1994020896 N94-25378

EVALUATION OF BIOIMPEDANCE FOR THE MEASUREMENT OF PHYSIOLOGIC VARIABLES AS RELATED TO HEMODYNAMIC STUDIES IN SPACE FLIGHT

Final Report
NASA/ASEE Summer Faculty Fellowship Program--1993
Johnson Space Center

Prepared By:	Bruce C. Taylor, Ph.D.
Academic Rank:	Associate Professor
University and Department	The University of Akron Biomedical Engineering Akron, Ohio 44325-0302

NASA/JSC

Directorate:	Space and Life Sciences
Division:	Medical Sciences
Branch:	Space and Biomedical Sciences Research Institute
JSC Colleague:	Janice M. Yelle, M.S.
Date Submitted:	August 13, 1993
Contract Number:	NGT-44-001-800

ABSTRACT

Orthostatic intolerance, following space flight, has received substantial attention because of the possibility that it compromises astronaut safety and reduces the ability of astronauts to function at peak performance levels upon return to a 1g environment. Many pre- and post-flight studies are performed to evaluate changes in hemodynamic responses to orthostatic challenges after Shuttle missions. The purpose of this present project was to validate bioimpedance as a means to acquire stroke volume and other hemodynamic information in these studies.

In this study, ten male and 10 female subjects were subjected to simultaneous measurements of thoracic bioimpedance and Doppler ultrasonic velocimetry under supine, 10^{o} head down and 30^{o} head up conditions. Paired measurements were made during 6 periods of 5 seconds of breath holding, over a 2 minute period, for each of the three positions.

Stroke volume was calculated by three bioimpedance techniques and ultrasonic Doppler. The three bioimpedance methods included calculation of stroke volume:

1. using Kubicek's basic equation and obtaining peak dz/dt by numerical differentiation of the delta-z waveforms ex post facto. Resistivity values, taken from the literature, were 135Ω-cm for all cases.
2. using Sramek's modifications of Kubicek's equation and obtaining dz/dt by numerical differentiation of the delta-z waveforms ex post facto.
3. from the digital output of the BoMed® NCCOM3 Cardiovascular Monitor in which peak dz/dt is determined by electrical differentiation and an internal, noise-eliminating, algorithm.

Regression analysis showed no discernible relationship between any of the three bioimpedance techniques and Doppler ultrasound. R^2 values were <0.1 in all cases. Percent change in stroke index from the supine to head up or head down position showed all four methods demonstrated significant differences as a function of tilt with no significant differences between the 4 methods ($P<0.05$). However, additional analysis demonstrated that the major changes in stroke volume measurements were due, in part, to thoracic fluid shifts and subsequent changes in Thoracic Fluid Index (Basal Impedance).

The results of this study demonstrate a poor correlation between Doppler ultrasound and electrical bioimpedance measurements of stroke volume. The study also indicated that apparent changes in stroke volume were due, in part, to changes in basal impedance and not due to changes in dz/dt or ventricular ejection time. At this time, bioimpedance measurements, using the methods described in this paper, are not recommended for quantitative determinations of stroke volume and cardiac output in the US space program. Measurements of relative changes in stroke volume and cardiac output may be possible on the same subject however further analysis of the data will be required to determine statistical significance.

INTRODUCTION

The phenomenon of orthostatic hypotension is manifested as pre syncope or syncope that occurs in some individuals undergoing postural changes from a supine (or seated) to an upright position. The effect is caused by the sudden movement of blood from the upper body to the lower extremities during standing. This causes a reduction in the amount of blood flowing to the heart (reduced end-diastolic volume) which responds by reducing the force of contraction (Frank-Starling Law). This effect is normally short-lived because baroreceptors sense a reduction in blood pressure and respond, within a few seconds, by sending commands to correct the deficit. The normal response mechanism is complex but includes an increased heart rate, increased force of contraction and peripheral vasoconstriction. If these mechanisms fail, the net result is a reduction in oxygenated blood to the brain and subsequent syncope. Figure 1 shows an episode of orthostatic hypotension that occurred during a "Stand Test" in the cardiovascular laboratory. The test results were more pronounced, in this case, because of voluntary fluid depletion on the part of the subject.

