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Dr. Vinograd

CARDIOVASCULAR STUDIES ON U. S. SPACE CREWS
AN OVERVIEW AND PERSPECTIVE

G. WYCKLIFFE HOFFLER, M.D.

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Author's mailing address:

Mail Code DB2

NASA - Johnson Space Center
Houston, Texas 77058

ABSTRACT

Early concerns for adverse effects upon man from exposure to the weightlessness of space have proved to be largely unfounded. Nevertheless, significant symptomatology and physiological alterations do occur apparently as adaptive phenomena, both upon entry into orbit and upon return to earth gravity. The cardiovascular system figures prominently in much of the observed changes, which include weight loss, decrements in leg mass, cephalad shift of body fluids, decreased blood volume and heart size, and variations in orthostatic tolerance and exercise capacity.

Accumulation of sufficient data from which a composite picture can be pieced and by which reasonable hypotheses could be formulated have required multiple investigative teams working with crews of many and varied space missions. Development of special and unusual procedures and techniques have become necessary. Parallel ground-based studies designed to reproduce as nearly as possible inflight findings have greatly aided integration and understanding of the space data. Challenges continue, however, and await more sophisticated, or perhaps orthodox, investigations which the Space Shuttle era promises.

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CARDIOVASCULAR STUDIES ON U. S. SPACE CREWS

INTRODUCTION AND BACKGROUND

Well before orbital space flight became a reality, much conjecture and hypothesizing had dealt with possible and probable effects of weightlessness upon man's cardiovascular system (Berry, 1973). This concern was in large part due to, and perhaps justified by, the very mobile character of the contents of the vascular tree. Accompanying early experience with manned flights, significant consequences of exposure to the space environment were seen in clinical symptomatology and in physiological test observations of a generally reduced postflight orthostatic tolerance (Catterson, et al., 1963 and Berry and Catterson, 1967). Orthostatic tolerance may be defined as that ability of primates to stand and function in the upright position by means of developed and adapted anatomical structures and physiological mechanisms of the cardiovascular system for countering hydrostatic forces imposed by gravity.

Since man functions usually in the erect stance with the long axis of his body oriented parallel to the gravitational force vector at the surface of the earth, this position may be considered his normal state. The price, however, is a continuous contest against fluid drift or pooling into the dependent end of the body, the ultimate consequences of which produce syncope. Routine and habitual departures from erect posture, such as horizontal sleep, induce significant cyclical internal alterations and a diurnal pattern has been determined for human orthostatic tolerance (Aschoff and Aschoff, 1969).

Because the cardiovascular system obeys many aspects of a closed hydraulic design, redistribution of hydrostatic pressures accompanies changes in body posture.

A teleological objective of the primate circulatory system is to maintain adequate cerebral pressure, circulation, and perfusion, which normally operate at the low pressure, or cephalad, end of the long axis of the body.

For a rigid system, internal hydrostatic pressures would be a function of the angle this long axis makes with the horizontal and the distance from a pivotal or zero reference point. This latter hydrostatic indifference point has been measured slightly below the diaphragm in erect human beings (Gauer and Thron, 1965).

Since human beings, and certainly their vascular systems, are not rigid, this transitional zone shifts headward with head-down tilt or headward acceleration stress. It may be presumed to shift at least qualitatively in like fashion in space where no acceleration forces impinge on the total organism. In any case, all mechanisms and functions normally combatting the inexorable force of gravity on earth suddenly become unopposed upon entry into the weightlessness of orbital flight. The net result is the symptomatology and postflight consequences noted above, apparently sequelae of whatever adaptive processes take place during this non-natural state (Gauer and Henry, 1963 and Klein, et al., 1969).

So simple and certain a finding as reduced postflight orthostatic tolerance has therefore not proved as easily explained. A plausible etiology for reduced orthostatic tolerance has been sought in diminished circulating blood volume, plasma and/or red cell mass; in increased peripheral venous compliance, altered central pump dynamics; disturbed neurological control of the cardiovascular system; and in renal-hormonal changes induced by varying gravity vector and pressure forces.

In actuality, the truth probably encompasses a little of them all, and relates directly and/or indirectly to the peculiar hypodynamia attendant exposure to weightlessness (Berry, 1973).

This overview intends to examine currently relevant data and their permissible interpretations as of the present moment, viz., after Skylab and the Apollo-Soyuz Test Project (ASTP) missions. Much effort has been expended by many medical, physiology, and engineering teams in attaining this current level of accomplishment. The amassed data are literally astronomical and only the more obvious and pertinent determinations have received open publication. No distinctive integrative work has yet taken place. This paper is an attempt to put into perspective from available information one major physiological area. Documented, factual returns will be accorded priority. Consideration will then turn to selected extrapolations which may be reasonably surmised. Finally, questions which may become grounds for important early Shuttle investigations are entertained. This summation must necessarily fall short of adequate comprehension and represents only the present step, based on incomplete knowledge, toward fully understanding physiological functions in this newly experienced space environment.

FACTUAL DATA

Weight Loss

One of the most consistent determinations following space flight has been weight loss. Because this entity bears importantly on much of the succeeding development for cardiovascular findings, the following details are to be emphasized. The astronaut pilot lost nearly eight pounds (3.5 Kg, 5.3%) during the 34-hour Mercury 9 flight in 1963 (Catterson, et al., 1963). Of eighteen Gemini crewman on flights from 5 to 331 hours duration, only one returned without weight loss and the group mean loss was 5.6 pounds (2.5 Kg) or 3.4% of preflight weight (Unpublished data, Johnson Space Center, Houston, Texas). A virtual duplication of this picture was seen in 33 Apollo crewmen flying missions from 6 to 12.6 days duration. Based on launch day weights, only two showed no decrement in weight postflight, with the group mean loss being 6.2 pounds (2.8 Kg) or 3.7%. Using preflight mean weights from several measurements as early as 30 days before launch, all lost weight and the mean decrement was even larger (7.8 pounds, 3.5 Kg, or 4.5%) (Hoffler, Wolthuis and Johnson, 1974).

Data from the Skylab missions appear to offer further corroboration with a mean weight loss for the nine crewmen of 3.5 Kg (4.9%) (Unpublished data, Johnson Space Center, Houston, Texas). But for these missions widely varying in durations (28, 59 and 84 days), another interpretation may be legitimate, namely an inverse relationship between weight loss and mission duration. The three Skylab crewmen of each mission average 5.7, 3.8, and 1.1 Kg weight loss respectively. The three

ASTP crewmen in a 9-day mission averaged 2.0 Kg (2.5%) weight loss (Unpublished data, Johnson Space Center, Houston, Texas).

Figure 1 presents graphically the percentage weight loss versus mission duration for all U. S. space fliers. The average overall weight loss has been 2.8 Kg or 3.8%. This plot allows several significant statements. Whatever may be the etiology of weight loss in the space environment, the disturbing stressors are at work very early after launch and they persist for several weeks. It is not possible to determine if this weight loss may be wholly a function of deficit intake. However, it does appear that a stabilizing effect, or perhaps even reversing trend, has begun in the longer duration missions.

Leg Volume Decrements; Headward Mass Shift

Nearly as well documented as weight loss is the fact of a headward migration of body mass while in weightlessness. Early hypotheses of centripetal displacement of blood to the thoracic region led to predictions that a relative blood volume excess would be appreciated by volume receptors or indirectly by baroreceptors (Gauer and Henry, 1963). This in turn would evoke circulatory, hormonal, and renal responses in order to reequilibrate intravascular volume. Participation by other body fluid compartments in these adjustments to the absence of gravity has apparently received little consideration.

But measurements of maximal calf girth during early Apollo missions revealed invariably large decrements postflight. This finding was firmly quantitated throughout the Apollo program with an average calf girth decrease for 24 crewmembers of

almost three percent. At that time it was reasoned that this loss represented, at least in part, atrophy of a muscle group prominently employed for human movement in one-g, but relatively little used in weightlessness (Hoffler, et al., 1974).

This type of measurement was amplified on crewmen of the last two Apollo missions in order to approximate true volume determinations. On the supine crewmen multiple circumferences were taken pre- and postflight from above the malleoli to as high on the thigh as practicable, using bony landmarks for repetitive accuracy (Figure 2). Accuracy of the method is about one percent. Calculated lower limb volumes based on assumed circular geometry showed an average loss per crewman of nearly a liter for the combined volume of both legs, or 5%. The largest loss of these six crewmen was 10%. This calculates as more than the total preflight leg blood volume; it is, therefore, clearly obvious that the leg volume deficit must be accounted for by other than vascular contents.

Skylab provided not only confirmation of this change in leg size with even greater postflight size deficits, but also a time course of the alteration in flight. Maximal calf girths measured preceding every orthostatic tolerance test (Lower Body Negative Pressure, v.i.) revealed rapid, early (by fourth day) in flight decrements with very gradual flattening of the regression curve. In even the 84-day flight, it is not fully clear that maximal calf girth has reached a stable plateau (Figure 3). Inflight loss in calf girth averaged well over 7%. This approximates 3.5% volume decrement for that immediate anatomical region.

Actual limb volume determinations by the previously described method

employing multiple circumferences yielded postflight combined losses averaging for all nine Skylab crewmen 1.5 liters (9.1%); the largest loss was 2.3 liters (13.2%) on the SL2 pilot. Inflight left leg volumes obtained only on the three Skylab 4 crewmen were considerably lower than those obtained shortly after recovery. These three averaged for the left leg alone 1.1 liters (14.6%) deficit inflight, but only 0.7 liter (9.4%) immediately after recovery. Approximately 80% of the net inflight decrement occurred by the third or fifth day in orbit when their first leg volume measurements were obtained (Figure 4).

Further information on this rather significant migration of body mass cephalad was acquired by the Apollo-Soyuz (ASTP) crewmen. The left leg of the Command Module Pilot showed a half liter (6%) decrease in volume by six hours in orbit. All three averaged two-thirds liter deficit (8.3%) by 32 hours; the last inflight volumes obtained at 205 hours averaged 0.9 liter (11.3%) below preflight mean values. Earliest recovery values yielded a mean deficit of only a half liter (5.9%) (Figure 5).

In conjunction with almost universal inflight symptoms of head fullness and nasal stuffiness, crew observations and photographs of facial plethora and distended neck and scalp veins, the foregoing data on leg mass changes confirm rather voluminous fluid shifts headward. This, no doubt, involves interstitial and lymphatic as well as vascular compartments. Perhaps even intracellular fluids might undergo a redistribution in weightlessness but there is yet little factual support.

Blood Volume Decrements

Special hematologic data obtained on the three longer Gemini missions (4, 8 and 14 days duration) initially presaged a hemolytic process (Fischer, Johnson,

and Berry, 1967). Red cell mass deficits up to 20% measured by radioisotope dilution were observed postflight. This has subsequently been attributed to the pure oxygen atmosphere of the Gemini vehicle. Somewhat lesser decreases in plasma volume were seen in four of the six crewmen evaluated by the isotope technique. The 14-day mission yielded converse results in plasma volume, i.e., increased postflight plasma volume.

More extensive blood studies were conducted on 21 Apollo crewmen of seven missions (Johnson, P., 1975). Again, postflight blood volume changes varied widely. Red cell mass changes ranged from +2.3% to -17.0% of preflight values, but the 21-crewman average of -7.5% is a highly significant decrement ($p < 0.001$). Curiously, a statistically significant difference between the average change for the six crewmen of Apollo 7 and 8 (mean = -2.2%) and the 15 other crewmen (mean = -9.5%) can be shown. This has been attributed to the fact that atmosphere in the 7 and 8 Apollo vehicles never was purged to pure oxygen content, which was the case on all the other Apollo missions, and, of course was the launch status of Gemini vehicles.

Plasma volume measured on 18 Apollo crewmen was likewise significantly decreased by an average of 6%. No difference between the crewmen exposed to the two types of cabin atmospheres could be demonstrated, however. Likewise, total blood volume significantly decreased by 6.3% and no difference for atmosphere effect occurred (Johnson, P., 1975).

For the much longer Skylab missions, nine crewmen averaged postflight 11.1% loss in red cell mass and 10.8% loss in plasma volume, both highly significant decrements. In these missions a two-gas atmosphere prevailed most of each mission

but periodic exposures to 100% oxygen occurred. An unexpected finding obtained, however, in that the mean difference in red cell mass loss between the three crewmen of the 28-day mission and the three of the 84-day mission was significantly less for the longer mission, while their losses in plasma volume showed a reverse effect. Three astronauts in the 56-day Skylab Medical Experiments Altitude Test (SMEAT, a ground-based chamber test designed to simulate many aspects, including atmospheric, of the Skylab) showed a mean plasma volume change of +1.6% and mean red cell mass change of -2.7%, in no way comparable to changes of either Skylab crew (Johnson, P., 1975).

The etiology and complexity of intravascular volume losses is poorly understood, but it must be clear that intravascular volume decrements are an integral element accompanying space flight.

Decreased Orthostatic Tolerance

Since decreased blood volume would be expected to lower orthostatic tolerance, the former determination has been considered a paramount factor in lessened orthostatic tolerance observed almost universally after space flight. Tendency toward spontaneous syncope has, in fact, occurred in several crewmen immediately after their recovery. In virtually all cases where specific orthostatic stress testing was employed, decreased tolerance has become evident (Shvasty, 1972).

