National Space Biomedical Research Institute
Grant Application

NSBRI-RFP-05-01-0005

1a. TITLE OF PROJECT
Quantification of the Effects of Hypogravity, Resistive Load, and Exercise Modality on Bone and Muscle Forces during Resistive Exercise

1b.
CRL 4
TRL 3

1c. PRIMARY TEAM
Muscle Alterations and Atrophy

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAMS ANNOUNCEMENT
Number: NSBRI-RFP-05-01
Title: NSBRI Announcement Soliciting Postdoctoral Fellowship Applications

3. APPLICANT		4. MENTOR	
Name	Andrew Abercromby, M.Eng	Name	R.D.Hagan, Ph.D.
Degrees		Degrees	Ph.D., M.A., B.A.
Title	Research Scientist	Title	Exercise Lead
Organization	NASA JSC	Organization	NASA JSC
Department	Human Adaptation and Countermeasures Office	Department	Human Adaptation and Countermeasures Offic
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5. HUMAN SUBJECTS	5a. If Yes, Exemption no. or IRB approval date	5b. Assurance of compliance no.	6. VERTEBRATE ANIMALS	6a. If Yes, IACUC approval date	6b. Animal welfare assurance no.
Yes	Pending	None	No		

7. DATES OF PROPOSED OF SUPPORT From	Through	8. TYPE OF ORGANIZATION	9. ENTITY IDENTIFICATION NUMBER DUNS NO. (if available)	Congressional District
1/16/2006	1/14/2008	State		Texas 18t

10. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE		11. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION	
Name	Melvin Buderer, Ph.D.	Name	Melvin Buderer, Ph.D.
Title	Deputy Chief	Title	Deputy Chief
Address	Human Adaptations & Countermeasures Office NASA Johnson Space Center: Mailcode SK 2101 NASA Parkway Houston TX 77058	Address	Human Adaptations & Countermeasures Office NASA Johnson Space Center: Mailcode SK 2101 NASA Parkway Houston TX 77058
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12. APPLICANT ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.	SIGNATURE OF APPLICANT NAMED IN 3. *(In ink. "Per" signature not acceptable.)* Signature Page Received	DATE --------
13. MENTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.	SIGNATURE OF MENTOR NAMED IN 4. *(In ink. "Per" signature not acceptable.)* Signature Page Received	DATE --------
14. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Service terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.	SIGNATURE OF OFFICIAL NAMED IN 10. *(In ink. "Per" signature not acceptable.)* Signature Page Received	DATE --------

ABSTRACT

Existing resistive exercise (RE) devices and regimens onboard the International Space Station do not prevent crewmembers from losing bone and muscle strength compared to pre-flight levels, which can affect performance and increase injury risk during and after space flight. This may be due, at least in part, to bone and muscle forces (BMF) that are less than those experienced in 1-g at the same resistive load. The contribution of body weight to BMF is absent during RE in weightlessness and cannot be recreated by a single resistive load. This will be the first study to quantify BMF during RE in weightlessness and to investigate the effects of resistive load, exercise modality and gravity level on BMF.

The long-term objective of this research is to develop a spaceflight RE device and exercise regimens that more closely replicate BMF experienced during 1-g RE with the aim of reducing or preventing bone and muscle deconditioning. This objective is consistent with NSBRI's goals of identifying more suitable high-resistance exercise prescriptions to prevent or reduce muscle and bone loss.

This study will test three hypotheses: 1) Hypogravity significantly reduces BMF experienced during RE at the same external load. 2) Increasing the magnitude of a single RE load in hypogravity does not eliminate significant differences in BMF between hypogravity and 1-g RE. 3) Application of multiple discrete segmental RE loads in hypogravity can eliminate significant differences in BMF between hypogravity and 1-g RE.

The specific aims are to test the hypotheses as follows: A) Develop and validate a biomechanical model that quantifies BMF during RE under different resistive loads, exercise modalities, and gravity levels. The model will be developed and validated using motion capture, EMG, and force data from 24 subjects during squats and dead-lifts under three different resistive loads using free-weights (1-g) and Advanced Resistive Exercise Device (1-g and parabolic flight). B) Quantify the effects of hypogravity, resistive load, and exercise modality on BMF during RE. C) Minimize differences between 1-g and hypogravity BMF by using the model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness and simulated Lunar- and Martian-gravity. This approach will enable more accurate description of this and other RE devices and associated exercise modalities in terms of potential efficacy for bone and muscle strength maintenance.

PERFORMANCE SITE(S)

Organization	*Location*
Exercise Physiology Laboratory, NASA JSC	Houston, Texas

KEY PERSONNEL

Name	*Organization*	*Role on Project*
R.D.Hagan, Ph.D.	NASA JSC	Mentor
Andrew Abercromby, M.Eng	NASA JSC	Applicant

Research Grant
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Appendix

BIOGRAPHICAL SKETCH

Name	*Position*
R.D.Hagan, Ph.D.	**Exercise Lead**

EDUCATION/TRAINING

Institution and Location	*Degree*	*Year*	*Field of Study*
CSU Northridge, Northridge, CA	B.A.	1964	Physical Education
UC Santa Barbara, Santa Barbara, CA	M.A.	1966	Physical Education
U Oregon, Eugene, OR	Ph.D.	1975	Scientific Basis of Physical Education
UC Santa Barbara, Santa Barbara, CA	Fellowship	1977	Exercise and Environmental Physiology

RESEARCH AND PROFESSIONAL EXPERIENCE

A. Positions and Honors

Positions and Employment::
2001- Exercise Lead, Human Adaptation and Countermeasures Office, NASA/JSC, Houston, TX
1991-2001 Senior Scientist, Geo-Centers, Inc., Naval Health Research Center, San Diego, CA
1983-1991 Associate Professor, University of North Texas Health Science Center (UNTHSC), Fort Worth, TX
1983-1986 Director of Research, Institute for Human Fitness, UNTHSC, Fort Worth, TX
1977-1983 Director of Exercise Physiology Division, Cooper Institute for Aerobics Research, Dallas, TX
1981-1988 Adjunct Associate Professor, Texan Woman’s University, Denton, TX
1973-1975 Graduate Student Teaching Assistant, Men’s Service Program, University of Oregon, Eugene, OR
1969-1971 Secondary School Teacher, Los Angeles Unified Schools, Los Angeles, CA

Other Experience and Professional Memberships:
1980 present Member, American Physiology Society
1976 present Member, American College of Sports Medicine

Honors:
1979 Fellow, American College of Sports Medicine,
1986 Ambassador, American College of Sports Medicine,

BIOGRAPHICAL SKETCH

Name	*Position*
Andrew Abercromby, M.Eng	**Research Scientist**

EDUCATION/TRAINING

Institution and Location	*Degree*	*Year*	*Field of Study*
University of Edinburgh, Edinburgh, UK	BSc	2000	Mechanical Engineering
University of Edinburgh, Edinburgh, UK	MEng	2002	Mech. Engineering with Management Techniques
University of Houston, Houston, TX	Ph.D.- ABD	2005	Kinesiology

RESEARCH AND PROFESSIONAL EXPERIENCE

EMPLOYMENT:

Teaching Assistant: Jan - Jun 2000
School of Mechanical Engineering, University of Edinburgh, UK
Tutored students in engineering principles.

Pilot-in-Training: Nov 1997 - Jan 2000
Royal Air Force Reserve Forces, RAF Leuchars, UK
Youngest ever applicant accepted into the Reserve Forces of the Royal Air Force. First solo flight flown July 1998 from RAF Woodvale, England. Participated in organization of inter-squadron events, squadron expeditions, and squadron leadership. Opted out of 20 year commission application.

Human Test Subject Facility: Jul – Dec 2001
NASA-Johnson Space Center, Houston, TX
Participated as a test subject in space-related life-sciences research. Completed Physiological Training program required for flight on the KC-135.

Titan-Astronautics Engineering Intern: Feb – Dec 2001
Flight Mechanics Laboratory, NASA-Johnson Space Center, Houston, TX
Coordinated an engineering project, between four departments within Johnson Space Center (TX) and Kennedy Space Center (FL). Project involved the integration of real spacecraft imagery and telemetry into an X-38 / Crew Return Vehicle Human-in-the-Loop Visual Attitude Determination simulation.

Teaching Fellow: August 2002- December 2003
Department of Health and Human Performance, University of Houston, TX
Lectured undergraduate motor control classes; developed and monitored internet-based courses for the Department of Health and Human Performance. Participated in experimental design, and the gathering, processing, and analysis of data in motor control and biomechanics laboratory research.

National Space Biomedical Research Institute Intern: May-Aug 2003 & May-Aug 2004
Neurosciences Laboratory, NASA-Johnson Space Center, Houston, TX
2003: Researched, conducted, and documented a pilot-study evaluating the use of existing EMG and computerized dynamic posturography hardware in a novel application to measure muscle tone.
2004: Conducted a full research investigation of biomechanical and neuromuscular responses to whole-body vibration during standing.

Clinical Gait Analysis Workshop: A Focus on Interpretation; Science Museum of Minnesota, St. Paul, MN: May 13-15 2004

Biography Continuation Page for Andrew Abercromby, M.Eng

National Space Biomedical Research Institute Intern: May 2005-present
Anthropometrics and Biomechanics Facility, NASA-Johnson Space Center, Houston, TX
Analyzing kinematic, accelerometry, and EMG data. Participating in ongoing research projects within the Biomechanics and Anthropometrics Facility.

Research Assistant: January 2004-present
Laboratory of Integrated Physiology, University of Houston, TX
Conducting a project to develop an innovative technique to conduct bilateral inverse dynamics gait analysis using optoelectronic and digitized virtual markers. Acquisition, integration, and synchronization of hardware including force platforms, motion capture system, and EMG. Inverse dynamics model parameter definitions and data analysis using Matlab. Kinetic and kinematic gait parameter calculation for use in forward dynamic gait analysis. Review and develop designs and technologies for a mechanical foot stimulation research tool in collaboration with Department of Mechanical Engineering.

HONORS:
Ford Group Engineering Design Award: 2000
University of Edinburgh
Award for excellence in the development of a novel wheelchair design.

Outstanding Achievement Award: 2001
Titan-Astronautics, NASA-Johnson Space Center, Houston, TX
Outstanding Achievement Award for role in development of a spacecraft attitude determination technology.

First Class Honors (Summa Cum Laude): 2002
University of Edinburgh, Scotland
Awarded highest degree classification possible in MEng Mechanical Engineering with Management Techniques degree

National Award: Best Graduating Mechanical Engineering Student: 2002
Institution of Mechanical Engineers (IMechE), Scotland

Robert and Elizabeth Houston Scholarship: 2004
University of Houston, TX
Awarded for excellence in leadership and academic performance.

College of Education Alumni Association Scholarship 2005
University of Houston, TX
Awarded for excellence in leadership and academic performance. (Current GPA: 3.98)

PUBLICATIONS:
Layne, C.S., Forth, K.E., Abercromby, A.F.J. “Using Patterned Stimuli and Varied Muscle Spindle Input to Modify Neuromuscular Reflexes.” Annual Meeting of the Society for Neuroscience, New Orleans, LA, November, 2003.

Layne, C.S., Forth, K.E., Abercromby, A.F.J. Kyparos, A., Clarke, M.S.F., Feeback,D.L., “Proprioceptive and Muscle Maintenance for the Injured Athlete.” Presented - VIIth IOC Olympic World Congress on Sports Sciences, Athens, Greece, October 2003.

