ESTIMATING TRABECULAR BONE MECHANICAL PROPERTIES FROM NON-INVASIVE IMAGING

Final Report
NASA/ASEE Summer Faculty Fellowship Program--1996
Johnson Space Center

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Division:	Medical Sciences
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ABSTRACT

An important component in developing countermeasures for maintaining musculoskeletal integrity during long-term space flight is an effective and meaningful method of monitoring skeletal condition. Magnetic resonance imaging (MRI) is an attractive non-invasive approach because it avoids the exposure to radiation associated with X-ray based imaging and also provides measures related to bone microstructure rather than just density. The purpose of the research for the 1996 Summer Faculty Fellowship period was to extend the usefulness of the MRI data to estimate the mechanical properties of trabecular bone. The main mechanical properties of interest are the elastic modulus and ultimate strength. Correlations are being investigated between these and fractal analysis parameters, MRI relaxation times, apparent densities, and bone mineral densities.

Bone specimens from both human and equine donors have been studied initially to ensure high-quality MR images. Specimens were prepared and scanned from human proximal tibia bones as well as the equine distal radius. The quality of the images from the human bone appeared compromised due to freezing artifact, so only equine bone was included in subsequent procedures since these specimens could be acquired and imaged fresh before being frozen. MRI scans were made spanning a 3.6 cm length on each of 5 equine distal radius specimens. The images were then sent to Dr. Raj Acharya of the State University of New York at Buffalo for fractal analysis. Each piece was cut into 3 slabs approximately 1.2 cm thick and high-resolution contact radiographs were made to provide images for comparing fractal analysis with MR images. Dual energy X-ray absorptiometry (DEXA) scans were also made of each slab for subsequent bone mineral density determination. Slabs were cut into cubes for mechanical using a slow-speed diamond blade wafering saw (Buehler Isomet). The dimensions and wet weights of each cube specimen were measured and recorded. Wet weights were also recorded. Each specimen was labeled and marked to denote anatomic orientations, i.e. superior/inferior (S/I), medial/lateral (M/L), and anterior/posterior (A/P). The actual locations of each cube cut were documented and images distributed to define ROI locations for other analyses (to Raj Acharya for fractal analysis, to Jon Richardson at Baylor College of Medicine for DEXA, and to Chen Lin at Baylor College of Medicine for T2* MRI analysis). Quasi-static mechanical testing consisted of compressive loading in all three mutually perpendicular anatomic directions. Cyclic loading was applied for 10 cycles to pre-condition the specimen and results calculated for the eleventh. For one of three directions tested on each specimen, the 10 cycles were followed with loading to failure. Testing is currently proceeding and once completed the results will be correlated with data from the other analyses. One of the main points of interest is the relationship between fractal dimension and mechanical properties. Throughout preparation and testing all specimens were maintained hydrated with physiological saline and stored frozen when not being used.

INTRODUCTION

An important component in developing countermeasures for maintaining musculoskeletal integrity during long-term space flight is an effective and meaningful method of monitoring skeletal condition. Magnetic resonance imaging (MRI) is an attractive non-invasive approach because it avoids the exposure to radiation associated with X-ray based imaging and also provides measures related to bone microstructure rather than just density. Much of the initial work in this area deals primarily with the lower limb because of its prominence in overall skeletal function. Recent Summer Faculty Fellowship participants have devised methods for non-invasively determining the size and shape of the main load-bearing bones, such as the femur & tibia (Todd, 1994), and also estimating muscle forces and joint kinematics during exercise (Figueroa, 1995). The bone dimensions and geometry are derived from magnetic resonance images (MRI) since this avoids exposure to ionizing radiation as is customary with X-ray and similar methods. Finite element models of the femur can be constructed from the geometry data and the applied loads derived from physiological muscle force data. The goal is to use such models to predict the stresses and strains within the bone, and from them identify and assess regions of weakness and potential fracture risk. This detailed and quantitative insight will allow individualized evaluation of skeletal condition (pre-, post-, and in-flight) and prescription of exercise protocols for in-flight counter-measures as well as post-flight rehabilitation.

