Semi-Annual Status Report - NASA Research Grant NGR 24-003-001

April 1, 1971

STUDIES OF THE EFFECTS OF GRAVITATIONAL AND INERTIAL FORCES ON CARDIOVASCULAR AND RESPIRATORY DYNAMICS

This report consists of brief status reports of the investigative projects which have received support from this grant.

1. Roentgen biplane videometry - with Erik L. Ritman and Ralph E. Sturm

Left posterior and anterior oblique projections of the left ventricle plus the ECG and time course of injection of 0.5 ml 69% renovist/kg are recorded on a videodisc which allows stop-action display of single video fields. A flying-spot scanner video image processor provides operator interactive masking out of noncontributory portions of the images to facilitate automatic recognition of the borders of the ventricular chamber. The video signal is then fed into a video quantizer border recognition assembly (Mayo Clinic Proceedings 43:803, 1968) which brightens the video beam at each of the four instants in time when this beam encounters the borders of the two silhouettes during the successive 60-80 horizontal lines constituting the images. The proximity of the bright spots to the cardiac borders is used by the operator to adjust the assembly to obtain an accurate fit of the automated border recognition points to the borders of the opacified chamber. When this procedure is completed for the single video fields at end-diastole and end-systole, the border recognition proceeds for every 60-per-second field recorded throughout the cardiac cycle. Clock times of the border pulses are fed in real time into a CDC 3300 computer programmed to calculate the volume and display the shape of the ventricle for each video field. Values for volumes and shape of the left ventricle of anesthetized dogs are reproducible and volumes of test objects accurate to within 0.5 ml.

Silastic casts of canine left ventricles, supplied by Dr. Harold Sandler, were impaled on thin rods along the longitudinal axis and mounted at an adjustable angle from the plane of the x-ray beams of the biplane video system (J. Appl. Physiol. 24:724, 1968) and centered at the intersection of these beams. Biplane roentgen images of the cast and its angular position about its longitudinal axis were recorded on videotape (every video field 60 times per second) as the cast was rotated 360° in two seconds. This procedure was repeated at different angles of the longitudinal axis and for casts made at different stages of cardiac contraction. Orthogonal diameters of the ventricle were measured for real time by videometry at 50 to 80 positions along its longitudinal axis for each video field and its volume and shape calculated by the time-shared digital computer (CDC 3300) sixty times each second (Federation Proc. 26:72, 1970).

Three sets of values for ventricular volumes were calculated based on three assumed shapes of this chamber, as follows:

1. It was assumed that the shape of each of the 60-80 cross sections of the ventricle delineated by each of the 60-80 horizontal lines was elliptical and that the orthogonal biplane silhouettes passed through the actual major and minor diameters of each of these assumed elliptical discs. The volume of each disc was calculated on the basis of this assumption, and the total volume of the ventricle obtained in accord with Simpson's rule as the sum of the volumes of these discs.

2. It was assumed that the ventricular cavity is spheroidal in shape and that major and minor diameters of each silhouette in the biplane images were the true major and minor axes of this spheroid.

3. It was assumed that the ventricular cavity was a prolate spheroid in shape. Based on this assumption, the volume of the cavity was calculated from each monoplane image.

The calculated values were always greater than the true volume of the cast. A 90° periodicity in the variation of these calculated values in relation to the angular position of the cast was obtained. This results from observation in two fixed orthogonal planes of a rotating object which has a dominant dimension, such as occurs in a box or an ellipse. Analysis of this periodicity of calculated volume during rotation of the cast provides information as to the effective shape of the rotating object (i.e., the roentgenographic image). The simultaneous volume values calculated on the basis of all three assumptions show that the monoplane data has a 180° periodicity, and that values obtained by summing the 78 assumed elliptically shaped cross-sections of the cast (Method 1) gave values closest to the true volume at all angular positions. Values based on the ellipsoid assumption (Method 2) using four axes measured from the orthogonal silhouettes, resulted in a greater overestimate than Method 1, whereas the values based on monoplane views (Method 3) generally gave the greatest overestimate.

When these observations were carried out using casts obtained at different phases of the cardiac cycle, similar patterns in the variation of the calculated volumes were obtained. In all cases, however, the values based on biplane measurements showed 30 to 50% less variation with rotation than the values obtained by the monoplane method. Values based on the ellipsoid model differed from the elliptical disc model by a fixed volume offset, and the two sets of values exhibited a nearly 1:1 relationship. On the average, the calculated volume values for the four different casts (made at different phases of the cardiac cycle) obtained by the ellipsoid method and the monoplane method, respectively, were 3 and 7%, respectively larger than the values obtained by the multiple elliptical disc method.

Preliminary verification of the accuracy of the system in intact animals has been obtained by comparing volumes determined by roentgen videometry with values measured simultaneously by accepted independent methods such as the conventional indicator-dilution technique, and beat-to-beat measurements of stroke volume by chronically implanted aortic electromagnetic flowmeter and analysis of aortic pressure pulses.

The inter-relationships of the dynamic changes in the shape and volume of the ventricular chamber with the blood pressures and flows generated by these changes and the associated stresses and strains (i.e., the length-tension relationships) in the myocardium producing these changes are the essence of cardiovascular function. Therefore, in addition to developing techniques for dynamic displays of the changes in shape and volume during individual cardiac cycles, it is necessary to relate these changes to simultaneous pressure and flow data plus the tensions and length changes derived therefrom. These changes must be displayed so that they can be easily related to specific anatomical regions covering the full spatial extent of the ventricle and temporally to all phases of the cardiac cycle.

Descriptions of the considerable progress which has been made in this laboratory in the development and application of computer graphic techniques, particularly in the display of these dimensional data have been published (1,2).

These techniques, which produce data-dense readily comprehensible displays of multidimensional data, are proving to be of great value as an aid in the comprehension and interpretation of biplane videometric and associated data.

These studies demonstrate that the roentgen videometry system can be used as an independent quantitative technique for more detailed and sophisticated investigations of ventricular function for which beat-to-beat data concerning changes in shape and volume of the left ventricle during individual cardiac cycles are required and not accessible by conventional means in animals or man studied without thoracotomy.

It is believed that this system, coupled with computer processing of high volumes of data which cover the full anatomical and temporal extents of the ventricle and individual cardiac cyles, respectively, will provide cardiac physiologists and cardiologists with a degree of power for detailed rapid analysis of the temporal and physical inter-relationships of cardiac function in health and disease which has heretofore been unattainable.