During Gemini missions tilt table testing from a supine control position to 70° head-up tilt utilized heart rate, blood pressure, and change in leg volume as evaluation criteria (Figure 6). Comparison of pre- and postflight results yielded

a simple but meaningful and quantitative assessment of orthostatic tolerance from cardiovascular responses to this form of controlled orthostatic stress. For the 18 Gemini crewmen with available pre- and postflight data, supine resting heart rates increased an average of 29% and tilt-stressed heart rates 51% after flight (Unpublished data, Johnson Space Center, Houston, Texas).

By means of special apparatus enclosing the lower half of the body and with an adequate waist seal, reduced atmospheric pressure can be applied to this isolated region. The effect of the differential pressure is to displace blood and other body fluids footward with much the same cardiovascular effects as erect posture in earth gravity. The level of lower body negative pressure (LBNP) may be varied; the LBNP protocol shown in Figure 7 has been determined to produce orthostatic stress comparable to that of one gravity. Eighteen Apollo crewmen underwent this slightly unorthodox orthostatic test called LBNP; six other Apollo crewmen were tested by simple passive standing. A typical LBNP response is depicted in Figure 8 while a direct comparison of heart rate response to LBNP and tilt table orthostatic stresses in the same crewman is graphically demonstrated by Figure 9. Overall Apollo results yielded average immediate postflight elevations of 11% ($p < 0.02$) in supine resting heart rate and 42% ($p < 0.001$) during orthostatically stressed heart rate. Postflight pulse pressure was reduced in the supine resting state by 8% (N.S.) and by 25% ($p < 0.02$) during orthostatic stress, with at least seven crewmen experiencing pre-syncopal symptoms during their immediate postflight test.

Apollo plethysmographic measurements of the change in calf size as a function of fluid shifts into the legs during LBNP stress have provided additional

physiological information. Maximal change in calf size during postflight LBNP was surprisingly 12% (N.S.) less than preflight values. This has been a troublesome determination, for similar measurements during Gemini tilt tests had indicated a larger leg volume expansion postflight. Skylab revealed an amplifying detail. LBNP stress inflight produced an average 83% greater calf volume increment than the same stress preflight. Immediately after flight this measurement was only 10% greater than preflight, not too unlike the postflight Apollo average.

Moreover, during Skylab missions, LBNP was employed inflight as well as postflight for assessing orthostatic tolerance (Figure 10). Inflight tolerance decreased quite comparable to that seen immediately postflight as determined by heart rate elevations (Figure 11); postflight findings were again like data on Apollo crews. Compared to preflight reference responses, Skylab heart rates further increased during inflight LBNP tests an average of 30% ($p < 0.01$) and 33% ($p < 0.005$) immediately on recovery. Resting heart rate elevations in both phases of the missions, averaged only 10% and 3%, respectively, and were not statistically significant from preflight values. An apparent exception, however, was that resting heart rate actually decreased inflight for the three Skylab 2 crewmen. An interesting and significant positive correlation has been shown to exist between LBNP stressed heart rate and the preceding supine resting heart rate (Figure 12). Average pulse pressure, however, though encompassing great individual variability, was not significantly reduced. Even so, there were 15 inflight episodes of presyncope occurring among six of the nine crewmen and their total 139 inflight LBNP assays; one episode occurred on recovery day (Johnson, et al., 1974).

Decreased Heart Size

The only other discrete data available from which regional body or organ volumes may be derived are chest X-rays and echocardiographs. Standard posterior-anterior chest X-rays have been taken as a clinical routine before and after each U. S. space flight on every crewman. A review of these films provides a large base for assessing heart size in this planar projection (Figures 13 and 14). The simplest determination with some experiential sanction is perhaps the cardiothoracic (C/T) ratio. Figure 15 tabulates C/T ratio measurements on the basis of diametral and areal dimensions for 8 Skylab crewmen. Summing data from four Mercury crewmen making orbital flights, 18 Gemini, 30 Apollo and 9 Skylab crewmen, a postflight decrement in the C/T ratio of -0.018 is shown to be statistically significant at $p < 0.001$ (Unpublished data, JSC, Hoffler, et al., 1974 and Nicogossian, et al., 1974).

Pre and postflight echocardiograms were obtained only on Skylab 4 and ASTP crews but postflight data on the latter were compromised by the noxious gas episode. Two of the three Skylab crewmen showed modest postflight decrements in resting left ventricular end-diastolic volume and stroke volume. Return to preflight dimensions occurred between 11 and 31 days after recovery (Henry, et al., 1974).

Collectively, these data strongly support a hypothesis of decreased postflight cardiac filling and stroke volume, probably directly related to decreased blood volume. An immediate consequence is decreased orthostatic tolerance long observed and now well documented. In the great majority of specific tests, crewmen have demonstrated adequate cardiovascular compensation by one or more

methods — especially by elevated heart rate and possibly by altered peripheral resistance.

Altered Exercise Capacity

In a somewhat counter, but further confirmatory argument, exercise capacity, quantitated by bicycle ergometry, which has almost universally been reduced postflight, never deteriorated inflight for Skylab crewmen. On the contrary, they demonstrated progressively increased levels of exercise activities in the succeeding missions (Michel, et al., 1974). It may be reasoned that, regardless of the absolute blood volume deficit induced by orbital flight, the effective resting volume was adequate for basal metabolic needs. It is also probable that, with a facilitated cardiac return postulated from headward fluid shifts and perhaps enhanced by any lower extremity activity, cardiac output satisfied inflight metabolic requirements of even high levels of work output. Apparently only during application of an orthostatic stress (LBNP or gravity by tilt or by stand, inflight or postflight) while absolute blood volume is decreased, is the net volume deficit functionally manifest.

Summary

The keystone datum in support of this hypothesis, therefore, probably involves an inverse relationship between orthostatically stressed heart rates (Hoffler, et al., 1974 and Johnson, et al., 1974) and blood volume (Johnson, P., 1975). Since both of these measurements have been made pre- and postflight on a large number of space crewmen, it is possible to express a sort of population response. Figure 16 depicts percentage changes in these data after flight for 21 Apollo, 3 Skylab

Medical Experiments Altitude Test (SMEAT, v.s.), and 9 Skylab crewmen. The negative correlation is highly significant ($r = -0.54$, $p < 0.005$) and would seem to offer strong support for the hypothesis.

SURMISED DETERMINATIONS

If a hypothesized decrease in total absolute blood volume be granted, with central blood volume either maintained or perhaps even augmented, certain indirect evidences of these blood volume changes may have been detectable. Among these are systolic time intervals, vectorcardiographic elements, leg blood flow, and leg compliance.

Systolic Time Intervals

Systolic time intervals (STI) are temporal measurements derived from non-invasive sensors yielding important physiological and clinical assessment of contraction characteristics of the heart. The major signals and intervals required are shown in Figure 17. Taken pre- and postflight on the last three Apollo crewmen and on all nine Skylab crewmen (Bergman, Hoffler, and Johnson, 1974) STI seem perhaps to allow some inferences regarding cardiac performance (Figure 18). It is well documented that application of LBNP causes a pooling of blood in the lower part of the body, especially in the legs (Wolthuis, Bergman, and Nicogossian, 1974 and Wolthuis, et al., 1975). This leads to decreased central venous pressure and probably decreased right atrial filling or preload as evidenced by increased pre-ejection period (PEP). In any case, left ventricular performance is diminished with decreased stroke volume and ejection time.

During preflight LBNP stress tests, the pre-ejection period (PEP) considerably lengthened on all crewmen while left ventricular ejection time (ET) shortened. The resulting PEP/ET ratio changed markedly and is therefore a strong determinant of the

degree of altered ventricular performance. During postflight evaluations, the PEP/ET ratio at supine rest was more than 20% greater than preflight recordings. Under LBNP stress, this ratio was around 30% greater postflight, and required several days to descend to preflight values.

Of course, one could as well argue that these STI data are due to depressed ventricular contractility rather than to a decreased ventricular filling, or to both factors. And no direct inflight data exist to confirm or refute. It would seem rather illogical, however, that inflight exercise capacity demonstrated by Skylab crewmen throughout flight even to deorbit time could be so well maintained in the presence of significant myocardial dysfunction. The immediate exercise decrements postflight must be due to some more acute process which is rapidly reversible. The fluid displacement theory fits the picture.

Vectorcardiogram

A further step using indirect data can be made with vectorcardiographic data taken pre- and postflight on the last nine Apollo crewmen and on all nine Skylab crewmen inflight as well (Hoffler, et al., 1973, 1974 and Smith, et al., 1974). In passing it should be noted that no pathological abnormalities of ultimate clinical concern have been seen, although most crewmen have demonstrated occasional ectopic and rhythm aberrations. It has been shown that certain elements of the vectorcardiogram are consistently and predictably altered upon application of LBNP (Figure 19), which, like gravity, readily displaces blood footward. Among the more sensitive respondents to LBNP is the maximal vector magnitude of the

P-loop. At -50 mmHg LBNP this maximal P-wave vector is increased in the normal adult male approximately 30%. On Apollo crewmen postflight, there was an increase of 56% during LBNP. Skylab crewmen demonstrated an astonishing 75% increase postflight, but more importantly, inflight values averaged 78% greater than the corresponding measurement at rest. A bit perplexing, however, is the fact that this P-vector at rest inflight, when one might postulate an increased blood volume, was also greater by 24% than the preflight reference. Of course, the earliest inflight VCG was not made until the fourth mission day and the true time course of proposed fluid shifts can only be guessed.

If one will allow some inference from the P-vector response during LBNP when caudad blood shifts occur, it will be easy to surmise that a relatively larger effect should be assumed inflight. Without attempting an explanation of the etiology or a correlation between cardiac electrical and mechanical elements, the data stand firmly in support of a reproducible event probably related to degree of atrial filling.

Leg Blood Flow

On the opposite end of these fluid shifts are leg blood flow data derived inflight only on Skylab 4 crewmen. Using an arm blood pressure cuff from onboard medical equipment and the leg band plethysmographs from the LBNP experiment, measurements of calf blood flow were undertaken at cuff occlusion pressures of 30 mm and 50 mmHg. Both the initial slope and the later slope continuing for 20 seconds were measured from three pressurization cycles at each of seven test periods over

the 84-day mission (Thornton and Hoffler, 1974).

The initial slope more closely approximates true leg blood flow since after venous capacity is exceeded, inflow occurs against progressively increasing tissue back pressure. During three preflight reference tests, initial slopes (Figure 20) of blood flow ranged between 2-4 volumes percent/minute. The second slope preflight generally was ≤ 1 volume percent/minute. Inflight values of the initial slope varied widely, but ranged as high as 10-12 volume percent/minute and were nearly always above 4 volumes percent/minute. The second slope inflight rarely exceeded 4 volumes percent/minute, but still was usually about twice preflight levels. In many cases there was no evidence of a lessening slope over the 20 seconds occlusion interval, normally an indication of increasing back pressure.

Admittedly these data are crude and suffer from variation in hand inflation of the cuff, improvisation of design, and other operational discrepancies, but they point distinctly to increased inflight leg blood flow. This for the present is attributed to the decreased leg volume offering less impedance to regional arterial flow rather than to an actual increase in cardiac output as such. This, of course, needs verification.

Leg Compliance

One related datum is maximal percentage leg volume change attained during LBNP with the described plethysmograph. As already noted, in all normal subjects two distinct slopes may be described. The early and greater slope is usually attributed to the zone of free venous distensibility and the later, more shallow slope, at least

in part, to stress relaxation and fluid transudation from the vascular compartment. The latter presumption is also supported by the fact that calf volume after release of LBNP almost never returns completely to pre stress levels.

Apollo and Skylab data regarding maximal change in calf size during LBNP have already been described with respect to amount of blood pooled. Postflight changes have been not different from preflight, while inflight Skylab data showed almost a doubling of preflight values. Since the LBNP stressing protocol remained unchanged, it is clearly evident that an inflight compliance change must have occurred. Whether this is totally a functional phenomenon of vessels, is primarily due to altered turgor of adjacent tissue, or is some combination effect involving the whole limb, matters perhaps little. Any increased compliance of the legs would materially enhance pooling of blood out of the usable circulating compartment while a reduced absolute blood volume had already compromised cardiovascular reserves. This is the presently interpreted state of returning space crews. Not until new evidences have been made available can we more objectively understand and perhaps prevent this condition.

OUTSTANDING QUESTIONS - CONCLUSIONS

The vantage available at this juncture should allow relatively free reign in conceptualization and design of future ground-based and inflight experiments which will further resolve and clarify principal aspects of cardiovascular function in the space environment.

Perhaps among the first basic questions should be a more refined evaluation of absolute volumes and their redistributions and time course involved in fluid shifts in space. Definitive measurements will likely necessitate multiple radio-isotope or other markers for specific fluid compartments with serial quantitative determinations.

Development of techniques, preferably noninvasive, for measuring regional blood flow and perfusion are integral to volumetric evaluations. Liberal use of such devices as the gamma camera and ultrasonic probe should be encouraged. Provision must be made for continuous and/or rapidly repetitive measurements during the critical phases of flight - launch and deorbit. And, not least, there must be decision making capability for the onboard investigator and provision for his real-time inputs into the progress and direction of researches.

Completeness requires that other organ and functional body systems be explored concurrently. Precise and definitive fluid balance studies have yet to be performed in space. Insensible water loss very likely is significant. Not only must urine output be well documented, but renal blood flow as well as neuro-endocrinological aspects accompanying hemodynamic control of urine production

need unveiling. Moreover, the receptors which detect and initiate action upon perceived increases or decreases in volume or pressure are in many respects hypothetical. An understanding of mechanisms is essential to intelligent and optimal therapeutic and preventative measures. Much of this is necessarily the determination and application of basic physiology.

