics could not easily be implemented to locate initiation of LVET; hence a digital procedure was devised to identify the initiation of carotid pulse upstroke. Because of the variation of carotid pulse from individual to individual, the end of LVET was difficult to locate. In actual testing, the LVET termination could be detected most easily by using the negative going time derivative. This testing was accomplished over a wide range of pulses. Five different variations in wave shapes were observed to account for the majority of cases. In Figure 5 (I), the pulse includes only one readily identified notch; therefore, a single sawtooth is generated marking the end of LVET. In Figure 5 (II, III, IV), two detectable notches appeared on the pulse with the second marking the end of LVET. The analog computer generates separate sawtooth pulses on different channels for each notch with the digital program automatically selecting the second of two notches. In one other variation, wherein the pulse has more than one notch but the first is the correct one, the input parameter of the digital program provides for the selection of the first sawtooth (Fig. 5 (V)).

As illustrated in Figure 2, following the identification of ST by analog computer and marking by sawtooth pulses, all analog channels are digitized at a frequency of 125 samples/sec. This sampling rate, required for accurate definition of the carotid pulse events, is used on all channels. The data are stored on 1/2" digital magnetic tape and batch processed on an IBM 360/65 digital computer. Sawtooth waveforms are decoded into ST on a beat-by-beat basis.

HEART
SOUND



HEART
SOUND
SAWTOOTH



EKG



Figure 4. Oscilloscope tracing of heart sounds, sawtooth pulses generated by analog circuitry, and electrocardiogram. Note sawtooth pulse is not generated where heart sounds are not well defined.

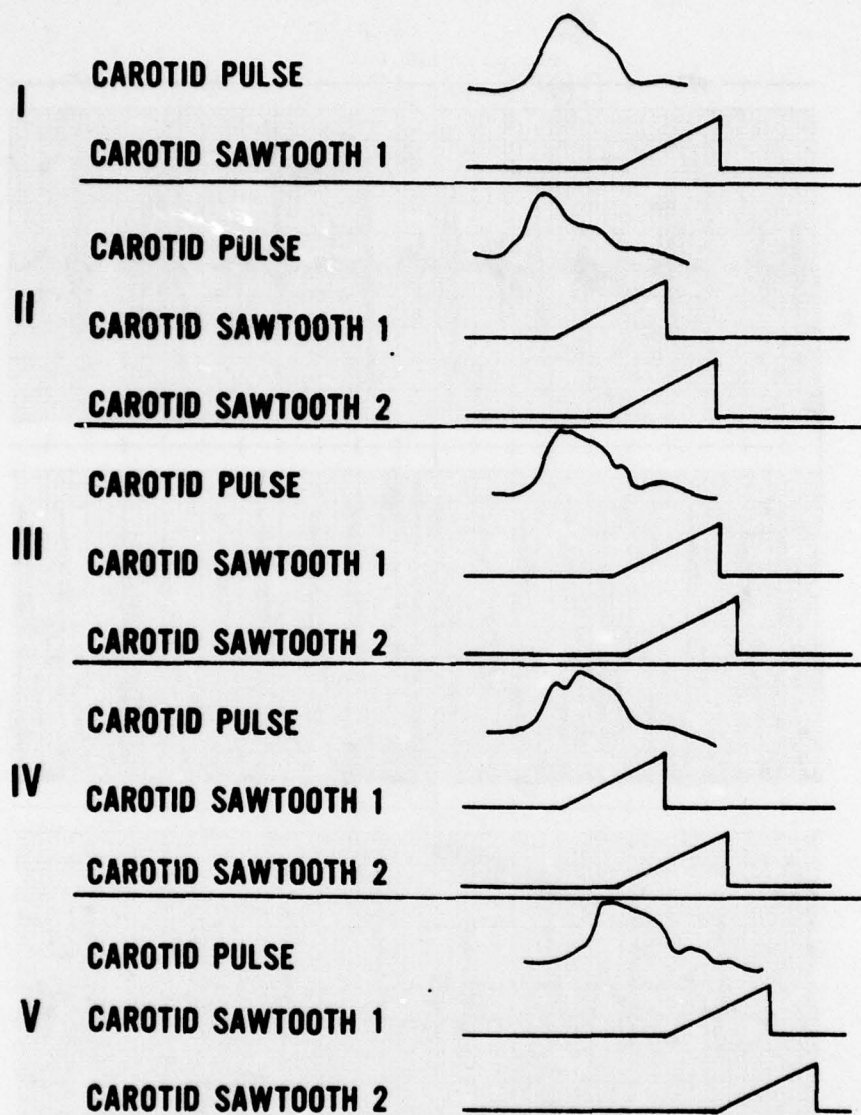


Figure 5. Five different variations in carotid pulse wave shape that were observed to account for the majority of cases.

