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REVIEW

Artificial Intelligence for Osteoporosis Diagnosis, Risk Prediction and Therapy: Current Advances, Clinical Challenges, and Future Perspectives

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Abstract: Osteoporosis (OP) is a chronic systemic skeletal disorder that predominantly affects the elderly. It is characterized by an imbalance in bone homeostasis, reduced bone mass, microarchitectural deterioration of bone tissue, and increased bone fragility, ultimately leading to a higher risk of fractures and related complications. With the progression of global population aging, the prevalence of OP continues to rise, underscoring the importance of early diagnosis and timely intervention. However, the diagnosis and management of OP—particularly its early detection—remain limited by material constraints such as diagnostic equipment and by subjective factors including clinician experience, which hinder widespread screening. In recent years, artificial intelligence (AI) has emerged as a transformative technology with advantages of efficiency, objectivity, and scalability, and has been increasingly integrated into various medical domains. For example, AI-assisted musculoskeletal measurements on leg and foot radiographs can reduce the measurement time from 166 seconds to 40 seconds, resulting in an overall efficiency improvement of approximately 70%. Applying AI to the diagnosis and treatment of OP can reduce human error, save labor costs, and improve diagnostic accuracy and clinical efficiency. Numerous studies have investigated AI-based approaches in OP-related research and clinical practice. Despite these promising developments, several important limitations should be acknowledged. Considerable heterogeneity exists among published studies regarding patient populations, AI algorithms, and evaluation metrics. Besides, consistent external validation remains insufficient in many studies. Challenges related to data imbalance and potential selection bias further highlight the need for standardized reporting frameworks and multicenter collaborative research to promote safe clinical adoption of AI technologies in osteoporosis management. This review summarizes current AI applications in OP diagnosis, risk prediction and therapy. We highlight key methodological limitations and emerging trends, aiming to guide future research and facilitate safe clinical implementation of AI in OP management.

Keywords: artificial intelligence, osteoporosis, image recognition, big data, bioinformatics

Introduction

OP is a chronic systemic skeletal disorder characterized by an imbalance in bone homeostasis, decreased bone mass, alterations in trabecular microarchitecture, and increased bone fragility.[1] Epidemiological data indicate that in China alone, approximately 49 million women and 22.8 million men aged over 50 years are affected by OP, highlighting a substantial disease burden in the world's largest aging population.[2] Similarly, in the United States, musculoskeletal disorders affect more than 121 million individuals and remain one of the leading causes of disability across all disease categories.[3] It primarily affects elderly individuals, particularly postmenopausal women. According to data from the International Osteoporosis Foundation (IOF), one in three women over the age of 50 worldwide are affected by OP, and

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many eventually develop serious complications, the most prominent of which is osteoporotic fracture (OF).[4,5] Globally, OP is estimated to cause 8.9 million fractures annually.[6] With the acceleration of population aging, improving early identification and management of OP has become an urgent public health priority.

Currently, the diagnosis of OP mainly relies on dual-energy X-ray absorptiometry (DXA). When a patient's bone mineral density (BMD) is equal to or less than 2.5 standard deviations below the mean value for healthy young adults, OP can be diagnosed,[7].[8] However, both the availability and utilization rate of DXA remain relatively low, and patient adherence to DXA screening is often poor,[9] creating a significant barrier to early diagnosis. On the treatment side, OP management still depends heavily on traditional drug development, which is time-consuming, costly, and has a high failure rate, thereby increasing the difficulty of effective intervention.[10]

AI —which is rapidly advanced in the past three decades[11]—has been increasingly integrated into diverse areas of medicine,[12] including automated medical image recognition,[13] early disease diagnosis,[14] and drug discovery.[10] Key enabling technologies include machine learning (ML), deep learning (DL),[15] large-scale foundation models,[10] and Generative AI.[16] In recent years, with the development of big data analytics, the convergence of AI and large-scale biomedical data has opened new directions for medical research and clinical applications.[17]

The unique capabilities of AI provide promising solutions to the challenges faced in OP diagnosis and treatment. In diagnostics, AI enables identification of osteoporotic features from common imaging modalities such as X-ray,[18] computed tomography (CT),[19] magnetic resonance imaging (MRI),[20] and ultrasound,[21] offering potential for opportunistic screening. Moreover, AI can identify risk factors and predict the likelihood of OP and OF occurrence.[22] In therapeutics, AI contributes to the discovery of key genetic targets for OP,[23] supports drug development,[10] and predicts clinical outcomes.[24] Despite these promising developments, growing evidence indicates substantial variability in patient populations, algorithm selection, and evaluation strategies, which may limit the comparability, reproducibility, and clinical translation of current AI models.[10,25–27]

Therefore, a comprehensive review that not only summarizes existing applications but also critically examines methodological limitations, validation challenges, and barriers to real-world implementation is needed. This review aims to summarize current applications of AI in OP screening, diagnosis, risk prediction, and treatment research, while critically discussing methodological challenges and future directions to support safe and effective clinical adoption.

Methods

This narrative review aimed to summarize current applications of AI in osteoporosis OP research and clinical practice. Relevant literature published in English was retrieved from PubMed and IEEE Xplore databases up to May 2026.

In PubMed, both Medical Subject Headings (MeSH) terms and free-text keywords were used. The primary MeSH terms included "Artificial Intelligence" and "Osteoporosis". Additional keyword searches were also performed using terms such as "machine learning", "deep learning", "radiomics" and "osteoporotic fracture" to identify studies related to AI-assisted diagnosis, prediction, and treatment of OP. Furthermore, broader searches using the keyword "artificial intelligence" were conducted to support the introductory overview of AI technologies and concepts.

In IEEE Xplore, literature searches were performed using combinations of keywords including "artificial intelligence and medicine", "artificial intelligence and orthopedics", and "artificial intelligence and osteoporosis" to identify engineering- and technology-oriented studies relevant to musculoskeletal medicine and OP research.

Original research articles, reviews, and clinically relevant studies focusing on AI applications in OP diagnosis, prediction, molecular analysis, imaging, or treatment were included. References from relevant articles were also manually screened to identify additional studies of relevance.

Overview of AI Technologies in Osteoporosis

With the rapid advancement of modern technology, AI has evolved into several major subfields, including ML, DL, natural language processing (NLP), and robotics and automation.[28] Each of these branches has found distinct yet complementary applications in medicine. For instance, ML is widely used for feature extraction and patient data analysis;[29] DL has become fundamental in medical image recognition and classification;[30] NLP assists clinical decision-making by supporting treatment planning, providing alerts, and monitoring adverse events,[31] while robotics and automation are primarily applied in surgical assistance[32] and patient rehabilitation.[33] Although these AI subfields differ in their core methodologies and application domains, they are often interrelated and integrated in clinical research and practice. The interconnections among these branches are illustrated in Figure 1.

Machine Learning for Osteoporosis Data Analysis

ML is a fundamental branch of AI that has been widely applied in healthcare.[28] It is good at the extraction and interpretation of complex data patterns, particularly for image feature extraction,[40] risk factor assessment,[22] and bioinformatics-based prediction.[23] OP-related data are typically characterized by high dimensionality, heterogeneous data sources (eg., imaging, clinical indicators, and molecular data), and relatively limited sample sizes, which makes ML particularly suitable for OP research. Now ML plays a critical role in disease diagnosis and prognosis, drug discovery and design, gene and molecular mechanism analysis, and risk factor prediction.[41–44]

ML for Diagnosis and Prognosis of Osteoporosis

Among all the directions, the use of ML for OP diagnosis and prognosis prediction has attracted the most attention. Because in X-ray imaging, manual measurement of OP-related indicators requires substantial manpower and time, which results in low reproducibility of manual classification methods. ML can extract quantitative features such as size, shape, and texture heterogeneity from segmented images, thereby overcoming the above limitations.[45,46] This line of research mainly follows three approaches: image recognition,[47] radiomics,[48] and bioinformatics.[43] Image recognition–based diagnosis and prognosis prediction of OP currently represents one of the most extensively studied directions in ML research. For example, Galbusera F et al applied ML to MRI and X-ray images of the lumbar spine for OP detection. Their study found that two models—CatBoost and Gradient Boosting Classifier (GBC)—achieved the best performance, with CatBoost showing optimal accuracy for MRI (0.90) and GBC for X-rays (0.88).[49] In radiomics-based studies, Zhang et al integrated clinical variables such as CT values and cross-sectional areas (CSA) of the L1 vertebral body, psoas major (PM), and paraspinal muscles (PVM), along with patient demographics, DXA T-scores, and follow-up data. Using a Support Vector Machine (SVM) algorithm, they constructed a multimodal model that combined BMD, CT features, and radiomic–DL signatures to predict OF risk. Furthermore,[40] in bioinformatics-driven analyses, Hu et al identified

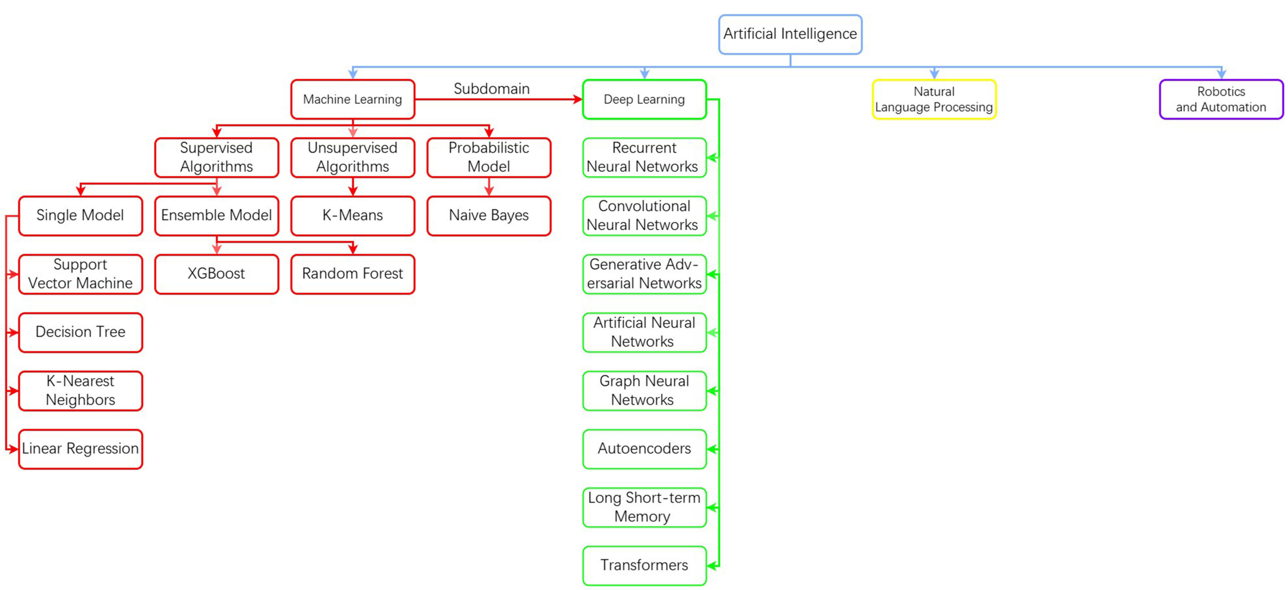

Figure 1 Relationships among commonly used AI technologies.[1,28,34–39] Blue boxes and arrows AI and its relationships with related domains. Red boxes and arrows indicate ML and its subfields, while green boxes and arrows denote DL and its associated areas. Yellow boxes represent NLP, and purple boxes represent robotics and automation. AI mainly consists of four subfields: ML, DL, NLP, and robotics and automation.ML primarily includes three types of algorithms: supervised algorithms, unsupervised algorithms (eg., K-means), and probabilistic models (eg., Naïve Bayes). Supervised algorithms can be further divided into single models (eg., LR, SVM, k-NN, and decision trees) and ensemble models (eg., XGBoost and RF).DL is a subfield of ML; however, it has increasingly evolved into a relatively independent research area parallel to traditional machine learning. Its main categories include CNN, RNNs, generative adversarial networks (GANs), ANNs, graph neural networks (GNNs), autoencoders, LSTMs, and transformers.