1. Coulam, C. M., W. H. Dunnette, and E. H. Wood:
A computer-controlled scintiscanning system and associated computer graphic techniques for study of regional distribution of blood flow.
Computers and Biomedical Research 3:249-272 (June) 1970.

2. Greenleaf, J. F., J. S. Tu, and E. H. Wood:
Computer-generated three-dimensional osicllоscopic images and associated techniques for display and study of the spatial distribution of pulmonary blood flow.
IEEE Transactions on Nuclear Science 17:353-359 (June) 1970.

2. Myocardial force-velocity-length curves from biplane angiograms: comparison of three commonly used models - with A. A. Bove and P. R. Lynch

High-speed biplane cineradiographs were exposed during injection of radiopaque contrast into the left ventricle (LV) of dogs under morphine-pentobarbital anesthesia. LV stress (LVS) and circumference(LVC) were estimated at intervals at 15 msec, and continuous curves of LVS and LVC and their time derivatives were obtained. These four parameters provide enough information to calculate contractile element force (Fce) and velocity (Vce) using an assumed mechanical model of myocardium at 15 msec intervals throughout the heart cycle. Values for series elastic (SE) and parallel elastic (PE) constants were taken from published data. Three-dimensional force-velocity-length curves show little difference among three commonly used models. The Voigt model with a stiff PE and a model with no PE show no significant difference in either Fce or Vce in any phase of contraction. The stiffness of the PE, however, is critical in eliminating differences between these models. The Maxwell model gave 8.5% higher values for mean Vce ($P < .001$) and a 12% higher value for Vmax ($P < .001$) than the Voigt model. Fce showed little difference among the three models. The value of Fce during isometric contraction for all three models was sensitive to small changes in the initial value of the SE force-length relation. Thus, the choice of the constant B in the SE equation: $dF/dl = AF + B$ is of some importance. Values of Vce and Fce derived from stress and length data on intact hearts are different when the Voigt or Maxwell model is used or if the PE is excluded, although the differences are small. The choice of SE and PE constants in any model, however, is critical since Vce and Fce are sensitive to changes in these constants. Because of the assumptions made concerning the shape of the ventricular chamber required to convert pressure and major diameters to stress and then to Fce and Vce, these data represent only approximations to actual values of these myocardial parameters. This method, however, may be useful in evaluating force-velocity relations in clinical studies.

3. Effect of magnitude and duration of G acceleration on spatial distribution of pulmonary blood flow - with James F. Greenleaf

The effect of duration and magnitude of the gravitational-inertial force environment on the spatial distribution of pulmonary blood flow (D-PBF) was measured using radioactive microspheres in six dogs in the left lateral decubitus position. D-PBF was determined from the regional concentration of 35μ diameter radioactive microspheres resulting from their injection into the right ventricle. Microspheres tagged with different isotopes were injected during 1G control, and at two successive points in time during two-to-three minute exposures to centripetal acceleration of 5.6-8G. High resolution measurements of the D-PBF in the dogs were obtained by scanning individual 1 cm thick cross-sections of the excised fixed lungs. Pressures in the thoracic aorta, pulmonary artery, right ventricle, left atrium, and left pulmonary vein were recorded. Three cuvette oximeters measured oxygen saturation of blood continuously withdrawn from the thoracic aorta, pulmonary artery, and left pulmonary vein. Results indicate: 1) the fraction of blood flow traversing the left and right lungs is independent of duration and magnitude of acceleration, but 2) is strongly affected by the occurrence or absence of fast deep breaths which cause an increase or decrease, respectively, in ventilation and concurrently in blood flow through the dependent lung, and 3) $+G_y$ acceleration caused a significant increase in blood flow in the midlung region concurrent with a decrease in the superior portion of the lobes of the right lung. Result 2 may be mediated primarily by the physical and possible regional gas tension effects of changes in regional alveolar volume associated with the increase in weight of the thoracic contents and the pattern of ventilation as modified by the respiratory musculature. Thus, these effects resulting from changes in the regional geometry of the lung are superimposed on and may override the hydrostatic effects of acceleration on the distribution of pulmonary blood flow.

4. <u>Effects of $+G_y$ acceleration on blood oxygen saturation and pleural pressure relationships in dogs breathing first air then liquid fluorocarbon in a whole body water immersion respirator</u>
with Donald J. Sass

A total body water immersion, mechanical respirator, body support assembly has been used with dogs on the human centrifuge to compare effects of $+1G_y$ and $+6G_y$ acceleration on cardiovascular and respiratory function in dogs under three conditions: 1) normal respiration in air; 2) totally immersed in a saline-filled respiratory chamber providing control of respiratory rate, tidal and residual volumes when breathing air or oxygen; and, 3) when respired in the same manner with oxygenated liquid fluorocarbon. Intrathoracic pressures were recorded by strain-gauge manometers connected to fluid-filled catheters introduced without thoractomy into the thoracic aorta, pulmonary artery, right and left atria, left pulmonary vein, and right and left pleural spaces. Three cuvette oximeters measured oxygen saturation of blood continuously withdrawn from the thoracic aorta, pulmonary artery, and left pulmonary vein. Oxygen saturation measurements and intrathoracic pressures were analyzed on-line by the CDC 3300 digital computer. The results indicate that: 1) arterial hypoxemia due to dependent pulmonary arteriovenous shunting caused by acceleration is not minimized by water immersion alone; 2) dogs can be respired with liquid fluorocarbon for four hours or longer, without clinical signs of respiratory distress, with arterial PCO_2 values maintained at will between 16 and 40 mm Hg, with arterial blood fully oxygenated at breathing rates between four and eight per minute, and with minimum histological evidence of pulmonary injury due to breathing fluorocarbon; 3) liquid respiration prevented dependent pulmonary arteriovenous shunting at $+6G_y$; 4) vertical gradients in pleural pressure were approximately 0.7 cm H_2O/cm vertical distance between pleural catheter tips in air breathing dogs in contrast to greater than 1.0 cm H_2O/cm vertical distance in liquid-breathing experiments; and, 5) liquid breathing prevented inertial displacements of the heart and other mediastinal structures to dependent sites in the thorax and roentgenographically evident pulmonary atelectasis in dependent regions. During exposures to $+6G_y$, the heart floated upward into the superior hemothorax with somewhat over expansion of the dependent left lung. The specific gravity of the fluorocarbon was 1.7.