The digital program initially identifies two consecutive R wave sawtooth pulses and computes indices for these two events. The R wave indices are used as fiducial points to bracket the events in a single cardiac cycle. A search is then initiated for the Q wave sawtooth at a maximum distance of 64 msec preceding the first R wave index. If no Q wave is found, the R wave is accepted as the beginning of electro-mechanical systole. A character (*) is then printed on the right margin of the printout for this beat to signify that no Q wave was found.

S_1 and S_2 sawtooth pulses are contained on the same digital channel, requiring timing consideration for correct identification of the sound pulses. S_1 is required to be located within the initial 25% of the time for R-R interval occurrence to be counted as a first heart sound. A search for the second heart sound is limited to the remaining 75% of the R-R interval.

The end of LVET is transferred to digital form by sawtooth pulses on two digital channels, depending on the individual variation in the notches of the carotid pulse (Fig. 5). With most cases wherein sawtooth pulses are recorded on both channels, the second channel sawtooth is used to mark the true end of LVET (Fig. 5 (II, III, IV)). The program automatically selects the second of the two notches. In Figure 5 (V), the first of two sawtooth pulses marks the correct end of LVET. This pulse is enabled when analog processing and input parameters are selected to cause the program to identify the first sawtooth at digital processing time. When the carotid pulse had only one notch and a single corresponding sawtooth pulse was present, the program used it as LVET termination. A character (#) is also printed on the printout's right margin to indicate which channel is used for LVET termination.

B, the beginning of LVET, is located in digital mode. A search is made on the carotid pulse channel for the maximum point, X, between two consecutive R waves (Fig. 6). The minimum point, N, is located between the first R wave and X. Six points are selected between N and X, with a least-squared technic used to find line 1. Line 2 is a horizontal line intersecting the minimum point, N. The intersection of these two lines at B is then computed to mark the beginning of LVET.

The STI are calculated from the ST from single cardiac cycles. This includes $Q-S_2$, LVET, $Q-S_1$, PEP [$(Q-S_2) - LVET$], and IVCT [$(S_1-S_2) - LVET$]. The STI indices are computed beat by beat, using the standard Weissler equations shown in Table 1. All STI and STI indices are printed in milliseconds. Measurements of the beat number, the heart rate (beats/min), the period of R-R interval, and the ratio of PEP to LVET are also computed and printed as shown in Figure 7. At the top of each page, the program prints a heading with subject name, date of experiment, type of stress, analog tape number, and time code (analysis period). If the STI had a missing component, S_1 not found, asterisks are printed for this beat in the column requiring S_1 ($Q-S_1$, S_1-S_2 , and IVCT) (Fig. 7).

