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CARDIOVASCULAR INSTRUMENTATION FOR SPACEFLIGHT

By Roger T. Schappell, John T. Polhemus
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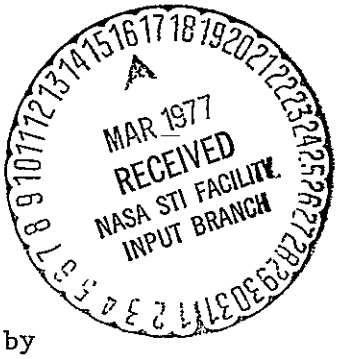

Prepared under Contract No. NAS2-9062 by
MARTIN MARIETTA CORPORATION
Denver, Colorado 80201

for

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
Ames Research Center, Moffett Field, California 94035

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FOREWORD

This report summarizes the results of a cardiovascular performance monitoring instrumentation investigation. It contains the results of our investigation of numerous techniques and instruments applicable to the space-flight cardiovascular deconditioning problem.

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INTRODUCTION

Future manned space missions can be planned and executed only if the conditions assuring man's well-being and effectiveness are defined. Furthermore, the selection of instrumentation for space-flight physiological experiments must be a function of a specific set of criteria. The Apollo and Skylab missions demonstrated that changes do take place in the major physiological systems of the body during space flight and that an accurate time profile of these changes, as a function of weightlessness, is required to determine the true nature of these biological alterations.

This report summarizes the historical space-flight observations, discusses applicable instrumentation, and provides recommendations for future research and development activity required for cardiovascular deconditioning monitoring.

The following assumptions made in the performance of this study stimulated enthusiastic and significant response from the biomedical community at large:

1) More sophisticated biomedical instrumentation may possibly be flown than in previous space flight missions;

2) Extensive bed-rest studies will be conducted;

3) Human surrogates will be flown in unique animal-holding facilities;

4) The Space Shuttle flight potential for biomedical mission specialists is high;

5) Significantly greater European participation is planned;

6) Broad biomedical science community participation is essential.

The objectives for establishing a rationale for cardiovascular performance assessment were best described by Dr. E. McCutcheon, NASA-ARC, in table I.

This study is primarily concerned with the observation mechanisms dealing with pressure, flow, morphology, temperature etc. The approach taken in the performance of this study was to (1) review ground and space-flight data on cardiovascular function, including earlier related ground-based and space-flight animal studies, Mercury, Gemini, Apollo, Skylab, and recent bed-rest studies, (2) review cardiovascular measurement parameters required to assess individual performance and physiological

TABLE I.- CARDIOVASCULAR DECONDITIONING PROBLEM

Passenger Selection Criteria and Indices
What restrictions must be placed on passenger candidates for flight? Which indices will identify susceptible individuals and guide decisions on exclusion or protective measures?
Fundamental Mechanisms
What causes the changes identified as cardiovascular deconditioning? What are the critical variables?
Safety Monitoring
What are the tolerance limits; what physiological penalties are imposed by the deconditioning-induced loss of physiological reserve? Which tests should be performed and which variables should be monitored?
Protection: Prevention/Countermeasures
Which techniques are most effective? Which technique or combination is most practical?

alterations during space flight, (3) perform an instrumentation survey including a literature search as well as personal contact with the applicable investigators, (4) assess instrumentation applicability with respect to the established criteria, and (5) recommend future research and development activity.

It is concluded that, for the most part, the required instrumentation technology is available but that mission-peculiar criteria will require modifications to adapt the applicable instrumentation to a space-flight configuration.

OBSERVATIONS/FUNCTIONS

The cardiovascular system basically consists of the vascular system, the blood and blood volume and its control and regulation, and the heart and the control and regulation of its output. Since it is not the intent of this report to provide a dissertation on cardiovascular physiology, the reader is referred to Rushmer (1972) for further information on structure and function.

To obtain a level of knowledge of the cardiovascular system and the effects on it of space-flight stresses that will permit long-duration manned missions to be planned with assurance, a systematic program of ground-based and inflight experimentation and testing using atraumatic noninvasive techniques on humans is essential. A program is also required that will include complementary experiments with animals in which chronically implanted, telemetered data sources are emphasized. Due to time-line and scheduling constraints, it is essential that as much ground testing as practical be conducted and flight experiments be limited to those requiring zero-g and other space-flight conditions not possible to simulate. To accomplish this, a particular set of instrumentation and techniques for biomedical measurements and monitoring is essential and is discussed herein.

Before proceeding, it is significant to note that a rather thorough dissertation on the physiological problems of manned space flight can be found in a report of a study conducted in 1966 by the Space Science Board of the National Academy of Sciences National Research Council, Publication 1485A, Volume I, "Circulation."

This report contains extensive discussions of (1) control and regulation of the vascular function, (2) control and regulation of organ circulation, (3) control and regulation of blood volume and cardiac output, and (4) stress factors in manned space flight.

Based on the results of previous space-flight and bed-rest studies and on discussions with the medical personnel at the respective NASA centers, it was concluded that the assessment of cardiovascular deconditioning due to weightlessness during space flight would include the following primary observations:

1) Fluid distribution changes and vascular compliance;

2) Increased loading of the heart;

3) Instability of cardiac electrical activity;

4) Modifications of cardiovascular regulation pattern;

5) Blood volume shifts during dynamic states such as re-entry and postflight one-g conditions;

6) Postflight orthostatic tolerance due to space flight;

7) Thermal stress effects;

8) Isolation stress effects;

9) Circadian rhythm effects;

10) Cellular alterations.

Tables II and III were therefore assembled to provide a candidate set of observations for cardiovascular deconditioning assessment for man and for human surrogates.

Based on these measurements, candidate sensors were investigated and are discussed in the Instrumentation section of this report. Obvious instrumentation such as a centrifuge blood sample processor and freezer for obtaining and storing blood plasma were not included in this report but are included in the listing of CORE equipment in the appendix.

TABLE II.- HUMAN STUDIES

Measure blood pressure - Systolic/diastolic
Determine venous capacitance
Determine arterial flow in limbs
Determine renal blood flow
Acquire blood samples and separate plasma
Collect urine daily and measure volume
Determine body fluid compartment volumes
Determine heart chamber volumes
Record ECG/VCG/pulse
Derive stroke volume
Derive cardiac output
Perform environmental monitoring
Perform biochemical analyses
Measure pulmonary capillary blood volume and flow

TABLE III.- HUMAN SURROGATE STUDIES

Record chamber pressures
Determine chamber volumes
Derive ventricular compliance
Perform intercardiac catheterization
Measure organ blood flow
Record ECG/VCG/pulse
Derive stroke volume
Derive cardiac output
Collect blood samples and separate plasma
Collect urine daily and measure volume
Derive body fluid compartment volumes
Record food and fluid intake
Have provisions for histological and biopsy procedures
Perform biochemical analysis
Perform environmental monitoring

As pointed out previously, many of the measurements and observations in tables II and III resulted from discussions with individuals from the biomedical community. Typical suggested protocols are tabulated.

R. Whittingham, MD, RAF at NASA-JSC	Response to cardiopulmonary stress testing Observation of cardiovascular control mechanisms Observation of fluid volumes, flow, and distribution of extracellular, interstitial, and intercellular fluids Vascular observations of central, peripheral, and microcirculation
S. A. Bergman, MD, NASA-JSC	Measurement of fluid shift and interthoracic blood volume Observation of pulmonary and lung compliance Measurement of leg circumferences Drug infusion experiments with primates Dimensional measurements of the heart Injection of microspheres into primates Cerebral flow measurements for analysis of motion sickness and head fullness
D. O'Hanley, PhD, JPL	Ultrastructure analysis of cellular structures resulting from cardiovascular deconditioning Analysis of vascular permeability effected by space flight
Wen Ko, MD, PhD, Case Western Reserve University, Cleveland	Muscle stimulation experiments for primates Increase heart rate and blood pressure and observe effects Electrically stimulate the vagal nerve Study control mechanisms of heart Position electrodes on ventricle, stimulate heart, and observe changes
David Flemming, Md, PhD, Case Western Reserve	Exgometer-type centrifugal exerciser to be used as a gravity simulator and for stress testing
G. W. Hoffler, MD, NASA-JSC	Monitoring of invasive parameters using chronically instrumented animals Development of an ultrasonic system for Shuttle

Craig J. Hartley, PhD, and Henry G. Hanley, MD, Baylor researchers at Methodist Hospital in Houston, have been involved in physiological and pharmacological animal studies for a number of years and have developed a system for chronically instrumenting healthy animals and studying the effects of experimental cardioactive drugs on them. This system consists of a multichannel pulsed Doppler flowmeter system for the simultaneous measurement of regional blood flow to several tissues, Konigsberg pressure gages, and a multichannel ultrasonic segment-length monitor for measuring regional myocardial dimensions. Their current capability enables simultaneous monitoring of four regional blood flows, three regional myocardial dimensions, and arterial and left ventricular pressure.

The many more suggestions received from the biomedical community are too extensive to list. Nevertheless, all inputs were considered and used in the development of the candidate observations and functional analyses summarized in tables II and III.

HISTORICAL REVIEW OF CARDIOVASCULAR PERFORMANCE MONITORING

During this study, the cardiovascular experiments performed in the Mercury, Gemini, Apollo, Skylab, and ground-based studies, i.e., Skylab medical experiments altitude test (SMEAT) and bed-rest studies, have been summarized in terms of mission constraints, experiment objectives, instrumentation, and results.

Mercury Flight

The Mercury flight program consisted of six manned flights and four human surrogate flights. The pilots of the Mercury flights all withstood the stresses of preflight, flight, and postflight phases with no evidence of degradation. One symptom of the pilot's functional integrity, or the static hypertension accompanied by accelerated pulse response, was exhibited in post-flight examination. This condition returned to normal while the pilot was sleepting 9 to 12 hours after landing.

The specific results, experiments, and instrumentation of the MA-9 mission are presented for Astronaut L. Gordon Cooper, Jr. and are exemplary for the Mercury project.

Preflight observations.- Medical examinations of Astronaut Cooper were conducted both before and after six preflight space-craft checkout tests and a session in the Cape Kennedy procedures trainer, all of which required the pilot to wear the full pressure space suit. Also, special examinations to assess the pilot's fitness for flight were conducted 11 and 3 days before launch. A final examination was performed by the NASA flight surgeon on launch morning. The examination included measurement of heart rate via electrocardiogram R-waves and blood pressure. The preflight data were collected to establish the baseline physiological response of the MA-9 astronaut specifically using the flight biomedical instrumentation. This consisted of two sets of ECG leads and a blood pressure measuring system (BPMS). The latter was made up of a microphone, pressure cuff, and automatic controller.

The ECG from the preflight observation period was scanned repeatedly. The collective opinion of numerous observers of the ECG was that marked normal sinus arrhythmia was present with frequent occurrences of a wandering cardiac pacemaker. At times, sinus node suppression was sufficient to allow activation by the atrioventricular (A-V) node with escape and fusion beats. This and other variants were considered acceptable for this individual on the basis of extensive preflight testing.

The flight data are summarized in tables IV and V along with preflight and postflight data. No significant anomalies were noted during flight.

TABLE IV.- SUMMARY OF HEART RATE DATA

Preflight					
Date	Procedure	Duration of observation, hr:min	Overall Mean	Range of mean rates	Range of ±2 standard deviations
			Heart rate, beats/min	Heart rate, beats/min	Heart rate, beats/min
September 1951 to May 15, 1963	Centrifuge simulations and checkout procedures	56:23	72	62 to 83	39 to 104

Inflight						
Date	Procedure	Duration of observation, hr:min	Mean Heart rate, beats/min	Heart Rate ±2 standard deviations, beats/min	Range of Mean Rates Range, beats/min	Respiration rate Number of values
May 15 and May 16, 1963	Orbital flight	34:16	89	62 to 116	55 to 180	151

Postflight						
May 16 and May 17, 1963	Physical examination	(*)	77	72 to 82	56 to 88	1

*Not determined, not time-critical.

The medical examination performed immediately after the MA-8 recovery suggested an alteration in the pilot's cardiovascular responses to position changes. To obtain more quantitative measurements of these responses, an operational tilt procedure was developed for shipboard use using a Stokes' litter with crossbars added for lifting and stabilization.

Heart rate and blood pressure measurements were taken at least every minute in all tests and were chosen as the primary indicators of altered functions, in conjunction with observation of visible reactions and subjective comments. Operational use called for minute heart rates calculated from 15-second counts of the right radial pulse, with clinical blood pressures taken from the left arm. Greater capability in the Space Medicine Laboratory in Hangar S permitted simultaneous determination of both clinical and

TABLE V.- SUMMARY OF BLOOD PRESSURE DATA

Date	Procedure	Duration, hr:min	Mean blood pressure, mm Hg	Systole			Diastole			Mean pulse pressure, mm Hg
				Number of values	±2 standard deviation, mm Hg	Range, mm Hg	Number of values	±2 standard deviation, mm Hg	Range, mm Hg	
Preflight, clinical										
February 1959 to May 15, 1963	Crew selection examination, special tests and preflight examinations	a	113/79	95	99 to 127	88 to 124	95	69 to 89	64 to 88	34
Preflight, blood pressure measuring system										
September 1961 to May 15, 1963	Centrifuge simulations and preflight test procedures	56:09	112/79	160	86 to 138	79 to 148	160	58 to 90	61 to 124	33
Inflight, blood pressure measuring system										
May 15, and May 16, 1963	Orbital flight--------	34:16	119/81	12	b	109 to 131	12	b	73 to 89	38
Postflight, clinical										
May 16 and May 17, 1963	Postflight physical examinations	a	91/66	16	75 to 107	86 to 100	16	55 to 77	52 to 82	25

[a]Not determined; not time-critical.

[b]Not applicable.

BPMS blood pressures and continuous recording of respiration rate and ECG from the biosensor system. Minute heart rates were determined from the directly recorded biosensor data by using 12-second counts made every 30 seconds.

Minute respiration rates were determined from 30-second counts made each minute. There were no apparent differences between the clinical and biosensor values.

In short, the preflight tilt test produced expected cardiovascular compensatory reactions that could be demonstrated by heart rate, blood pressure, and ECG data, and all of these tests were well-tolerated. The postflight tilt tests demonstrated the presence of moderate orthostatic hypotension, with far greater heart rates required to maintain effective cardiovascular function. Compensation was achieved, however, and the pilot did not develop even near-syncope. Tilt studies of responses after stresses similar to those experienced during flight are not available. Contributing stress factors, including heat stress, the effect of prolonged confinement, dehydration, fatigue, and a possible effect of weightlessness *per se*, are thought to be the principal elements responsible for this change. The picture is further clouded by residual effects of the dextro amphetamine.

A device for calibrated work consisting of a short plastic handle and expansible bungee cords was fixed within the spacecraft near the astronaut's feet. A limiting cable ensured repeatability of handle travel, requiring 65 pounds of force for each full extension. At 2:25:00 and again at 7:41:00 GMT, the astronaut recorded his blood pressure, pulled the device 30 times in as near 30 seconds as possible, and again recorded his blood pressure. The results of these two work periods were compared with five such periods performed at normal gravity in the spacecraft and in the procedures trainer.

Subjectively, the astronaut could tell little difference between the work performed under normal gravity and under zero gravity; the effort under zero gravity was, if anything, slightly easier. During flight he felt his postwork breathing was not as labored as it was following control runs, and he thought his heart rate returned to prework values more rapidly. The data, however, do not support this statement.

Analysis of the data does not show any striking differences between the one-g and zero-g work periods. Inflight mean heart rates during the calibrated work period were 16 beats per minute higher than preflight, but the astronaut's inflight mean heart rate before work was 15 beats per minute higher. (Return to prework values was slower following the inflight exercise.) The results are presented graphically in figure 1. One preflight

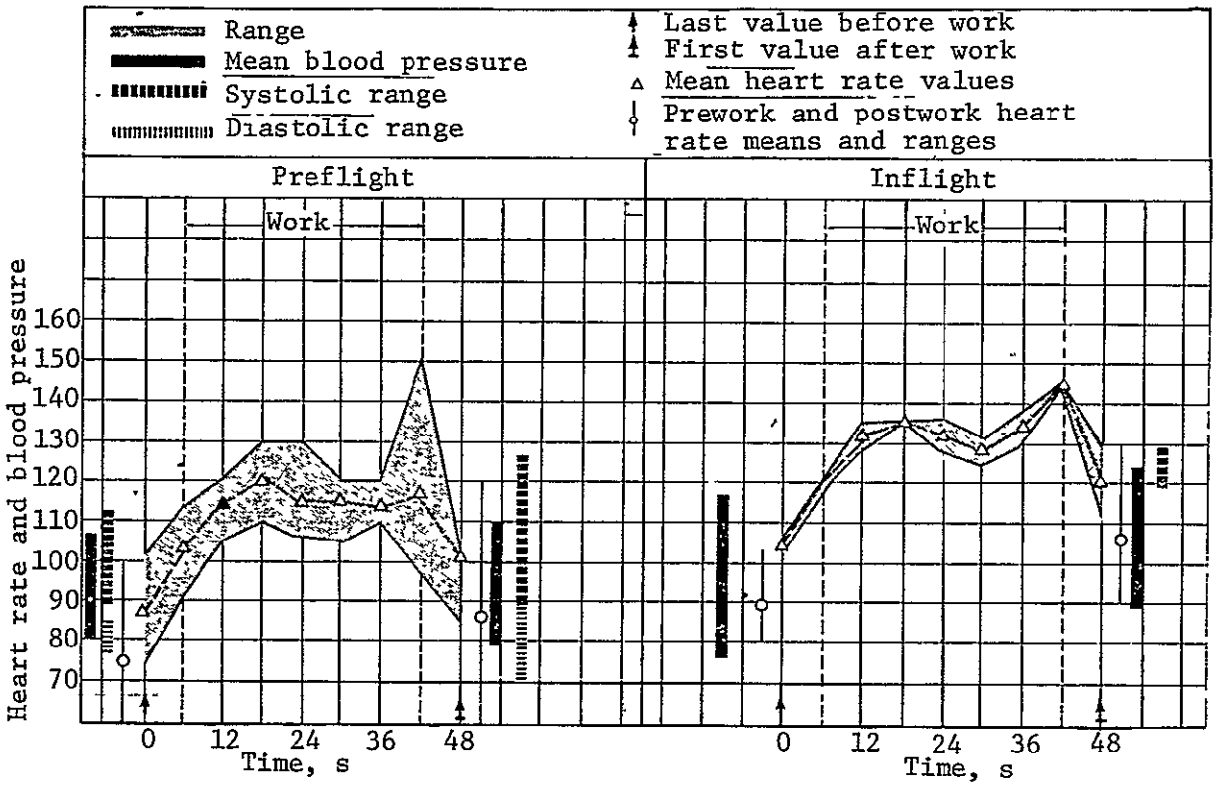

Figure 1.- Calibrated work, MA-9.

heart rate during during work was 160 beats per minute. This value occurred at the only time in one of the seven periods in which the astronaut worked over 0.7 minute and probably reflects the prolongation of the work period rather than indicating a higher workload. During the 18-second recovery period after the test, the preflight mean heart rate dropped to 11 beats per minute over the preflight value, while during the flight it fell to 17 beats per minute over the prework mean.