Perhaps that such enigmas as the loss of red cell mass and the space sickness syndrome of the early orbital period have etiological foundations in circulatory disturbances can be justifiably conjectured. The latter condition has certain elements quite akin to hyperemesis gravidarum and to the presumed hydrops of Ménière's disease. Since the mechanisms involved in red cell production have so far escaped clinical investigators, here is a rather fertile field perhaps ready made for space researchers.

Consideration of and compensation for variations in other aspects of the space environment must be assured. It is not yet known to what extent, if any, a hypobaric atmosphere, altered atmospheric content, maintained low humidity, or other perhaps unperceived conditions influence the subject in question. Neither can one be certain of the degree of transference permitted between so-called ground-based analogs of weightlessness and the true environment of orbital space flight.

Thus, a fitting final question might be, with what may the weightlessness of space be legitimately compared? Immobilization is not the preferred analogue. Astronauts are ever so active. Immersion has much to speak for it: universal

buoyancy and a measure of equilibrated external forces tending to produce a centripetal shift of body mass. The diuresis accompanying water immersion perhaps has biased our thinking on what, in fact, occurs upon "space immersion." Perhaps a clear distinction should be made between the two forms of centripetal forces; the one in space is more properly cephalad in direction. Water exerts essentially equal pressure over the whole body surface. A sensation of head fullness is not appreciated. On the other hand, in weightlessness, elastic tissue forces of the lower body, always previously conditioned by the inexorable counter-
ing force of gravity, suddenly become unopposed. Tissues of the upper body are not so conditioned and experience immediately an anomalous distension, poorly opposed. And, of course, the internal organs all share equally the absence of gravitational force, which is not the case in immersion. What might be the effect, for instance, upon renal blood flow? Or upon cerebral or coronary dynamics? An intelligent guess seems not yet possible.

The last and most widely used analogue for weightlessness is bed rest. Magnitude of experience, breadth of associated studies, and simplicity of performance concede to bed rest pre-eminence. There are also many ancillary contributions in clinical medicine dealing with fluid shifts, particularly in congestive heart failure. A slight modification recently entertained by Russian and American investigators adds perhaps an additional degree of realism - namely, head-down tilt (Yarullin, et al., 1972 and Nicogossian, et al., 1975).

As of the present moment, with very few studies available, it is not possible

to state categorically if head-down tilt achieves any further fidelity, or if such gain is even justified in the face of some increased subject discomfort. Nor has an optimal angle of head-down tilt been determined. But, at least subjectively, certain elements of the space syndrome are more nearly reproduced. Here is an area presently amenable to laboratory investigations. Basic physiologists and clinicians could, no doubt, contribute importantly with proposals suggested by this new ability to manipulate body fluids.

In conclusion, the cardiovascular system figures prominently in all of man's endeavors, in his sicknesses and his health, in his inner emotions and external conduct, in his exertions, failures, and achievements. It is not likely that it will preclude his frontier advances in space, for the cardiovascular system has always been adaptable. But a better understanding of its sometimes puzzling responses to the space environment will not only help lessen the cardiovascular strain from man's inquisitiveness and adventuresomeness, but also assist man in assuring optimal adaptation and function of this truly cardinal system for his overall well-being in the new environment called space.

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NATO CARDIOVASCULAR PRESENTATION

1. NASA-S-75-12448 PERCENT WEIGHT LOSS vs. MISSION DURATION
2. NASA-S-74-3274 METHOD OF LEG VOLUME MEASUREMENT
3. NASA-S-75-12447 SKYLAB 4 CALF GIRTHS
4. NASA-S-75-12446 SKYLAB 4 LEG VOLUMES
5. NASA-S-75-12445 ASTP LEG VOLUMES
6. NASA-S-66-778 GEMINI 7 TILT TEST - HR, BP, PERCENT
CHANGE LV (After Berry and Catterson, 1967)
7. NASA-S-74-3245 LBNP PROTOCOL
8. NASA-S-69-4315-V APOLLO 8 LBNP TEST - HR, PERCENT CHANGE LV
9. NASA-S-69-4271-X COMBINATION 7+9 FOR HEART RATE
10. NASA-S-74-20161 SL PHOTOS OF LBNP
11. NASA-S-74-3235 HR SL 3 SPT
12. NASA-S-74-3244 HR - STRESS vs. REST
13. NASA-S-71-3131-S CHEST X-RAYS APOLLO 10 CMP
14. NASA-S-74-4937 CHEST X-RAYS SKYLAB 4 SPT
15. NASA-S-74-4549 SL C/T RATIOS (SYSTOLIC & DIASTOLIC
(After Nicogossian, et al., 1974)
16. NASA-S-75-12450 PERCENT CHANGE HEART RATE vs. PERCENT
CHANGE BLOOD VOLUME
17. NASA-S-74-4940 STI EXPLANATION (After Bergman, et al., 1974)
18. NASA-S-74-4330 SYSTOLIC TIME INTERVALS - SKYLAB 4
(After Bergman, et al., 1974)
19. NASA-S-74-4866 VCG AMPLITUDE MEASUREMENTS - SKYLAB
20. NASA-S-75-12449 LEG BLOOD FLOW - SKYLAB 4 SPT

FIGURE LEGENDS

- Figure 1. Percentage weight loss of U. S. space crewmen as a function of mission duration, based on preflight (usually the mean of multiple values) and immediate postflight weights.
- Figure 2. The method of leg volume measurement by obtaining multiple circumferences. Calculation is based on assumed circular geometry and summation of multiple, truncated, conical volumes.
- Figure 3. Maximal left calf girths in centimeters for all three Skylab 4 crewmen. Pre-, in-, and postflight mission phases are indicated. Variation in individual measurements does not obscure the exponential decrease in calf size during the flight, nor the rapid restitution of size after return to earth gravity. Time course and magnitude of this measurement are important in assessing fluid shifts headward.
- Figure 4. Left leg volume in liters for all three Skylab 4 crewmen. Earliest inflight values for two crewmen are on Mission Day 3. Volume decrement seems more abrupt and of greater magnitude than the single maximal calf measurement in Figure 3.

Figure 5. Left leg volume in liters for all three ASTP crewmen. The earliest inflight value for one crewman is at 6 hours mission elapsed time and 32 hours for all three. In this, as in Figure 4, immediate postflight leg volumes are considerably greater than the corresponding last inflight value.

Figure 6. Heart rate (beats per minute), blood pressure (systolic and diastolic, in millimeters of mercury), and change in leg volume (in percentage) during a 25-minute, 70° tilt test protocol, the first and last 5 minutes being in the horizontal, supine position. Preflight mean curves are solid lines and the first postflight test values are dashed (or hatched). The crewman was Command Pilot of the 14-day Gemini 7 flight (After Berry and Catterson, 1967.)

Figure 7. The Lower Body Negative Pressure (LBNP) protocol used for Apollo and Skylab assessments of orthostatic tolerance. It is, like the tilt test used for Gemini crew evaluations, 25 minutes in duration with the first and last 5 minutes being at supine rest, ambient pressure conditions. Step-wise decreases in the lower body stressing pressure provide multiple levels of orthostatic stress.

Figure 8. Heart rate (in beats per minute) and change in leg volume (in percentage) during a 25-minute LBNP test protocol. Preflight

mean curves are dashed and the first postflight test data 3 hours after splashdown are solid lines. The crewman was Commander of the Apollo 8 flight - the same crewman depicted in Figure 6 tilt test data.

Figure 9. Heart rate (in beats per minute) during both 25-minute 70° tilt and LBNP test protocols. Preflight mean curves and immediate postflight curves are differentiated and labeled accordingly. The same crewman flew both named space missions. See Figures 6 and 8.

Figure 10. Operational set-up for performing the Skylab LBNP test protocol in the one-g trainer where most preflight tests occurred, in the Cardiovascular Mobile Laboratory where most postflight tests were performed, and in the orbiting Skylab itself where the crew conducted all such tests.

Figure 11. Composite plot of supine resting and -50 mmHg LBNP stressed (the maximal level) heart rates (in beats per minute) for the Skylab 3 Science Pilot for every LBNP test over all three mission phases. Vertical lines delineate launch and recovery dates. Elevations in both resting and orthostatically stressed heart rates during the flight and in the immediate postflight period are clearly apparent.

Figure 12. Maximal attained stressed (-50 mmHg LBNP) heart rate as a function of the corresponding and immediately preceding supine, resting heart rate (both in beats per minute) for all three crewmen of the Skylab 3 mission. Regression equations obtained from multiple tests during all three mission phases have significant r -values.

Figure 13. Standard 6-foot posterior-anterior chest roentgenograms of the Apollo 10 Command Module Pilot taken 5 days before launch and on recovery day. The change in heart size is visually apparent. Both films were randomly exposed with respect to the cardiac cycle.

Figure 14. Standard 6-foot posterior-anterior chest roentgenograms of the Skylab 4 Science Pilot taken 10 days before launch and on recovery day. Both films were exposed by electrocardiographic signal triggering to correspond in time to peak systole.

Figure 15. Determinants of cardiac size by diametral and areal cardio-thoracic ratios averaged from eight Skylab crewmen based on standard 6-foot posterior-anterior planar roentgenograms. Two other independent measures of heart size are also tabulated. Triggering from electrocardiographic signals provided both systolic and diastolic exposures. Differences between pre- and postflight sizes are statistically shown. (After Nicogossian, et al., 1974.)

Figure 16. The change in immediate postflight orthostatically stressed heart rates (in percentage) from preflight mean reference values as a function of change in corresponding post- and preflight total blood volumes (in percentage) measured by radioisotope dilution methods. Both LBNP and passive 90° standing orthostatic stress techniques are included. The equation of the best fit linear regression through all 33 data points is given and the r-value of -0.54 is statistically significant ($p < 0.005$).

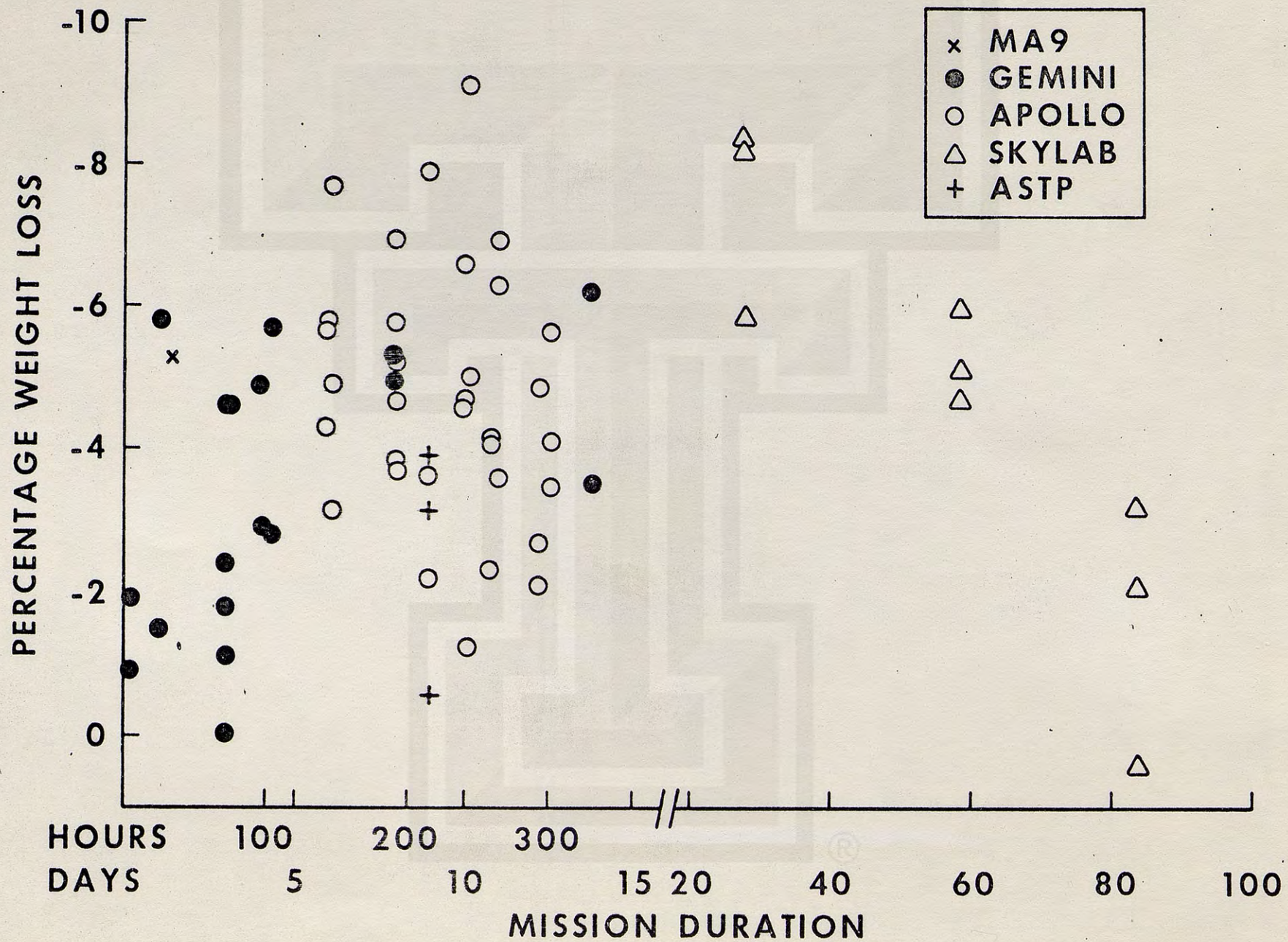
Figure 17. A composite of traces from an electrocardiogram lead, a carotid pulse wave, a phonocardiogram, and a pneumogram to show the temporal relationships from which systolic time intervals (STI) are derived. PEP=pre-ejection period, ET=left ventricular ejection time, Q=initiation of the QRS complex, S₂=initiation of the second heart sound, and R-R=the cardiac cycle interval. All temporal values are usually expressed in milliseconds. (After Bergman, et al., 1974.)