Layne, C.S., Forth, K.E., Abercromby, A.F.J. “Spatial Factors Influence the Generation of Neuromuscular Responses to Foot Stimulation.” 14th Humans in Space Conference, Banff, Alberta, Canada , May, 2003.

Biography Continuation Page for Andrew Abercromby, M.Eng

Layne, C.S., Forth, K.E., Abercromby, A.F.J. "Does Varying Muscle Spindle Input Modify Neuromuscular Responses to Foot Stimulation?" 14th Humans in Space Conference, Banff, Alberta, Canada , May, 2003.

Layne, C.S., Forth, K.E., Abercromby, A.F.J., "Spatial factors and muscle spindle input influence the generation of neuromuscular responses to stimulation of the human foot," Acta Astronautica, Volume 56, Issues 9-12, May-June 2005, Pages 809-819.

Abercromby, A.F.J., Arellano, C., Neptune, R.R., Ambrose, C.A., and Layne, C.S. "Inverse Dynamics Gait Analysis Using Optoelectronic and Digitized Virtual Markers." The Houston Society for Engineering in Medicine and Biology, The 22nd Annual Houston Conference on Biomedical Engineering Research, February, 2005.

Abercromby, A.F.J., Amonette, W.E., Paloski, W.H., Hinman, M.R., Layne, C.S., "Effect Of Knee Flexion Angle On Neuromuscular Responses To Whole-Body Vibration" To Be Presented – 28th NSCA National Conference and Exhibition, Las Vegas, July 2005.

Amonette, W.E., Abercromby, A.F.J., Paloski, W.H., Hinman, M.R., Layne, C.S., "Neuromuscular Responses To Two Whole-Body Vibration Modalities During Dynamic Squats" To Be Presented – 28th NSCA National Conference and Exhibition, Las Vegas, July 2005.

OTHER SUPPORT

Name

Andrew Abercromby, M.Eng

NO OTHER SUPPORT

OTHER SUPPORT

Name

R.D.Hagan, Ph.D.

Active

SMS00403 (Babs Soller (UMass) and R. Donald Hagan (NASA))	07/01/2004-06/30/2006	5%
NSBRI/NASA	$700,000	
Development and Testing of a Noninvasive Sensor fo		

Develop and demonstrate a portable, noninvasive, optical instrument which can accurately measure muscle metabolism during exercise, for use to clinically evaluate physical fitness and readiness for operational objectives during spaceflight.

MENTOR SUPPORT

I am pleased to give my support to the National Space Biomedical Research Institute post-doctoral fellowship application of Mr. Andrew Abercromby to work in the Exercise Physiology laboratory at the NASA Johnson Space Center. Mr. Abercromby has previously worked in other JSC laboratories conducting biomechanical evaluations of space-related operations. The work that he is proposing will be a part of our long-term desire to better understand the effect of weightlessness on exercise performance, and to develop better exercise countermeasure devices and prescriptions for long-duration space inhabitants.

At JSC, I am the Exercise Lead for the Human Adaptation and Countermeasures Office, and manager of the Exercise Physiology Laboratory. As such, I am involved in many activities related to the Exercise Countermeasures Program onboard the International Space Station. The responsibilities associated with these activities allow me to mentor, advice, and assist graduate students and post-doctoral fellows interested in space and life sciences. In addition, our laboratory personnel are well-versed in academic pursuits and will be able to enhance the mentoring experience.

Our programs and laboratory are unique in that we support both medical operations and research activities. The goals and objectives of the Exercise Physiology Laboratory are four fold: 1) to support pre-flight, in-flight, and post-flight medical physical fitness testing operations, 2) to assist in the development of astronaut physical conditioning programs, 3) to evaluate and validate exercise countermeasure equipment, procedures, protocols, and conditioning programs related to the maintenance of crew health and performance during ISS missions, and 4) to study the effects of micro- and reduced gravity upon human performance during and after exposure to micro- and reduced gravity and space flight. The work proposed by Mr. Abercromby will support all of these goals and objectives.

We are regular contributors to scientific programs in the exercise and life sciences, and often give presentations and lectures to graduate school programs related to space operations and activities. In addition, we support NASA and NSBRI summer internships. I feel that we will be able to provide Mr. Abercromby with a unique educational program and research opportunity. Thus, I gave my full support to the proposal submitted by Mr. Abercromby to conduct post-doctoral fellowship work in our Exercise Physiology laboratory.

RESOURCES

FACILITIES

Laboratory:

Exercise Physiology Laboratory, NASA/JSC: Laboratory equipment (see 'Major Equipment') will be used for data collection protocols. The Advanced Resistive Exercise Device (ARED), electromyography, load sensing, and motion capture systems to be used in the proposed project are all located in the NASA/JSC Exercise Physiology Laboratory. The laboratory is onsite at NASA/JSC, where the project will be based. The Mentor for this Postdoctoral Fellowship Application is R. Donald Hagan, Ph.D. who is the Exercise Lead for the Human Adaptations and COuntermeasures Office at NASA/JSC.

Clinical:

Human Test Subject Facility, NASA/JSC: All test subjects will be recruited through the NASA/JSC Human Test Subject Facility, which is located onsite at NASA/JSC.

Animal:

Not applicable.

Computer:

Dell Precision 670 computer with MS Office Pro and HP Laserjet 1300n printer will be used for project management and administration. Computers and software programs (MATLAB, SmartAnalyzer, LifeMOD, Statistica, MS Excel) will be used for data processing and analysis. All requisite computing hardware and software will be available for use in the Exercise Physiology Laboratory.

Office:

Office space will be available for the Princioal Investigator within the Exercise Physiology Laboratory at NASA/JSC.

Other:

Information technology, electronics, and machine shop support facilities will all be available to the project onsite at NASA/JSC.

MAJOR EQUIPMENT

C-9 parabolic flight aircraft: Parabolic flight testing will be used to investigate resisitive exercise during short periods of microgravity. The flights will be based from Ellington field, which is approximately 10 miles from NASA/JSC. The C-9 and the requisite equipment to conduct onboard testing will be available to the project.

Advanced Resisitive Exercise Device (ARED): Exercise Physiology Laboratory, NASA/JSC. ARED enables performance of resistive exercise in 1-g and microgravity environments. The device is instrumented to record the requisite load data and is certified for use onboard the C-9 parabolic flight aircraft. Although not the primary focus of the research project, the use of ARED will also enable the findings of the research to be applied to the utilization of the ARED which is intended for use on the International Space Station.

Free Weights: Exercise Physiology Laboratory, NASA/JSC. Free weights will be used as a well-understood resistive exercise modality with which to compare the ARED. Free weights will not be used onboard the C-9.

Electromyography (EMG): Exercise Physiology Laboratory, NASA/JSC. Surface EMG will provide a non-invasive method of measuring muscle activation during resistive exercise. Muscle activation data will be used to validate the optimization method used by comparing the mathematically calculated muscle onsets and offsets with the muscle onset and offset data collected using EMG.

Strain gauges: Exercise Physiology Laboratory, NASA/JSC. Strain gauges (load cells) are needed to measure the amplitude and direction of all forces acting on the subject during resistive exercise. This kinetic data is used in conjunction with kinematic data to calculate the forces and moments throughout the body, and subsequently in individual bones and muscles. The load sensing equipment to be used in the proposed research project has been successfully used by the Exercise Physiology Laboratory personnel in previous parabolic flights.

eMotion SMART system (Motion Capture): The calculation of bone and muscle forces requires that the position of each body segment is measured accurately with respect to time over the duration of the resistive exercise. This system has capability to measure body sgement positions with errors of less than 1mm. The motion capture equipment to be used in the proposed research project has been successfully used by the Exercise Physiology Laboratory personnel in previous parabolic flights.

GOALS

The long-term objective of this research is to develop a spaceflight resistive exercise (RE) device and exercise regimens that more closely replicate bone and muscle forces (BMF) experienced during 1-g RE with the aim of reducing or preventing bone and muscle deconditioning. This objective is consistent with NSBRI's goals of identifying more suitable high-resistance exercise prescriptions to prevent or reduce muscle and bone loss.

This study will test three hypotheses: 1) Hypogravity significantly reduces BMF experienced during RE at the same external load. 2) Increasing the magnitude of a single RE load in hypogravity does not eliminate significant differences in BMF between hypogravity and 1-g RE. 3) Application of multiple discrete segmental RE loads in hypogravity can eliminate significant differences in BMF between hypogravity and 1-g RE.
The specific aims are to test the hypotheses as follows: A) Develop and validate a biomechanical model that quantifies BMF during RE under different resistive loads, exercise modalities, and gravity levels. The model will be developed and validated using motion capture, EMG, and force data from 24 subjects during squats and dead-lifts under three different resistive loads using free-weights (1-g) and Advanced Resistive Exercise Device (1-g and parabolic flight). B) Quantify the effects of hypogravity, resistive load, and exercise modality on BMF during RE. C) Minimize differences between 1-g and hypogravity BMF by using the model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness and simulated Lunar-, and Martian-gravity.

This approach will enable more accurate description of this and other RE devices and associated exercise modalities in terms of potential efficacy and efficiency for bone and muscle strength maintenance. More efficient devices and regimens will require crewmembers to spend less time exercising, thereby making more time available for other duties.

Section 2

Research Plan

Quantification of the Effects of Hypogravity, Resistive Load, and Exercise Modality on Bone and Muscle Forces during Resistive Exercise

Applicant: Andrew F. J. Abercromby, Ph.D. – ABD
Mentor: R. Donald Hagan, Ph.D.
Organization: NASA Johnson Space Center, Exercise Physiology Laboratory

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A. Specific Aims

A priority in current space biomedical research is the development of exercise devices and regimens that prevent bone and muscle deconditioning more effectively and more efficiently during hypogravity (particularly weightlessness, Lunar- and Martian-gravity). **The long-term objective of this research is to develop a spaceflight resistive exercise device and exercise regimens that more closely replicate bone and muscle forces experienced during 1-g resistive exercise regimens with the purpose of reducing or preventing bone and muscle deconditioning**. This objective is based on the following observations. First, the principle of Specific Adaptations to Imposed Demands (SAID), which explains that human muscle and bone adapt specifically to the stresses (biomechanical loads) imposed upon them [1,2]. Second, the purported efficacy of current resistive exercise (RE) countermeasure devices and regimens are based on empirical data derived from training studies in 1-g and not in weightlessness [3]. Third, in weightlessness, body segment weights do not contribute to joint loading, with the result that the training stimulus (biomechanical loading) on the human body will be less than that which results from the same RE in 1-g; ground reaction forces during RE in weightlessness are more than 50% smaller than during equivalent RE in 1-g [4]. Fourth, despite performance of dynamic exercise activities during space flight, crewmembers continue to experience loss of lower extremity muscle size and strength [5, 6] and loss of bone density [5, 7, 8].

Towards this long-term objective, this research project aims to test three specific hypotheses:

1) Weightlessness significantly affects bone and muscle forces during RE.

2) Increasing RE load during weightlessness does not eliminate significant differences in bone and muscle forces during RE in 1-g and in weightlessness.

3) Significant differences in predicted bone and muscle forces during RE in 1-g and in hypogravity can be eliminated by the (simulated) application of discrete segmental resistive loads in weightlessness, and in simulated Lunar- and Martian-gravity.

