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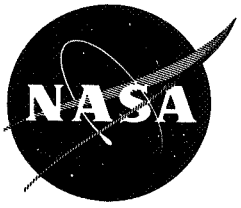
TECHNOLOGY SURVEY

Technology Utilization Division

NASA Contributions to:

CARDIOVASCULAR MONITORING



NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

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NASA Contributions to:
CARDIOVASCULAR MONITORING

by

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Foreword

That American business can benefit from technological advances prompted by requirements for space missions is becoming obvious. That research sponsored by the National Aeronautics and Space Administration also may help prolong thousands of persons' lives is less generally realized. This survey of recent developments in cardiovascular monitoring emphasizes applications of achievements in aerospace work to civilian medicine.

The Technology Utilization Division of NASA was established to disseminate information rapidly that appears likely to be useful in industry. Members of the staff of the Bioengineering and Biosciences Technology Department of the Westinghouse Electric Corporation Research Laboratories in Pittsburgh undertook this survey for NASA. Their report both reviews several significant developments and discusses the potential market for new products that now can be readily envisioned.

GEORGE J. HOWICK,
Director, Technology Utilization Division,
National Aeronautics and Space Administration

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CHAPTER 1

Scope of This Study

Physiological monitoring is the continuous or periodic measurement of quantitative physiological data in a form suitable for evaluation, recording or storage. This monograph is concerned primarily with these techniques as they apply to an intact human subject, although many of them are equally applicable to other biological subjects. Most physiological monitoring systems are designed to measure properties of the organism itself; however, some measurements of the physical properties of the organism's environment may have sufficient biological significance to warrant classification as physiological monitoring.

Physiological monitoring systems consist of three primary elements: the transducer or sensor which performs the actual measurement, the communication equipment which transmits this data from the point of measurement to the point of analyses or reproduction, and the data handling system which analyzes, reproduces and/or stores the data.

The transducer or sensor detects the values of the biological parameters and makes them available for measurement. The term transducer ordinarily denotes a device which transforms energy in one form to energy in another form. Many physiological transducers operate by transforming heat, motion, pressure, etc., into electrical signals. Exceptions are those "transducers" which are used to measure bioelectric phenomena. Electrodes used to detect potential differences for instance do not transform energy but, together with associated amplifiers and signal conditioning equipment, make it available for measurement.

The communication sub-system consists of three elements: the data transmission device which receives energy from the transducer and transmits it, the communication link, and the data receiving unit. The communication link may be either wired or wireless. The data transmitter usually amplifies, conditions, and modulates the signal received from the transducer before transmitting it to the data receiving unit. At the receiving unit, the signal is demodulated and often further amplified.

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A variety of data reproduction units may be used with physiological monitoring systems. Almost any unit which generates a visual display may be used to exhibit the measurements in real time (as they are received). Oscillographs, typewriters, and other printing units that produce records may provide both a real time visual display of the measurements and a permanent record of the data. Sometimes the data is analyzed and certain computed functions are displayed instead of or in addition to the signal itself. The signal obtained from an electrocardiogram, for example, can be processed to provide pulse rate and acceleration, and quantitative respiratory data. In a more sophisticated system, data analysis could be routinely performed and only unusual or significant deviations from the normal or expected values displayed or recorded. This would enormously decrease the amount of data to be examined.

In surveying physiological monitoring systems and their applications, we have focused attention on the sensors involved. These elements are of necessity tailored specifically for biomedical use, while data transmission and data handling systems differ only slightly from those used in other sensing and display systems. Current and previous surveys[1] have covered the major technological advances in these areas.

The primary emphasis of this report is upon the methodology involved in making physiological measurements and the sensing systems used. This limitation in scope, however, is not intended to derogate the importance of other areas in the development of practical monitoring systems. In fact, one of the major stumbling blocks to the use of continuous monitoring techniques is the vast amounts of data generated, and the subsequent need for an intelligent programmed technique for analyzing and evaluating it. Such techniques are indeed essential to the extensive use of continuous monitoring techniques.

A further reduction in the scope of this study is in regard to the physiological systems considered. The circulatory and respiratory systems are inherently and directly sensitive to the environmental conditions of space flight, and consequently a preponderance of NASA-supported research and development efforts have been concerned with monitoring of the significant parameters of these systems. For the respiratory system, the principal efforts were to evaluate and adapt existing monitoring techniques to the flight application. However, existing monitoring techniques for the circulatory system were inadequate, and a concentrated effort was necessary to produce acceptable flight hardware. In view of current medical interest in the treatment of certain types of heart disease in special coronary care wards equipped for continuous monitoring of circulatory param-

Superior figures refer to References on p. 43.

eters, technology concerned with the circulatory system may now have considerable economic significance.

This monograph was written to encourage the commercial exploitation of this technology by industrial organizations that are willing to undertake such further development or adaptation as may be required to render these devices and techniques useful to civilian medicine. It is also intended to serve members of the biomedical community who need new techniques but may not be aware of the technological advances resulting from the space effort.

The literature surveyed was limited by design to unclassified, unlimited distribution documents. Some errors of omission and commission have undoubtedly occurred. A number of NASA advances were alluded to in the general literature, but in many cases detailed development reports were not available; thus these developments could not be well evaluated.

No evaluation of the potential for transfer of technology from indirectly related fields has been attempted. Typical examples of such indirect transfers that have occurred in the past are the use of space-developed gas bearings in ballistocardiography and electronic filtering techniques in phonocardiography.

CHAPTER 2

Techniques of Cardiovascular Monitoring

Before describing NASA advances in cardiovascular monitoring, we shall briefly discuss the nature and significance of the system parameters measured and the present and proposed techniques for monitoring these parameters.

The circulatory (or cardiovascular) system consists of the heart and blood vessels which distribute nutrients and oxygen to all parts of the body and carry away the wastes and carbon dioxide produced. Of major importance in monitoring the activity of this system are the electropotentials generated by the heart muscles (electrocardiography), heart sounds (phonocardiography), blood pressure and oxygenation, pulse rate and rate of change, and flow rate of blood through specific arteries or body tissues.

BLOOD PRESSURE

Blood pressure is the result of the pumping action of the heart which empties blood into a closed system of elastic blood vessels. The volume capacity of this system changes as a result of the stretching of the vessels and by caliber changes in response to nervous and chemical stimuli.

During ventricular systole, blood is forced into the highly elastic arterial system faster than it can escape into the arterioles, capillaries and veins, and the arteries are stretched to greater capacity. But since blood is constantly passing into the capillaries, the pressure falls when the flow of blood into the arteries is stopped at the end of ventricular systole. The elastic recoil of the arterial walls forces the blood onward through the capillaries at a constantly decreasing pressure until the arteries regain their pre-systolic caliber. The energy that was stored in the arterial walls during the stretching of the vessels is expended between heart beats, insuring a relatively continuous flow of blood through the arterioles and capillaries. The pulsations of the arteries are convenient indications of heart rate.

The blood pressure is maintained at a normal level by a combination of five factors: cardiac output, peripheral resistance, blood volume, elasticity of the arterial walls and blood viscosity.

Blood pressure is a major parameter in monitoring the circulatory system. The pressures recorded at various points on the body are different, however, since blood would not flow if there were not a pressure gradient from the large arteries to the smaller arteries, the arterioles, the capillaries and the veins. Therefore, to be comparable, blood pressure information must be recorded at the same place. Almost all blood pressure measurements are presently made on the forearm. At this location, it is quite easy to measure both systolic pressure (the maximum pressure which occurs during ventricular systole) and diastolic pressure (the minimum pressure which occurs as a result of arterial recoil during ventricular diastole). The difference between the systolic and diastolic pressures is called the pulse pressure.

BLOOD PRESSURE MEASUREMENT BY OCCLUSION

A physician normally measures arterial pressure by encircling the arm with an inflatable cuff, and placing a stethoscope, microphone, or other listening device over the brachial artery below the cuff in a position where the pumping sounds of the heart are clearly audible. The cuff is inflated until the pressure in the cuff is greater than the arterial pressure; at this point, no sounds are heard, since arterial pressure is insufficient to force blood past the cuff. The pressure in the cuff is released slowly until the lumen in the compressed artery is opened enough to allow the passage of a jet of blood with each heart beat (ventricular systole). The pressure in the cuff at this point, recognized by the sound of the pulsing blood flow in the partially occluded artery (Korotkoff sounds), represents the systolic pressure. As the cuff pressure is reduced further, the sounds change in quality and disappear completely when the blood flows continuously through the artery. The pressure in the cuff at this point is the diastolic pressure.

This general technique of blood pressure measurement by occlusion and detection of pulsatile blood flow can be used at almost any point on the body where a uniform pressure field can be applied to an artery. The ausculatory (listening) method is extremely sensitive to noise artifacts which makes automatic interpretation of the data difficult to perform reliably. Other methods available for the detection of pulsatile blood flow include electrical impedance plethysmography and ultrasonic and electromagnetic flow meters. (These techniques are discussed in detail later in connection with blood flow rate measurement.)

The changing opacity of flesh to light can also be used to indicate changes in blood flow rate or volume. Either reflected or transmitted light may be employed. Disadvantages of the reflective technique include increased susceptibility to motion artifacts, reduced sensitivity due to direct light transfer over the skin surface, and the effect of

skin color upon the output. The transducer may be located at almost any convenient site on the body. In contrast, the transmitted light technique requires that the transducer be placed on a site where it can easily straddle a web of flesh.

Several methods have been proposed that use the motion or force that a pulsating artery imparts to the skin as an indication of blood flow. When transmitted to the skin, however, any physical changes imparted by the vascular system are extremely small compared to motion produced by normal activity. Thus, such systems are extremely sensitive to motion artifacts.