The results of such a study, in addition to their academic interest, are of practical importance in relation to the problems of development of dependent atelectasis in immobilized patients, and the arterial hypoxemia and occasional instances of damage to pulmonary parenchyma which have been observed at levels of acceleration encountered during the launch and re-entry phases of space flight and the frequent injury to the thoracic contents caused by impact acceleration (vehicular crashes) and blast. If a safe and practical technique for breathing of a liquid with a specific gravity similar to that of blood and tissue can be developed, it appears possible that combination of this technique with immersion in water would allow humans to withstand levels of acceleration of over 50G, such as could be encountered during uncontrolled re-entry of the earth's atmosphere from outer space or during a crash situation.

Liquid breathing also has potential applications in extending man's capability for withstanding sustained or transient extreme changes in environmental pressure such as associated with explosive blasts, sudden decompression, and deep-sea diving. Extravehicular survival by the use of liquid breathing in the extreme depths of the ocean may also be feasible.

Beat-to-beat measurements of left ventricular stroke volume have been made in relation to the phase of respiration in right lateral decubitus dogs breathing first air, then oxygenated liquid fluorocarbon in a water-immersion respirator providing control of respiration rate, tidal and residual lung volumes. An electromagentic flowmeter was implanted around the root of the aorta of a dog nine weeks prior to this study. Aortic blood flow, oxygen saturation of blood continuously withdrawn from the thoracic aorta and pulmonary artery, right and left pleural pressures, immersion tank (body surface) pressure, intratracheal and other intrathoracic pressures, circulatory pressures, and other variables were recorded simultaneously on digital magnetic tape. Measurements of cardiac output from indicator dilution curves following indocyanine green dye injection at different phases of respiration were used to calibrate the aortic flowmeter. Left ventricular stroke volume was calculated on-line by a CDC 3300 digital computer and the beat-to-beat values were plotted versus time by a computer-driven incremental plotter along with concomitant measurements of intrathoracic pressures, body surface pressure, and other variables.

The plots of left ventricular stroke volume versus time were approximately sinusoidal and synchronized with respiration (9 to 10 per minute when breathing air, and 3 to 4 per minute when breathing fluorocarbon). Maximum stroke volume occurred soon after the start of the inspiratory phase when the dog breathed air, and just prior to full inspiration when the dog breathed fluorocarbon. The average stroke volume was approximately one-third greater, and the peak-to-peak changes in stroke volume were roughly twice as great, comparing plots from liquid-breathing and air-breathing experiments, respectively.

These results indicate that the phasic variations in body surface pressures and concomitant induced changes in intrathoracic, airway, and other internal body pressures required to maintain adequate respiratory gas exchange with liquid fluorocarbon, produce large respiratory variations in cardiac output which are reflected by variations in the oxygen content of mixed venous blood.

5. Simultaneous indicator dilution curves at selected sites in the coronary circulation and determination of blood flow in coronary artery-saphenous vein grafts by roentgen videodensitometry - with Hugh C. Smith

Since the advent of selective coronary angiography by Sones in 1962, much data has been gathered on normal anatomy of the coronary arteries and the anatomic abnormalities encountered in coronary heart disease. Little has been written on the measurement of coronary blood flow in the intact animal or man, although indocyanine green and various radioisotopes have been used to estimate coronary flow by the indicator-dilution or precordial washout techniques. The theoretical and technical difficulties with these techniques make the videodensitometric methods of determining coronary blood flow attractive, particularly since it is anticipated that this method will allow the simultaneous determination of vessel anatomy and blood flow at any specific site within the coronary circulation. Rutishauser and coworkers have applied roentgen cinedensitometric techniques to the determination of coronary blood flow in dog and man.

Following a single injection of contrast material, simultaneous indicator-dilution curves may be obtained from every site in the circulation within the x-ray field by roentgen videodensitometry. This noninvasive sampling technique has enabled workers in this laboratory to study blood flow across the mitral and aortic valves under normal and various abnormal conditions. The roentgen videodensitometric system and methods developed in this laboratory for studies of this type have been described in detail in papers by Sturm and Wood.

This noninvasive sampling technique is usually limited to circulatory sites not superposed on other structures containing contrast medium. In this study, angiograms were recorded on videotape during injection of 69% renovist into the left ventricle or aortic root of anesthetized dogs. On replay of the tape, roentgen density-time curves were obtained with the sampling window on a selected coronary site. Compensation for nonspecific roentgen changes due to vessel motion and change in cardiac size and position was achieved in real time by a time-shared digital computer (CDC 3300). Usual indicator curves were not obtained due to persistence of contrast medium in cardiac walls and recirculation in cardiac chambers superposed in the sampling window. A second background curve obtained from an area of the heart immediately adjacent to the coronary artery was subtracted from the coronary plus background curve to give dilution curves of contrast medium in any selected 2-5 mm segments of a coronary artery alone. Differences in geometry at the two sites were minimized by superposing the two curves so that roentgen densities were identical prior to injection and 15-18 seconds after injection when uniform renovist distribution was assumed (Figure 1).

ROENTGEN VIDEODENSITOMETRIC DILUTION CURVES RECORDED OVER AND ADJACENT TO LEFT CORONARY ARTERY DURING INJECTION OF 12 ml 69% RENOVIST INTO ASCENDING AORTA

(Dog 15.4 kg, Morphine - Pentobarbital Anesthesia)

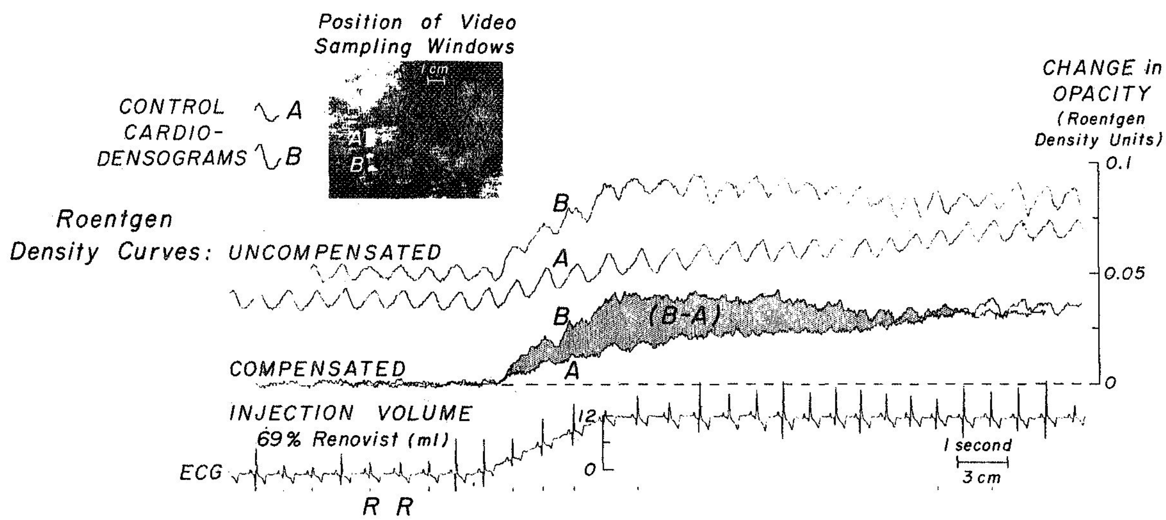

Figure 1 The uncompensated curves from both sites (B and A) are a direct computer replot of the digitized videodensitometric data. The compensated curves (B-A, lower) are obtained by subtraction of the respective nonspecific cyclic variation in roentgen density (control cardiodensograms A and B) from the uncompensated curves. The computer-generated small vertical bars below the ECG (two of which are marked R) indicate the instants in time at which the computer recognized successive R-waves of the electrocardiogram.