The specific aims are to test the hypotheses as follows: **A)** *Develop and validate a biomechanical model to quantify bone and muscle forces during RE under different resistive loads, exercise modalities (squats and dead-lifts), and gravity levels*. The model will be developed and validated using force, motion capture, and muscle activation (EMG) data collected from 12 male and 12 female subjects during RE in 1-g and in weightlessness (parabolic flight). Each subject will perform squats and dead-lifts at 3 different resistive loads using free-weights (1-g) and the Advanced Resistive Exercise Device (1-g and weightlessness). **B)** *Quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during RE.* **C)** *Minimize differences between 1-g and hypogravity bone and muscle forces by using the model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness and simulated Lunar- and Martian-gravity.*

The methodological approach to be used in this project will utilize both direct measurement and mathematical modeling to quantify bone and muscle forces associated with real and simulated RE in 1-g and hypogravity. Using the validated model, bone and muscle forces will also be predicted for simulated RE conditions. This approach will enable more accurate description of this and other exercise countermeasure devices and associated exercise modalities in terms of potential effectiveness for bone and muscle strength maintenance and also potential for injury risk reduction. Quantitative information on exercise countermeasure devices and modalities will allow development of specific dose-response (frequency, duration, and intensity) models for their use, thereby allowing for the development of safer and more effective and efficient exercise devices and regimens.

B. Background and Significance

This section will explain that current exercise countermeasure devices and exercise regimens do not adequately prevent bone and muscle deconditioning during weightlessness, and possible reasons for this ineffectiveness will be discussed. The importance of bone and muscle forces in resistive exercise (RE) training is described and it is explained why these forces are affected by weightlessness and hypogravity. Finally, the significance of the proposed research will then be explained in terms of the design and development of exercise countermeasures, injury risk assessment, and the development of a quantitative dose-response model for individualized exercise regimens.

Existing RE countermeasures do not prevent deconditioning in weightlessness. In 1996, Baldwin *et al* concluded that no activity-specific countermeasures exist which adequately prevent or reduce musculoskeletal deficiencies [9]. They further remarked that "it seems apparent that counter-measure exercises that have a greater resistance element, as compared to endurance activities, may prove beneficial to the musculoskeletal system". In 2000, Leblanc *et al* discussed the results of pre- and post-flight DEXA scans from 18 crewmembers each of whom had spent from 4 to 14 consecutive months in weightlessness [10]. The results led them to conclude that the in-flight exercise regimens used during that period were not sufficient to prevent bone and muscle loss during weightlessness. More recent data confirms that International Space Station (ISS) crewmembers continue to experience losses in bone mineral density (BMD), muscle strength and endurance, and aerobic conditioning, as compared to pre-flight values despite the use of cycle, treadmill, and RE countermeasures. Preliminary data indicate that ISS crewmembers completing missions of 3–4 months in duration have on average lost 6–7% of BMD in the proximal femur, and 1–4% of BMD in the lumbar spine. Muscle (quadricep and hamstring) strength and endurance is decreased an average of 20–30% on the fifth day after landing. Aerobic capacity declined 10–15% during the first 30–60 days of flight [5]. Collectively, these alterations reduce mobility and functional capacity to perform tasks, and increase the risk of injury upon return to increased gravity environments. The purpose of this study is to quantitatively investigate a possible reason for this ineffectiveness and evaluate a potential solution.

Bone and muscle forces during RE affect bone and muscle integrity. The principle of Specific Adaptations to Imposed Demands (SAID) dictates that human muscle and bone adapt specifically to the stresses (biomechanical loads) imposed upon it [1,2]. If the forces imposed on bones and muscles during RE in weightlessness are not as large as the forces imposed on the same bones and muscles during RE in 1-g then the SAID principle dictates that those bones and muscles will adapt to the less demanding weightless environment. Thus, decreased BMD and muscle strength and endurance will result. This conclusion is further substantiated by studies that have demonstrated that exercise produces region specific changes in bone mineral density [12-14] and muscle strength [15] and that the effect on bone mineral density and muscle strength varies with exercise modality [13, 15, 16].

To maintain bone and muscle condition, spaceflight countermeasures should reproduce the 1-g training stimulus. As far back as 1992, Cavanagh *et al* suggested that exercise during space flight must be considered from both a biomechanical and physiological perspective [11]. They found that peak loading rates at the feet for running, rowing, and cycling in 1-g were in the ratio 34.7:1.9:1, respectively. The corresponding values for peak foot loads were in the ratio 5.3:1:1.2. They concluded that the large variation in loading with exercise mode highlights the need for quantifying body loading during exercise if optimal countermeasure responses are to be obtained.

Crewmembers typically perform regular RE prior to spaceflight. Free-weight RE regimens in 1-g have been shown to be effective in increasing BMD and muscle strength and volume [3]. It follows that to compensate for the relative absence of incidental bone and muscle stimulation during spaceflight, those bones and muscles must be subjected to training stimuli at least equivalent to those which are experienced during RE preflight (i.e. in 1-g) in order to maintain bone and muscle in pre-flight condition. A resistive exercise device, known as the Advanced Resistive Exercise Device (ARED; see Figure 4, Section C), has been designed to more closely approximate the effects of free weights by providing both a constant force simulating static weight, and an inertial component dependent on acceleration. The premise behind this approach is that the RE loading stimulus during weightlessness should be as similar as possible to the loading stimulus that occurs during RE in 1-g. However, as described below, this device may not adequately reproduce the 1-g training stimulus because of its failure to adequately compensate for the effect of body weight.

Body weight does not contribute to resistive load during RE in weightlessness. In 1-g, the amount of force experienced within and between individual muscles and bones during upright RE is primarily affected by a) the amount of external resistance (load) being lifted, and b) the weight of the person's own body, which must also be lifted. This fact was demonstrated by a study performed at the NASA/JSC Exercise Physiology Laboratory, details of which are included in Section C. For squats, deadlifts, and heel raises performed with the same resistive load in 1-g and in weightlessness mean ground reaction forces and mean index of total work per repetition were reduced in weightlessness by

55% and 65%, respectively [4]. This problem can be illustrated using a simplified diagram of distributed static loading during a 1-g squat compared to a weightless squat (see Figure 1; also Appendix 1 for larger image). Assume that in 1-g the subject's upper body weighs 100 lbs, the upper legs combined weigh 60 lbs, and the lower legs combined weigh 40 lbs. If a 150 lb barbell is lifted in 1-g (left image), the weight of each body segment will contribute to loading at the joints below that segment. As a result, the total static weight load contributions to the hip, knee, and ankle joints are 250 lbs, 310 lbs, and 350 lbs, respectively. In weightlessness, body segment weights do not contribute to joint loading. If a 150 lb load is applied to the shoulders by a resistive exercise device (middle image), then the hip, knee and ankle joints will each see a static weight of only 150 lbs.

Segmental body masses cannot be "replaced" by a single load applied at the shoulders. It is not adequate to "replace" the effect of body weight by increasing the applied resistive load at the shoulders. While this approach may be successful in matching the ground reaction forces between 1-g and hypogravity conditions, it will not replicate the bone and muscle forces experienced in 1-g. Referring back to Figure 1, if the subject attempts to compensate for the lack of body weight by increasing the RE device load to 350 lbs to make up for the missing 200 lbs of body weight (right image), then the hip, knee, and ankle will all see the full 350 lbs. The ankle will be subject to a load equivalent to that in the 1-g exercise, but the knee and hip will experience excessive loads, giving rise to a risk of injury. It may be difficult for the subject to bear the high loading at the shoulders without experiencing significant discomfort or even injury to the shoulders or back. In reality, muscle forces and inertial effects would also contribute to joint loading, further compounding the differences between 1-g and weightlessness. Furthermore, in weightlessness, the crewmember may alter their form (body motions) in response to the altered load distribution and to maintain their balance against the applied load without relying on body weight. In spite of these facts, it is not currently feasible to perform controlled exercise training studies in weightlessness which means that the purported efficacy of current RE devices and regimens are based on empirical data derived from training studies in 1-g and not in weightlessness [3].

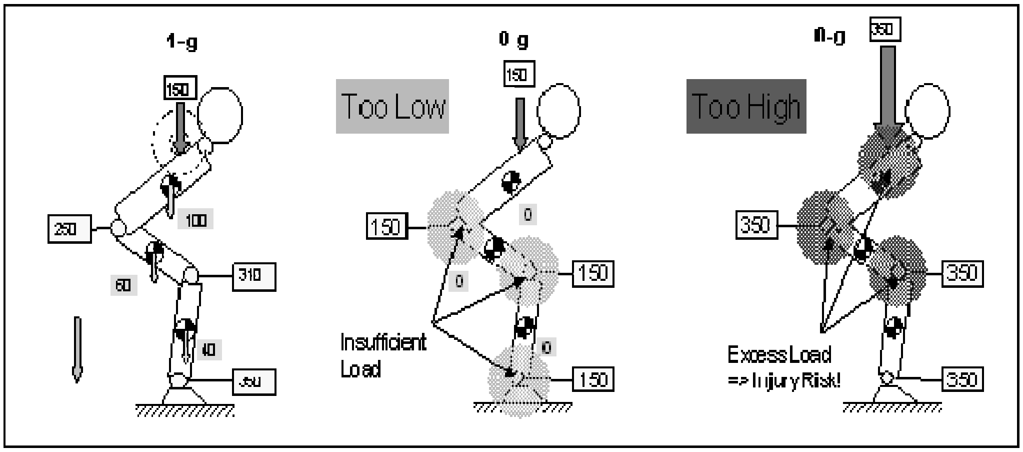


Figure 1: The role of gravity in vertical loading during resistive exercise.

It is necessary to quantify bone and muscle forces in 1-g, weightlessness, and simulated altered gravity. The reduced efficacy of RE training regimens in the weightless environment may be attributable to crew compliance factors, hardware reliability problems, the relative lack of incidental bone and muscle forces experienced in day-to-day activity during spaceflight, and/or the side-effects of other physiological adaptations to weightlessness such as fluctuating levels of glucocorticoids and anabolic steroids [17, 18]. However, as the evidence cited above suggests, continued bone and muscle deconditioning might also be a consequence of significantly lower bone and muscle forces experienced during RE in weightlessness compared with 1-g. The long-term objective behind this study is to evaluate this possibility quantitatively.

Quantification of these forces requires a combination of direct measurement and mathematical modeling. Biomechanical methods involving motion capture, external force measurement, and inverse dynamics have been shown to be highly effective in demonstrating quantitative differences in musculoskeletal loading based on exercise mode and form, improving athletic performance through training, and injury risk prediction [12, 13]. Commercially available human modeling software such as LifeMOD (see Figure 2) has reduced the time and difficulty associated with developing biomechanical human models. Rasmussen *et al* [19] showed that human body modeling can be used in the optimization of exercise machines. Their analysis showed that even small dimensional changes in the exercise machine would significantly change the fraction of overall body work performed by the Latissimus Dorsi muscle. No such model has been previously developed to quantify the effects of weightlessness or altered gravity on biomechanical loading during RE. In addition to enabling the calculation of individual bone and muscle forces, the model will allow the simulation of RE with multiple external loads applied to different body segments and the simulation of RE in partial gravity environments.