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differentially expressed genes (DEGs) associated with OP through bioinformatic screening and subsequently built an SVM classification model capable of accurately distinguishing osteoporotic samples.[50]

ML in Molecular Mechanism Research

In addition to imaging analysis, ML has also been increasingly applied to molecular mechanism exploration in OP research. By integrating bioinformatics techniques with ML algorithms, researchers can identify disease-related genes, signaling pathways, and molecular biomarkers associated with OP progression. For instance, Zhang et al investigated the molecular pathways underlying plasticizer-induced OP by employing ten ML algorithms (including Lasso, SVM, and Random Forest [RF]) to build 113 predictive models, ultimately identifying six core genes: CKM, TACR3, SOAT2, ERAP2, SGK1, and MMP12.[51] Similarly, Yang et al examined the genetic correlation between chronic hepatitis B virus (HBV) infection and OP. Using LASSO regression, recursive feature elimination (RFE), and three ML models (RF, SVM, and Gradient Boosting Machine [GBM]), they screened for disease-associated genes and identified 18 key genes, including USP10, ERAL1, and ECM1.[52] These approaches demonstrate the potential of ML to improve the efficiency and precision of molecular-level investigations. Detailed applications of AI in genetic and molecular studies of OP are further discussed in Artificial Intelligence in Genetic and Molecular Studies of Osteoporosis.

ML for Risk Factor Prediction

Risk factor prediction represents another major application area of ML in OP research. Chang et al compared the predictive accuracy of ML algorithms with multiple linear regression (MLR) for changes in BMD (ΔT-score) among 1,698 postmenopausal women. By incorporating biochemical and lifestyle variables, and using RF, XGBoost, Naïve Bayes (NB), and Stochastic Gradient Boosting (SGB) algorithms, they identified key determinants such as educational level that significantly influenced bone density variation.[53] Similarly, Xu et al integrated demographic variables and blood-based biomarkers into ML models, demonstrating that serum biomarkers can effectively distinguish individuals with low BMD, thereby highlighting their potential as noninvasive diagnostic indicators.[54]

ML for Drug Design in Osteoporosis

Although studies applying ML to drug design for OP remain limited, emerging work has demonstrated promising results. Yang et al combined LASSO, SVM-RFE, and RF algorithms with bioinformatics analyses to identify shared diagnostic genes for comorbid OP and sarcopenia, including CHST3, PGBD5, and SLIT2. These genes were subsequently queried in the Connectivity Map (CMap) database to predict potential therapeutic compounds, such as PU-H71, Scandenin, and BMS-345541.[55]

In summary, ML has shown broad and expanding applications in OP research, encompassing diagnostic imaging, molecular biology, pharmacology, and clinical risk assessment. With ongoing advances in data integration and algorithmic modeling, ML-based approaches are expected to play an increasingly significant role in future OP studies.

Deep Learning in Osteoporosis Imaging

DL is a subfield of ML that enables computational models composed of multiple processing layers to learn data representations at various levels of abstraction. DL models demonstrating remarkable capability in feature learning.[34] In the medical domain, DL has been extensively applied to the analysis and interpretation of medical imaging data.[30] So DL is particularly well suited for OP -related imaging tasks, as it enables automatic extraction of hierarchical features from raw radiographic and CT images. These models can capture complex trabecular and cortical bone patterns that are difficult to quantify manually, reducing reliance on handcrafted features and improving robustness across different imaging conditions.[46]

In the context of OP, DL has primarily been used for image-based diagnosis and auxiliary detection.[56] Large-scale application of DL models can significantly reduce manual workload, shorten image reading time, and minimize the impact of human subjectivity. For example, Ho et al developed a DL model named DeepDXA-Hand, based on the efficient convolutional neural network (CNN) architecture HarDNet, to detect OP noninvasively using hand X-rays. The model achieved high diagnostic performance, with a sensitivity of 0.73, specificity of 0.83, and accuracy of 0.80.[57] Similarly, Pan et al constructed a DL-based segmentation framework that integrated multiple radiomic features to classify OP from chest CT scans. Their model achieved outstanding area under the curve (AUC) values of 0.992 for normal bone density, 0.973 for osteopenia, and 0.989 for OP, demonstrating exceptional diagnostic capability.[58]

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Beyond imaging applications, DL has also been explored in drug discovery and optimization related to OP. According to Xu et al, DL techniques can facilitate drug target identification, lead compound screening and optimization, prediction of physicochemical properties, drug–drug interaction modeling, and synthetic route design. Compared with traditional drug discovery methods—which are often costly, time-consuming, and have low success rates, DL-based approaches offer higher efficiency and scalability. However, specific studies applying DL to OP drug development remain limited, suggesting that this may become a promising direction for future research.[10]

Potential Roles of Other Models in Osteoporosis Research

In addition to traditional ML and DL approaches, large models have recently emerged as one of the most actively studied branches of AI. Current research on the application of large models in OP primarily focuses on evaluating their potential utility in OP-related drug development.[10] Although no concrete clinical or laboratory studies have yet been conducted, the intrinsic advantages of large models—such as their ability to process high-dimensional data, perform multitask learning[10]—suggest significant potential for future applications in OP research. In OP research and clinical practice, large language models may play a supportive role by processing unstructured clinical narratives, guideline documents, and electronic health records(EHRs).[59]

While AI encompasses a wide range of techniques and methodologies, its most mature and clinically impactful applications in OP to date have been concentrated in disease detection and diagnosis. In particular, advances in ML and DL have enabled the extraction of subtle skeletal features from routine medical images, laying the foundation for AI-assisted imaging-based diagnosis.[60]

AI in Osteoporosis Diagnosis

With the progression of population aging, the incidence of OP has been increasing steadily each year, making early case identification particularly critical. Although DXA remains the gold standard for diagnosing OP, its limited accessibility and low screening coverage mean that a large proportion of patients with OP have never undergone DXA examination.[9] An alternative method, quantitative computed tomography (qCT), also faces challenges due to its high operational cost and limited feasibility for large-scale screening.[61]

Over the past few decades, the rapid rise of AI technologies has provided a promising solution to these diagnostic challenges. With powerful image recognition capabilities, AI systems offer high accuracy, rapid processing speed, and cost-effectiveness, making it feasible to diagnose OP using routine imaging modalities.[62] Beyond imaging-based diagnosis, risk factor screening and prediction models powered by AI have also become active areas of current research, offering complementary tools for early and noninvasive identification of OP.

Image Recognition

AI possesses powerful image recognition capabilities and has been applied across multiple imaging modalities.[63] In the field of OP, numerous studies have explored AI-assisted diagnostic approaches based on medical image analysis.

X-Ray Imaging

Different imaging modalities contribute unequally to AI-based OP diagnosis. X-ray imaging has emerged as the most extensively studied modality due to its high accessibility, low cost, and widespread clinical use.[64] However, unlike dual-energy DXA, conventional X-rays are not sufficiently sensitive to detect OP, limiting their diagnostic utility. With advances in AI, especially in ML and DL, it has become possible to extract subtle image features imperceptible to human observers. That enabling the construction of large-scale datasets required for robust AI training.[65] Consequently, a larger body of literature has focused on X-ray–based approaches, whereas studies involving MRI and US remain comparatively limited. The use of standard X-rays for OP diagnosis has gained increasing attention, particularly over the past five years (Table 1). Among studies applying AI to X-ray images for OP diagnosis, the most commonly used anatomical sites include the chest,[66] spine,[67] pelvis and hip,[68] hands[69] and feet,[70] and or maxillofacial region.[47]

Chest radiographs are among the most common medical images, and several studies have investigated their utility in OP diagnosis. For example, Lin et al and Asamoto et al both developed DL models trained on chest X-rays to detect OP.

Table 1 Recent Studies Applying AI for OP Diagnosis Using X-Ray Imaging

Parts	Researchers	Year	Purpose	Algorithms Evaluated	Dataset	Best-Performing Algorithm	Performance Metrics of Best-Performing Algorithm
Knee	Naguib SM et al[71]	2024	Develop a new deep-learning approach to categorize knee X-ray images into OP, osteopenia, and normal classes	AlexNet, ResNet50	Knee X-ray images	Superfluity DL model	AUC0.8116(CI: Not given)
	Xie H et al[72]	2024	Develop a FSL framework for the diagnosis of osteopenia and OP in knee X-ray images	VGG, ResNet, Xception	Knee X-ray images, chest x-ray images	FSL models	Accuracy0.728(CI: Not given)
	Sarmadi A et al[73]	2024	Compare the ability of OP detection between vision transformer and neural networks	CNN, ViT	Knee X-ray images	vit_r50_l32_fe	Accuracy0.6380(CI: Not given)
	Srinivasan D et al[74]	2025	Improve the accuracy, speed, and reliability of early-stage OP detection by ANNs	ANN	Knee X-ray images	BoneVoyage model	Accuracy0.972(CI: Not given)
	Muhammad I et al[75]	2025	Introduce an advanced deep-learning methodology to enhance the accuracy and efficiency of osteoporosis detection through knee X-ray analysis	DenseNet169, Vision Transformer (ViT), Attention Model (AM)	Knee X-ray images	Fusion model	Accuracy0.8611(CI: Not given)
	Qureshi MB et al[76]	2025	Detect OP from knee X-rays using DL, specifically employing the ResNet-50 model with transfer learning, as a strategy to address existing challenges	VGG-16, ResNet-18, ResNet-50	Knee X-ray images	ResNet-50	Accuracy0.90(CI: Not given)

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Chest	Jang M et al[66]	2021	Develop and evaluate the DL approaches for screening OP using the classified chest radiographs based on the DXA-based diagnosis of OP	CNN	Chest X-ray images	OsPor	Internal validation AUC 0.91(95%CI: 0.90–0.92),External validation AUC 0.88(95%CI: 0.85–0.90)
	Lin C et al[77]	2024	Evaluate the effectiveness of DXA screening in high-risk patients with OP identified by an AI model using chest radiographs.	CNN	Chest X-ray images	DenseNet	Positive predictive value 75% (CI: Not given)
	Asamoto T et al[78]	2024	Verify the usefulness of DL model for predicting BMD of femoral neck in external validation	ResNet-50	Chest X-ray images	ResNet-50	Osteopenia AUC 0.80, OP AUC 0.83(CI: Not given)
	Tsai DJ et al[79]	2024	Develope a DL model to identify OP from chest X-ray features	DenseNet	Chest X-ray images	CXR-OP	Internal validation AUC 0.930(CI: Not given),External validation AUC 0.892(CI: Not given)
	Ohta Y et al[80]	2025	Develop and evaluate two DL models to detect low BMD in the femoral neck and lumbar vertebrae	ResNet-50	Chest X-ray images	ResNet-50	Femoral neck AUC0.82(CI: Not given); Lumbar vertebrae AUC0.96(CI: Not given)
	Tang J et al[81]	2025	Provide an automatic screening method for OP using chest X-rays	Inception v3, VGG-16, ResNet-50	Chest X-ray images	ResNet-50	Internal validation AUC 0.945(CI: Not given) and 0.957(CI: Not given),External validation AUC 0.904(CI: Not given)
	Iwao Y et al[82]	2025	Predicts BMD from chest radiographs using clavicular features	U-Net	Chest X-ray images	U-Net	Accuracy0.68(CI: Not given)
	Park J et al[83]	2025	Develop and validate a DL model for the opportunistic detection of low bone mass using routine chest X-rays	OsPenScreen	Chest X-Ray Images	OsPenScreen	AUC0.95 (95% CI: 0.94–0.97)

(*Continued*)

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Table 1 (Continued).

