Review Co-

HEMODYNAMICS OF THE LOWER LIMBS

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Background

Significant among the medical findings following space flight have been reduced orthostatic tolerance and ergometric work capacity. Changes in hemodynamics of the legs with increased blood pooling must be considered one of the primary causes of these effects. This concern plus the marked tissue changes occurring in the legs during flight[1] prompted the addition of several procedures to evaluate changes in arterial blood flow, venous compliance, and muscle pumping. Impromptu studies were implemented during the latter portion of the SL-3 mission. Results were of sufficient value to include more comprehensive studies on SL-4. Results from SL-4 raise a number of issues which will require additional study, but also they provide previously unavailable insight into some fundamental mechanisms. For convenience the experiment will be described under two headings: (1) Arterial Flow and Venous Compliance, and (2) Muscle Pumping.

5th M.I.S.

[1] Skylab 1/2 Preliminary Biomedical Report, JSC 08439: September 1973. Section 2.4, Measurement of Crew Somatic and Functional Changes; Section 3.1, Mineral Balance; Section 3.3, Specimen and Body Mass Measurements; and Section 3.5, Lower Body Negative Pressure.

Skylab-3 Preliminary Biomedical Report, JSC 08668; February 1974. Section 2.4, Anthropometric and Functional Changes on Skylab; Section 3.1, Mineral Balance; Section 3.3, Specimen and Body Mass Measurements; and Section 3.5, Lower Body Negative Pressure.

Methodology

Arterial Flow and Venous Compliance - If an occlusive cuff placed around a limb segment is inflated somewhat above venous pressure, arterial flow will be little affected, but venous flow will be stopped until venous pressure exceeds cuff pressure. If volume change is also measured, the initial rate of change with time, before appreciable back pressure develops, is arterial inflow. There are many assumptions and sources of potential error in this measurement and those pertinent to this study will be discussed.[2,3]

Vascular compliance, i.e., Change in Volume/Change in Pressure, which in this case is assumed to be venous compliance, may be qualitatively estimated from the shape of the volume curves from a tracing following cuff inflation, and a single numerical value may be obtained at cuff pressure, or 30 mm Hg in this case.

Data for these two studies were obtained, as shown in figure 1, with an arm BP cuff above the left knee and a capacitance Limb Volume Measuring System (LVMS) band around the maximum girth of the calf. Volume changes actually measured are only those in the segment directly beneath the cuff and are recorded in percent of segment volume. The BP cuff was used to isolate the smallest practical segment to reduce systemic disturbance to a minimum. The least modified response from the vessel was sought as opposed to a measurement which induces many compensatory changes such as LBNP.

[2] Abramson, David I. Circulation in the Extremities. Ch. V. 1967, Acad. Press, New York and London.

[3] Burch, George E. Digital Plethysmography. Ch. I. 1954, Grune and Stratton, New York.

Blood flow was recorded three times each test session by rapidly inflating the cuff to and maintaining it at 30 mm Hg for 10 seconds. This sequence was repeated at 50 mm Hg cuff pressure. Curves for such a series at 30 mm Hg are shown in figure 2. For compliance studies, three minutes later in the mission, the cuff was inflated to and held at 30 mm Hg for 12 minutes; and the resulting volume curve was recorded. An example is shown in figure 3.

Muscle Pumping - The crewman was left in the LBNP apparatus after completion of M092 and the LVMS system was brought to zero and recalibrated, and a negative pressure of 30 mm Hg was applied for three minutes. At the end of this time the subject made ten maximum effort isometric contractions of his leg muscles, relaxed for one minute and repeated the maneuver. Changes in a left calf volume segment were recorded from the LVMS, as shown in figure 4.

Results and Analysis

The entire series of procedures was performed three times preflight, seven times inflight, and three times postflight. The original inflight schedule was minimal but was reduced, by scheduling even further during periods critical to the experiment. Several trials were lost or severely compromised by artifacts which appeared to be electrical. Other than these problems, the data were collected without difficulty.

Blood flow was calculated by manually drawing a tangent to the slope and measuring this slope in terms of Δ volume/Δ time. Several artifacts may be present in this curve. Somewhat surprisingly, there was an increased rate of volume change during cuff inflation which, in view of the distance between plethysmograph segment and cuff, must be venous reflux. This initial slope and artifact were avoided during measurement. Another possible error, but which could not be avoided, was flow of blood from or into areas not typical of the segment under measurement, e.g., the foot. Flows were calculated in terms of 100 ml of tissue under the capacitance band and are shown in figures 5 and 6. These two curves at differing cuff pressure correspond well and indicate that the arm cuff provided relatively complete occlusion at these venous pressures.