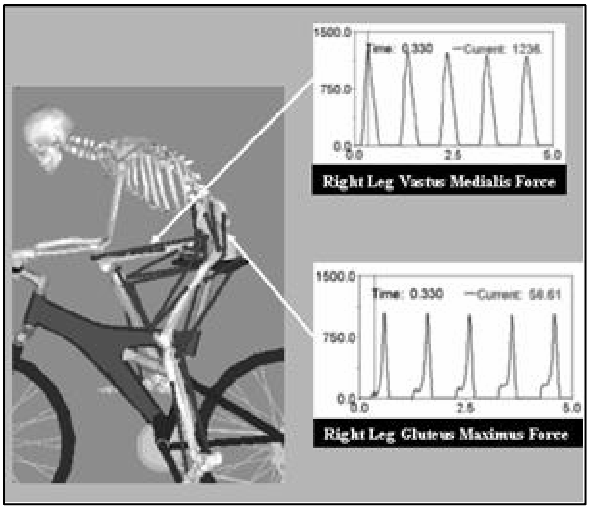


Figure 2: An example of muscle force calculation using LifeMOD modeling.

Results of this study will enable more accurate description of this and other exercise countermeasure devices and associated exercise modalities in terms of potential effectiveness and efficiency for bone and muscle strength maintenance and potential for injury risk. Quantitative information on exercise countermeasure devices and modalities will allow development of specific dose-response (frequency, duration, and intensity) models for their use. In accordance with the long-term objective of this study, this will enable the development of exercise devices and regimens which aim to more effectively and efficiently counteract muscle deconditioning by replicating 1-g biomechanical loading. For the same reasons, the bone and muscle forces and mechanical power exertion associated with treadmills, centrifuges, vibration platforms, and any other countermeasure which aims to impart forces throughout the body should also be quantified. Indeed, the development of the model described in Section D is consistent with NSBRI's objectives of **a)** modeling the effects of microgravity on biomechanical loading in the human body, **b)** aiding in the development and testing of existing and future exercise countermeasures, and, **c)** developing and applying a biomechanical research technique which could subsequently be utilized in bone loss, muscle alterations, cardiovascular alterations, physical fitness and rehabilitation research investigations.

C. Preliminary Studies/Progress Report

The research project will be conducted at the NASA/JSC Exercise Physiology Laboratory (EXL) in cooperation with the personnel listed in Section I. In addition to the evidence presented in Section B, previous studies conducted within the EXL provide the rationale for the testing of the research hypotheses and also demonstrate the capability to safely and successfully conduct research studies using resistive exercise (RE) protocols, electromyography, ground reaction force, and motion capture data both in laboratory settings and during parabolic flights. Research studies conducted by the Principal Investigator demonstrate experience in biomechanical study design, hardware integration and synchronization, data collection, data processing, biomechanical modeling, inverse dynamics, statistical analysis, project management, and interdisciplinary collaboration.

NASA/JSC Exercise Physiology Laboratory

Recent research conducted within the NASA/JSC Exercise Physiology Laboratory investigated the effects of weightlessness on ground reaction forces during RE using the interim Resistive Exercise Device (iRED). The purpose of this project was to compare ground reaction force during iRED exercise in normal gravity (1-g) vs. weightlessness achieved during parabolic flight. Four subjects performed three exercises (squat, heel raise, and dead-lift) using the iRED during 1-g and weightlessness at a moderate intensity (60% of maximum strength during dead-lift exercise). Ground reaction force was measured in the three orthogonal axes using a force platform, and the magnitude of the resultant force vector was calculated. Linear displacement (LD) was measured using a linear transducer. Peak force (Fpeak) and an index of total work (TWi) were calculated and paired t-tests were used to test differences between 1-g and weightless RE. Results indicated that Fpeak (Figure 3) and TWi measured in the resultant axis were significantly decreased (p <0.05) in weightlessness for each of the exercises tested. During weightlessness, Fpeak was 42-46% and TWi was 33-37% of that measured during 1-g. LD and average time to complete each repetition were not different from 1-g to weightlessness. The finding that ground reaction forces are significantly reduced during RE in weightlessness is consistent with the hypothesis that bone and muscle forces are significantly affected by weightlessness. Individual bone and muscle forces were not calculated in this study, however their magnitudes are known to be proportional to the magnitude of the ground reaction forces.

Pilot data is currently being collected for the 1-g component of the proposed study. Kinetic, kinematic, and EMG data have been collected synchronously from 6 subjects during parallel back squats and deadlifts using ARED and free-weights in 1-g. The primary purpose of the pilot study is to verify that the necessary exercises can be performed with the necessary loads and instrumentation without occlusion of motion capture markers or interference with kinetic and EMG data collection. As a result of the pilot study, a suitable data collection protocol and instrumentation configuration have been developed and data have been collected which demonstrate the requisite integrity to perform the subsequent analysis which would be performed during the proposed research project. A 39-marker, 19-segment model will be used. All data collection was performed with appropriate NASA/JSC CPHS approval.

Principal Investigator: Andrew Abercromby, Ph.D. – ABD

Mr. Abercromby has previous experience as a Principal Investigator on research projects at both the University of Houston and at the Johnson Space Center:

Mr. Abercromby is currently the Principal Investigator on a biomechanical analysis study in the Laboratory of Integrated Physiology at the University of Houston (*"Inverse Dynamics Analysis Using Optoelectronic and Virtual Markers"*). Mr. Abercromby has developed an innovative technique to perform bilateral inverse dynamics gait analysis using an OptoTrak optoelectronic motion capture system (Northern Digital, Inc, Waterloo, Canada) with a single camera array. The technique reduces the duration and discomfort of data collection protocols for subjects and allows for near-real-time biomechanical modeling and analysis of gait. Joint forces and torques are calculated using the Visual3D inverse dynamics software program (C-Motion, Rockville, MD). Mr. Abercromby's technique will be used in a collaborative project with the University of Texas Health Science Center and the University of Texas at Austin (*"Biomechanical Implant Wear Mechanisms during Human Locomotion"*). Details of the technique were presented at a biomedical engineering conference [20] and prompted ongoing discussions between Northern Digital, Inc and C-Motion (manufacturers of the Visual3D software) with a view to a collaborative project on the basis of the capability developed by Mr. Abercromby. The capabilities and the model-building techniques learned and enhanced in this study will be directly applicable to the data collection, model development and analysis to be performed in the proposed research project.

Mr. Abercromby is currently the Principal Investigator on a research project within the Human Adaptations and Countermeasures Office at NASA/JSC (*"Neuromuscular and Biomechanical Responses to Whole-Body Vibration during Standing"*). The study involves collaboration between the Neurosciences Laboratory, Countermeasure Evaluation and Validation Project, Exercise Physiology Laboratory, and the University of Texas – Medical Branch. Electromyography (EMG), motion capture, and accelerometry data were collected on 16 human subjects during two different modes of whole-body vibration (WBV) while performing static and dynamic unloaded squats. The study is investigating the effects of knee angle, WBV mode, height, weight, and motion artifact on the measured neuromuscular responses to two different modes of WBV. It is also the first study to quantify the severity of vibration associated with WBV training platforms according to international standards for human vibration exposure (ISO 2631). Results of the preliminary analyses will be presented in two oral presentations at the National Strength and Conditioning Association Conference in July 2005 [21, 22]. Manuscripts are being prepared for submission to peer-reviewed journals. Mr. Abercromby has participated in several other similar EMG studies as a co-investigator [23-27].

In 2001, Mr. Abercromby led a 10-month interdisciplinary research and development project involving approximately 20 scientists and engineers at both the Johnson Space Center and Kennedy Space Center (*"Ground-Based Detailed Test Objective: Spacecraft Visual Attitude Determination"*). The project involved the development and subsequent evaluation of a human-in-the-loop spacecraft attitude determination technology. The project required collaboration across multiple technical disciplines and locations and was successfully completed on-time and within budget. Mr. Abercromby received the Titan-Astronautics Outstanding Achievement Award for his role in the project and was also recognized with a National Award from the Institution of Mechanical Engineers (IMechE).

D. Research Design and Methods

In this study, skeletal joint force (bone force) and muscle tension (muscle force) will be determined during resistive exercise (RE) in 1-g and in weightlessness (parabolic flights). This will be accomplished through the use of direct measurement, inverse dynamics, and human body modeling. Direct measurement will be used to quantify the kinematics (joint position, velocity, and acceleration) associated with body motions, and the external loads (forces and moments) imposed on the subject by the device and other supporting structures. A combination of direct measurement and empirical math formulae are used to account for the subject's anthropometry (body geometry) and mass properties (mass and moments of inertia of segments). Mathematical models will be used to describe joint degrees of freedom, and bone and muscle form and function. Inverse dynamics methods will be used to calculate the joint forces and joint torques associated with the measured external loads (kinetic data) and kinematics. The individual muscle forces that contribute to joint force and joint torque, and the forces acting upon bones, will be determined through mathematical modeling and optimization.

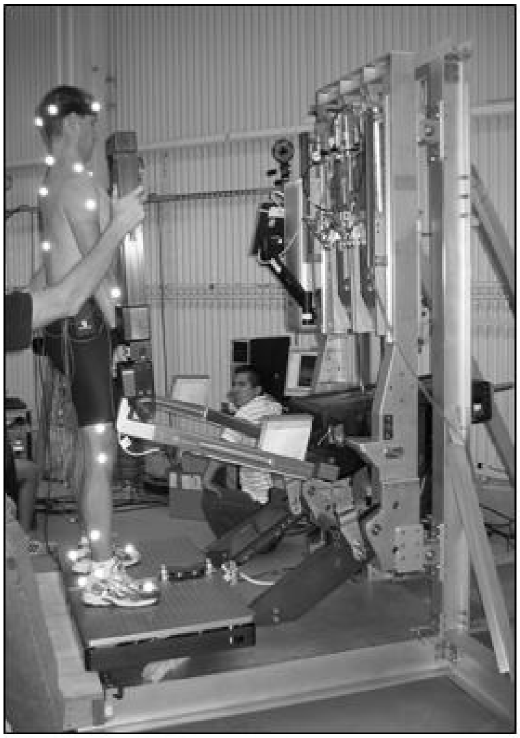


Figure 4: Collection of EMG, kinetic, and kinematic pilot-data using the Advanced Resistive Exercise Device (ARED).

RE will be studied in two environments: ground-based laboratory (1-g) and C-9 research aircraft (weightlessness). Within the laboratory environment, squat and dead-lift exercises performed using the Advanced Resistive Exercise Device (ARED; see Figure 4) will be compared with the same exercises performed using free weights (barbell). Studies performed on the C-9 will involve only the ARED device, which is designed for use in weightless environments. The study design is shown in Table 1. To the extent possible, the order of sessions 3 through 14 will be balanced across subjects. Scheduling constraints for the C-9 flights may limit the extent to which sessions 15 and 16 can be included in the balancing process. The parabolic trajectories flown by the C-9 aircraft are imperfect and thus weightlessness can only be maintained within a few hundredths of 1-g. Furthermore, only about 25 seconds of near weightlessness can be sustained per parabola before the aircraft is required to pull out of its dive. Multiple parabolas are used to make up the overall duration of weightlessness required.

Twenty-four subjects (12 male and 12 female) will perform the experiments in the laboratory and on the C-9. A power analysis suggested between 8 and 16 subjects would be adequate for a univariate analysis of the data. Available data in the literature, however, do not support a multivariate power analysis. To get around this limitation, the number of subjects in the study design has been increased to 24.