BLOOD PRESSURE MONITORING

Blood pressure may be monitored by partially or completely automating the occlusive procedure. The occlusive device is pressurized rapidly to a level above any anticipated systolic pressure, after which the pressure is gradually reduced. The initiation and cessation of pulsatile blood flow are detected by the transducer and when combined with a pressure signal from the occluding device, produce an indication of systolic and diastolic blood pressure.

Cyclic-occlusion techniques have several inherent limitations. The long period required to make a single determination of systolic and diastolic pressure obviously makes this technique somewhat less satisfactory than a dynamic measurement. The major disadvantage, however, is that the cyclic-occlusive phenomena produces considerable discomfort when used continuously on a major artery. If used on a minor artery or arteriole, continuous measurements may be possible, but the inherent accuracy of measurement on the peripheral circulation system is limited. All the influences related to the change of peripheral circulatory resistance, such as temperature, position and the autonomic nervous system, present complications in the measuring problem and may profoundly influence the displayed values of arterial blood pressure.

NON-OCCLUSIVE INDIRECT METHODS

Several methods of indirect non-occlusive measurement of blood pressure have been proposed, but the transducer remains the difficult area of development. At present, the most promising method appears to be the direct force-balance probe which is placed against the arterial wall (or the tissue directly above it). The transducer is responsive to the arterial pressure wave and can display the dynamic waveform, but there are still many problems associated with this method. The exact placement of the transducer over the arterial wall and the maintenance of this position is the major obstacle. This is true of all of the probe balance systems presently under investigation.

Pulse wave velocity has been advocated as an indirect measure of blood pressure, but many investigators strongly believe that the reliability of this technique is questionable.

PULSE RATE

As blood leaves the heart under high pressure, some of its flow energy is expended in distending the elastic walls of the large arteries. The recoil of these arteries then forces the blood through the system after ventricular systole. This distension and recoil is responsible for the pluse wave which can be felt in any artery. A pulse occurs with every systole; therefore, the pulse rate can be measured to determine heart rate.

A transducer may be placed over any artery to pick up the pulse. The most common position is on the wrist where the radial artery runs just below the skin. Pulse rate or heart rate also may be measured by using electrocardiographic leads to pick up cardiac muscle potential. In this case, the potential picked up by the leads is passed through a filter to eliminate high frequency electromyographic potentials. The resulting wave is clipped so that only the peak of the ventricular systole potential remains, and this information is amplified and fed into a counter (cardiotachometer) to record the heart rate.

Gross body movement and muscular activity create random signals that interfere with pulse rate measurements at the wrist or at the chest. All types of instrumentation for measuring pulse rate require filters to eliminate these random signals. In addition, there are other problems resulting from the use of electrocardiographic leads to record pulse rate which are similar to those described for monitoring the cardiac cycle.

CARDIAC ACTIVITY

Cardiac activity is commonly monitored by the (1) electric potentials stimulating the contracting heart muscles (electrocardiography), (2) small movements produced in various parts of the body under the influence of displacement of the heart and blood (ballistocardiography, vibocardiography, etc.), or (3) heart sounds obtained by intracardiac catheterization or by acoustic pickup with a chest microphone (phonocardiography).

ELECTROCARDIOGRAPHY

The activities of the cardiac muscles, as previously noted are initiated by electrical changes. These potential changes are transmitted to the surface of the body where they may be recorded and correlated with heart action. Since it is important for standardization purposes that potentials be read from the same places each time, and

since the limbs are the only locations that are equipotential over a large area, three standard combinations of instrument lead connections have been adopted universally. Standard limb lead I measures the potential difference between the right and left arms; lead II measures the potential between the right arm and left leg; and lead III measures the potential between the left arm and left leg.

Electrocardiography has well-established standard values that are given in numerous handbooks. Primarily, the electrocardiogram permits the monitoring of the electrical signals which control the heart rate and rhythm. The frequency of ventricular systole indicates the heart rate. Also, the presence of fibrillation (and premature atrial contractions), tachycardia, heart block and hypoxia can be detected from the EKG.

Since the peak voltage appearing in an electrocardiograph signal using standard electrode arrangements is approximately 2 millivolts, the signal must be amplified considerably, and the amplifiers and recording equipment must be selected carefully to avoid introducing excessive artifacts. The electrodes must not be placed over large muscle masses where they can detect electromyographic potentials. In addition, they must be attached to the body firmly to prevent the skin from moving beneath the electrodes. Artifacts are introduced through impedance changes resulting from changes in galvanic skin reflexes, but little can be done about these except to try to avoid locations where there are numerous sweat glands, and to recognize the artifacts when they appear in the record.

BALLISTOCARDIOGRAPHY

Ballistocardiography is the measurement of the total body motions produced in response to the pumping actions of the circulatory system. The measurement of this parameter has evolved along two basic lines. In the first technique, ultra-low frequency devices attempt to support the body in the direction of interest with a spring-damping system which has a natural frequency much less than the exciting frequency of the cardiovascular activity. A second technique uses a high frequency suspension system and attempts to measure forces without motion. This technique allows the natural resilience of the body to play an important role.

Despite practical difficulties with equipment and artifacts, ballistocardiography is an impressive prognostic tool. The diagnosis of coronary deficiencies is claimed to be practical, but the real value to date has proven to be in the area of qualitatively evaluating the myocardium.

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APEXCARDIOGRAPHY

Apexcardiography is the measurement of the displacements of the precordial area immediately over the apex of the heart. These low frequency displacements of 0.1 to 20 cps indicate information relative to certain anatomic factors in the same manner as manual palpation of the pericardium but with greatly extended sensitivity. Atrial and ventricular hypertrophy is made evident, and certain valvular malfunctions can be ascertained.

VIBROCARDIOGRAPHY

Vibrocardiography is the measurement of the acceleration produced at the chest wall by the pumping motion of the myocardium. This technique is also known as the precardial ballistocardiogram, stethogram, mechanogram and kinetogram. The vibrocardiogram can be obtained by differentiating the apexcardiogram twice (and vice versa) if comparable frequency response transducers are used. The information is essentially the same, but the acceleration display delineates certain periods of the cycle more clearly. The duration of the isometric contraction and the ejection phase can be accurately measured, and it is believed that these two parameters are valuable in estimating the strength of the heart.

The biggest single problem confronting this and related techniques discussed above is that of attaining general acceptance as valid diagnostic and prognostic information. Much of this difficulty is caused by the lack of a uniform technique and instrumentation. Noise and spurious signals have also been a serious problem. Generally speaking, the major limitation involved with this technique is physiologic and anatomic correspondence. The cardiovascular system is extremely complex and its external manifestations present investigators with a large number of unexplained physiological phenomena.

PHONOCARDIOGRAPHY

Phonocardiography is an objective method of graphically presenting the sound vibrations produced by the action of the heart. It differs from vibrocardiography only in the frequency range of interest. Cardiac auscultation is one of the classic diagnostic methods obligatory in the examination of a patient; it usually yields the most complete presentation of the dynamics of cardiovascular activity and its disorders. However, the subjective character of auscultation and the limitations of the human ear in an analysis of time relationships eventually led to phonocardiography as a more objective method of presenting heart sounds. The normal phonocardiogram presents the

change of sound pressure with time, although a spectrum analysis presentation is also used.

BLOOD FLOW RATE

Measurement of blood flow rate is important for detecting changes in the internal resistance of blood vessels as well as for diagnosing circulatory ailments. The flow of blood may be monitored directly by electromagnetic and sonic flow meters. Electromagnetic flow meters employ an electromagnetic field in which a blood vessel is placed. The flow of the conductive fluid (blood) through this magnetic field generates a potential difference across the vessel which can be directly or indirectly measured.

Ultrasonic blood flow meter techniques involve signal injection into an artery and downstream detection of the transfer of this signal which is modified by blood flow. Systems utilizing this technique are troubled by coupling problems at the input and output sites, artifacts, and critical placements of the transducers.

Plethysmography offers the advantage that the veins or vessels need not be exposed to be monitored. With impedance plethysmographic techniques, the change in the volume of body tissues is used to indicate the quantity of blood they contain. A low voltage, radio-frequency signal is passed through the subject's finger or some other portion of the body. The received signal indicates the rhythmical variations in electrical impedance resulting from pulsatile volume changes (and consequently heart beat). This impedance curve may be correlated with cardiac output, or the information may be fed into a differentiating network to yield the relative change in the velocity throughout the cardiac cycle in a given pulse region. This technique is generally considered "delicate" and difficult to standardize.

Blood flow rate also may be monitorized by plethysmographic methods using strain-type gages. A strain gage is connected to a strap encircling the subject's finger, arm or calf to measure the girth of the limb. An occluding cuff is provided below the gage to occlude arterial flow (except on the finger), while another cuff above the gage (on the heart side) occludes venous flow. The change in girth may be calibrated to record flow rate. This type of device could be integrated with the occluding cuff used for determining blood pressure, thereby reducing the discomfort to the subject being monitored.

OXYGEN SATURATION OF BLOOD

The oxygen saturation of the blood may be determined by measuring the percentage of hemoglobin in the blood in oxygenated form with a photoelectric photometer. Oxygenated and reduced hemoglobin absorb light of wavelengths in the region of 640 millimicrons (red)

quite differently, while light of 800 millimicrons wavelength is absorbed equally by both forms of hemoglobin. A device can be constructed, therefore, using a photocell for each wavelength (640 and 800 millimicrons). The light of each wavelength is transmitted through a thin section of the body, such as the projecting part of the external ear, and is detected by the photocells. The difference between the readings at each wavelength is a function of the oxygen saturation of the blood.

To correct for the ear tissue interposed in the optical path of the device, a pressure device (mechanical or pneumatic) can be used to force blood from the ear so that the light absorption of the bloodless tissue can be measured. The light absorption of the blood alone would be the difference between the readings with the ear occluded and with the ear open to circulation. This technique is subject to artifacts from acceleration forces and vibration that affect equipment performance.