Parts	Researchers	Year	Purpose	Algorithms Evaluated	Dataset	Best-Performing Algorithm	Performance Metrics of Best-Performing Algorithm
Spine	Zhang B et al[67]	2020	Develop a DCNN model to classify osteopenia and OP with the use of lumbar spine X-ray images	DCNN	Lumbar spine X-ray images	DCNN	Test dataset 1 OP AUC 0.767(95%CI: 0.701–0.824), Test dataset 1 osteopenia AUC 0.787(95%CI: 0.701–0.824); Test dataset 2 OP AUC 0.726(95%CI: 0.646–0.796), Test dataset 2 osteopenia AUC 0.810(95%CI: 0.737–0.870)
	Lee S et al[84]	2020	Evaluated ML models for identifying individuals with abnormal BMD through an analysis of spine X-ray features	AlexNet, VGG, Inception-V3, ResNet-50, SVMC, KNNC, RFC	Spine X-ray images	RFC with VGG-16	AUC0.74(CI: Not given)
	Hsieh CI et al[85]	2021	Present an automated tool to identify fractures, predict BMD, and evaluate fracture risk using plain radiographs	VGG-11, VGG-16, ResNet-18, ResNet-34	Pelvis/ lumbar spine X-ray images	VGG-16, ResNet-34	Hip OP AUC 0.89(CI: Not given);Spine OP AUC 0.89(CI: Not given)
	Mao L et al[86]	2022	Construct a CNN model for screening primary osteopenia and OP based on the lumbar radiographs	DenseNet	Lumbar X-ray images	The model based on the anteroposterior\lateral channel	AUC0.909(95%CI: 0.909–0.950),0.937(95% CI: 0.883–0.930)
	Dong Q et al[87]	2023	Develop a DL classifier for spinal osteoporotic compression fractures	GoogLeNet	Spine X-Ray images	GoogLeNet	AUC0.99(95%CI: 0.98–1.00)
	Hong N et al[88]	2023	Develop DL scores to detect OP and VF based on lateral spine radiography and investigate whether their use can improve referral of high-risk individuals to bone-density testing	EfficientNet-B4	Spine X-Ray images	VERTE-X pVF, VERTE-X	Vertebral fractures AUC 0.926(95%CI: 0.908–0.944); OP AUC 0.848(95%CI: 0.827–0.869)
	Dong Q et al[89]	2024	Build an automated opportunistic OCF radiograph screening tool with three primary sequential components	GoogLeNet, Inception-ResNet-v2, EfficientNet-B1, two ensemble algorithms	Thoracic and lumbar spine X-ray images	Ensemble Model	Local dataset's AUC 0.948(95%CI: 0.933–0.961),MrOS dataset's AUC 0.936(95%CI: 0.910–0.959)
	Moro T et al[90]	2025	Develop an AI-assisted diagnostic system that estimated not only lumbar BMD but also femoral BMD from anteroposterior lumbar X-ray images	ANN	Lumbar X-ray images	ANN	AUC>0.8(CI: Not given)

	Hong N et al[91]	2025	Develop DL models to detect prevalent vertebral fracture and OP	CNN	Lateral spine X-Ray images	VERTE-X	VERTE-X OP AUC 0.926 (95% CI 0.908–0.955),0.848 (95% CI 0.827–0.869)
	Hong J et al[92]	2025	Develop a DL -based model to predict pediatric BMD using plain spine radiographs	ResNet-18	Spine X-Ray images	ResNet-18	AUC0.85(CI: Not given)
	Tamai K et al[93]	2025	Validate the diagnostic yield of a DL algorithm for detecting osteopenia/ OP using cervical radiography and compare its diagnostic accuracy with that of spine surgeons	EfficientNetB2	Cervical spine radiography	EfficientNetB2	AUC0.869 (95% CI: 0.822–0.916)
	Boonrod A et al[94]	2025	Propose the DL models to screen for OP and measure its accuracy on OP detection from lumbar spine radiographs	MobileNet-V2, AlexNet, DarkNet-19, ResNet-18, CiRA32	Lumbar X-ray images	ResNet-18	AUC0.79 (95%CI 0.76–0.82)
Mouth	Kavitha MS et al[47]	2015	Determine whether individual measurements or a combination of textural features and mandibular cortical width (MCW) derived from digital DPRs are more useful in assessment of OP	k-NN, SVM, NB	Panoramic radiography	SVM	Femoral neck BMD accuracy 0.963(CI: Not given);Lumbar spine BMD accuracy 0.958 (CI: Not given)
	Kavitha MS et al[95]	2016	Propose a new automated screening system based on a hybrid genetic swarm fuzzy (GSF) classifier using digital DPRs to diagnose females with a low BMD or OP	GSF classifier	Panoramic radiographs	Hybrid GSF with optimized MF and RS	Lumbar spine accuracy 0.9601 (95% CI: 0.903–0.995) Femoral neck accuracy 0.989 (95% CI:0.920–1)
	Hwang JJ et al[96]	2017	Develop an OP detection model based on panoramic radiography	decision tree, SVM	Panoramic radiography	SVM	Accuracy 0.969(CI: Not given)
	Lee JS et al[97]	2018	Evaluate the diagnostic performance of a DCNN-based computer-assisted diagnosis (CAD) system in the detection of OP on panoramic radiographs	DCNN	Panoramic radiographs	SC-DCNN	AUC0.9991(CI: Not given)
	Alzubaidi MA et al[98]	2019	Explores the use of 13 different feature extractors for detection of reduced bone density in dental radiographs	SVM	Panoramic radiographs	The models based on SOM and LVQ using Gabor Filter, Edge Orientation Histogram, Haar Wavelet, and Steerable Filter feature extractors	Accuracy 0.926(CI: Not given)

(*Continued*)

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Table 1 (Continued).

Parts	Researchers	Year	Purpose	Algorithms Evaluated	Dataset	Best-Performing Algorithm	Performance Metrics of Best-Performing Algorithm
	Nakamoto T et al[99]	2022	Develop computer-aided screening systems that could predict OP	AlexNet, VGG-16, GoogLeNet	Panoramic radiographs	GoogLeNet	Lumbar spine OP accuracy 0.74(95% CI:0.654–0.823),0.79(95% CI:0.710–0.870),0.79(95% CI:0.710–0.870). Femoral neck OP accuracy 0.70(95% CI:0.610–0.790),0.75(95% CI:0.665–0.835),0.75(95% CI:0.665–0.835)
	Tassoker M et al[100]	2022	Compare five CNN for predicting OP based on mandibular cortical index (MCI) on panoramic radiographs	AlexNet, GoogleNet, ResNet-50, SqueezeNet, ShuffleNet	Panoramic radiographs	AlexNet	C1, C3 AUC 0.9987±(0.0012) (CI: Not given)
	Sukegawa S et al[101]	2022	Investigate the use of DL to classify OP from DPRs	ResNet, EfficientNet	Panoramic radiographs	Ensemble model of EfficientNet-b7	AUC0.921 (95%CI:0.917–0.925)
	Yadalam PK et al[102]	2025	Classify bone loss severity (normal, mild, or severe) from OPG notes using a novel dual-embedding FSL framework	DualFit	Panoramic radiographs	DualFit	Accuracy of 0.9898(CI: Not given)
	Roebers P et al[103]	2025	Investigate the use of NN to predict potential OP using the Panoramic Mandibular Index derived from panoramic radiograp	ResNet-50	Panoramic radiographs	ResNet-50	Accuracy 0.895(CI: Not given)

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Hip	Sapthagirivasan V et al[68]	2013	Evaluate the ability of a kernel-based SVM with respect to diagnosis and add to knowledge about the trabecular features of digital hip radiographs for identifying subjects with low BMD	SVM	Hip X-ray images	SVM	Accuracy 0.90 (95%CI:0.82–0.98)
	Yamamoto N et al[104]	2020	Consider the use of DL to diagnose OP from hip radiographs, and whether adding clinical data improves diagnostic performance over the image mode alone	ResNe-t18, ResNet-34, GoogleNet, EfficientNet b3, EfficientNet b4	Hip X-ray images	EfficientNet b3	AUC 0.9374(CI: Not given)
	Jang R et al[105]	2021	Predict OP via simple hip radiography using DL algorithm	VGG-16	Hip X-ray images	VGG-16	AUROC0.867(CI: Not given)
	Yamamoto N et al[106]	2021	Evaluate the OP identification ability of DL by combining hip radiographs with patient variables	ResNet-18, ResNet-34, ResNet-50, ResNet-101, ResNet-152	Hip X-ray images	ResNet-34 ensemble model	AUC0.892 (95% CI: 0.890–0.894)
	Nguyen TP et al[107]	2021	Proposing a DL -based method for evaluation of BMD based on the X-rays of hips and biological parameters.	CNN	Hip X-ray images	CNN	Correlation coefficient 0.8075(CI: Not given)
	Acosta-Batlle J et al[108]	2025	Develop and validate an AI-based tool for the diagnosis of OP	CNN	Hip X-ray images	CNN	AUC0.866(CI: Not given)
Hands and feet	Areeckal AS et al[69]	2017	Propose an automated low-cost tool for early diagnosis of onset of OP using cortical radiogrammetry and cancellous texture analysis from hand and wrist radiographs	ANN	Hand and wrist X-ray image	ANN	Training accuracy 0.943 (CI: Not given); Test accuracy 0.885 (CI: Not given)
	Singh A et al[109]	2017	Extract discriminatory statistical features of different orders used for ML for the classification of two populations composed of osteoporotic and healthy subjects	SVM, NB, ANN, k-NN	Calcaneus X-ray image	SVM	Classification rate 98% (CI: Not given)
	Gharehmohammadi F et al[70]	2025	Create a DL model to screen for OP /osteopenia in patients by using radiographs of the foot or ankle	CNN, FCNN	X-rays of the foot or ankle	CNN	AUC 0.87(95% CI:0.85–0.94)

(*Continued*)

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Table 1 (Continued).

Parts	Researchers	Year	Purpose	Algorithms Evaluated	Dataset	Best-Performing Algorithm	Performance Metrics of Best-Performing Algorithm
	Ho CS et al[57]	2025	Develop a HarDNet-based DL regression model for hand BMD prediction.	CNN	Hand X-ray images	DeepDXA-Hand	Osteopenia accuracy 0.82 (95% CI:0.80–0.84); OP accuracy 0.80(95% CI:0.78, 0.82)
	Hwang U et al[110]	2025	Propose a method to predict OP using hand and wrist X-ray images	U-Net, SimCLR, SupCon, SwAV, VICReg	Hand X-ray images	SimCLR	AUC0.81(CI: 0.78–0.84)
	Lee KA et al[111]	2026	Perform segmentation and classification on metacarpal radiographs to accurately detect OP	OMO-Net	Hand X-ray images	OMO-Net	AUC0.99(CI: Not given)
Others	Liu J et al[112]	2019	Present an improved OP diagnosis algorithm based on U-NET network	U-Net	Pelvic X-ray image	U-Net	SO-S1 AUC 0.6921(CI: Not given);SO-S2 AUC 0.7011(CI: Not given);S1-S2 AUC 0.6348(CI: Not given)
	Zhou K et al[113]	2025	Explore the feasibility of using a hybrid DL framework (HDLF) to establish a model for BMD prediction and classification based on BPX images	CNN	Biplanar X-ray radiography	CNN	AUC0.97(CI: Not given)
	Yen TY et al[114]	2024	Explore the possibility of predicting the BMD and classifying high-risk patient groups using KUB radiographs	DeepDXA-KUB (a DL model)	Kidney-ureter-bladder radiographs	DeepDXA-KUB(a DL model)	Lumbar vertebrae AUC 0.939(CI: Not given); Left hip AUC 0.947(CI: Not given)
	Quagliato L et al[115]	2025	Develop an ML algorithm that performs binary classification of OF risk based on 2D-DXA-derived geometry and material parameters	XGBoost, SVM, MLP	2D-DXA	XGBoost	Raw data AUC0.77(CI: Not given), Synthetic data AUC 0.99(CI: Not given)

Abbreviations: AI, artificial intelligence; AM, Attention Model; ANN, artificial neural network; BMD, bone mineral density; BPX, biplanar X-ray imaging; CAD, computer-aided diagnosis; CI, confidence interval; CNN, convolutional neural network; DCNN, deep convolutional neural network; DL, deep learning; DXA, dual-energy X-ray absorptiometry; FSL, few-shot learning; GSF, genetic swarm fuzzy; HDLF, hybrid deep learning framework; HU, Hounsfield unit; k-NN, k-nearest neighbors; KNNC, k-nearest neighbors classifier; LR, logistic regression; LVQ, learning vector quantization; MCW, mandibular cortical width; MF, membership function; ML, machine learning; MLP, multilayer perceptron; NB, naïve Bayes; OCF, osteoporotic compression fracture; OF, osteoporotic fracture; OP, osteoporosis; OPG, orthopantomogram; OVF, osteoporotic vertebral fracture; ResNet, residual neural network; RFC, random forest classifier; ROI, region of interest; RS, rule set; SC-DCNN, single-channel deep convolutional neural network; SOM, self-organizing map; SVM, support vector machine; SVMC, support vector machine classifier; U-Net, U-shaped convolutional neural network; ViT, vision transformer; VF, vertebral fracture; AUC, area under the receiver operating characteristic curve; AUROC, area under the receiver operating characteristic curve; ACC, accuracy.