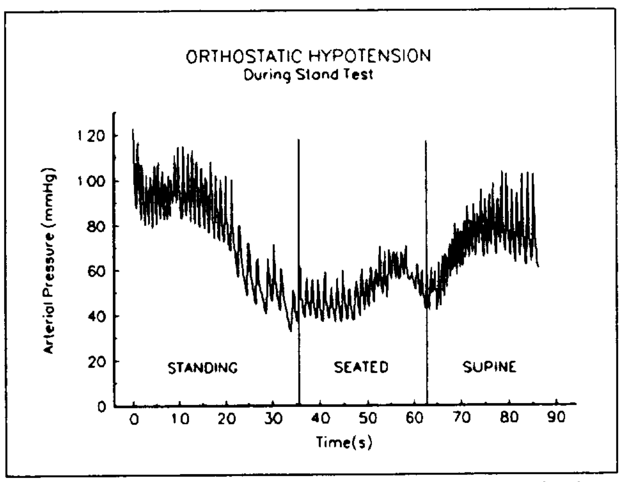

Figure 1.-An episode of orthostatic hypotension that occurred during a Stand Test. The substantial decrease in arterial pressure was corrected when the subject resumed a supine position.

In the space program this same phenomenon has been reported in a substantial number of astronauts after space flight. Microgravity exposure produces a redistribution of blood from the lower extremities. The body responds to this anomalous fluid challenge by eliminating apparent excess fluid while in microgravity. When the individual returns to the 1g environment, in a fluid-depleted-state, he is more susceptible to orthostatic hypotension. This orthostatic intolerance can cause key personnel to function below peak performance levels. Potential problems of this type are of concern and attempts are being made to eliminate the hazard.

Cardiac output is one of the most important physiologic variables to be monitored in the study orthostatic intolerance. At present non invasive cardiac output is measured, in the Cardiovascular Laboratory at JSC, using B-Mode and continuous wave Doppler ultrasonic velocimetry. The process requires measurement of the aortic outflow tract diameter just distal to the aortic valve using pulsed echo (B-Mode) ultrasound. Beat-by-beat continuous wave (CW) Doppler measurements of aortic outflow blood velocity are then made at the suprasternal notch. Stroke volume is computed by integrating over time, the area under the ejection velocity curve to obtain mean ejection velocity for one cardiac cycle. The mean velocity times the aortic cross sectional area times the ventricular ejection time gives **stroke volume**. Stroke volume times **heart rate** gives **cardiac output**. The process of determining cardiac output using ultrasound requires sophisticated, expensive equipment and highly skilled technical support. Other non invasive methods of cardiac output measurement such as radio nuclide imaging using gated blood pool scans, magnetic resonance imaging and procedures using inhaled gases are not appropriate for use in the space Shuttle or pre- and post- landing phases of Shuttle flight.

We proposed that the measurement of stroke volume and cardiac output could be simplified through the use of electrical bioimpedance measurements. Bioimpedance cardiac monitors are less expensive, easier to apply to the test subject, require less training for proper use and are less bulky than Doppler ultrasound. Impedance cardiology, first described by Kubicek (1966) has the potential of being a major contributor to the field of non invasive cardiology except that the source of the cardiac bioimpedance signal, despite numerous attempts, has never been adequately identified. In a 1988 note on "Continuous Cardiac Output Monitoring by Electrical Bioimpedance" the American College of Cardiology concludes "Due to limitations in accuracy in certain subgroups, the use of empirical formulas, and a relative lack of correlation with other presently used non-invasive methods, the technique is considered investigational." Although numerous investigators (Geddes, et al. 1966, Judy, et al., 1969, Baker, et al., 1971, Pate, et al., 1975) have evaluated the efficacy of cardiac output by bioimpedance the space program has not accepted bioimpedance as a viable means to acquire cardiac output information.

It was the purpose of this present study to attempt to validate cardiac bioimpedance measurements using the BoMed® NCCOM3 Cardiovascular Monitor already in-house at the Johnson Space Center to compare against simultaneously-acquired ultrasonic Doppler measurements of stroke volume. Since the analog output of the NCCOM3 included ΔZ it was also possible to determine stroke volume using the Kubicek, *et al.* classic equation and the modified equation proposed by Sramek (1982) and Bernstein (1986).

Development of the Bioimpedance Equations used in this Study

Impedance plethysmography studies(Nyboer, 1970) have demonstrated that, for a volume conductor, a change in volume, ΔV, is related to a changes in electrical impedance, ΔZ, by the following equation

$$\Delta V = -\frac{\rho L^2}{Z_0^2}\Delta Z \qquad (1)$$

where

ρ is the electrical resistivity of blood at the excitation frequency used;

L is the distance between voltage sensing electrodes;
Z_O is the mean basal impedance between voltage sensing electrodes.

If ΔZ is taken as the extrapolated maximum impedance change during systole(Ventricular Ejection Time) then ΔV represents the volume change during systole or stroke volume(SV). Kubicek determined that the peak value of the first time derivative of the ΔZ waveform, dz/dt, could be used instead of the extrapolated value. Figure 2 demonstrates this concept.