The next major step in developing this capability is to determine the material properties of the bone tissue within the bones. With methods available to generate the geometry and loads, a complete and more accurate model also requires information on the material properties of the bone or bones of interest. A major challenge at this point is to devise a way to estimate these properties from MRI data, which is a process essentially unexplored to date. Another recent Summer Faculty Fellowship participant has been studying methods for calculating fractal parameters from high-resolution MRI data in order to characterize the microarchitecture of trabecular bone tissue (Acharya *et al.*, 1995). The purpose of the research for the 1996 Summer Faculty Fellowship period has been to examin the potential usefulness of the MRI data to estimate the mechanical properties of trabecular bone. More specifically, correlations are being studied between the fractal parameters and elastic modulus, ultimate strength, apparent density, and bone mineral density. Considerable attention is being given to developing the detailed protocols and procedures needed and conducting preliminary tests to establish parameters and identify potential limitations

EXPERIMENTAL PROCEDURES

Overview

Much of the time and effort during the summer research period has been spent establishing and improving the detailed protocols and procedures required to execute and coordinate the research plan. The research involves collaboration between several different laboratories and personnel so extensive and effective coordination is essential. The main steps in the overall process can be summarized as follows:

1. Acquire whole bone specimens, cut to size, and embed for whole bone" MRI scanning.
   (at University of Texas Medical School, Orthopaedic Biomechanics Laboratory)

2. MRI scan region 3-4 cm long using "high-resolution" coil.
   (at Baylor College of Medicine/Methodist Hospital, Medical Physics)

3. Cut piece into slabs approximately 1.2 cm thick.
   (at University of Texas Medical School, Orthopaedic Biomechanics Laboratory)

4. Scan slabs for bone mineral density using dual energy X-ray absorptiometry (DEXA).
   (at Baylor College of Medicine /Methodist Hospital, Medical Physics)

5. Make high-detail contact X-rays to provide alternate images of trabecular architecture.
   (at Texas A&M University, Veterinary Radiology)

6. Cut slabs into cubes for mechanical testing and define regions of interest (ROI).
   (at University of Texas Medical School, Orthopaedic Biomechanics Laboratory)

7. Conduct mechanical tests and calculate mechanical properties of interest.
   (at University of Texas Medical School, Orthopaedic Biomechanics Laboratory)

8. Determine wet and dry densities and ash weights.
   (at University of Texas Medical School, Orthopaedic Biomechanics Laboratory)

9. Calculate fractal dimensions from MRI and X-ray images.
   (at State University of New York at Buffalo, Biomedical Imaging Group)

10. Determine bone mineral densities and T2* effective relaxation times from DEXA and MRI data, respectively, for each ROI corresponding to test specimens.
    (at Baylor College of Medicine /Methodist Hospital, Medical Physics)

Once the experimental tests are completed and the data analyzed, correlations will be examined between mechanical properties and other parameters. The mechanical properties of interest are the elastic moduli (in all 3 orthogonal directions) and the ultimate strength. The main microstructural parameter is the fractal dimension of the trabecular architecture. The fractal dimension is a novel quantity not commonly used for such purposes but recent studies have shown it to be a unique measure in distinguishing between normal and osteoporotic bone (Ruttimann *et al.*, 1992; Majumdar *et al.*, 1993; Weinstein and Majumdar, 1994). This suggests that the fractal dimension may likewise be a promising parameter for predicting mechanical properties. Addressing this question is therefore a major goal of the current research. For completeness and reference with other studies, additional microstructural measures to be included in correlation studies are the wet and dry densities and the ash weights.

Specimen Preparation and Imaging

Whole bones were acquired either through the University of Texas Medical School (human tibia) or the Texas A&M University College of Veterinary Medicine (equine radius). The bones were cut down to roughly one-third of the total length to isolate the metaphaseal regions containing significant trabecular bone. These pieces (proximal tibia for human bone and distal radius for equine bone) were then embedded using bone cement to mount them to plexiglass base plates. An embedded specimen is shown schematically in Figure 1.

