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LFD info — M071

Discuss ASAP! Status??

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
MANNED SPACECRAFT CENTER
HOUSTON, TEXAS 77058

MSC-DA

March 19, 1971

REPLY TO
ATTN OF:

TO: AB/Deputy Director, Manned Spacecraft Center

FROM: CB/Dr. D. L. Holmquest

SUBJECT: Scientific activities in support of manned spaceflight

One of the major physiological responses to prolonged weightlessness is a decrease in the calcium content of the skeleton. The significance of this reaction in terms of diminished skeletal strength is partially understood at best because of the inability to accurately simulate zero gravity conditions; however, the problem unquestionably exists and must be evaluated carefully before we can intelligently design future missions for man in space.

One of the major medical experiments of Skylab, M071, is a mineral balance experiment which seeks to assay, by carefully measuring all mineral intakes and outputs, the net loss in calcium and other minerals from the bones. This same experiment was attempted on Gemini VII and failed miserably. Despite heroic efforts by the principal investigators and the medical personnel here at MSC, the data obtained from the experiment, although published, is not considered valid by most investigators who are familiar with the problem and this study. An inadvertent disruption of the dietary protocol by the crew and a failure of the urine volume measuring hardware were the major factors which contributed to the loss of useful data.

For the past nineteen months, I have allocated a significant portion of my time to following the Habitability Support System of Skylab; in particular I have worked closely on those subsystems which affect the M071 experiment, the fecal urine collection systems, the food, and the Specimen Mass Measurement Device. All of these subsystems affect the success of the calcium balance experiment and all have displayed considerable difficulty in meeting the stringent requirements imposed by the experiment. The requirements of this experiment alone have escalated enormously the cost of these systems, to say nothing of the price the crew pays operationally in time. Nevertheless, the medical data from this experiment is critically important, and we should do everything possible to support this experiment.

I personally and professionally have a strong interest in the field of Nuclear Medicine and have been studying part time in this medical specialty for over six months. Over the past year it has become apparent to me that we critically need an alternative means of studying long-term calcium balance, both as a back-up method for the very complex and potentially fallible methodology of Skylab and as a primary, inexpensive technique for future missions. The method of _in vivo_ neutron activation analysis provides such a method, and I have developed over the past year, with the collaboration of Dr. Joe Allen of our office, a proposal to create a facility in Houston that would support such a methodology. The neutron activation analysis technique allows one to measure the total amount of calcium in the body of the crewman; and by this method, one can measure the net loss of calcium over a mission by measuring total body calcium on a pre- and post-flight basis, with no inflight hardware and no impact on crew diet, time, or operations. We have been discussing this approach with the Medical Directorate since last September and hope shortly to be funded adequately to proceed with development. I enclose for your information a copy of the research proposal from Baylor College of Medicine in Houston, where I plan to house the facility. I am not listed on the proposal as an investigator since I hope to function as the MSC contract monitor.

I offer these comments to you because of the present concern over what to do with scientist-astronauts. Since MSC management seems to feel that a crew of two pilot-astronauts and one scientist-astronaut is appropriate to a mission composed of ten hours of spacecraft maneuvering and 27 and 55 days of science, it would indeed appear that some of us have a long wait in store for us before a spaceflight. It is my intention, therefore, to use this time to the fullest extent possible to pursue research and development efforts which will enhance our ability to perform significant scientific experiments in space and to maintain my competence as a research scientist and physician. It seems to me that these activities are appropriate to what should have been all along the job description of the Scientist-Astronaut who is not actively assigned to a flight crew. However, because we ultimately plan to function as crewmen on future spaceflights, I feel that it is critically important, at the same time, to preserve intimate ties with the present Astronaut Office and to maintain high-performance jet aircraft proficiency.

As a means of achieving these ends, I propose to accept, over the next two to three years, a 90 percent leave of absence to the Baylor College of Medicine in Houston. This allotment of time will allow me to give my undivided attention to the development of the neutron activation facility I have described, which can be so essential as a secondary source of medical information on Skylab. I am presently an Assistant Professor of Radiology and Physiology at Baylor, and I plan to function in that position during this leave. I should like to retain a 10 percent employment as a means of continuing my position within the Astronaut Office and would use that time to attend to scientific affairs within NASA, maintain important office correspondence, cover category 1 and 2 speaking engagements, and maintain T-38 proficiency. I have already submitted to the Astronaut Office a proposed budget which covers travel for scientific purposes during fiscal 1972. Funds for scientific research will be covered by the research proposals submitted to the Medical Research and Operations directorate through NASA headquarters. Ninety percent of my salary will be paid by Baylor College of Medicine.