Compliance was calculated at the single known pressure point, 30 mm Hg and plotted versus time in figure 7. The units used were percent volume change/ 30 mm Hg pressure.

Relative and absolute volume of blood removed is the only aspect of muscle pumping examined thus far. The volume of blood pooled in the legs by 30 mm Hg negative pressure is calculated, as is the amount remaining after muscle pumping. These are plotted versus mission time in figure 8. Only values for the SPT and CDR are shown for graphic clarity. The response of the PLT was similar to that of the SPT.

Interpretation

A major problem in interpretation of this blood flow data, figures 5 and 6, is that blood from calf and foot cannot be separated and these segments may respond in different fashion to changes produced by weightlessness. Factors controlling blood flow in the legs with postural changes have not been adequately documented. It is known that posture affects leg blood flow, e.g., it is increased with up to 15^{o} leg elevation with the subject supine and decreased with the leg dependent.[4] At least a portion of this change is felt to be a function of change in arteriole-venule diameter influenced by extrinsic tissue pressures. It was demonstrated on SL-4 that up to 15 percent of the crewmen's leg volume had been lost by MD 3 (see Anthropometric Change and Fluid Shift), and it would not be unreasonable to postulate decreased leg tissue pressure with a possible increase in diameter of the resistance vessels. On MD 5 the flow had slightly increased in the CDR and increased more than twofold in the PLT. On MD 13 the first measurement of the SPT showed more than a threefold increase, while the other crewmen were relatively unchanged from MD 5. There were two days of sharp increase in flow followed by a return to previous values, but it has been impossible to relate these to either instrumental error or other factors.

There is great variability in the flow data. Some of this variability probably results from changes in temperature and in relationship of the time of measurement to food ingestion and exercise. None of these factors were controlled or adequately known to compensate for. In spite of the variability, it seems safe to say that flow was elevated throughout the flight over pre- and postflight levels. Such a picture is not inconsistent with the increase in muscle flow[5] seen in elevation of the legs or other maneuvers to increase intra-thoracic venous pressure, a mechanism which apparently releases sympathetic vasoconstrictor action. It was shown (see Anthropometric Changes and Fluid Shifts) that fluid and blood from the legs were shifted cephalad on exposure

[4] Ludbrook, John. Venous Function in the Lower Extremities, Ch. 4, 1966. Charles C. Thomas, Springfield, Illinois, U.S.A.

[5] Shepherd, John. Physiology of the Circulation in Human Limbs in Health and Disease, Ch. 2, 1963. W. B. Saunders Company, Philadelphia and London.

to weightlessness and this must have produced transient increase in venous pressures which probably were not completely restored to 'normal' throughout the flight.

No real inflight trends could be established, but one had the impression that CDR and PLT values were decreasing their rate while the SPT was more or less stable. If there were a decreasing trend, this might be consistent with a decreasing central pressure either as an adaptation or through decreased blood volume. On recovery the SPT and CDR were in the preflight range while the PLT was slightly elevated. The cause of either this increase in flow and difference in individual response can only be surmised. A decreased tissue pressure with increase in vessel diameter is one possibility. All of the CDR's responses are consistent with relatively higher tissue pressure.

Venous compliance and muscular pumping of venous blood can only be understood in terms of the unique features of leg veins which include a network of superficial veins with heavy muscular walls and many one-way valves, many interconnecting veins or penetrating branches with centrally directed one-way valves, and large thin-walled veins surrounded by muscles which, in turn, are frequently surrounded by fascia and are also equipped with numerous centrally directed one-way valves. These deep veins typically contain 80 to 90 percent of venous blood in the legs.[6]

It was originally postulated that the shifts of fluid and loss of tissue from the legs and particularly from enclosed fascial compartments would produce reductions in effective venous tone, especially those of the deep veins, through reduction in tissue pressures and elasticities external to the veins.

A plot of venous compliance at +30 mm Hg pressure, i.e., percent volume/30 mm Hg press, is shown in figure 7. Responses of the SPT and PLT have been combined in the upper curve. It is obvious that more points are needed and that one point makes a marked difference. This one point has been tested for validity in every possible way and until some error is found, this point will be considered significant.

There are several obvious features of this plot including:

- A marked difference in magnitude of response in the CDR as compared to the SPT and PLT.

[6] Ludbrook, op. cit., pp. 55 and 72.

. A severalfold increase in compliance in two crewmen which, however, requires some two weeks to reach a maximum.

. After this initial increase in compliance, there was a decrease, or at least stability, until mission end.