Figure 1 (continued)

These blips serve to verify that the computer program for recognizing and subtraction of the cardiodensogram is operating in the correct temporal relationship with respect to each cardiac cycle. The difference (B-A, stippled area) between the compensated coronary plus background curve (B) and the compensated background roentgen density curve (A) represents the change in roentgen opacity due to the transit of contrast medium through the coronary artery alone. This is valid only when the videodensitometer gain and the window settings are unchanged and the geometrical differences between the sampling sites, indicated by A and B in the photo insert, are minimized by superposition of the curves so that the roentgen density signals are identical prior to contrast medium injection and 15 to 18 seconds after injection when uniform mixing the contrast material is assumed. The photo insert is a segment of a picture of the television monitor of the videodensitometer exposed during replay of the videotape recorded aortogram. The 1 cm scale mark is superposed on the opacified silhouette of the aorta. The variations in amplitude of the R wave of the electrocardiogram are the artifactual results of the relatively slow, 60-per-second, analog-to-digital sampling rate used to input the ECG into the computer.

Similar curves have been obtained in this laboratory from videotape recordings made during coronary artery angiographic studies carried out in patients with coronary heart disease (Figure 2). These data, which have heretofore been impossible to obtain or available only by time consuming frame-by-frame analysis, can now be used for the determination of blood flow in individual vessels in man in the clinical setting, as illustrated in the following study.

The present assessment of the efficacy of saphenous vein-coronary artery implants in patients with coronary artery disease is limited to an objective assessment of exercise tolerance and electrocardiographic data following recovery from surgery or the subjective assessment of coronary and saphenous vein graft flow during graft and coronary angiography. Using videodensitometry, we have obtained compensated indicator-dilution curves of contrast medium at selected sites within the coronary circulation following injection of small amounts (3-6 ml) 69% renovist into the aortic origin of the vein graft in coronary implant recipients (Figure 2). The measurement of mean transit time of contrast material between two sites on the graft (Figure 3) a measured distance apart, plus determination of the vessel dimension by biplane angiograms after appropriate corrections for x-ray image mangification, allow flow to be calculated as the product of mean blood velocity and corss-sectional area. Computer analysis of vessel coordinates transferred from biplane orthogonal angiograms facilitates accurate measurement in three dimensions of the distance between sampling sites along a vessel and its cross-sectional area, regardless of vessel tortuosity or patient position. An example of measurement of blood flow in a coronary artery vein graft in a patient is shown in Figure 3.

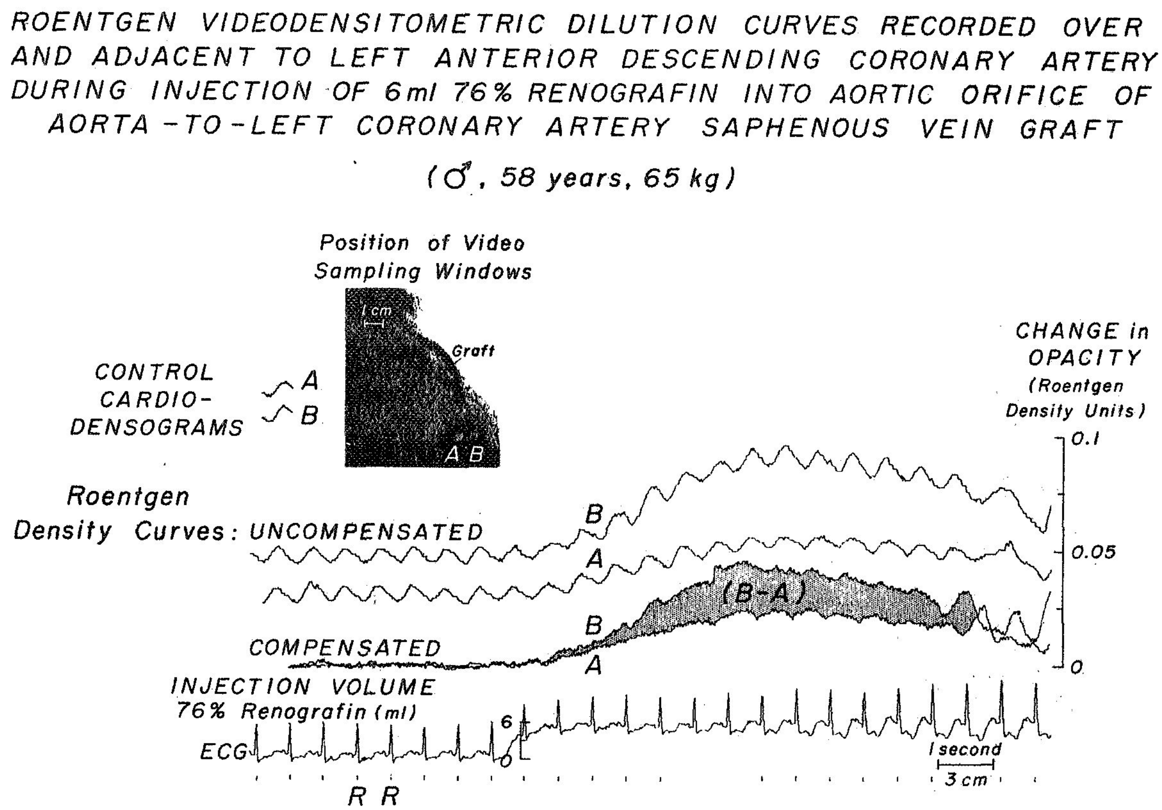

Figure 2 Computer-generated plots of roentgen density dilution curves of renografin recorded over and adjacent to the left anterior descending coronary artery just distal to the downstream orifice of an aortic-to-left coronary artery saphenous vein implant in a patient with severe coronary artery disease.