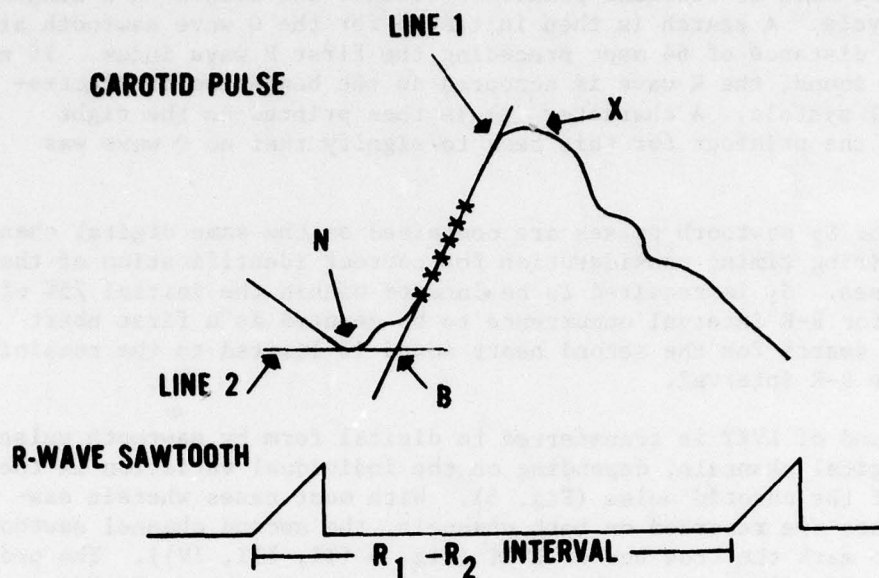


Figure 6. The R wave sawtooth pulses are used to bracket the events in a cardiac cycle. Six points are selected between N (minimum value) and X (maximum value) with a least-squared technic used to find line 1. The intersection of line 1 and line 2 (horizontal line drawn through N) marks the beginning of LVET.

TABLE 1. STI INDICES EQUATIONS^a

Systolic interval	STI index
Total electromechanical systole (Q-S ₂)	$Q-S_2I = 2.1 \text{ HR} + Q-S_2$
Preejection period (PEP)	$PEPI = 0.4 \text{ HR} + \text{PEP}$
LV ejection period (LVET)	$ETI = 1.7 \text{ HR} + \text{LVET}$

^aStandard Weissler equations (men) corrected for heart rate.

IMMEDIATE RECOVERY 36 200AB75 TAPE 102 TIME CODE 11750-11825										GROUP NO: 701			
BEAT	TIME (SEC)	HR (H/100)	PERIOD (MSEC)	PER (MSEC)	PPPT (MSEC)	10FT (MSEC)	21 (MSEC)	Q-51 (MSEC)	Q-52 (MSEC)	Q-521 (MSEC)	Q-52 (MSEC)	10FT (MSEC)	PER/10FT
1	0.597	68.8	871	112	160	236	351	67	366	891	278	88	.878
2	1.468	68.8	932	123	169	219	328	70	361	836	272	53	.563
3	2.401	66.6	901	117	166	227	340	72	364	884	272	85	.817
4	3.362	69.9	859	118	162	231	350	75	368	891	270	39	.881
5	4.160	75.6	798	132	162	218	346	75	358	508	275	57	.688
6	4.958	78.9	761	138	170	221	355	888	358	525	888	888	.626
7	5.215	75.1	799	136	166	221	349	990	357	515	888	888	.617
8	6.518	68.9	871	136	168	231	388	71	366	511	281	62	.588
9	7.385	63.3	987	181	166	230	318	78	370	503	296	66	.611
10	8.332	62.8	961	125	150	200	386	71	368	895	291	51	.520
11	9.298	63.0	853	126	151	236	383	71	361	891	288	53	.533
12	10.286	68.1	881	130	157	231	387	76	361	508	286	58	.561
13	11.127	70.8	887	131	159	236	356	75	367	516	293	56	.556
14	11.975	67.6	888	133	160	237	352	75	370	512	295	58	.559
15	12.863	66.7	899	138	165	239	352	78	377	517	303	68	.575
16	13.762	66.7	899	137	168	235	388	70	371	511	301	67	.582
17	14.661	67.2	893	18	85	235	349	54	252	383	188	888	.075
18	15.558	67.7	887	135	162	232	387	76	366	508	281	59	.581
19	16.881	68.5	863	133	161	228	387	77	362	508	285	56	.583
20	17.388	76.2	787	188	178	218	388	77	363	523	286	68	.663
21	18.091	79.8	752	136	168	221	358	77	359	527	282	58	.611
22	18.883	78.3	767	150	181	221	384	888	372	536	888	888	.680
23	19.610	73.1	820	138	163	281	365	76	375	528	288	58	.588
24	20.830	67.9	888	133	160	218	354	69	372	515	303	68	.588
25	21.318	65.3	818	138	160	236	387	73	370	507	287	61	.565

Figure 7. Computer printout of sample output showing beat-by-beat analysis of ST1.

RESULTS

The STI for baseline stress conditions were manually calculated and compared to computerized values. In all baseline and stress recovery cases, the automated computations (c.f. Fig. 7) agreed with manually reduced values within 2% for mean levels. Because the phonocardiograms and carotid pulse signals became noisy with large D.C. artifacts during stress periods, both automated and manual STI were inconsistently detected during stress periods. Nevertheless, the manual and automatic values for periods of reliable signals agreed within 10% in all cases.