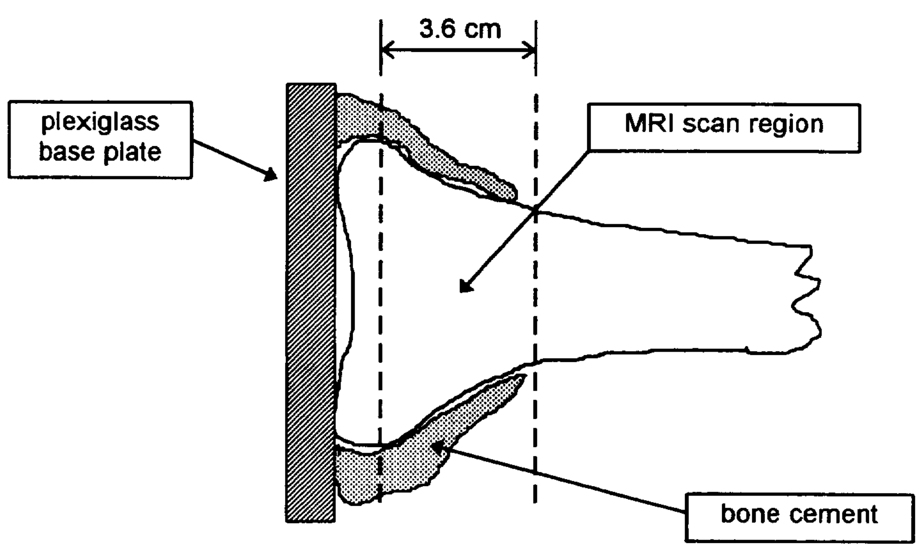

Figure 1. Embedded specimen for MRI scanning.

Each mounted specimen was transferred to the Baylor College of Medicine for MRI scanning by Dr. Chen Lin. In order to obtain images with high enough resolution to depict the microstructural architecture within trabecular bone tissue an orbit coil was used. The in-plane resolution of the orbit coil is 0.125 microns. Nine axial scans were made spanning a 3.6 cm long region on each specimen. Each scan was 2 mm thick with a 2 mm space between scans. Each 3.6 cm section was cut into 3 slabs approximately 1.2 cm thick on a band saw with custom fixtures for maintaining parallel, even cuts. The slabs and MRI scans are depicted in Figure 2. A coronal scan was also made for documenting the location of the axial scans. In order to maintain maximal clinical relevance, human proximal tibia bones were studied first. Upon reviewing the images from these bones, however, artifacts due to air pockets were observed, particularly in the central portions of the pieces where the porosity is high. Thus, an attempt was made to fully hydrate the specimens by storing in water overnight under a vacuum. The images from the re-hydrated specimens were still not as clear as *in vivo* or fresh bone, so further study was restricted to equine bone since these could be acquired fresh without being frozen before scanning. A total of 5 equine radius bones were prepared and scanned. The images were then sent to Dr. Raj Acharya for eventual fractal analysis.

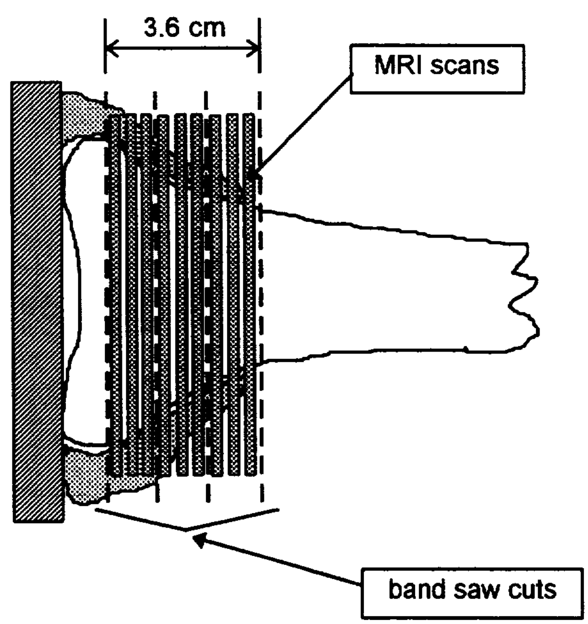

Figure 2. MRI scan and slab cutting details.