Lin et al employed a CNN based on the DenseNet architecture, while Asamoto et al integrated imaging data with patient age and sex. Both models achieved diagnostic accuracies above 75%, and Asamoto's group further externally validated a femoral BMD prediction model with similar accuracy approaching 80%.[77,78] Jang et al developed a supervised DL model named OsPor-Screen, which demonstrated even higher performance, achieving AUCs of 0.91 and 0.88 on internal and external test datasets, respectively highlighting the strong potential of chest X-rays for OP screening.[66]

Dental panoramic radiographs (DPRs) have also been widely explored for OP detection, with research in this area dating back nearly a decade. In 2015, Kavitha et al used DPRs to train NB, k-Nearest Neighbors (k-NN), and SVM models, utilizing fractal dimension (FD) and gray-level co-occurrence matrix (GLCM) features to classify OP. All three models achieved accuracies exceeding 90%,[47] and subsequent model refinements increased performance to over 95%.[95] With the advent of DL, Lee et al (2018) trained Deep Convolutional Neural Network (DCNN) models with two architectures: a single-column DCNN (SC-DCNN) using a region of interest (ROI) below the mandible, and a multi-column DCNN (MC-DCNN) using bilateral mandibular ROIs. The SC-DCNN achieved an accuracy of 92.5%, SC-DCNN (with data augmentation) 98%, and MC-DCNN 98.5%.[97] Subsequent studies by Sukegawa,[101] Tassoker,[100] and Nakamoto[99] applied pretrained models such as AlexNet and GoogLeNet. Notably, Nakamoto et al extended their trained models to lumbar spine and femoral neck X-rays, achieving diagnostic performance comparable to that of experienced radiologists. A distinct line of research has focused on feature extraction from DPRs.[99] For instance, Alzubaidi et al utilized 13 feature extractors, including pixel intensity histograms, and trained Self-Organizing Map (SOM) and Learning Vector Quantization (LVQ) models. Among them, SOM/LVQ models incorporating Gabor filters, edge orientation histograms, Haar wavelets, and steerable filters demonstrated the best OP detection accuracy.[98]

Spinal radiographs are widely used in orthopedic diagnostics and have become a popular research focus in AI-based OP detection. Many studies have employed pretrained CNN architectures, such as those by Lee et al[84] and Dong et al[87] demonstrating the feasibility of spinal image–based OP recognition. Other studies have applied deep DCNNs to spine imaging, including works by Zhang et al[67] and Hong et al[88] Notably, Hong's team explored whether integrating clinical parameters (such as age, sex, or biochemical markers) with DCNN-derived imaging features could improve diagnostic performance. Their findings confirmed that the combination of imaging and clinical data yielded superior diagnostic accuracy for OP compared with imaging alone.[88] Recent research has advanced beyond OP diagnosis alone, using DL models to simultaneously identify OP, vertebral fractures, and fracture risk from spinal radiographs.[91] These developments suggest that DL-based spinal imaging analysis may eventually expand to the diagnosis of other spinal disorders as well.

Pelvic and hip radiographs have also become major areas of interest for AI-based OP diagnosis.AI analysis of hip X-rays began relatively early: in 2013, Sapthagirivasan et al applied an SVM-based model that extracted trabecular bone features from hip radiographs, achieving an average accuracy of 90%.[68] Later, DL methods were introduced into this field. Liu et al employed a U-Net model, though its accuracy was limited,[112] while Yamamoto et al achieved improved results using pretrained CNNs, surpassing earlier traditional ML performance.[104] Building on these efforts, Nguyen et al integrated a Sobel gradient–based CNN mapping model with biological parameters to predict OP, achieving a correlation coefficient of 0.8075 compared with DXA measurements, indicating strong predictive capability.[107] Furthermore, Srinivasan et al developed a dual-core model named BoneVoyage for hip radiographs, which combines ShuffleNet for efficient feature extraction with artificial neural networks (ANNs) for classification. This hybrid model achieved an impressive 97.2% accuracy, significantly outperforming conventional diagnostic approaches and pointing toward a promising direction for future multimodal AI models.[74]

Research on knee X-rays for OP diagnosis has been relatively limited compared with other imaging modalities, largely because such images are more commonly used for evaluating osteoarthritis rather than bone density. However, studies published in 2024 by Sarmadi et al,[73] Xie et al,[72] and Naguib et al[71] have renewed interest in this area. These researchers primarily employed pretrained DL models, with notable innovation by Xie et al, who implemented a few-shot learning (FSL) approach to address the challenge of limited imaging data. Their results demonstrated that the FSL model achieved higher accuracy and sensitivity than radiologists, underscoring the potential of AI even in small-sample OP datasets.[72] This also provides a potential approach to addressing the algorithmic fairness issues that inherently exist in the use of artificial intelligence for disease diagnosis.[116] Compared with knee images, hand and foot X-rays are more complex due to the intricate bone structures and overlapping features, making feature extraction challenging.

Nonetheless, advances in AI have made it possible to utilize these images for OP diagnosis. In 2017, Singh et al applied four ML algorithms—SVM, k-NN, NB, and ANNs—to analyze trabecular bone features in calcaneal X-rays. All classifiers achieved accuracies above 95%, with SVM performing best (97.87% accuracy).[109] More recently, Ho et al (2025) developed an advanced DL model named DeepDXA-Hand, which analyzed multiple hand regions—including the capitate, trapezoid, hamate, triquetrum, and second metacarpal head—and achieved an overall accuracy of 0.80.[57] This model demonstrated the feasibility of using AI to perform noninvasive OP screening based on standard hand radiographs.

Beyond the imaging sites above, several studies have explored the potential of alternative X-ray modalities for OP detection. For instance, Zhao et al used ML to diagnose OP from shoulder radiographs;[117] Yen et al developed a CNN-based model for detecting OP from kidney–ureter–bladder (KUB) X-rays;[114] Zhou et al applied DL to biplanar radiography for bone density estimation;[113] and Ashok Kumar et al utilized forearm X-rays to predict the risk of future OF in women.[118] Although the number of studies in these areas remains limited, they collectively illustrate the growing versatility and potential of AI in diverse radiographic applications for OP diagnosis.

In summary, due to its high accessibility, low cost, and widespread clinical use, X-ray imaging,[64] when combined with SVM or pretrained DL models (such as VGG and ResNet) for feature extraction and classification, enables a low-cost, simple, and automated diagnosis of OP patients.[85,95]

CT

CT is a widely used imaging modality in clinical diagnosis, known for its high spatial resolution and three-dimensional (3D) imaging capability. A notable derivative of CT technology, qCT, has been recognized as a potential alternative to DXA for diagnosing OP.[119] Current AI-based CT studies on OP mainly focus on chest,[120] abdominal,[121] spinal,[122] and oralmaxillofacial[123] regions, with an increasing number of investigations also aiming to enhance the diagnostic performance of qCT[124] (Table 2).

Although chest, abdominal, and spinal CT scans are frequently performed in routine clinical practice, they are not traditionally used for OP diagnosis, because they cannot directly visualize reductions in BMD. However, with the advent of AI, it has become feasible to detect OP using these common CT datasets.[168] Most AI approaches follow a two-step workflow: (1) vertebral segmentation and (2) feature extraction and classification,[63].[169]

For vertebral segmentation, various methods have been proposed. Asaka et al manually extracted L1–L4 vertebral levels from unenhanced abdominal CT scans to train a CNN model, achieving an AUC of 0.965 (internal) and 0.970 (external validation), demonstrating excellent diagnostic accuracy.[122] Similar frameworks were employed by Tariq et al[140] and Tomita et al[120] More recent studies have adopted automatic segmentation using DL architectures. For instance, Fang et al used U-Net for automatic segmentation followed by DenseNet-121 for BMD estimation, achieving a very high correlation with qCT-measured BMD ($r > 0.98$).[158] Comparable approaches have been reported by Oh,[41] Pan,[155] and Li,[56] all employing U-Net-based pipelines. Alternative models have also been explored: Breit et al proposed a CNN using wavelet-based and geometric constraints for segmentation;[126] Pan et al (2023) utilized a landmark detection network combining Single Shot Multibox Detector (SSD) and VGG-16;[156] Peng et al used a VB-Net–based pretrained model;[127] and other studies have applied Vision Transformers.[136] Although 2D segmentation is possible, Hathaway et al demonstrated that 3D segmentation provides superior accuracy.[157]

Following segmentation, CNNs are commonly employed for OP classification. Dzierżak et al compared six transfer learning models—VGG16, VGG19, MobileNetV2, Xception, ResNet50, and InceptionResNetV2—to address small-sample challenges, with VGG16 performing best (accuracy 95%).[146] Tang et al developed an automated CNN framework for lumbar CT analysis, comprising a Mark-Segmentation Network (MS-Net) and a BMD-Classification Network (BMDC-Net). The model achieved a classification accuracy of 76.65% on the test dataset, demonstrating strong potential for automated OP diagnosis.[145]

With the rise of radiomics, this technique has become increasingly relevant in CT-based OP research. A typical radiomics workflow involves five steps:

(1) Image Acquisition: Single-source dual-energy CT scans generate 70-keV virtual monochromatic images of the lumbar spine with a bone-density calibration phantom.