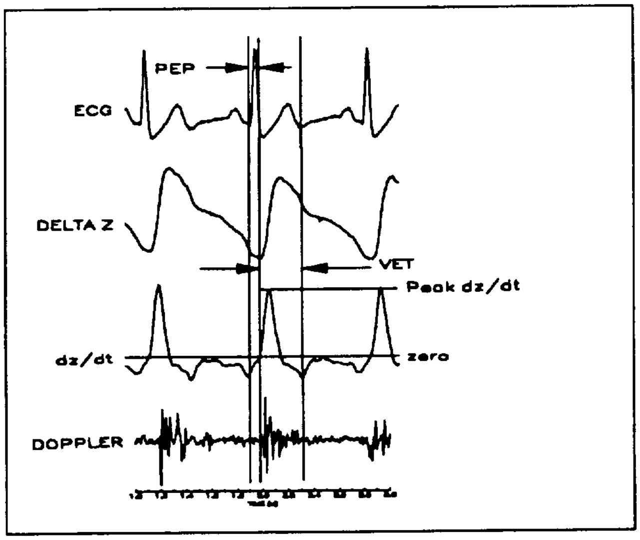

Figure 2.-An example of ECG, ΔZ, dz/dt and CW Doppler ultrasound signals taken simultaneously from the same subject. The diagram clearly demonstrates that the positive dz/dt corresponds to the ejection phase and that the peak negative dz/dt indicates the end of systole. The difference, in seconds, between these two events is the Ventricular Ejection Time (VET).

Kubicek's modification of equation (1) for stroke volume(SV_K) then becomes

$$SV_K = \frac{\left[\frac{dz}{dt}\right]_{peak} VET \rho L^2}{Z_0^2} \qquad (2)$$

where peak dz/dt and VET are taken from the analog signal as described in Figure 2.

Quail, *et al.* (1981) rearranged the Kubicek equation to solve for ρ such that

$$\rho = \frac{SV \cdot Z_0^2}{L^2 \left[\frac{dz}{dt}\right]_{peak}} \qquad (3)$$

Using dogs as test subjects, by varying hematocrits and other physiological parameters and using an electromagnetic flowmeter to measure stroke volume, Quail and his associates determined that ρ was essentially constant at 135Ω-cm. Given this observation, Bernstein (1986) rearranged the Kubicek equation (2) to eliminate ρ. Since

$Z = \frac{\rho L}{\pi r^2}$ solving for ρ such that $\rho = \frac{Z \pi r^2}{L}$ and substituting in equation (2) the modified Kubicek equation becomes

$$SV = \frac{\left[\frac{dz}{dt}\right]_{peak} VET \cdot L \cdot \pi r^2}{Z_0} \tag{4}$$

Sramek determined that the $\pi r^2 L$ represented a "Volume of Electrically Participating Tissue" (VEPT) a truncated cone whose volume was determined, experimentally, to be 1/3 that of a cylinder of the same radius and that the distance, L, between voltage sensing electrodes was 0.17*Height. Bernstein provided a nomogram to assist in the calculation of VEPT from the subject's height and weight which took into account the differences between male and female subjects. The Sramek (SV_S) equation, modified from (4) above was

$$SV_S = \frac{\left[\frac{dz}{dt}\right]_{peak} \cdot VET \cdot VEPT}{Z_0} \tag{5}$$

Equation (5) is the same equation used by the BoMed NCCOM3 Cardiac Monitor, SV_{BM}. The difference between SV_S and SV_{BM} lies in the method that the peak dz/dt is obtained. This is explained further in the Methods section.

MATERIALS AND METHODS

Ten normal female and 10 normal male volunteers, who had current NASA Class III physical examinations, were selected for this study. The subjects read and signed the NASA Human Research Minimal Risk Informed Consent Form prior to testing. Each subject drank 0.5 Liters of water just prior to the test in order to assure a reasonable level of hydration. The height and weight of each subject was recorded and entered into the BoMed® NCCOM3® Cardiovascular Monitor (BoMed Medical Manufacturing, Ltd., Irvine, CA 92718). Each subject was fitted with BoMed #04-030 Pre-gelled disposable electrodes . Two electrode pairs were placed on the neck with the uppermost member of each pair(current electrodes) even with the angle of the jaw. Two lower pairs of electrodes were placed on each side of the thorax with the uppermost electrode of each pair at the level of the ziphoid process.

The vertical distance, L, between the two innermost (sensing) electrodes was recorded for use in calculating stroke volume by Kubicek's method. Circumferential band electrodes were not used in this study .

Ultrasound measurements were made on a Biosound Genesis II®(Biosound Corporation, Indianapolis, IN 46250) echocardiograph system with a 2.0MHz CW Doppler probe. Two dimensional images of the Aortic Outflow tract (Ao2D) were also made with the Genesis II operating in the B-Mode.

Data for each subject were recorded on a TEAC (Teac, America Inc., Montebello, CA 90640) MR-30 Cassette Data Recorder running at 9.52 cm/s. This speed provided bandwidths of 100Hz - 18.8kHz in the direct-record mode used for the CW Doppler signals and DC - 2.5kHz in the FM mode.

