Level I Project Proposal

Real-Time Bone Density Loss Monitoring Device

Prepared by Rice University senior bioengineering students:
Charlie Foucar, Leslie Goldberg, Bodin Hon, Shannon Moore, and Evan Williams

Working under Dr. Maria Oden, Rice University, Department of Bioengineering: moden@rice.edu
and Dr. Tara Ruttley, NASA, Biomedical Systems Division: tara.m.ruttley@nasa.gov

October 6, 2008

NASA Space Grant Consortium Design Competition
# Table of Contents

I. Introduction..................................................................................................................2

II. Research Group..........................................................................................................3

III. Collaborators.............................................................................................................4

IV. Team Taurus Member Profile....................................................................................6

V. Topic Background Information..................................................................................9

VI. Design Objective.......................................................................................................13

VII. Project Timeline.....................................................................................................14

VIII. Budget Plan............................................................................................................16

IX. Conclusion...............................................................................................................17

X. References................................................................................................................18

XI. Appendices..............................................................................................................19

   A. Expense Report

XII. List of Figures:

   A. Figure 1: Markers for Assay-Based Analysis

   B. Figure 2: Project Design Plan

   C. Figure 3: First-semester Budget

   D. Figure 4: First-semester Timeline
**Introduction**

Numerous studies on astronauts exposed to prolonged periods of weightlessness have indicated that the human skeletal structure undergoes a significant level of bone mineral density (BMD) loss as a result of hypodynamia (decreased forces) and hypokinesia (fewer movements) [Vico, 2000]. The event of a bone fracture presents a significant risk to the safety of astronauts and the success of a proposed exploration mission to Mars. Current countermeasures employed to mitigate this phenomenon include various exercise regimens and pharmaceutical agents, none of which have been fully effective [White, 2001]. One method used to measure the pathology of osteoporosis uses specific biochemical bone markers. For example, markers such as urinary galactosyl hydroxylysine are used to assess specific bone resorption activities such as bone collagen destruction [Collet, 1997]. Using this and other markers found in bodily fluids, we propose a non-invasive device that monitors the systemic bone loss by measuring the concentration of bone markers in sweat or urine. The design and construction of this device will allow mission control to actively assess the efficacy of the proposed countermeasures and adjust them accordingly.
Research Group

In addition to the five Rice University senior bioengineering students who are the heading the project, the following is a list of the mentors for the design process:

**Dr. Tara Ruttley [JSC-EB]**
Biomedical Systems Division  
NASA Johnson Space Center  
2101 NASA Road 1 - Houston, TX 77058  
Email: tara.m.ruttley@nasa.gov  ph: (281) 483-9615  
  * Dr. Ruttley is a member of the Biomedical Systems Division at NASA. Her previous work includes her role as Lead Hardware Engineer on the Health Maintenance System on the ISS.

**Dr. David Tomko – NASA Headquarters**  
Advanced Capabilities Division - Human Research Program  
NASA Johnson Space Center  
2101 NASA Road 1 - Houston, TX 77058  
Email: dtomko@nasa.gov  ph: (202) 358-2211  
  * Dr. Tomko is a member of NASA's Advanced Capabilities Division.

**Emily Burdett – Rice University**  
Graduate Student of the Department of Bioengineering  
Department of Bioengineering  
P.O. Box 1892 MS-142  
Houston, TX 77251  
Email: emilyburdett@rice.edu  
  * Emily Burdett is a graduate student in Rice University's department of bioengineering. She is a member of Dr. Mikos' research laboratory.
Collaborators

Dr. Susan A. Bloomfield – Texas A&M University
Department of Health & Kinesiology and Intercollegiate Faculty of Nutrition Director of the Bone Biology Laboratory
Email: sbloom@tamu.edu
Phone: (979) 862-1181
  • Dr. Bloomfield will be an invaluable resource to the team. She specializes in bone biology under microgravity conditions. In addition to a tour of her research laboratory, she will be able to help determine the feasibility of the design.

Dr. Nancy Butte – Baylor College of Medicine
USDA/Agricultural Research Service’s Children’s Nutrition Research Center
Email: nbutte@bcm.tmc.edu
  • Dr. Butte will provide necessary insight pertaining to the urine assay component of the design. She has offered to give a tour of her laboratory as well as the laboratories of her colleagues so that the team can get a personal, in-depth understanding of the current detection methods currently used.