GEMINI FLIGHT

The Gemini program consisted of 10 manned space flights involving 20 individuals, two on each flight. A summary of these flights is shown in table VI.

The principal physiological changes noted were orthostatism (orthostatic hypertension) for some 50 hours after flight as measured with a tilt table. The Gemini program also provided extravehicular activity and the resultant monitoring of the cardiovascular system under these new stress conditions.

TABLE VI.- GEMINI MANNED SPACE FLIGHTS

Gemini mission	Crew	Launch date	Description	Duration, day:hr:min
III	Grissom Young	March 23, 1965	Three-revolution manned test	0:04:52
IV	McDivitt White	June 3, 1965	First extended-duration and extra-vehicular activity	4:00:56
V	Cooper Conrad	August 21, 1965	First medium-duration flight	7:22:56
VII	Borman Lovell	December 4, 1965	First long-duration flight	13:18:35
VI-A	Schirra Stafford	December 15, 1965	First rendezvous flight	1:01:53
VIII	Armstrong Scott	March 16, 1966	First rendezvous and docking flight	0:10:41
IX-A	Stafford Cernan	June 3, 1966	Second rendezvous and docking; first extended extravehicular activity	3:01:04
X	Young Collins	July 18, 1966	Third rendezvous and docking; 2 extravehicular activity periods; first docked target-vehicle-propelled high-apogee maneuver	2:22:46
XI	Conrad Gordon	September 12, 1966	First rendezvous and docking initial orbit; 2 extravehicular activity periods; second docked target-vehicle-propelled high-apogee maneuver; tether exercise	2:23:17
XII	Lovell Aldrin	November 11, 1966	Rendezvous and docking; umbilical and two standup extravehicular activity periods; tether exercise	3:22:37

The cardiovascular system was the first of the major body systems to show physiological change following flight; as a result, it has been extensively investigated by various means (table VII). As previously reported, the peak heart rates have been observed at launch and at reentry; the rates normally reached higher levels during the reentry period. The midportions of all the missions have been characterized by more stable heart rates at lower levels with adequate response to physical demands.

TABLE VII.- CARDIOVASCULAR OBSERVATIONS

Experiment	Objective	Instrument	Time	Measurement
Cardiac	Heart condition mechanics	Synchronous phonocardiograph ECG	Before, during, and after flight	Heart sounds QRS complexes
M003 cardiovascular stress	Cardiovascular under stress	ECG, SPCG BPMS Bungee device	Before, during, and after flight	Heart sounds QRB waves Korotkov sounds Brachial pressure
Cardiovascular	Heart rate Mean blood pressure	ECG, BPMS Tilt table	Before, during, and after flight	Heart sounds QRB waves Korotkov sounds Brachial pressure
Cardiovascular	Heart rate Mean blood pressure	Bicycle Ergometer	Before, during, and after flight	Heart sounds QRB waves Korotkov sounds Brachial pressure

The electrocardiogram has been studied in detail throughout the Gemini missions. The only abnormalities of note have been very rare, premature, auricular and ventricular contractions. No significant changes have been detected in the duration of specific segments of the electrocardiogram.

Blood pressure measurements obtained during the Gemini VII mission revealed that systolic and diastolic values remained within the envelope of normality and showed no significant changes throughout 14 days of flight. As previously reported, this included the pressures taken at the time of reentry.

Some insight into the electrical and mechanical phases of the cardiac cycle was gained during the Gemini flights. The data were derived through synchronous phonocardiographic and electrocardiographic monitoring. In general, wide fluctuations in the duration of the cardiac cycle, but within physiological limits, were observed throughout the missions. Fluctuations in the duration of electromechanical systole correlated closely with changes in heart rate. Stable values were observed for electromechanical delay (onset of ventricular activity, QRS complexes, to onset of first heart sound) throughout the missions, with shorter values observed

during the intervals of peak heart rates recorded during liftoff, reentry, and extravehicular activity. The higher values observed for the duration of systole and for electromechanical delay in certain crew members suggest a preponderance of cholinergic influences (vagal tone). An increase in adrenergic reaction (sympathetic tone) was generally observed during liftoff, reentry, and in the few hours preceding reentry.

As a further measure of cardiovascular status, experiment M003, inflight exerciser, determined the heart rate response to an exercise load consisting of one pull per second for 30 seconds on a bungee device (force at full extension of 12 in. equaled 70 lb). The results of the 4-day Gemini IV and the 14-day Gemini VII mission did not differ. This variant of the step test revealed no physical or cardiovascular decrement after as much as 14 days in a space-flight environment.

In contrast to the Mercury project results, orthostatism resulting from any Gemini mission has not been detectable except by means of passive tilt-table provocation. Typically, the heart rate and blood pressure responses to a 15-minute, 70-deg tilt performed after flight are compared with identical preflight testing of the same crewmen. Consistently, such testing has demonstrated a greater increase in heart rate, a greater reduction in pulse pressure, and a greater increase in leg volume, as interpreted from lower limb circumference gages during the preflight tilt (fig. 2). The changes observed in these variables may be most significantly illustrated by examining the heart rate changes observed during preflight and postflight tilt-table studies. When the postflight increases in heart rate during tilt are expressed as percent of the preflight tilt heart rate for each of the Gemini crews, the postflight increases are from 17 to 105% greater than those exhibited before flight.

The Gemini flights have also provided some excellent examples of human variability and have emphasized the necessity for care in making deductions. In making projections based on very limited results in a few people, the current trend is to bank heavily on comparisons in a given individual; that is, differences between baseline data, and responses observed during and after a flight. The crewmen who have flown twice have shown variability between flights in the same manner as have different men on the same flight. Figure 3 shows the heart rates for one crewman during the launch phase of both his Mercury mission and his Gemini mission. The two curves show little correlation and could easily have come from different individuals.

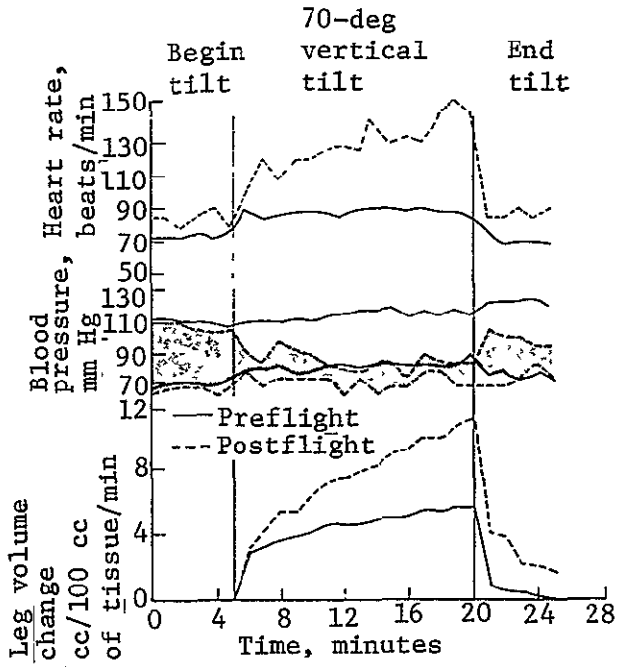

Figure 2.- Typical tilt-table response.

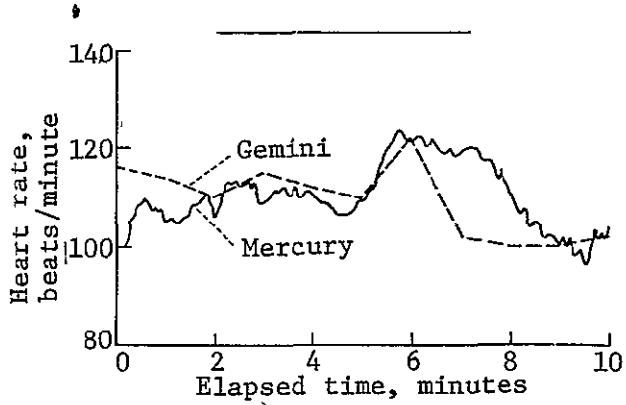

Figure 3.- Command pilot heart rate comparisons.

Apollo Flight

The Apollo program consisted of 11 manned flights including lunar landing. A summary of these flights is given in table VIII.

TABLE VIII.- APOLLO MISSION CHARACTERISTICS AND ORTHOSTATIC EVALUATION TECHNIQUES

Apollo mission	Type of mission	Time from liftoff to lunar landing, hr	Length of lunar stay, hr	Time from lunar liftoff to splash-down, hr	Total mission duration		Type of orthostatic evaluation performed
					Hours	Days	
7	Earth orbital				260.1	10.8	LBNP
8	Lunar orbital				147.0	6.1	LBNP
9	Earth orbital				241.0	10.0	LBNP, Stand
10	Lunar orbital				192.0	8.0	Stand
11	Lunar landing	102.7	22.2	70.9	194.0	8.1	Stand
12	Lunar landing	110.5	31.5	102.0	244.5	10.2	--
13	Lunar-abort				142.9	6.0	--
14	Lunar landing	108.2	33.5	74.3	216.0	9.0	--
15	Lunar landing	104.7	67.0	123.6	295.0	12.3	LBNP
16	Lunar landing	104.5	71.0	90.3	265.8	11.1	LBNP
17	Lunar landing	110.3	75.0	116.5	301.8	12.6	LBNP

Reductions in orthostatic tolerance following flight were observed with the late Mercury flights. Elevated heart rate, reduced pulse pressure, and increased pooling of fluid in the lower extremities were found consistently during 70-deg upright tilts in the early postflight period.

Several techniques were used to induce cardiovascular responses. They include the tilt table and the lower body negative pressure (LBNP) systems as simulators of orthostatic stress.

In addition, antihypotensive garments were tested. These included Jobst waist-length leotards and a garment employing the capstan principle for the application of lower body positive pressure. The methods and conditions affecting orthostatic evaluation are described in the following section.

Lower body negative pressure device.- The device for measuring LBNP consisted of a chamber of sufficient size to accommodate the lower body, an airtight waist seal, and a regulated vacuum source (Wolthuis et al., 1970; Wolthuis et al., 1972). The type of physiological measurements taken during the LBNP protocol varied slightly from mission to mission. Measurements made in conjunction with the Apollo 7 to 9 missions included continuous axillary and sternal lead electrocardiograms, indirect blood pressure taken every 30 seconds by the Korotkov sound technique (using the NASA Gemini blood pressure measuring system), and changes in calf circumference measured by double-strand, mercury-in-silastic strain gages.

For the Apollo 15 to 17 evaluations, the limited two-lead electrocardiogram was replaced with a modified Frank lead vectorcardiogram (VCG) and wideband precardial heart sounds (vibrocardiogram) were recorded with a capacitance microphone system. The respiration rates of the Apollo 16 and 17 crewmen were measured with a mercury strain gage attached to the lower thorax. The carotid pulse trace was recorded for Apollo 17 crewmen.

A Jobst waist-length elastic leotard was used in the Apollo 16 mission. This garment produced a pressure at the ankle of 40 to 45 mm Hg (53 x 10^2 to 60 x 10^2 N/m^2) that decreased linearly to approximately 10 mm Hg (13 x 10^2 N/m^2) at the waist. To accommodate expected reductions in limb size during flight, garments were made in three separate sizes.

A lower-body garment using the capstan principle to apply pressure to the lower limbs was provided for the Apollo 17 command module pilot to use following splashdown. Capstan pressure was read from an aneroid gage and was inflated with a hand bulb, both of which were concealed in a zippered pocket. The capstan exerted the pressure of the garment over the skin at the ankle in a 2:1 ratio. This pressure diminished linearly to approximately

10 mm Hg (13 x 10^2 N/m^2) at the waist. Preflight testing with pressure sensors between the garment and the skin verified the ratio and the diminishing gradient of pressure from ankle to waist. To accommodate anticipated loss of limb girth, laces were provided for reducing the garment size slightly before stowage in the command module. The capstan itself accommodated moderate changes (±2.5 cm) in limb girth.

Accessory cardiovascular and related measurements were made to evaluate orthostatic changes. Before orthostatic evaluation of the Apollo 7 to 11 and 15 to 17 crewmen, the circumference of the calf at its maximum girth was measured during supine rest. The total lower limb volume of Apollo 16 and 17 crew members were calculated from multiple leg circumference measurements made at discrete intervals from the ankles to the groin while the crewman was supine with the legs extended and slightly elevated. Standard 1.8-m (6-ft) posterior-anterior chest X-rays were taken of every crew member at his last major preflight medical examination and first postflight evaluation. The cardiothoracic ratio was determined by standard clinical methods. The ambient temperature and the oral temperature and body weight of each crewman were recorded at each evaluation.

Results.- Of the various cardiovascular measurements obtained from Apollo crew members during their evaluations, heart rate was the most easily measured and yielded the most accurate and predictable values. Table IX contains heart rate data on individual crew members during three conditions of orthostatic stress evaluations: (1) resting supine control, (2) the highest level of LBNP [-50 mm Hg (-67 x 10^2 N/m^2)], and (3) passive standing. The resting supine heart rate was elevated significantly in 13 of 24 crewmen (54%) at the first postflight evaluation; the group response was elevated at the 2% level of confidence. A trend toward preflight values was subsequently evident. By the third postflight evaluation, only three of 15 individuals (20%) showed significant elevations in the resting supine heart rate, and the group mean value was not statistically different from the preflight group mean heart rate (n = 15, paired).