Output signals from the NCCOM3 include the following signals: $\Delta Z(1V = 0.1\Omega)$, $dz/dt(1V = 1\Omega/s)$, ECG(1v = 1mV) and Digital Signals(RS-232 9600 Baud, 11 bit format, 1 Start bit, 7 data bits, even parity, 2 stop bits)

In the slow mode, the NCCOM3 averages 16 beats and outputs the following derived parameters via the serial I/O port: Cardiac Output (L/m), Stroke Volume(ml), End Diastolic Volume(ml), Peak Flow(ml/s), Ejection Fraction(%), Heart Rate(beats/m), Thoracic Fluid Index (Z_0), Index of Contractility(sec^{-1}), Ejection Ratio(%), Systolic Time Ratio(%), Acceleration Index(sec^{-2}), Time (every minute)

In the fast mode, the NCCOM3 provides the following data on a beat by beat basis: Cardiac Output(L/m), Stroke Volume(ml), End Diastolic Volume(ml), Peak Flow(ml/s), Ejection Fraction(%), Heart Rate(beats/m), Time(every minute)

Data stored on magnetic tape included the following: CW Doppler audio from the echocardiograph(direct record mode); ECG from the NCCOM3; ΔZ from the NCCOM3; dz/dt from the NCCOM3; Event Marker; Serial (RS-232, 2400 Baud) Baud rate shifted data from the NCCOM3 and Voice

Video and audio output from the Genesis II echocardiograph were also recorded on a Panasonic 6300 Video Cassette Recorder for post processing of Ao2D and CW Doppler signals. Serial data from the NCCOM3 were at 9600 Baud which required a bandwidth beyond the capability of the TEAC MR-30 recorder. Baud rates were shifted to 2400 Baud through the use of a Black Box® (Black Box Corporation, P.O. Box 12800, Pittsburgh, PA 15241-0800) CMA02A interface adapter. The CMA02A buffers the incoming 9600 Baud data and outputs it at 2400 Baud. The 2400 Baud signals are then recorded on the TEAC Recorder on an FM channel.

After the subject was fully instrumented, appropriate data entered into the NCCOM3 and recorded on tape, the Ao2D measurements were taken with the Genesis II Echocardiograph while the subject was placed left-side-down. After the aortic dimensions were measured, the subject was required to lie in the supine position on a Stryker Circle® Bed (Stryker Corporation, Kalamazoo, MI 49001).

During the next four minutes of testing, the following protocol was followed for each subject at each of three (supine, 10^{o} head down and 30^{o} head up) positions.

Minute 1
NCCOM3 set to the Slow Mode (averages every 16 "good" beats) and CW Doppler measurements made at the Suprasternal Notch.
Minutes 2 and 3
The NCCOM3 was switched to the Fast Mode (beat x beat analysis of stroke volume and cardiac output) and CW Doppler signals taken.
Subject was required to breath normally for 15 seconds then hold breath for 5 seconds. This process was repeated 6 times over the next two minutes.
Minute 4
One minute period of data acquisition during which the NCCOM3 was placed in the Slow Mode and ultrasound measurements taken.

Sequencing was done through the audio channel on the VCR and TEAC tapes, event marks on the TEAC tape and Image Reversal (Flash) on the Genesis II Echocardiograph.

ECG, ΔZ and event waveforms were transcribed to PC floppy disks by playing back the FM analog tapes through a DATAQ (DATAK Instruments, Akron, Ohio) analog to digital converter using DATAQ's CODAS Signal analysis software. Each data channel was digitized at 100 samples per second. The dz/dt data were not digitized because dz/dt could be obtained by differentiating the ΔZ channel using the CODAS software. Peak values of dz/dt and VET could then be determined manually for the SV_K and SV_S and automatically, via the NCCOM3 unit for SV_{BM}

Figure 3 shows representative tracings of the transcribed data used for analysis. This protocol permitted collection of 4 successive heart beats and the associated impedance signals. For individuals with extremely low heart beats, with R-R intervals exceeding 1.25s, only 2 or 3 successive beats were acquired.

RESULTS

After data collection, the analog and serial data were transferred to PC-compatible floppy disks. Analog data were separated by event (supine, 10^{o} head down, 30^{o} head up). ECG, ΔZ and event mark were transcribed initially. Then using the CALC feature of the CODAS Signal Processing Software, the ΔZ data were differentiated to produce a dz/dt channel. Peak dz/dt(referred below as IMPSIG) and VET measured during each breath-hold sequence were then manually determined and transferred to a Quattro® (Borland International, Inc., Scotts Valley, CA 95067-0001) spread sheet for processing. Stroke volumes using Kubicek's and Sramek's formulae were then calculated using the following equations:

$SV_K = (IMPSIG/10*VET*135*L^2)/TFI^2$
$SV_S = (IMPSIG/10*VET*VEPT)/TFI$

Since TFI data were not available on a beat-to-beat basis, the TFI values were determined just before and just after the 2 minute test series. The two readings, when different, were averaged.