Figure 18. The ratio (unitless) of the pre-ejection period (PEP) to the left ventricular ejection time (LVET or ET) averaged for all three crewmen of Skylab 4, under supine resting and LBNP stressed conditions, at specified pre- and postflight test dates. No inflight data for this determination have been obtained. (After Bergman, et al., 1974.)

Figure 19. Amplitude measurements of the vectorcardiograms from the nine Skylab crewmen. Changes (percentage) are based on the nine crewmen group mean, preflight, supine resting values as reference. Changes are given for the effect of LBNP alone in the LBNP preflight column and for the effect of space alone in the flight in-flight column. Compound effects are registered in other columns due to various combinations of LBNP, the orbital state, and recovery conditions. Pmax MAG = P-wave maximum vector magnitude, QRSmax MAG = QRS complex maximum vector magnitude, QRS-E CIRC = QRS spatial Eigenloop circumference, and STmax MAG = ST-wave maximum vector magnitude (all in millivolts in the preflight reference column). Statistical significance is indicated under P or was not computed under * columns.

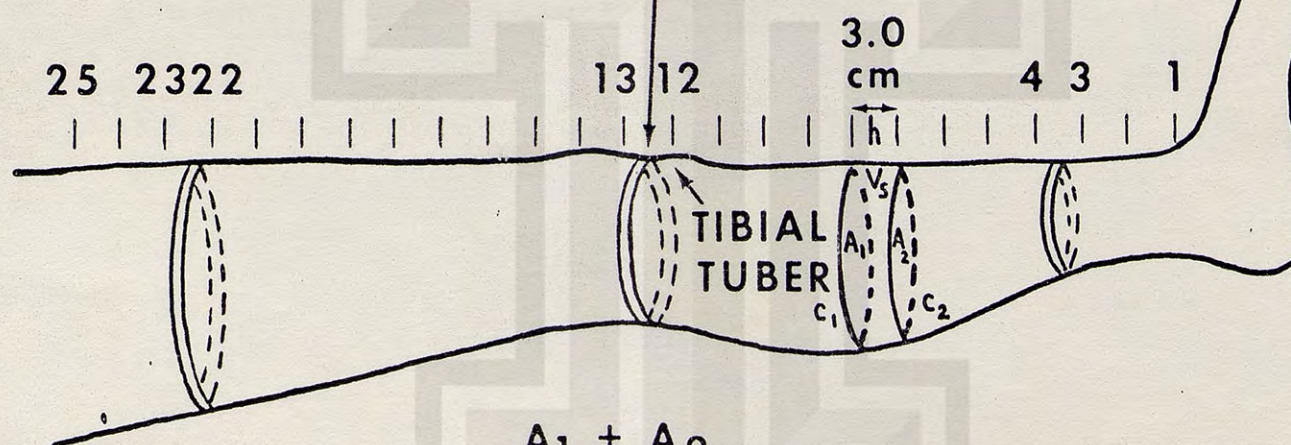
Figure 20. Calf blood flow (in volumes percent per minute) at various tests pre-, in-, and postflight for the Skylab 4 Science Pilot, based on occlusion cuff plethysmography using capacitance bands for volume determination. Slope 1 is the initial rapid volume change after inflation of the occlusion cuff; slope 2 is that after a definite hip or reduction in volume change has become evident. Bars depict ± 1 standard deviation from 3 successive 20-second occlusion traces at each test. The inset at left shows one typical volume trace following cuff occlusion. Cuff occlusion pressure was 50 mmHg.

NASA-S-75-12448



LEG VOLUME MEASUREMENT BY CIRCULAR CONE SEGMENTS

MIDDLE VELCRO STRAP = INDENTATION BETWEEN
ANATOMICAL REFERENCE KNEE CAP AND
TIBIAL TUBEROSITY



$$V_s = \frac{A_1 + A_2}{2} \cdot h$$

$$= \left[C_1^2 + C_2^2 \right] \cdot \frac{h}{8\pi}$$

A = CIRCULAR AREA
C = CIRCUMFERENCE
h = HEIGHT = 3.0 cm
V_s = CIRCULAR CONE
VOLUME

Handwritten notes:

$$A = \pi r^2$$

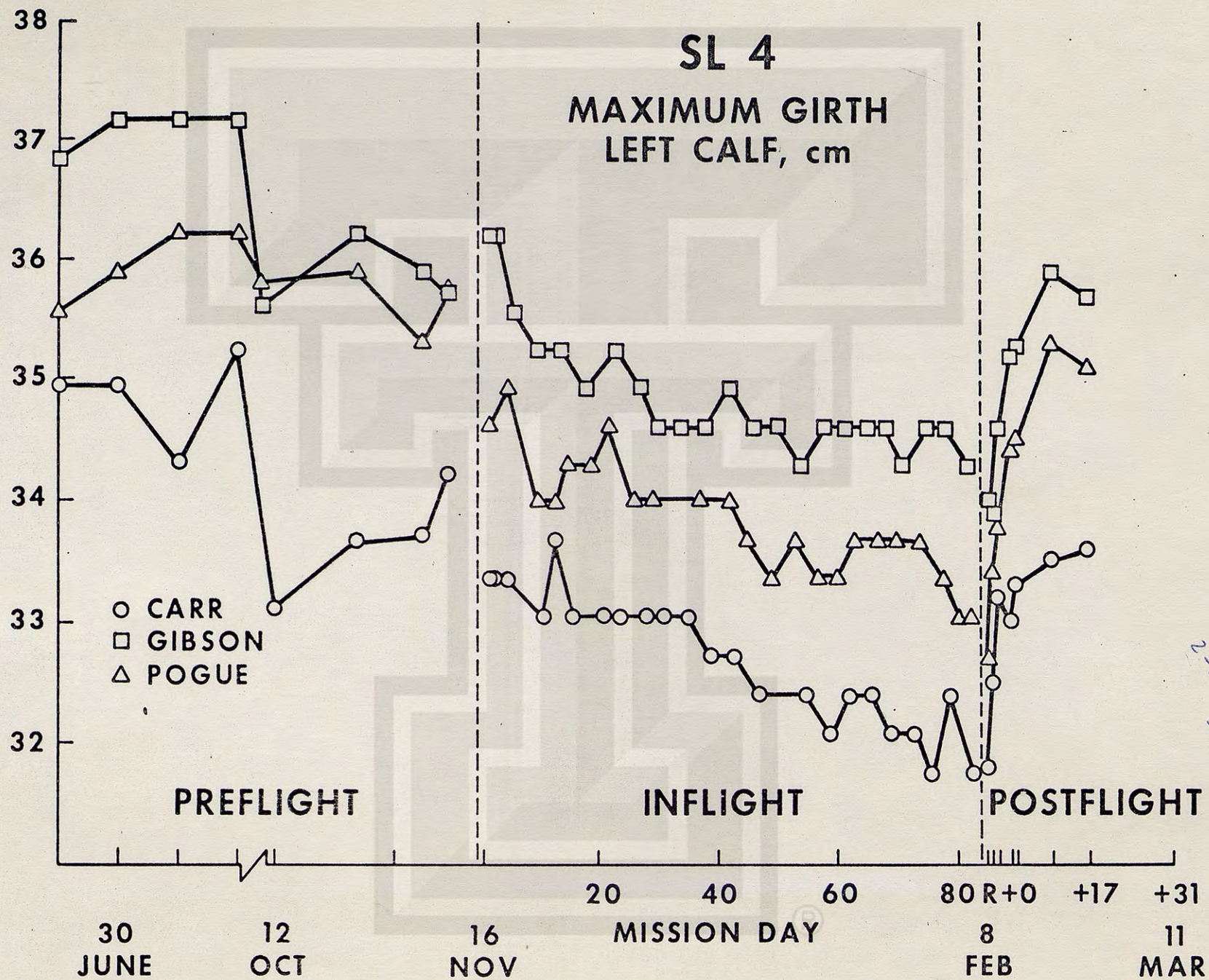
$$= \pi \left(\frac{C}{2\pi} \right)^2$$