Dr. Melissa Knothe-Tate – Case Western Reserve University
Experimental and Computational Mechanobiology Laboratories
Email: knothetate@case.edu
Phone: (216) 368-5884
  • Dr. Knothe-Tate holds a joint appointment in the Biomedical and Mechanical Engineering departments at CWRU. She is specifically interested in bone biology and the mechanobiological influences on bone, and has performed research regarding bone strength in microgravity. She will be a valuable resource for helping us to determine which bone degradable products will be most feasible to test.
**Dr. Adrian D. LeBlanc** – Baylor College of Medicine
Departments of Medicine and Orthopedic Surgery
Director of Division of Space Life Sciences
Email: leblanc@dssl.usra.edu
Phone: (713) 793-1131

- Dr. LeBlanc is interested in building systemic bone loss monitoring device for use in space flight. His efforts focus primarily on imaging techniques, but his expertise would serve as a valuable resource to the design project.

**Dr. James F. Young** and **Dr. Richard Baraniuk** – Rice University
Department of Electrical and Computer Engineering
Email: young@ece.rice.edu and richb@rice.edu (respectively)
Phone: (713) 348-4721 and (713) 348-5685 (respectively)

- Dr. Young and Dr. Baraniuk have extensive research interests in electrical engineering design that will be useful during the design process of the analysis component of the device. In particular, Dr. Baraniuk explores signal-processing algorithms that accommodate low power consumption for long-term battery operation. Dr. Young is an expert in the development of optical devices, which will likely be necessary for the design.

**Ali Arya Mokhtarzadeh** – Rice University
Senior Mechanical Engineering and Material Science Major
Email: Arya@rice.edu
Phone: (304) 561-4881

- Arya will help with material selection and device component design.
Team Taurus Member Profiles

Team Taurus is comprised of five senior bioengineering majors at Rice University working on a senior design project for BioE 451, Bioengineering Design I. This class is the senior design course and covers topics ranging from design to economics. “Taurus” was chosen both in reference to the zodiac sign, which signifies determined and disciplined individuals, and to the bull itself, a hardy animal with great physical prowess.

From left to right, Team Taurus is: Charlie Foucar, Leslie Goldberg, Shannon Moore, Evan Williams, and Bodin Hon.
Charlie Foucar serves as the team leader. His interests include cancer cell biology and neuroscience. After graduation, Charlie plans to attend a research oriented medical school in order to earn a medical degree and possibly either a master's degree or PhD. Charlie’s career goal is to utilize both his engineering and medical degrees to do translational research in the field of neurology. [cfoucar@rice.edu]

Leslie Goldberg manages the group deadlines, maintains the Gantt chart, and compiles the weekly TSGC reports. Her future plans include earning an M.D./Ph.D. after gaining work experience over the next year. In her spare time she enjoys reading, swimming, traveling, and learning new languages. [leslie.a.goldberg@rice.edu]

Bodin Hon grew up in Hong Kong and New Zealand before attending college at Rice. His role is the team’s digital media specialist. His interests include device component design using CAD, as well as prototype fabrication. In the past two summers, he has spent time learning the design process with the Waste Management Subsystem (WMS) team for the Orion’s Crew Exploration Vehicle. [bodin.hon@rice.edu]
Shannon Moore serves as the team's financial manager. Her specific interests include tissue engineering, biomaterials and the amazing phenomena of bones. She is also actively involved in Engineers Without Borders and spends her free time working on a water distribution system for a community in El Salvador. Her plans for the future involve earning a Ph.D. and working on international scientific collaboration.

[ShannonM@rice.edu]

Evan Williams is the team's editor and organizer. His interests lie in the underlying genetic differences behind disease susceptibility, including osteoporosis and type II diabetes. He is an active bioinformaticist whose future goal is to develop hands-on experience to supplement his *in silico* work and to earn a Ph.D. in genetics. [egw4693@rice.edu]

Dr. Maria Oden – Rice University, Department of Bioengineering  
P.O. Box 1892 MS-142  
Houston, TX 77251  
Email: moden@rice.edu

- Dr. Maria Oden is member of the Department of Bioengineering at Rice University. She is also the director of the new Oshman Engineering Design Kitchen at Rice in addition to designing products with third world health applications. Dr. Oden is Team Taurus’s faculty advisor.
Topic Background

One of the major concerns of long-term space travel is the significant decrease in bone mineral density resulting from the absence of gravity. Similar to the effects of osteoporosis, microgravity-induced BMD loss increases the risk of bone fracture, with the deleterious effects being magnified as the duration of the mission increases. Currently, NASA measures bone density loss by using imaging techniques before launch and upon return. Monitoring real-time changes in bone composition, however, will lead to a better understanding of BMD loss over the course of the mission. Understanding the time dynamics of bone density loss could also aid in the optimization of the proposed solutions involving combinations of drug therapy and exercise. The outcome of the project will benefit not only astronauts involved in extended space travel, but physicians wishing to perform bone density analysis in situations where access to expensive and complicated traditional imaging methods are limited.