Stroke volumes from the BoMed NCCOM3 were taken directly from the serial output data for the same time interval as the impedance data and entered into the spread sheet as SV_{BM}. Doppler echocardiographic data were obtained from the Genesis II Echocardiograph . These data were obtained for the same beats as the impedance data. In some cases, all 4 beats were not obtainable because of frame misalignment on the VCR. In these cases data were obtained for as many beats as possible.

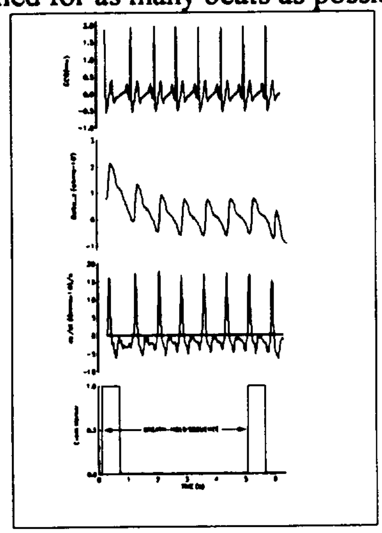

Figure 3.-Digitized data showing event marker that denotes start and finish of 5 second breath-hold sequence. Six of these sequences are performed during a 2 minute test interval at each position. The breath-hold sequence(arrows) eliminates the respiration artifact in the impedance signals.

The data were reduced by averaging the beats taken during the 5 second breath-hold sequences. In this way, each data point represents the average stroke volume, for Doppler and Impedance methods, for each 5 second period. To normalize the data for size differences between subjects, each Stroke Volume value was divided by Body Surface Area (BSA) to obtain **Stroke Index**.

An Analysis of Variance (ANOVA) was performed to test significant effects for replications, sex, and event(tilt). The results are Shown in Table I with values <0.05 considered to be statistically significant.

These results indicated there were no significant differences in replications so that the 6 data points for each condition could be combined. Also of note is the fact that there was a significant interaction for the sex-by-tilt grouping. Analysis of simple effects showed that all impedance methods were highly significant for sex($P \leq 0.001$). Doppler was not significant for sex except for the 30^{o} head-down tilt case which was highly significant ($P \leq 0.001$)

Table 1.-ANOVA results to test the significant effects for sex, replications(REPS) and tilt.

	SEX	REPS	TILT	SEX by REPS	SEX by TILT	TILT by REPS	3 way
SI_{BM}	.0001	.9922	.0001	.8044	.0046	.999	.999
SI_K	.0001	.9802	.0001	.98	.0922	.9917	.984
SI_S	.0001	.9878	.0001	.9813	.0026	.9878	.910
SI_D	.0001	.6037	.0001	.9181	.0132	.9919	.946

To observe the effects of tilt, the percent change in stroke index for the three tilt events, using combined data, were plotted. These results are shown in Figure 4. Statistical analysis ($P \leq 0.05$)showed that differences between events 1 and 2 were not significant but that event 3 was different from both groups 1 and 2. There were no significant differences between groups, i.e., all 4 methods produced equivalent results. Scatter plots of stroke indices of all three impedance methods are shown in Figure 5.

To test the validity of the NCCOM3 algorithm to detect and differentiate the ΔZ signal, a scatter plot of SI_S by SI_{BM} was done and shown in Figure 6.

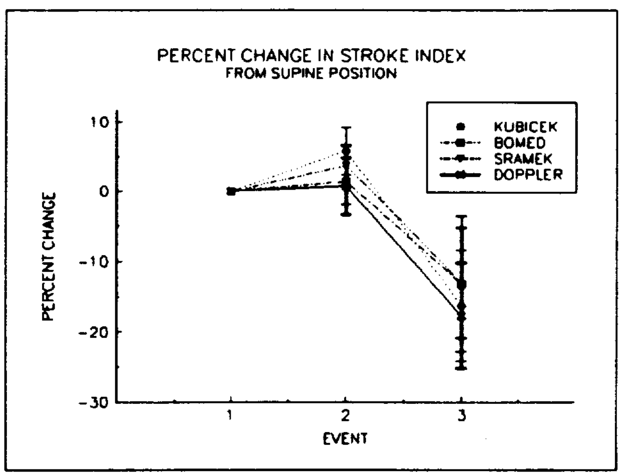

Figure 4.-Combined data showing percent change in stroke index as caused by head-up(2) and head-down(3) tilt from the supine(1) position. Vertical bars are 95% confidence limits.