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High-resolution contact radiographs were made of each slab to provide images for comparing fractal analysis with MR images. The X-ray images were also used to plan cutting cube specimens for mechanical testing. X-rays were made at 3 mA and 28 kV for two exposure times (45s and 60s) on a berryllium window GE model 2001437 unit in the Large Animal Radiology Lab of the College of Veterinary Medicine at Texas A&M University. In addition, each slab was radiographed in two orientations, with the superior surface "down" touching the film packet and with the inferior surface "down". The developed films were scanned into a PC to create TIF files (600dpi). A sample is shown in Figure 3. These images were also sent to Dr. Acharya for fractal analysis. Each of the slabs was also scanned by Mr. Jon Richardson of Baylor College of Medicine on a DEXA (dual energy X-ray absorptiometry) scanner for subsequent bone mineral density determination.

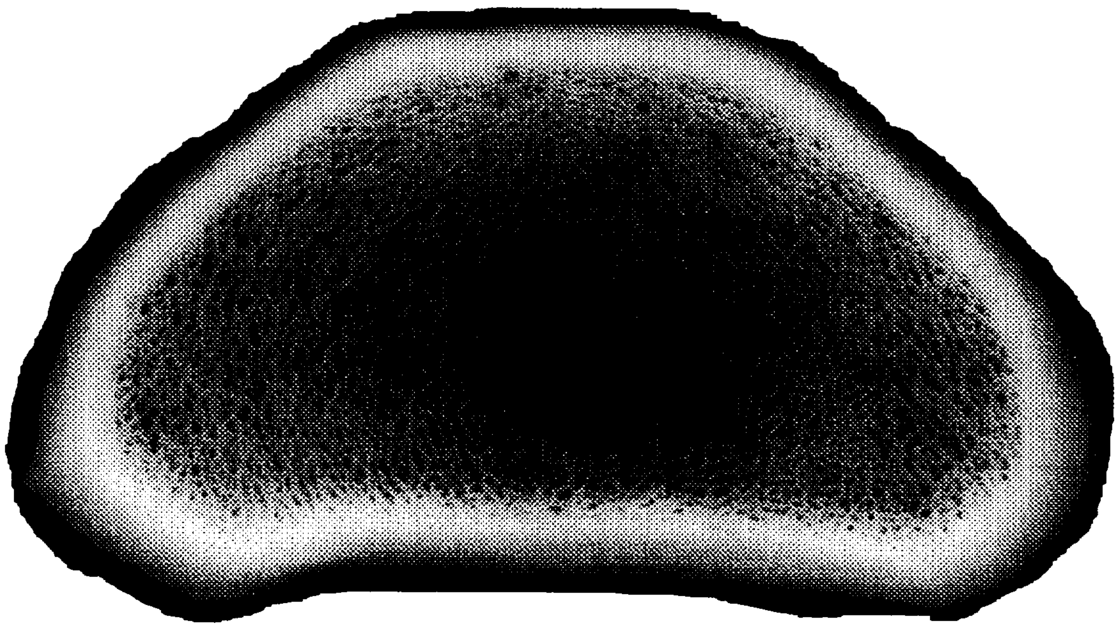

Figure 3. Sample X-ray image (scanned at 600dpi).

Mechanical Testing

Before actually cutting the cube specimens, the number and location was planned graphically. A lower resolution (300dpi) scan was made of the X-ray encompassing all 3 slabs cut from each of the 5 bones. The TIF file was imported into CorelDraw and a 12 x 12 mm grid overlaid and positioned so as to maximize the number of cubes and allow adequate gripping in the saw. A sample image is shown in Figure 4 for bone "E3". Each of the bones was labeled E1 through E5, and the slabs from each were labeled A, B, and C from smallest to largest (i.e. superior to inferior, or proximal to distal), respectively.