Following the same comparisons, the application of 50 mm Hg (-67 x 10^2 N/m^2) LBNP produced significantly elevated heart rates in 14 of 17 Apollo crewmen (82%) at the first postflight evaluation, with a group elevation significant at the 0.1% level. The Apollo 15 lunar module pilot experienced presyncope during the last seconds of -40 mm Hg (-53 x 10^2 N/m^2) LBNP and was not tested at -50 mm Hg (-67 x 10^2 N/m^2) LBNP on recovery day. Five other crew members (the Apollo 8 command module pilot, the Apollo 8 lunar module pilot, the Apollo 9 lunar module pilot, the Apollo 16 command module pilot and the Apollo 16 lunar module pilot developed presyncopal symptoms at some point before protocol

TABLE IX.- INDIVIDUAL APOLLO CREW MEMBER HEART RATE DATA
(ARROWS INDICATE p <0.05)

Protocol condition	Apollo mission	Crew member	Preflight evaluations			Preflight summary		Postflight evaluations		
			F-30 days	F-15 days	F-5 days	Mean	±SD	First	Second	Third
Resting supine control period	7	CDR	56	59	54	56	2.6	77 ▲	59	--
		CMP	81	74	78	78	3 1	78	76	--
		LMP	57	64	66	62	4 4	75 ▲	70	--
	8	CDR	74	69	70	71	2.6	87 ▲	70	80 ▲
		CMP	84	69	66	73	9 7	94	76	66
		LMP	77	74	72	74	2.4	91 ▲	81 ▲	71
	9	CDR	76	63	68	69	6.8	64	78	80
		CMP	56	59	58	57	2 0	57	54	53
		LMP	59	55	57	57	2 1	50 ▼	50 ▼	50 ▼
	10	CDR	62	70	59	64	5.7	81 ▲	73	--
		CMP	65	59	55	60	5.0	65	62	--
		LMP	59	62	52	58	5 1	80 ▲	79 ▲	--
	11	CDR	61	62	67	63	3 2	69	79 ▲	--
		CMP	53	46	51	50	3.6	67 ▲	65 ▲	--
		LMP	68	69	70	69	1.0	62 ▼	81 ▲	--
	15	CDR	51	50	55	52	2 6	54	50	52
		CMP	66	69	70	68	2 1	83 ▲	84 ▲	73
		LMP	52	56	57	55	2.6	66 ▲	66 ▲	66 ▲
	16	CDR	57	57	55	56	1 2	70 ▲	60 ▲	61 ▲
		CMP	49	49	45	48	2 1	56 ▲	48	56 ▲
		LMP	60	53	54	56	3 9	57	61	60
	17	CDR	55	62	59	59	3.2	67 ▲	70 ▲	64
		CMP	78	76	68	74	5.1	67	64	69
		LMP	50	50	51	50	0.6	55 ▲	56 ▲	52
	Group Mean		62 8	61 5	60.7	61.6		69 7	67 2	63.5
	±SD		10.47	8.53	8.41	8.60		12.19	10.90	9 88
	LMP					t-Test		p<0.02	ns	ns
-50 mm Hg* LBNP	7	CDR	72	61	59	64	6.7	90 ▲	67	--
		CMP	94	92	90	92	2.1	137 ▲	94	--
		LMP	76	74	76	75	1.1	108 ▲	87 ▲	--
	8	CDR	100	86	94	93	6 7	159 ▲	108	101
		CMP	116	89	94	99	14 5	129	121	88
		LMP	97	105	106	103	4.8	146 ▲	137	102
	9	CDR	82	67	78	76	7.9	100 ▲	94	93
		CMP	63	73	76	71	6.9	81	70	68
		LMP	74	70	67	70	3.3	87 ▲	75	65
	15	CDR	62	59	61	61	1.5	76 ▲	--	65
		CMP	79	81	81	80	1.2	131 ▲	109 ▲	93 ▲
		LMP	58	56	64	59	4.2	--	84 ▲	78 ▲
	16	CDR	79	71	72	74	4 1	109 ▲	101 ▲	83
		CMP	62	67	58	62	4.2	99 ▲	74 ▲	79 ▲
		LMP	82	72	83	79	5.9	112 ▲	98 ▲	98 ▲
	17	CDR	67	78	71	72	5 3	112 ▲	91 ▲	78
		CMP	87	86	79	84	4.3	87	78	90
		LMP	59	69	60	63	5.4	82 ▲	80 ▲	60
	Group Mean		78 3	75.3	76.1	76.5		108.5	92.2	82.7
	±SD		15.97	12.61	13 70	13.27		24.58	18.85	13.76
						t-Test		p<0.001	p<0.02	ns
Passive Stand	9	CDR	81	73	79	78	4.2	93 ▲	100 ▲	96 ▲
		CMP	66	75	72	71	4.6	88 ▲	72	70
		LMP	71	67	69	69	2.0	93 ▲	79 ▲	65
	10	CDR	86	93	86	88	4.0	111 ▲	92	--
		CMP	88	85	70	81	9 6	100	81	--
		LMP	80	74	70	75	5.0	121 ▲	109 ▲	--
	11	CDR	73	83	85	80	6.4	112 ▲	105 ▲	--
		CMP	76	69	65	70	5.6	91 ▲	88 ▲	--
		LMP	73	76	79	76	3.0	89 ▲	100 ▲	--
	Group Mean		77.1	77.2	75.0	76.4		99 8	91.8	77.0
	±SD		7.22	8.29	7.48	6.11		11.99	12.71	16 64
						t-Test		p<0.001	p<0.001	ns

*-67 × 10^2 N/m^2.

completion during their immediate postflight 50 mm Hg (-67 x 10^2 N/m^2) stress; the Apollo 15 commander experienced similar symptoms during his second postflight evaluation. Although more crew members immediately after flight demonstrated a larger heart rate increment over preflight values during LBNP stress than during the resting control period, statistically significant group differences disappeared by the third postflight evaluation. Passive vertical standing results indicated a similar increase in heart rate immediately after flight.

In table X, heart rates of Apollo crew members are compared with those of control subjects for three protocol conditions. Significant "postflight" heart rate changes among the control subjects onboard the recovery ship were not observed. Although the control subjects were exposed to similar environmental conditions, all had a five- to 10-day acclimatization period onboard the recovery ship preceding their evaluations.

TABLE X.- APOLLO CREW MEMBER VERSUS CONTROL SUBJECT HEART RATE DATA

Protocol condition	Apollo group	Preflight summary				Postflight evaluations					
		Response				First			Second		
		N	$\bar{X}$	SD_i	SD_t	N	$\bar{X}$	p	N	$\bar{X}$	p
Resting supine	Crew	24	61.6	8.60	1.06	24	69.7	0.02	24	67.2	0.05
	controls	22	69.7	6.93	1.00	22	69.4	ns	10	70.4	ns
-50 mm Hg* LBNP	Crew	18	76.5	13.27	1.55	17	108.5	0.001	17	92.2	0.02
	controls	16	85.1	8.14	1.49	14	87.3	ns	9	84.2	ns
Standing	Crew	9	76.4	6.11	1.24	9	99.8	0.001	9	91.8	0.01
	controls	7	79.6	6.40	2.72	7	81.1	ns	--	--	--

*-67 x 10^2 N/m^2.

Note: N = Number of subjects
$\bar{X}$ = Group mean
SD_i = Standard deviation of crew member preflight summary means
SD_t = Standard deviation of three preflight group means
p = Probability level

Skylab Medical Experiments Altitude Test (SMEAT)

The objectives of SMEAT were to provide a nearly full-scale simulation of a 56-day Skylab mission. Through this simulation, all crew procedures and equipment operations could be tested. The specific SMEAT objectives were to:

1) Obtain and evaluate baseline medical data for up to 56 days;

2) Evaluate selected experiments, hardware systems, and ancilliary equipment;

3) Evaluate data reduction and data handling procedures in a mission duration time frame;

4) Evaluate preflight and postflight medical support operations, procedures, and equipment;

5) Evaluate medical inflight experiment operation procedures and crew checklists;

6) Train the Skylab medical operations team for participation during the flight.

The specific experiments relating to the cardiovascular system are discussed in the following paragraphs.

M092 lower body negative pressure.- The objectives were to obtain baseline data concerning the time course of cardiovascular deconditioning during long-term residence in zero-g and predict the degree of physical impairment that may be experienced on return to earth's gravity, and to obtain verification of procedures and crew operational capability.

M093 vectorcardiogram - The objective was to determine reference data and changes in the electrical activity of the heart caused by exposure to the Skylab atmosphere and other specific stressors and to correlate the changes detected with those known to occur after specific stress in normal environments.

The equipment functioned well. Data loss was minimal and was mainly due to shortcomings in the software programs. The Skylab environmental specifications were maintained throughout this experiment with temperature ranging from 21 to 26°C. Despite the temperature fluctuations, there were no gross differences in cardiovascular responses and no signs of impending syncope. Table XI gives the mean physiological values for the prechamber, in-chamber, and postchamber periods and indicates statistically significant changes.

TABLE XI.- LBNP PHYSIOLOGICAL MEASUREMENTS

		Control						-50 mm Hg LBNP							
	N	Heart rate $\bar{X}$	±SD	Systolic BP $\bar{X}$	±SD	Diastolic BP $\bar{X}$	±SD	Heart rate $\bar{X}$	±SD	Systolic BP $\bar{X}$	±SD	Diastolic BP $\bar{X}$	±SD	PLVC $\bar{X}$	±SD
Commander															
Prechamber	5	51	4	99	2	65	3	56	2	99	4	67	4	3.1	0.3
In-chamber	18	52	3	102	4	64	3	60	6	101	5	65	3	3.2	0.4
Postchamber	1	61 ↑		110 ↑		73 ↑		69 ↑		100		65		3.4	
Scientist-pilot															
Prechamber	4	53	5	102	6	68	8	59	7	96	6	69	7	3.1	1.0
In-chamber	17	48	2	96	4	62	4	54	2	92	4	62	4	3.0	0.3
Postchamber	1	51		102		63		55		96		64		3.6	
Pilot															
Prechamber	4	70	9	119	3	69	4	75	11	112	7	74	1	3.0	1.0
In-chamber	18	77	6	123	9	69	5	82	5	116	10	76	5	3.0	0.4
Postchamber	1	69		112 ↓		61 ↓		77		97 ↓		63 ↓		2.5	

Note: Arrows indicate direction and statistical significance of change - one arrow $p>0.05$.
*p values were determined from fiducial limits computed by t-test.

Heart rate.- Since increased heart rate is one of the most effective ways of increasing cardiac output in the face of greater physiological demands, heart rate was used as the major single determinant of altered orthostatic response. In-chamber mean heart rates and postchamber individual values were compared with the prechamber mean. Table XI shows that throughout the 56-day test, the commander exhibited an increase in heart rate, both at rest and at reduced pressure. His postchamber values were significantly higher than the respective prechamber means. The scientist-pilot and pilot showed no significant changes in heart rate.

Blood pressure.- The blood pressure values of the commander showed increased postchamber control values, the scientist-pilot showed no significant variation, and the pilot exhibited a statistically significant decrease in both systolic and diastolic blood pressures. None of the crew members showed significant pulse pressure changes.

An unanticipated finding was detected during preliminary inspection of heart rate and blood pressure time graphs. Time series analyses for periods longer than one day produced statistically significant periodicity across different data sets for the same individual. All three crew members showed approximately monthly rhythms.

Vectorcardiography.- Compared to the prechamber baseline tracing, no significant changes of rhythm were observed in the crew members' VCG recordings. Any changes in the mean values of the PR, QRS, and QT intervals closely followed the changes observed in heart rate.

Percent Leg Volume Change.- Analysis of resting supine leg calf circumference showed a progressively decreasing linear trend. By statistical regression of the calf circumference values versus time, an estimate of the percent change was computed as the difference between intercepts at the first in-chamber day and postchamber day.

The decrease in leg calf circumference, together with the body weight loss, is summarized in table XII. The commander and scientist-pilot showed a decrease in both leg calf circumferences and a concomitant body weight loss. The excessive weight loss of the scientist-pilot can be partially attributed to a 500-calorie deficit in his daily diet. The pilot showed a decrease only in the right leg circumference.

TABLE XII.- CALF CIRCUMFERENCE AND BODY WEIGHT LOSS

	Commander	Scientist-pilot	Pilot
Initial left calf circumference, cm	35.8	42.4	38.7
Slope, cm/day	-0.011	-0.015	-0.000
Intercept (R + 0), cm	35.2	41.6	38.7
Percent decrease	1.7	2.0	0.0
Initial right calf circumference, cm	35.8	43.5	38.6
Slope, cm/day	-0.017	-0.018	-0.008
Intercept (R + 0), cm	35.0	42.5	37.8
Percent decrease	2.2	2.3	2.0
Body weight loss, kg	-1.81	-5.45	0.0

The percent leg volume change remained unaltered throughout all periods of the chamber study, and the experimental data suggest that a decrease in the absolute leg calf circumference had no effect on the percentage leg volume change during LBNP stress.

Both the Skylab LBNP hardware and data acquisition system operated satisfactorily. Previous studies of individuals confined in hypobaric chambers where physical activity was severely limited have shown evidence of reduced orthostatic tolerance. Similarly, it has been reported that even strict four-day chair

rest can produce this effect. In the M092 experiment, the astronauts entered the hypobaric chamber in good physical condition and exercised daily. These were undoubtedly factors in the maintenance of physical fitness. Impaired orthostatic tolerance, manifested by the increased heart rate, diminished systolic and pulse pressure, and increased tendency to syncope in the upright position (or during LBNP), was not observed in this experiment.

Skylab Flight

One of the objectives of the Skylab program was to study man's response to long-duration space flight. In the cardiovascular area it appears that cardiovascular deconditioning does occur during flight, that the change is adaptive in nature and stabilizes after a period of four to six weeks, that this change does not impair crew health or performance aloft, and that it is triggered by factors tending to reduce circulating blood volume. These changes and observations, as summarized by Dietlein (1974), are shown in tables XIII and XIV.

TABLE XIII.- SKYLAB CARDIOVASCULAR SUMMARY

- Cardiovascular deconditioning was observed during flight; changes appear adaptive in nature and tend to stabilize after 4 to 6 weeks.
- Cardiovascular changes do not impair crew health or ability to function effectively in weightless flight.
- Lower body negative pressure tests provide a fairly reliable predictive index of postflight cardiovascular status.
- Cardiac electrical activity, as measured by vectorcardiogram, was not significantly altered and remained within physiological limits.
- Decreased cardiac output noted in crewmen after flight; thought to be related to reduced venous return.
- Single episode of significant cardiac arrhythmia in one Skylab 2 crewman during exercise early in mission.
- No significant inflight decrement in work capacity or physiological responses to exercise.
- All crewmen have shown postflight decrease in exercise capacity and altered physiological responses.
- Skylab 3 and 4 crews returned to preflight cardiovascular status by the fourth and fifth day and the Skylab 2 crew on the 21st day after flight; increased exercise by Skylab 3 and 4 crewmen thought to be a factor in improved recovery rate.

TABLE XIV.- CARDIOVASCULAR SYSTEM

Findings
• Postflight orthostatic intolerance
• Postflight diminished exercise capacity
Probable etiological factors
• Decreased effective circulating blood volume after flight
• Diminished venous return at one-g
• Muscular imbalance occasioned by functional disuse atrophy of antigravity muscles
• Altered internal milieu (fluid/electrolyte dynamic flux) during early postflight period
• Altered venous reflexes/tone
• Fatigue

The lower body negative pressure test has proved to be a fairly reliable predictive index of postflight cardiovascular status. Cardiac arrhythmias have been rare; only one episode was noted early in Skylab 2 during intensive personal exercise and was interpreted as multiple, unifocal ventricular premature beats with no evidence of coupling.

Other arrhythmias observed have been limited to isolated rare to occasional premature beats. Cardiac electrical activity has been within physiological limits as judged from the vectorcardiographic data.

Exercise tolerance during flight was unaffected. It was only after return to earth that a tolerance decrement was noted.

Finally, the rapid postflight recovery of orthostatic and exercise tolerance following two of the three Skylab missions appears to be directly related to total inflight exercise as well as to a graded regular program of exercise during the postflight debriefing period.

There is no convincing incidence of myocardial damage as an etiological factor; however, transient cellular changes during the period of homeostatic perturbation would not be surprising or unusual. In animal oxygen toxicity studies we have observed such changes in lung, liver, and kidney.

The thrust of future cardiovascular investigations as summarized by Dietein (1974) is indicated in table XV. Continued human studies, as well as critical invasive experiments with animals, must be conducted to define the time course of pertinent mechanisms. The Gauer-Henry reflex has yet to be demonstrated. This will not be easy to demonstrate in man since the critical time period to be investigated is thought to coincide with the early operationally exacting first day of the mission.

TABLE XV.- SUGGESTED FUTURE INVESTIGATIONS

• In-depth, noninvasive cardiovascular dynamics monitoring
• Invasive pressure/volume/flow changes in early flight (animal)
• Demonstrate presence or absence of Gauer-Henry reflex
• Total body exercise regime to maintain integrity of antigravity as well as major muscle groups
• Assess role of venous (capacitance) vessels in observed deconditioning process
• Assess role of fatigue
• Devise exercise program for all major muscle groups
• Assess roles of capacitance vessels or veins in the deconditioning phenomena

Life Sciences Spacelab Payload Simulation I

During October 1974, NASA-JSC conducted a seven-day simulated life sciences mission in a Spacelab mockup. It contained 12 experiments in human biomedical and animal cardiovascular research, plant growth and microbiological studies, biochemical determinations, and other similar studies.

The objectives of the simulation included evaluation of in-orbit Spacelab operations, payload operations, related mission control functions evaluation, and preliminary Spacelab systems and ground support facilities design.

An experiment (LSI-2) on cardiovascular physiology and cellular repair was conducted in which chronically implanted sensors and Skylab noninvasive sensors were used to assess the cardiovascular system of a large mammal during simulated zero-g conditions. The objective was to evaluate the response of the cardiovascular system to standardized stresses such as fluid loading, drugs, and envrionmental factors. Healing responses and cellular analyses of specific organs were also evaluated to assess cardiovascular changes. The results of this simulation were useful in providing a better perspective of payload operations and future life science payload definition.

Life Sciences Spacelab Mission Simulation II

Fifteen experiments were performed during a seven-day simulated Shuttle mission to gain integration and operational insights of Shuttle life sciences mission planning and preparation. The experiments were selected as a function of relevancy and technical suitability. The experiments, as defined by NASA-JSC, are summarized in table XVI.

One significant observation was that individuals with tatoos or long-term markings for positioning the vectorcardiogram leads exhibited less deviation than those without position indicators.

Bed-Rest Studies

Recent bed-rest studies have been performed. In July 1976, 28-day experiments for a Skylab I simulation were conducted. These experiments included the lower body negative pressure system. In studies involving orthostatic countermeasures via a dietary approach, it was found that beef boullion provided positive short-term effects. The normal parameters, i.e., systolic time intervals, absolute leg volume, etc were measured.