DISCUSSION

In looking at the percent change (Figure 4) data there was a significant shift in the cardiac output from the 10^{o} head-down position to the 30^{o} head-up position. The magnitude of change from the head-down to head-up positions were roughly the same for all 4 methods. The Doppler and Sramek's method showed parallel effects. The BoMed method showed a slightly reduced sensitivity (lower slope) and the Kubicek method showed a slightly increased sensitivity(steeper slope) to positional changes. Using Duncan's Multiple Range Test to compare means there were no significant differences

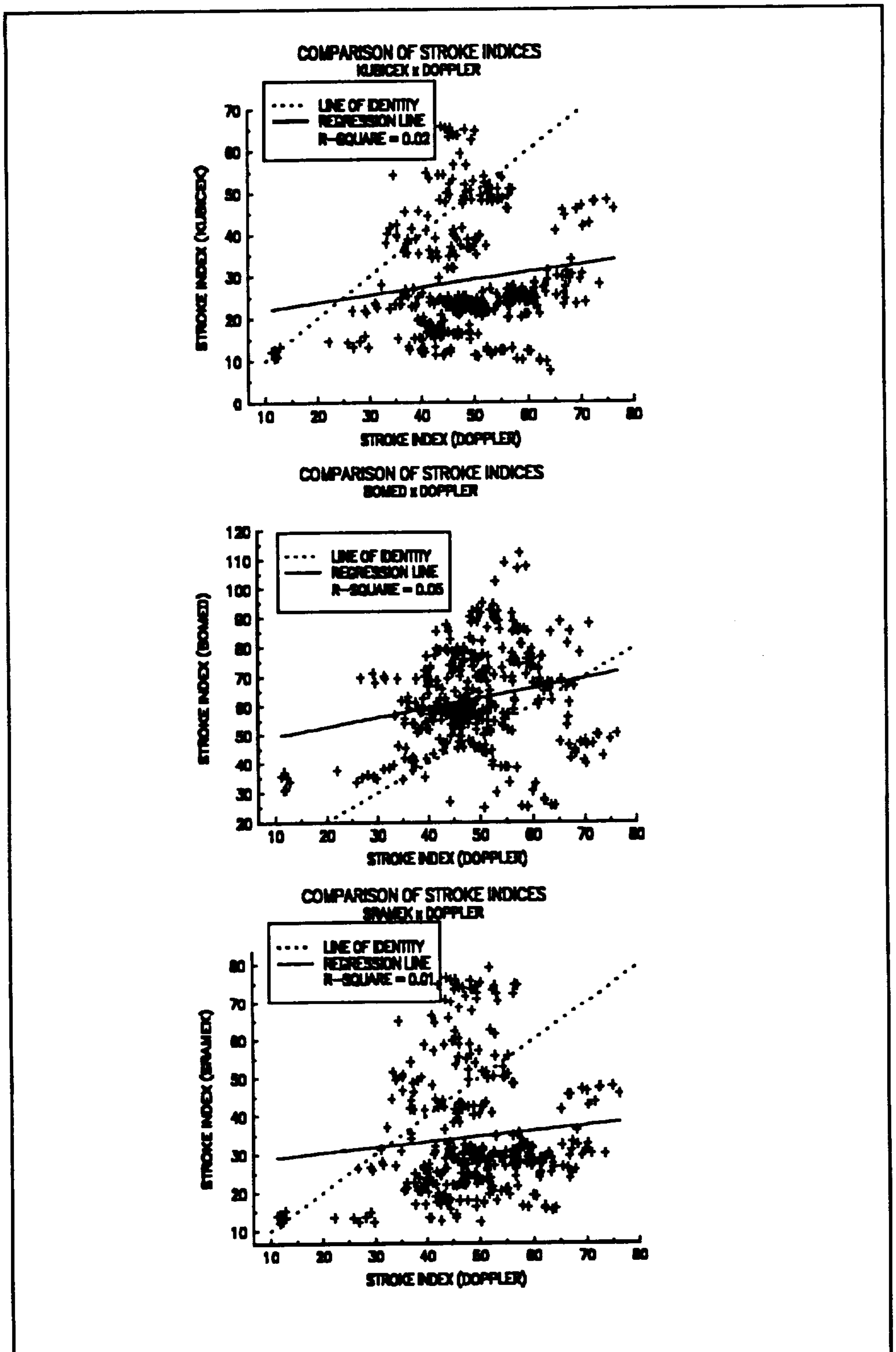

Figure 5.-Comparison of stroke indices of Kubicek x Doppler, BoMed NCCOM3 x Doppler and Sramek x Doppler. The solid line represents the linear regression line for the data. The dotted line represents the line of identity along which the data would lie if the variables were equivalent. R^2 values for the three groups are 0.02, 0.05 and 0.01 respectively.

among any of the 4 methods within any treatment group (degree of tilt) however there were significant interactions between degree of tilt and sex.