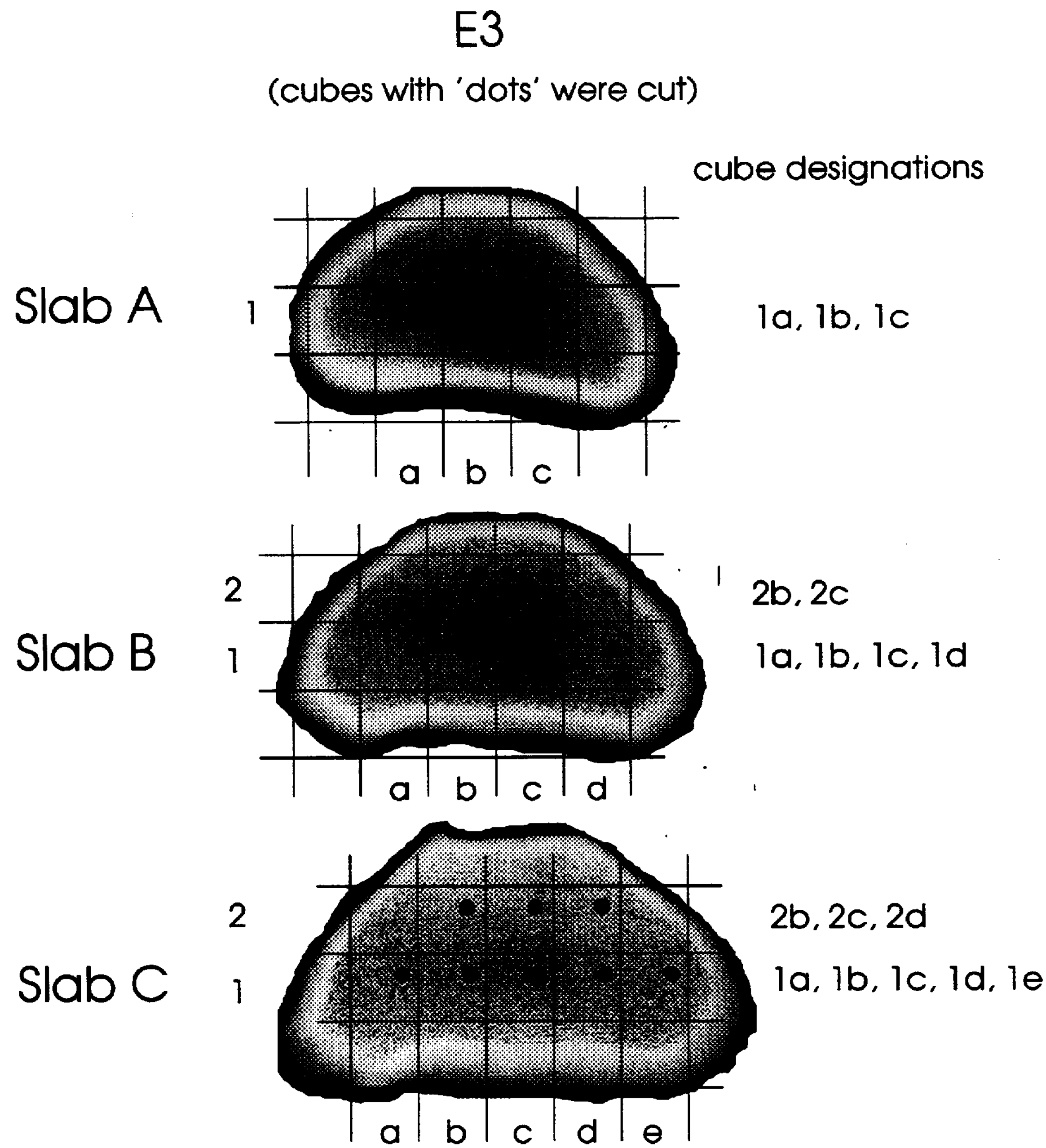

Figure 4. X-ray image with grids overlaid for planning cube specimen cuts.