$$= \frac{C^2}{4\pi}$$

$$2\pi r = C$$

$$r = \frac{C}{2\pi}$$

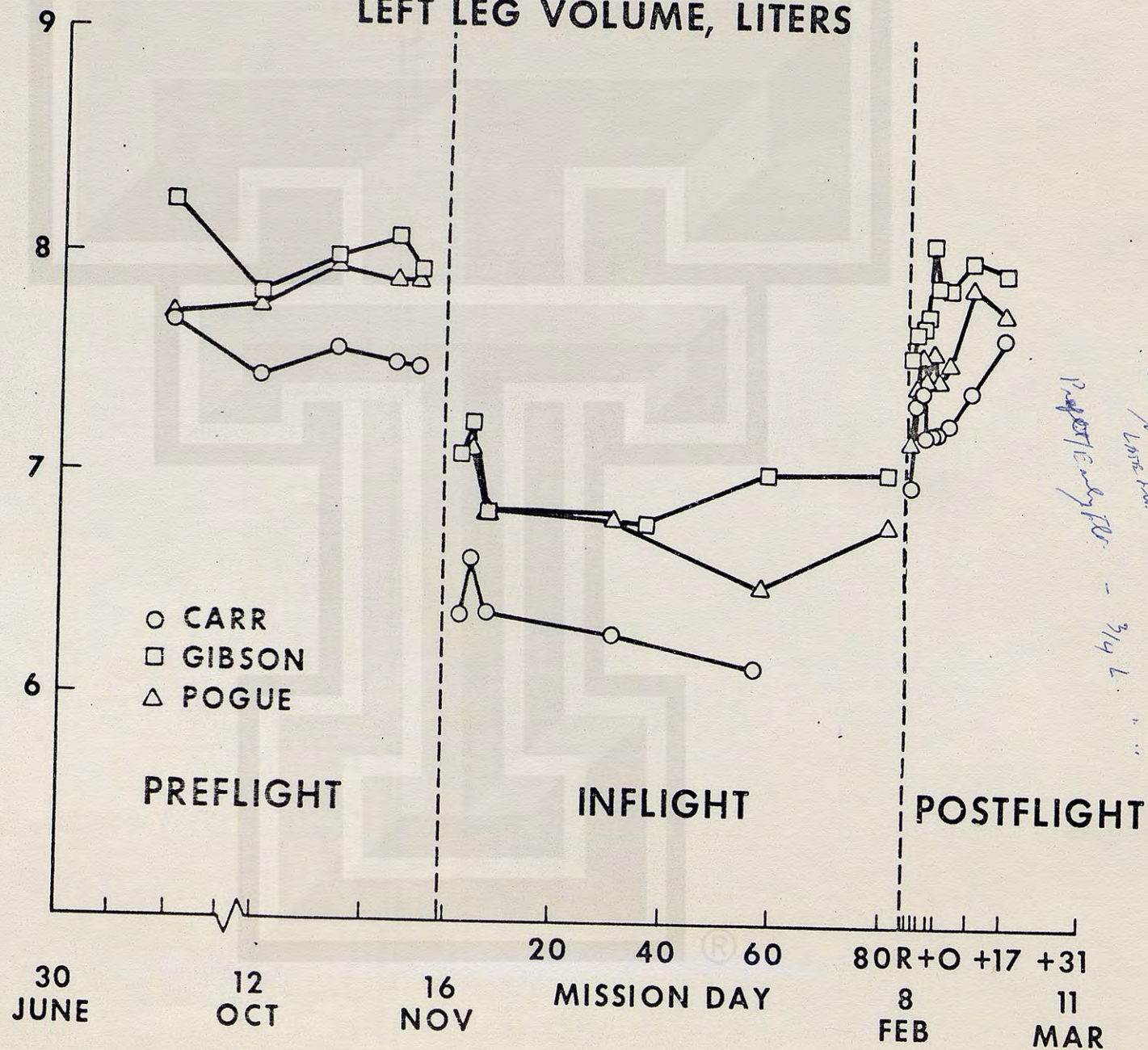
NASA-S-75-12447



2-2 1/2 in. scale

SL 4

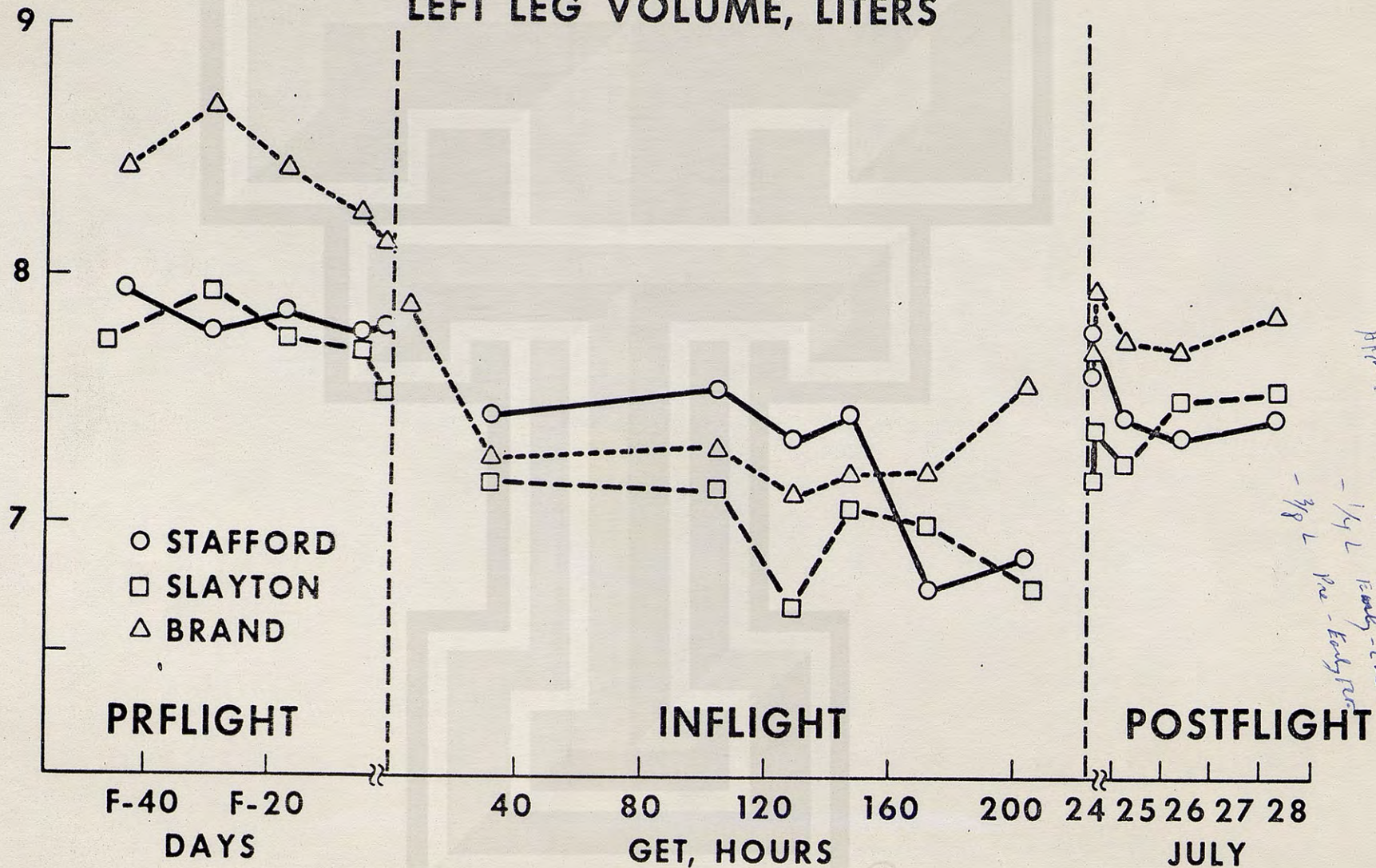
LEFT LEG VOLUME, LITERS



NASA-S-75-12445

ASTP

LEFT LEG VOLUME, LITERS



break
- 1/4 L pre-post
- 1/4 L early-1st post
- 3/8 L pre-early post

LAUNCH
15 JULY 75

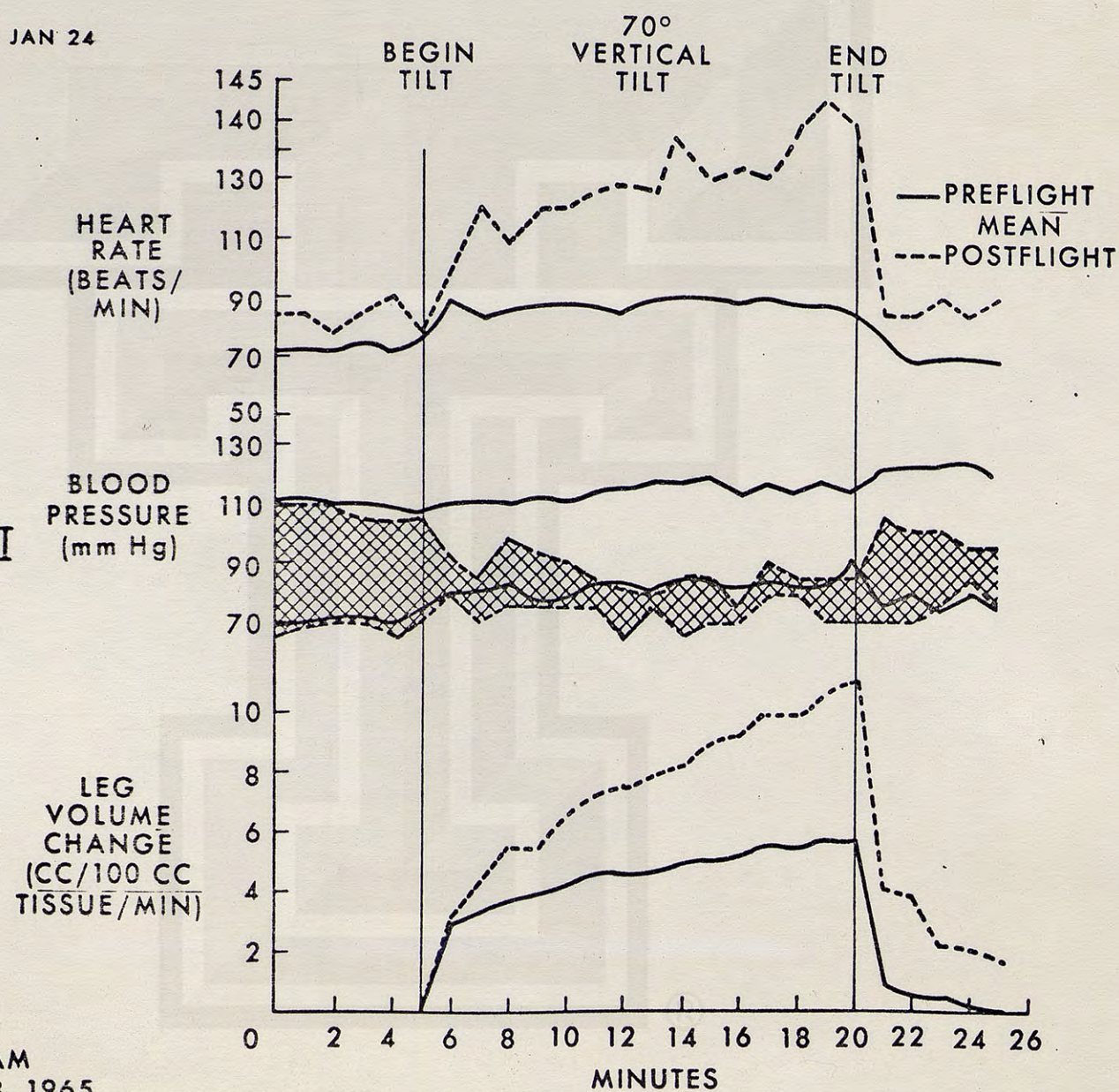
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NASA-S-66-778 JAN 24

MISSION
GEMINI VII

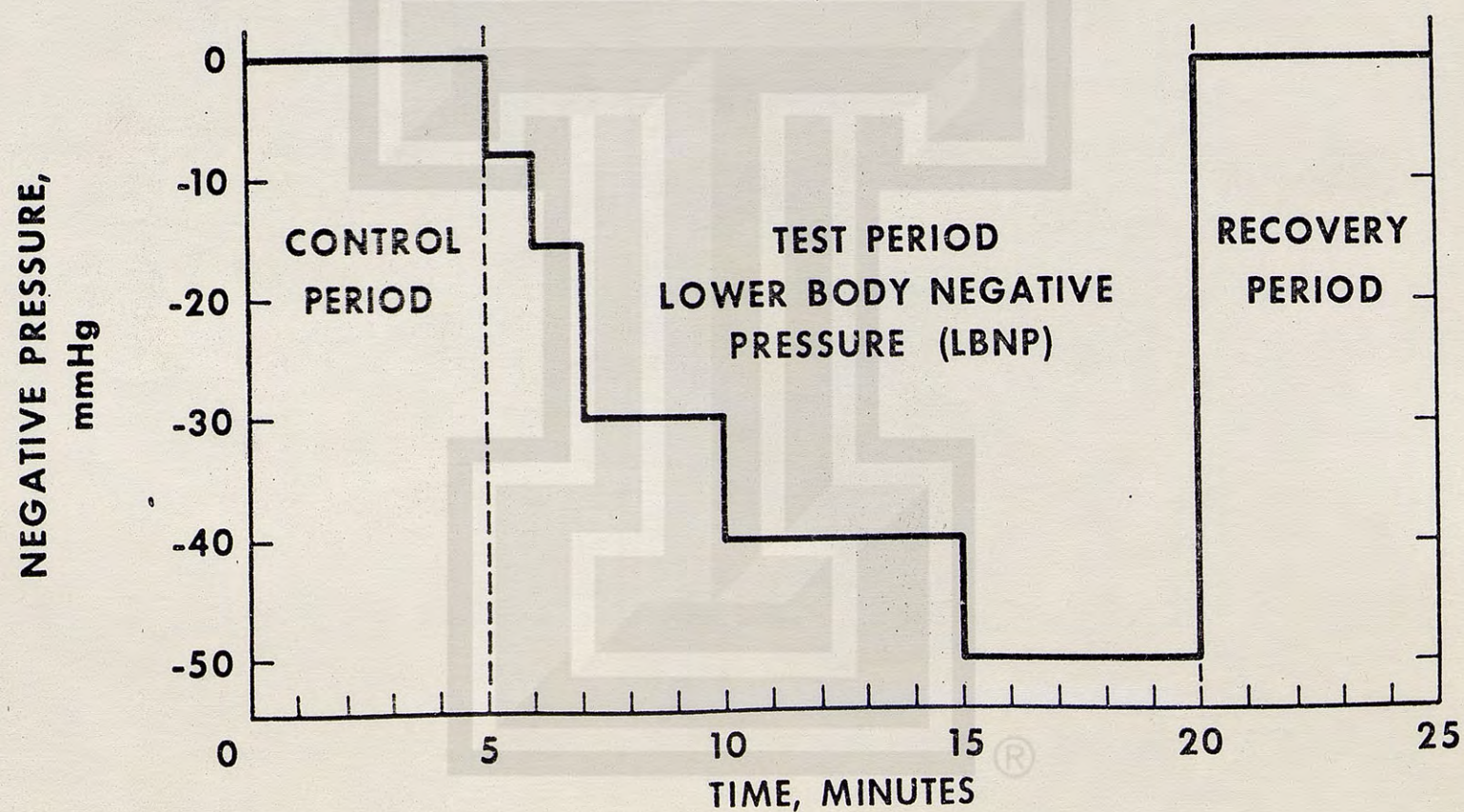
TILT
TABLE
DATA

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TILT: NO. 1
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DATE: DEC 18, 1965