CHAPTER 3

NASA Technological Advances

NASA has supported a variety of in-house and industrial programs to develop physiological monitoring systems to be used in the space program. This section will briefly review the major technological advances most applicable to patient monitoring. The status of these developments is evaluated in terms of the required performance, and the remaining development or adaptation is identified.

Our review is limited to those areas in which major technological advances were achieved through a computer search of NASA unclassified, unlimited distribution documents. Briefly, these include the indirect measurement of blood pressure, new EKG electrode techniques, and vibrocardiography. The use of an electrical impedence pneumograph to monitor respiratory rate and volume appears to be a significant advance, but sufficient evidence was not available to clearly identify NASA's role in the development or adaptation of this device.

BLOOD PRESSURE

Research and development in blood pressure measurement has proceeded in several directions. An automated sphygmomanometer system for periodic blood pressure measurement was developed and used in the flight program. Concurrently, a major effort was carried on to develop an indirect non-occlusive blood pressure monitoring technique that could be used continuously with little or no inconvenience to the subject. However, because of a decision not to monitor blood pressure on Apollo flights, some promising devices and techniques were only partially developed or tested. Many of these show considerable promise for clinical use.

AUTO-SPHYGMOMANOMETER [2, 14]

On Mercury and Gemini flights, an automated sphygmomanometer system has been used that AiResearch developed under contract to NASA. It is based on the same principle used in clinical sphygmomanometry. An inflatable occluding cuff on the left arm is inflated to a pressure in excess of the maximum expected value of systolic pressure. As the pressure gradually decreases, a microphone under

the lower half of the cuff over the brachial artery listens for the Korotkoff sounds indicative of pulsatile blood flow. The signal from the microphone is amplified and mixed with a signal from a pressure transducer which transmits the cuff pressure. In order to determine the systolic and diastolic pressure it is necessary to identify the points of inception and cessation of the microphone signal on the cuff pressure signal.

As originally conceived, the blood pressure measuring system (BPMS) would be initiated from a tracking station through the command receiver, by an automatic sequencing device on board, or by the pilot. The automatic system included special safety circuits to dump the cuff pressure if the cuff stayed above 60 mm Hg for more than 2 minutes. This feature provided for a situation in which the pilot was unconscious and the automatic system failed to bleed off the cuff pressure. The cuff pressure in the automatic system was decreased in a linear manner from 220 mm Hg to 60 mm Hg by a special pressure regulator in which the reference spring tension was varied by a motor-driven cam. The pneumatic system consisted of an oxygen storage flask, solenoid fill valve, motor-driven regulator, dump solenoid valve, cuff pressure transducer and suit reference manifold.

When the preliminary system was tested on astronauts and other flight personnel it became evident that the standard 5-inch clinical cuff was unsatisfactory because of its stiffness, bulk, and restriction to arm movement. A new cuff (Figure 1) was devised by NASA which was acceptable on all points and is almost unnoticeable when not inflated. Tests were performed to compare the new cuff with the standard cuff and the resulting data were identical. It is believed

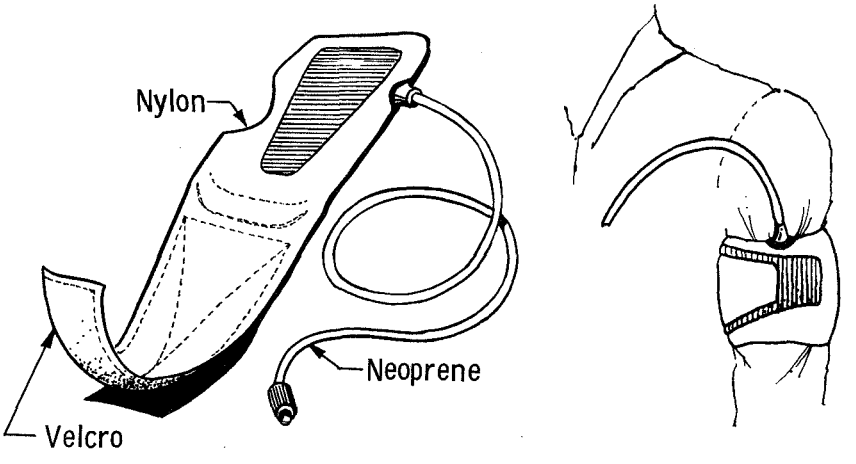

FIGURE 1.—Mercury Blood Pressure Cuff.

that the new cuff type can be used wherever comfort, light weight, ease of application and unrestricted arm motion are desired.

If the microphone signal is filtered so that only frequencies between 32 and 40 cps are used, the various artifacts due to movements and ambient noise level are greatly attenuated, while the component that allows the discrimination of the systolic and diastolic points is passed. A specially damped, piezoelectric microphone was developed for flight use. The instrument is about 3.5 cm in diameter and 0.5 cm thick and is so constructed that sensitivity to ambient noise is greatly reduced. The microphone signal leaves the suit through the bioconnector and enters the amplifier in the blood-pressure unit. The BPMS amplifier consists of a shielded preamplifier and two high-gain amplifiers which determine the response characteristics. Each amplifier is designed to have greatly attenuated response outside the 32 to 40 cps band by means of R–C filtering circuits in each feedback loop. The amplifier output is gated so that unless a signal of sufficient amplitude is present there is no output signal, and this gating results in a marked reduction in the output noise level for improved readability of the signal.

The cuff pressure is measured by a potentiometer-type transducer powered by two mercury batteries to give the zero-centered +1.5 volt output necessary for telemetering. The signal from the pressure transducer passes through a miniature transformer where it is mixed with the output from the microphone and then on to the output clipping circuits that protect the telemetry system from excessive voltages that can cause cross-channel interference.

To compare this method with direct arterial measurement, a special centrifuge unit was fabricated and installed on the human centrifuge at the University of Southern California (USC). Then a series of tests was performed by personnel from USC, NASA, McDonnell, and AiResearch. Subjects equipped with the blood pressure measuring system on the right arm and an arterial catheter on the left arm were tested at various acceleration levels. Spot checks were also made with a clinical cuff and stethoscope. The results showed that at 1 g the BPMS read about 5 mm lower on systole and about 5 mm higher on diastole compared with the direct arterial readings.

There was an increased scatter in the points as acceleration increased which is thought to have been partly due to the "eyeballs down" position of the subject causing a pooling of blood in the lower arm. Comparison of the data from the BPMS with clinical and arterial tests can be summarized as follows: The BPMS is more accurate than the clinical method when both are compared with the direct arterial measurements, and the BPMS readings compared with the clinical readings

are higher on systole and lower on diastole, a fact which is probably due to the increase in sensitivity of the microphone over the stethoscope. Problems in spacecraft integration later required the elimination of the gas pressure source, regulator, and motor programmer and the installation of a hand-pumped inflation system with a simple orifice to release cuff pressure. Subsequent flight systems provided a gas pressure source and a simple switch actuation to initiate the cycle.

DIRECT FORCE BALANCE PROBE [3, 4, 5]

The direct force concept of arterial blood pressure measurement originated at the Stanford Research Center under NASA funded research studies. The objective of this research was to investigate techniques for the continuous monitoring of arterial blood pressure by external means. It was required that the transducer be designed so as not to encumber the subject and not itself affect the pressure being measured.

Initial work was directed toward measurement of superficial effects of arterial distention. Measurements were conducted in an effort to relate skin displacement above an artery to blood pressure causing arterial distention. Several skin deflection transducers were designed and constructed that measured the difference between the skin elevation directly over the artery and the skin elevation adjacent to the artery, and a novel method of applying a constant force to hold a transducer against the skin was devised. These techniques resulted in a reasonably stable measuring system that would respond to changes of skin elevation.

During the course of the project, however, it was determined that skin displacement effects could not be related to blood pressure to the exclusion of other physiological influences such as skin tension and muscle tone. For example, certain drugs for the reduction of blood pressure have an effect on the patient's tissue tone such that arterial distention actual increases. The displacement type transducer would then measure an increase instead of a decrease in blood pressure.

During the Stanford research, an alternate concept of a direct force type of measurement evolved. This technique involves restraint of the arterial deflection and simultaneous measurement of the force required to provide the restraint. This effectively immunizes the transducer against the effects of variations and non-linearities in skin and tissue elasticity by reducing the skin deflection to a negligible value.

Transducer Design and Construction

To obtain a more accurate description of the nature of this blood pressure measuring system, a mathematical model of the system

characteristics was used. This model was based on the assumption that the deflections involved are so small that non-linearities are insignificant, and therefore compressible and extensible tissues are represented as linear springs. The artery is assumed to rest on a firm base, to have elastic walls, and to be surrounded by uniform tissue. The transducer is assumed to have side structures to allow it to rest on the skin, and a center structure that responds to arterial pressure.

Design of the direct force measuring transducer was based on the requirements resulting from the consideration of this mathematical model. Since the basic assumptions that determine the validity of this model demand that the deflections of the skin surface and artery be small to avoid non-linearities, it is essential that the transducer spring constant be much greater than the effective spring constant which normally determines arterial deflection. An additional requirement that must be satisfied for the practical utilization of this technique is that the arterial rider diameter be somewhat smaller than the artery to provide assurance that it can be easily positioned entirely over the artery.

Previous measurements with the deflection transducer had revealed the unrestrained motion of the skin surface over the temporal artery to be approximately 120 micro-inches with a pulse pressure of 40 mm Hg. To obtain a true force measurement, the transducer spring constant was made about ten times as great, producing a resultant deflection on the order of 12 micro-inches.