The grid was transferred to each slab by making transparencies of the images, trimming around the edge of the bone, and then using this template to mark line positions. The lines were drawn with a fine point permanent marker pen. Cubes were cut in a slow-speed diamond blade wafering saw (Buehler Isomet) under continuous irrigation with distalled water. A dual blade tandem arrangement was employed to allow pairs of parallel cuts. Once the cubes were cut the confirmed positions were distributed as regions of interest (ROI) to the other investigators for fractal analysis (Raj Acharya), DEXA analysis (Jon Richardson), and MRI relaxation time determinations (Chen Lin). The ROI information included in Figure 4 is annotated to include a numbering system devised to uniquely identify each cube in the study. For example, the cube on the lower left of slab B shown would be designated E3B1a, where the first two digits identify the "parent" bone (E3), the next digit the slab (B), and the next two digits the "row/column" position within the slab (row 1, column a). After each cube was cut, the wet weight was measured on a microbalance and the dimensions determined using a digital caliper. The length for each of the 3 orthogonal anatomic directions was measured in six locations and averaged to give dimensions in the superior/inferior (S/I), anterior/posterior (A/P), and medial/lateral (M/L) directions. The cubes were wrapped in saline-soaked gauze in individually sealed plastic bags and stored frozen.

Mechanical testing was conducted in the Orthopaedic Biomechanics Laboratory at the University of Texas Medical School in Houston in collaboration with Drs. Timothy Harrigan and Catherine Ambrose. Procedures were developed similar to those of Goulet et al. (1994), Keller (1994), and Linde et al. (1992). A servo-hydraulic MTS 810 load frame was used to apply quasi-static compressive loading in each of the three anatomic directions. Polished aluminum platen fixtures were fabricated with the lower one articulated for self-aligning. The platens were lightly lubricated with glycerol just before mounting the specimens in place. Cyclic loading was applied at a rate of 1%/s to a level of 1% strain for 15 cycles. Force and displacement output were digitized at 50Hz and stored to disk. Data from the loading portion of the eleventh cycle was used for estimating the elastic modulus from the best-fit linear region. The first 10 cycles are for pre-conditioning the specimen to stabilize the response to consistent behavior. For the last of the three directions tested on each specimen, the 10 cycles were followed with loading to failure. A sample output plot for this case is shown in Figure 5. The ultimate strength is then calculated from the maximum load achieved. The direction for failure loading was randomized between S/I, M/L, and A/P. Thus, the mechanical testing of each specimen gives the elastic modulus in all three directions and the ultimate strength in one direction.

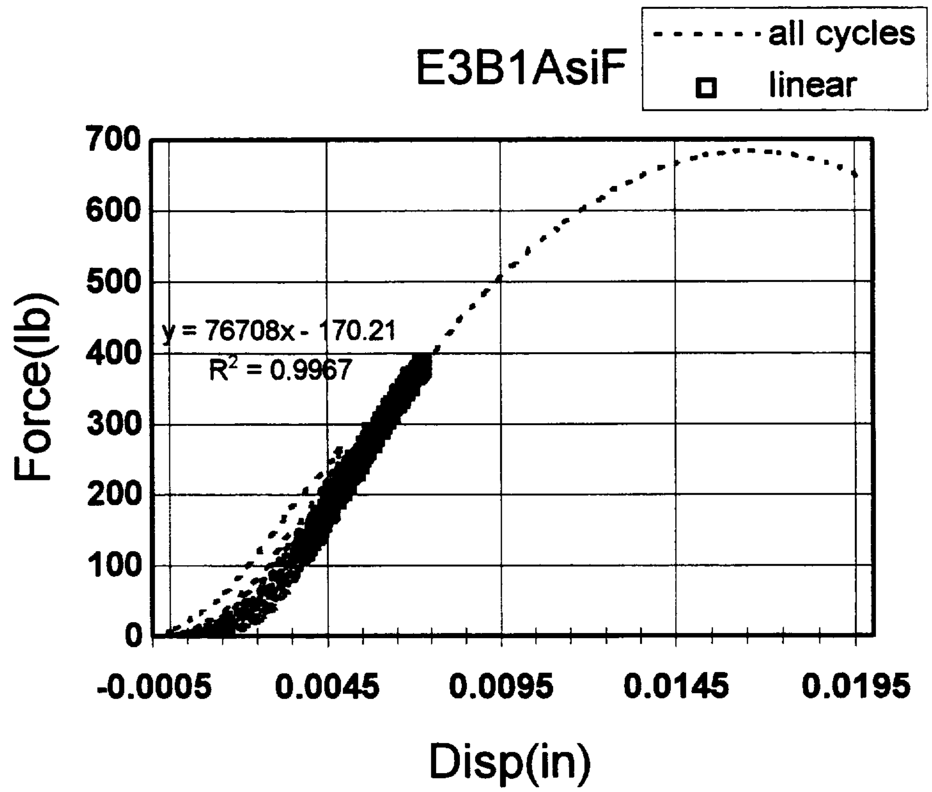

Figure 5. Force-displacement results for cyclic loading and failure overload.