Table 2 Applications of AI in OP-Related Tasks Based on CT Imaging

Task	Parts	Researchers	Year	Purpose	Algorithms Evaluated	Dataset	Performance Metrics
Osteoporosis Diagnosis	Chest	Yang J et al[125]	2022	Explore the value of the attenuation values of all thoracic vertebrae and the first lumbar vertebra measured by AI on non-enhanced chest CT to do OP screening	AI-Rad Companion	Chest CT	Osteopenia AUC0.831(95% CI: 0.800–0.862); OP AUC0.972(95% CI: 0.961–0.983)
	Chest	Breit HC et al[126]	2023	Assess the performance of an AI-based CNN-Algorithm for the detection of low bone density on routine non-contrast chest CT	CNN	Chest CT	Accuracy0.75(CI: Not given)
	Chest	Peng T et al[127]	2023	Explore the feasibility of using DL to establish a model for OP classification and bone density value prediction based on opportunistic CT scans and to verify its generalization and diagnostic ability using an independent test set	DenseNet, VB-Net	Opportunistic CT	Normal AUC0.999(95% CI: 0.999–1.000); Osteopenia AUC0.970(95% CI: 0.949–0.990); OP AUC0.933(95% CI: 0.906–0.960)
	Chest	Li J et al[56]	2024	Develop a DL model to automatically measure BMD and improve the diagnostic rate of OP	GCN, 3D-Unet, 3D-ResNet	Chest or abdominal paired CT	Accuracy0.88(CI: Not given); 0.91(CI: Not given); 0.91(CI: Not given)
	Chest	Park H et al[128]	2024	Examine the diagnostic efficacy of automated deep learning-based bone mineral density (DL-BMD) measurements for OP	2D U-Net	Chest CT, abdomen CT, spine CT	Low BMD AUC0.790(95% CI 0.733–0.839); OP AUC0.769(95% CI 0.710–0.820)
	Chest	Pan J et al[58]	2024	Develop a multi-feature DL model based on chest CT, combined with clinical information and radiomics to explore the feasibility in screening for OP based on estimation of volumetric BMD	DCNN	Chest CT	Normal AUC0.992(CI: Not given), Osteopenia AUC0.973(CI: Not given), OP AUC0.989(CI: Not given)
	Chest	Lin X et al[129]	2024	Investigate the feasibility of utilizing radiomics technology based on chest CT images to screen for opportunistic OP	SVM	Chest CT	Internal AUC0.892(95% CI 0.8399–0.9445); External AUC0.7960(95% CI 0.7361–0.8563)
	Chest	Fang K et al[130]	2024	Assess the possibility of using radiomics, DL, and transfer learning methods for the analysis of chest CT scans and combine these techniques with bone turnover markers to identify and screen for OP	SVM, KNN, RandomForest, ExtraTrees, XGBoost, LightGBM, NaiveBayes, AdaBoost, GradientBoosting, LR, MLP, alexnet, densenet121, densenet169, googlenet, mnasnet1_0, mobilenet_v2, mobilenet_v3_large, mobilenet_v3_small, resnet101, resnet152, resnet18, resnet34, resnet50, resnext50_32x4d, squeezenet1_0, squeezenet1_1, vgg11, vgg11_bn, vgg13, vgg13_bn, vgg16, vgg16_bn, vgg19, vgg19_bn, shuffleNet	Chest CT	Best performance:3D DL model; AUC0.906(95% CI 0.846–0.966)
	Chest	Tong X et al[131]	2024	Develop two bone status prediction models combining DL and radiomics based on standard-dose chest computed tomography (SDCT) and LDCT	VB-Net, RF	SDCT, LDCT	LDCT AUC0.97 ± 0.01(CI: Not given);SDCT AUC0.94 ± 0.02(CI: Not given)
	Chest	Wang S et al[132]	2024	Develop an intelligent diagnostic model for OP screening based on LDCT	SVM, RF	LDCT	Best performance: Aseg model; First-level model: internal AUC0.985(CI: Not given); external internal AUC0. 965(CI: Not given).In the second-level model: internal AUC0.933(CI: Not given); external AUC0.907(CI: Not given)
	Chest	Li Y et al[133]	2025	Explore the feasibility of DL -enhanced, fully automated BMD measurement using the ultralow-voltage 80 kV chest CT scans	DenseNet, ResNet	80kV chest CT, 120kV lumbar CT	Best performance:80 kV CNNs; OP AUC0.997–1.000 (CI: Not given);Low BMD AUC0.997–0.998(CI: Not given)
	Chest	Li Y et al[134]	2025	Propose a DL method for osteoporosis diagnose using LDCT and lumbar CT scans across CT scanners from different manufacturers and hospitals	CNN	120kV chest CT, 120kV lumbar CT	AUC0.993–1.000 (95% CI:0.988–1.000)

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Table 2 (Continued).

Task	Parts	Researchers	Year	Purpose	Algorithms Evaluated	Dataset	Performance Metrics
	Chest	Zhou K et al[135]	2025	Investigate the feasibility of using DL to establish a system for vBMD prediction and OP classification based on LDCT scans	CNN	LDCT	OP AUC0.800(CI: Not given); Osteopenia AUC0.878 (CI: Not given)
	Chest	Kuo DP et al[136]	2025	Introduces an ensemble framework to leverage their complementary strengths, generating visualized and decision-transparent recommendations for DXA scans from chest LDCT.	ViT, CNN	LDCT	Best performance:ViT–CNN model; Development cohort: normal AUC0.97(CI: Not given), OP AUCof 0.94(CI: Not given); Test cohort, normal AUC0.93 (CI: Not given), OP AUC0.99(CI: Not given)
	Chest	Li Y et al[137]	2025	Explore the feasibility and accuracy of using 100 kV low-voltage chest CT scans obtained for lung cancer screening in opportunistic osteoporosis diagnose	CNN	100 kV chest CT, 120 kV chest CT	Best performance:100 kV chest CT CNN model; AUC1.000(CI: (1.000–1.000))
	Chest	Wei L et al[138]	2025	Evaluate the diagnostic accuracy of AI in chest CT for osteoporosis/osteopenia screening in a Chinese population	Yizhun BMD AI system	Chest CT	T10 AUC 0.84 (95% CI: 0.81–0.87), T11 AUC0.83 (95% CI: 0.80–0.86), T12 AUC0.81 (95% CI: 0.79–0.84), L1 AUC0.83 (95% CI: 0.80–0.87),
	Chest	Zhang Y et al[139]	2026	Develop a DL model for OP screening based on images of thoracic vertebrae obtained from 100 kV chest CT	CNN	100 Kv chest CT	AUC0.983 (CI: 0.966–1.000)
	Abdomen	Lim HK et al[121]	2021	Evaluate the prediction performance of femoral OP using machine-learning analysis with radiomics features and APCT	RF	Abdomen-pelvic CT	Training AUC0.959(95% CI 0.937–0.981); Validation AUC0.960(95% CI 0.932–0.988)
	Abdomen	Tariq A et al[140]	2023	Develop an AI model for opportunistic screening of low bone density using both contrast and non-contrast abdominopelvic CT exams	CNN	Non-contrast abdominopelvic CT	Best performance:fusion model; AUC0.86(95% CI 0.84–0.87)
	Abdomen	Yuan X et al[141]	2024	Evaluate the performance of ML analysis based on proximal femur of abdominal CT scans in screening for abnormal bone mass in femur	LR	Abdominal CT	Training AUC0.917 (95% CI: 0.867–0.967); Testing AUC0.963 (95% CI: 0.919–0.999)
	Abdomen	Adarve-Castro A et al[142]	2025	Assess the proficiency of supervised ML techniques in discriminating between normal and abnormal BMD by leveraging clinical features and texture analysis of spinal bone tissue in patients diagnosed with primary hyperparathyroidism (PHP)	NB, LR, NN, Mixed model NN and NB	Abdominal CT	Best performance:Bayes; AUC0.916(CI: Not given)
	Abdomen	Paukovitsch M et al[143]	2025	Measure volumetric bone mineral density (vBMD) in clinical routine thoraco-abdominal CT using an AI-based algorithm	CNN	Thoraco-abdominal CT	AUC0.96(95% CI: 0.93–0.98)
	Abdomen	Sarquis Serpa A et al[144]	2026	Develop and do multicenter validation on an algorithm that screens for OP from abdominal CTs	ResNet34, 2D U-Net	Abdominal CT	Internal dataset AUC0.96 (95% CI: 0.89–1.0); External dataset AUC0.82 (95% CI: 0.74–0.89)
	Spine	Yasaka K et al[122]	2020	Investigate whether a DL model can predict the BMD of lumbar vertebrae from unenhanced abdominal CT images	CNN	Lumbar spine CT	Validation dataset I: OP AUC0.965 (95% CI: 0.887–1.000), Osteopenia AUC0.955 (95% CI: 0.901–1.000); Validation dataset E: OP AUC0.970 (95% CI: 0.915–1.000), Osteopenia AUC0.903 (95% CI: 0.823–0.983)
	Spine	Tang C et al[145]	2021	Design a novelty diagnostic method for OP screening by using the CNN	U-Net, DenseNet-121	Lumbar spine CT	AUC0.9167(CI: Not given)
	Spine	Dzierżak R et al[146]	2022	Assess the possibility of using deep DCNNs to develop an effective method for diagnosing OP based on CT images of the spine	VGG16, VGG19, MobileNetV2, Xception, ResNet50, InceptionResNetV2	Spine CT	Best performance:VGG16; AUC0.985(CI: Not given)
	Spine	Cheng L et al[147]	2023	Construct a combined model that integrates radiomics, clinical risk factors, and ML algorithms to diagnose OP in patients and explore its potential in clinical applications	SVM, RF, LR	Lumbar spine CT	Best performance:combined model; Training AUC0.959 (95% CI: 0.9412–0.9763); Testing AUC0.910 (95% CI: 0.8690–0.9506)

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	Spine	Wang J et al[148]	2024	Develop and validate a predictive model for OP and osteopenia prediction by fusing deep transfer learning (DTL) features and classical radiomics features based on single-source dual-energy CT virtual monochromatic imaging	SVM	Lumbar spine CT	Best performance:radiomics models; Training AUC0.999 (95% CI: 0.997,1.000); Testing AUC0.943 (95% CI: 0.905,0.981)
	Spine	Chen B et al[149]	2024	Extract radiomics from CT images to screen OP in the elderly	RF, SVM, kNN	Lumbar spine CT	Best performance:RF; Training AUC0.925 (95% CI: 0.922–0.939); Test AUC0.826 (95% CI: 0.809–0.836)
	Spine	Liu J et al[150]	2024	Proposed a transformer-enhanced DL framework to automatically acquire features from the entire lumbar vertebral body and the cancellous compartment to develop radiomics models for OP screening in routine CT	RF, Transformer	MDCT	Training AUC0.95(95% CI: 0.91–0.99), Test AUC0.97 (95% CI: 0.93–1.00)
	Spine	Küçükçiloğlu Y et al[151]	2024	Develop unimodal and multimodal deep-learning-based diagnostic models to predict bone mineral loss of the lumbar vertebrae using MRI and CT imaging	CNN	Lumbar spine MRI or CT	Best performance:multimodal model; Accuracy0.9890 (95% CI: 0.984–0.994)
	Others	Xu Y et al[152]	2013	Propose a novel method based on machine-learning method performed on micro-CT images to diagnose OP	SVM, kNN	Micro-CT	Precision1.00(CI: Not given)
	Others	Namatevs I et al[123]	2023	Examine the capabilities of deep DCNNs for diagnosing OP through cone-beam computed tomography (CBCT) scans of the mandible	ResNet-101	CBCT	Training Accuracy0.9885(CI: Not given); Validation Accuracy0.9399(CI: Not given)
	Others	Sebro R et al[153]	2024	Evaluate whether the CT attenuation of bones seen on shoulder CT scans could be used to predict low BMD	SVM, kNN	Shoulder CT	Best performance:SVM; AUC0.857(CI: Not given)
	Others	Du C et al[154]	2025	Establish an automated OP detection model based on low-dose abdominal CT	RF	Proximal femur images from LDCT	OP AUC0.960 (95% CI: 0.913–1.000); Osteopenia, AUC0.828 (95% CI: 0.747–0.909).

(*Continued*)

Table 2 (Continued).

Task	Parts	Researchers	Year	Purpose	Algorithms Evaluated	Dataset	Performance Metrics
BMD Envaluate	Chest	Pan Y et al[155]	2020	Develop a DL -based system to automatically measure BMD for opportunistic OP screening using low-dose chest computed tomography (LDCT) scans	U-net	LDCT	OP AUC0.927(95% CI: 0.896–0.951); Low BMD AUC0.942(95% CI: 0.914–0.964)
	Chest	Pan Y et al[156]	2023	Develop and evaluate a fully automated method based on DL and phantomless internal calibration for BMD measurement and opportunistic low BMD (osteopenia and OP) screening using chest LDCT scans	CNN	Chest LDCT	VCI: OP AUC0.964(95% CI:0.947–0.976); Low BMD AUC0.943(95% CI:0.923–0.959); VCII: OP AUC0.968 (95% CI:0.940–0.985); Low BMD AUC0.984(95% CI:0.962–0.995)
	Chest	Hathaway QA et al[157]	2025	Determine whether nnU-net can measure 3D vertebral body BMD across consistently imaged thoracic levels (T1–T10) at any conventional, noncontract chest CT examination.	nnU-net	Chest CT	Best performance:3D vertebral BMD with FRAXnb; AUC =0.82(CI: Not given)
	Abdomen	Oh J et al[41]	2024	Train DL models to localize the center axial slice from the CT scan of the torso, segment the vertebral bone, and estimate BMD for the top four lumbar vertebrae	U-Net, DenseNet169	Abdominal CT	MAE0.066, Pearson's r0.907 (P<0.001), R2 of 0.78(CI: Not given)
	Spine	Fang Y et al[158]	2021	Develop a fully automatic method based on deep DCNN for vertebral body segmentation and BMD calculation in CT images	U-Net, DenseNet-121	Lumbar spine CT	Minimum average dice coefficients 0.823 (95% CI: 0.815–0.831), 0.786 (95% CI: 0.773–0.799), and 0.782 (95% CI: 0.769–0.797)
	QCT	Oh S et al[159]	2024	Describe a new DL algorithm for vertebral segmentation and localizing of L1 and L2 vertebrae in routine clinical chest, abdomen, and lumbar spine CT scans and automatically draw a ROI from each vertebra to calculate volumetric QCT BMD	DL, U-Net	QCT	Low-BMD AUC0.847(CI: Not given); OP AUC0.770 (CI: Not given)
	QCT	Li Y et al[160]	2025	Evaluate the diagnostic efficacy of AI-based automated BMD measurement system for opportunistic OP screening using lumbar DECT scans	3D RetinaNet, U-Net	DECT, QCT	OP AUC0.979(95% CI: 0.935–0.997); Low BMD AUC0.980 (95% CI: 0.935–0.997)
	Others	Schmidt D et al[161]	2022	Evaluate a fully automated DL -based method for lumbar vertebral segmentation and measurement of vertebral volumetric trabecular attenuation values	CNN	Non-contrast-enhanced CT	Mean L1 attenuation value 140 HU ± 54(CI: Not given)
Fracture Detection or Risk Prediction	Chest	Tomita N et al[120]	2018	Developed a system to detect osteoporotic vertebral fractures (OVFs) on CT exams	LSTM, ResNet34	Chest CT, abdomen CT, pelvis CT	Accuracy0.892(CI: Not given)
	Spine	Biamonte E et al[162]	2022	Evaluate radiomics features on CT images of the lumbar spine in subjects with or without fragility vertebral fractures	LSVM	Lumbar spine CT	Training AUC0.839(CI: Not given); Testing AUC0.789 (CI: Not given)
	Spine	Zhang J et al[163]	2024	Develop and validate a predictive model for OVFs risk by integrating demographic, BMD, CT imaging, and DL radiomics features from CT images	CNN, SVM, KNN, LR, RF, Extratrees, XGBoost, LightGBM, MLP	Spine CT	Best performance:fusion model; Training AUC0.980 (95% CI: 0.959–1.000); Test AUC0.971 (95% CI: 0.928–1.000)