The sensing element used in the first transducer was a semi-conductor strain gage with a gage factor of 110. The arterial rider was 0.065 inches wide and 0.250 inches long, with a resulting rider area of 0.0156 square inches. The arterial pulse pressure of 40 mm Hg. (0.77 psi) produces a rider force of 0.0121 lb. Thus, to limit arterial deflection to 12 micro-inches, a spring constant of approximately 1000 lb/in. was utilized in the form of a simply supported beam.

The rider dimensions were a compromise between the small size needed to position the rider over an artery and a size sufficiently large to provide adequate force and signal level. Taken together the requirements for a stiff transducer and small rider resulted in quite low levels of strain in the beam. In practice, pulse amplitude levels of 650 microvolts were recorded. Although the resulting signal levels were low, the low-impedance input of the system resulted in negligible electrical noise, so that the signal-to-noise ratio was large.

In testing this gage, it was determined that the rider was still too large to satisfy fully the strictest requirements for using this technique. It was concluded that ideally the arterial rider should be about 0.020 inches in diameter for application to an artery of the temporal group. However, several serious design penalties are en-

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countered as the rider size and contact area are reduced. The most serious consequence is that as a result of the proportionate reduction in blood pressure force, the transducer becomes more sensitive to inertia forces produced by movements of the transducer.

Another problem with this gage was its excessive temperature sensitivity, which was found to be about 2 mv per degree Centigrade, as compared to a pressure sensitivity of 1 mv per 100 mm Hg. It was concluded that temperature sensitivity must be reduced by at least an order of magnitude.

Continued development resulted in an improved strain gage transducer which displayed greater sensitivity and linearity, and greatly decreased temperature sensitivity. This transducer used a 0.030 by 0.125 inch rider and was designed for use on the radial artery. It used a double cantilever beam configuration (Figure 2).

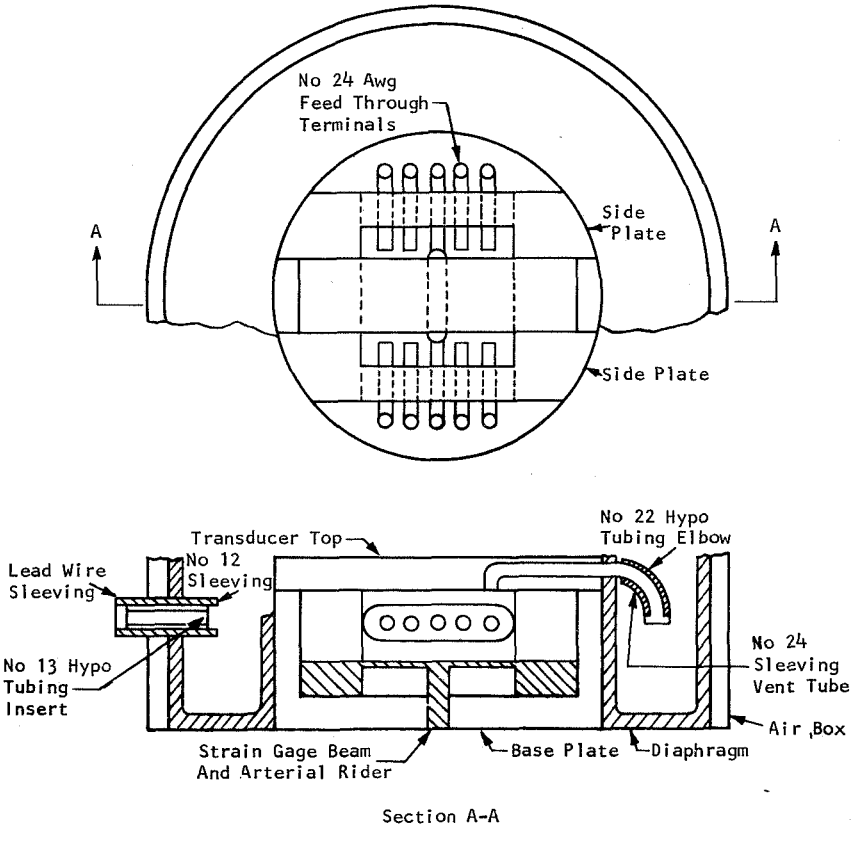

FIGURE 2.—Direct Force Strain Gage Transducer.

The general problem of measuring a small force with a near-zero displacement has been solved in other applications through the use of a feedback force-balance system. This has an inherent advantage in that the basic position sensor need not be a linear element, but need only be sensitive to position and possess an inherently stable zero or reference position. One form of this device, using a Hall-effect transducer was constructed as a laboratory bench model. This device displayed the basic sensitivity and stability required, but the construction of a working blood pressure transducer of the size desired would have required much more development work.

Still further work in the design of a transducer for the temporal artery resulted in a diaphram-suspension of differential-transformer design with a 0.020 inch rider diameter (Figure 3). The major advantages of this design over the previous strain gage models is that it permits greatly reduced overall size and acceleration sensitivity. Reduced acceleration response was achieved by using a minimum mass arterial rider and suspending the differential transformer coil, which then acted to compensate for inertia forces.

Two models of differential transformers were constructed. The first of these had a relatively large commercially available transformer, but was useful in validating the operational concept of the device. With this transducer it was possible to obtain calibrated pulse recordings from the temporal artery. A miniature transducer specially con-

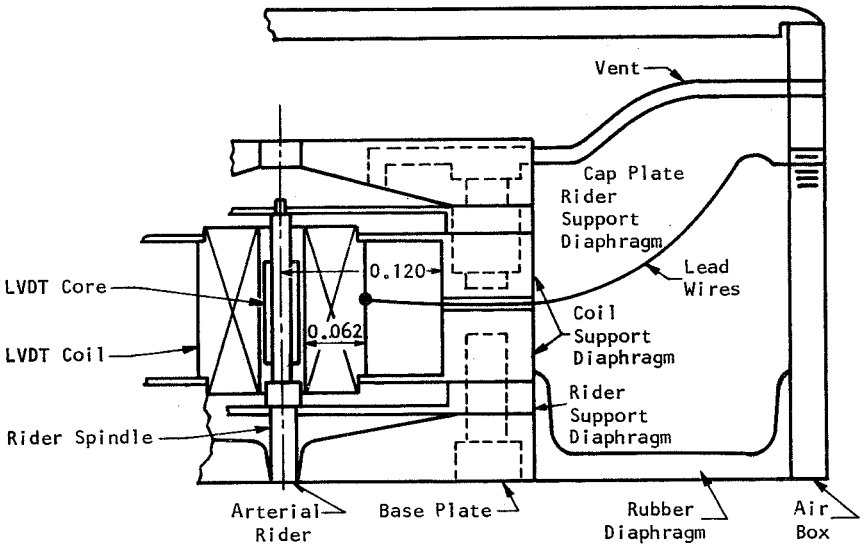

FIGURE 3.—Direct Force Differential Transformer Transducer.

structed with an ⅛-inch diameter x ⅛-inch high coil performed similarly, but presented three major areas of difficulty:

1) A zero-level adjustment was not provided for the core. Proper null settling of the core is necessary to permit higher amplifier gain without saturation and higher excitation frequencies with a concommitant increase in transformer sensitivity.
2) The excitation voltage must be limited to low voltage RMS.
3) The low impedance of transformer increases sensitivity to variations in cable resistance.

Calibration

One of the major advantages of the direct force principle of blood pressure measurement is that ideally, absolute calibration should be possible. Calibration could be performed on the instrument prior to use, and be independent of the individual or location. The two requirements on the measuring device in order to achieve absolute calibration are:

1) The artery surface below the transducer must be flattened,
2) The flattened area of the artery must cover the entire measuring surface of the transducer.

Under these conditions the transducer can be calibrated by means of an "artificial artery." Present transducers, however, do not appear to be able to produce proper calibration reliably in this manner. This inability to obtain absolute calibration is a difficulty shared by all presently available externally applied non-occlusive blood pressure measurement systems. The direct force system is considered to be the one concept with which it is at least theoretically possible to achieve an absolute calibration, and which has been shown under actual conditions to agree with such a calibration within the accuracy of the sphygmomanometer used for comparison.

Problem Areas

Prototype transducers based upon the direct force principle have demonstrated the validity of the technique, and displayed adequate accuracy, sensitivity, response and freedom from electrical noise and artifacts. The major problem is the proper positioning of the transducer over an artery and the maintenance of this position.

A manual technique of moving the transducer and searching for the maximum pulse amplitude appears to work, but it will not give a subsequent indication of improper positioning if the transducer is accidentally moved. Studies were conducted to determine the feasibility of various methods of sensing and indicating proper position of the transducer over the artery. A method using a null signal from

piezoelectric pressure sensitive crystals appears to hold promise, but was never incorporated into a working model.[5]

Even if efforts at initial positioning are successful, maintaining proper position is apparently very critical. Thus an effective mounting and re-locating scheme must be developed that allows the establishment and maintenance of proper transducer position.

EAR PULSE PRESSURE TRANSDUCER[6, 16]

Another method of indirect blood pressure measurement studied under contract to NASA was an ear-located transducer which uses the cyclic-occlusive method. The primary advantage of this transducer location is that continuous cyclic-occlusion of the ear pina can be performed with no apparent discomfort to the subject. An inherent disadvantage is that it deals with peripheral circulation, and thus may be susceptible to a variety of influences which may limit its inherent accuracy.

Description

The ear transducer developed for NASA by Corbin-Farnsworth, Inc., incorporates an annular-shaped occlusion bellows and is designed for installation on the ear pina. Systolic and diastolic pressure are detected by means of a pulsatile blood flow detector which measures variations in opacity of the ear capillary bed to infrared light. The principal advantage of this light transmission technique of detecing blood flow is its inherent insensitivity to motion and noise artifacts. Conversely, the main disadvantage is that it must be located at a body site where the transducer can look through a web of flesh. Previous work at the Mayo Clinic established the ear pina as the most promising measurement site.