TABLE XVI.- SMS II EXPERIMENTS

Number	Title	Description
SMS II-1	Hemodynamic changes following exposure to weightlessness	Study quantitative changes in limb blood flow and relative pulse wave velocity/ time during and after flight.
SMS II-2	Central and peripheral hemodynamic responses during isometric exercise	Evaluate the effect of space flight on cardiovascular responses to isometric exercise.
SMS II-3	The effect of orbital fluid shifts on cardiovascular dynamics	Determine by myocardial responses reflected in systolic time intervals, central volume loading effects caused by headward fluid shifts and temporal course after orbit.
SMS II-4	The effect of zero-g fluid shifts on the vectorcardiogram	Determine by inflight vectorcardiogram, etiology and consequences of fluid shifts, and potential countermeasures.
SMS II-5	Echocardiography	Evaluate changes in dimensions and cardiac mechanical and electrical function throughout cardiac cycle.
SMS II-6	Hemopoietic function of bone marrow	Collect samples of bone marrow and hemopoietic tissue from experimental animals to evaluate functional aspects of the hemopoietic processes during space flight.
SMS II-7	Pulmonary blood flow	Obtain data on the time course and magnitude of changes in central blood flow/ volume relationships in zero-g by measuring pulmonary blood flow.
SMS II-8	Respiratory physiology and pulmonary function	Examine physiological mechanisms involved in adaptation of pulmonary system in zero-g and readaptation to earth gravity.
SMS II-9	The effect of zero-g fluid on thermoregulation	Assess the effect of zero-g on the rate of heat transfer from the body.
SMS II-10	Vestibular function	Obtain electronystagmograph responses of human vestibular system to variable angular acceleration.
SMS II-11	Acute fluid and electrolyte metabolism responses to space flight	Identify acute changes in systemic physiologic factors that occur upon introduction of zero-g.
SMS II-12	Study of skeletal muscle muscle function in space flight	Evaluate muscle dysfunction characteristics and consequences resulting from space-flight disuse.
SMS II-13	Salivary analysis	Measure selected parameters of parotid saliva and relate to both oral and general health.
SMS II-14	The effect of zero-g on muscle-like contractile proteins	Determine effects of zero-g using rhythmic reversible protoplasmic streaming of the myxomycetes.
SMS II-21	Cosmic ray magnetic spectrometer	Measure the momentum and electrical charge of nuclei from cosmic radiation.

INSTRUMENTATION

Numerous biomedical instruments to detect and quantitatively measure the various living processes within the body have been developed. Numerous techniques and transducers have also been developed with the intent of converting physiological events into observable and recordable signals. This has resulted in the eventual development and utilization of specialized signal processing and display devices. The ultimate use of implantable transducers has, in some cases, even necessitated the use of biotelemetry transmitters to provide the observed subject with full physical freedom.

Various methods are used to convert a physiological event to an observable, e.g., resistance, capacitance, inductance, fluidic, ultrasonic, chemical, electromagnetic, mechanical, and electromechanical techniques.

This chapter is intended to summarize the various generic types of instrumentation applicable to cardiovascular deconditioning monitoring. Both invasive and noninvasive instrumentation are included. While this summary is inclusive of representative state-of-the-art instrumentation, it is not all-inclusive in that candidate selection was tempered by the intended space-flight application and no attempt was made to provide an historical treatise on biomedical instrumentation. Furthermore, the fundamental principles used to transduce physiological phenomena into electrical signals are best described in detail in textbooks such as Geddes and Baker (1975).

Techniques and instrumentation are required that will allow better observation of man in space to determine physiological changes as a function of the spacecraft environment over a given period of time. Selection of applicable cardiovascular performance monitoring instrumentation is a function of many factors, including:

1) Specific physical properties to be measured;

2) Mission and spacecraft constraints;

3) Development/modification and implementation costs;

4) Historical techniques and instrumentation used;

5) Experimenter bias;

6) Human application versus human surrogate use;

7) Interfacing with common operational research equipment;

8) Developmental status or clinical use;

9) Class of life sciences laboratory;

10) Intended use as flight hardware or for ground-based use.

Because of several of the above factors, interviews were conducted with various knowledgeable biomedical experimenters including those not necessarily associated with the current Space Shuttle/Skylab program. The intent was to gain a fresh insight into what might constitute a near-optimum set of cardiovascular deconditioning monitoring instrumentation.

Results of previously completed NASA studies provided a baseline set of data defining life sciences cardiovascular research requirements for Spacelab. These data were analyzed and updated to incorporate inputs from recent life sciences space research results and other inputs obtained during working sessions with NASA scientists and the biomedical community at large. The new inputs were integrated with applicable baseline data into a set of related function and measurement requirements and a suggested time sequencing of research activities. Figure 4 illustrates the work flow employed to reach the objectives of this task.

A literature search was initiated by a thorough review of pertinent data defining life sciences space research requirements. The data extracted from the multiple input sources resulted in the generation of a set of requirements for assessment of cardiovascular deconditioning during space flight.

The pertinent sources used in the literature search for the evalution of instrumentation and techniques were:

1) MEDLARS;

2) JSC archives;

3) Industry report;

4) Denison Library, University of Colorado Medical Center;

5) Research reports acquired during visits to the biomedical community and conferences.

The individuals listed in table XVII were contacted at their respective institutions to gain a more current insight into potentially applicable techniques and instrumentation. Because the published literature must necessarily lag actual developments, researchers known to be active in cardiovascular instrumentation were contacted for update data in their respective areas.

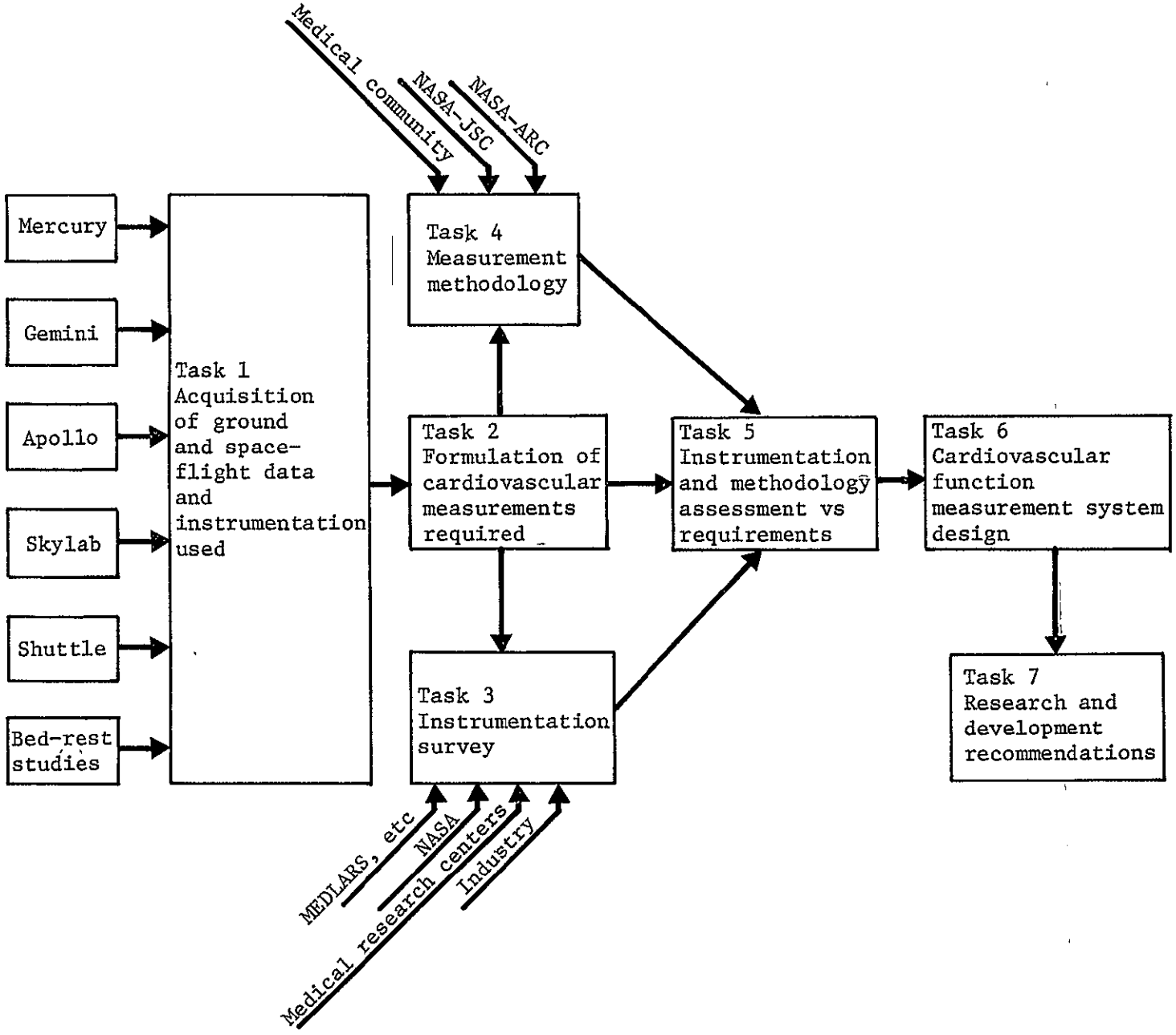

Figure 4.- Cardiovascular measurement system flow chart.

TABLE XVII.- BIOMEDICAL COMMUNITY CONTACTS

Name	Institution
E McCutcheon, MD	Chief Medical Officer in Cardiovascular Research Lab - NASA-ARC
R. Simmons, VMD	NASA-ARC Veterinarian
J Tremor	Program Manager for Animal Holding Facility - NASA-ARC
Bruce Payton, MD	Department of Surgery, University of Colorado Medical Center (UCMC)
Robert Grover, MD	Department of Surgery, UCMC
Clyde Tucker, MD	Department of Surgery, UCMC
Jack Reeves, MD	Department of Surgery, UCMC
Natalio Banchero, MD	Physiology Department, UCMC
Don Dick, PhD	Biomedical Engineering Department, UCMC
James D Meindl, PhD	Integrated Circuits Laboratory, Stanford University
Ingvar Sodal	Instructor of Medicine, UCMC
Francis D McLeod, PhD	Department of Physiology and Biophysics, Colorado State University
Slonim N Balfour, MD, PhD	Cardiopulmonary Diagnostic Lab oratory in Denver
Robert Johnson, MD	Space/Clinical Medicine Branch - NASA-JSC
G W. Hoffler, M D	Space/Clinical Medicine Branch - NASA-JSC
Stuart A Bergman, MD	Space/Clinical Medicine Branch - NASA-JSC
Sam Pool, MD	Chief, Space/Clinical Medicine Branch - NASA-JSC
Margaret M. Jackson	Space Physiology Branch, Respiratory Physics - NASA-JSC
C J. Hartley, PhD	Methodist Hospital, Texas Medical Center, Houston
Charles F Savin, PhD	Space Physiology Branch, Respiratory Physics - NASA-JSC
H G. Hanley, MD	Cardiovascular Research, Methodist Hospital, Texas Medical Center, Houston
P. Wittingham, MD	RAF Life Sciences Collaboratory at NASA-JSC
Gene Schmidt, MD	Biomedical Technology Transfer Team, Stanford University School of Medicine
Wen Ko, PhD	Case Western Reserve University
Dough O'Hanley, PhD	Technology Utilization, JPL
David Flemming, MD	Case Western Reserve University
Thomas B Fryer	Head, Invasive Biomedical Sensor Technology - NASA-ARC
Samuel Fox, MD	Georgetown University
Dennis Battock, MD	Rose Memorial Hospital
Edward Miller, MD	Chairman, Department of Medicine, General Rose Memorial Hospital, Denver CO
William Rector, MD	Director, Division of Ultrasound, Department of Radiology, General Rose Memorial Hospital, Denver CO
Phil Green	Program Manager for Ultrasonics, SRI

Many of their comments and thoughts have been incorporated in this study. Information sought throughout the technology review included future research requirements considered essential to the space program planners and science community.

Previous manned space programs showed that the cardiovascular system exhibited adaptive changes after entry into the zero-g environment that reduced the normal tolerance for reentry and landing stresses. The referenced source documents in the bibliography contained numerous recommendations for both noninvasive human studies and invasive animal studies that would enable a basic understanding of the mechanisms of cardiovascular adaption to zero-g.

Three primary areas were emphasized for detailed future space flight experimentation:

1) Altered vascular flow, volume, pressure relationships in zero-g;

2) Presence or absence of a compensatory body fluid redistribution mechanism;

3) Cardiovascular regulatory responses to exercise in zero-g.

During the process of instrumentation selection, it is evident that certain techniques and instrumentation applicable to humans are also applicable to animals. The use of an acceptable number of implanted devices in any animal must also be considered since this will ultimately be determined by the experiment objectives and the principal investigator. Furthermore, for certain measurements such as pressure or flow, several alternative methods are available, including both invasive as well as noninvasive devices. It is further assumed that invasive devices will be surgically implanted during the preflight period. Still another major consideration is cost. Where appropriate, instrumentation successfully employed in previous space missions should receive full consideration for future Shuttle/Spacelab missions. Typical examples would be the Skylab blood and urine collection equipment.

Common operations research equipment (CORE) must also be considered in the selection. CORE, as summarized in the appendix, was developed by NASA with the support of industry and represents the basic hardware complement of a general life sciences laboratory. The equipment items were derived from a variety of sources that included off-the-shelf Skylab, SRT, new developments, and Spacelab. Off-the-shelf items will require modifications for the Shuttle environment but are generally commercially available. An example of the use of CORE is as follows. For the potential cardiovascular studies, such as the investigation of the Gauer-Henry reflex, the hemotology/urology kits, the freezers, and the centrifuge CORE equipment would be required.

Still another consideration is the class of life sciences laboratory (or payload) under consideration. A number of these are categorized as being carry-on laboratories, minilaboratories, or dedicated laboratories.

All of these factors will ultimately have to be considered in the selection of cardiovascular deconditioning assessment hardware. Furthermore, several advanced technology concepts will require additional laboratory development and testing if they are to be ready for Shuttle. These are discussed in the remainder of this chapter.

Flow and Pressure Measurement

The following instrumentation review includes several of the classical techniques for information purposes only. Table XVIII summarizes the blood flow measurement methods and is followed by a discussion.

TABLE XVIII.- BLOOD FLOW MEASUREMENT METHODS

Extracorporeal measurement
Time accumulation
Orifice meter
Pitot-static tube with manometer
Rotameter
Vessel-invasive measurement
Hot-wire anemometer
Bristle flowmeter
Indicator dilution techniques
Sampling
Roentgen videodensitometry
Blood pressure techniques
Strain gage
Piezoelectric bimorph
Shock-excited tuning fork or crystal
Plethysmograph
Thermal flow-velocity transducer
Electromagnetic flowmeter
Ultrasonic techniques
Pulsed transit-time flowmeter
CW doppler flowmeter
Pulsed doppler flowmeter
Swept-frequency CW doppler flowmeter

Extracorporeal measurement.- The following techniques are most useful in combination with a heart-lung machine or dialysis, but generally are not suitable for chronic use.

The accumulation method requires drawing off the flow into a graduated container and timing the accumulation. It is unsuitable for obvious reasons.

The orifice meter requires that the blood flow through an iris that distends more widely with greater volume flow rate. The area of the orifice is proportional to the quantity of blood passing through it in a given time. Conceivably, this method could also be employed intracorporeally but is still unsatisfactory because the apparatus must come into contact with the blood to function.

The pitot-static tube used with a manometer is principally a laboratory instrument. A pressure differential, created by the moving blood stream, causes a displacement of the fluid in the U-shaped manometer (fig. 5). The difference in the fluid levels is an indication of the flow velocity. The apparatus is much too large for implantation and is also position-sensitive.

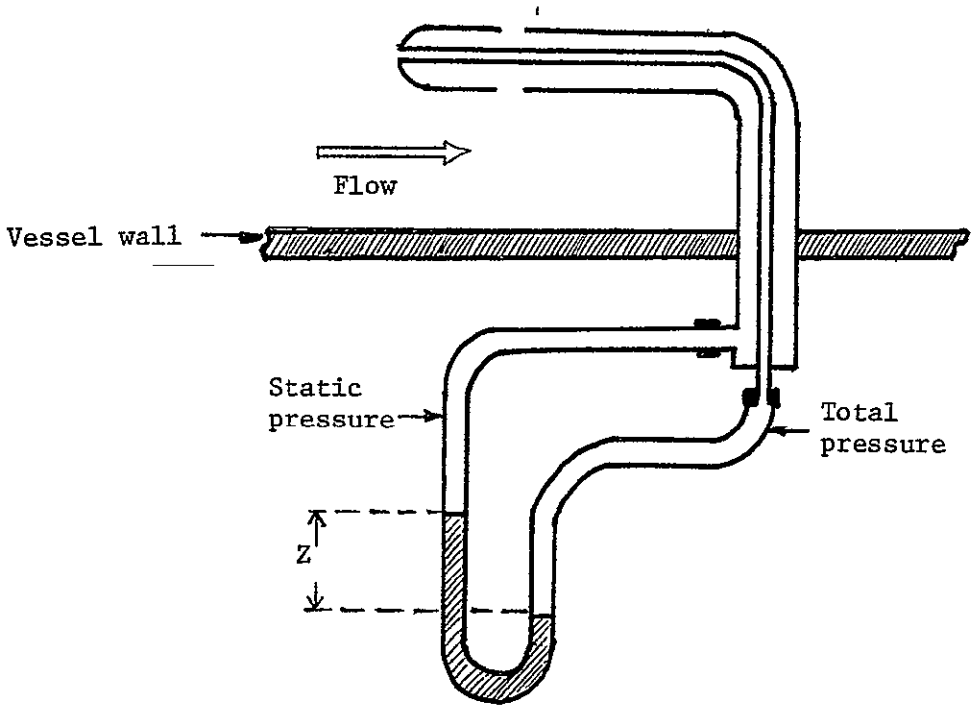

Figure 5.- Pitot-static tube with manometer.

As shown in figure 6, the rotameter consists of a ball inside a graduated tube. The ball rises inside the tapered tube until the force of gravity just balances the force of the fluid as it rises. The position of the ball thus corresponds to the volume flow rate. It is position-sensitive, will not measure reverse flow, and is unsuitable for implantation.