Because the beat-to-beat variations in STI stand out as a unique advantage of the automated methodology, mean values will not be considered here. Rather, the instantaneous values will be presented as depicted in Figure 7. Figure 7 lists reduced STI data for the recovery period immediately following +3 G_z acceleration exposure. The cardiac period oscillates between values of approximately 750 and 950 msec, with relatively relaxed breathing. Computed STI are listed on an individual beat basis in both uncorrected (PEP, LVET, Q-S₂) and rate-corrected (PEPI, ETI, Q-S₂I) form. In all cases, the rate-corrected figures are larger than uncorrected, as expected by the use of Weissler correction factors. Figures 8-10 display a typical set of baseline determinations including cardiac period, uncorrected electromechanical systole, and heart rate-corrected preejection period as plotted on a beat-to-beat basis. The relatively regular oscillations in cardiac period (Fig. 8) follow the frequency of respiration, apparently reflecting normal sinus arrhythmia and central blood volume changes during normal breathing. Total electromechanical systole (Fig. 9) closely follows the same oscillatory pattern, with maximal lengths of systole corresponding to, or slightly preceding, maxima for the cardiac period. The preejection period of Fig. 10, although corrected for changes in the instantaneous heart rate, similarly varies with respiration. The occurrence of maximal preejection periods, however, corresponds in most cases to minimal cardiac period and hence to reduced duration of total electromechanical systole. At beat numbers 12, 20, and 26, for example, the PEP is at high peak values while cardiac period and Q-S₂ are at minima. The oscillatory phenomena, occurring in response to normal resting respiration, characterize the individual's cardiovascular responses to the rather well-defined mechanical and neurologic events accompanying lung inspiration and expiration.

In Figure 11 similar beat-to-beat phenomena are demonstrated for a human subject recovering from acceleration. Because of the relatively high heart rate and respiration rate during this recovery period, the respiration-induced oscillations in both cardiac period (Fig. 11) and LVET (Fig. 12) are faster with relatively sharper peaks. As noted for Q-S₂ during baseline the LVET maxima and minima are in phase with those for cardiac period. The data plotted in Figures 8 through 12 are typical for all subjects measured in the respect that respiration-induced oscillations in STI intervals, with corresponding relationships between individual intervals, were of the same nature.

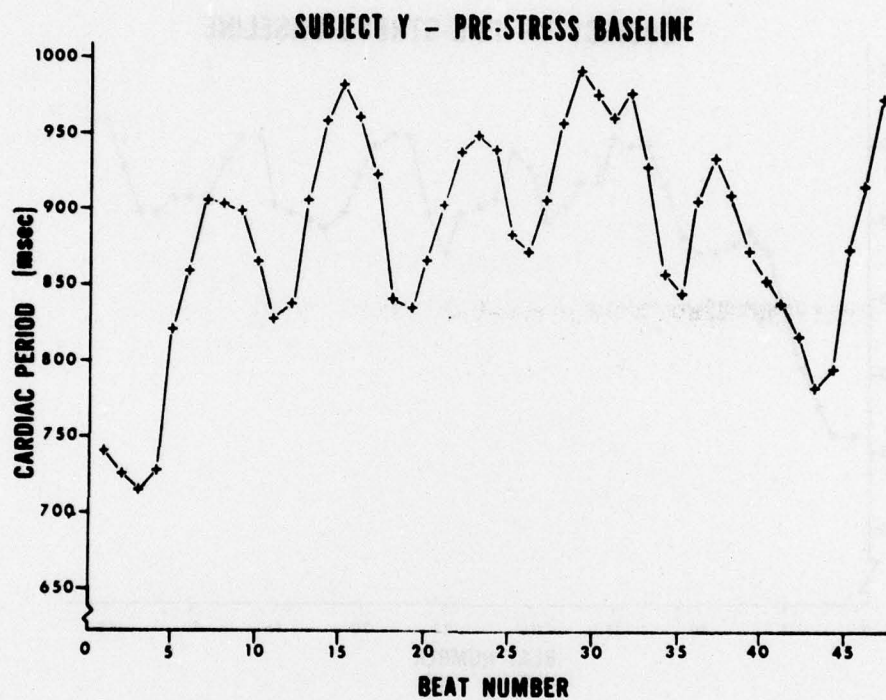


Figure 8. Beat-by-beat prestress baseline intervals for human subject during cardiac period.