. On return to one-g after 24 hours or less, there was a return to or even beyond preflight values.

The increase in compliance is not surprising, but its relatively slow rate of increase as compared to loss of fluid from the leg[7] was unexpected. Again, no explanation of the changes can be given. Loss of tissue pressure through decreased fluid volume, loss of somatic muscle tone, and changes in reflexes must all be considered.

Muscle pumping is effected by pressure exerted on the veins by surrounding contracting muscles. This pressure can exceed 200 mm Hg in some calf muscles.[8] Such pressures propel the blood cephalad through a series of one-way valves. Unfortunately, quantitative data, especially as regards the effectiveness of removal of blood from connected superficial veins, is not available.

A plot of the amount of blood (in terms of percent of volume in the calf segment measured) added to the legs by three minutes of -30 mm Hg pressure and the amount remaining after ten isometric contractions of leg muscles are shown in figure 8. Only the CDR's and SPT's results are plotted. The PLT's response is similar to the SPT's. Again, data from a crucial period was missing. The

[7] See Anthropometric Change and Fluid Shifts

[8] Ludbrook, op. cit. p-60.

upper two curves are the amount of blood pooled by negative pressure in the SPT and CDR respectively, while the lower curve is an approximation of the blood remaining after muscle pumping in both the SPT and CDR.

Two features of the muscle pumping curves appear significant: (1) there is the relatively slow development of a marked increase in compliance which paralleled that already seen and which was followed by an immediate postflight reduction and (2) the CDR and SPT show an identical percentage of blood remaining after pumping. It is unfortunate that we do not have some other evidence for the relative distribution of blood in superficial and deep veins here. In the absence of such evidence, there is no assurance where the blood remains after pumping, but it seems reasonable to conclude that much of it is in the superficial veins since muscle pumping should more effectively remove the deep portion.[9] Another point to be considered is whether this volume represents blood or if an appreciable portion is extravasate produced by increased hydrostatic pressures. If such significant extravasation occurred, one would expect a continuing upward slope on the volume curve and an appreciable volume remaining after rapid cuff deflation. Neither of these features is prominent enough in the records to suggest that appreciable fluid, other than blood, was pooled in the legs.

Also of interest is comparison of changes produced by 30 mm Hg negative pressure to the 30 mm Hg pressure by occlusive cuff. One of the major reasons for using

[9] If this is truly the amount of blood remaining in the superficial veins, then the great change in compliance should be in the deep veins or rather their surrounding tissue.

cuff occlusion was that it involved a small segment of the vascular system and hence would provoke a minimal response in the remainder of the cardiovascular system, i.e., differences in response from the two methods were expected. Conversely, the volume of blood trapped by either method should be the same or, if anything, reduced under negative pressure by compensatory responses, but they appear to be some 20 percent higher which can be most reasonably attributed to incomplete transmission of occlusion pressure by too narrow a cuff.

clarify

Conclusions

A major significance of this study will not be attained until the findings are correlated in detail with those of experiment M092 (LBNP). While the responses to LBNP may be considered the final[10] hence significant response, they are, in effect, the end of a long series of events, a series of events which must be isolated and followed to understand the total response. As demonstrated here, the initial or provocative response is the volume change of capacitance vessels as a function of pressure under static and dynamic conditions and it should be the point of departure for other studies, both inflight and in bedrest. At the same time these studies, particularly compliance, when combined with the decrease in blood volume and red cell to mass, demonstrated by Dr. Kimzey and others in M110, provide some basis for interpretation of experiment M092 results. In all of the results seen here the CDR demonstrated much less change in blood flow compliance and muscle pumping than the other two crewmen. The trend charts for experiment M092 (LBNP) show similar decreased heart rate and blood pressure

[10] It should not be forgotten that LBNP is a simulation of orthostatic stresses and in itself differs from walking or standing under one-g, especially after the crewmen have a few hours to equilibrate under one-g.

changes for this crewman at maximum LBNP.

Such a finding is not inconsistent with previous findings of a wide range of responses to orthostatic stresses in the human which, in some cases, could be attributed to physiological and anatomical differences. It would seem desirable to develop a way to predict individual response and bedrest studies, or more severe negative pressure stresses might be initial avenues of approach.

A second impression, strongly shared by the crew, was that after a week of weightlessness, LBNP became increasingly stressful and after a few weeks, much less so. Data does not obviously support this and, unfortunately, this critical period was lost to priority problems; but again, what remains indicates that compliance reached a peak in the two to three-week period and then decreased. If one could now add a decreasing red cell mass and blood volume, and a variable state of hydration to these effects, the primary stresses would probably be delineated.