The stippled area labeled (B-A) is the roentgen density-time curve caused by the transit of the roentgen contrast medium-blood mixture through the segment of the left anterior descending coronary artery viewed by the video sampling window, labeled B in the x-ray photo insert. See legend of Figure 1 for additional details.

It is apparent from the photo that multiple simultaneous indicator-dilution curves may be obtained within the coronary

Figure 2 (continued)

circulation from the single injection of contrast material and associated x-ray exposure by repositioning of the video-densitometer sampling window during each videotape replay of the resulting coronary arteriogram.

ROENTGEN VIDEODENSOMETRIC DILUTION CURVES RECORDED OVER PROXIMAL AND DISTAL SEGMENTS OF AORTA-TO-LEFT CORONARY ARTERY SAPHENOUS VEIN GRAFT DURING INJECTION OF 6 ml 76% RENOGRAFIN INTO AORTIC ORIFICE OF GRAFT

(♂, 55 years, 76 kg)

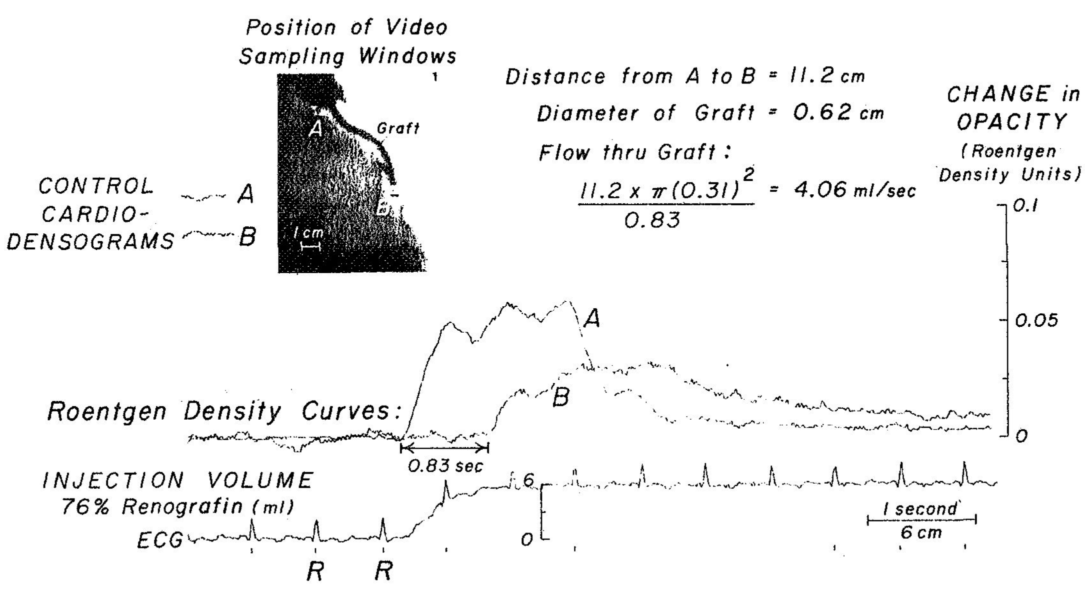

Figure 3 Computer-generated roentgen density curves recorded simultaneously over proximal (A) and distal (B) segments of an aorta-to-coronary artery saphenous vein graft in a patient with severe coronary artery disease.

Determination of the difference in the appearance time of the contrast medium at the two sites of 0.83 seconds and the measured length of the graft between the two sites of 11.2 cm provides the basis for an estimation of the velocity of blood flow between these sites. The approximate volume rate of blood flow through the graft of 4.06 ml/second can then be estimated as the product of blood velocity and vessel cross-sectional area. Measurement of vessel dimensions (length and

Figure 3 (continued)

diameter was achieved by three-dimensional analysis of the vessel from biplane angiogram x-rays corrected for x-ray magnification. Blood flow of 160 ml per minute through this graft was determined by electromagnetic flowmeter following completion of extracorporeal circulation and implantation of the graft at the time of surgery. Subsequent determination of blood velocity obtained from a measured difference in mean transit time (ΔMTT) of 1.38 seconds gives a volume rate of blood flow of 170 ml per minute.

The measurement of blood flow in single coronary arteries of dogs and man by roentgen cinedensitometry has been reported, but the presence and influence of contrast material in the superposed structures upon mean transit time measurements were not examined. Persistence of contrast material in the cardiac walls and recirculation in the cardiac chambers superposed in the vessel sampling window will result in an artifactual prolongation of the mean transit time and may lead to an underestimation of vessel flow. On the other hand, in our preliminary studies, our measurement of the difference in appearance time (ΔAT), as illustrated in Figure 3, could cause an overestimation of vessel flow as the velocity profile of the contrast bolus becomes more parabolic in shape as the leading edge moves farther in advance of the main portion of the bolus in its progress downstream. This vessel blood flow overestimation is probably greater in the long nonbranched saphenous vein graft than the short branched coronary vessels where fully developed parabolic flow is less likely to occur and accounts for the difference in shape of the indicator-dilution curve at vein graft sampling sites A and B (Figure 3). Subsequently, all blood flow determinations were derived from blood velocity values obtained from the differences in mean transit time of the contrast material between two sites on the graft a measured distance apart.

Postoperative measurements of flow in the saphenous vein-coronary artery grafts have been carried out in sixteen patients. The flow data were obtained from single small injections of contrast material from a single catheter with brief (20-40 seconds) x-ray exposure during routine postoperative catheterization. This technique allows the simultaneous determination of anatomic abnormalities in a coronary artery, and the flow through the vessel, thus providing an assessment of the functional derangement resulting from altered structure.

Preoperative determination of flow in the individual coronary arteries of patients being considered for saphenous vein-coronary artery grafts, and the postoperative measurement of the flow in the graft(s) and in the recipient arteries, together with pre- and postoperative assessment of cardiac performance should provide meaningful objective data upon which the results of surgical revascularization procedures can be assessed.

The technique is also applicable to studies of coronary blood flow in intact primates studied under orbiting space laboratory (zero gravity) conditions.