In order to properly address the problem of decreased in bone mineral density in space, research was done on osteoporosis, the current methods used to diagnose bone mineral density loss, and future methods in development.

Osteoporosis

Osteoporosis is classified as a significant decrease in bone strength due to the loss of mass and certain material properties of the bone. The mechanism behind this change in properties involves two cell types: osteoclasts and osteoblasts. These two cell types are responsible for the constant remodeling of bone whereby old bone is replaced by new bone. Bone remodeling occurs at distinct sites on the bone, known as
bone multi-cellular units (BMUs). At the onset of osteoporosis, a decrease in bone density occurs because of both an increase in the number BMUs and an imbalance in the remodeling process that results in more bone resorption than bone formation [Clunie, 2008].

According to the rules set forth by the World Health Organization (WHO), bone density loss can be classified into two categories based upon the relative amount of loss. Osteoporosis represents a bone density that is 2.5 standard deviations below the accepted value for an individual. Osteopenia is a less severe classification given to a patient with a measured bone density 1 to 2.4 standard deviations below the accepted value [Clunie, 2008]. We believe the active treatments of bone loss proposed by NASA will likely allow astronauts to maintain the classification of osteopenia. Therefore, detecting and monitoring bone loss in the range defined by osteopenia will be the main focus of the design project.

**Current Methods of Diagnosis**

The two most prominent and reliable methods for testing region-specific bone loss are dual energy x-ray absorptiometry (DEXA) and qualitative ultrasound (QUS). Qualitative ultrasound devices are non-invasive, global-specific, and non-radiative, and serve as an excellent tool for diagnosis. However, QUS devices are not yet fully mature. Approximations, such as measuring the calcaneus as a model for the hip, which is too deep in tissue for most ultrasound systems to test directly, must be used [Akrout, 2002]. DEXA systems have the best precision for scanning for BMD loss, but are large,
consume considerable amounts of power, and expose subjects to ionizing radiation [Stewart, 2000].

In extended space travel, such as a moon colony or a manned mission to Mars, the primary concern is combating systemic bone density loss—not only bone-specific risk factors [Iwamoto, 2005]. Since the primary benefit of QUS and DEXA over assay-based methods is to gain specificity at the cost of space, power use, and operation time, those methods of testing were ruled out in favor of assay-based techniques.

Currently, measuring the loss in BMD over time for astronauts is performed by freezing collected samples in space and subsequently analyzing the samples upon return to Earth. This is done by measuring for a specific marker correlated with BMD loss in blood, sweat, or urine, and then comparing the change in the marker’s levels over time [Leach, 1979]. Real-time measurements using assay-based techniques are primarily performed using antibody based- or radioimmuno- assays; these methods can quickly measure the concentration of a particular substance in the collected sample utilizing the specificity of the reaction of between an antibody to its antigen [Yalow, 1960].

ELISA (Enzyme-Linked Immunosorbent Assay) is the biochemical technique mainly used to determine the concentration or the presence of either an antigen or antibody in a given sample [Engvall, 1971]. The unknown quantity of antigen in the sample is firstly immobilized on a surface; its specific antibody which had been previously linked with an enzyme is then washed over the fixed surface so all the
antigens are bound with its antibody/enzyme complex. A substance containing the enzymic substrate is then added to the surface, reacting with the immobilized enzyme linked to the antigen/antibody complex to produce a visible signal [Engvall, 1971]. The mixture’s colorimetric property can then be quantitatively used to determine the concentration of the substance in the sample using a standard curve.

The predecessor to ELISA was radioimmunoassay (RIA), which presents a health concern as it involves the use of radioactive signal. The technique involves marking a known quantity of antigen with radioactivity before mixing it with a known amount of its specific antibody; as a result the two chemically bond to each other. Subsequently, the sample containing the non-radioactive variant of the antigen is added to the mixture, thus resulting in competition over the antibody binding site with the radioactive antigen. The radioactive variant is then displaced, and the amount left in the supernatant can be measured, thus enabling a quantitative evaluation of the amount of antigen in the sample [Yalow, 1960].

**Potential Markers**

A range of biochemical markers found in various bodily fluids have been determined to be fundamentally intertwined with the activities of bone formation and bone loss. Assessing the levels of these markers over time may prove to be crucial to monitoring of the health of the crew’s bones. Systemic Ca\(^{2+}\) is one such candidate that can be tracked as its transfer to and from the bone to the blood indicates bone resorption or formation. Tracking the level of parathyroid hormone (PTH), which is the primary hormone driving the activity of osteoblasts and osteoclasts, may also be used for this sort of detection. Nevertheless, more
specific biochemical markers have been found whose levels can correlate to specific activities such as osteoblast differentiation and osteoblast maturation [Collet, 1997].