Initial experiments with a non-occlusive opacity transducer indicated that the pulse wave information obtained was purely qualitative and could not be calibrated to measure arterial blood pressure. Subsequent experiments utilized a similar configuration but with the addition of the pneumatically operated translucent membrane stretched over the light source. This membrane design did not work well for diastolic pressure determination, and the annular shaped occluding bellows was finally arrived at as the most acceptable design (Figure 4).

The inlet side of this bellows is connected to a hydraulic system. A second bellows at the other end of the hydraulic line is attached to the plunger of a solenoid. Pressure at the occluding ear piece is increased or decreased by varying the dc current through the solenoid coil. The coil is driven by a transistor power amplifier. The frequency response of the hydraulic-electrical system was from 0 to 10 cps, with some response up to 30 cps.

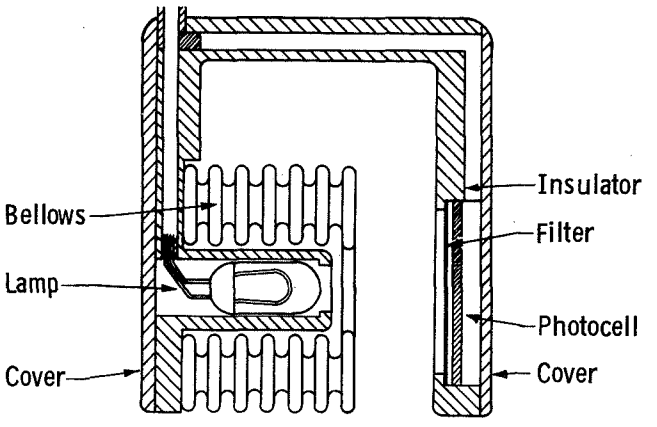

FIGURE 4.—Ear Opacity Transducer.

The light source used in the transducer is a "grain of wheat" lamp mounted in the center of the annular occluding bellows. Environmental light artifacts were successfully eliminated by the use of an infrared filter and an infrared sensitive photocell.

Test Results

In a previous study of 17 subjects E. H. Wood made simultaneous blood pressure determinators using auscultation of the brachial artery, ear opacity pulse pressure determinations, and a direct indwelling catheter in the radial artery. His results [7] showed that pulse pressure determinations at the ear were reliable and also more accurate than the auscultatory method. American Heart Association Studies have shown that determinations by sphygmomanometry typically produce systolic pressures that are a minimum of 8 mm Hg too low and diastolic pressures that average 8 mm Hg too high. Test results with the Corbin-Farnsworth ear transducers on four subjects produced consistent results in which systolic pressure was typically 15 mm higher and diastolic pressures 5 mm Hg lower than sphygmomanometry. Thus the measurements with the ear transducer should correlate quite well with a direct indwelling catheter.

In the above tests little or no discomfort was noted during occlusion of the capillaries in the ear pina. In fact, it was difficult for the subject to know when pressure was being applied. One subject wore the transducer for more than an hour with partial occlusion and suffered no discomfort. Thus the ear transducer appears to be applicable to continuous blood pressure monitoring.

Further Development

The development of this transducer appears to be technically complete. Further experimentation is needed to evaluate the accuracy of the ear pulse pressure under various patient conditions and its susceptibility to artifacts. The hydraulic pressurization system has a fast response time and its developers have suggested that a servo system might be utilized to make the occlusion pressure follow the waveshape of arterial blood pressure. Such a servo system would permit a complete indication of blood pressure waveshape rather than simply the systolic and diastolic pressure points.

VIBROCARDIOGRAPHY

NASA has supported the development of externally derived cardiovascular diagnostic procedures with grants to the Institute for Medical Research at Cedars of Lebanon Hospital.[8] The technique is based upon sensing the external manifestation of the forces of cardiovascular dynamics, or more specifically, the local relative motion of the chest wall due to movements of the heart itself. The technique is variously known as apexcardiography, kinetocardiography, vibrocardiography and phonocardiography, depending primarily upon the frequency range and choice of motion derivative to be displayed.

Vibrocardiography, which is the measurement of precordial accelerations, has been shown to have a high degree of correlation with hemodynamic events. It has been found that measurement of the phases of isometric contraction, ejection, systole and diastole can be obtained from the precordial vibration tracing with an accuracy as good as that realized with direct cardiac catheterization. Further, comparisons of these phase intervals under stress procedures in human and animal subjects show significant changes which serve to differentiate the normal from the cardiac injured subject. These changes correlate well with other physiological parameters during maximum stress.

A further means of evaluation is based on the measurement of cardiac vibrational energy level during specific phases of the cardiac cycle. These measurements have shown consistent changes during stress and may well provide a means of determining cardiac mechanical force. Recent experimentation has also shown that the vibrocardiogram will provide a method of measuring relative stroke volume, thereby yielding a measurement of cardiac output. These findings have been compared with known methods of cardiac output and heart force determinations and, in preliminary experiments, have shown excellent correlation.

To implement clinical research in vibrocardiography, it has been necessary to develop transducers and instrumentation for its measure-

ment. In line with the overall objective of this report, this technical review will be limited to a description of the hardware that has been currently developed and utilized in NASA supported research work.

VIBRATION RECORDING TRANSDUCERS

Extensive study and evaluation of various types of vibration recording transducers has resulted in a delineation of the desirable qualities of these transducers with respect to the particular application of precordial vibration recording. These qualities include (1) a displacement flat response from at least 2 cps to 2000 cps to permit the recording of the total energy spectrum of the heart in a form (displacement) which has been found to be most valuable; (2) a wide dynamic range such that the lower amplitude high frequencies as well as the higher energy low frequencies are reproduced; and (3) lightweight and minimal dimensions to permit usage on human subjects during stress procedures.

Since none of the available transducers fulfilled these needs, further development of an "ideal" transducer was necessitated. To this end, engineers of Ling Temco Vought, Inc., working with members of the staff of the Institute for Medical Research at Cedars of Lebanon Hospital have developed a transducer with the desired specifications. Two models have been used thus far in experiments. These units are transistorized for minimal size, have a frequency response of 1.6 to 3000 cps (± 3 db) and a dynamic range of 90 db. Both of these units have been used in experiments with gratifying results.

A third model of the LTV transducer was announced during the preparation of the referenced report. The new unit, designated LTV–3, incorporates a number of improvements. Following are several features of the new microphone, which is shown in Figure 5:

- The height has been reduced to $\frac{3}{4}''$, plus pad. The microphone projects $\frac{3}{32}''$ from the base plate and the tentative coupling pad is $\frac{1}{4}''$ thick silicone rubber.
- The case is made of chrome plated brass with an anodized aluminum cover. The microphone diaphragm is now stainless steel and is additionally protected with Mylar as before.
- To avoid overloading, the sensitivity has been reduced approximately 15 db. The noise level remains low as before.
- An emitter follower has been incorporated in the unit which provides a low impedance, 600 ohm output thus reducing cable noise and hum pickup. The output voltage is not affected by this addition.
- The low frequency cut-off is adjustable within limits and can be readily modified for acoustic equalization.
- The battery box (shown in the bottom figure) has been enlarged for increased battery life (four flashlight cells are used) and a meter incorporated which shows the battery condition and indicates when

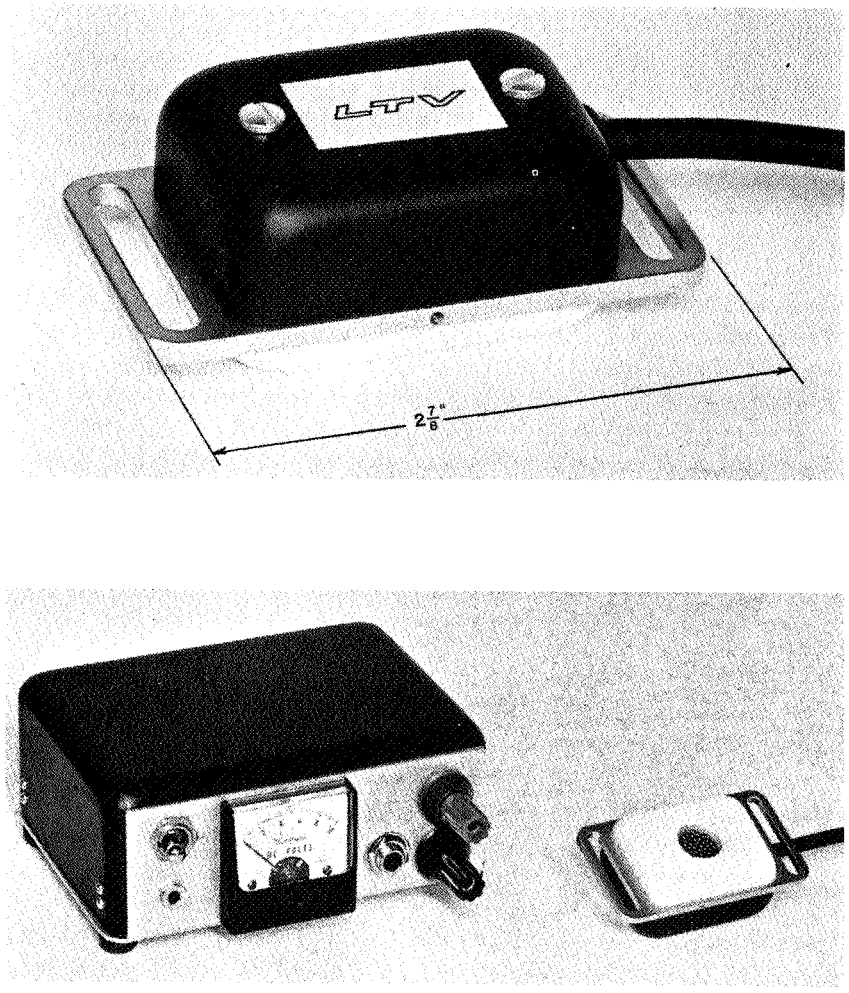

FIGURE 5.—Vibrocardiographic Transducer.

the unit is switched on. A switch, GR, BNC, and phono outputs are provided.