Parallel back squats and deadlifts will be examined. Parallel back squats and deadlifts are considered to be particularly effective at targeting the bones and muscles most affected during prolonged weightlessness. Subjects will perform each of the exercises at 65, 75, and 85% of their one repetition maximum load (1RM). For the C-9 portion, a fourth load level of 75% of 1RM plus 60% of the subject's body weight will be added. This fourth load level will partially compensate for the lack of body weight loading in the weightless environment. Since the fraction of body weight above the hip is estimated to be 60% of the total body weight, this fourth load level is expected to provide an approximate match with the hip loading for the 75% of 1RM load level in 1-g. Five repetitions will be performed at each load level. Cadence will be controlled at 3 sec: 1 sec (Eccentric: Concentric) using a metronome.

Session	Environment	Device[1]	Exercise[2]	Load	Purpose
1	Lab (1-g)	FW	Squat	Harman protocol	Determine 1RM
2			Deadlift	Harman protocol	
3	Lab (1-g)	FW	Squat (5 reps/set)	65%, 75%, 85% 1RM	Kinematics, Kinetics, EMG
4				65%, 75%, 85% 1RM	
5				65%, 75%, 85% 1RM	
6			Deadlift (5 reps/set)	65%, 75%, 85% 1RM	
7				65%, 75%, 85% 1RM	
8				65%, 75%, 85% 1RM	
9	Lab (1-g)	ARED	Squat (5 reps/set)	65%, 75%, 85% 1RM	
10				65%, 75%, 85% 1RM	
11				65%, 75%, 85% 1RM	
12			Deadlift (5 reps/set)	65%, 75%, 85% 1RM	
13				65%, 75%, 85% 1RM	
14				65%, 75%, 85% 1RM	
15	C-9 (0-g)	ARED	Squat (5 reps/set)	65% 1RM	
				75% 1RM	
				85% 1RM	
				75% 1RM + 60% BW	
16			Deadlift (5 reps/set)	65% 1RM	
				75% 1RM	
				85% 1RM	
				75% 1RM + 60% BW	

[1]: The order of devices used in sessions 2 and 3 will be balanced among subjects. [2]: The order of exercises will be randomized.

Table 1. Detailed description of subject sessions in terms of environment. device. exercise. and load.

Collecting the requisite data during each training session requires at least three test operators, and will involve the placement of electrodes and tracking markers on subjects. In this technique, erroneous marker placement will introduce errors into the bone and muscle force calculations. However, the PI and the personnel in the NASA/JSC EXL have considerable experience with both EMG and motion capture data collection protocols and the test operators gained further experience with this specific protocol during the pilot data collection described in Section C. These potential error sources are inherent in any protocol involving motion capture over multiple sessions.

Kinematic (position), kinetic (force), and EMG (muscle activation) data will be measured in both the laboratory and C-9 environments. Ground based and C-9 kinematic data will be collected using six 120 Hz eMotion SMART infrared strobe cameras (BTS Bioengineering, Milan, Italy) while subjects perform RE. Small, lightweight, retro-reflective markers will be affixed to the subject over appropriate bony landmarks of body segments necessary for task analysis. All markers will be affixed to the subject via non-abrasive standard adhesive tape or Velcro straps. The motion capture system will track the 3-dimensional position of all markers during each trial using stereophotogrammetry. Pilot data collection at the NASA/JSC Exercise Physiology Laboratory successfully tested a marker set which is not occluded by other equipment and instrumentation (see Figure 4). A force sensing platform (Advanced Mechanical Technology Inc, Watertown, MA) and load cells will be used to measure all forces acting on subjects during RE (i.e., ground reaction forces and forces resulting from resistive load). All force sensing equipment will be calibrated prior to each use. Electromyography (EMG) measurements will be recorded for the 18 muscles of interest (see Table 2) using bipolar surface electrodes (Therapeutics Unlimited Model 544, Iowa City, IA). Standard EMG data collection procedures will be followed in accordance with manufacturer's and Institutional Review Board requirements. All data will be recorded synchronously while the subject performs the appropriate task. The raw data will be monitored, amplified, filtered, and recorded on a computer hard drive.

Advances in motion capture technology have greatly increased the accuracy and processing speed of marker position data for humans performing exercise movements and motions. The use of force plates and load cells for measurement of forces and moments generated by human body interaction with external objects (floor, barbell, etc.) has also demonstrated a high degree of accuracy and consistency. Thus, the measurements of applied forces and marker positions are expected to be highly accurate. Kinematics calculations (segmental and joint angular positions, velocities, and accelerations) are made with the assumption that marker data can be used to reconstruct body segments accurately. Because the markers are placed on the subjects' skin the axes of rotation of a body segment are determined through extrapolation. This approximation may lead to small errors in kinematic measurements, however it is not anticipated that the resulting errors will be appreciable. Small error rates are expected in biomechanical studies involving motion measurement.

Joint, muscle and bone forces will be calculated using inverse dynamics and biomechanical modeling. The process of calculating individual muscle forces involves two steps. The first step will be the calculation of joint motions and loads using the SmartAnalyzer inverse dynamics software program (eMotion, Milan, Italy)). Kinematic (position) data will be used to build a software model of each subject, from which joint motions can be plotted over time. Incorporating the kinetic (force) data into the model allows derivation of joint forces and torques using standard inverse dynamics procedures embedded within the SmartAnalyzer software program.

In the second step, the joint kinematics and external load parameters calculated using SmartAnalyzer will be used as inputs to a dynamics and simulation software analysis application called LifeMOD (Biomechanics Research Group, San Clemente, CA). The individual muscle forces are resolved by means of a model that assumes that muscles are activated in an optimal way. The model, which will be developed using LifeMOD software, will be used to compute the specific bone and muscle forces associated with each joint. Forces will be quantified for the bones and muscle listed in Table 2. <u>These bone and muscle forces will be the dependent variables used to statistically test Hypotheses 1 and 2.</u> The benefits of calculating bone and muscle forces rather than simply ground reaction forces are explained in Section B; identical ground reaction forces can result from very different biomechanical loading distributions. It is ultimately the loading distribution and not ground reaction forces which will affect bone and muscle condition. LifeMOD software has already been validated in terms of its ability to predict both ground reaction force [28] and inter-segmental forces [29].

Bones	Muscles	
Calcaneus	Sartorius	Rectus Femoris
Tibia	Iliacus	Biceps Femoris
Fibula	Psoas	Semitendinosus
Femur	Gluteus Maximus	Semimembranosus
Pelvis	Gluteus Medius	Adductor magnus
Sacrum	Gluteus Minimus	Gastrocnemius
Vertebrae	Vastus Lateralis	Soleus
	Vastus Medialis	Latissimus Dorsi
	Vastus Intermedius	Erector Spinae

Table 2: Bones and muscles for which forces will be quantified.

To reduce the uncertainty associated with the muscle activation model, direct measurements of muscle activation using EMG will be compared with the model predictions. For muscle and bone forces, the human body may be modeled as a system of connected rigid bodies with degrees of freedom sufficient to describe motion relevant to the bones and muscles of interest. This approach assumes that motion in secondary joints, such as those of the hand; do not have a significant impact on other joints of interest (the knee, for example). The assumption of rigid bodies is a limitation that avoids the complexity of the deformable mass of soft tissue connected to the skeleton. Modeling body segments with constant mass and moments of inertia properties is not considered to significantly affect the accuracy of forces calculated at the whole bone and whole muscle level and is the only non-invasive method by which to calculate these forces.

The biomechanical model will be validated and used to predict bone and muscle forces under simulated resistive loads and simulated gravity levels. Calculations of bone and muscle forces in 1-g and weightless conditions will be derived from the actual kinetic and kinematic data collected during each trial, as described above. Bone and muscle forces calculated during simulated conditions (1/3-g and 1/6-g and different external loads) will be based on the assumption that the kinematics (body motion) in these conditions would be unchanged and only the internal bone and muscle forces would change. The magnitude of the simulated resistive load applied by the RE device can be varied and additional loads can be applied to different parts of the body.

In addition to the model validation described above, bone and muscle forces will be calculated for the weightless condition using the kinematic data from the equivalent trial in 1-g, and compared with the bone and muscle forces calculated using the actual weightless kinematic data. The resistive ARED load inputs will be the same in both models. Comparison of the results of "real" and simulated data will provide an indication of the accuracy with which the biomechanical model can predict bone and muscle forces under simulated conditions. Similarly, 1-g bone and muscle forces will be predicted using the kinematic data from the equivalent trial in weightlessness. The same approach will be used to compare results between "real" and simulated levels of resistive load in both 1-g and weightlessness. Predictions will be repeated across all trials, subjects, and conditions with the purpose of characterizing the model with respect to its ability to predict bone and muscle forces using "real" kinematic data and other simulated inputs. On the basis of these comparisons, statistical confidence intervals will be calculated as an indication of the accuracy with which the model can predict bone and muscle forces during altered resistive load levels and in 1-g versus weightlessness. The biomechanical model will then be used to predict bone and muscle forces under varied simulated loading conditions and simulated gravity states with the objective of matching bone and muscle forces to those experienced during 1-g RE. The predicted bone and muscle forces under these simulated conditions will be the dependent variables in the statistical testing of Hypothesis 3.

The use of the biomechanical model in a predictive role provides insight into the potential effectiveness of exercise devices and regimens in situations which could not otherwise be tested without significant cost and possible risk to human subjects.

Data Analysis and Interpretation

Data from LifeMOD will be processed using MATLAB (The Mathworks, Natick, MA). For each of the bones and muscles listed in Table 2, the time history, the peak value, average value, and time integral (force impulse or work) will be determined in each condition. The average and peak rate of change of compressive and tensile forces will also be calculated for bones. Data analysis will be performed using MATLAB and Statistica (StatSoft, Tulsa, OK). As described above, a large number of dependent variables will result from the biomechanical analysis. Accordingly, a combination of multivariate and univariate approaches will be used in which processed bone and muscle force parameters described above will be the dependent variables. In the hypothesis testing, multivariate models will be used for omnibus tests in which data from all joints are tested concurrently. In all instances, appropriate follow-up tests will be used to test the hypotheses in individual joints, muscles, bones, and for squats versus deadlifts. The probability of a Type-I error (α) will be controlled at 0.05 using a Bonferroni or similar adjustment for each hypothesis. If no significant gender effects are found, the data will be combined into a single group for hypothesis testing.

Hypothesis 1: *Weightlessness significantly affects bone and muscle forces and mechanical power exertion during RE.* A 2x2x2 (Gravity x Exercise x Gender) repeated measures (RM) Multivariate Analysis of Variance (MANOVA) will be conducted. A significant Gravity (1-g vs. weightlessness) main-effect is expected and would indicate that – averaged across all loads, all exercises, all bones, and all muscles – weightlessness significantly affects bone and muscle forces, supporting Hypothesis 1.

Hypothesis 2: *Increasing RE load during weightlessness does not eliminate significant differences in bone and muscle forces and mechanical power exertion during RE in 1-g and in weightlessness.* A 2x5x2 (Exercise x Loading Condition x Gender) RM MANOVA will be conducted. The five loading conditions will be the 1-g 65% 1RM condition and all four weightless loading conditions. Planned simple contrasts will be performed in which each of the four load levels in the weightless condition are compared with the 1-g 65% 1RM condition. If, as expected, significant differences are observed between the 1-g condition and each of the weightless conditions then the data will be considered to support Hypothesis 2.