6. Effect of the magnitude and direction of the gravitational-inertial force environment on the spatial distribution of lung parenchyma - with Hugh C. Smith

High resolution methods of measuring regional distribution of pulmonary blood flow during $+G_y$ acceleration have been developed in this laboratory. Greenleaf et al, examining the spatial distribution of radioactive microspheres injected into the pulmonary circulation during $+G_y$ exposure, found that the dependent portions of the lungs showed no significant changes in flow during +6G exposure even though the perfusion pressure in these dependent lung regions increased by an average of 10 cm H_2O from the 1G condition. Atelectatic areas have been noted radiologically in these dependent areas, and this is not surprising in view of the large positive pleural pressures determined in these regions during $+6G_y$ acceleration. The increased pulmonary vascular resistance in these areas may result from the decrease in dependent lung volume to the point of atelectasis.

The measurement of the spatial distribution of pulmonary blood flow per alveolus requires that the lungs be inflated so that the alveoli maintain a uniform size during the scanning procedure. The relationship between regional lung volumes in vivo, during $+6G_y$ exposure, to the regional volumes of the excised inflated lungs is not precisely known, and it is, therefore, difficult to relate the in vitro spatial distribution of blood flow at 1G to the in vivo distribution at 1G or 6G.

To establish the relationship between in vitro and in vivo regional lung volumes, and to correlate regional changes in lung volume with regional changes in pulmonary vascular resistance during G_y acceleration, the pulmonary parenchyma has been tagged with small (0.5-0.8 mm) radiopaque stainless steel tags. These are introduced one to two weeks prior to $+G_y$ exposure to all lobes of the lung percutaneously (Figure 1) using a custom designed needle. Minimal pulmonary fibrosis or foreign body response to the tags is evident microscopically (Figure 2), and insertion is accomplished without significant pneumothorax, hemorrhage, or pleural adhesions.

Computer analysis with correction for the geometric magnification of the roentgenograms taken during changes in direction and magnitude (1-6G) of the force environment indicate that the superior lobes expand, and the dependent lobes are compressed when the dog is rotated to a lateral recumbent position at 1G (compare x-ray, Figure 1, with A-P x-ray, Figure 3, and computer plot, Figure 4). Little further lung parenchymal distortion occurs during $+G_y$ exposure (Figure 4) in this body position.

Preliminary evidence suggests that the excised lungs, when inflated with air, expand isotropically, and the spatial distribution of pulmonary blood flow data determined from the inflated excised lungs may be applied to the in vivo state.

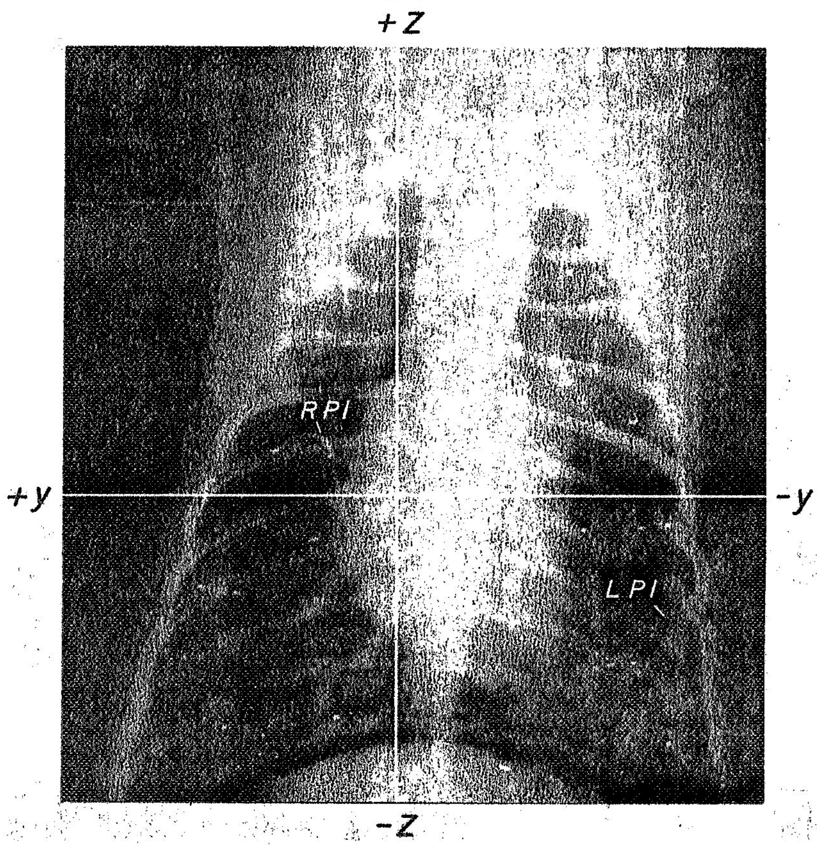

Figure 1 Chest roentgenogram with a 15.2 kg dog in the prone position following insertion of stainless steel beads as lung tags. Pleural pressures were monitored during the insertion procedure

Figure 1 (continued)

by pleural catheters (RPl, LPl) in the right and left pleural space. The bead distribution is fairly uniform in this position, but significant alteration in pulmonary parenchymal geometry occurs when the dog is rotated to the left decubitus position at 1G (P-A roentgenogram, Figure 3, and computer-generated plot of bead positions at 1G (solid circles) Figure 4).

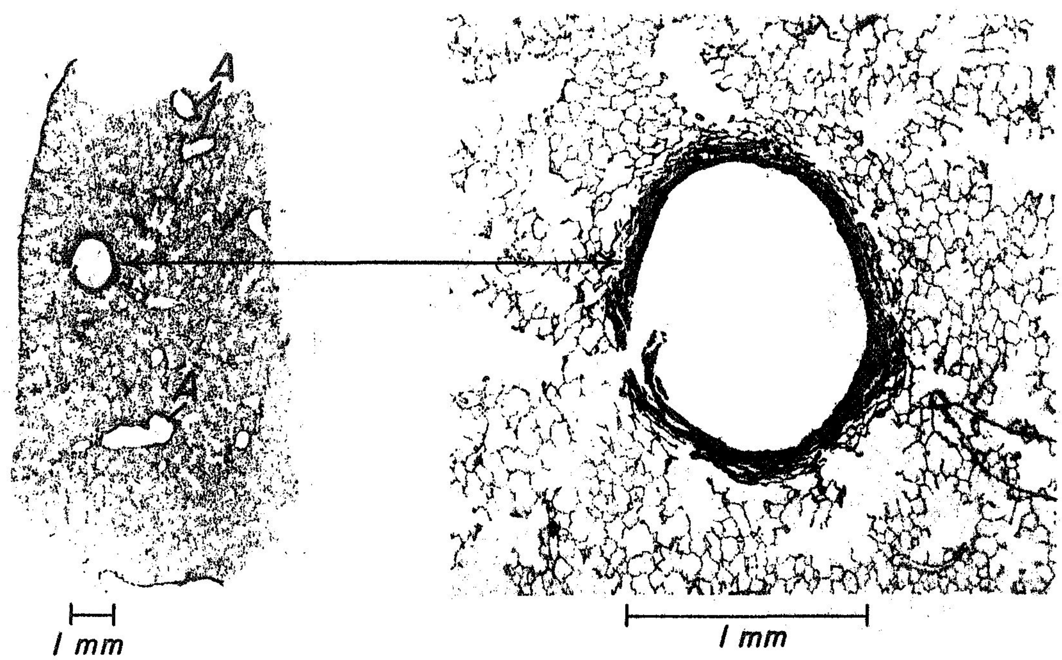

Figure 2 Photomicrographs of a fixed inflated section of right lower lobe of a dog two weeks following insertion of lung tags. The tag, whose position is indicated by the capsule (double-ended arrow) was removed prior to microtome sections.