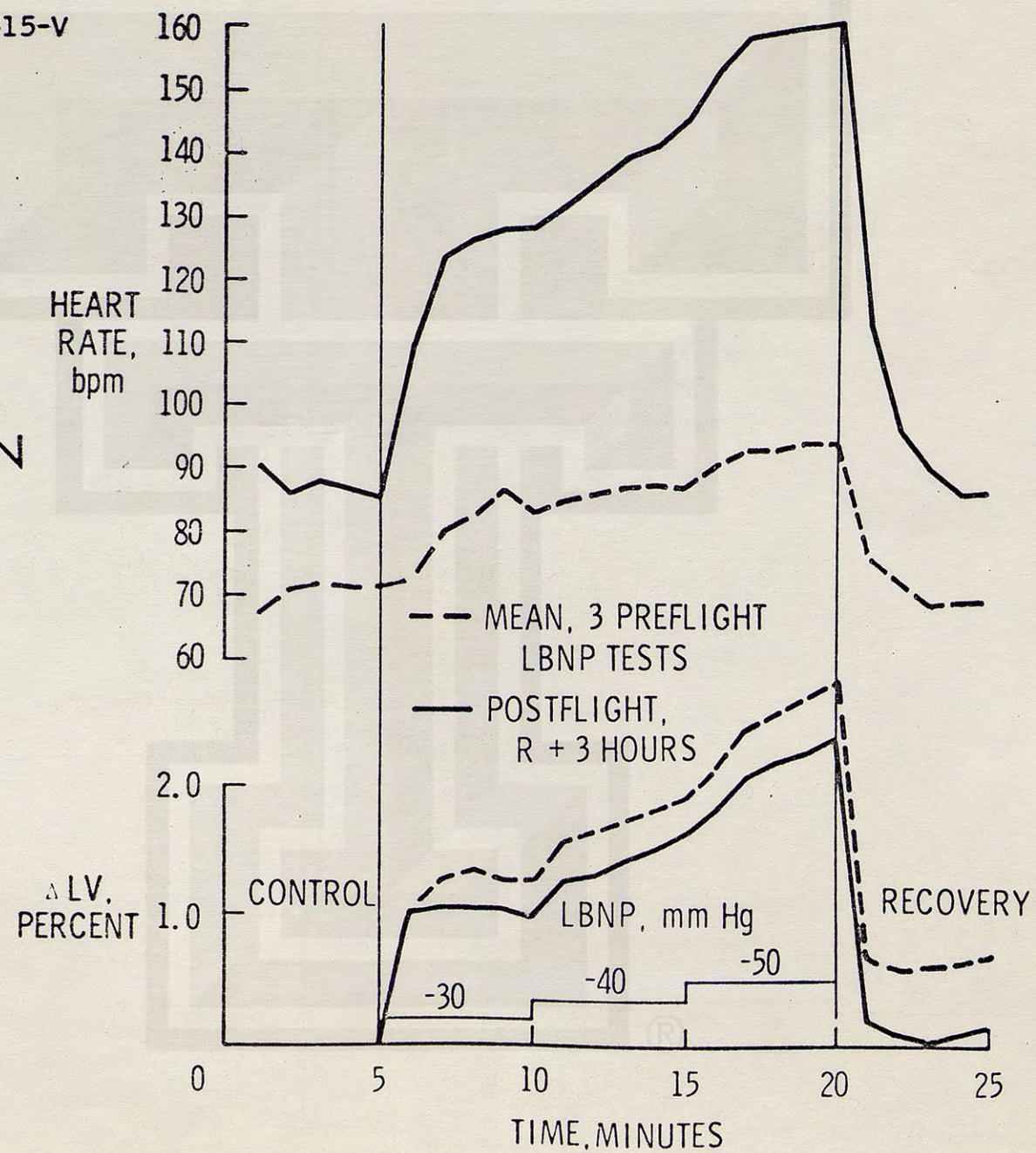
NASA-S-74-3245

THE LOWER BODY NEGATIVE PRESSURE PROTOCOL USED FOR SKYLAB CARDIOVASCULAR EVALUATIONS ASSESSING ORTHOSTATIC TOLERANCE



NASA-S-69-4315-V

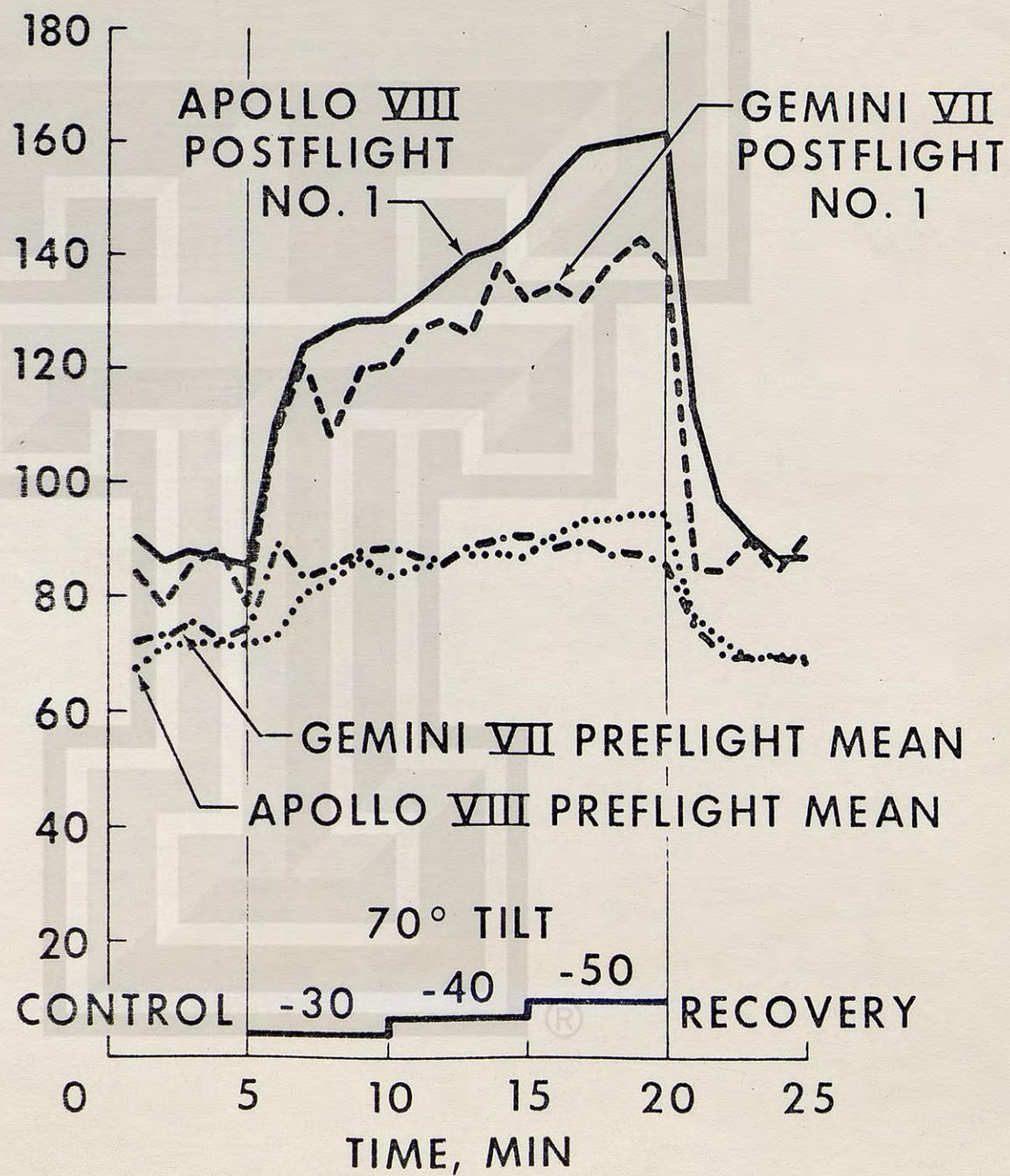
BORMAN

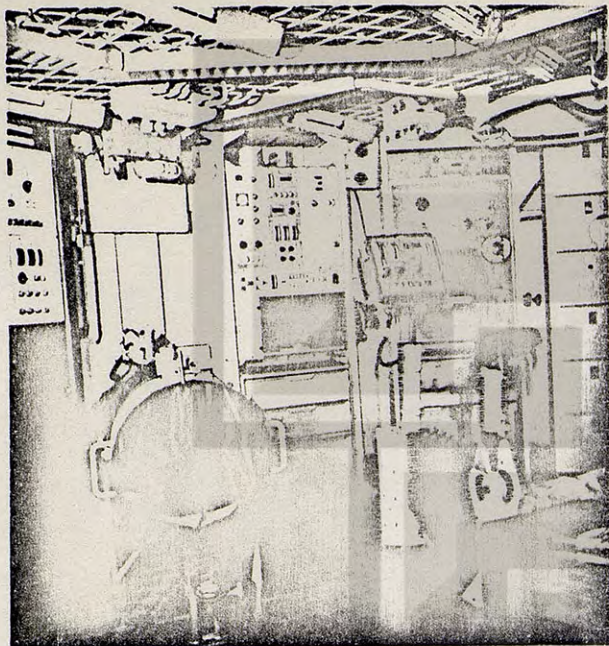


NASA-S-69-4271-X

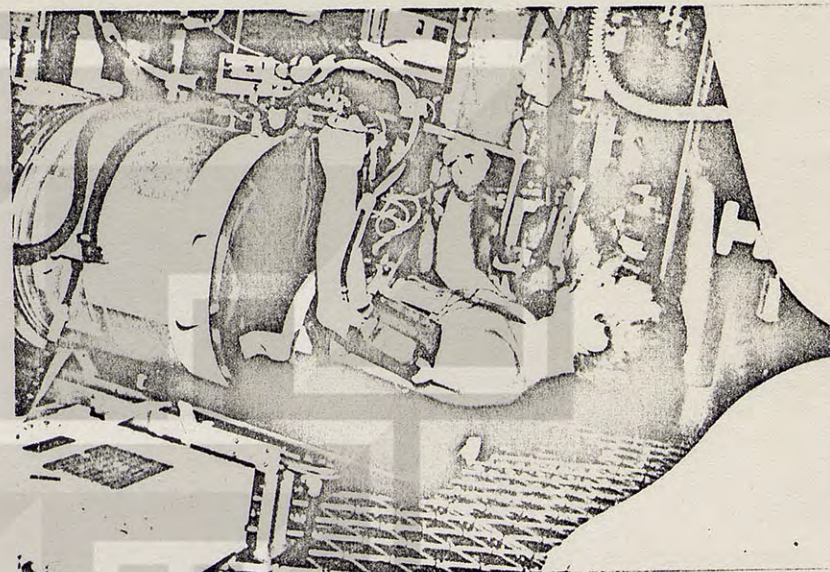
BORMAN

H R,
BPM





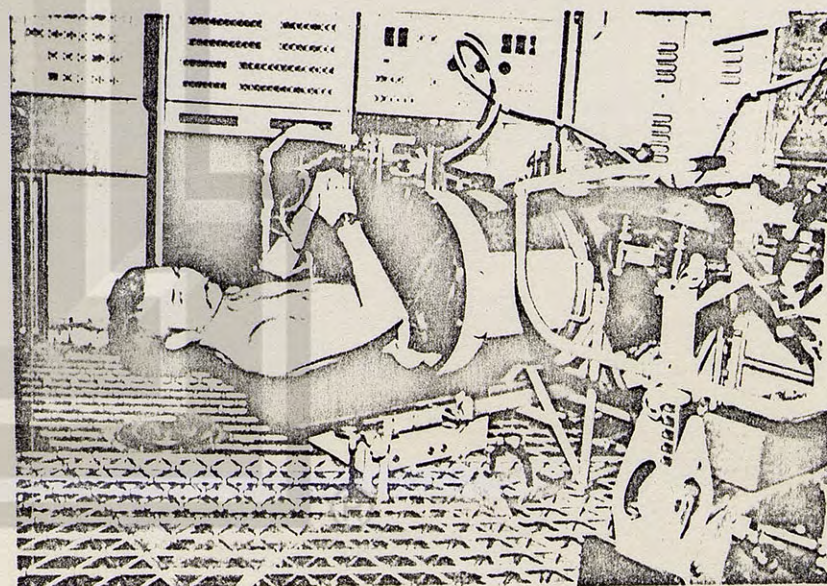
I-G TRAINER



SKYLAB-3 OWS



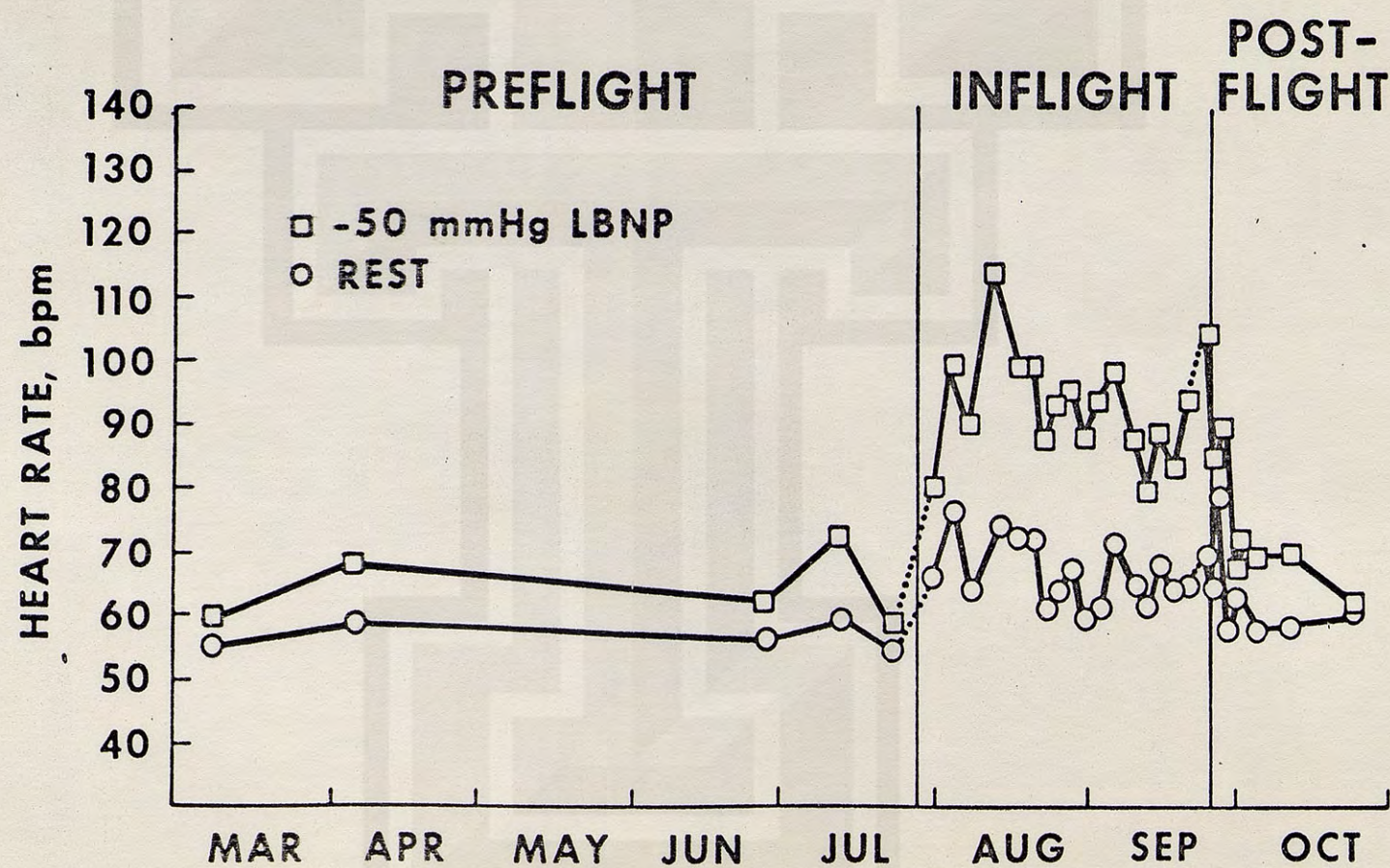
SKYLAB MOBILE LABORATORIES
(CARDIOVASCULAR)