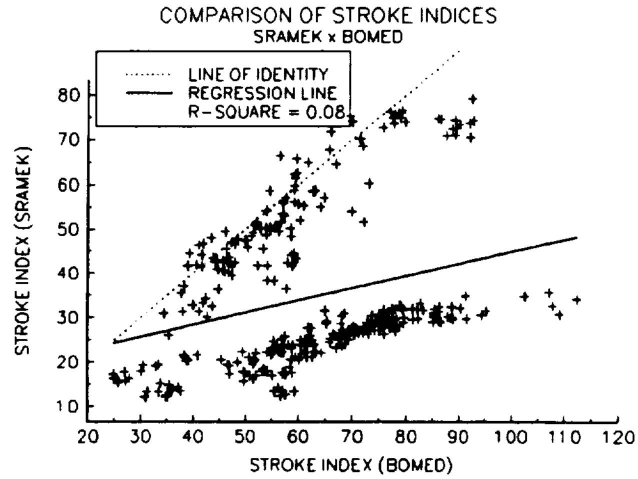

Figure 6.-Scatter plot of stroke index calculated by Sramek's equation and the BoMed NCCOM3 cardiovascular monitor. The data should fall on the line of identity with an R^2 value of 1.0. The data exhibit a bi-modal distribution with a low R^2 value of 0.08. The reason for this distribution is not clear.

Looking at the scatter plots of the three impedance methods and Doppler, there appeared to be no correlation among any of the events. Correlation coefficients were less than 0.1 in all cases. This indicates that either impedance (all three methods) or Doppler or both are not measuring stroke volume. Since the Doppler echocardiographic analysis of percent change studies produced the expected results, one can suspect that the echocardiograph is measuring a real quantity, namely stroke volume. On the other hand, one cannot assume this of the bioimpedance signals because of the changes in TFI that occur with postural changes.

One is then led to consider these two apparent contradictory results, namely acceptable results when percent change from supine is considered and random results when comparing Doppler to bioimpedance. The assumption must be that something else is affecting the impedance signals. A likely culprit is the TFI signal which also varies with positional changes. A look at equations (2) and (5) show that a change in TFI will produce changes in stroke volume in the direction observed. It should also be noted that the change in SV_K will produce a steeper slope because of the squared term that appears in the denominator.

In order to determine to what extent the TFI changes would have on stroke volume or stroke index, the data were recalculated by keeping all variables constant except for TFI. The constant was taken as the mean dz/dt, mean VET, mean L and mean VEPT over all trials. For the Kubicek equation, ρ was taken as 135Ω-cm. The results of this investigation were plotted against the percent change data and are shown in Figure 7.

This analysis demonstrates that a major portion of the change that is seen in the three test groups is due to changes in TFI and not due to measured changes in dz/dt and

VET. Statistical analyses demonstrated highly significant differences in the TFI data by sex, by tilt and by sex*tilt ($P \leq 0.001$).

A second set of statistical analyses keeping TFI constant showed the following:

For the Kubicek Data, sex was not significant but tilt was ($P \leq 0.05$) when moving from the head-down(2nd) to the head-up(3rd) position.
For the Sramek data, sex and tilt were both significant ($P \leq 0.05$) when moving from the 2nd to 3rd position.

Comparison of the stroke index as calculated from Sramek's formula and the digital output of the NCCOM3 showed no overall correlation but some of the data did appear to fall on the line of identity. The rest of the data accumulated around a second slope giving the data a bi modal appearance. At this time it is not known why this bi modal distribution occurred nor is it known which data belong to what group.

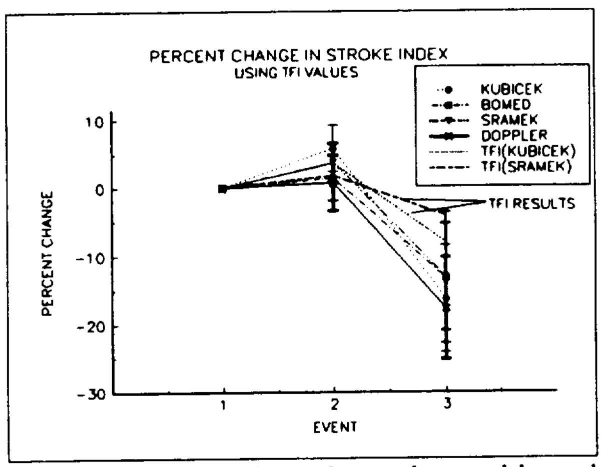

Figure 7.-Percent change in stroke index from the supine position with TFI results added. The TFI data represent changes in stroke index that can be attributed to TFI only.