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Bone Quality or Microarchitecture Prediction	Spine	Yoshida K et al[164]	2023	Evaluate the feasibility of using DL with a CNN for predicting BMD and bone microarchitecture from conventional CT images	ResNet50	Lumbar spine CT	Osteopenia AUC0.921(95% CI: 0.793–0.973); OP AUC0.969 (95% CI: 0.872–0.993)
	QCT	Zhang K et al[124]	2024	Develop a novel multi-domain diagnostic method for learning domain-invariant features from CT images, enhancing OP analysis generalization across varied CT regions and accommodating dose or device variations	DeepmdQCT, AlexNet, ResNet-50, ResNet-101, DenseNet-101, ShuffleNet, EfficientNet, DSNet, DLGNet	QCT	Dose domain image Accuracy0.910(CI: Not given); Device domain images Accuracy0.905(CI: Not given)
Technical Development	Spine	Feng E et al[165]	2025	Develop an AI model for automatically detecting Hounsfield unit (HU) values at the L1 vertebra in preoperative thoracolumbar CT scans	nnU-Net	Thoracolumbar CT	High Dice coefficient 0.91(CI: Not given)
	Abdomen	Song J et al[166]	2026	Assess whether integrating volumetric vertebral and body composition features obtained from DL segmentation of CT images enhances the prediction of BMD and the classification of OP	3DnnU-Net	Abdomen CT	AUC0.95(CI: Not given)
	Spine	Hiyama A et al[167]	2026	Evaluate the utility of L1–L4 average HU values from lumbar spine CT in predicting OP using multiple ML models	LR, RF, SVM, KNN, NB, DT, XGBoost	Lumbar spine CT	Best performance: KNN; AUC0.705(CI: 0.659–0.751)

Abbreviations: AI, artificial intelligence; BMD, bone mineral density; vBMD, volumetric bone mineral density; OP, osteoporosis; OVF, osteoporotic vertebral fracture; CT, computed tomography; QCT, quantitative computed tomography; DXA, dual-energy X-ray absorptiometry; ROI, region of interest; HU, Hounsfield unit; CNN, convolutional neural network; DCNN, deep convolutional neural network; U-Net, U-shaped convolutional neural network; DenseNet, densely connected convolutional network; ResNet, residual neural network; VB-Net, volumetric bone network; LSTM, long short-term memory network; RF, random forest; RFC, random forest classifier; SVM, support vector machine; KNN, k-nearest neighbors; KNNC, k-nearest neighbors classifier; LR, logistic regression; MLP, multilayer perceptron; VMC, virtual monochromatic imaging; AUC, area under the receiver operating characteristic curve; ACC, accuracy; SEN, sensitivity; SPE, specificity; MAE, mean absolute error; RMSE, root mean square error; CI, confidence interval.

(2) ROI Segmentation: Radiologists manually delineate volumetric regions of interest (VOIs) in vertebral bodies using 3D Slicer, excluding cortical bone and venous plexuses.
(3) Feature Extraction: First-order, shape, and texture features are extracted via PyRadiomics, while transfer learning features are derived from a pretrained ResNet50 model.
(4) Feature Selection: Redundant features are removed through reproducibility testing, Spearman correlation, and LASSO regression.
(5) Application: Selected features are used to train a two-level SVM classifier, which distinguishes OP from non-OP cases and further differentiates osteopenia from normal BMD (Figure 2). [148–150]

Studies such as those by Liu et al and Du et al have successfully applied radiomics to extract lumbar vertebral features from abdominal CT scans,[154,170] enabling quantitative and high-dimensional OP diagnosis. Radiomics allows for the integration of imaging, molecular biology, pathology, and data science, and is likely to represent a promising analytical direction for future CT-based OP research.

Oromaxillofacial CT is another clinically common modality, offering practical potential for OP diagnosis. In 2023, Park et al developed a DL-based QCBCT-Net model to analyze quantitative cone-beam CT (QCBCT), achieving a root mean square error (RMSE) of 83.41 mg/cm³, indicating high precision.[171] Similarly, Namatevs et al created a DCNN-based AI tool for detecting OP from CBCT images, reporting a classification accuracy of 93.99%.[123] These findings highlight the feasibility of using oromaxillofacial CT for OP assessment and suggest a promising research direction for automated dental OP screening. Integration of AI with qCT to improve its diagnostic power is another emerging trend. In 2024, Oh et al developed

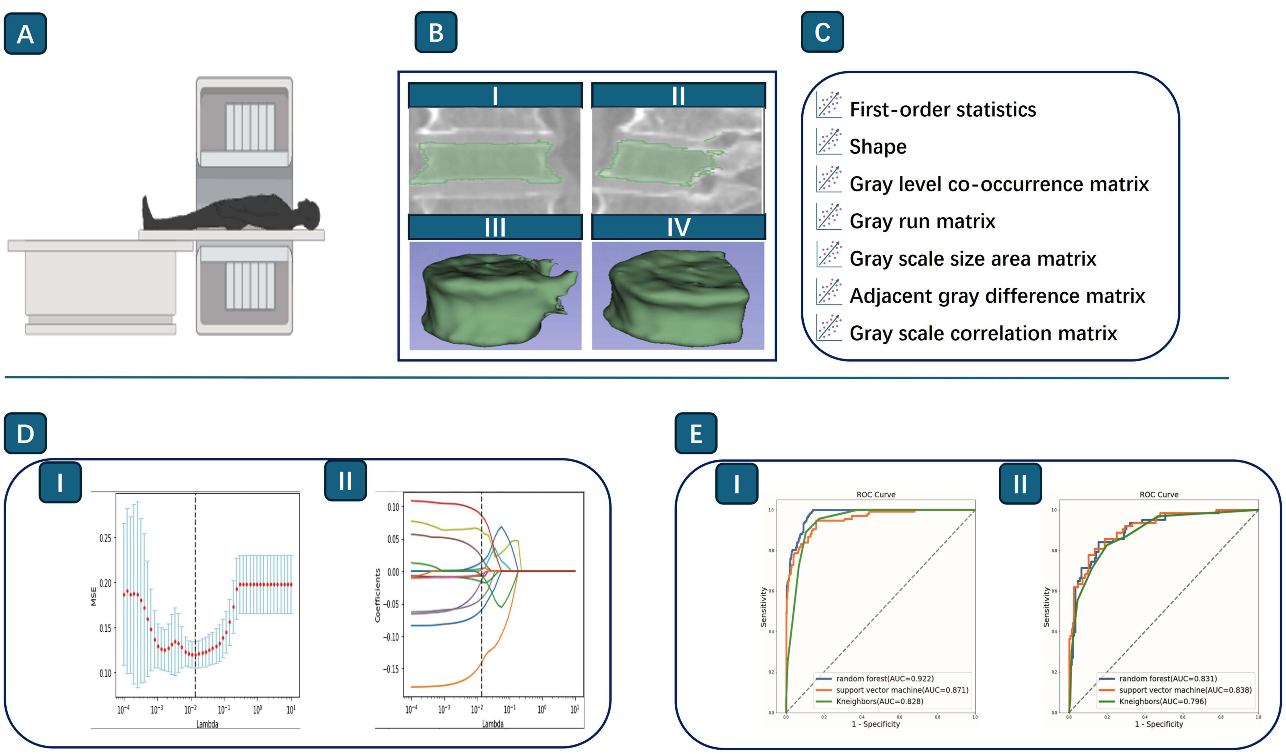

Figure 2 A schematic workflow of CT-based OP diagnosis using radiomics, illustrated using lumbar spine CT as an example. (Adapted and redrawn based on Figures 2,3 and 4 from Cui Z et al, "Application of radiomics model based on lumbar computed tomography in diagnosis of elderly osteoporosis," with permission.).[148–150] (**A**) Image Acquisition: Use CT to acquire the image of the target part of the body. (**B**) ROI Segmentation: ROI are delineated by radiologists using 3D Slicer. BI. Segmentation of image coronal section. BII. Segmentation of sagittal slice of image. BIII. 3D model construction. IV. Model construction processing. (**C**) Feature Extraction: Features are extracted via PyRadiomics. (**D**) Feature Selection: Useful features are selected by LASSO regression. DI. Best lasso value. A ten-fold cross-validation procedure was applied to identify the optimal lambda parameter. The y-axis shows the mean squared error (MSE), while the x-axis represents the lambda sequence. Vertical dashed lines denote the optimal lambda value, defined as the lambda yielding the minimum average MSE regardless of its spread. DII. LASSO coefficient profile of radiomic features. Coefficient trajectories of fourteen radiomic features are plotted against the lambda sequence. The vertical dashed lines indicate the optimal lambda value. (**E**) Application: Selected features are used to train models. EI. ROC curves of training set. EII. ROC curves of test set.

a DL model based on Python (v3.8.5) and TensorFlow-GPU (v2.4.0) to automatically measure BMD from qCT images. Using DXA as a reference, the model achieved AUCs of 0.847 and 0.770 for distinguishing low BMD and OP, respectively.[159] In the same year, Zhang et al addressed the issue of inter-device variability by developing a DeepmdQCT model built on a ResNet architecture with a comprehensive attention-guided module (CAGM) that integrates both global and local features. The model achieved average accuracies of 91% (normal dose) and 90.5% (low dose), maintaining consistent performance across Philips and Siemens imaging systems—demonstrating strong generalizability.[124]

From the above studies, it can be observed that CT can provide three-dimensional structural information of the measurement sites,[172] and when combined with CNN-based models, it enables accurate bone mineral density analysis.[126] However, compared with X-ray imaging, CT is associated with higher costs and greater radiation exposure.[173] Therefore, although CT-based approaches offer advantages in terms of diagnostic accuracy, their widespread use in large-scale or initial screening is limited.

MRI and Ultrasound Imaging

Compared with X-ray and CT imaging, studies that combine MRI or ultrasound (US) with AI for OP diagnosis remain relatively limited.