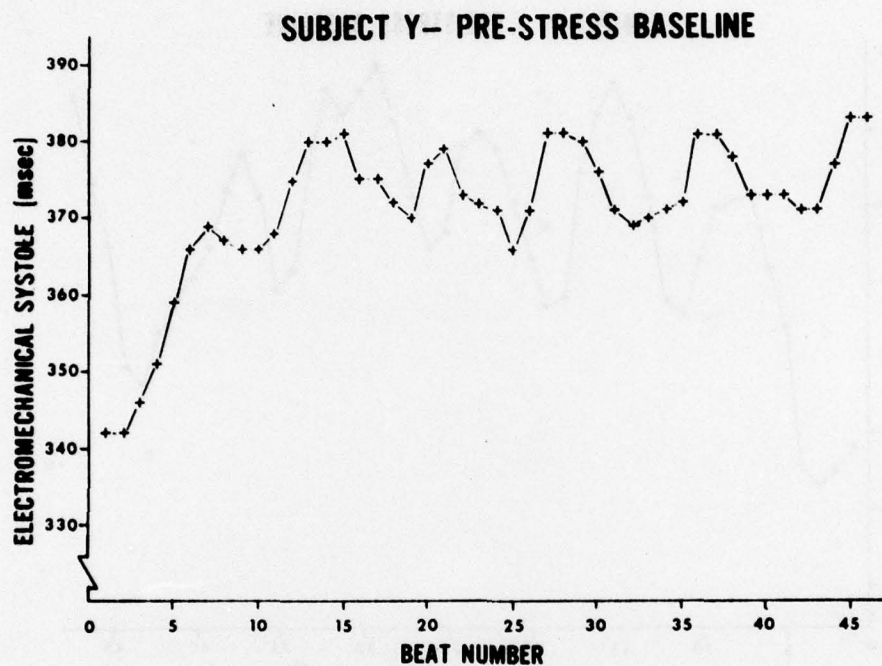


Figure 9. Beat-by-beat prestress baseline intervals for human subject with uncorrected electromechanical systole.

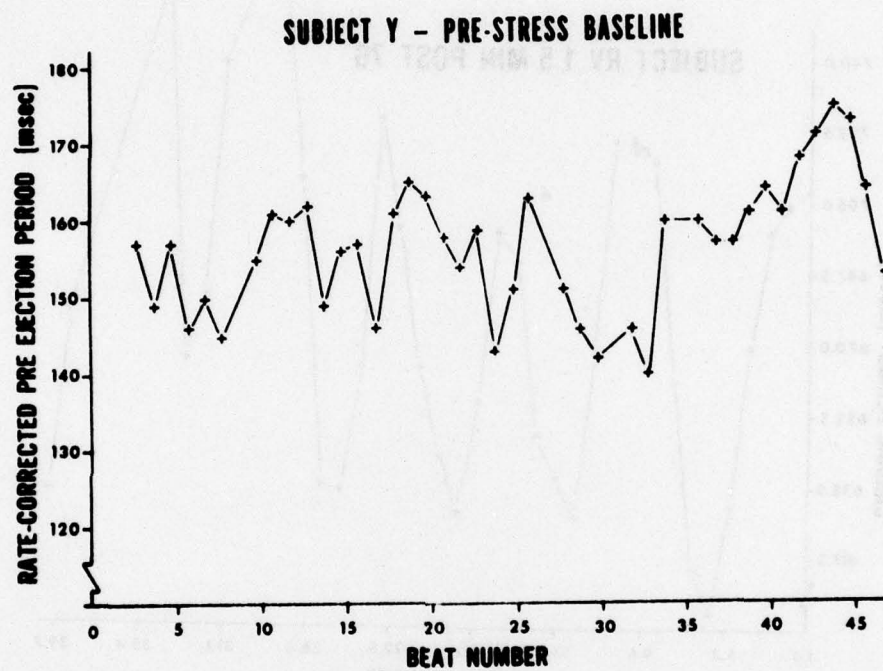


Figure 10. Beat-by-beat prestress baseline intervals for human subject with electromechanical systole corrected for heart rate.