SKYLAB-3 OWS

NASA-S-74-3235

SKYLAB 3 - SPT

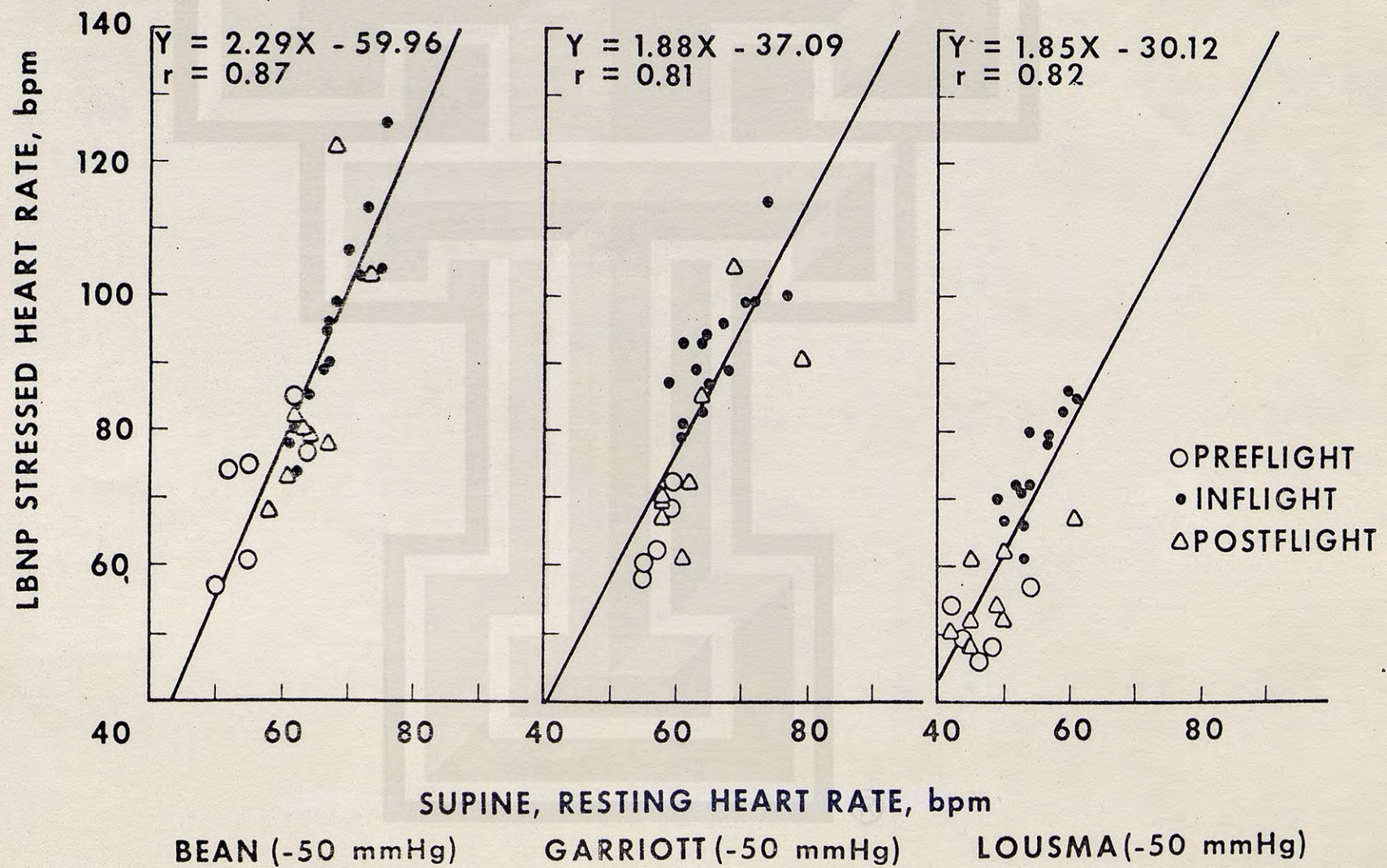


SKYLAB 3

CDR

SPT

PLT

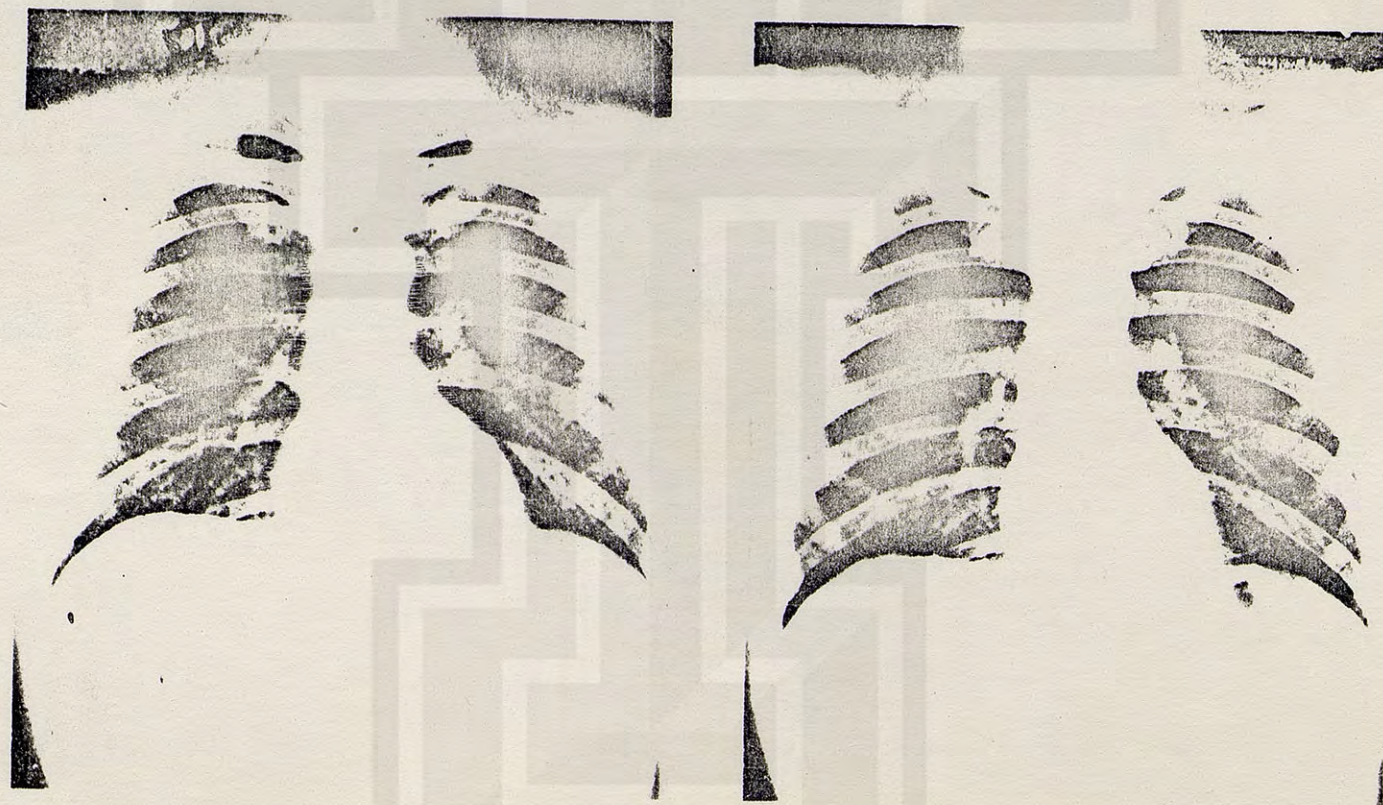


NASA-S-71-3131-S

APOLLO 10 COMMAND MODULE PILOT

PREFLIGHT

POSTFLIGHT



MAY 13, 1969

MAY 26, 1969

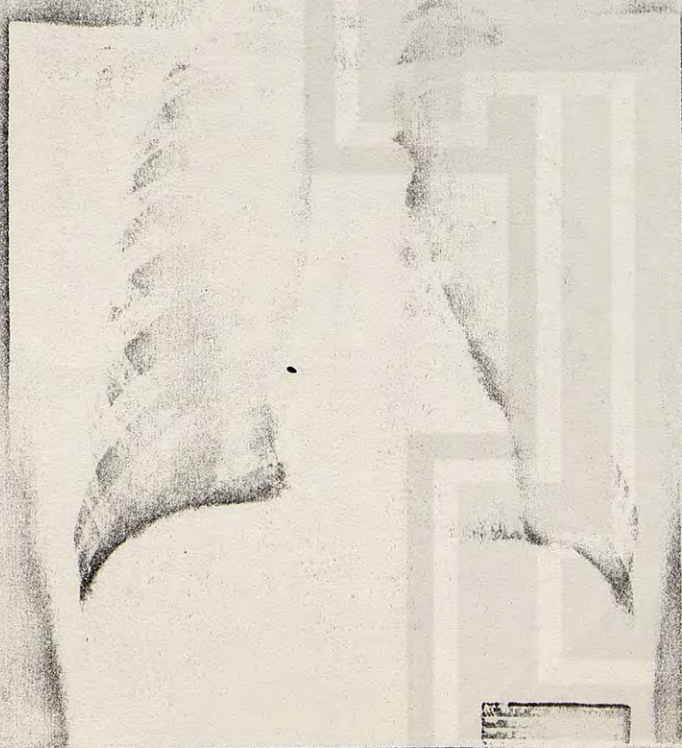
NASA S 74 4937

SKYLAB 4 SCIENCE PILOT

SYSTOLIC CHEST X-RAY

PREFLIGHT

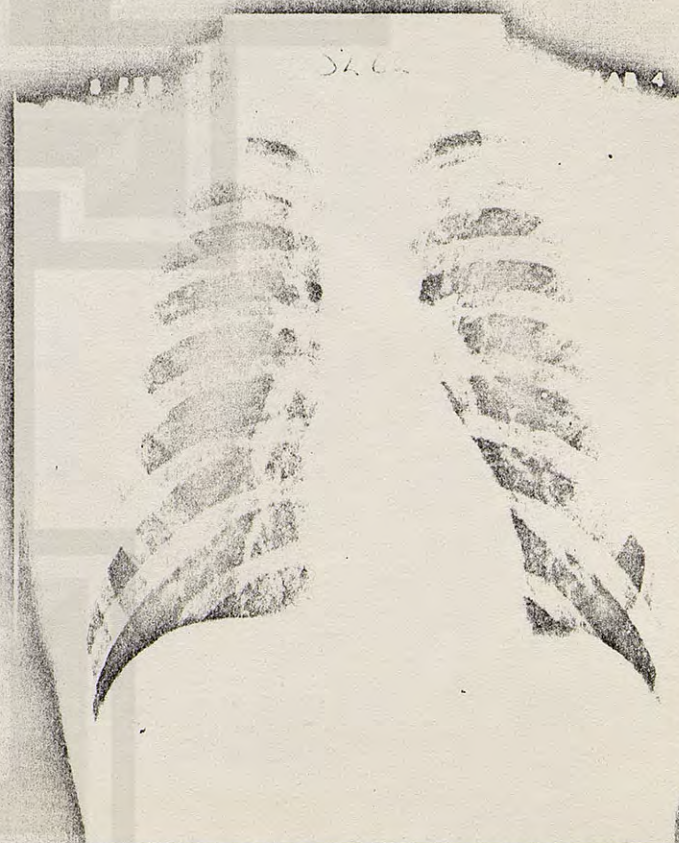
SL 60



6 NOV 73

POSTFLIGHT

SL 60



8 FEB 74

DETERMINANTS OF CARDIAC SIZE FROM ROENTGENOGRAMS

CARDIAC PHASE	MEASUREMENT	PREFLIGHT		POST FLIGHT (R+0)		STATISTICAL SIGNIFICANCE
		MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	
SYSTOLE	C/T_D^A	0.416	0.029	0.390	0.018	$p^E < 0.05$
	C/T_A^B	0.180	0.019	0.166	0.018	$p < 0.01$
	$D_1 \times D_2^C$	238.87(cm ²)	38.13(cm ²)	221.90(cm ²)	40.82(cm ²)	N.S. ^F
	PLAN. ^D	123.81(cm ²)	13.31(cm ²)	114.22(cm ²)	12.74(cm ²)	$p < 0.05$
DIASTOLE	C/T_D	0.403	0.018	0.399	0.021	N.S.
	C/T_A	0.177	0.015	0.164	0.020	$p < 0.01$
	$D_1 \times D_2$	248.41(cm ²)	28.28(cm ²)	212.27(cm ²)	34.09(cm ²)	$p < 0.05$
	PLAN.	121.71(cm ²)	7.74(cm ²)	111.67(cm ²)	12.20(cm ²)	$p < 0.01$

N = 8 (R+0 FILM UNSATISFACTORY ON SL-3 PILOT)