The capsule, approximately 100μ thick, was composed primarily of compressed alveoli with minimal fibrosis and foreign body reaction (right panel). The adjacent pulmonary parenchyma and pleural surface are normal.

A = terminal bronchioles.

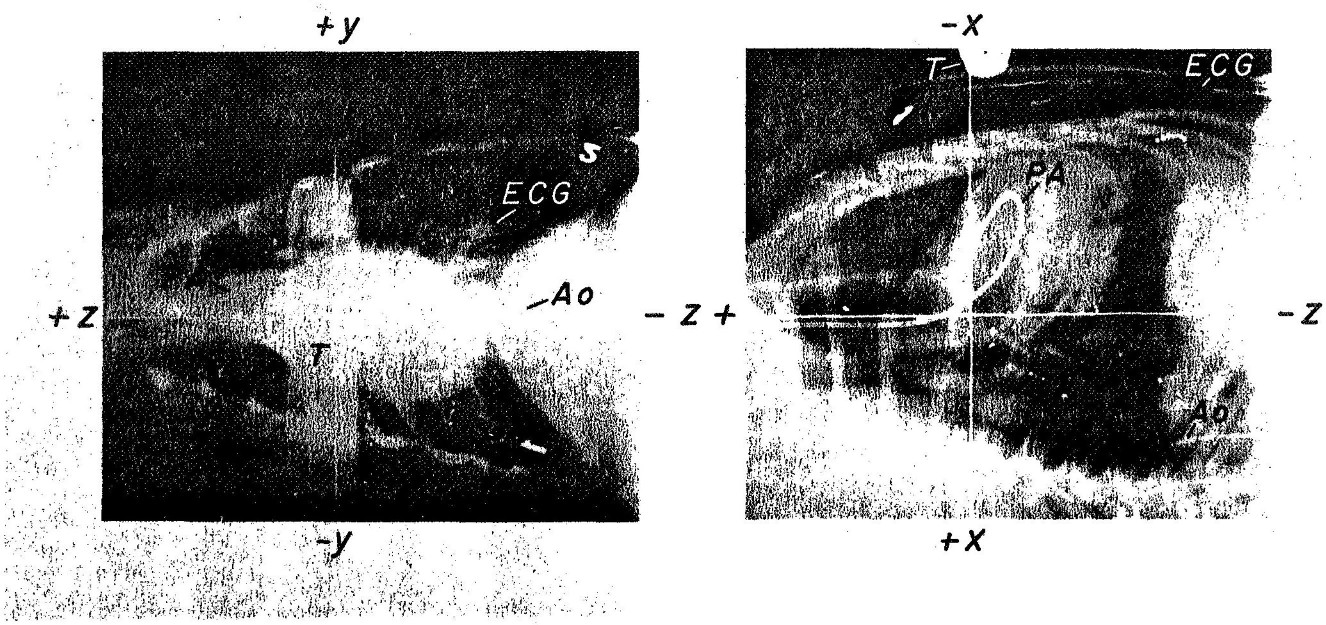

Figure 3 A-P and lateral roentgenograms of dog shown in Figure 1, maintained in left decubitus position by molded half-body cast in centrifuge cockpit.

ECG - ECG leads sewn to skin; T - thistle-tube system for zero reference purposes; PA and Ao - catheters with tips in pulmonary artery and aorta, respectively.

Comparison of the tag positions in this A-P roentgenogram of the dog in the left decubitus position with the tag positions in the P-A roentgenogram in the prone position (Figure 1) and the computer-generated plot (Figure 4) indicate that significant expansion of the superior lobes, and compression of the lower lobes occurs following rotation to a left decubitus position at 1G.

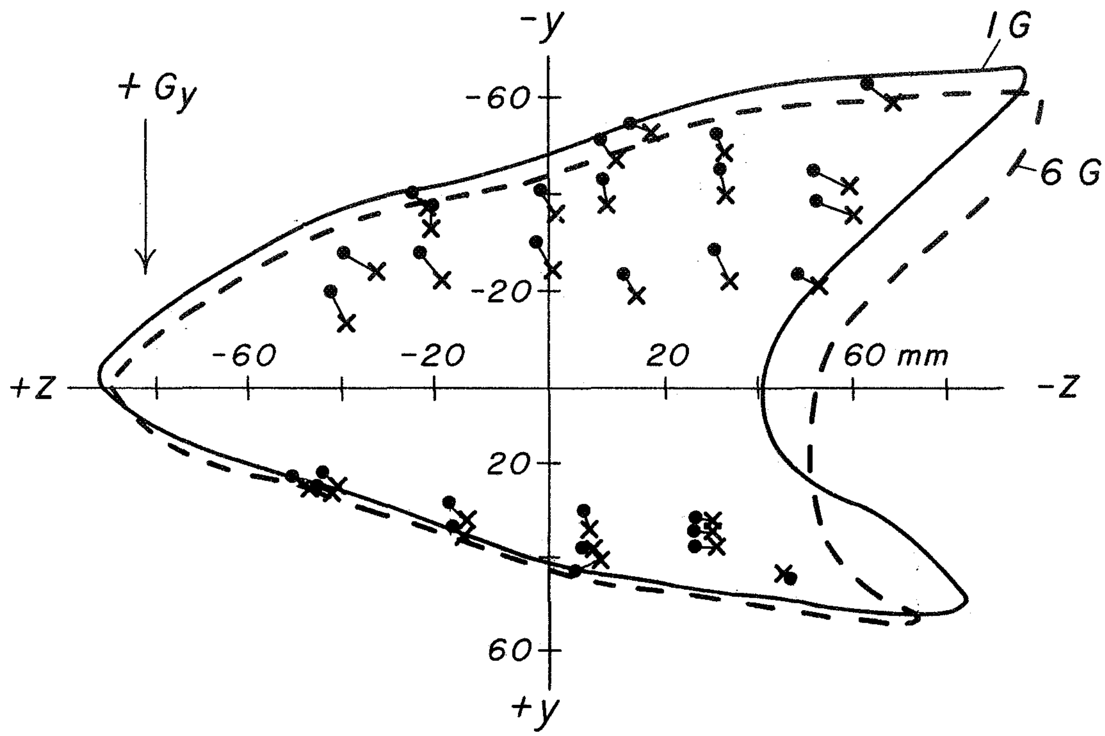

Figure 4 Computer-generated plot of positions of lung parenchymal tags in dog at $1G_y$(●), and during exposure to $+6G_y$ in the left decubitus position (x), A-P projection.