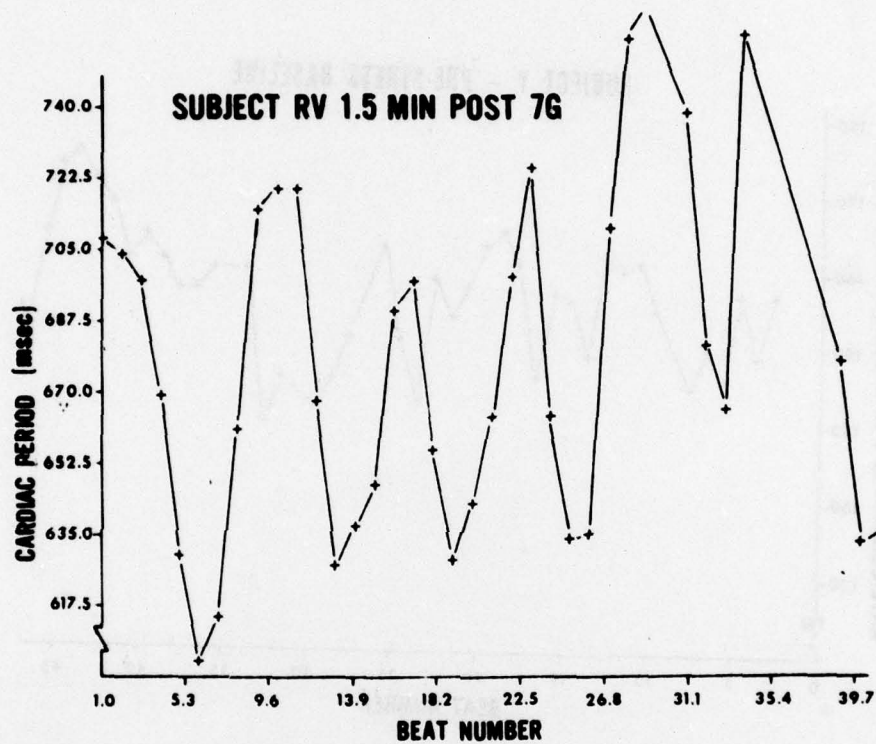


Figure 11. Beat-by-beat intervals for human subject following acceleration exposure in cardiac period.

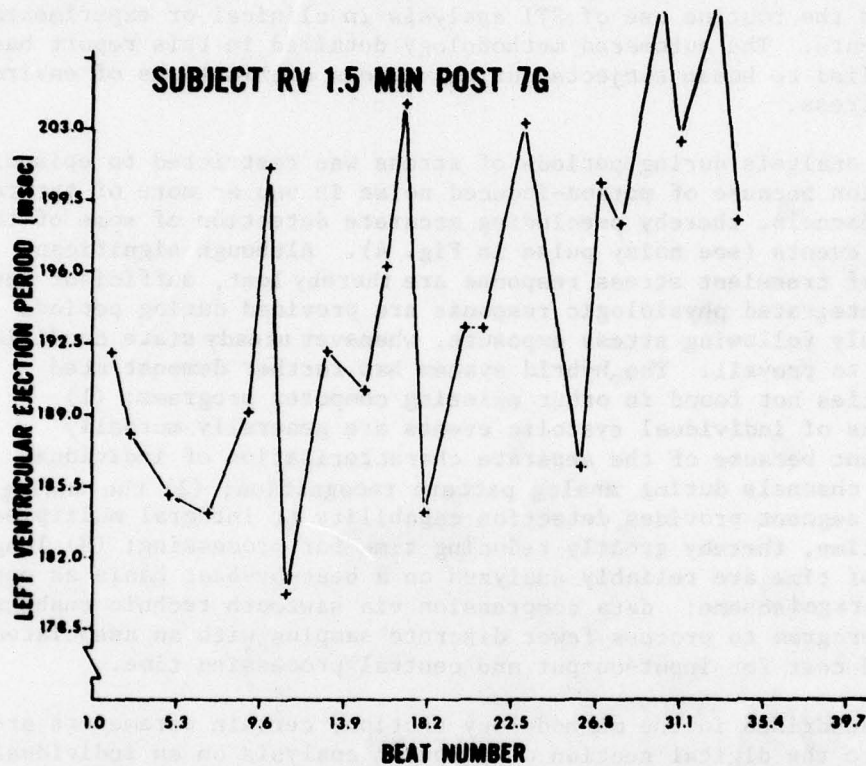


Figure 12. Beat-by-beat intervals for human subject following acceleration exposure in uncorrected left ventricular ejection period.