CONCLUSIONS

This study was initiated in order to validate the bioimpedance measurements of stroke volume and cardiac output. Doppler echo velocimetry has been used in the cardiovascular laboratory and on several missions aboard the space Shuttle. The problem with the technique is the cost of the equipment and the skill level necessary to use it. Bioimpedance, on the other hand, has been purported to be accurate yet inexpensive and does not require the skill level of echocardiography.

This study, however, does not support the use of bioimpedance measurements in conjunction with the space program. Analysis of the data collected during this study show no correlation between stroke volume measured by echocardiography and that measured by bioimpedance. Furthermore, it appeared that the changes that were detected were due to shifts in thoracic fluid and consequential changes in Thoracic Fluid Index (Basal Impedance, Z_0).

Comparisons of the BoMed NCCOM3 monitor with manually derived values, using the same equations, showed no overall correlation though a small group of data points did appear to correlate well. This result indicates that the algorithm that is internal to the NCCOM3 does not agree well with manually-derived results and that neither of the methods is particularly quantitative.

Reasons for the apparent lack of correlation are unknown at this time. If we assume that the manual calculations of Kubicek's and Sramek's equations were faulty, then the BoMed results should have been acceptable, but they were not. If we assume that the BoMed internal algorithm was faulty, then Kubicek's and Sramek's methods should have worked out well, but they did not. Several of the subjects dz/dt waveforms were difficult to interpret because of double dz/dt peaks or because of indistinct VETs. These data were in the minority and would not affect the overall results.

It is possible that the BoMed NCCOM3 used was producing noisy ΔZ signals which would lead to noisy, randomized results. It is also possible that the BoMed electrode system used is not at all suitable for this type of study. Until these questions are answered, however, use of this system to study stroke volume and cardiac output is not recommended. Relative changes in stroke volume or cardiac output and the measurement of TFI may find some use in the program but further research needs to be conducted..

It is recommended that this series of experiments be repeated with the following changes:

Use a different bioimpedance monitor, for example use the Minnesota Impedance Cardiograph or build one.

Since the Ventricular Ejection Time is sometimes difficult to determine using the dz/dt waveform, it would be better to identify systole acoustically with a phonocardiograph microphone.

Use circumferential electrodes since it is not clear whether the BoMed electrodes provide the uniform current densities that this technique requires.

Continue to use Kubicek's and Sramek's formulae since variables for Sramek's formula are easier to obtain and do not require calculations based on the subject's hematocrit.

REFERENCES

Baker, LE, Judy, WV, Geddes, LA, *et al*. The measurement of cardiac output by means of electrical impedance. *Cardiovasc, Res. Ctr. Bull.*, 9:135-145, 1971.
Bernstein, DP A new stroke volume equation for thoracic electrical bioimpedance:Theory and rationale. *Crit. Care Med.* 14:904-909, 1986.
Geddes, LA, Hoff, HE, Mello, *et al*. Continuous measurement of ventricular stroke volume by electrical impedance. *Cardiovasc. Res. Bull.* 4:118-131, 1966.
Judy, WV, Langley, FM, McCowen, KD, *et al*. Comparitive evaluation of thoracic impedance and isotope dilution methods for measuring cardiac output. *Aerosp. Med.* 40:532-536, 1969
Kubicek, WG, Karnegis, JN, Patterson, RP, *et al*. Development and evaluation of an Impedance Cardiac Output System. *Aerospace Med.* 37:1209-1212, 1966.
Nyboer, J. *Electrical Impedance Plethysmography* (2nd ed.), Charles C. Thomas, Springfield, Il, 1970.
Pate, TD, Baker, LE and Rosborough, JP The simultaneous comparison of the electrical impedance method for measuring stroke volume and cardiac output with four other methods. *Cardiovasc. Res. Ctr. Bull.* 14:39-52, 1975.
Quail, AW, Traugott, FM, Porges, WL, *et al*. Thoracic resistivity for stroke volume calculation in impedance cardiography. *J. Appl. Physiol.* 50:191-195, 1981.
Sramek, BB Cardiac output by electrical impedance. *Med. Elect.* April:93-97, 1982
Note:
W.G. Kubicek has compiled and published *A Bibliography of Publications Related to Impedance Cardiography* which contains 546 listings on the subject. This compendium of civilian and space flight, can be obtained by writing to:

W.G. Kubicek, Ph.D., Professor Emeritus
University of Minnesota Medical School
4180 Edmund Blvd.
Minneapolis, MN 55406

Also note that numerous publications by Sramek, the developer of the competing BoMed Impedance Cardiograph, do not appear to be listed in this compendium. Sramek, tends to publish in "throw-away" magazines (Medical Electronics, Critical Care Medicine and his own publications) and it is possible that Dialog Information Services, Inc. (the source of Kubicek's bibliography) does not index these magazines.