- A terminal board is provided in the battery case which can incorporate a preamplifier of greater output voltage if required, or electrical equalization if it is desired to reduce the low frequency amplification in order to better fit the dynamic range of typical tape recorders.
- The unit can be completely filled with a silicone potting compound to render it impervious to moisture, vibration and similar environmental influences. Also, the diaphragm spacing in the microphone has been doubled to provide greater moisture resistance as well as to control the sensitivity.

INSTRUMENTATION

Instrumentation for the instantaneous determination of cardiac vibrational energy has been completed by modification of a Ballantine RMS voltmeter. This unit has been adapted to determine the energy level of the vibrocardiogram simultaneous with its recording and will be used in both human and animal experimentation.

In addition, circuitry has been developed which will allow the measurement of vibrational energy during the isometric contraction and ejection phase of systole. This equipment provides wave recognition circuitry for the location of the significant virbrocardiographic waves and gating circuitry which permits measurement and display of both energy levels and time between any of these points.

ELECTRODES

FLUID ELECTRODE

Despite half a century of clinical use of the electrocardiogram, a great deal of development was necessary to produce an EKG electrode acceptable for flight use. Essentially the problem is identical to that of recording the EKG during exertion. Many types of electrodes were available for use on a working subject, but they were not of sufficiently low resistance. In addition, most of these systems use standard electrode paste or an electrolyte which is hypertonic. After 24 hours of contact, the hypertonic nature of the electrode paste causes considerable irritation to the skin. As the paste dries it loses conductivity and effectiveness.

After a number of trials with various experimental models, a "fluid electrode" was finally developed with the desired characteristics. The basic principle of this approach is to glue firmly to the skin a nonconducting cup containing a non-irritating electrode paste and to use this paste as the lead off the skin. The potential is picked up from the paste by a shielded wire attached to a metal electrode buried in the paste but suspended in the cup so as not to touch the skin. The resistance of such electrodes stays constant if the paste is hygroscopic and the cup is well sealed to prevent drying out.

PROJECT MERCURY ELECTRODE TECHNIQUES [9, 10]

The first problem was to find an electrolyte that would remain moist and be non-irritating for the duration of a mission. After considerable testing, an electrolyte was developed for the Mercury Program that consisted of 3.0 grams of calcium chloride in 10 cc of water with 15 grams of bentonite (aluminum silicate powder) to bring it to a paste. This electrolyte produced no irritation after 48 hours of use.

The EKG electrodes consisted of rings composed of silicone rubber, constructed to support a disk of 40-mesh stainless steel screen, 30 mm in diameter and approximately 2 mm above the skin. The center conductor of a miniature-type coaxial cable is brought through a strain-relieving projection in the rubber ring and soldered to the screen. A piece of thermally shrinking plastic tubing seals the cable shield at the entrance into the ring to keep out moisture.

Before the electrode is applied to the washed and shaved skin, a coating of elastoplast adhesive is put on the bottom surface of the electrode ring and allowed to dry. The ring cavity is then filled with electrolyte and applied. After checking the ring cavity and eliminating voids, the assembly is sealed with tape and a 4-inch square of moleskin is placed over the entire sensor area.

This electrode appeared to give less background noise than the standard metal plates used in clinical electrocardiography, and also less baseline shift when the region to which they were attached was actively moved.

GEMINI ELECTRODE TECHNIQUES [11, 13]

Electrodes used on the Gemini flights were modified slightly from those developed for Mercury. The more important changes included the use of silver-silver chloride electrodes and the preparation of a long-term non-irritating electrode paste.

Electrode Construction

The stainless steel mesh used initially because of its corrosion resistance produced considerable motion artifact, probably caused by electrochemical irreversibility. The unprotected compound metal junction of the solder joint was also a source of spurious potentials. The present electrode (Figure 6) is fabricated from a pure silver perforated disk. After applying a coat of epoxy resin to insulate the compound metal junction, the disk is anodized in salt solution to produce a coating of silver chloride.

The electrode housing, injection molded from Dow Corning S–6015–A silicone rubber, is designed to support the electrode disk above the skin in a circular groove. A wide flange facilitates good adhesion to the skin. Electrodes fabricated in this manner may be used repeatedly.

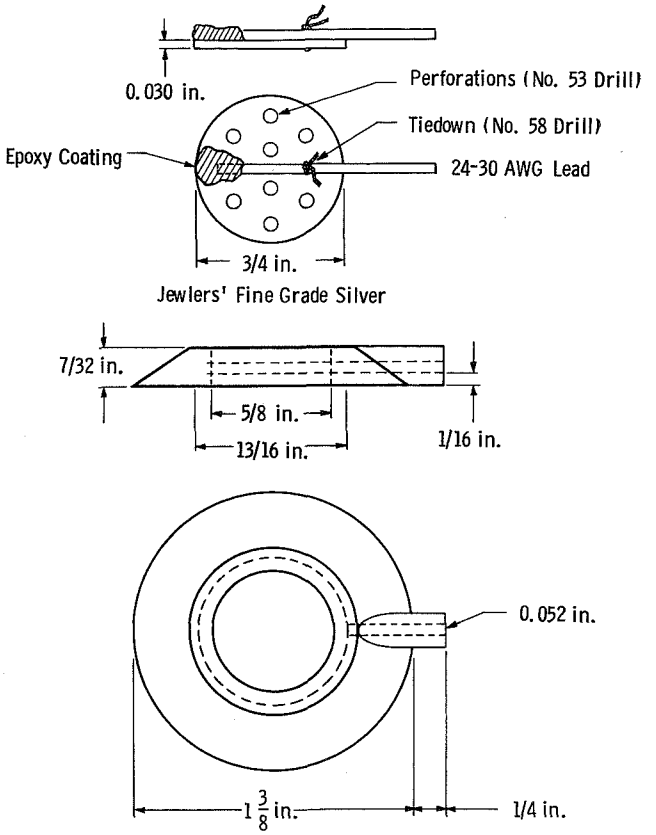

FIGURE 6.—Gemini Electrode Construction.

Electrode Paste

This electrodes may be used with any electrode paste which contains chloride ions. For the repeated long-term applications necessary in the space programs, however, a special non-irritating paste was developed. Standard EKG pastes are irritating for long periods, especially if rubbed in, because the paste contains an abrasive.

An electrode paste with the same ionic content as ten times that of Mammalian Ringer's solution provided a relatively low resistance with minimal skin irritation for periods of one week. This paste contains no abrasive. Details of the formulation of the present electrode paste for EKG and impedance pneumography are presented in Reference 13. The paste is relatively non-irritating, non-sensitizing, and has a long shelf life. This paste must not be used for galvanic skin response, skin resistance, or skin potential measurements since it is intended to reduce skin resistance.

Electrode Application

This electrode can be applied in less than 3 minutes by an experienced technician. A strong non-toxic double-backed tape* is first applied to the flange. The flange side of the electrode is then filled with electrode paste. The skin is lightly swabbed with acetone to remove skin oils, and the electrode firmly applied. The outer compartment of the electrode is then filled to just below the top. A 1-inch square of Mystic† tape is applied to close the opening. A 3-inch square of Micropore‡ tape is then applied to cover the entire electrode. After removing the electrode, the skin is cleansed with Zepharan chloride and an antiseptic skin lotion is applied. In more than 3 year's experience with this procedure, neither irritation nor infection has occurred.

Long-Term Electrode Tests

In addition to numerous short-term tests performed during the development of the electrode system, a series of longer duration tests was carried out. In one of these a group of 21 volunteers, in good health with no history of dermatitis, wore the electrodes for four days (96 hours). The subjects continued their routine jobs, engaged in active sports, and took daily showers. The only skin preparation was a gentle swabbing with acetone to remove skin oils.

Except for an initial high resistance that occurs in the first several hours while the paste and skin reach equilibrium, the mean skin resistance was quite low (less than 25 kilohms) throughout the duration of the test. Upon removal of the electrodes, an examination of the sites revealed no skin irritation under the electrode paste. Some mild irritation was observed under the electrode housing and under the Micropore tape; however, this irritation was believed to be largely due to mechanical irritation, and uncommon in a relatively inactive subject.

SPRAY-ON ELECTRODE [12]

Conventional electrode techniques have disadvantages in many situations. They demand special site preparation, relatively large electrode areas and considerable time to install. To permit routine monitoring of test pilots at the NASA Flight Research Center, Edwards, Calif., a goal of pilot instrumentation and checkout in less than three minutes had to be met. One result of the requirement was the abandonment of conventional electrode techniques for the more quickly applied conductive paint electrode. This electrode is sprayed on and

*Scotch No. 1500 Stomaseal (Colostomy) Tape.
† Mystic Silicone Tape No. 7010.
‡ Scotch Micropore Surgical Tape No. 530.

dries almost instantly. A coat of protective spray is applied to the finished product. The wires leading to the electrode are Teflon-covered copper, approximately the diameter of a hair. An additional advantage of this electrode technique is that it is much more comfortable than conventional electrodes, although of considerably higher impedance.

CHAPTER 4

The Medical Market

The prolongation of human lives is the most significant contribution that aerospace biomedical technology can make to the national economy.

The full benefits of aerospace medical research and development will be realized, however, only if the technology and hardware generated are modified and, where necessary, further developed to satisfy the specific needs of civilian medicine. In many cases, a considerable investment of money and time may be necessary to implement these modifications. To expedite this further development and adaptation by private industry it is of utmost importance to demonstrate, where possible, that such investments are economically justifiable in terms of financial benefits to the potential manufacturer.