In the MRI-based research field, one of the earliest studies was conducted by Ferizi et al, who applied multiple ML algorithms to predict the risk of OF using MRI data. They evaluated 15 ML models, including SVM and k-NN, while incorporating patient-level features such as age, body weight, and height. Among the tested models, RUS-boosted trees, logistic regression(LR), and linear discriminant analysis (LDA) achieved the best predictive performance.[174] More recently, in 2024, Küçükçiloğlu et al integrated MRI and CT data for multimodal AI training. They developed four distinct models: (1) a single-modality MRI model, (2) a single-modality CT model, (3) a combined single-modality model trained on merged MRI–CT data, and (4) a multimodal model treating MRI and CT as separate inputs. The multimodal model achieved the highest performance, with a balanced accuracy of 98.90% on MRI–CT datasets and similarly strong accuracy in patient-level validation.[151]

In the US-based domain, Vogl et al (2019) introduced an AI-assisted framework using low-frequency guided waves to assess acoustic parameters of the tibia, followed by SVM classification for OP diagnosis.[175] However, because low-frequency guided waves are not standard in clinical ultrasonography, the practical applicability of this method remains uncertain. In the same year, Mohanty et al estimated cortical bone microstructural parameters from US frequency-dependent attenuation, combined with 2D finite-difference time-domain (FDTD) simulations to generate simplified cortical models. These were refined using CT-derived structural data and subsequently used to train an ANN to predict pore diameter, pore density, and porosity. The ANN demonstrated high prediction accuracy, suggesting that AI-augmented US could become a promising tool for OP assessment.[176] In recent years, Ferguson HE proposed combining CNNs with US backscatter to assess BMD, achieving promising results. This further demonstrates the feasibility of US applications in the field of OP.[177]

Overall, the relatively limited use of MRI and US in AI-assisted OP diagnosis may be attributed to their lower prevalence in orthopedic imaging and the inherent limitations of these modalities for bone evaluation,[178].[179] Nonetheless, the ability of AI to extract subtle diagnostic information from MRI and US data suggests that AI-enhanced multimodal imaging could represent a valuable future direction in OP research.

Although imaging-based AI has demonstrated strong performance in identifying OP and related fractures, these approaches primarily focus on phenotypic manifestations of the disease. To understand the mechanisms of the disease, researchers have increasingly turned to bioinformatics and genetics. By integrating AI with molecular-level data, it has become possible to explore the genetic basis and biological pathways underlying OP.

Identification of Diagnostic Genes

In addition to imaging-based diagnosis, AI and ML models have also been applied to gene-based diagnostic prediction in OP. In these studies, selected genes or gene-expression profiles are commonly used as input features for classification models aimed at distinguishing osteoporotic from non-osteoporotic populations.[180] Unlike studies focusing on molecular mechanisms, these approaches primarily aim to develop predictive or classification models capable of distinguishing osteoporotic

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individuals from non-osteoporotic populations. For example, Hu et al identified five key DEGs—CCR1, CD33, HCK, LILRB2, and CYBB—through bioinformatics analysis and subsequently constructed an SVM classification model based on these genes, achieving accurate classification and prediction of OP samples.[50] Similarly, Ding et al and Zheng et al adopted comparable approaches: Ding integrated gene expression profiles with clinical features using both MLR and ANN models,[181] while Zheng systematically evaluated diagnostic performance across different gene combinations to determine the optimal gene subset.[43] Building upon this concept, Lin et al focused on the effect of smoking on BMD. Using bioinformatics methods, they identified gene modules associated with BMD in both smokers and non-smokers and selected ten shared genes (including TNS4 and IRF2) to construct an SVM–RFE model. This model effectively distinguished high- and low-BMD individuals in both groups, achieving an AUC > 0.9, thereby demonstrating strong potential for identifying individuals at high risk of OP.[182] These studies demonstrate the potential of combining bioinformatics and AI for OP diagnosis and risk stratification. Broader applications of AI in molecular mechanism exploration and biomarker discovery are discussed further in Artificial Intelligence in Genetic and Molecular Studies of Osteoporosis.

Non-Imaging AI-Based Diagnostic Technologies

Beyond imaging and genomics, several novel AI-based diagnostic methods have been proposed. For instance, Yang et al suggested that surface-enhanced Raman scattering (SERS) spectral features from blood samples could be analyzed using SVM to construct an OP diagnostic model.[183] Although this represents a promising alternative approach, the current mainstream of AI-assisted OP diagnosis still relies predominantly on medical imaging. In 2026, Liang Q et al conducted a study that did not utilize any medical imaging, relying solely on ordinary facial photographs to diagnose OP, thereby further facilitating its detection.[184] Nevertheless, these emerging diagnostic modalities offer broad opportunities for future exploration and may complement imaging-based AI strategies in clinical practice.

Artificial Intelligence in Genetic and Molecular Studies of Osteoporosis

Bioinformatics is an interdisciplinary field that applies computational, mathematical, and statistical methods to analyze biological data, such as genomic and proteomic information.[185] It has been extensively used to explore disease-associated genes and proteins, providing potential diagnostic and therapeutic targets for various diseases. With the rapid development of AI, bioinformatics has gradually merged with AI technologies, a trend that has revolutionized biomedical research. The integration of AI and bioinformatics has already yielded promising results in gene sequence alignment and annotation, non-coding RNA prediction, protein folding analysis, protein–protein interaction modeling, and drug discovery and development,[186].[187,188] In the field of OP, beyond diagnostic applications[23] AI has increasingly been utilized to investigate the molecular mechanisms underlying OP, for example, therapeutic targets,[189] as well as for the identification of genes shared with other diseases.[190] Recently, AI techniques have been increasingly incorporated into these studies, significantly improving efficiency and analytical depth.

AI-Based Biomarker Identification for Osteoporosis

Bioinformatics is frequently applied to identify diagnostic and therapeutic targets for various diseases. In OP research, several studies have utilized bioinformatics to uncover such targets. For example, Zhang L et al identified the methylation biomarker MAP3K5 as associated with OP and validated its potential therapeutic value through immune cell infiltration analysis.[191] With the advancement of AI, integrating intelligent algorithms into bioinformatics pipelines has become an emerging trend, greatly accelerating research progress. As early as 2010, Guan Y et al proposed combining functional genomics with AI for disease-gene prediction. They constructed functional relationship networks and employed SVM to predict phenotype associations, successfully identifying BMD-related genes such as Timp2 and Abcg8. Experimental validation in mice confirmed that knocking out these genes significantly reduced BMD, demonstrating the feasibility of AI-assisted genomic analysis in OP research.[192] Feng ZW et al (2024) followed a similar workflow.[193] In 2019, Yang C et al identified DHTKD1, OSTF1, and GPR116 as key genes associated with OP, and validated their relevance using multiple ML models, including SVM, decision tree, and RF, though without animal validation.[194] In addition, Long SW et al used a RF model to identify five ferroptosis-related hub genes (CP, FLT3, HAMP, HMOX1, SLC2A3), constructed diagnostic models, and confirmed their roles experimentally, establishing these genes as potential biomarkers for OP.[195]

Some other studies combined traditional bioinformatics-based gene screening with AI validation, which were discussed earlier and will not be elaborated here. Overall, AI can play a major supporting role in identifying OP-related diagnostic and therapeutic biomarkers, and future studies are expected to expand in this promising direction.

AI-Driven Molecular Mechanism Exploration

Beyond identifying diagnostic biomarkers, AI has been increasingly applied to elucidate the molecular mechanisms underlying OP by analyzing gene networks and signaling pathways. Understanding the molecular mechanisms underlying disease pathogenesis is crucial for developing targeted treatments. In OP, bioinformatics-based molecular analyses have long been conducted, but the introduction of AI has injected new vitality into this research area. Xiao KW et al investigated how monocytes affect BMD through the ribonucleoprotein complex biosynthesis pathway. After identifying key genes via gene set enrichment analysis (GSEA), they built an elastic net regression model to predict BMD. It is an early but imperfect attempt to apply AI to mechanistic studies of OP.[196] Subsequent research has increasingly focused on immune-related mechanisms. Hao S et al used LASSO and mSVM-RFE algorithms to identify CCR5 and IAPP as key BMD-related immune genes, validating their roles experimentally—the first study to combine bioinformatics and ML to identify immune-related OP genes.[197]

Similarly, Chen L et al (2024) analyzed postmenopausal OP (PMOP) using LASSO and RF models, identifying PYGM and POMP as regulators of immune response and proteolysis, marking their first report in PMOP.[198] Zhang B et al further revealed that neutrophils modulate BMD via inflammatory cytokine secretion.[199] Li J et al (2025) focused on FBXW4, applying ML to identify its co-expressed hub genes and discovering that FBXW4 may regulate OP progression via antiviral defense, cytokine production, and immune response modulation. Beyond immunity, other mechanisms have been explored.[200] Wang X et al used ML to identify ferroptosis-related molecular subtypes in diabetic osteoporosis (DO) and identified IDH1 as a key gene.[201] Feng Z et al[202] Bi K et al[203] and Li S et al[204] focused on pyrimidine metabolism genes (PyMGs), cellular senescence, mitochondrial biomarkers, and smoking-related genes, broadening the mechanistic landscape of OP. In 2025, Zeng HB et al also focused on the role of mitochondrial dysfunction in OP, identifying three key genes—ALAS1, HSPB1, and VPS35. They further proposed that overexpression of VPS35 inhibits osteoblast differentiation by suppressing the ERK/PI3K/AKT signaling pathway, a process regulated by miR-142-5p.[205] A particularly novel study by Zhang X et al combined network toxicology, ML, and molecular docking to examine plasticizer-induced OP. Using 113 ML models (LASSO, SVM, RF, etc.), they identified core genes linking plasticizer exposure to OP, pioneering research into the toxicological mechanisms of OP. This integrative framework—combining target screening, model optimization, and molecular validation—offers new perspectives for future studies.[51]

AI-Based Cross-Disease Genetic Analysis

A growing number of studies have revealed shared genes between OP and other diseases, such as atherosclerosis (Mishra BH et al)[206] and type 2 diabetes mellitus (T2DM) (Du A et al).[207] Investigating shared genetic profiles can uncover common disease mechanisms, reveal potential therapeutic targets, and facilitate personalized and multi-disease intervention strategies. The incorporation of AI has accelerated progress in this area. For example, Zhao R et al focused on OP and T2DM. Using LR, cross-analysis, and RF algorithms, they identified three hub genes.[208] In another study, Liu J et al applied XGBoost to identify pyroptosis- and crosstalk-related hub genes between periodontitis and OP providing insights into shared mechanisms.[209] Yang J et al examined chronic HBV infection and OP using differential gene expression and LASSO regression, identifying three shared genes—USP10, ERAL1, and ECM1—which may assist in the diagnosis and management of HBV-related OP.[52] Similarly, Xu G et al explored inflammatory bowel disease (IBD) and OP, using LASSO combined with NETs-related gene analysis to identify HDAC6, IL-8, and PPIF as diagnostic genes. Their study revealed potential neutrophil extracellular trap (NET) involvement in the connection between IBD and OP.[210] In 2026, Tang H et al employed ML to investigate shared genes between OP and chronic kidney disease (CKD), ultimately identifying four genes—FAM184A, NFKBIA, RP2, and HIRA—providing a molecular-level explanation for the high prevalence of OP in CKD patients.[211] Collectively, these findings highlight AI's ability to uncover shared molecular mechanisms among diseases. However, most current research focuses on pairwise disease associations; future work should aim to investigate multi-disease gene networks, ultimately enabling multi-target therapeutic strategies.

Beyond these primary areas, the cross-disease genetic analysis has also been explored in drug discovery. For instance, Yang X et al identified shared genes between OP and sarcopenia using ML models and subsequently employed the CMap database to predict potential therapeutic compounds.[212] Zhang C et al investigated the shared genes between peri-implantitis and OP, identifying three common DEGs, namely ALDH1A3, MGP, and CYBB. They further explored potential drug targets associated with these hub genes.[213] In the same year, Lv Y et al applied ML models, including LASSO, to identify five shared genes between sarcopenia and OP—APOC1, ENPP5, FBXL22, IRS1, and PAQR4—revealing the common molecular mechanisms underlying these two age-related degenerative conditions.[214] These applications will be discussed in detail in the following section on AI-assisted treatment of OP.

Insights gained from AI-driven genetic and molecular analyses not only enhance the understanding of OP pathogenesis but also provide a foundation for individualized risk assessment. Building upon these mechanistic findings, AI has been further applied to predict disease risk, stratify patient populations, and estimate future clinical outcomes.