Hypothesis 3: *Significant differences in predicted bone and muscle forces during RE in 1-g and in hypogravity can be eliminated by the (simulated) application of discrete segmental resistive loads in weightlessness, and in simulated Lunar- and Martian-gravity.* During the simulation phase, discrete external loads will be applied to body segments during RE in weightlessness with the objective of approximating the effect of segmental weights during RE in 1-g at 75% 1RM. Within the LifeMOD model, constraints will be defined on the basis of practical issues of how and where external loads can be applied to the modeled human. Within the bounds of these constraints, LifeMOD will derive an optimal combination of external loads for each subject in weightlessness, simulated 1/3-g and simulated 1/6-g, which will most closely approximate the bone and muscle forces experienced during RE in 1-g.

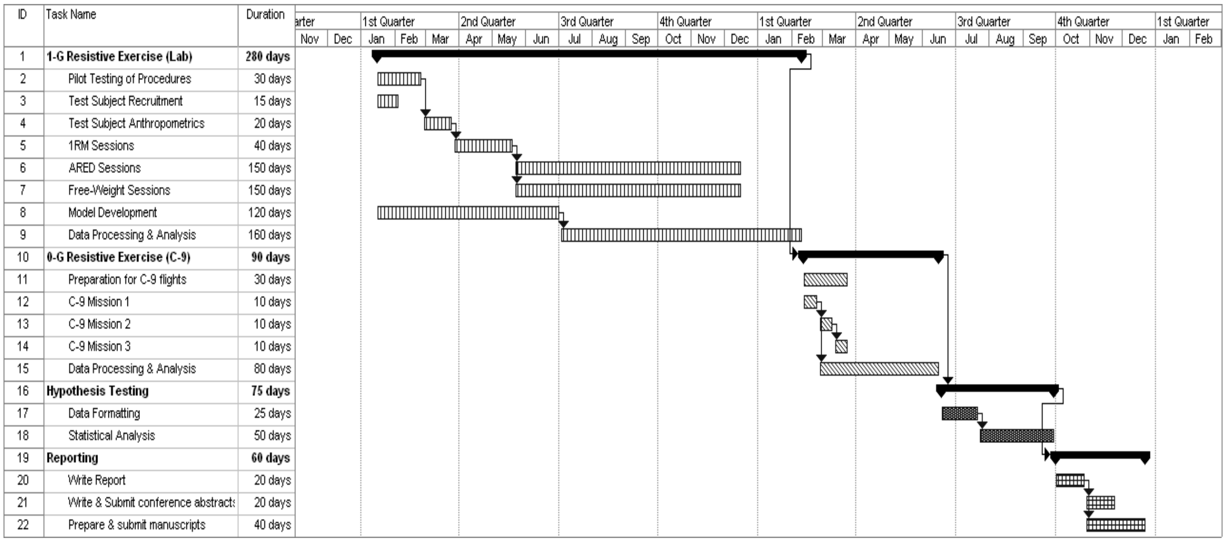
The bone and muscle forces predicted during the optimized simulated RE for each gravity level will be statistically compared with those calculated during actual RE in 1-g using both ARED and free-weights. A 2x5x2 (Exercise x Condition x Gender) RM MANOVA will be conducted. The five conditions will be 1-g ARED, 1-g FW, simulated 1/3-g ARED, simulated 1/6-g ARED, and weightlessness ARED, all performed at 65% 1RM resistive load. Planned simple contrasts will be performed in which each of the three reduced gravity conditions are compared with each of the 1-g conditions. If, as expected, no significant differences are observed between the 1-g ARED condition and each of the reduced gravity conditions then the data will be considered to support Hypothesis 3. Furthermore, if no significant differences are observed between the 1-g free-weight condition and each of the reduced gravity conditions then the data will also be considered to support the assertion that the application of discrete segmental loads during RE in weightlessness can be used to replicate the bone and muscle forces experienced during free-weight RE in 1-g, which is known to stimulate both bone and muscle.

Data Sharing

Data will be supplied to the NSBRI/NASA Bioinformatics Initiative within the two-year timeframe of the proposed research project. Additionally, findings of the study will be presented at National scientific meetings and will be submitted to peer-reviewed journals for publication.

Projected Timeline

A Gantt chart illustrating a projected timeline for the study is shown in Figure 5 (larger version in Appendix 2).



ID	Task Name	Duration
1	**1-G Resistive Exercise (Lab)**	**280 days**
2	Pilot Testing of Procedures	30 days
3	Test Subject Recruitment	15 days
4	Test Subject Anthropometrics	20 days
5	1RM Sessions	40 days
6	ARED Sessions	150 days
7	Free-Weight Sessions	150 days
8	Model Development	120 days
9	Data Processing & Analysis	160 days
10	**0-G Resistive Exercise (C-9)**	**90 days**
11	Preparation for C-9 flights	30 days
12	C-9 Mission 1	10 days
13	C-9 Mission 2	10 days
14	C-9 Mission 3	10 days
15	Data Processing & Analysis	80 days
16	**Hypothesis Testing**	**75 days**
17	Data Formatting	25 days
18	Statistical Analysis	50 days
19	**Reporting**	**60 days**
20	Write Report	20 days
21	Write & Submit conference abstracts	20 days
22	Prepare & submit manuscripts	40 days

Figure 5: Projected 2-year timeline.

Procedures, situations, or materials that may be hazardous to personnel and the precautions to be exercised

1) Due to the nature of parabolic flight, it is possible that test operators will experience disorientation, nausea, and vomiting. Symptoms are likely to occur among some operators but are temporary and do not have lasting deleterious health effects. Motion sickness medication will be available through the NASA-JSC Test Subject Facility as prescribed by a qualified physician. In addition, operators will carry motion sickness bags to contain vomit as necessary. A flight surgeon will be immediately available on the flight to assist as necessary. **2)** During parabolic flight, unexpected forces may be exerted upon test operators by sudden changes in the flight pattern. This may result in a loss of balance resulting in musculoskeletal injury. Personnel will use foot and hand restraints as necessary to provide the requisite postural support. Also, personnel will closely monitor the flight accelerometer to anticipate pull-out and the onset of gravitational forces. During hypergravity no exercises will be performed. Potentially hazardous situations for test subjects are addressed in Section E.

E. Human Subjects Research

1. Risks to the Subjects

Human Subjects Involvement and Characteristics: Human subjects will perform dynamic and repetitive resistive exercise. Exercise will be performed by those subjects in a laboratory setting and also in a research aircraft which will fly in parabolas to induce multiple periods of short-duration (20-30 seconds) of weightlessness). Up to 12 male and 12 female human subjects will be recruited through the NASA/JSC Human Test Subject Facility. Anticipated age range is 25-40 years. All subjects will have passed a Class III Air Force Physical Examination and will be screened for cardiovascular and orthopedic contraindications to resistive exercise.

Sources of Materials: Data collected from individual subjects will include measures of height, weight, body dimensions, strength, and physical activity level. Data describing body forces and movements and muscle activation during resistive exercise will be recorded. All data collected will be used directly in this study and will be coded such that identifiers are eliminated. The code key will be kept in a locked file cabinet by the principal investigator. All raw and collated data will be kept in locked file cabinets. Published data will not include identifiers. No use will be made of pre-existing specimens, records, or data.

Potential Risks: **1)** Subjects in this study will perform dynamic and repetitive resistive exercise. Potential hazards from this activity include muscle soreness and possible strain to the muscle, tendon or joint. Some degree of muscle soreness is expected to occur in all subjects since this is a normal result of resistive exercise. The occurrences of muscle, tendon or joint strain are rare with resistive exercise. The risks associated with this type of exercise are reasonable and are unavoidable in research investigations of resistive exercise. **2)** Due to the nature of parabolic flight for this evaluation, it is possible that subjects will experience disorientation, nausea, and vomiting. Symptoms are likely to occur among some subjects but are temporary and do not have lasting deleterious health effects. **3)** During parabolic flight, unexpected forces may be exerted upon subjects by sudden changes in the flight pattern. This may result in a loss of balance or improper performance of the exercise. Without protection against this risk, there is a high probability of this occurrence. Possible consequences of loss of balance include musculoskeletal injury due to falling. An alternative to parabolic flight is exercise testing in the weightlessness onboard the ISS. Cost and schedule restrictions preclude this as a possibility for this study. **4)** Subject confidentiality could be compromised through the publishing or theft of personally identifiable information. There is low likelihood of this occurring but this risk has potentially considerable seriousness for subjects in terms of psychological, and/or social harm. Personal information must be recorded for all subjects in order to test the research hypotheses.

2. Adequacy of Protection against Risks

Recruitment and Informed Consent: All subjects will be recruited from the NASA/JSC Human Test Subject Facility (HTSF). Potential participants will be identified from a HTSF database of human test-subjects and contacted via telephone by HTSF staff. Standard NASA informed consent procedures will be followed for this study. The study is first verbally described to each subject and preliminary questions are asked to determine whether the subject is willing and suitable for this study. Subjects attend a briefing session where the study is described in detail, experimental equipment and procedures are described and/or demonstrated, and a written layman's summary and consent form are presented. The subjects are encouraged to ask questions or to obtain further clarifications of the study purpose, risks, or procedures. Next subjects are carefully screened for medical risk factors (Air Force Class III physical or equivalent). Once medically cleared, a written informed consent is obtained. Subjects are free to withdraw from the study at any time. The study will have been reviewed and approved by the NASA JSC Committee for the Protection of Human Subjects. Signed statements of informed consent will be kept in a locked file cabinet by the principal investigator.

Protection Against Risk: Subjects will be protected against the risks described in Section E1 as follows: **1)** All subjects will perform light stretching prior to exercise. Exercise repetitions will be performed in a ramp fashion, starting with 8–10 repetitions at 50% of maximal effort and ending with 5–6 repetitions at 80% of maximal effort. Subjects will be reminded that they may end the exercise at any time and to communicate any degree of discomfort to the test operator. These precautions will likely reduce the extent of muscle soreness and the likelihood of suffering a strain to the muscle, tendon or joint. **2)** Motion sickness medication will be available through the NASA-JSC Test Subject Facility as prescribed by a qualified physician. In addition, subjects will be encouraged to carry motion sickness bags to contain vomit as necessary. A flight surgeon will be immediately available on the flight to assist as necessary. These precautions are expected to reduce the incidence and severity of motion sickness. **3)** Spotters will closely monitor subjects and will be within reach and available to assist, should problems occur. Also, spotters will closely monitor the flight accelerometer to instruct subjects to stop exercising prior to pull-out. During hypergravity no exercises will be performed. These precautions are expected to significantly reduce the likelihood that a subject will suffer musculoskeletal injury as a result of a fall. **4)** All data will be coded such that personal identifiers are eliminated. The code key will be kept in a locked file cabinet by the principal investigator. All raw and collated data will be kept in locked file cabinets. Published data will not include identifiers. These precautions will significantly reduce the likelihood that any subject's personally identifiable information will be made available to the public. A flight surgeon will be present during all C-9 and 1-RM testing protocols. During all other testing protocols, an HTSF physician will be on call in the event that medical assistance is required. All participants in the study will be encouraged to inform an HTSF physician at any time should they feel there may be any adverse effects or potential for adverse effects during participation in the study.

3. Potential Benefits of the Proposed Research to the Subjects and Others

Wyle Laboratories and NASA personnel will be provided with a charge number to which they can charge their time at their normal labor rate. Non-affiliated test subjects will be paid at a rate of $10/hour. Although subjects will receive no personal benefit from this study, the information derived from this study will potentially help in the design of effective exercise countermeasures for crewmembers during long duration spaceflights.