Most fundamental of the problems is identification of causes for the changes seen here. It was originally postulated that a reduction in tissue pressure through loss of fluid and atrophy would directly affect the contiguous vessels. In all three crewmen the major volume loss occurred quickly, within a day or so, and there was a sharp increase in blood flow by the time of the first inflight measurement and also a sharp drop on recovery. This is in keeping with flow being affected, possibly by venule size or by pressure outside the vessels.

Compliance changes developed more slowly reaching a peak not earlier than two weeks after achieving weightlessness such that the same mechanism as blood flow can hardly be invoked. A slow adaptation of smooth muscle reflexes might fit this picture but further evidence is needed to support pooling of a large quantity of blood in the superficial vessels containing such muscle. Such a hypothesis would also contradict the one proposed in muscle pumping. Reflex changes in the deep vessels and their surrounding structures are, to my knowledge, uninvestigated and unknown. It is to be hoped that bedrest and other simulation studies of the future will take proper cognizance of these fundamental areas.

Finally, it must be recognized that crewmen on SL-4 were on ~~different~~ increase food and exercise regimens from those of SL-1/2 and SL-3 and that any responses seen will differ not only from those of unprotected individuals exposed to weightlessness, but also from the responses of crewmen on the other missions. Most importantly, the changes seen here did level off and possibly improve and promptly reverted to preflight baseline on return to one-g.

LIST OF ILLUSTRATIONS

Leg Hemodynamics

FIG. 1 Arrangement for arterial flow and compliance measurements. Subject was in the open LBNP apparatus.