Donald L. Holmquest, M.D., Ph.D.

cc: Dr. R. R. Gilruth/AA
Mr. D. K. Slayton/CA
Col. T. P. Stafford/CB
Dr. C. B. Berry/DA
Dr. Homer E. Newell, NASA Headquarters/AA
Mr. Dale D. Myers, NASA Headquarters/M
Dr. James W. Humphries, NASA Headquarters/MM
Dr. Sherman P. Vinograd, NASA Headquarters/MM

SUMMARY

Baylor College of Medicine, in close collaboration with the University of Washington, proposes to develop, construct, and operate, within the Texas Medical Center near the Manned Spacecraft Center, a neutron activation analysis facility to support biomedical research on future manned missions (including, if schedule permits, Skylab). This development program will concentrate initially on early construction of a facility that can measure changes in total body content of calcium, phosphorus, nitrogen, and potassium that occur in astronauts exposed to long-duration weightlessness. Subsequent to construction, the investigators will use the facility not only to support pre- and post-flight studies of flight crew body composition but also, working with phantoms, animals, and human subjects, will further refine the technique with regard to improving accuracy, decreasing radiation exposure, developing partial body activation procedures, and possibly developing an apparatus that can be used for inflight activation analysis of man or animals.

PRELIMINARY

DESCRIPTION OF RESEARCH

In order to move rapidly toward a capability in Houston for measuring changes in flight crew body content of calcium, phosphorus, potassium, and nitrogen, we are proposing a joint effort between the University of Washington and Baylor College of Medicine to: 1) further refine the present techniques for measurement of total body calcium with emphasis on maximum accuracy and minimum radiation exposure, 2) pursue further the measurement of total body phosphorus and its partition into skeletal and extraskeletal components, (by correlation with total body potassium) as a potential means of studying skeletal mass with significantly reduced radiation exposure, 3) investigate further the techniques for measuring total body nitrogen simultaneously with phosphorus as a means of following changes in nitrogen balance (muscle mass), and 4) construct and operate within the Nuclear Medicine Laboratory of St. Luke's Hospital a neutron activation facility capable of applying these advanced techniques to the measurement of mineral metabolism on flight crews exposed to long duration weightlessness and to the development of other nuclear methods for studying physiological funtion in spaceflight. ~~As soon as~~ If it can be demonstrated that the Baylor facility will be functional in time to satisfactorily measure mineral balance in Skylab astronauts, the principal investigators from the two institutions plan to submit, as co-principle investigators, an Experiment Proposal for approval as a Skylab experiment, It is hoped that the pre- and post-flight nature of this experiment and its relatively low cost will facilitate its acceptance at a time fairly late in Skylab development. We also should not forget that major spaceflight projects, particularly Skylab, have a long history punctuated with delays and postponements; and any such delay in Skylab, while unfortunate, would probably allow sufficient time for this facility to be operating smoothly. On the other hand, the neutron activation methodology has great potential for use in future manned space programs for the study of both man and animals; and the investigators would, in the absence of an opportunity to study Skylab flight crews, continue to refine present techniques and develop further the potential applications of this technology to biomedical research in space.

The following development schedule shows a breakdown of related efforts and fund requirements in time and between the two institutions.

SIGNIFICANCE.

While there is considerable evidence from ground based bedrest studies to suggest that the absence of gravitational stress results in a loss of skeletal and muscular mass, there is only scanty data thus far to support the hypothesis that this phenomenon holds true also for spaceflight. When adequate scientific evidence is available, it may be that this physiological response to weightlessness will remain as the major limitation to man's prolonged existence in space; on the other hand, it is also possible that this response will be found to be quite small and self-limiting, and thus all efforts at development of artificial gravity, special diets, hormone supplements, and special garments to prevent this deterioration can be abandoned.

Actual studies in spaceflight thus far have been limited to pre- and post-flight measurements of bone density and one inflight calcium balance study (GeminiVII). Thus far the bone density measurements in the hand and foot have shown slight but quite variable decreases over the relatively short mission durations examined. However, the one attempt at performing a calcium balance study on a space mission (1) encountered so many operational difficulties that the results are of questionable validity in supporting or disproving the significance of the problem (2), ~~Rub.~~ Rev.

