Osteoporosis is a prevalent disease marked by diminished bone mineral density (BMD), significantly increasing the risk of bone fractures. Dual-energy x-ray absorptiometry (DXA) and quantitative computed tomography (QCT) are the established gold standards for BMD measurement and osteoporosis diagnosis. However, their routine application is limited due to higher costs and increased radiation exposure. Standard X-ray imaging for BMD assessment offers a promising alternative for early osteoporosis detection through opportunistic screening. Traditional methods that directly regress BMD from X-ray images often require extensive training datasets and complex preprocessing.

Addressing these limitations, we introduce a generative adversarial network (GAN) approach to estimate BMD from X-ray images. Our method simultaneously synthesizes two types of digitally reconstructed radiographs (DRRs) for four lumbar spines (L1 – L4) via multi-channel image synthesis, facilitating the estimation of both DXA-based BMD and CT volume BMD (CT-vBMD). This method was evaluated using a dataset of 300 cases, supplemented by pretraining on simulated x-ray images derived from a comprehensive CT dataset (exceeding 9000 scans) with 5-fold cross-validation. The results demonstrate the correlation coefficient of 0.808 and 0.728 between our method’s predictions and the actual BMD measurements obtained through DXA and QCT in anteroposterior (AP) views. Our proposed method provides a new approach for estimating CT-vBMD from x-ray images with the capability to improve the accuracy of DXA-BMD and CT-vBMD simultaneously.