INTRODUCTION
Disuse osteopoenia affects mineral density, microstructure and integrity of bone, which lead to increased risk of osteoporosis and fracture. Bone integrity is dependant on not only the mineral density, but also the quality of bone which includes the strength and structural parameters. Advents in quantitative ultrasound (QUS) provide a unique method for evaluating both bone strength and density. The objective of this study has two folds, 1) to evaluate the efficacy of a scanning confocal acoustic navigation (SCAN) QUS system for a 90-day microgravity analog study with the comparison to the standard Dual X-ray absorptiometry (DXA) in localized interested region, e.g., calcaneus; and 2) to test a guided ultrasound in mitigating bone loss in an estrogen deficient model of osteopenia.

METHODS
Bedrest Study: The human subjects experimental protocol was approved by both Stony Brook University and University of Texas Medical Branch (UTMB) at Galveston IRB Committees. The longitudinal evaluation of bone quality using SCAD and DXA was performed in 90-day continuous bed rest. The subject are skeletal matured and in the healthy conditions. QUS was processed to calculate the ultrasound attenuation (ATT; dB), wave ultrasound velocity (UV), and the broadband ultrasound attenuation (BUA; dB/MHz). Both QUS and DXA measurements were conducted in day 0 (baseline), day 60 and day 90. The scanning region converged in the middle of the median plane of the calcanei, covering an approximate 40x40 mm\(^2\) with 0.5 mm resolution. BMD was also measured at corresponding 0, 60, and 90 days using a DXA machine (Hologic, MA). Interrelationships between QUS parameters and DXA determined BMD were evaluated through multiple correlations, with Student T-test and the significance level was set at \(p < 0.05\).

Ultrasound Inhibit Bone Lose: 72, 16 w.o. Sprague-Dawley rats were divided into six groups including baseline control and US treatment groups. Low intensity ultrasound was delivered transversally at the L4/L5 vertebrae, 20 min/day, 5 days/week for 4 weeks. Vertebrae were imaged using \(\mu\)CT at 15 \(\mu\)m and evaluated for bone volume fraction (BVF), structural model index (SMI), trabecular number (Tb.N.) and trabecular thickness (Tb.Th.). Specimen specific, voxel based, finite element (FE) models (E=18GPa & \(v=0.3\)), were generated using \(\mu\)CT image data and 1% axial compressive strain was simulated using a nonlinear FE solver (ABAQUS).

RESULTS
QUS indicated that disuse alone induced -1.2+/-.04% bone loss via UV, and decreased 2dB/MHz (-2.27%) for BUA, while disuse plus vibration treatment mitigated bone loss (UV, +0.19%; BUA, +0.5%) in calcaneus. Longitudinal subtle changes were predicted by the UV and BUA comparing disuse plus treatment and disuse alone. DXA measurement showed heel bone mineral density (BMD) changed -4.50% for control subjects and -2.18% for vibration subjects. Correlation test between QUS and DXA demonstrated a strong correlation between QUS determined values and DXA measured BMD (BUA and BMD: \(r^2=0.69\); UV and BMD: \(r^2=0.54\); Combined: \(r^2=0.70\)). US treatment significantly increased BVF compared to OVX controls for the 100mW/cm\(^2\) treated group. Additionally, SMI, and Tb.N showed significant improvements compared with OVX for the 100mW/cm\(^2\) treated groups.

DISCUSSION
It has been demonstrated that the \textit{in vivo} assessment of bone quality using QUS predicts overall BMD distributions in all pooled subjects following a longitudinal testing. SCAN has shown its capability to sense subtle changes in bone in the longitudinal BMD alteration, i.e., prediction of 2.5% UV reduction for 90 day bed rest. The high correlations were observed between QUS and BMD in the treated skeletal sites, i.e., calcaneus. These preliminary data suggest that prolonged exposure to simulated disuse may be assessed by SCAN, which then could be used for the longitudinal and instant follow-up of bone demineralization occurring during long-term space flights. Guided ultrasound can significantly mitigate bone loss in the selected region, which may provide early treatment for bone loss and accelerate fracture healing. Ultimately, it may provide a portable, noninvasive device for bone loss assessment and treatment in space and on Earth. [Supported by the National Space Biomedical Research Institute through NASA Cooperative Agreement NCC 9-58.]