A reliable, economical, accurate and operationally feasible method of evaluating spaceflight effects on the body will become more essential as longer duration missions are carried out and as special physiological support measures are attempted. While it is true that a carefully designed balance type experiment already exists for evaluating mineral metabolism on the Skylab astronauts, there are several cogent reasons for developing an additional method for studying mineral metabolism in spaceflight.

a. The present mineral balance experiment seeks to study a potential major stumbling block to manned spaceflight; and, as a mission critical experiment, it should have a backup means of obtaining the required data.

b. The inflight mineral balance experiment places enormous constraints on flight hardware requirements, crew diet and meal preparation, waste management hardware and procedures, and crew time. As soon as possible, a simpler method, preferably pre- and post-flight in nature, should be developed.

c. Longer missions, such as those envisioned for subsequent space stations, cannot tolerate the heavy return payload requirements of a balance study, and an alternative method will be required.

d. In some instances, such as on Skylab, the assessment of the safety of undertaking additional longer missions will depend upon early evaluation of the results of the studies of mineral losses. Whereas the results from mineral balance type experiments will require a period of weeks for calculation and interpretation of results, the post-flight analysis of body composition by neutron activation analysis should be available within 24 to 48 hours after performing the measurement.

BASIC METHODOLOGY

Neutron activation analysis is a well-established analytical technique that has been used, since its discovery in 1936 by Hevesy and Levi ( ), primarily for detection and ~~quantitation~~ quantification of elements that are present in physical or biological materials in trace amounts. In vivo neutron activation analysis is a relatively new application of the principles of this technique to the non-destructive, quantitative measurement of the total content of certain elements within the living body. In 1964, Anderson and co-workers used total body neutron activation analysis to measure total body sodium and chlorine and estimate body calcium ( ). Investigators at the University of Washington who were interested in a new approach to the study of calcium metabolism in a variety of calcium-wasting diseases several years ago teamed with nuclear physicists at the Battelle Northwest Laboratories to devise a system for ~~quantitation~~ quantification of total body calcium ( ). These investigators have now utilized this system in a number of clinical studies on human subjects and have found good correlation of their results with those obtained by other methods. The method has been particularly valuable in those clinical settings where the slow progress of the calcium-wasting process overy many months makes the classic calcium balance technique impractical and expensive.

Neutron activation analysis is basically a two-step procedure. First, the material to be analyzed is subjected to bombardment by neutrons of known energy. As the neutrons collide with atoms of the element of interest, these atoms absorb the neutrons and, after emitting some type of nuclear radiation (gamma photon, neutron, proton or alpha particle e.g.) assume a new nuclear configuration. The neutron energy is normally chosen such that the resulting nuclear species, whether a different element or merely an isotope of the original element, is unstable. The second step is thus to count in a suitable scintillation counter the gamma photons produced by the unstable atoms. By simultaneously irradiating a suitable standard containing a known amount of the element with the same neutrons at the same distance from the neutron source, one can compare the resulting gamma counts and calculate quite accurately the amount of the desired element in the unknown sample. Although the atoms of many different elements may be activated by the neutron flux, one can control the unwanted reactions by chosing a neutron energy that excludes many of the likely conflicting activations; those unstable products that do result from unwanted elements can be further eliminated on the basis of their gamma photon energies or their differing half-lives.

In vivo neutron activation analysis thus requires complex equipment capable of delivering a uniforn dose of neutrons of proper energy to the body tissues. Subsequent to the activation procedure, precise counting of induced gamma activity requires a total body counting chamber with sufficient sensitivity and adequate shielding. Since most of the unstable elements produced by this technique have very short half-lives, it is essential that total body counting commence as soon as possible after termination of the neutron irradiation. In the system employed presently at the University of Washington, a cyclotron is used as one step in the neutron generating system (22 Mev deuterons bombarding a beryllium target); the total body counter consists of four nine-inch sodium iodide crystal detectors which scan over the body in a non-linear fashion that compensates for the rapid decay of the short-lived radionuclides. This system is presently in use in clinical studies of calcium metabolism and is capable of determining changes in total body calcium content within accuracies of 2 - 3 percent. With current techniques, the radiation dose resulting from each calcium measurement is both calculated and measured to be about 200 millirads. By using a different neutron source which provides higher energy neutrons (14 Mev), these same investigators have also developed a capability for measuring total body phosphorus in animals (   ) that can also be applied to humans with a total neutron radiation dose of only 20 millirads. It appears quite feasible that total body nitrogen can be determined simultaneously with the phosphorus measurement with no additional radiation exposure to the subject.