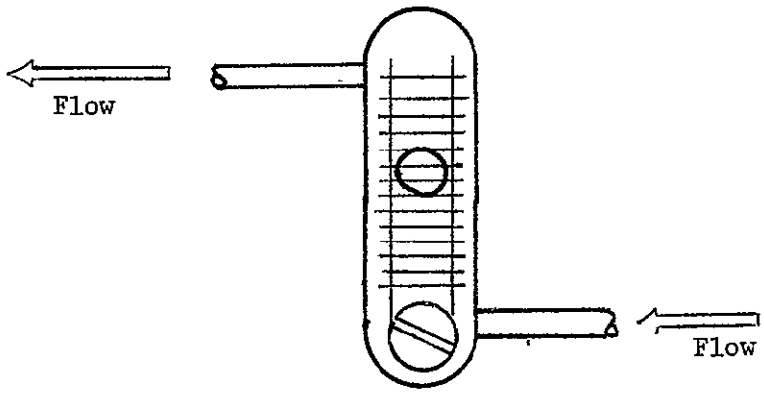

Figure 6.- Rotameter.

Vessel-invasive measurement.- The following techniques are characterized by good measurement accuracy, but must be used intravenously to operate.

The hot-wire anemometer has an advantage in that it can be made very small. It generally consists of a heating element separated by a short distance from a temperature sensor. The blood is heated slightly by the heating element. The temperature sensor reads the highest temperature with zero flow. As velocity increases, the temperature sensed decreases. The hot-wire anemometer has been made in catheter and hypodermic needle tip configurations.

The bristle flowmeter consists of one or more "bristles" encased in a cannulating probe and placed at an angle to the fluid flow. As the flow increases the angle changes. The flow velocity can be converted to an electrical signal by a strain gage coupled to the bristles.

Indicator dilution techniques.- Indicator dilution begins with the injection of an indicator into the bloodstream. The indicator used and the techniques for extracting the desired information, however, vary widely.

The historical application of dye- or radioisotope-dilution consists of injecting a quantity of the indicator and allowing the indicator to become distributed according to the assumption that the circulation is a steady-state system. Samples are withdrawn and the concentration of indicator is measured. If the concentration in the area of interest is as expected the vessel is assumed to be functional. The drawbacks are immediately apparent. No information is obtained about the pulsatile nature of the flow.

A more recent method, which shows promise, involves the injection of a radiopaque contrast material and recording the roentgenographic images on videotape. The videotape images may then be analyzed on a per frame basis to extract the desired information. In coordination with biplane angiograms to determine vessel geometry, good quantitative data concerning pulsatile blood flow have been obtained. Correction of the image for motion of the heart and arteries is applied by a digital computer. At present this technique requires a very complex instrumentation setup to reduce the data and more-than-desirable exposure to X-rays by the patient on a periodic basis.

Blood pressure techniques.- The simplest measurement of blood pressure is palpation; however, statistical studies have shown that measurement of blood pressure is not sufficient to guarantee that a vessel is capable of transporting blood. The transducers discussed here measure blood pressure externally and indirectly by sensing the distension of the vessel due to the pulsatile pressure variations. None of these transducers used singly will provide the required flow information. However, by using them in pairs, located axially from each other, some valid flow information can be obtained. As the pressure pulse propagates along a functioning artery, the vessel distends at the site of the proximal transducer slightly before it distends where the distal transducer is situated. The waveforms from the sensors will therefore differ in phase. All parts of the vessel will distend at nearly the same time and the phase shift at the sensors will be absent. Phase shift depends on flow direction, which satisfies another of the system requirements. Because these methods are indirect, the output must be correlated with an accurate temporary sensor during surgery. Moreover a change in elasticity of the vessel wall with time could invalidate the calibration.

The strain gage is a device that changes resistance when it is stretched. The resistance change can be converted to a modulating voltage or current for transmission out of the body.

The piezoelectric bimorph consists of two piezoelectric crystals cemented together so one crystal expands and the other contracts if the assembly is bent. If the bimorph is attached to a clamp that clamps lightly around the vessel as in figure 7, the expansion and contraction of the vessel will cause the bimorph to produce a potential difference between its crystals. The electrical output can be processed to measure the distension of the vessel.

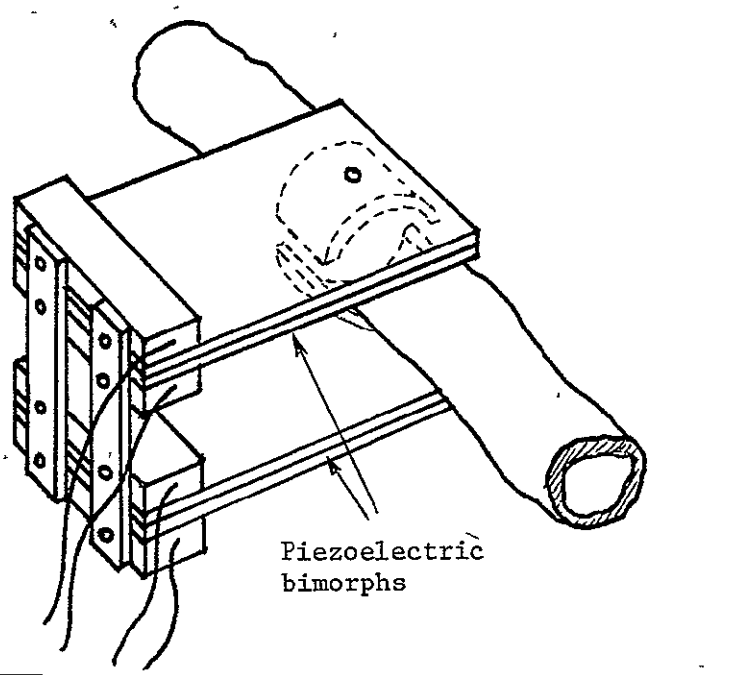

Figure 7.- Piezoelectric bimorph transducer.

Possibly the simplest system for transporting information about an individual blood vessel out of the body is the ultrasonic tuning fork or crystal. The distension of the vessel wall is used to shock-excite a tuning fork or piezoelectric crystal. The crystal will continue to oscillate at its resonant frequency. Figure 8 shows the system and its output, a damped oscillatory waveform. The information content is restricted to the peak of the pressure pulse, but two of these sensors located axially could provide a qualitative indication of flow in the vessel.

Operation of the plethysmograph is based on the higher conductivity of blood than most other body tissues. As the systolic pressure wave propagates through the arteries, they distend at the expense of surrounding tissue and the conductivity momentarily rises. In the implanted version, the plethysmograph applies a constant high-frequency current to electrodes emplaced on opposite

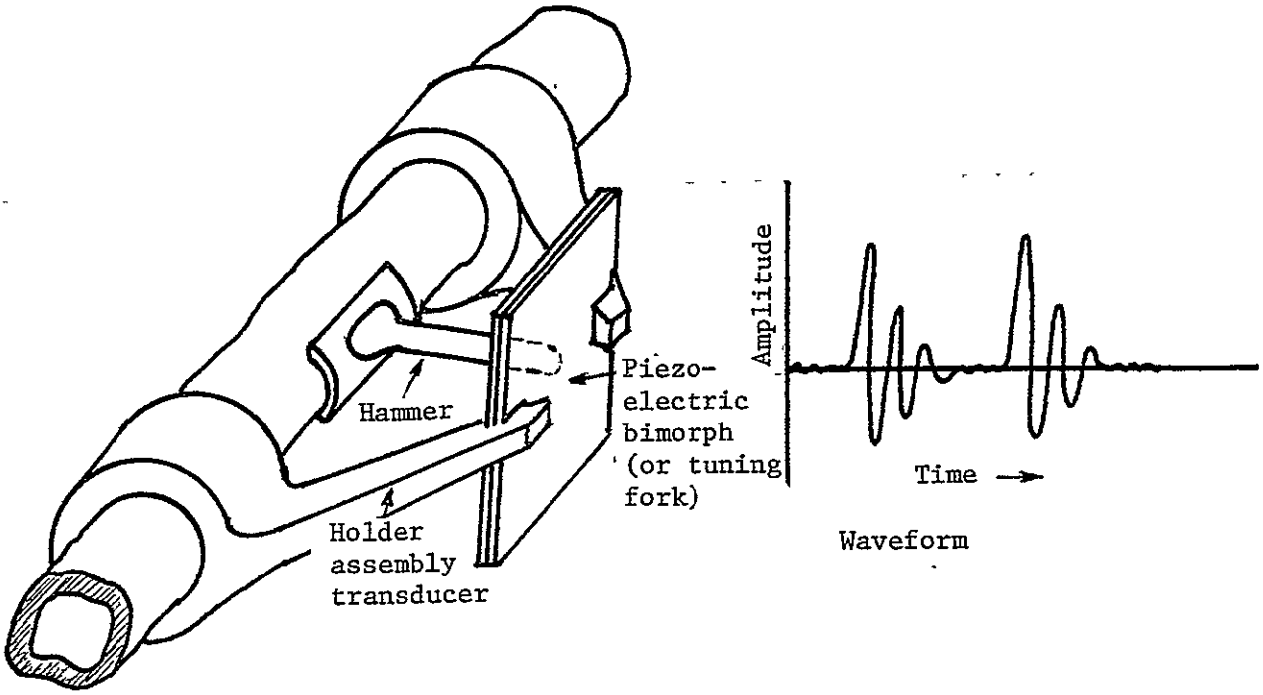

Figure 8.- Shock-excited resonant mechanical transducer.

sides of the vessel. As the conductivity changes, the voltage across the electrodes changes. This voltage change is the sensor output and is often attributed to blood flow. However, like the other techniques discussed, the principal parameter sensed is the distension of the vessel due to pressure.

Thermal flow-velocity transducer.- Figure 9 shows the "Thermo-Stromuhr." Radio frequency power is applied to the capacitor plates on opposite sides of the vessel. The RF heats the blood between the plates and the temperature differential measured by the thermocouples provides a voltage output. The slower the flow, the more the blood heats up and an increased voltage is obtained at the output. This transducer is also sensitive to direction of flow. The system has been used to measure flow rates from 10 to 300 mℓ/min; however, the response is only marginal for observing pulsatile flow.

Electromagnetic flowmeters.- The EM flowmeter shown in figure 10 is one of the oldest and most widely used sensors of blood volume flow rate. An alternating magnetic field is applied to pole pieces on opposite sides of the vessel. A magnetic field at right angles to the flow is produced. Blood flowing through the vessel cuts the lines of force and generates a voltage that is picked up by electrodes on the vessel walls. The magnitude of the sensed voltage is directly and linearly proportional to the volume flow rate. The instrument is also sensitive to direction. Unfortunately, the EM flowmeter is sensitive to a number of errors that decrease its

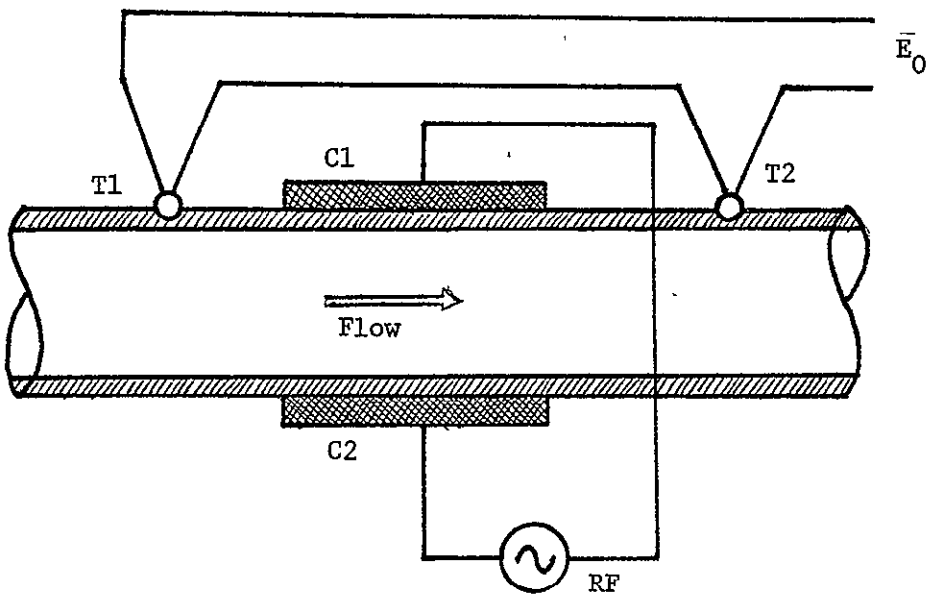

Figure 9.- "Thermo-Stromuhr" transducer.

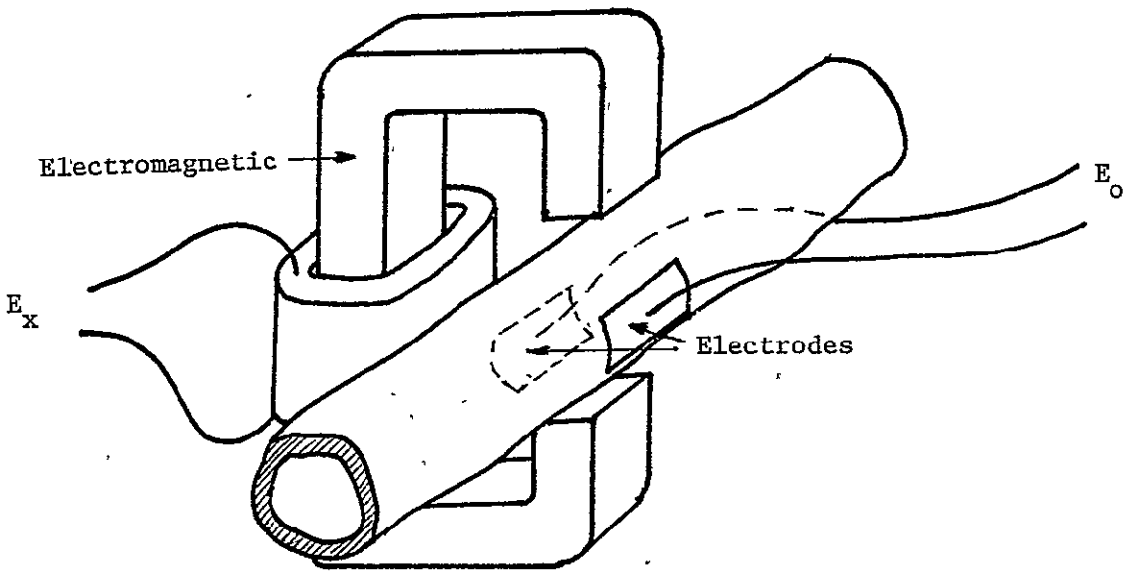

Figure 10.- Electromagnetic flowmeter.

usefulness, e.g., the electrode circuits can act as a transformer secondary with respect to the strong field applied by the electromagnet. This action produces extraneous signals that alter the desired blood flow signals. The instrument is also difficult to calibrate for zero flow. Another problem is poor reliability of the electrode contact with the vessel wall. Finally, the electromagnet requires more power than is desirable. Thus, despite its potential ability to yield the most accurate data for pulsatile blood volume flow, it must be considered a poor candidate for implantation.

Ultrasonic techniques.- Several distinct blood velocity techniques employing ultrasound (high-frequency mechanical waves) have been developed. They all have in common the use of piezoelectric transmitters to transform an RF signal to a mechanical vibration and a receiver to perform the reverse function. They have the additional advantage of requiring no electrical contact with the vessel, thus eliminating a potential source of artifacts. They can also be made quite small and their power and circuitry requirements are also less than for most other sensors. The primary drawback of the ultrasonic systems is that they are sensitive to flow velocity rather than to volume flow rate. Volume flow rate can be determined with reasonable accuracy with knowledge of the vessel diameter. Pitfalls associated with their use have been discussed by Flax et al. (1973).

As shown in figure 11, the pulsed sonic flowmeter employs two piezoelectric crystals (usually barium titanate) facing each other diagonally across the blood vessel. The crystals serve alternately as transmitter and receiver. A pulse from one crystal is sent across the vessel lumen to the receiver. The transit time is measured. Then the process is reversed and a pulse from the second crystal is sent to the first. The difference in transit times is a measure of flow in the vessel, being zero for zero-flow velocity.

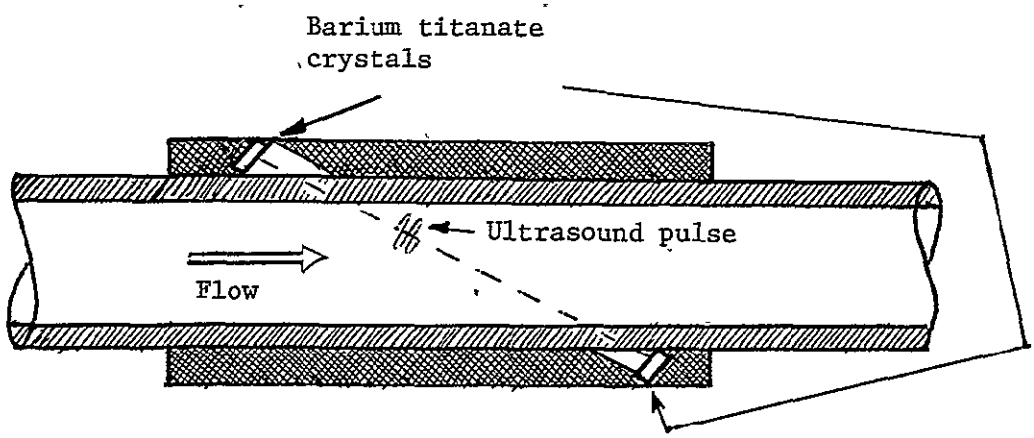

Figure 11.- Pulsed-ultrasonic transit time flowmeter.