ARTERIAL FLOW/VENOUS COMPLIANCE MEASUREMENT

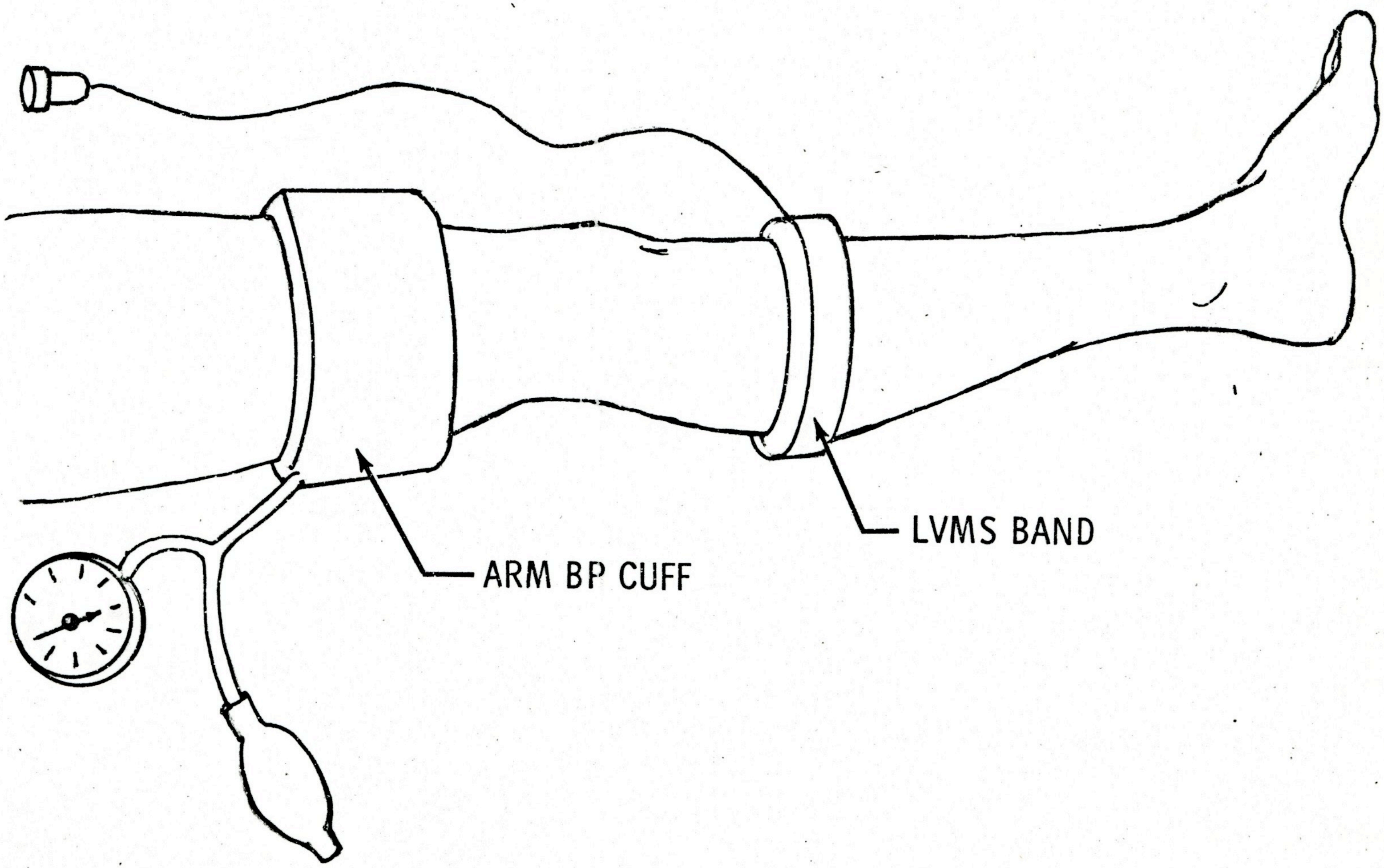
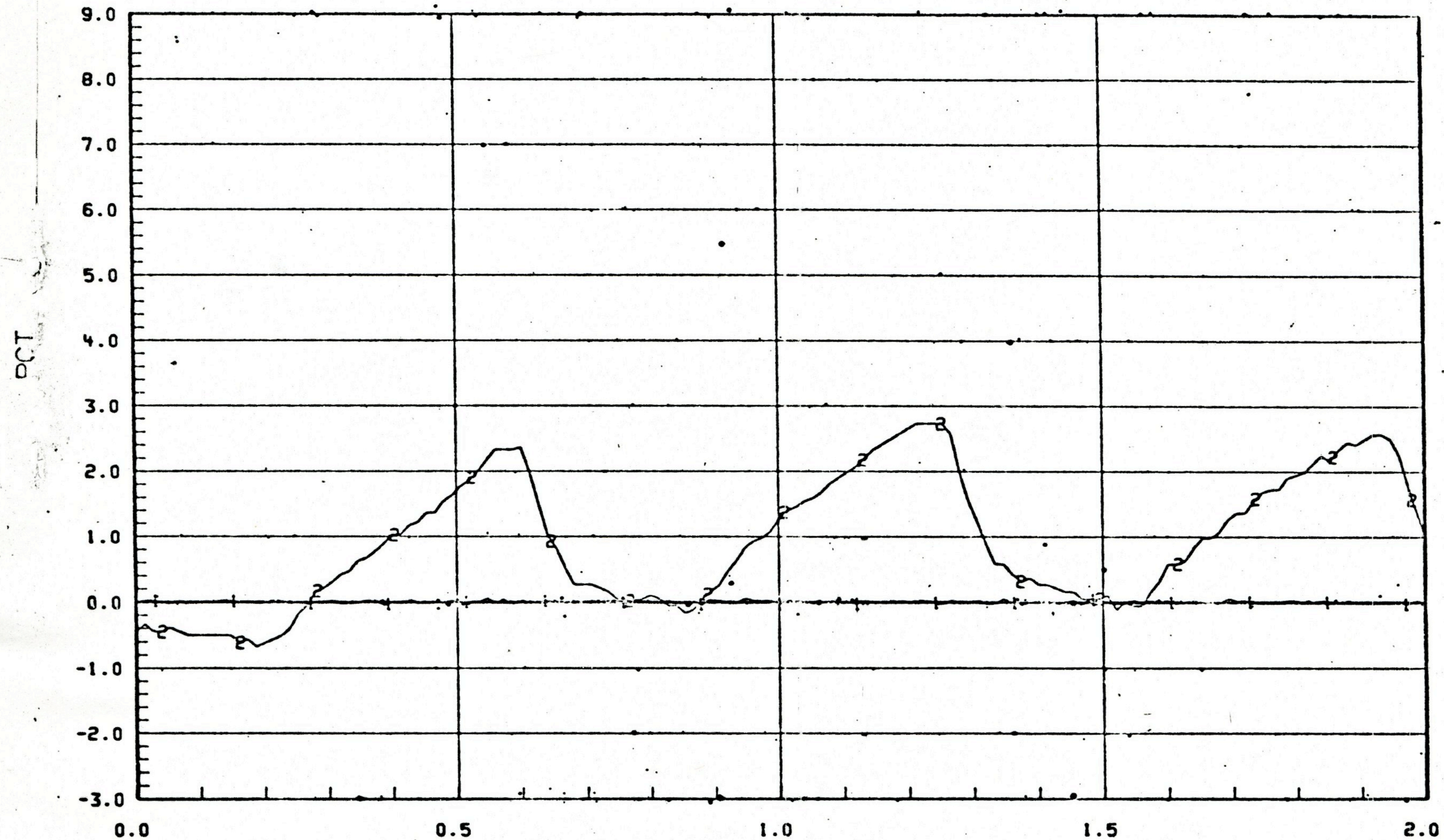


FIG. 2 Recording of limb segment volume change for three cuff inflations to 30 mm Hg. for determination of arterial flow.

