Microgravity and aging induced bone loss is a critical skeleton complication occurred particularly in the weight-supporting skeleton, which leads to osteoporosis and fracture. Adveits in quantitative ultrasound (QUS) provide a unique method for evaluating both bone strength and density. Using an imaging-base confocal scanning ultrasound diagnostic system (SCAD), the goals of this work were to non-invasively characterize bone quality at proximal femur, and longitudinally monitor effectives of calcaneus bone loss in a 90-day bedrest. QUS scanning was performed at proximal femur (cadaver) and calcaneus (bedrest subjects) regions with QUS images of 80x80 mm² for hip and 40x40 mm² for calcaneus. QUS was processed to calculate the ultrasound attenuation (ATT; dB), wave ultrasound velocity (UV), and the broadband ultrasound attenuation (BUA; dB/MHz). Human cadaver proximal femurs have been measured with the SCAD, micro-CT, DXA, and mechanical strength test. Human calcaneus of bedrest subjects were measured using SCAD and DXA in day 0 (baseline), day 60 and day 90. Results demonstrated that QUS measurement has the capability to predict bone BMD, microstructure and mechanical properties in human bone, and indicated significant sensitivity to the progressive change of bone quality, particularly in the trabecular bone region with remodeling activities.