Transit time is longer upstream than downstream. The system requires little power and is sensitive to direction of flow. A major disadvantage is that the crystals must be widely separated (2 cm or more) for low flow rates, making the transducer somewhat larger than desirable for many applications.

Doppler flowmeters operate on the principle that ultrasound waves are back-scattered from moving blood cells. Figure 12 illustrates the transducer arrangement. The transmitter emits a continuous wave of ultrasound energy into the vessel at an angle, usually about 45 deg. A receiver crystal located diametrically opposite the transmitter and aimed toward the vessel lumen at the same angle picks up the reflected energy. Some of the transmitted ultrasound reaches the receiver crystal directly and is, in fact, much greater in amplitude than the back-scattered ultrasound. Back-scattered energy from stationary cells comes to the receiver exactly at the transmitted frequency and is "swamped out" by the large direct component. But reflections from moving cells arrive at a higher or lower frequency due to the Doppler effect and frequency-modulate the signal at the receiver crystal. Due to the mixing effect of the direct and reflected energy, sum and difference frequencies are also produced. The difference frequency consists of the modulation only, which is an audio frequency. The audio frequency can be amplified and used to produce an output. Unfortunately, this directly converted waveform cannot distinguish the direction of flow -- it responds identically to flow in both directions. Therefore, the ultrasound frequency at the receiver crystal is sometimes processed by other means to retain the directionality information. Doppler flowmeters normally operate between 2 and 10 MHz. At these frequencies the receiver signal may be amplified and transmitted out of the body without further frequency

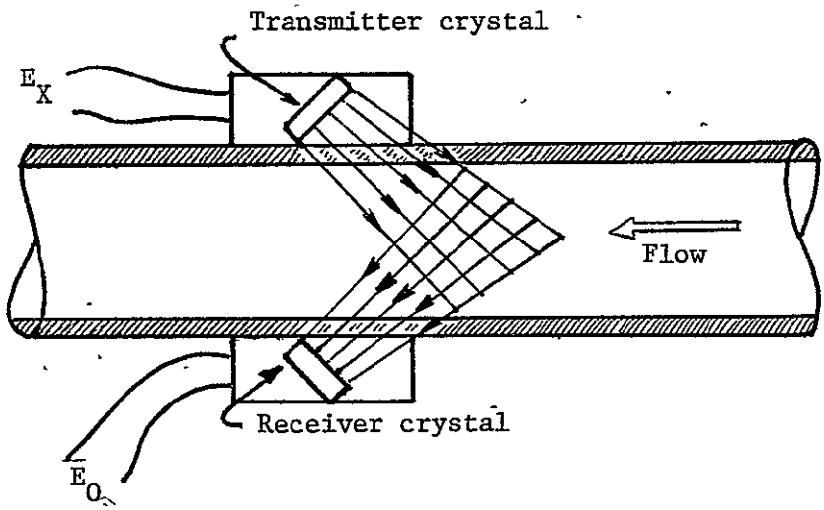

Figure 12.- CW Doppler flowmeter.

conversions. It can also be made small enough for implantation in very tight areas. It is therefore a high-ranking candidate for use in an experimental system.

Another ultrasound technique uses two crystals diagonally but asymmetrically opposite across the vessel lumen as in figure 13. The barium titanate crystals are excited simultaneously in phase opposition by a continuous wave signal at 5 MHz. Thus each crystal acts as a transmitter and receiver at the same time. With no flow, the signal on each crystal is identical -- the sum of its own excitation signal, the direct received signal, and reflections from stationary objects like the vessel wall. These identical signals are canceled at the input to a differential amplifier. When blood is flowing in the vessel, however, the signals passing through the lumen are phase-modulated, the upstream signal now being different in phase than the downstream signal. These signals are no longer canceled at the amplifier input and an output signal is produced. The interferometer is an interesting concept but the system balance is quite critical and the baseline may exhibit serious instability over a period of time. Another serious disadvantage is that the asymmetrical design makes the probe even larger than that of the pulsed-sonic flowmeter.

Two other techniques for Doppler flowmeters are deserving of mention although the additional information to be gained from them probably does not justify the increase in system complexity in this instance. Both are used to obtain a velocity profile across the

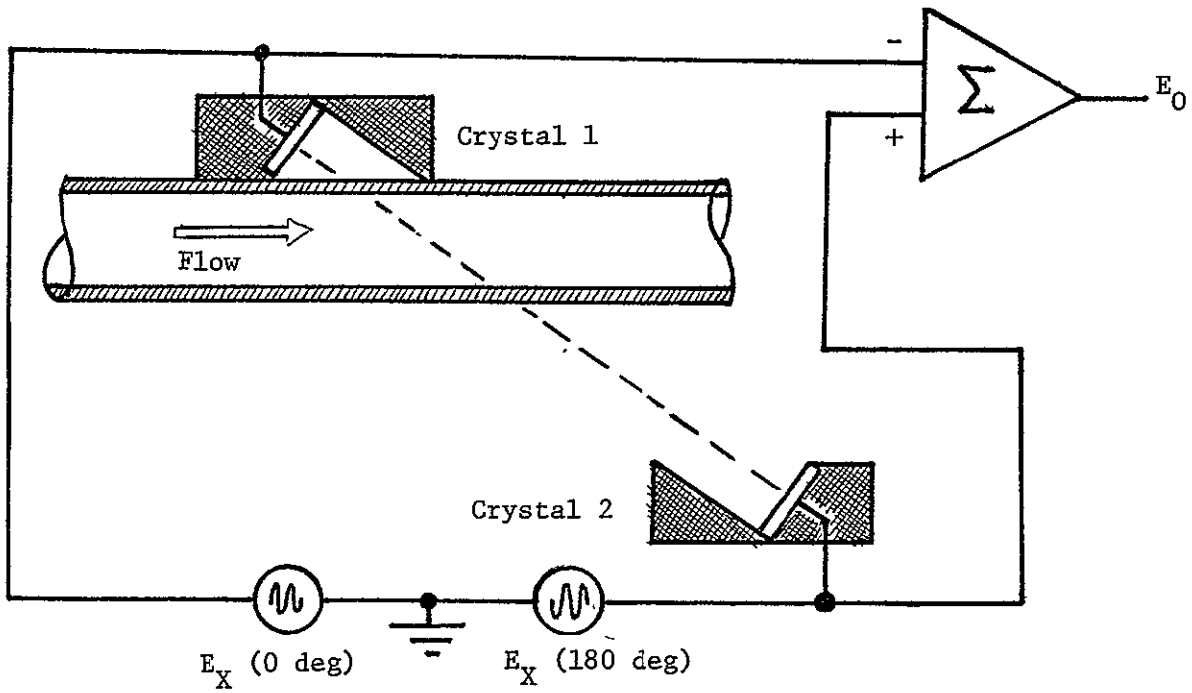

Figure 13.- Ultrasonic interferometric blood flowmeter.

vessel lumen. The first is a pulsed-Doppler single-crystal tranceiver. A pulse of ultrasound energy is directed into the vessel at a 45-deg angle. The reflected energy is received at the same crystal after a transit time depending on the distance to the crystal -- very similar to a pulse radar system. A range gating system is used to divide the vessel into range intervals. A cancellation circuit is used to eliminate echoes that return at exactly the transmitted frequency and represent static elements. Doppler-shifted moving elements are processed within their range intervals. In this manner, using the information received for each range interval, a velocity profile across the lumen is developed.

Pulsed Doppler catheter tip flowmeters that measure instantaneous flows within the vessel have been reported (Hartley and Cole, 1974; Pardue et al., 1975).

A second method uses a frequency-modulated, CW Doppler signal. The transducer is identical to that shown in figure 12 but is excited by a sawtooth frequency sweep. The frequency difference reflected onto the receiver crystal is now a combination of the range of the reflector and its velocity. By comparing the instantaneous transmitter and receiver signals, a velocity profile can be developed as in the pulsed-Doppler system.

Power Sources

Sources of power for devices implanted within the body fall within three distinct categories -- implanted storage sources, biological energy sources, and extracorporeal energy sources as illustrated in Table XVIII.

TABLE XIX.- POWER SOURCES FOR IMPLANTED SENSORS

- Implanted stored-energy sources
  - Electrochemical power sources
    - Pacemaker cells
    - Solid-electrolyte batteries
  - Nuclear power sources
- Biological energy sources
  - Biochemical energy sources
    - Biofuel cells
    - Ionic concentration cells
    - Biogalvanic cells
  - Biomechanical energy sources
- Extracorporeal energy sources

Implanted storage sources.- This category includes electrochemical and nuclear power sources housed in sealed containers and surgically implanted. At present these energy supplies are used primarily to power cardiac pacemakers.

Although considerable research is in progress, the field of implantable cells is incredibly small. The most widely used pacemaker battery is the Mallory RM-1, a 1.35-V, 1-A-h cell. Although designed for a three- to four-year lifetime at currents in the 30- to 40-μA range, most are replaced at around two years due to losses within the cells. Several batteries with a solid electrolyte such as lithium-iodine, silver-iodine and lithium-iodide salt have been proposed and evaluated. However, these experimental cells have not proved to be significantly better than the RM-1. It is possible that the zinc-mercury RM-1 would be acceptable for intermittent use if it were turned on only when measurents were taken. Magnetic reed switches have been successfully implanted and used this way.

The Model 50 Betacel made by McDonnell Douglas Astronautics is a promethium-fueled nuclear battery. It has a volume of 1.8 cc (about half the size of the zinc-mercuric oxide cell discussed earlier). When new, the battery has a terminal voltage of 2.0 V and a short-circuit current of 42 μA. Promethium 147 has a 2.63-year half-life and the battery capacity decreases accordingly, whether used or not.

Biological energy sources.- The search for ways to produce electrical energy from processes within the body has produced some interesting results. The experiments have been frustrated, however, by the cyclical nature of body functions and the mechanisms by which the human organism tends to surround any foreign object with a mass of tissue. Both chemical and mechanical methods have been attempted.

Biofuel cells make use of the body's metabolism in an oxidation-reduction reaction. An example biofuel cell uses platinum black electrodes bonded to a tantalum mesh. The electrodes act as a catalyst to oxidize glucose at the anode and reduce oxygen at the cathode. In vivo experiments showed that the cell worked, but only for a few days before the catylitic action at the anode was poisoned by proteins.

Ionic concentration cells have also been tried. These cells depend on different ionic concentrations in different areas of the body. So far the differences in concentrations have been found to be too small or the fluctuations too large for a practical cell to be constructed.

Biogalvanic sources have met with some moderate success. Galvanic pairs of metal electrodes are used with body fluids serving as the electrolyte. As in electrochemical batteries, the electrodes and the electrolyte are consumed in the reaction, a process that limits the useful life.

The growth of tissue can also render the cells useless in a short time although inert materials with selective permeability have had some effect in prolonging the cell life as well as preventing pathological reaction in the tissues.

A converter similar to the bimorph pressure transducer in figure 7 can produce electric power. If a larger version is placed on the aorta, the more active pulsing could conceivably generate enough power to operate a blood flow transducer system. Unfortunately, the constant flexing of a sufficiently large and thick crystal would lead to fatigue failure in a relatively short time. In addition, the defensive tissue growth would tend to reduce the output.

Extracorporeal energy sources.- By transporting energy into the body only when needed, an extracorporeal power source overcomes the difficulties inherent in using implanted sources. To maintain isolation, dc current paths through the body and RF induction methods are normally used. A flat external coil is placed over the area of a similar implanted coil as in figure 14. RF energy is coupled from the external primary coil to the internal secondary through mutual inductance. The secondary energy is then rectified and filtered to produce the dc operating voltages for the implanted flowmeter sensor. A storage capacitor would normally be used to provide continuous operation during short interruptions of the input power. The transfer of sufficient energy into the body to power the sensor and electronics is no particular problem. It is anticipated that the total power requirement will be considerably under 1W. Power transfer of 1000 W into the body of a dog has been attained with no apparent tissue damage and only a 7°F temperature rise immediately beneath the transmitter coil after 90 minutes of operation. The primary drawback -- and the point that should receive considerable attention -- is the possibility of interference with other instrumentation. [A thorough review of power sources for bioinstrumentation is given by Fryer (1970; 1974)].

Telemetry Technology

Implanted telemetry transmitters have been in use for many years and the technology is well developed. The most comman application has been for remote monitoring of physiological parameters of unrestrained animals. The primary considerations are range, choice of frequencies, multiplexing, and special considerations for implanted transmitters such as tissue damage and interference with other instrumentation. The receiving range varies from just

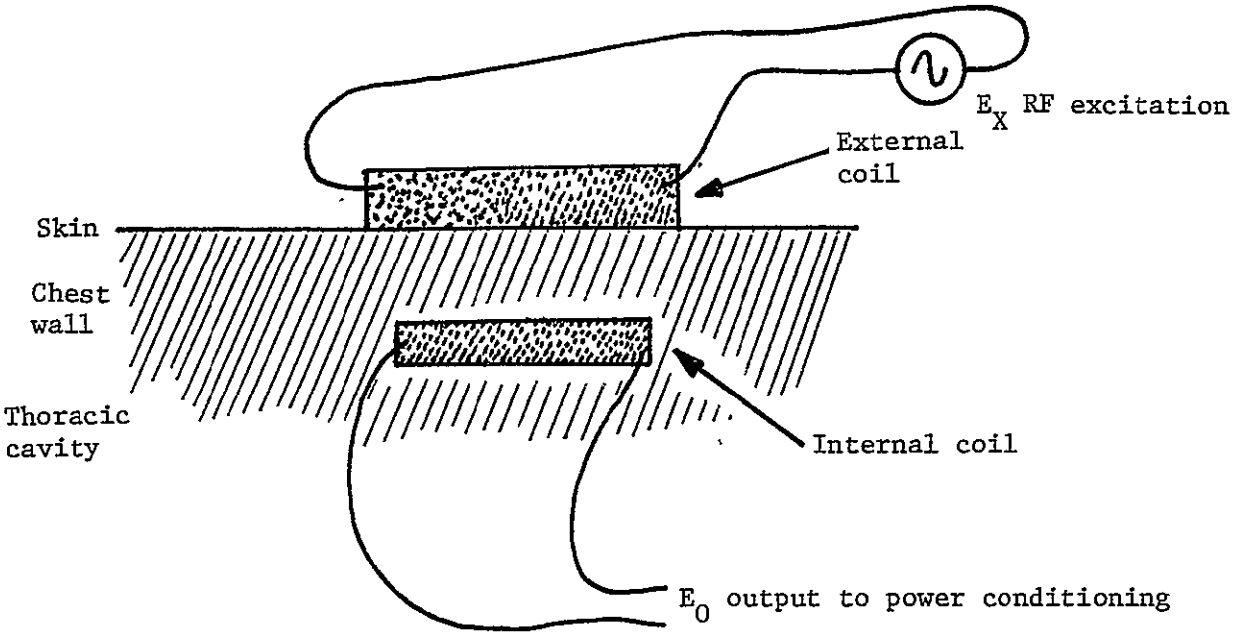

Figure 14.- Transcutaneous induction energy transfer.

outside the skin to many miles, depending on transmitter power, frequency, modulation method, and antennas. Frequency modulation is often employed, in part because it is simple to generate, but mostly because it maintains better data fidelity than other simple systems such as amplitude modulation. The choice of frequencies is usually in the VHF region -- 30 to 300 MHz. It has been common practice to place the telemetry transmitter between 88 and 108 MHz and use a high-quality standard FM receiver. The Federal Communications Commission has authorized frequencies in the 460-MHz band for medical telemetry but the intent is for telemetry from an emergency vehicle to the hospital emergency room rather than from an implanted transmitter to the laboratory equipment. The frequencies chosen for flowmeter telemetry will depend on the transducer used. For example, when using a CW Doppler sensor it would simplify the implanted circuitry to use the 5- to 10-MHz excitation frequency as the telemetry frequency as well.

Multichannel telemetry systems [Biotelemetry, Vol 3 (1): 1-64, (1976), Fryer (1970) and Sandler, et al., (1972)] are commonly employed when the use of more than one sensor is desired. It is not economical to have a separate transmitter for each sensor. Most biological parameters are in the audio to subaudio frequency range. These fairly low frequency signals easily permit the output of several sensors to time-share the same transmitter carrier

by sampling each sensor output in turn. The reverse process restores the original information at the telemetry receiver. The advent of CMOS integrated circuits now makes possible a multichannel system that takes very little more power than a single-channel system.

Cardiovascular Noninvasive Instrumentation

Cardiovascular deconditioning assessment will require a wide range of noninvasive instrumentation such as that illustrated in table XX. This table is intended to provide the reader with a brief summary of applicable existing cardiovascular performance monitoring hardware.

Technology Status

Ultrasound considerations.- The use of ultrasound devices in cardiovascular measurement has greatly increased in the last decade and now holds great promise in many areas of diagnosis and monitoring. Although some of the major advances do not seem closely related to space medicine and cardiovascular measurements, many do. Two major technology areas germane to these areas of interest are organ system visualization, in this case, echocardiography relating to the heart and great arteries and measurements of hemodynamics related to heart output and activity, and the peripheral vessel system.

The literature covering even these restricted fields has become voluminous; however, several excellent review works are available [Popp & Harrison, 1974; Goldberg, 1973; Harrison, Sandler and Miller (Eds), 1975] and the material covered in them will not be repeated in detail here.

The key features of the ultrasound technique that make it attractive are the options of using it invasively or noninvasively, safety, comfort, and feasibility of continuous measurements of mobile subjects. The equipment, including the data handling electronics, can be small, at least for peripheral vessel monitoring systems. Transducers of barium titanate and lead titanate zirconate, as well as others, are typically operated at 2 to 8 MHz and have diameters of 2.5 to 10 mm.