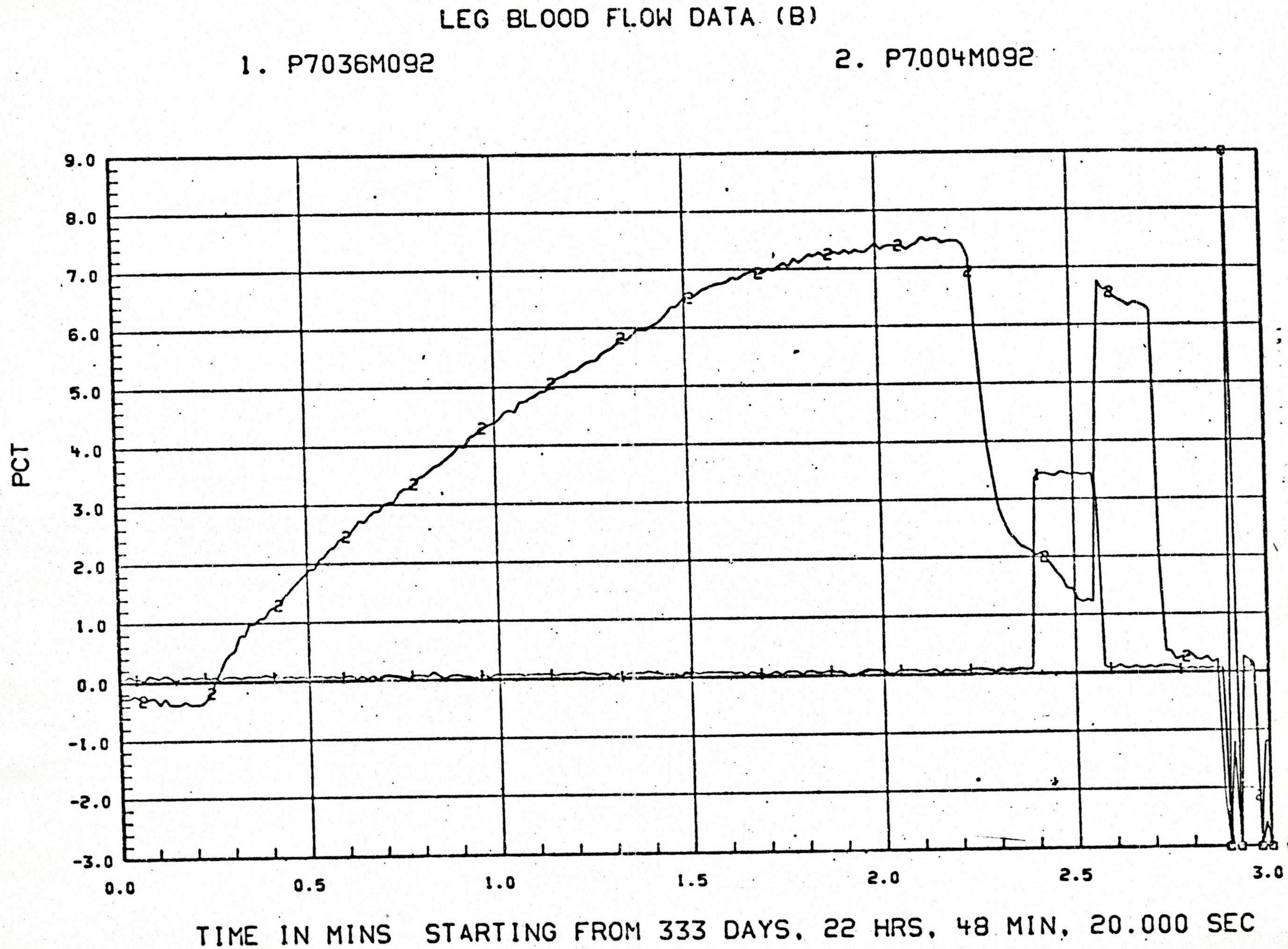
LEG BLOOD FLOW DATA (A)

1. P7036M092 2. P7004M092



TIME IN MINS STARTING FROM 333 DAYS, 22 HRS, 42 MIN, 40.000 SEC

FIG. 3 Recording of limb segment volume change produced by cuff inflation to 30 mm. Hg. for determination of compliance.