4. Importance of the Knowledge to Be Gained

The methodological approach to be used in this project will determine bone and muscle forces associated with resistance exercise in 1-g and weightlessness. The mathematical model that will be built and validated with data from this study will allow for the development of resistive exercise devices and regimens which are not only more effective in preventing bone and muscle deconditioning but may also help prevent injuries by identifying exercise conditions which induce excessive forces in muscles and bones. The future utilization of the mathematical model may reduce the need for human test subjects in future studies and will allow for the simulation of potentially dangerous exercise conditions without endangering human beings. These results will also allow more accurate description of resistive exercise countermeasures in terms of their potential effectiveness for bone and muscle strength maintenance. The quantitative information on exercise countermeasure modalities will allow the development of specific dose-response (frequency, duration, and intensity) models for these exercise modalities. The development of better dose-response models will allow for the development of better exercise prescriptions, which will in turn lead to more effective and efficient exercise regimens. Given the precautions that are in place to reduce the likelihood and severity of potential risks to human subjects in this study, the considerable benefits described above justify the minimal risks faced by the human test subjects.

5. Collaborating Sites

All work will be performed at NASA/JSC and onboard the NASA C-9 parabolic flight aircraft and is covered by the current NASA/JSC Committee for the Protection of Human Subjects (CPHS) approval (see Appendix 5). No other organizations will collaborate on the proposed project.

F. Vertebrate Animals

Not applicable.

G. Literature Cited

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H. Consortium/Contractual Arrangements

This Postdoctoral Fellowship Application is a formal request to become an NSBRI Postdoctoral Fellow in response to NSBRI-RFP-05-01. Other than the funding described in NSBRI-RFP-05-01, no additional funds are being requested from NSBRI. All other funding to conduct the planned study described in this proposal has been sought from internal sources at NASA/JSC.

If selected, the Principal Investigator will begin work as a Postdoctoral Fellow on January 16th 2006 and will be based in the Exercise Physiology Laboratory at NASA/JSC under the supervision of R. Donald Hagan, Ph.D.

I. Consultants

Mentor:	**R. Donald Hagan, Ph.D.**, (NASA) Exercise Lead, EXL, JSC
Co-Investigators:	**Grant Schaffner, Ph.D.**, (Wyle Laboratories) Senior Engineer, EXL, JSC
	John K. DeWitt, M.S., (Bergaila Engineering), Biomechanist, EXL, JSC
Consultants:	**William E. Paloski, Ph.D.**, (NASA) Principal Scientist, Human Adaptations and Countermeasures Office, JSC
	Sudhakar Rajulu, Ph.D., (NSBRI), Technical Monitor, Anthropometry and Biomechanics Facility, JSC

Dr. Schaffner and Mr. DeWitt will work part-time as co-investigators on the project and will contribute to the project as described in their letters of participation (Appendices 3 and 4). Dr. Paloski and Dr. Rajulu will be available for consultation on technical issues, particularly biomechanical modeling, throughout the duration of the project. Dr. Paloski and Dr. Rajulu will provide letters of recommendation directly to NSBRI and will also indicate their roles in the project.

Section 3

Critical Path Roadmap
Professional References

CRITICAL PATH ROADMAP (CPR) FORM

Hypotheses	**Risk Number** (from Critical Path Roadmap)	**Critical Question Number** (from Critical Path Roadmap)	**Critical Question** (from Critical Path Roadmap)	**Specific Aim**
Quantitative description of the specific distribution of bone and muscle loading associated with specific exercise modalities will enable the development of dose-response models based on exercise duration, intensity, and frequency; optimal exercise regimens will replicate the quantity and amplitude of biomechanical loading distributions and mechanical power exertion which are experienced during free-weight resistive exercise regimens in 1-g; this can be achieved through application of discrete segmental resistive loads..	Risk #1	1E	What are the specifics of the optimal exercise regimen with regard to mode, duration, intensity and frequency, to be followed during exposure to hypogravity so as to minimize decreases in bone mass?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar- and Martian-gravity.

Bone mass and bone strength losses can be minimized or prevented by utilizing exercise countermeasure devices and regimens which replicate the biomechanical loading distributions which are experienced during free-weight resistive exercise regimens regimens in 1-g; this can be achieved through application of discrete segmental resistive loads.	Risk #1	1L	What regimen (exercise, pharmacological, nutritional, or biomechanical including impact loading or artificial gravity exposure) will most effectively hasten restoration of bone mass and/or bone strength (geometry and architecture) to pre-flight values in returning crewmembers?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.

Exercise countermeasures which more closely replicate joint and intervertebral forces experienced during exercise in 1-g while preventing excessive loads will protect joint and intervertebral soft tissues from microgravity or partial gravity-related damage; this can be achieved through application of discrete segmental resistive loads.	Risk #3	3C	What countermeasures will protect joint and intervertebral soft tissues (e.g. discs and ligaments) from microgravity or partial gravity-related damage?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.

Skeletal muscle mass, strength, and endurance will be preserved or increased using resistive exercise countermeasure devices and regimens which replicate the muscle forces experienced during free-weight resistive exercise regimens in 1-g; this can be achieved through application of discrete segmental resistive loads.	Risk #11	11A	Can any one or combination of non-invasive modalities (exercise regimens, artificial gravity, etc.) protect or build skeletal muscle mass or maintain skeletal muscle strength or preserve skeletal muscle endurance during an ISS, lunar, or Mars mission?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.

Skeletal muscle strength will be preserved or increased using exercise countermeasure devices and regimens which replicate the muscle forces experienced during free-weight resistive exercise regimens in 1-g; this can be achieved through application of discrete segmental resistive loads.	Risk #11	11B	Can non-invasive countermeasures (resistive exercise, artificial gravity, etc.) aimed at counteracting atrophy processes during an ISS, lunar, or Mars mission maintain those deficits in skeletal muscle strength that appear to occur independently of the atrophy process?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.

Skeletal muscle mass, strength, and endurance will be preserved using exercise countermeasure devices and regimens which replicate the muscle forces experienced during free-weight resistive exercise regimens in 1-g; this can be achieved through application of discrete segmental resistive loads.	Risk #11	11D	What hardware and/or technology is/are reliable and effective in preserving skeletal muscle mass, strength, and endurance during an ISS, lunar, or Mars mission?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.
Incorporating kinetic and kinematic instrumentation into resistive exercise countermeasure devices will enable quantification of muscle forces during maximal and/or submaximal resistive exercise during spaceflight.	Risk #11	11E	What technologies (e.g., ultrasound) can be used to monitor and quantify changes in skeletal muscle size, strength, and endurance during space flight?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise.

Skeletal muscle mass, strength, and endurance losses can be minimized or prevented by utilizing exercise countermeasure devices and regimens which replicate the muscle force distributions which are experienced during free-weight resistive exercise regimens in 1-g; this can be achieved through application of discrete segmental resistive loads.	Risk #11	11K	What prescription modality(ies) (exercise regimens, physical therapy, etc.) facilitate recovery of skeletal muscle mass, strength, and endurance in crewmembers returning from an ISS, lunar, or Mars mission?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.
Reduced bone and muscle forces result from resistive exercise countermeasure devices and regimens which do not adequately compensate for the absence of segmental body masses in weightlessness and hypogravity, thereby contributing to the accelerated rate of bone loss in the central and peripheral skeleton.	Risk #11	11P	Does site-specific skeletal muscle atrophy contribute to the accelerated rate of bone loss in the central and peripheral skeleton because of countermeasures targeting select muscle groups and/or reduced forces at the tendon insertion sites during space flight?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise.

Increased resistance to skeletal muscle and associated connective tissue injury can be achieved through the development of countermeasure devices and regimens for which effective but non-hazardous bone and muscle forces have been quantified for each individual.	Risk #12	12A	What prescription guidelines and compliance factors facilitate increased resistance to skeletal muscle and associated connective tissue injury in crewmembers prior to space flight?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise.
Muscle structure will be effectively preserved using exercise countermeasure devices and regimens which replicate the muscle forces experienced during free-weight resistive exercise regimens in 1-g; this can be achieved through application of discrete segmental resistive loads.	Risk #12	12B	What hardware and/or technology is/are effective in preserving muscle structure during an ISS mission?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.

Muscle structure will be effectively preserved using exercise countermeasure devices and regimens which replicate the muscle forces experienced during free-weight resistive exercise regimens in 1-g; this can be achieved through application of discrete segmental resistive loads.	Risk #12	12C	What hardware and/or technology is/are effective in preserving muscle structure during a lunar mission?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.

Muscle structure will be effectively preserved using exercise countermeasure devices and regimens which replicate the muscle forces experienced during free-weight resistive exercise regimens in 1-g; this can be achieved through application of discrete segmental resistive loads.	Risk #12	12D	What hardware and/or technology is/are effective in preserving muscle structure during a Mars mission?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.
Susceptibility to skeletal muscle damage during space flight will be minimized through the development of exercise countermeasure devices and regimens for which effective but non-hazardous muscle forces have been quantified for each individual.	Risk #12	12I	What are the prescription guidelines and compliance factors needed for countermeasures (exercise, AG, etc.) during space flight to minimize susceptibility to skeletal muscle damage?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise.

Injury-free skeletal muscle rehabilitation will be facilitated by the development of exercise countermeasure devices and regimens for which effective but non-hazardous muscle forces have been quantified for each individual.	Risk #12	12L	What prescription guidelines and compliance factors facilitate injury-free skeletal muscle rehabilitation in crewmembers returning from an ISS mission?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise.
Injury-free skeletal muscle rehabilitation will be facilitated by the development of exercise countermeasure devices and regimens for which effective but non-hazardous muscle forces have been quantified for each individual.	Risk #12	12M	What prescription guidelines and compliance factors facilitate injury-free skeletal muscle rehabilitation in crewmembers returning from a lunar mission?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise.

Injury-free skeletal muscle rehabilitation will be facilitated by the development of exercise countermeasure devices and regimens for which effective but non-hazardous muscle forces have been quantified for each individual.	Risk #12	12N	What prescription guidelines and compliance factors facilitate injury-free skeletal muscle rehabilitation in crewmembers returning from a Mars mission?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise.
Bone and muscle strength will be maintained pre-landing through use of exercise countermeasure devices and regimens which replicate the muscle forces experienced during free-weight resistive exercise regimens in 1-g; this can be achieved through application of discrete segmental resistive loads.	Risk #21	21A	What are the primary, secondary and tertiary preventive strategies needed to ensure post-landing performance for a Mars mission?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.

Bone and muscle strength will be maintained post-landing through use of exercise countermeasure devices and regimens which replicate the muscle forces experienced during free-weight resistive exercise regimens in 1-g; this can be achieved through application of discrete segmental resistive loads.	Risk #21	21B	What are the essential technologies, resources, protocols, skills and training necessary for post landing rehabilitation (including psychological, cardiovascular, neurosensory, musculoskeletal and nutritional)?	A: Develop and validate a biomechanical model of different resistive exercise modalities and intensities in 1-g and hypogravity environments. B: Using data and the biomechanical model, quantify the effects of hypogravity, resistive load, and exercise modality on bone and muscle forces during resistive exercise. C: Minimize differences between 1-g and hypogravity bone and muscle forces by using the biomechanical model to optimize the simulated application of discrete segmental resistive loads during RE in weightlessness, Lunar, and Martian-gravity.