BACKGROUND

The clinical study of bone physiology and pathophysiology has long been a tedious process involving indirect approaches and inaccurate, difficult procedures. The primary investigative tool has been the metabolic balance study in which the subject meticulously consumes all of a carefully constructed, usually non-varying diet while all urine and feces are collected, and, if possible, the mineral content of the sweat is estimated. Various chemical compounds or minerals are measured in these studies, but usually calcium, phosphorus, and, in some cases, ~~recently~~ hydroxyproline are the main constituents of interest. While the balance study does provide a quantitative estimate of the net flux of calcium, phosphorus, and perhaps protein into and out of the total skeletal pool, its usefulness is limited by its extreme difficulty.

On the opposite extreme lies the radiographic study of the skeleton which with relative ease provides a qualitative estimate of the bone density in localized regions of the skeleton. This technique has been useful in establishing the presence of relatively advanced skeletal wasting such as is seen in advanced osteoporosis; however, its very limited accuracy and its susceptibility to distortion by overlying body tissues have limited its usefulness in following small, progressive changes in the skeletal mass.

Since there is a need to document progressive changes in bone structure that may be more prominent in some skeletal sites than others, the newer technique of photon absorption bone densitimetry will likely replace the x-ray as a means of measuring with ease qualitative changes in bone ~~density~~ mass. Because of its greater accuracy, lower sensitivity to overlying tissues, and potential portability, this technique may be put to use in the future in an inflight experiment that will provide investigators with the relative rates of skeletal changes at several sites throughout the skeleton in addition to the time course of the observed changes. A technique which would measure quantitatively the amounts of skeletal mineral gained or lost in localized regions of the skeleton throughout the duration of the spaceflight would be even more valuable.

Although bone densitometry can provide much of the necessary information on skeletal changes, there remains a requirement to assess accurately in quantative terms the net decrement in skeletal mass that occurs in spaceflight. Until recently this assessment could only be made by a balance study; however, the stringent requirements that such a study imposes on the flight crew subjects have encouraged those associated with the operational problems of spaceflight to search for newer methods of accomplishing the experimental goals.

1972

		Totals
Total Body Counter + Neutron Source		
. Equipment	$	
12 Crystals	81600	
Multichannel Analyzer	18000	
Analyzer Readout	3000	
Kaman Neutron Generator	18000	
Spare Generator Head	1600	
High Voltage Supply, Divider, Adjust	2000	124200
B. Materials		
Neutron shielding	30000	
Irradiation enclosure	7000	
Cadavers - 3 @ $150	450	37450
C. Labor		
Irradiation room	5000	5000
I Personnel Costs.		
Physicist - Murphy 50%, Cushing 5%	12000	
John Burdine - 10%	—	
Donald Holmquest - 40%	~~6000~~ 1200	
Secretary	5000	
Inst. Technol - 50%	3500	
Technician - 50%		
Employee benefits / Indirect costs	13250	39750
II. Travel		
BCM - UW - BNW	1500	
Scientific meetings	2000	3500
II Misc Costs		
Computer	800	
Misc. Lab Supplies	2000	
Office Supplies	300	
Art, photos, reprints, drafting	400	3500

1971

Total Body Counter

		Totals
Equipment		
12 Crystals	$81600	
Shielded room - concrete	5000	86600
Materials		
Counter Assembly	4000	
Lead Bricks	10000	14000
Labor		
Design Counter	2000	
Consultant Fees (incl. travel)	2000	
Const. Shielded Room - TBC	10000	14000
Personnel Costs.		
Physicist (Murphy 50%, Bushong 5%)	6000	
John Bordnie - 10%		
Donald Helmquist - 40%		
Secretary - 50%	1500	
NM Technologist - 50%	2000	
Employee benefits } Indirect Costs. }	4750	14250
Travel		
BCM - UW + BNW	900	
Scientific Meetings	1500	2400
Misc. Costs		
Computer	400	
Misc Lab Supplies	1000	
Office Supplies	200	
Art, photos, drafting, etc	300	
		1900