LEG BLOOD FLOW DATA (B)
1. P7036M092
2. P7004M092
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
-2.0
-3.0
PCT
0.0
0.5
1.0
1.5
2.0
2.5
3.0
TIME IN MINS STARTING FROM 333 DAYS, 22 HRS, 48 MIN, 20.000 SEC

FIG. 4 Recording of limb segment volume changes produced by 30 mm. Hg. negative pressure and two sets of 10 each isometric contractions for evaluation of muscle pumping effectiveness.

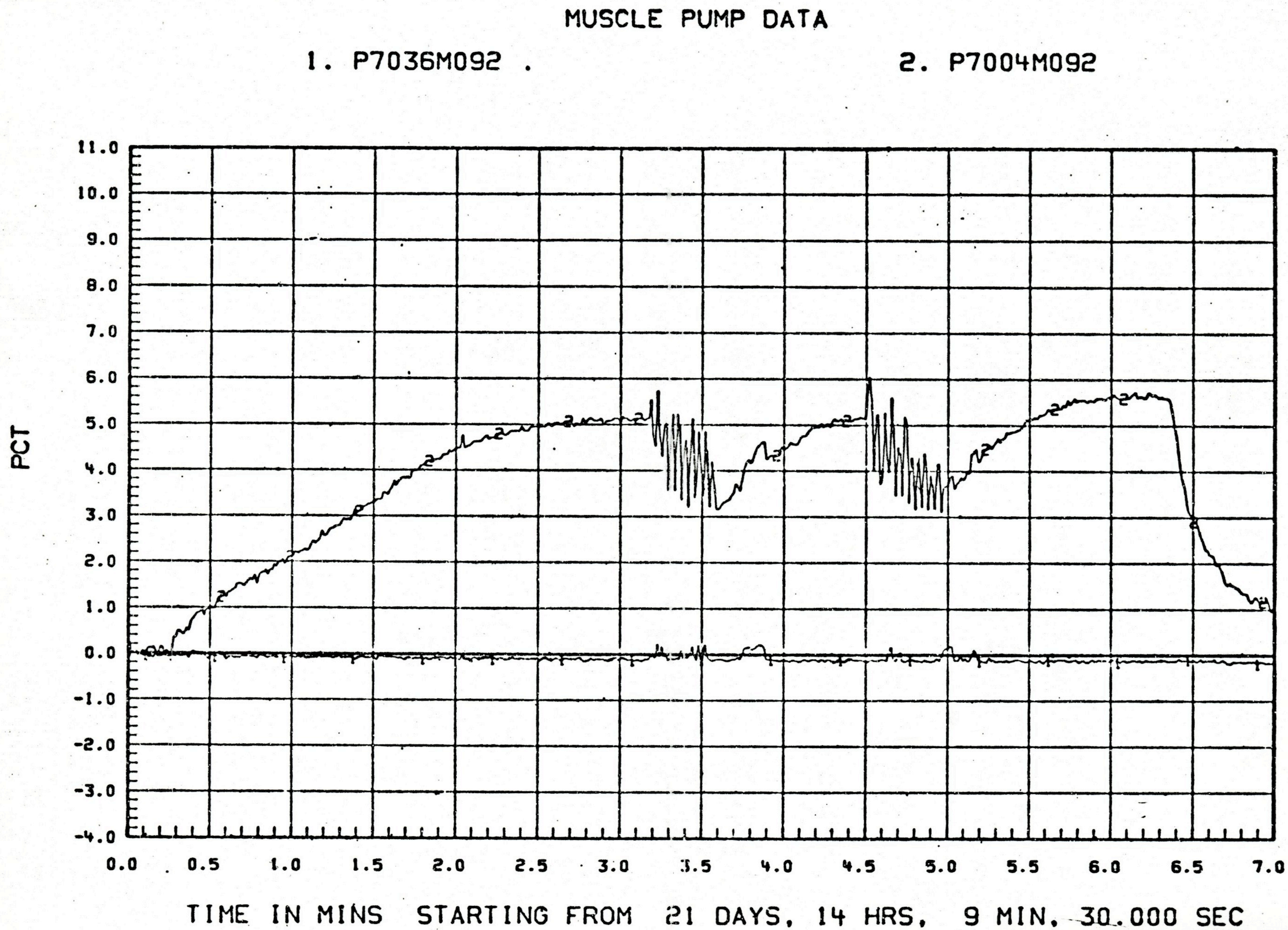

MUSCLE PUMP DATA
1. P7036M092 .
2. P7004M092
PCT
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
-2.0
-3.0
-4.0
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
TIME IN MINS STARTING FROM 21 DAYS, 14 HRS, 9 MIN, 30.000 SEC