DISCUSSION

The recording and analysis of systolic time intervals provide clinicians and physiologic researchers with a noninvasive, atraumatic means of characterizing the cardiovascular system's condition. The extensive time and effort required for manual reduction of data have precluded the routine use of STI analysis in clinical or experimental environments. The automated methodology detailed in this report has been applied to human subjects during various combinations of environmental stress.

STI analysis during periods of stress was restricted to episodic information because of motion-induced noise in one or more of the raw-signal channels, thereby precluding accurate detection of some of the systolic events (see noisy pulse in Fig. 4). Although significant periods of transient stress response are thereby lost, sufficient details of the integrated physiologic response are provided during periods immediately following stress exposure, whenever steady state conditions continue to prevail. The hybrid system has further demonstrated capabilities not found in other existing computer programs: (1) detections of individual systolic events are generally mutually independent because of the separate characterization of individual waveform channels during analog pattern recognition; (2) the analog computer segment provides detection capability at integral multiples of real time, thereby greatly reducing time for processing; (3) long periods of time are reliably analyzed on a beat-by-beat basis as opposed to an averaged scheme: data compression via sawtooth technic enables the digital program to process fewer discrete samples with an associated decreased cost for input-output and central processing time.

As described in the methodology section, certain parameters are input into the digital section of computer analysis on an individual subject basis. This provision assures accurate identification of complicated or special carotid pulse waveforms and thereby takes into consideration individual variations among subjects. Only minor modifications are required for conversion of the technic to real-time capability; but the authors feel that the nature of phonocardiogram and carotid pulse recordings requires special analytical preparation and, at least in the research setting, large quantities of information could be lost or deteriorated by inappropriate analog setting occurring in real-time operation.

Sample data, depicted in Figures 7 through 12, demonstrate beat-to-beat variations in STI that oscillate with the frequency of respiration. The instantaneous changes in preejection period (Fig. 10) during resting ventilation reflect the neurological and mechanical influence of lung inflation and deflation on left heart function. In particular, the amplitude of PEP oscillatory change represents a quantitative measure of left ventricular filling and sinoatrial node electrical activity. The LVET values, during recovery from acceleration (Fig. 12), further

demonstrate two simultaneous dynamic processes: (1) gradual increase in ejection time over the complete period of 40 beats corresponding to an increasing cardiac period (Fig. 11), with concomitant return of venous blood to the central volume; (2) oscillatory changes corresponding to lung inspiration and expiration. These early differentiated long- and short-term changes in LVET reflect the underlying cardiovascular processes of increasing venous return, decreasing systemic resistance, increasing central blood volume, decreasing myocardial inotropy; and reduced ventilation. The relative contributions of these individual components in the integrated physiologic response can be quantitatively assessed by comparing the dynamic changes in STI among one another and serially evaluating individual values with reference to baseline control.

The cardiovascular effects of certain pharmacological agents with positive inotropic effects, for instance, could be evaluated via this automated scheme with respect to individual subject response by assessing serial changes in PEP, LVET, and PEP/LVET. While the time and effort required for manual reduction of the STI in such a clinical or physiologic investigation would be prohibitive, the application of the automated method converts the study to a routine level. The method's outstanding capability to process long periods of data enables a complete cardiovascular response profile, including transients and steady states.

The capability of the automated STI analysis to provide beat-to-beat values over long periods of time extends the applications and values of noninvasive cardiac records. The literature to date has reported mean values for STI (c.f. ref. 5 and 15) with little or no reference to instantaneous changes and their significance. The method reported here, however, has evidenced the potential informational value of individual heart beat analysis. Respiration and its interaction with cardiac and vascular dynamics has been shown here to be a useful perturbation when assessing cardiac status via STI. Both long-term (multibeat) and short-term (beat-to-beat) changes in systolic intervals can be accurately monitored and assessed as reflectors of cardiac response components (with quantitation ensured by the computerized scheme). Investigators can thus ascertain reliable physiologic and pathologic response data with noninvasive means. Minor programming changes are easily accommodated with this methodology, thus ensuring satisfaction of individual investigator preference for special analog filtering and digital computation correction.

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