The investment required to adapt or further develop aerospace technology and hardware to meet the requirements of civilian medicine is difficult, if not impossible, to predict precisely. It will depend upon the capabilities, previous experience, and financial structure of the particular company involved. In some cases, even with unlimited effort, development problems will not be amenable to practical solution. No attempt is made in this report to quantify or even generalize investment costs. Estimates of this type must be made by the prospective manufacturer.

Estimates of the potential market for specific hardware items are, however, intrinsic to the functional capabilities of that hardware, and not subject to extreme manufacturer-dependent variation. The purpose of this chapter, therefore, is to explore the nature of the civilian medical market, and to develop estimates of the potential dollar volume market associated with the principal hardware items described in the foregoing sections.

COURSE OF DEVELOPMENT

The course of development of medical hardware and its introduction to the market place is considerably different from the normal industrial course. It is important that firms contemplating entrance to the biomedical field be aware of these differences, and the influence they have upon the investment of capital funds in product development.

Acceptance of new developments in the medical field generally follows a pattern which can be separated into three phases. The first is a period of research, development, evaluation on experimental animals, and prototype testing. The second phase involves limited clinical testing and evaluation, usually carried on by only one or two investigating groups; during this period the true clinical value of the technique is determined as it is gradually refined and the results are published in medical journals. In the third phase the technique is gradually introduced into the routine of regular medical practice in several locations. Only after these three phases are successfully completed will the new medical product find its way into general use.

The rate of progression of a medical device through these three phases depends upon the fundamental medical technology upon which the device is based. For rapid progression, the device must be based on technology which is widespread and presently understood by a majority of practicing medical professionals. If the device involves new medical technology, the progression will be slow because of the educational time required to incorporate such technology into general practice.

To illustrate this problem, consider the now common technology of electrocardiography. The first phase was completed in the 1920's, but it was nearly twenty years later that the method found its way into general use. In fact, as recently as 1959, more than 10 percent of the nation's hospitals still had no EKG equipment. These several decades were required to incorporate the basic technology of EKG into the curricula of schools which produced the practitioners versed in the art of electrocardiography and created the demand for instrumentation of this type.

At present there is an immediate market for EKG equipment which is faster, easier, "better" or cheaper because these adjectives have readily apparent meaning to practicing cardiologists. Consequently, the rate of progression through the three development and acceptance phases should be extremely rapid for a clearly superior EKG device.

The medical profession often has been accused of ultra-conservatism in the incorporation of new technology into general practice. The problem is deeper, however, than professional conservatism. In fact, doctors engaged in research are eager to try new techniques and may incorporate new technology very quickly. Unfortunately, the research device represents only a limited market. A company may fail to appreciate the time lag problem if it deals only with groups practicing medicine far ahead of that taught in medical schools. The medical product market, then, must have considerations factored into it relative to the level of medicine generally practiced.

Equipment manufacturers are largely dependent upon the medical profession for carrying out the three phases described above. Independent investment to accomplish this work is rarely required because of the eagerness of medical research groups to explore new techniques. Moreover, the results of clinical work done *within the medical profession* are the only results likely to be accepted promptly by the medical community. A cooperative effort by private industry, the medical community, and often governmental agencies is frequently a rational approach to product development in the biomedical field.

PATIENT MONITORING MARKET NEEDS

Technological advances sponsored and funded by NASA in the area of physiological measurements reflect the differences between aerospace applications and more conventional applications of these measurement techniques. The major needs which characterize an aerospace application are (1) measurement techniques which are remote, continuous or semi-continuous, automated, and of relatively long duration, and (2) measuring equipment of high reliability, small size, weight and power requirements which can operate in an environment of high acceleration and vibration without severely restricting or causing discomfort to the subject.

There are a number of medical applications in which these characteristics offer unique advantages. The most important application is patient monitoring. In many situations the physician is faced with monitoring critically ill persons for protracted periods. For a few hours, as in surgical recovery rooms, standard monitoring methods such as the blood pressure sphygmomanometer, rectal temperature, and observed pulse and respiration rate are perhaps adequate. If the patient requires longer periods of monitoring, however, automated remote measurements become a necessity, both in terms of effectiveness and economics.

Although equipment now available is intended to fill this need, a number of problems remain. These are related primarily to the transducer or sensing system. Present electrode techniques are subject to degradation and require periodic repositioning. Monitoring devices require frequent calibration and considerably restrict the activity and comfort of the subject. Techniques developed for continuous monitoring of subjects during extended space flights are of necessity designed to minimize such problems.

INTENSIVE CARE WARDS

In the last few years, clinical experience has demonstrated the usefulness of an intensive care ward which is predicated upon close observation of the patient and more frequent measurement of vital

physiological, electrical, and biochemical variables. The value of this approach was first proved in surgical recovery rooms, later by medical and surgical intensive care wards, and more recently by the advent of coronary care wards.

It has been estimated that properly functioning coronary care wards could save the lives of 100,000 hospital patients each year.[14] The Committee of Clinical Cardiology of the American Heart Association and the Heart Disease Control Program of the U.S. Public Health Service have recommended that victims of acute myocardial infarction be cared for in electronically equipped coronary care areas for the first few days "since the detection and treatment of potentially lethal cardiac arrhythmias require constant observation and prompt action." About 85 percent of all deaths from this disease take place in the week following the attack.

According to this report, coronary care units seem desirable and practicable in general hospitals, especially those admitting 100 or more cases of acute myocardial infarction each year.

SURGICAL AND POST-OPERATIVE RECOVERY AREAS

Until a few years ago, continuous monitoring of physiological variables in the operating room was limited to the electroencephalogram and the electrocardiogram. At best, these bioelectric potentials reveal only gross malfunctions. More recently, methods of obtaining medical data from the surgical patient have undergone drastic changes, and electronic oscillographs and elaborate data acquisition and display systems have become standard aids in several surgical procedures and are even found in surgical wards. Blood pressure is a parameter of particular importance in surgical procedures and during post-operative recovery since it gives an indirect indication of blood volume and thus blood loss.

A simple automated monitor and alarm system designed specifically for minor operations could be extremely useful in many situations where an anesthesiologist is not needed for other reasons. Such a system could allow the physician to concentrate completely upon his primary work, yet receive early indication of danger. In such applications the complexity and convenience of the equipment must be weighed carefully against the desired information. True fidelity and exact reproduction of electrical waveshapes are not required, which are important factors in cost reduction. Continuous information on the heart's activity is most desirable. Respiration observations are also valuable. Most important, however, would be an automatic alarm which would enable the operating physician and other medical personnel to concentrate upon their specialized functions.

OTHER APPLICATIONS

Another important area of application is diagnostic monitoring. A simple, unencumbering and artifact-free monitoring system would be very useful as a diagnostic tool in individual patient examinations. Presently, a medical examination is restricted to incomplete information while the patient is at rest or at some time after exercise. A wireless transmitter attached to the patient could give a continuous picture of the body's changing physiological responses during all phases of stress—information which has been thus far unobtainable.

Still other important areas of application are medical research and public health. Long-term monitoring of normal and abnormal subjects might result in quantitative descriptions of these abnormalities and aid in diagnosis. Rapid techniques developed for screening astronauts might also be of use in the mass screening of subjects in public health work.

PATIENT MONITORING MARKET POTENTIAL

Approximately 5,600 non-Federal short-term general and other special hospitals account for over 90 percent of all hospital admissions in this country. Federal, psychiatric, tuberculosis and long-term hospitals number about 1,500. Of the short-term hospitals which are of principal interest, about 2,100 hospitals have 100 beds or more. In hospitals of these sizes there are 520,000 beds.

Applications for patient monitoring within these hospitals exist in operating rooms, post operative recovery rooms, intensive care wards and coronary care units.

Almost all intermediate and larger sized hospitals have post-operative recovery facilities, either as separate suites adjoining the operating rooms, or within the intensive care wards. The average length of stay in such facilities is on the order of several hours. The number of operating rooms is typically 1.5–3% of the number of hospital beds. Assuming an average of one monitoring facility per operating room and one for post-operative recovery, one finds a total market potential of approximately 15,000 units in surgical and post-operative recovery areas.

The introduction of intensive care wards to meet the needs of critically ill patients more effectively has proceeded to the point where it is estimated that more than 1,000 hospitals have such units. These are usually on a one-per-hospital basis, and of such a size that about four intensive care beds are provided for each 100 beds in the hospital. Coronary care units are just beginning to be introduced into hospitals to accommodate victims of myocardial infarctions. About 30 of these units are now in use. It is desirable to have them located

in proximity to the intensive care wards so that service personnel may be shared when emergencies arise. A hospital can expect an average of about two coronary cases per year for each regular bed in the hospital. The length of patient stay varies between three and seven days, depending on the practice in the given hospital. If an average stay of five days is taken as typical, then 2.5 coronary care beds are required for each 100 total beds in the hospital. This figure corresponds well with the number found to be adequate in practice. Present practice is that a cardiac monitor is provided for each bed in the unit. In hospitals having 100 beds or more, the saturation potential would be 13,000 coronary care beds.

In order to estimate the number of early installations, the growth history of intensive care units was examined. In the case of coronary care units, consideration was given to the need that hospitals will have for additional space for this new facility adjacent to their intensive care wards. It is estimated in this manner that during the period of most rapid growth, the installation of monitoring units may occur at a rate of 2,500 per year.

In discussing the potential market for any device, it is important to recognize that there may be several alternate devices that compete to satisfy a need. It is necessary to modify overall estimates by the expected participation in this market. The most important factor in determining the extent of participation are the performance and cost of the product. In the following sections, individual products are examined as to their functional performance relative to established needs and their projected selling price to determine annual dollar volume of the potential market.