Echocardiography.- Echocardiography has been used primarily to detect such abnormalities as aneurysms or occlusions in the vessels and pericardial effusions, valve malfunctions, and heart tumors. Left ventricular stroke volume, ventricular wall thickness, and wall motion can also be determined and, with two-dimensional transducer arrays, a three-dimensional image of the heart is feasible (Beaver, et al., 1975).

TABLE XX.- CARDIOVASCULAR SYSTEM PERFORMANCE MONITORING HARDWARE

Number	Identification	Parameter(s) Measured	Physical Principle Used	Restrictions on Use	Development State	Remarks
1	Electrocardiograph	Time history of muscular and electrical events during heart beats	Time histories of electrical potentials on surface points of thorax indicate desired parameters	Clinics or labs required, patients' movements limited by facilities	High, readily available	Highly standardized methods and interpretation
2	Vectorcardiograph	Time history of muscular and electrical events during heart beats	One additional electrode allows 3-dimensional vectorial interpretation of electrical potentials	Clinics or labs required, patients' movements limited by facilities	High, more specialized than item 1	Many different instruments, needs standardization
3	Sonocardiograph	2-dimensional outline of heart and 3-dimensional picture of side of heart	Sonically senses heart with matrix of sensors at 40 frames per second	Clinics or labs required, display on CPT	Developmental, prototype built and tested at NASA-ARC	Can be used for heart stroke volume measurement
4	Lower body negative pressure device	Cardiovascular capability as a function of time spent in zero-g environment	Size (volume) of lower body at negative pressures indicates cardiovascular capability	Specialized setup, demands total patient availability during test	Developed especially for Skylab	Can be used both on ground and in large spacecraft
5	Wearable blood pressure recording system	Pressure vs time with suitable superficial arteries	Tiny silicon diaphragms with diffused boron resistors sense artery through skin	Unrestricted	Developmental prototypes are in being	Development continuing at Stanford Research Institute
6	Wearable ECG recording system	Same as item 1, usually with reduced number of leads and capabilities	Same as item 1	Largely unrestricted, patient must carry instrumentation	High, developed for both civilian and space environment	Self-contained recorder or telemetry required, can be combined with other instruments
7	Apex cardiograph (kinetocardiograph)	Left ventricular pressure vs time	Microphone records chest displacements at maximum impulse location from 0 1 to 20 0 Hz	Patient in specified position, lying down	High, more specialized than item 1	Nonstandardized, easily assembled
8	Piezoelectric pulse pickup	Arterial pulse	Piezoelectric crystals respond to pressure changes	Practically none	High	Readily fabricated, inexpensive
9	Phonoarteriograph	See item 11 below				
10	See item 11 below	Hepatic (tracings)				
11	Echocardiograph	Actual motions of heart components, e g , anterior mitral valve leaflet	Sound waves are reflected by body components	Clinics or labs required	High, but expensive	Considerable technical skill required for adequate tests
12	Cinefluorograph	Functioning of prosthetic heart valves	Direct visualization and cinephotography by means of x-ray fluoroscopy	Used only for specialized studies of prosthetic valves	High, cine frame rates up to 180 per second	Image intensifier tubes used
13	Radionuclide imaging	Gross heart component dimensions, blood flow volumes, etc	Concentrations of nucleides are shown by scintillation cameras	Low resolution in scintillation camera limits use to gross measurements	Developmental	Extremely high data rates available
14	Impedance cardiograph	Volumetric blood flow	Thoracic impedance of 20 to 100 kHz can be calibrated in terms of blood flow	Clinics or labs required	Developmental	Can be combined with ECG
15	Cardiotachometer	Heart beat rate	Measures time between beats	See items 1 and 6	High	Incorporated in items 1, 2, 4, 7, 8, 9, 10, 12, 13, etc

Miniaturized equipment does not seem essential for echocardiography since displays for A and B scans are ordinarily required in the form of cathode ray tubes, which are quite bulky. While there is no fundamental reason why the transducers and electronics associated with driving and data handling cannot be miniaturized, the nature of usage of echocardiography would seem to rule out the sensibility of such miniaturization. Such reviews of echocardiography are available (Popp and Harrison, 1974; Popp, 1975).

Scanning can be accomplished mechanically by moving the transducer. Also acoustic or electric scanning is possible by focusing a two-dimensional array of transducers with an electronic array of charge coupled device (CCD) circuits (Beaver, et al., 1975).

Miniature two-dimensional arrays developed by several workers (Bom, et al., Beaver, et al., 1975; Kisslo, et al., 1975) permit rather accurate visualization of organs with stationary transducers. One- and two-dimensional acoustical imaging devices providing 2-mm resolution at 20 cm and a frequency of 2.25 MHz have been described (Fraser et al., 1974; Kino, 1974). These devices may have application to biomedical measurements, although they were not designed specifically for this purpose. Surface acoustical wave techniques are used to scan optical or acoustical images and for electronic focusing of acoustical images.

Doppler ultrasonic cardiovascular measurements.- Doppler techniques permit ultrasound to be used for either diagnosis or monitoring of the heart or vessels. A splendid review of basic concepts, techniques, and some of the problems of Doppler measurements has been given by Gill, et al., (1975). Monitoring in space medicine has received more emphasis than diagnosis, and this trend will be reflected in the following discussion.

Heart wall motion can be detected by continuously monitored Doppler techniques. Esophageal probes and implanted probes can continuously monitor flow rates and cross sections of the vessels approximate to the heart. These techniques, however, seem likely to be limited to experimental animals or human surrogates in space in spite of the fact that some of the best results in measuring blood flow by Doppler have been obtained by invasive techniques. Invasive measurements on the aorta have been quite successful, either with or without percutaneous connections, the latter permitting subjects to engage in activity regimes (Foletta, et al., 1974).

The fluid-mechanical aspects of blood flow have been characterized by Talbot and Berger (1974), showing clear relationships between blood pressure and velocities at various sites along the arteries.

Theoretical analyses of both CW and pulsed Doppler flowmeters published by several workers (e.g., Brody and Meindl, 1974; Gill, et al., 1975; Hottinger and Meindl, 1974; McLeod, 1974) have provided a basis for sophisticated digital data handling techniques.

Velocity profiles across vessel sections are being characterized by McLeod of Colorado State University using his multichannel Doppler flowmeter techniques (McLeod, 1974; McLeod, et al., 1974). They provide a potential basis for estimating total blood flow from average velocity and vessel diameter, a much simpler task electronically than measuring velocities of the total vessel cross section.

Foletta, et al., (1974) pointed out that only a pulsed Doppler shift is capable of measuring blood flow from one side of a vessel. This seems to be the most likely candidate noninvasive technique for man in space. Noise problems are severe, however, and the signals will require extensive processing, which is not necessarily prohibitive if done digitally.

Doppler techniques employing wideband transmitted frequencies have been recently described and analyzed. Better range and resolution are claimed using these techniques than are available with the usual pulsed deterministic transmitted signal Jethwa and Olinger, 1975; Newhouse, et al., 1976).

Vessel wall motion can be parametrically related to blood pressures. A 55 dB S/N ratio can be obtained from vessel walls compared with erythrocyte back-scattering. A blood pressure indicator embodying Doppler ultrasonics, a stored parametric relationship between brachial and radial artery parameters (for a given subject), and a microprocessor is based on this principle. This work is being done by Martin Marietta personnel at the Denver Division.

Computer processing.- Considerable work has been done on computer processing of data produced by ultrasound. Most of this work has been directed at echocardiograph images of the heart and great vessels (Hirsch, et al., 1973; Saunders and Harrison, 1975) but some work has also been done on data derived from smaller vessels, the latter unpublished work by the Martin Marietta Corporation. One of the key technology items pacing the use of computers for cardiovascular parameter analysis is the development of hardware preprocessors to effectively detect the onset (usually a rising wavefront) of a cardiac event. Some of the successes of computer processing of biomedical images have been reviewed by Preston (1976) and the future discussed. The advent of microprocessors at low cost along with substantial commitments from their manufacturers to provide software and operating systems will undoubtedly enhance the widespread use of digital computers in cardiovascular measurement systems.

Gas analysis.- Sodal and coworkers at the University of Colorado have had considerable success in using mass spectroscopy for monitoring the pulmonary and cardiovascular parameters listed in table XXI.

TABLE XXI.- MASS SPECTROSCOPY PARAMETERS

1)	Standard pulmonary functions; a) Vital capacity, b) Forced vital capacity, c) Maximum breathing capacity, d) Lung volumes, e) Closing volumes, f) Occlusion pressures, g) Flow volume curves;
2)	Hypoxic and hypercapnic ventilatory drive;
3)	Oxygen uptake;
4)	CO_2 production;
5)	Cardiac output (noninvasively, gaseous method);
6)	Lung water;
7)	Arterial PO_2 and PCO_2 (noninvasive);
8)	Arterial PO_2-PCO_2 and arterial O_2 and CO_2 content on drawn blood samples;
9)	Distribution of V/Q ratios (method of Wagner and West).

A miniature, fully computerized respiratory mass spectrometer has been developed in their laboratories over the past several years. This instrument is now completed to the point where it could perform the first five measurements indicated in Table XXI. Preliminary work has been conducted at this time to adapt this instrument to blood gas analysis, both measurement of content and gas tensions. This would make possible the use of the same instrument for measurements 6 through 8 in the same table.

The capability for noninvasively measuring arterial PO_2 and PCO_2 depends on transcutaneous outgassing. Previous work has been accomplished in Germany and England, but the measurements suffered from rather wide variations (Sodal, personal communications). The method used by Sodal, et al., is to heat the skin to 42 to 43°C, pull a vacuum against the skin across a few mil diameter capillary, and transfer a gas sample to the spectrometer inlet. The inlet system uses a servo-driven piezoelectric sapphire against a steel inlet valve with a sampling time per gas of 1-ms and a 30-ms settling time. A new ionizer has also been designed to permit fast response time and high efficiency.

The direct inlet system and ionizer are the prominent features of this 25-lb instrument, which can follow concentration profiles of all gas components during the entire breathing cycle. Several gas components, plus water vapor, can be monitored simultaneously.

Cardiac dimension measurement.- Two methods of cardiac measurement have been reviewed: (1) the method in which dimensions are evaluated from cineradiograms of cardiac chamber in which silver-tantalum clips have been sutured to the external surface of the ventricles, and (2) a noninvasive method in which echocardiograms are made with the use of ultrasonic transducers.

The first method (Harrison, et al., 1963) is implemented with silver-tantalum clips, which are nonreactive. These clips are sutured to three points on each cardiac chamber, forming a triangle on the anterior surface of the right ventricle with the apex of the triangle in the right ventricular outflow tract. Two clips are placed along the lateral surface of the left ventricle, one near its apex and the other near its base. The third clip is sutured to a point on the interior-posterior aspect of this chamber. Films are exposed in the frontal projection with a Picker image orthicon utilizing a 16-mm camera at 30 exposures per second. To detect any motion in the X-ray field, small metal markers were placed on the anterior and posterior surfaces of the chest wall. The individual frames of the films were correlated with specific points in the cardiac cycle with a mechanical indicator, which was triggered by the R-wave of the electrocardiogram. This permits precise correlation of each frame of the cineradiogram with the data recorded on the photographic recorder. The processed films are projected on a screen or a specially constructed cineradiographic analyzer, and the distances between clips on the magnified image were measured to the nearest millimeter. Measurements are reproducible to within 1.5%.

Recently a light-pen computer processing combination has been applied to angiograms for the determination of left ventricular volume (Alderman, et al., 1973). This method eliminates the tedious hand calculation of volume.

Another method involves the use of ultrasonic transducers directed from different orientations. The echoes from the cardiac chamber define the structure and thence the dimensions. Techniques to direct the ultrasonic transducers to a common location and thereby a common point of reference have been reported (Popp, et al., 1975; Popp, Brown and Harrison, 1975). The problem with this technique is repeatability of results. There is no standard interspace in the cardiac chamber, that is, standardization from one subject to another.

These limitations on ultrasonic transducers are not a limiting factor for the space experiment in which the subjects used can be clinically evaluated prior to the space activity. Standardization appears to be achievable and ultrasonic methods of dimensioning by measuring echoes appears to be a practical noninvasive method.

Blood pressure and flow.- Measurements of blood pressure and flow include the following parameters:

1) Velocity of blood in the vessel;

2) Changes in blood velocity;

3) Volume of blood flow;

4) Systolic and diastolic blood pressure.

The various instruments available or under development are summarized in table XVIII, and can be categorized as follows:

1) Noninvasive, suitable for space flight;

2) Invasive, suitable for space flight;

3) Invasive, not suitable for space flight.

Some of the instruments or techniques are largely of historical interest (e.g., manometers) described in tests such as Ruch and Patton (1965) and would not logically seem to be candidates for space use. Most of the invasive techniques are also well-covered in the older literature but are included here for the sake of completeness and their utility in human surrogates and other test animals.

The techniques of greatest interest at present are noninvasive and are the subject of considerable current research. The venous occlusion plethysmograph has been long known as a tool for estimating blood flow, and modern electronics have been used in recent developmental work on automating the cuff plethysmograph and identifying the associated Korotkov sounds for blood pressure measurements (Golden et al., 1974; Wolthuis, et al., 1974). Perhaps the greatest current interest centers around the use of ultrasound for both flow and pressure measurements because of the small size, wide variety of possible configurations, and the resulting electrical signals, the nature of which enables the application of digital processing. The advent of large-scale integrated circuits and microprocessors will almost certainly result in effective noninvasive peripheral cardiovascular measuring devices in the near future.

While there are apparently no commercially available ultrasound blood flow or pressure devices suitable for space use, several active research projects show considerable promise:

1) McLeod (McLeod et al., 1974) is establishing velocity profiles across vessel cross sections. In healthy subjects, parametric relationships can be established whereby vessel cross-sectional area and direct average velocity measurements can probably yield quite accurate estimates of flow;

2) Polhemus (unpublished) is using parametric relations between radial artery wall velocity at systole and measured systolic and diastolic pressures at the brachial artery to estimate blood pressure parameters. Additional measurement of artery diameter will permit estimates of flow when coupled with clinical characterization of a subject;

3) Under contract to NASA-ARC, McLeod (unpublished) is completing a system that uses two transducers oriented upstream along the vessel. Axial and radial components are measured simultaneously and flow direction is established unambiguously. Vessel diameter is estimated by low-frequency high-energy returns from the vessel walls. This method should provide good estimates of blood flow;

4) Baker, et al. (unpublished) uses a rotating pulsed Doppler scanner plus a stationary pulsed Doppler in an imaging system. The transducer position is established by use of a sonic microphone and spark gap. The vessel center is located at two positions several cm apart to determine the angle relative to the scanner. Information is obtained on vessel morphology, as well as artheroscloratic plaque, etc;

5) Meindl and coworkers have reported a number of Doppler flowmeters, so far restricted in practice to the great vessels. Some of the most interesting are the "angle-free" systems (Hottinger and Meindl, 1974; Gill et al., 1975) that give estimates of blood flow independent of lumen cross section, orientation, or velocity profile.

SUMMARY AND RECOMMENDATIONS

NASA has stated that the compensatory, adaptive processes produced by space flight could possibly create significant difficulties during reentry and postreentry survival situations and could pose problems for inflight emergencies and for long-term readjustment to earth conditions.

The potential for determining basic mechanisms of cardiovascular system response to zero-g and applying this knowledge to prevent or reduce orthostatic intolerance and other cardiovascular-related effects during Shuttle flight, reentry, and flyback is a necessary and important activity. Quantitative assessment of the following observations is deemed necessary to fully understand the short- and long-term effects of cardiovascular deconditioning as a result of space flight:

1) Shift in distribution of intravascular volume;

2) Instability of cardiac electrical activity;

3) Modification of integration and regulation pattern;

4) Blood volume shifts during reentry;

5) Orthostatic intolerance during tilt, LBNP, and centrifugation following flight or bed-rest exposure;

6) Cellular alterations.

Human bed-rest studies should continue to receive heavy emphasis to arrive at criteria that will enable optimization of crew performance, maximum safety, and candidate crew selection. Recent positive indications of orthostatic countermeasures via dietary techniques add further credulity to bed-rest studies. Continued emphasis is required on techniques for observing the time course of cardiac size, peripheral vascular compliance, and flow distribution, both in an unstressed and stressed environment during the bed-rest studies.

Table XXII summarizes the desired observable along with candidate instrumentation requirements. These can readily be compared to current NASA programs such as those tabulated in table XXIII. Our study results indicate that the instrumentation listed in table XXIV requires further development for future space flight. However, increased emphasis should be given to the types of instrumentation and studies outlined in the following sections.