^ACARDIOTHORACIC RATIO BASED ON THE RESPECTIVE DIAMETERS

^BCARDIOTHORACIC RATIO BASED ON THE RESPECTIVE AREAS

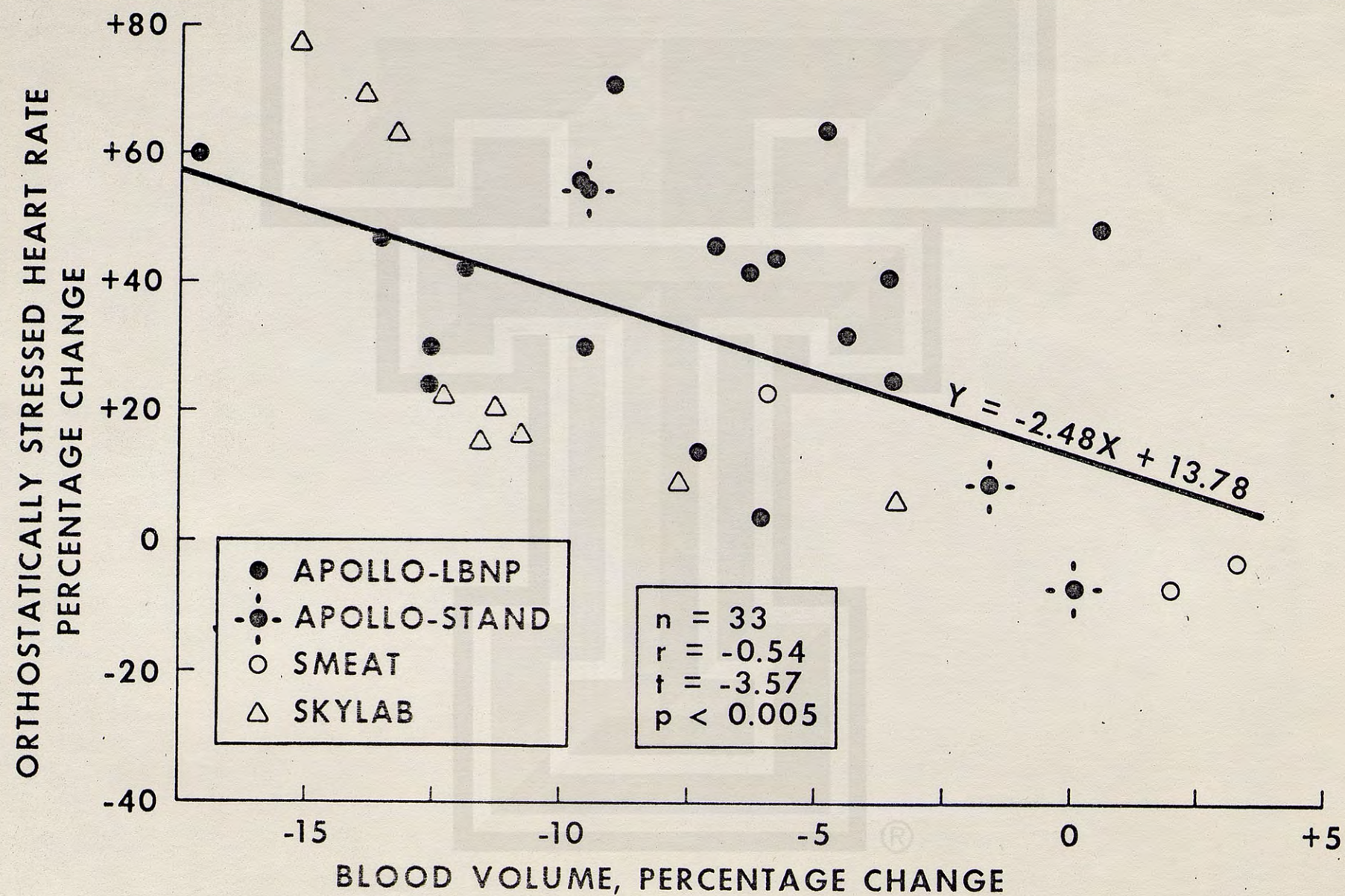
^CCARDIAC AREA DETERMINED FROM THE PRODUCT OF THE MINOR AND MAJOR DIAMETERS

^DCARDIAC AREA DETERMINED BY PLANIMETRY

^EPROBABILITY

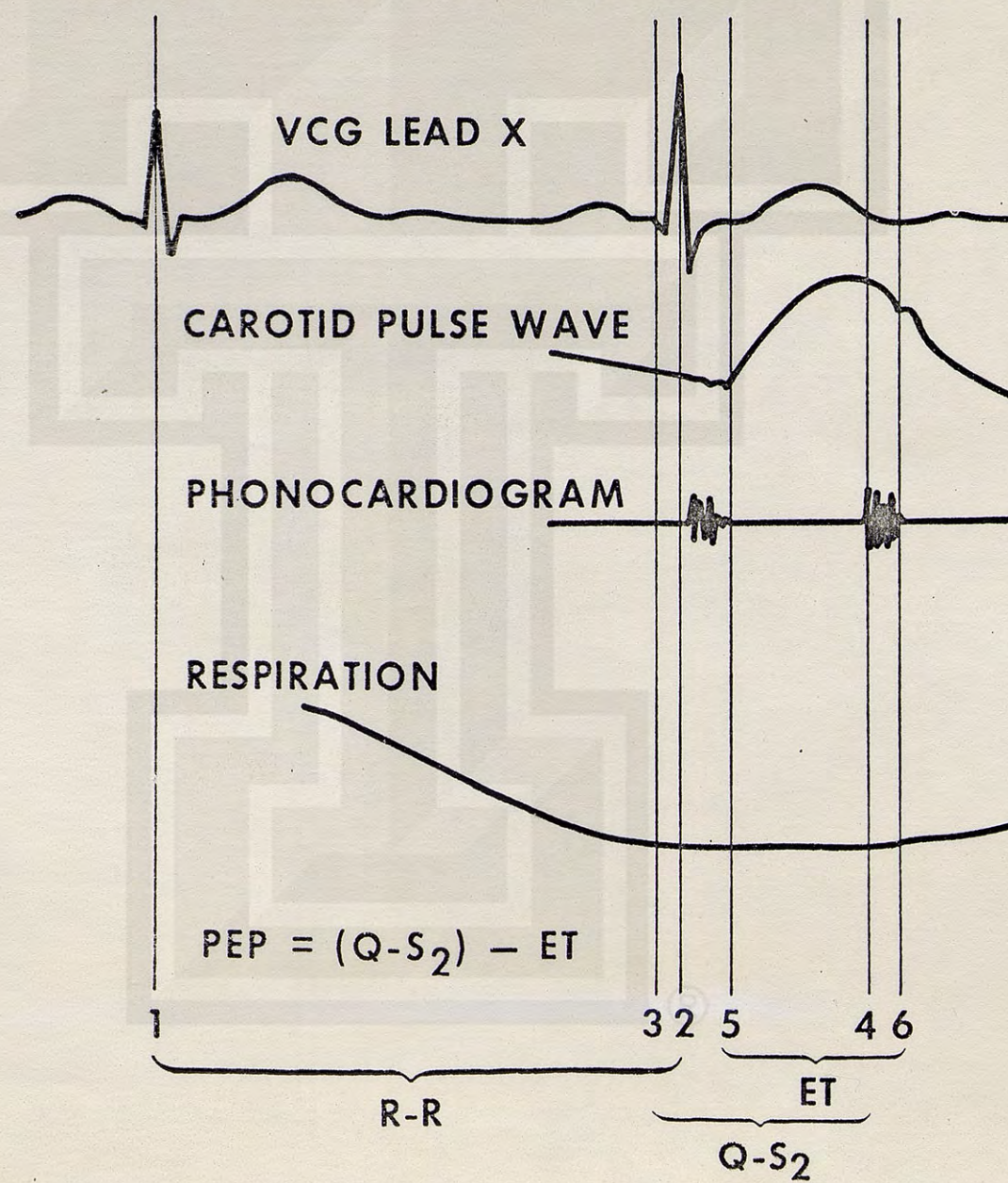
^FN.S. = NOT SIGNIFICANT

NASA-S-75-12450



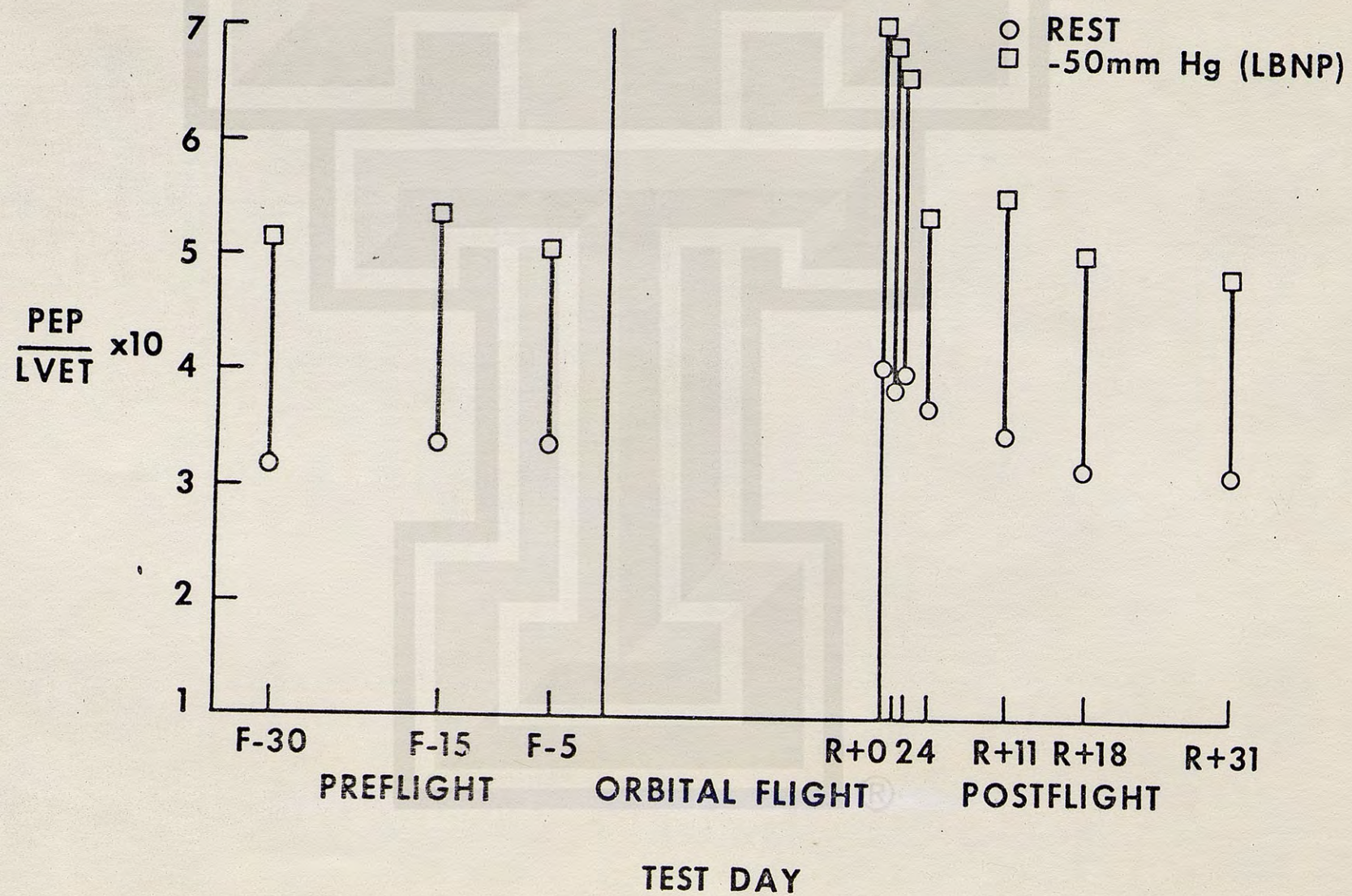
NASA-S-74-4940

SYSTOLIC TIME INTERVALS



NASA-S-74-4330

SKYLAB 4



AMPLITUDE MEASUREMENTS OF THE VECTORCARDIOGRAM

VCG MEASUREMENT	PREFLIGHT REFERENCE VALUES SUPINE, RESTING MEAN $\pm$ SD	CHANGE AFTER DESIGNATED CONDITION (%)									
		CONDITION = LBNP					CONDITION = FLIGHT				
		PREFLIGHT		IN-FLIGHT		POSTFLIGHT R + 0		IN-FLIGHT		POSTFLIGHT R + 0	
		$\bar{X}$	p	$\bar{X}$	*	$\bar{X}$	*	$\bar{X}$	p	$\bar{X}$	p
P _{MAX} MAG (mV)	0.122 $\pm$ 0.0332	+27	<0.001	+78		+75		+24	<0.02	+16	NS
QRS _{MAX} MAG (mV)	1.70 $\pm$ 0.373	- 6	<0.02	+13		+12		+12	<0.001	+18	<0.001
QRS-E CIRC (mV)	5.01 $\pm$ 1.027	+ 3	NS	+24		+32		+19	<0.005	+21	<0.001
ST _{MAX} MAG (mV)	0.646 $\pm$ 0.206	-15	<0.01	-32		-37		-10	NS	- 6	NS

* p VALUES WERE NOT COMPUTED FOR THESE COMPARISONS BECAUSE PERCENTAGE CHANGES ARE RECKONED FROM PREFLIGHT RESTING REFERENCES, AND COMPOUND TREATMENT EFFECTS (i.e., LBNP, SPACE AND/OR REENTRY) ARE INVOLVED. APPROXIMATE SIGNIFICANCE MAY BE JUDGED IN RELATION TO THE p VALUES FOR THE RELATIVELY 'PURE' TREATMENTS OF PREFLIGHT LBNP OR FLIGHT ITSELF.

SKYLAB 4 SCIENCE PILOT CALF BLOOD FLOW