The tag distances from the X-Z origin have been corrected for geometric magnification. The vertical displacement of the lung tags during exposure to the increased gravitational-inertial force environment is relative to a horizontal sagittal plane through the dog's thorax. The slight downward shift of the dependent portion of the dog's chest wall is due to sag in the supporting cast, and the greater downward shift of the superior portion of the dog's chest is due to chest compression.

Allowance for this shift and compression of the dog's thorax indicates that shifts in position of thelung tags are minimal relative to the dog's thorax, and are less than those encountered due to a change in body position at 1G (compare Figure 1 and left panel, Figure 3).

Publications

1. Reed, J. H., Jr., and E. H. Wood:
Effect of body position on vertical distribution of pulmonary blood flow.
Journal of Applied Physiology 28:303-311 (March) 1970.

2. Ritman, E. L., R. E. Sturm, and E. H. Wood:
A biplane roentgen videometric technique for dynamic studies of shape and volume of the left ventricle.
Federation Proceedings 29:719 (March-April) 1970.

3. Wood, E. H., C. M. Coulam, W. Dunnette, J. F. Greenleaf, D. Nathan, E. L. Ritman, and D. J. Sass:
Scintiscanning system for study of regional distribution of blood flow.
SAM-TR-70-6, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas pp 1-197, February 1970.

4. Wood, E. H. and R. E. Sturm:
Use of videometry and electronic data-processing for hemodynamic investigation by angiographic techniques.
Chapter, Proceedings of Conference on Pathophysiology of Congenital Heart Disease, sponsored by the American Heart Association, pp 419-434, April 1970 (University of California Press, Berkeley).

5. Sass, D. J., E. L. Ritman, J. F. Greenleaf, and E. H. Wood:
Effects of $+G_y$ acceleration on blood oxygen saturation in dogs restrained by water immersion.
Aerospace Medical Association preprints, April 27-30, 1970, p 69.

6. Avasthey, P., C. M. Coulam, and E. H. Wood:
Position-dependent regional differences in pericardial pressures.
Journal of Applied Physiology 28:622-629 (May) 1970.

7. Greenleaf, J. F., E. L. Ritman, D. J. Sass, and E. H. Wood:
Changes in distribution of pulmonary blood flow during acceleration.
The Physiologist 13:212 (August) 1970.

8. Ritman, E. L., R. E. Sturm, and E. H. Wood:
Comparison of volume of canine left ventricular casts and angiograms using biplane and monoplane roentgen videometry.
The Physiologist 13:294 (August) 1970.

9. Sass, D. J., E. L. Ritman, P. E. Caskey, N. Banchero, and E. H. Wood:
Modification of the cardiopulmonary effects of acceleration by water immersion and liquid breathing.
The Physiologist 13:301 (August) 1970.

10. Coulam, C. M., W. H. Dunnette, and E. H. Wood:
A computer-controlled scintiscanning system and associated computer graphic techniques for study of regional distribution of blood flow.
Computers and Biomedical Research 3:249-273 (June) 1970.

11. Katori, R., D. deS Amorim, R. A. Theye, and E. H. Wood:
Influence of body position on regional pulmonary arterial-venous shunts in intact dogs.
Journal of Applied Physiology 29:288-296 (September) 1970.

12. Sass, D. J., E. L. Ritman, P. Caskey, J. Greenleaf, N. Banchero, D. Mair, and E. H. Wood:
Effects of +Gy acceleration on blood oxygen saturation and pleural pressure relationships in dogs breathing first air, then liquid fluorocarbon in a whole body water immersion respirator.
Proceedings of 27th meeting Aerospace Medical Panel, AGARD-NATO, September 15-17, 1970, Garmisch-Partenkirchen, Germany.

13. Greenleaf, J. F., J. S. Tu, and E. H. Wood:
Computer generated three-dimensional oscilloscopic images and associated techniques for display and study of the spatial distribution of pulmonary blood flow.
IEEE Transactions on Nuclear Science, Vol NS-17, #3:353-359 (June) 1970.

14. Reed, J. H., R. A. Vandenberg, and E. H. Wood:
Effect of gravitational-inertial forces on vertical distribution of pulmonary blood flow.
Journal of Applied Physiology (in press).

15. Sturm, R. E. and E. H. Wood:
Roentgen image-intensifier, television, recording system for dynamic measurements of roentgen density for circulatory studies.
Proceedings International Symposium on Roentgen-Cine- and Video-densitometry, Kiel Germany, March 1969 (Georg Thieme Verlag, Stuttgart, Germany) (in press).

16. Ritman, E. L., R. E. Sturm, and E. H. Wood:
A biplane roentgen videometry system for dynamic (60/second) studies of the shape and size of circulatory structures, particularly the left ventricle.
Ibid.

17. Williams, J. C. P. and E. H. Wood:
Application of roentgen videodensitometry to the study of mitral valve function.
Ibid.

18. Amorim, D. deS, A. G. Tsakiris, and E. H. Wood:
Use of roentgen videodensitometry for detection of left-to-right shunts in dogs with experimental atrial septal defect.
Ibid.

19. Smith, H. C., R. E. Sturm, and E. H. Wood:
Simultaneous indicator dilution curves at selected sites in the coronary circulation.
Ibid.

20. Smith, H. C., R. E. Sturm, and E. H. Wood:
Simultaneous indicator-dilution curves at selected sites in the coronary circulation.
Federation Proceedings (March-April, 1971, in press).

21. Sass, D. J., E. L. Ritman, P. E. Caskey, and E. H. Wood:
Respiratory variations in left ventricular stroke volume during liquid breathing.
Aerospace Medical Association preprint (April, 1971, in press).

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