Testing is currently proceeding and once completed each specimen will be defatted and dried in an oven at 100°C for 24 hours. The dry weight will be measured (in g) and dry density calculated by dividing by the volume (in cm^3). The specimens will then be ashed in an oven at 500°C for 48 hours and weighed. The ratio of ash weight (in g) to dry weight (in g) is commonly expressed as a percentage and termed the "ash weight percent", or sometimes even just "ash weight". An ash density will also be calculated by dividing the ash weight (in g) by the volume (in cm^3). The wet density will likewise be estimated by dividing the wet weight (in g) by the volume (in cm^3). Once all testing and analysis is completed the following quantities will be determined directly from each cube specimen:

- wet density, fat-free dry density, and ash density
- ash weight percent
- elastic modulus in S/I, M/L, A/P directions
- ultimate strength in one direction

With proper identification of all ROI information between the various investigators, the following quantities will be calculated for the same specific tissue regions from which the cube specimens for mechanical testing were cut:

- fractal dimension
- MRI relaxation times (such as T2*)
- bone mineral density (BMD) and bone mineral content (BMC) from DEXA

Results will then be analyzed statistically to identify correlations between mechanical properties and fractal dimensions, T2*, BMD/BMC, and densities. The predictive ability of fractal dimension is of particular interest since this quantity reflects trabecular bone architecture and can be acquired non-invasively with X-ray exposure.

REFERENCES

Acharya, R. S., LeBlanc, A., Shackelford, L. C., Swarnarkar, V., Krishnamurthy, R., Hausman, E., and Lin, C. (1995) Fractal analysis of bone structure with applications to osteoporosis and microgravity effects. (manuscript submitted).

Ciarelli, M. J., Goldstein, S. A., Kuhn, J. L., Cody, D. D., and Brown, M. B. (1991) Evaluation of orthogonal medchanical properties and density of human trabecular bone from the major metaphyseal regions with materials tesing and computed tomography. *J. Orthop. Res.* **9**, 674-682.

Figueroa, F. (1995) Methodologies to determine forces on bones and muscles of body segments during exercise, employing compact sensors suitable for use in crowded space vehicles. *Final Report* NASA/ASEE Summer Faculty Fellowship Program.

Goulet, R. W., Goldstein, S. A., Ciarelli, M. J., Kuhn, J. L., Brown, M. B., and Feldkamp, L. A. (1994) The relationship between the structural and orthogonal compressive properties of trabecular bone. *J. Biomechanics* **27**, 375-389.

Keller, T. S. (1994) Predicting the compressive mechanical behavior of bone. *J. Biomechanics* **27**, 1159-1168.

Linde, F., Hvid, I., and Madsen, F. (1992) The effect of specimen geometry on the mechanical behaviour of trabecular bone specimens. *J. Biomechanics* **25**, 359-368.

Majumdar, S., Weinstein, R. S., and Prasad, R. R. (1993) Application of fractal geometry techniques to the study of trabecular bone. *Med. Phys.* **20**, 1611-1619.

Ruttiman, U. E., Webber, R. L., and Hazelrig, J. B. (1992) Fractal dimension from radiographs of peridental alveolar bone. *Oral Surg.Oral Med.Oral Pathol.* **74**, 98-110.

Todd, B. A. (1994) Finite element modeling of the lower extremities. *Final Report* NASA/ASEE Summer Faculty Fellowship Program.

Weinstein, R. S. and Majumdar, S. (1994) Fractal geometry and vertebral compression fractures. *J. Bone Min. Res.* **9**, 1797-1802.