PROFESSIONAL REFERENCES

Professional Reference 1

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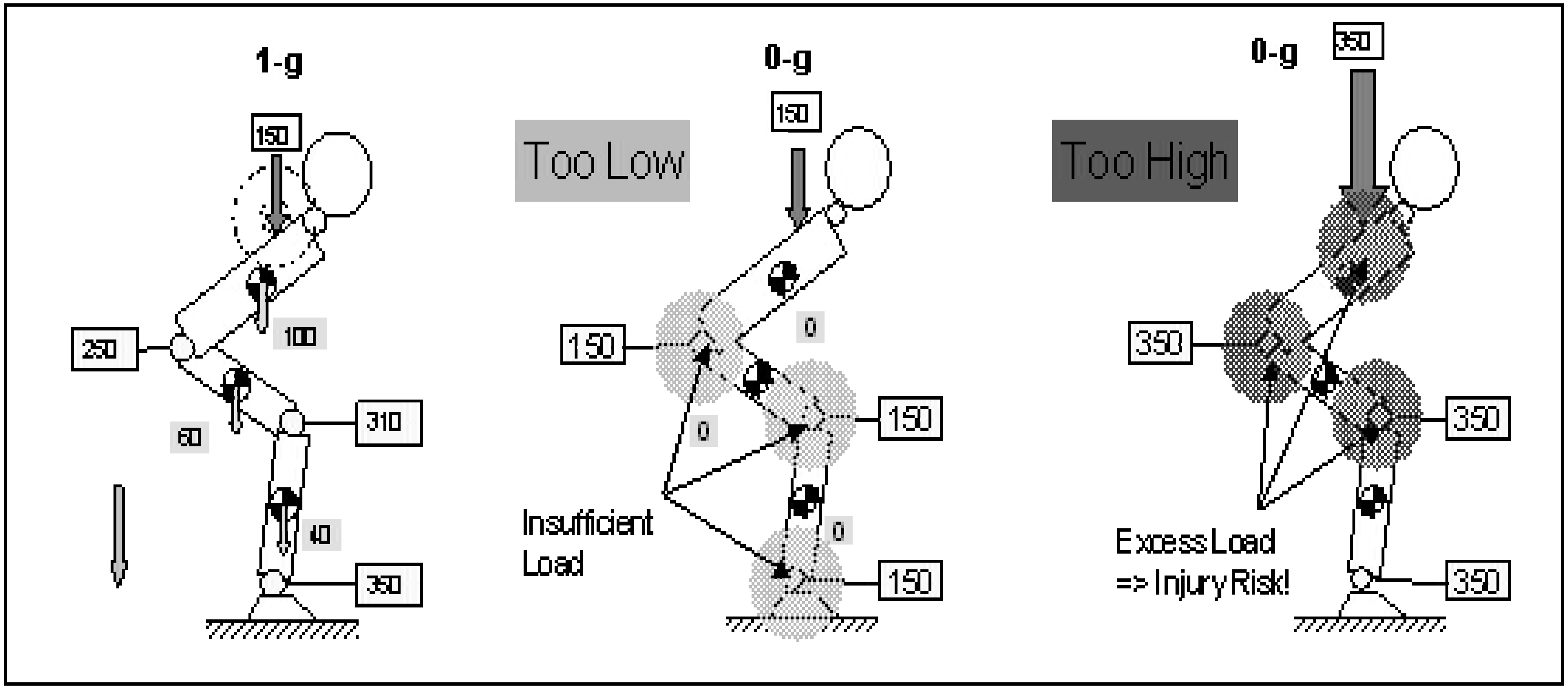
Appendix

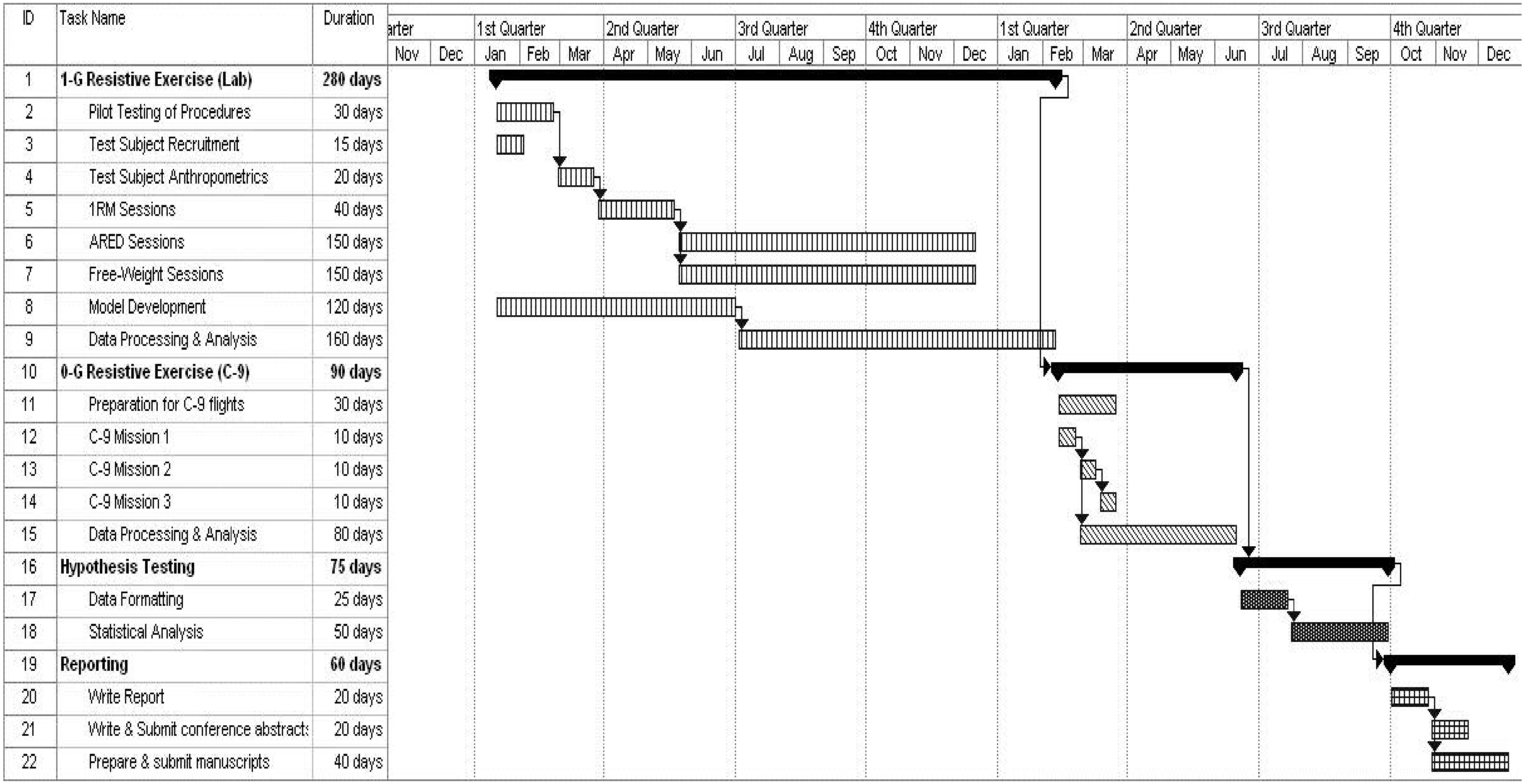
The Role of Gravity in Resistive Exercise

ROLE OF GRAVITY IN VERTICAL LOADING DURING RESISTIVE EXERCISE



Projected 2-year Timeline

PROJECTED 2-YEAR TIMELINE



ID	Task Name	Duration
1	**1-G Resistive Exercise (Lab)**	**280 days**
2	Pilot Testing of Procedures	30 days
3	Test Subject Recruitment	15 days
4	Test Subject Anthropometrics	20 days
5	1RM Sessions	40 days
6	ARED Sessions	150 days
7	Free-Weight Sessions	150 days
8	Model Development	120 days
9	Data Processing & Analysis	160 days
10	**0-G Resistive Exercise (C-9)**	**90 days**
11	Preparation for C-9 flights	30 days
12	C-9 Mission 1	10 days
13	C-9 Mission 2	10 days
14	C-9 Mission 3	10 days
15	Data Processing & Analysis	80 days
16	**Hypothesis Testing**	**75 days**
17	Data Formatting	25 days
18	Statistical Analysis	50 days
19	**Reporting**	**60 days**
20	Write Report	20 days
21	Write & Submit conference abstract	20 days
22	Prepare & submit manuscripts	40 days

Letter of Participation: Grant Schaffner, Ph.D.

wyle laboratories

Date: 22 June 2005

From: Grant Schaffner, Ph.D.

To Whom It May Concern:

Subject: Participation in study entitled “Quantification of the Effects of Hypogravity, Resistive Load, and Exercise Modality on Bone and Muscle Forces during Resistive Exercise”

I serve as the Senior Engineer for the Exercise Physiology Laboratory at the NASA Johnson Space Center. My role in this project will be to work with Mr. Abercromby on the development of a computational model that determines bone and muscle forces based on test data. I will spend 50% of my time on this project.

Letter of Participation: John DeWitt, M.S.

wyle
laboratories

Date: 22 June 2005

From: John K DeWitt, M.S.

To Whom It May Concern:

Subject: Participation in study entitled “Quantification of the Effects of Hypogravity, Resistive Load, and Exercise Modality on Bone and Muscle Forces during Resistive Exercise”

I serve as the Biomechanist for the Exercise Physiology Laboratory at the NASA Johnson Space Center. My role in this project will be to assist with data collection, analysis, and interpretation. I will spend 50% of my time on this project.

IRB Approval

National Aeronautics and
Space Administration
Lyndon B. Johnson Space Center
2101 NASA Parkway
Houston, Texas 77058-3696

June 27, 2005

JUN 27 2005

Andrew F.J. Abercromby, Ph.D./SK3
Exercise Physiology Laboratory
Human Adaptation Countermeasures Office
Lyndon B. Johnson Space Center
Houston, TX 77058

RE: Expedited Approval

Quantification of the Effects of Hypogravity, Resistive Load, and Exercise Modality on Bone and Muscle Forces During Resistive Exercise

Approval valid from June 27, 2005 to June 27, 2006

Dear Dr. Abercromby:

1. The Johnson Space Center (JSC) Committee for the Protection of Human Subjects (CPHS) has taken the following action with respect to the above named proposal:

   ( ) Accept the governance of the local Institutional Review Board (IRB).
   (X) Proposal is approved for 1-year.
   ( ) Proposal is approved with minor Board recommendations (See CPHS minutes).
   ( ) Proposal is tabled with Board recommended actions (See CPHS minutes).
   ( ) Proposal is rejected (See CPHS minutes).
   (X) Medical Monitoring designation: ( ) Not Required; ( ) Level I; ( ) Level II; (X) Level III; ( ) Level IV

2. Additional review of this proposal will be required:

   (X) Annually.
   (X) If there is any substantive change in protocol.
   (X) Should unexpected problems or unusual complications develop.

3. Method of review utilized:

   ( ) JSC CPHS Screening Process (NASA Funded Grants)
   ( ) JSC CPHS Full Board Review
   (X) JSC CPHS Expedited Review

Jerry Homick

6/27/05

Jerry L. Homick, Ph.D.
Alternate Chair, JSC Committee for the Protection of Human Subjects

Date