These markers can be divided two different categories: bone formation and bone resorption. Furthermore, these markers can be divided into their location of secretion: serum, urine, feces and sweat. Currently, lab analysis on the frozen samples returned to Earth have focused on the following:

![Fig. 1: Markers used to measure BMD loss [Collet, 1997].](image)

### Design Objective

The design objective is to create a non-invasive device that is able to monitor systemic bone loss during space flight through the assessment of biochemical bone markers found in bodily fluids.
Design Plan

Fig. 2: Year-long design plan flowchart for device development.
In initial research, four fundamentally different non-invasive approaches to measuring bone density loss in space were evaluated—qualitative ultrasound (QUS), dual energy x-ray absorptiometry (DEXA), body fluid analysis assays, and sweat patch measurements. For the fluids, research was focused on sweat or urine testing. The favorable and unfavorable criteria are currently being evaluated for each of the different options in a Pugh matrix in order to narrow down the selection. Urine and sweat analysis devices remained the two testing methods that serve as candidates for the final design.

Once a single device and testing method have been selected, the design process will begin, with CAD mockups, material purchases, electronic design, and coding for analysis software. It is in this stage of the process that the design criteria established earlier for size, weight, electronic, and material restrictions will be followed. Here, in the early stages of this process, any potential solution will be recorded, and flaws in any of the designs ironed out. Once the initial design work is done, we will perform a device review to ensure no major working points have been missed.

Once the initial design issues have been corrected, construction of the prototype will begin. As this prototype is built, any issues with the device’s construction or operation will be noted and modified for future construction and development. The prototype can then be tested and compared to other assays, or DEXA or QUS scans, to check accuracy and precision. As time allows, the device will continually be updated by building newer prototypes and reevaluating their efficacy. After the device is finalized and shown to work in standard laboratory conditions, it will be tested in the T-135 zero
gravity simulator to ensure practical use in the conditions of space. If any unforeseen problems arise in this simulation, changes will be made to the final product.

Once the device is shown to be fully functional, the design documents will be compiled and edited to form a comprehensive device manual, including detailed operation instructions and potential problems that could occur in extended use of the device. The entire process is outlined in figure 2.

**Project Timeline & Budget**

![Fig. 3: Budget plan for first-semester development of the device.](image)

The overarching goal of this project is to design, build and test a working prototype of a device or procedure for measuring systemic bone loss. The technical constraints include operation in microgravity, weight and size restrictions on the spacecraft, and resources such as water and electricity. We will work on this project throughout the school year (September 2008-May 2009) with a budget of about $2,500. The budget and timetable for the first semester are outlined in figures 3 and 4 respectively.
Conclusion

Initial research indicates that the design of a non-invasive systemic bone loss monitoring device is both feasible and necessary. During missions involving extended periods of space travel, NASA will be able to use this device to monitor the efficacy of their proposed treatments in real time. Using this data, mission control will be able to modify the treatment regimens to maximize their effectiveness. This document outlines the timeline, budget, and engineering approach that will be used to design and build the device.
References


Appendix

A: Expense Report

<table>
<thead>
<tr>
<th>INST</th>
<th>Rice University</th>
<th>TEAM NAME</th>
<th>Team Taurus</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEVEL</td>
<td>I</td>
<td>II</td>
<td>III</td>
</tr>
</tbody>
</table>

Teams are required to provide a Budget Report as an Appendix to each of the required reports for Levels I, II and III. The Budget Report will provide an overview of team expenditures for the time period preceding report submission. Ideally, it will help the team keep its budget in check.

<table>
<thead>
<tr>
<th>COMPLETED</th>
<th>LEVELS</th>
<th>OPTION AREAS</th>
<th>GRANT APPLICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
<td>III</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TEAM EARNINGS TO DATE</th>
<th>$0.00</th>
<th>TEAM EXPENSES TO DATE</th>
<th>$0.00</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>FUNDS REMAINING</td>
<td>$0.00</td>
</tr>
</tbody>
</table>

REPORT TIME PERIOD COVERED: I: Proposal /SOW  II: Mid-term  III: Final Rpt

<table>
<thead>
<tr>
<th>ITEM NAME</th>
<th>USE</th>
<th>RECPT?</th>
<th>COST</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TOTAL FOR THIS REPORT: $0.00

Was funding adequate/available to cover team’s project needs during this period? | YES