TABLE XXII - CARDIOVASCULAR PERFORMANCE AND DECONDITIONING ASSESSMENT

Observable	Assessment technique
1. Fluid distribution changes and vascular compliance	Photoplethymograph Limb plethysmograph
2. Orthostatic hypotension (fluid volumes, control and regulatory mechanisms)	Drugs Exercise program Flow sensors Biotelemetry systems Vibration facility Vibration transducer
3. Cardiopulmonary circulatory dynamics	Radioisotope equipment Doppler ultrasonic flow sensor Invasive flow transducers Vasoactive drugs
4. Cardiac dimensional analysis	Scanning echo device (3D) Low-dose X-ray system
5. Indices of functional alterations	Multisensor transducer for wall motion
6. Etiological mechanisms	Apexcardiogram Echocardiogram Scintillation angiocardiogram
7. Response to dynamic stress	LBNP Centrifuge Echocardiography Doppler transcutaneous flow sensors
8. Neurohumoral control of cardiovascular function	Implanted pressure transducers Implanted flow transducers Implanted pacemakers Implanted brain electrodes Pharmacologic tests
9. Cellular fine structures	Pharmacologic studies Image enhancement techniques Temperature transducer, implantable

TABLE XXIII.- CARDIOVASCULAR PERFORMANCE AND DECONDITIONING ASSESSMENT

	Measurement objective(s)	Subject	Observable(s)	Assessment technique	Equipment
1	Measure change in body, fluid distribution, and vascular compliance for cardiovascular deconditioning detection	Human	Limb compliance Volume Pressure	Noncontact limb volume technique using photoelectric principle	Photoplethysmograph for limb circumference measurement LBNP Centrifuge
2	Measure orthostatic hypotension processes	Human	Fluid volumes	Assess role of angiotension II in control of blood pressure and in postural homeostasis	LBNP Vectorcardiogram
3.	Determine effects of alterations in preload and afterload on ventricular function	Human	Headward body fluid shifts	Use LBNP to reduce left ventricular preload Drug effects studies	LBNP Nitroprusside intravenous infusion Nitroglycerin sublingually and intravenous infusion Catheter probes, etc
4.	Study circulatory dynamics, cardiovascular and pulmonary	Human	Cardiac output Stroke volume Pulmonary and systemic circulation times Ventilation/perfusion ratios Airway closing volumes	Radioisotope equipment Technitium 99 - CV circulatory dynamics Xenon 133 - Pulmonary circulatory dynamics	LBNP Tilt table Compare to ST I, echocardiography VCG, etc
5	Computer study of clinical vectorcardiograms for early detection of CV disease	Human (clinical use)	VCG parameters	Computer analysis of vectorcardiograms	Vectorcardiograph
6.	Evaluate indices of functional alterations with deconditioning	Human	Precordial wall motion Systolic time intervals Pulse transmission time	Multisensor transducer for wall motion detection Assemble statistics for ST I Use vasodilators and vasoconstrictors	Multisensor transducer for wall motion detection
7.	Plethysmograph refinement	Human	Limb circumference	Plethysmographic	Limb plethysmograph Arm plethysmograph
8	Observe left ventricle via 3D scan mechanization	Human	Left ventricular volume Cardiac output, X, etc	Echocardiography	Scanning echo device ECG
9.	Evaluate etiological mechanisms	Human (clinical use)	Cardiac output Stroke volume Diastolic and systolic volumes Ejection fraction Left ventricular end-diastolic pressure	Apexcardiography Systolic time intervals Echocardiography Scintillation angiocardiology Compare above with invasive measurement results	Apexcardiograph Echocardiograph Scintillation angiocardiograph Etc

TABLE XXIII.- CARDIOVASCULAR PERFORMANCE AND DECONDITIONING ASSESSMENT - Continued

	Measurement objective(s)	Subject	Observable(s)	Assessment technique	Equipment
10.	Measure degraded responses to exercise, +g acceleration, and LBNP	Human and animal	Marked increases in coronary blood flow	Bed-rest studies to determine cardiac function Invasive animal experiments	LBNP Centrifuge Echocardiograph Doppler transcutaneous flow sensors
11.	Measure changes in orthostatic tolerance due to space flight	Human	Mechanoreceptor stimulation response Orthostatic regulation	Apply stress, i.e., selective stimulation of major cardiovascular mechanoreceptor subgroups and observe response	LBNP Apply abdominal compression Positive pressure breathing Tilt table
12.	Hemodynamic measurements using ultrasonic techniques	Human	Volume blood flow Velocity Vessel dimensions	Noninvasive Doppler ultrasonics	Doppler ultrasonic flow system
13	Bandwidth reduction via compression of complex physiological system	Human or animals	ECG Pressure Flow Dimension } Process and condense	Hardware development	Data compression techniques Posttransmission reconstruction Frequency filtering
14.	Blood flow distribution via ultrasonics for understanding CV adaptive processes	Animals	Blood velocity profile and vessel cross-sectional area	Use implantable flow system to measure Renal Coronary Intestinal Cerebral flow	Doppler telemetry system Single crystal transducers Transcutaneous arrays Catheters
15.	Animal studies of blood flow	Animals	Cardiac and peripheral vascular changes Coronary blood flow Intravascular pressures Cerebral, renal, and splanchnic blood flow	Stress testing Vasoactive drugs	Implanted instrumentation Centrifuge LBNP
16.	Study of neurohumoral control of CV function	Animals	Ventricular pressure Atrial pressure Cardiac dimensions Ventricular flow Ventricular wall thickness	Pharmacologic tests Provocative stimulation of critical central nervous system areas via radio telemetry techniques	Transducers (implanted and hardwired telemetry LBNP Implanted pacemakers Brain electrodes
17	CV response of primates to orthostatic stresses	Animals	Arterial flow Venous flow	Measure arterial and/or venous flows in cerebral, renal, coronary, and mesenteric vascular beds Cardiac denervation (surgical and chemical)	Tilt table LBNP Hardwire transducers with back-pack telemetry system

TABLE XXIII.- CARDIOVASCULAR PERFORMANCE AND DECONDITIONING ASSESSMENT - Concluded

Measurement objective(s)	Subject	Observable(s)	Assessment technique	Equipment
18. Cellular consequences and ultrastructural effects of CV deconditioning	Animals	Cellular fine structures effects (cardiac muscle) Measure norepinephrine (NE) and NE granule distribution	Compare cellular fine structure morphologic changes with phsiologic function Apply various environmental forces	Centrifuge LBNP Kosmos 75 and '76 animals
19 Noninvasive direct measurement of CV dynamics	Human	Flow distribution Flow direction Flow velocity Cardiac structures	Application of ultrasonics to flow sensing	Gated Doppler velocity sensor Battery-operated echocardiograph Ultrasonic flow sensor (directional)
20 Fluoroscopic cardiac imaging for heart size	Human	Cardiac size during dynamic states	X-ray fluoroscopic techniques with stress testing	Low-dose x-ray system, fluoroscopic Centrifuge, human
21 Obtain inflight data on size and shape of various heart chambers or circulation	Human	Heart size and shape changes Circulation in heart Coronary Blood vessels	Roentgen video densitometry Computer-assisted data analysis 3D reconstruction of heart	Inflight x-ray system
22 Develop implantable CV bioinstrumentation	Animals	ECG Flow Pressure	Animal invasive studies using implantable transducers	RF inductive-coupled links Transducers for ECG, flow, and pressure
23. Small primate prototype CV flight experiment	Animals	ECG Temperature	Environmental testing of the rhesus monkey with implanted transducers and various power sources	Transducers for ECG and body temperature
24. Minimization of orthostatic intolerances via imposed dynamic acceleration	Human	Stimulation	Apply vibration and monitor with accelerometer	Vibration facility Externally applied vibration transducers
25. Math modeling of CV factors dependent on gravitational stimulus	N/A	Pressures Flows	Math modeling	LBNP
26. Develop biotelemetry packages	Animals (primates and rodents)	Inputs Body temperature ECG EEG Pressure Muscular activity pH and pO_2 of blood	Application of advanced ICs	Biotelemetry packages With batteries With inductive power sources
27. Develop multichannel telemetry system	Animal	Inputs ECG Temperature Pressure	Implant into artificial hearts in calves and sheep at University of Utah	Multichannel telemetry system

TABLE XXIV.- CANDIDATE INSTRUMENTATION REQUIRING FURTHER REFINEMENT

1.	Photoplethysmograph
2.	Improved LBNP
3.	Catheters for animals
4.	Echocardiograph
5.	Radioisotope equipment
6.	Multisensor transducer for wall motion
7.	Vectorcardiograph
8.	Limb plethysmograph
9.	Scanning echo device
10.	Implantable flow transducers
11.	Biotelemetry systems, implantable and backpacks
12.	Data compression electronics
13.	Radiotelemetry stimulators
14.	Low-dose X-ray system
15.	RF inductive power sources
16.	Temperature transducers, implantable
17.	Pressure transducers, implantable
18.	ECG "dry" leads
19.	Vibration stimulators
20.	Multichannel telemetry systems
21.	Ergometer

Noninvasive

Echocardiography.- A major direction for ultrasound usage in space medicine is the further development of linear and two-dimensional transducer arrays for three-dimensional imaging along with the concurrent development of improved display techniques. Heart size and other ventricular function measurements are essential.

Dietary and exercise studies.- Techniques must be developed to prevent or compensate for space-flight cardiovascular deconditioning. Improved dietary and exercise programs should be thoroughly evaluated during the bed-rest studies as a function of historical observations.

Plethysmography.- A reliable plethysmograph is required for blood flow and volume determination. The Skylab unit does provide a volume estimate via a capacitive technique; however, it is not easy to use due to postflight calibration requirements. If a microprocessor were used in conjunction with the plethysmograph, this would enable a real-time readout. This same microprocessor should be used to control the LBNP chamber pressures for maximum utility. Conversely, electrical impedance techniques are limited due to resistivity problems and are not recommended. The obvious advantage of the plethysmograph is that differential change can be related to an absolute volume.

Image analysis techniques.- Ultrastructure analysis of cellular structure as a result of cardiovascular deconditioning is recommended as a means of increasing resolution of electron micrographs. The image enhancement facility at JPL constitutes a unique tool for this activity.

Lower body negative pressure system.- The LBNP has proved its utility in Skylab and in recent bed-rest studies wherein increased heart rate during LBNP tests were generally shown to be the best single index in the assessment of orthostatic tolerance. By combining the circulatory effects of LBNP with echocardiographic analysis of ventricular volume, one would have a unique noninvasive method for assessment of the left ventricular function as well as for stress testing of the cardiovascular system in general. It is also recommended that control of chamber pressure be automated.

Roentgen videodensitometry.- Techniques for providing dynamic and stop-action, three-dimensional reconstructions of any part of the body are currently under development, e.g., the dynamic spatial reconstructor being developed at the May Foundation in Rochester, Minnesota, under the direction of Earl Wood (see Preston 1976). It is designed to sense and digitize at 60 frames per second 28 simultaneous planar projections that will be created by 28 video-scanned, pulse X-ray source-detector assemblies arranged in a semicircle. Computerized tomography in which data gathered from an X-ray scanner are fed into a computer to produce cross-sectional images of the human body certainly should be considered for future space flight as well as for preflight and postflight observation of the body. Development work in the areas of data storage and analysis, increase in computational speed, and hardware size reduction should continue for the Shuttle application.

Invasive Instrumentation

The chronic invasive instrumentation of animals has been facilitated by the advent of small reliable transducers. The small physical size and potential for long-term stability of presently available transducers permits rather extensive instrumentation of even small animals (cats, rats). The low expected mortality should permit animals to serve as their own controls, and rather complex protocols should be possible. Some development work beyond that already accomplished (e.g., by Hanley, Hartley, and others) will be necessary to adapt the instrumentation to space experiments.

We recommend that emphasis be placed on the necessary further development of catheter tip ultrasonic flowmeters, implantable pressure transducers, and a whole range of implantable ultrasonic blood velocity and organ morphology measuring devices.

Integrated Cardiovascular Measurement System

To arrive at an integrated cardiovascular measurement system, it is essential that (1) the necessary observables be defined, (2) the evolutionary instrument selection procedure be well established with appropriate alternatives, and (3) the environmental and experimental criteria be defined. More important perhaps is the necessity for a logical set of experiments that can best characterize the optimal approach to the determination of cardiovascular deconditioning processes. This experiment set is being solicited by NASA, both internally and from the biomedical community at large. Unfortunately, such an experiment set was not available for this study. Nevertheless, the results obtained from previous space flights and bed-rest studies are indicative of what further knowledge pertaining to cardiovascular deconditioning is required. Figure 15 illustrates a logical approach toward defining an integrated cardiovascular measurement system.

Iterative loops will be required to select a near-optimal set of instrumentation tailored to the required observables. Consideration must also be given to common equipment usage. A representative integrated biomedical measurement system for a Spacelab mission is as shown in table XXV wherein commonality of hardware is indicated. It should also be pointed out that the physical characteristics and mission objectives of a particular Skylab life sciences laboratory will influence instrumentation configurations and it is fully expected that the cardiovascular instrumentation configurations will be evolutionary.

Figure 15.- Development of an integrated cardiovascular measurement system.

TABLE XXV.- EXAMPLE OF AN INTEGRATED BIOMEDICAL MEASUREMENT SYSTEM

Experiment	Objectives and Observations	Required Hardware								
		Small Vertical Cages	Freezers	Mass Spectrometer	Automated Potentiometric Electrolyte Analyzer	Centrifuge, Blood	Hematology and Urology Kits	Physiology Kit	Recording System	Histology Kit
Cardiovascular	Altered vascular flow/volume/pressure relationships. Internal blood flows, pressures, urine and blood collection, freeze and store; food and fluid intake, biochemical analysis.	X	X			X	X	X		
	ECG/pulse, Doppler flowmeter.							X	X	
	Demonstrate myocardial degeneration resulting from zero-g.							X		X
Musculoskeletal	Absolute catabolic effects of zero-g. Food and fluid intake, histological preparations of bone, bone marrow, muscle.							X		X
Hematology	Invasive studies -- measure total blood volume, red blood cell mass, blood O_2 tension; obtain reticulocyte counts, collect, prepare and store blood samples		X		X		X	X		
Biochemical Reactions	Fluid and electrolyte balance, Ca regulation, adrenal function; urine collection, preservation and analysis; onboard and gound analysis.	X	X		X		X			
Pulmonary	*Respiratory gas analysis.*	X		X						

APPENDIX

PRELIMINARY CORE PRIORITY LIST

Accelerometer

Accelerometer, coupler

Adapters, TV microscope

Analyzer, general spectrophotometer

Atmospheric sampling manifold

Auto potenelectrolyte analyzer

Badges, radiation

Bags, plastic

Bicycle ergometer

Blood pressure system with cuff (noninvasive)

Body mass measuring device

Breathing regulator pressure demand

Calculator, portable

Camera controller

Camera mounts

Camera, cine

Camera, polaroid

Camera, video, B/W

Camera, video, color

Camera, 35 mm

Can crusher (Skylab)

Cardiopul analyzer system

Cardiotachometer

Cell counter

Centrifuge, table top

Centrifuge, reference high-speed

Chemical storage cabinet

Chemical containers

Chemical-radioactive, container

Cleaner, handiwipes

Cleaner, vacuum

Cleaner, hand washer

Commutator, gas manifold

Compactor, waste solids

Computer, digital

Counter, colony (manual)

Coupler, phono/vicrocardiogram

Coupler, vectorcardiogram

Coupler, gas-liquid flowmeter

Coupler, impedance pneumograph

Crew mobility aids

Crew restraints

Data management system buses

Digital voltmeter

Display - numeric

Display - keyboard, portable

DMS, control station

DMS, instrumentation modified

DMS, plotter/printer

Equipment restraints

Exercise equipment (Skylab)

ECG coupler

EEG coupler

Film

Filters, video (Skylab)

Flowmeter, breathing gas

Flowmeters, general-gases and liquid

Fluid handling kit

Freezer

Freezer, cryogenic

Freezer, low temperature (holding)

Gas analyzer mass spectrometer

Gas chromatograph

Gas supplies

General photometer

Holding unit, cells and tissues

Holding unit, invertebrate

Holding unit, plants

Holding unit, primates

Holding unit, small vertebrates

Incubator

Infrared gas analyzer

Kit, cleanup

Kit, general inventory

Kit, general tool

Kit, maintenance

Kit, stationary

Kit, tool - insection manipulator

Kit, urine acquisition

Lamp, portable high-intensity photo

Life sciences bioresearch center

Liquid tank

Log books

Lyophilizer

Mask, pressure breathing

Mass measuring device (macro)

Mass measuring device (micro)

Meter, pH

Meter, total solids refraction

Microprocessor

Microscope, dissecting

Microscope, comp-binocular

Microtome

Miniature fast analyzer

Mixer, temperature-controlled

Monitor, video

Oscilloscope

Paper, recording

Photocell (coupler)

Photocells

Plethysmograph, limb

Power supply and conditioning

Radiation counter biochemical sampler

Radiation detector, general

Recorder, multichannel biomedical

Refrigerator

Rotating litter chair

Signal conditioning rack

Small recorder, voice

Sound level meter

Staining system

Stop watch

Storage, film

Storage, general

Tape, video

Tape, voice recorder

Temperature block

Thermocouple coupler

Thermocouples

Timer, events

Tissue homogenizer

Transducer, plethysmograph

Trash can

Video ID date-time system

Video tape recorder

Volumetric measuring (liquid) kit

Vomitus bag & holder

Waste storage bag

Waste storage device

Waste storage, radiological and biological

Workbench, crew work station (ESRO)

Workbench, general experiments

Workbench, life support and protective system

Workbench modification, debris containment shroud

Workbench modification, environmental shroud

Workbench modification, surface airflow

Workbench, surgical

GENERAL INVENTORY KIT

Animal physiology kit

Chemical analysis kit

Hematology kit

Histology kit

Linear measurement kit

Microdissection kit

Microbiology kit

Organism holding kit

Physiology kit

Plant toools kit

Veterinary kit

Physical examining kit

Insect manipulation tool kit

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This constitutes a list of references cited throughout the report and a selected bibliography of recent and review works concerning cardiovascular measurements relating to spaceflight. No effort was made to include all applicable historical references since such a bibliography would be a major publication in itself. Reference to the review works cited here will lead to the pertinent literature.

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