BLOOD PRESSURE MEASUREMENT

Direct Force Blood Pressure Transducer

The direct force blood pressure measurement system produces a continuous external measurement of arterial blood pressure. Its principal advantages over comparable automated measurement systems are that the full pressure waveform is determined and, since there is no occlusion, monitoring is achieved for prolonged periods without discomfort. The signal obtained is also suitable for registering the pulse rate. The disadvantage is that the initial placement and maintenance of this placement may be a difficult problem that is as yet unresolved.

The needs that such a device can satisfy are in two broad categories: those where the complete blood pressure waveform is desired, and those where pressure levels only are required on a continuous basis. In the first category, present practice would limit the use to medical

research. However, as waveform analysis becomes more thoroughly investigated and more persons become experienced in interpreting the significance of specific waveforms, a potential exists for use of the device as a general diagnostic instrument. The second category, long continuous pressure level measurements, satisfies more established needs. Expected near term applications are in operating rooms for use by anesthesiologists, in post-operative recovery rooms, and in intensive care wards, particularly coronary care units.

Neither the manufactured cost nor the required selling price of the blood pressure monitoring system can be estimated with any certainty now. The manufactured cost depends on the proficiency of the fabricator and also upon the cost of whatever additional parts may be needed to solve the problem of insuring the proper continued positioning of the sensor over the artery. Another unknown variable is associated with the display unit. Standard oscilloscopes may be used. If specially designed, the accuracy and complexity of the display unit would have large effects on cost. A rough estimate at this time is that the sensor could be built for $100 to $200, and that a satisfactory but not elaborate display unit could be made for $200 to $300. Based on the customary factor of two between the manufactured cost and selling price, the hospital price for a sensor-plus-display package could run between $600 and $1,000. These figures are compatible with estimates of the required selling price based on corresponding prices of existing equipment performing a similar function. The demand might be quite elastic above about $1,000, and relatively inelastic at prices much below this figure. In other words, at prices much above $1,000 very few would be sold, and at some price well under $1,000, all who could use the product would buy it, so that any further price reduction would not significantly increase the number sold.

As a diagnostic instrument, a further potential exists, deriving its value from the possibility of showing the blood pressure waveform. If and when it is shown that analysis of these waveforms can produce useful diagnostic information, doctors having particular interest in cardiovascular disease would be expected to acquire the skill necessary to interpret these waveforms. The number so interested has been estimated at 5,000. Selling prices would probably have to be lower than those for the patient monitoring unit since many of the potential customers would be individuals rather than institutions. Required selling price is estimated at $400 to $600 which implies a manufacturing cost of $200 to $300. Some decrease in the sensor unit cost may be possible as compared to the patient monitoring unit because long term positioning is probably not a problem. The output display which is to show waveform probably will remain expensive. A simple oscilloscope might be used. A good many cardiac specialists may already have

oscilloscopes as part of their EKG equipment. In this case, the purchase of an additional display unit would not be required. A manufacturing cost of $100 for the sensor and $100 for the display unit are optimistic but not unreasonable. These figures are consistent with a $400 selling price.

Ear Opacity Blood Pressure Transducer

The ear opacity transducer permits the continuous external measurement of systolic and diastolic pressure. Its outstanding characteristics are the ease and uncritical nature of its application to the person, and the relative lack of discomfort during occlusion which permits semicontinuous, long-term monitoring. Potential disadvantages are associated with questionable accuracy which may occur if extraneous factors are present (certain anesthetics, drugs, possible sensitivity to patient position, etc.). Additional verification is needed to show that peripheral blood pressure measurement is consistently representative of the arterial pressure.

The clearest potential application for this device is a patient monitoring sensor. Measurements could be of the two-point type commonly made (systolic/diastolic), or simply systolic. The extent of this application was discussed previously.

Obtaining pressure waveforms is possible in principle either by using a servo to cause the applied pressure to follow the detected pressure continuously or by selecting points on the waveform from successive cycles. It might be expected that the higher frequency components of the waveform would be difficult to detect in the former instance and that cycle-to-cycle variations would lead to erroneous readings in the latter. Because these modes of operation have yet to be demonstrated, applications for them are not being considered here.

This transducer requires a source of varying pressure for its operation. The transducer output is compared with this source to determine the pressure at which occlusion occurs. Therefore, initial sale of the transducer will be accompanied by sale of the pressure controller and/or source and an electronic comparison and display unit.

At an estimated manufactured cost of $15 to $25 for the transducer, and $85 to $135 for the source-display unit, the total system cost would be $100 to $160. With a factor of two multiplier, the selling price would be $200 to $320. Because these figures are considerably lower than those for the direct-force system, more units are likely to be sold.

Subsequent to clinical evaluation, further development work will be required on the display unit to evolve a practical unit, and additional engineering will be needed to adapt it to production form.

Summary of Markets for Blood Pressure Indicators

The figures developed in the preceding sections are summarized in the table below. It is assumed that a display unit would be sold with each sensor. The two patient monitoring systems might be in competition with each other and with other similar units, so that sales of one would subtract from sales of the other. The direct-force blood pressure diagnostic instrument involves the display and perhaps analysis of the complete pressure waveform.

	Annual Quantity	Selling Price	Annual Market
Direct-force blood pressure patient monitor.	2, 500	$600–$1000	$1.5–2.5 million
Direct-force blood pressure diagnostic instrument.	500	$400–$600	$0.2–0.3 million
Ear occlusion blood pressure patient monitor.	3, 500	$200–$300	$0.7–1.0 million

VIBROCARDIOGRAPHY (VbCG)

The sensor which has been under development is an acceleration-sensitive transducer which produces an electrical output proportional to the mechanical input over a frequency range from a few cycles per second to several thousand cycles per second.

Its use as considered in this discussion is in measuring the mechanical events of the cardiac cycle. It is a natural companion to the electrocardiograph which is responsive to the electrical events of the cardiac cycle. The combination would be expected to give valuable information about the functional characteristics of the normal heart, and in the future to enable various abnormalities to be identified with a superior degree of certainty. Further, the determination would be made with little discomfort for the subject.

Work is currently being done in analyzing and interpreting the signals obtained from the VbCG sensor, as discussed previously. The results obtained to date show good correlation with measurements made in other ways for a number of parameters. Additional work is in progress to complete the clinical research necessary for this method to become accepted as reliable, informative, and practical. Until this work is finished there will be only a research market for equipment in this field.

The cost of the transducer is expected to be comparable to that of existing quality microphones. Prices range from a hundred dollars upward. Equipment for analyzing the phase, frequency and amplitude characteristics of the output signal from the transducer could be fairly expensive. This would be particularly true if a large number of accurate determinations needed to be made, each involving a different

kind of electronic operation. On the other hand, the amount of development work required on the analysis equipment will probably not be extensive because of the very large variety of electronic amplifiers, filters, phase detectors, etc., already developed and on the market.

The application progress in the field of vibrocardiography is expected to be similar to that of electrocardiography: a period of clinical research followed by trial use in a limited number of practical cases, and then upon demonstration of value in practice, a gradual acceptance as a standard technique. Also, as in EKG, the sensor may be sold separately from the analysis and display equipment.

The vibrocardiograph has a very sizable potential market, probably comparable to that of the electrocardiograph. However, because the vibrocardiogram is presently a research tool, the market for such a device in the predictable future is very small, and no attempt to predict the dollar volume of this market has been made.

Biopotential Electrodes

The functional improvements achieved by NASA developments over conventional electrodes are in the increased time period during which these new electrodes may be used, and the insensitivity to movement by the subject. A possible disadvantage is that the procedure of applying these electrodes is not as simple and quick as that for standard ones.

Applications where these improvements could be of advantage are in EKG and respiration monitors where long-term use of the electrode is important. These electrodes may also be used in diagnostic procedures for determining, without motion artifacts, the effects of exertion upon a subject.

These electrodes are essentially fully developed and ready for use; in fact, considerable transference of technology already has occurred. Several companies are offering for sale a variety of "fluid" electrodes, and investigators are using the technology to construct their own electrodes. For this reason, it was felt that this technology was not truly within the scope and purpose of this report, and it was not given further consideration.

CHAPTER 5

Summary and Conclusions

A number of NASA-supported technological advancements have been made in aerospace physiological monitoring to meet the particular requirements of the space program. Several of these requirements are quite comparable to existing patient monitoring needs in civilian medicine. Consequently, many of the improvements and new developments generated by the space medical program will also find extensive application in civilian medicine.

Developments which already have prompted considerable transfer of technology are exemplified by the auto-sphygmomanometer for remote automated blood pressure measurement, and NASA fluid electrode techniques for long-term monitoring of biopotentials of active subjects. Developments which show potential for transference soon include several transducers for the continuous external measurement of blood pressure. In addition, research and development is actively proceeding on vibrocardiographic evaluation of the activity of the heart and there is promise for future transference of this technology.

Consideration of the developmental status of promising devices for indirect blood pressure measurement and a forecast of the potential market for these devices has led to the following conclusions:

Direct Force Blood Pressure Transducer.—The direct force method of blood pressure measurement is a new technique for continuous indirect measurement, without occlusion, of the blood pressure waveform and shows great promise for both patient monitoring and diagnosis. This device performs a function offered by no other device on the present market. The remaining development problems, associated primarily with positioning, appear formidable though not insurmountable. An annual market potential of 2–3 million dollars exists for such a device if it is successfully developed.

Ear Opacity Blood Pressure Transducer.—The ear opacity transducer for blood pressure measurement shows promise as a simple, inexpensive monitoring device that can be easily applied and produces no irritation or inconvenience when used continuously. Although fully developed, further experimental evaluation and clinical use is necessary to establish its value relative to other similar semi-continuous devices. The potential market for such a monitor is 0.7–1.0 million dollars.

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