Age-, Sex-, and Obesity-Related Changes in Hip Bone Density During Skeletal Development and Maturation: A Population-Based Study of 11,756 Pelvic CT Scans

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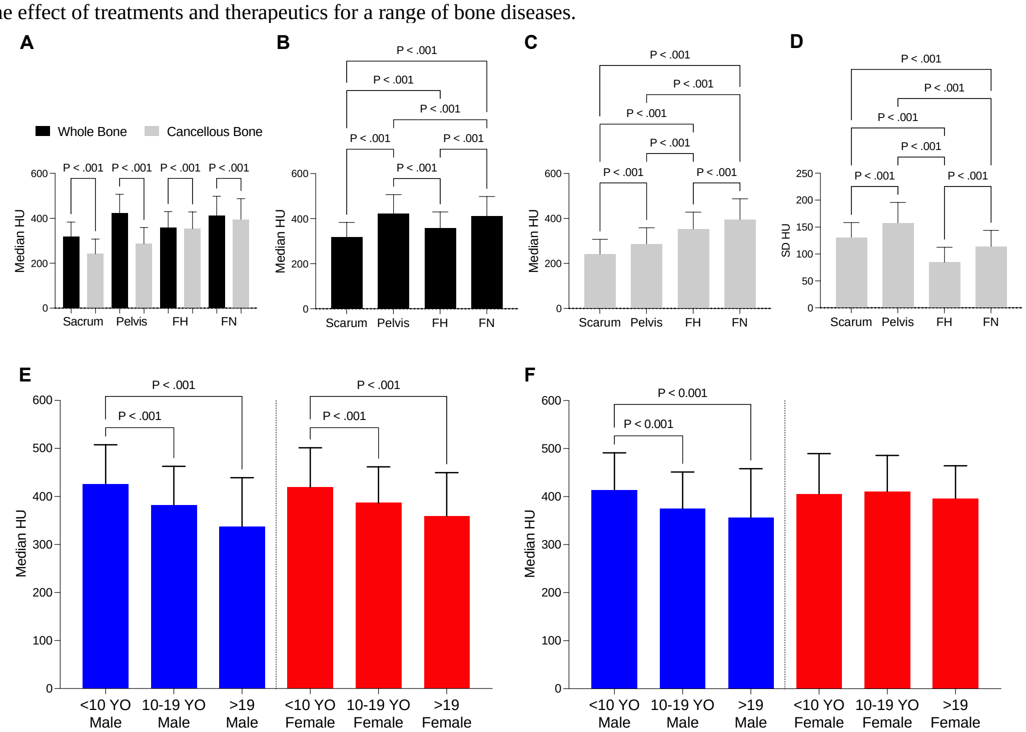
INTRODUCTION: Bone mineral density (BMD) is an important marker for bone health, especially for long term risks of bone fractures, with lower BMD associated with a higher risk of fractures. The most commonly used technique to clinically assess and measure BMD is a central dual energy x-ray absorptiometry (DEXA). Although DEXA is the standard technique for clinical assessment of BMD, DEXA may have errors associated with 2D projection and have low sensitivity to separate cortical and cancellous bones. Voxel-based x-ray attenuation based on Hounsfield Unit (HU) from clinical CT scans has become a recent area of interest as a surrogate for measuring BMD. If validated, such approach can allow a much more accurate and localized assessment of bone density. Here, we use a robust automated segmentation and landmark detection pipeline to measure global and regional HU (i.e., whole bone vs. isolated cancellous bone across pelvis, femoral head, femoral neck, and sacrum) in a large cohort of children, adolescents, and young adults who underwent pelvic CT scans without any reported bone or joint abnormalities. Afterwards, we investigate the changes in HU by age, sex, and obesity status.

METHODS: Following IRB approval, a validated natural language processing pipeline was used to process the clinical notes and radiology reports of all the patients who underwent pelvic CT scans from 2012-2022 in our institute and identified cases with no documented bone or joint conditions (accuracy of 0.98). A validated deep learning-based automatic segmentation and landmark detection pipeline (dice: 0.96-0.98) was used to segment pelvis, proximal femur, and sacrum, followed by isolating femoral neck and femoral head from identified "normal" CT scans. Then, the segmented masks were iteratively eroded to exclude cortical bones. Median and standard deviation of HUs were then extracted from the whole (cortical and cancellous bones) and eroded (only cancellous bone) masks. A mixed linear model was used to investigate the differences in HUs based on region, sex, age, and obesity status.

RESULTS: We identified a total of 11,756 CT scans which had no documented bone or joint conditions and adequate CT quality for accurate 3D segmentation (Age: 1-25; average 12 ± 6 years; 47% females). As expected, median HU was consistently higher in masks including both cortical and cancellous bones (whole bone) compared to cancellous bone only (P<0.001), with the highest difference in the pelvis and the lowest difference in the femoral head (Figure 1A). Median HU from the whole bone masks was highest in the pelvis and lowest in the sacrum (Figure 1B, P<0.001), while the median HU from cancellous bone masks was highest in the femoral neck and lowest in the sacrum (Figure 1C, P<0.001). The cancellous bone heterogeneity (HU standard deviation) was highest in the pelvis and lowest in the femoral head (Figure 1D, P<0.001). Median HU of the femoral neck decreased from childhood to early adulthood in both males and females with normal BMI (Figure 1E, P<0.001). However, in obese subjects, there were age-related reductions in males only (P<0.001), while females remained unchanged (Figure 1F). Similar trends were observed in other regions as well.

DISCUSSION: This is the first largescale study to use CT-based HU to study age, sex and obesity related changes during skeletal growth and maturation. The observed differences in HU measurements on whole vs. cancellous bone along with observed regional differences highlight the importance of region of interest selection when studying bone density from CT scans. The current findings also support the utility of HU measured from clinical CT scans to study variabilities in bone structure related to age, sex and other intrinsic or extrinsic factor, such as obesity. The observed reductions in HU by age are consistent with prior studies. However, the sex differences in how obesity may influence bone structure require further investigations. Future studies are focused on investigating the effect of image acquisition parameters (e.g., x-ray energy) on HU values and the relationships between CT-based HU and BMD measured from DEXA.

SIGNIFICANCE: A robust deep learning pipeline that can consistently measure HU from CT scans across different regions can help study bone structural development and its contributing factors. Such information has high clinical significance in studying healthy and pathological bone development, and can be used to measure the effect of treatments and therapeutics for a range of bone diseases.



Figrue 1. (A) Differences in median HU between whole bone and cancellous bone. (B) Regional differrences in whole bone median HU. (C) Regional differrences in cencellous bone median HU. (D) Regional differrences in cencellous bone HU standard deviations. (E) Age related differences in femoral neck median HU in subjects with normal BMI. (F) Age related differences in femoral neck median HU in obese subjects.