Figure 7. Compliance of Left Calf Segment of SL-4 Crewmen Plotted vs. Mission Duration

VASCULAR COMPLIANCE, LEFT LEG

SL-4 CREW - ΔP = 30mm Hg

(ORDINATE = ΔVOL.%)

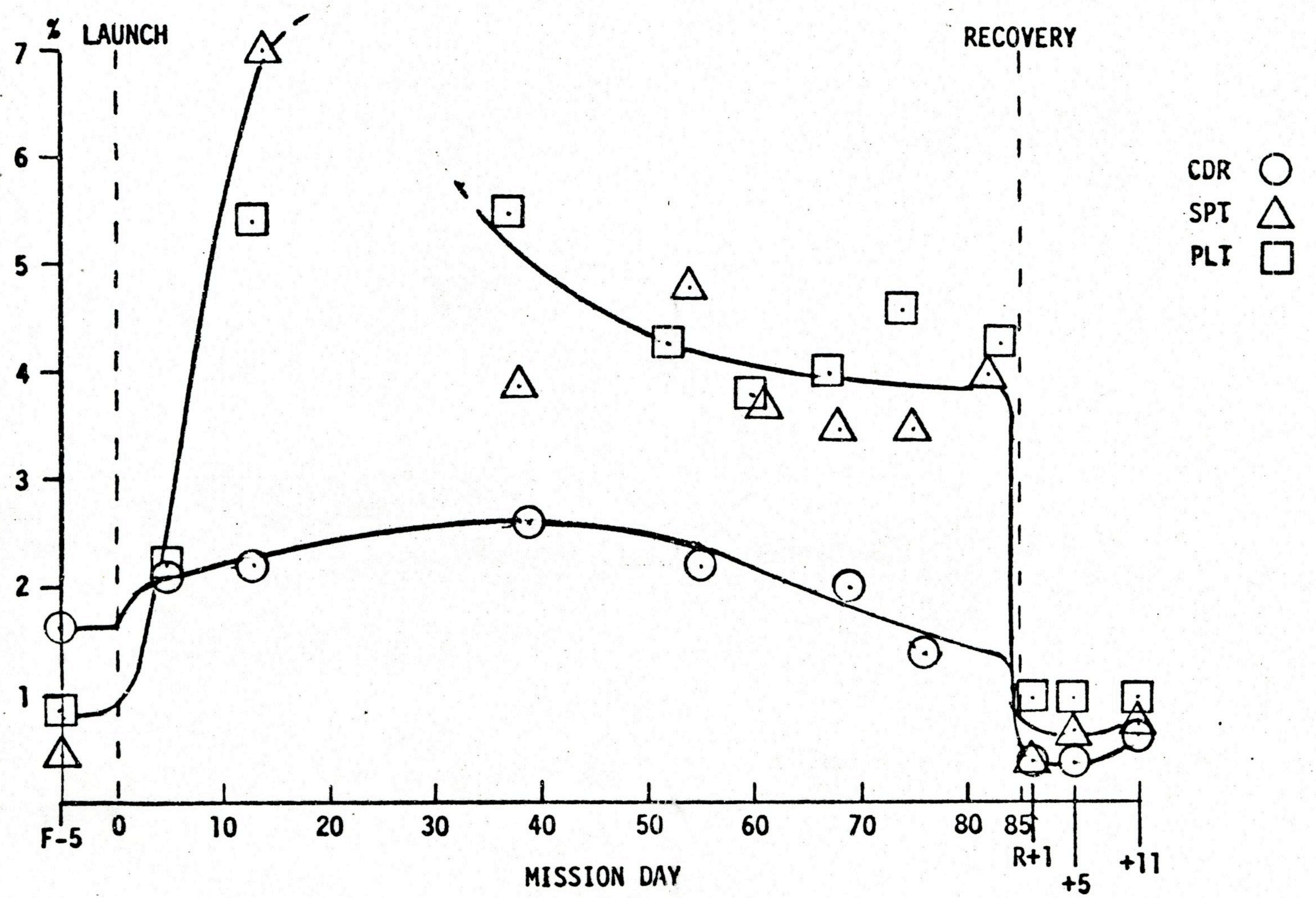


Figure 8. Volume of Blood in Leg Under Negative Pressure Before and After Muscle Pumping vs. Mission Duration

Leg Volume Changes from Muscle Pumping, SL-4