AI in Osteoporosis Prediction and Risk Stratification

Accurate identification of risk factors and prognostic prediction for OP are crucial for achieving precise diagnosis and stratified management.[212] These approaches not only optimize the use of medical resources but also spare patients from unnecessary examinations and treatments. In recent years, AI has been increasingly adopted to identify disease risk factors and predict clinical outcomes,[215].[216] For instance, Doppalapudi S et al employed ANNs, recurrent neural networks (RNNs), and CNNs to analyze demographic data, tumor site and morphology, disease stage, and treatment regimens, successfully predicting lung cancer prognosis.[217] Similarly, multiple studies have integrated AI into OP risk assessment and outcome prediction, demonstrating its growing potential in clinical decision support.

ML Applications

Since research on OP-related risk factors often involves structured data (eg., age, body mass index(BMI), blood markers), ML—rather than DL—is particularly well suited for this task.[218] PMOP has long been a major public health issue. Identifying predictive factors can facilitate early prevention. As early as 2013, Yoo TK et al applied several ML algorithms—SVM, RF, ANN, and LR—to analyze patient characteristics. They identified age, height, weight, BMI, duration of menopause, breastfeeding duration, estrogen therapy, hyperlipidemia, hypertension, osteoarthritis, and diabetes as key risk factors. Among these models, SVM achieved the best performance on both training and validation datasets.[219] Similarly, Jin W et al used EHRs from female patients, combining four feature-selection methods and eight ML algorithms to predict hip OP. Their final model achieved an external validation sensitivity of 0.775.[220] Beyond predicting OP, ML has been applied to OF prediction. In 2021, de Vries BCS et al compared multiple models—including random survival forest (RSF)—for predicting major osteoporotic fractures (MOFs), finding Cox regression performed best.[221]

For individuals below the recommended age for DXA screening, Park HW et al (2021) used XGBoost, LR, and multilayer perceptron (MLP) models to identify OP risk factors. The XGBoost model outperformed traditional risk assessment tools, with age, weight-related variables (BMI, weight, obesity), serum alkaline phosphatase (ALP), systolic blood pressure (SBP), blood urea nitrogen (BUN), and alcohol consumption identified as major predictors.[222] ML has also proven valuable for patients with chronic diseases, who are at higher risk of secondary OP. Peng Y et al used clinical data—including genetic markers—from elderly patients with cardiovascular risk to predict OP. Among four ML models compared with LR, the latter performed best, underscoring the value of model benchmarking in medical AI research.[223] Similar methods were employed by Hsu CT,[224] Wei Q,[225] and Yu X,[226] focusing on patients with CKD and type 2 diabetes, respectively. ML has additionally been applied to postoperative outcome prediction in OP treatment. Klemt C et al used neural networks and RF to predict surgical revision risks, identifying female sex, BMI > 35 kg/m², age > 70 years, ASA score ≥ 3, and T-score as the strongest predictors.[227] Beyond traditional demographic and clinical variables, some studies have incorporated imaging-derived features into ML models. For instance, Liu L et al developed a three-tier ML model for OP diagnosis: Tier 1 used only demographic features, Tier 2 incorporated clinical data, and Tier 3 added CT imaging features. The third-tier model performed best, demonstrating the added value of imaging information.[228] Recent studies have shifted toward bone microarchitecture and geometric analysis. Mateo J et al (2025) used trabecular bone score (TBS) and 3D-DXA–derived microstructural and geometric parameters to predict fracture risk in elderly women, achieving an internal validation accuracy of 89.24% ± 0.52% with an RF model.[229] Similar work by Quagliato L et al supported these findings.[115] Incorporating imaging data has further expanded predictive capabilities. Sebro R analyzed CT attenuation values from multiple skeletal regions on shoulder and chest CT to predict OP,[230];[231] Huang CB evaluated psoas muscle index (PMI) as a predictor;[232] and Zhang J et al used DL–extracted radiomic features for OP prediction.[163] Other studies have explored unconventional biomarkers. For instance, Kang SJ proposed metal element profiling in hair samples as a potential OP predictor.[233] A similar study was conducted by Huang W et al However, their study focused on heavy metals in the urinary tract.[234] Such innovative approaches may reveal new biomarkers for early OP detection in the future.

Other Artificial Intelligence Techniques

Beyond classical ML, other AI approaches have also been employed in OP risk prediction, particularly ANNs. As early as 1999, Queraltó JM et al used ANN models to predict bone loss in postmenopausal women, based on plasma estrogen, osteocalcin, parathyroid hormone (PTH), and urinary calcium and hydroxyproline.[235] Similarly, Sadatsafavi M et al (2005) used ANN models with age, body weight, menopausal age, corticosteroid and estrogen use, parity, menarche age, height, exercise, and smoking as inputs to predict BMD, achieving significantly higher AUROC than regression models.[236] Several comparative studies have evaluated ANN versus ML models. Yoo TK et al[219] Xu R et al[54] and Shim JG et al[44] all conducted such comparisons; while the first two found ML models superior, the latter reported ANN outperformed others—differences likely due to variations in input features and dataset characteristics. Interestingly, in contrast to the studies that primarily focused on elderly populations, the study by Jiang et al applied an ANN to investigate metabolic bone disease in neonates. Their work explored the effects of various prenatal and postnatal factors on disease risk and demonstrated that the ANN was effective in identifying key risk factors for neonatal OP. Among these, extremely low birth weight and antenatal magnesium sulfate exposure emerged as the two most significant contributors.[237] More recently, DL methods have gained traction. Suh B et al (2023) developed an interpretable DL model based on clinical features to screen for OP. Key predictors included sex, age, BMI, arm circumference, obesity prevalence, and socioeconomic status, with DL showing markedly higher accuracy than conventional models.[238] Similar DL-based approaches were reported by Hung WC[239] and Cho SW,[24] reinforcing DL's growing importance in OP risk assessment. In addition, Cho et al employed DL to extract imaging features from spinal radiographs and performed an analysis of spinal age. Their findings revealed a significant association between spinal age and OP. Although the study primarily focused on elderly patients with fractures, this observation nevertheless highlights the potential of DL-based approaches to capture osteoporosis-related imaging features from radiographs.[240] Compared with the previous study, Tang J et al not only extracted imaging features using a DL model but also integrated patients' clinical characteristics to construct a multimodal model. This multimodal model achieved an AUC of 0. 975.[241] As DL techniques evolve, their applications in OP prediction and prevention are expected to become increasingly refined and clinically impactful.

Risk prediction and stratification represent a critical step toward precision medicine in OP. Beyond identifying individuals at high risk, AI has also been explored as a tool to support therapeutic decision-making, drug discovery, and treatment outcome prediction, thereby extending its role from risk assessment to clinical intervention.

AI in the Treatment of Osteoporosis

Compared with its extensive applications in OP diagnosis, risk factor identification, prognosis prediction, and bioinformatics research, studies on the use of AI in OP treatment remain relatively limited. Current AI-assisted therapeutic research mainly focuses on identifying key genes within osteoporotic molecular pathways to discover potential therapeutic compounds,[55] optimizing and personalizing existing treatment strategies, and evaluating postoperative or long-term treatment outcomes.[242]

In drug discovery, bioinformatics-based AI approaches are most widely applied. For instance, Yang X et al utilized LASSO, SVM-RFE, and RF algorithms to identify CHST3, PGBD5, and SLIT2 as comorbidity-related diagnostic genes shared between OP and sarcopenia. These genes were subsequently analyzed using the CMap database to predict potential therapeutic agents targeting both diseases.[55] Similarly, Long SW et al employed an RF model to identify ferroptosis-related biomarkers from the GEO database and applied molecular docking to screen for small-molecule compounds with therapeutic potential against OP.[195] A recent study in this field by Li Q et al utilized Chemprop to develop a predictive model for cathepsin K (CTSK) inhibition. Experimental validation identified three compounds, including quercetin, that exhibited the strongest concentration-dependent CTSK inhibitory effects. These compounds represent promising candidate drugs for the treatment of osteoporosis.[243] Beyond novel target discovery, AI has also been used to explore repurposing of existing drugs for OP treatment. For example, Hung TNK et al investigated the pharmacological interactions between medications used for Paget's disease and OP, offering new insights into cross-disease drug repositioning.[42] In addition to identifying new or repurposed drugs, another important direction is using AI to recommend optimal treatment regimens from existing therapies. Bonaccorsi G et al developed a ML–based clinical decision system that integrates patient data to recommend personalized treatment strategies. The model demonstrated high predictive accuracy across various treatment-related decisions—including bone-protective therapy, vitamin D supplementation, and calcium administration—achieving accuracies approaching 90% in some cases.[244] Lin YT et al (2022) collected a comprehensive dataset of 33 clinical variables, encompassing patient demographics (age, sex, height, weight), laboratory data (serum calcium, phosphate levels), and medications (eg., alendronate, raloxifene, teriparatide), to train four ML models. These models successfully predicted therapeutic outcomes and assisted clinicians in adjusting individualized treatment plans.[242] Similarly, in 2026, Sugawara Y et al utilized patients' clinical and imaging features to train five ML models to assist clinical drug decision-making. They found that the LightGBM model among the five achieved an accuracy above 0.9, highlighting the potential of AI in supporting pharmacological therapy.[245]

In addition to drug discovery, AI has shown emerging potential in the optimization of rehabilitation strategies for OP. By integrating patient-specific factors such as age, BMD, fracture risk, physical function, and comorbidities, AI-driven models may assist in designing personalized exercise and rehabilitation programs aimed at improving bone strength, balance, and functional recovery. Such as Fasihi L et al trained an ML model incorporating patients' imaging features and covariate data to generate individualized exercise recommendations aimed at improving bone health and preventing fracture risk.[246] However, current applications in this area remain largely exploratory, and robust clinical studies focusing on AI-guided rehabilitation for OP are still limited. In the future, with continued technological advances, AI applications in OP may evolve in a manner like those used for fracture prevention, incorporating wearable devices to continuously monitor patient status. Such systems could assist with home-based exercise programs and nutritional management, thereby supporting disease management and promoting patient rehabilitation.[247]

AI has also demonstrated promising applications in surgical planning and intraoperative assistance across various surgical disciplines, including orthognathic surgery.[248] This suggesting potential future applicability in osteoporosis-related surgical management, though current evidence specifically addressing osteoporosis surgery remains limited. In terms of postoperative prognosis prediction of OP, Klemt C et al analyzed data from 350 patients and developed four ML models capable of predicting revision surgery risk following orthopedic procedures. This demonstrates the potential of AI in refining postoperative management and long-term outcome assessment.[227] Nevertheless, compared with diagnostic and pharmacological applications, AI-assisted surgical approaches in OP are underrepresented in the literature, highlighting a significant gap for future research.

While current AI-driven therapeutic research in OP predominantly focuses on drug discovery, its extension to rehabilitation optimization and surgical decision support represents a promising yet underdeveloped direction. Addressing these gaps will be essential for establishing a comprehensive AI-assisted management framework that spans diagnosis, treatment, and long-term functional recovery. Recent advances indicate that AI is increasingly involved in the translation of biomaterials,[249].[250] Moreover, biomaterials represented by metal–organic framework nanomedicine have demonstrated significant potential in OP therapy.[251] Therefore, the application of AI in biomaterials translation for OP is expected to become an emerging and promising research direction. In addition, nanomaterials are currently being used as contrast agents in multimodal imaging. Their integration with AI enables personalized imaging and image-guided therapy, a strategy that may also be extended to the diagnosis and treatment of osteoporosis in the future.[252] The rise of LLMs has provided a more convenient approach for clinical support in OP patients, and this direction may potentially become an integral part of comprehensive management for these patients in the future.[253]

Limitations

Despite these promising developments, several important limitations should be acknowledged. Considerable heterogeneity exists among published studies regarding patient populations,[25,169] AI algorithms,[26] and evaluation metrics,[27] which limits direct comparison and interpretation of reported performance outcomes. In addition, consistent external validation remains insufficient in many studies, raising concerns about model generalizability, robustness, and real-world clinical applicability,[169].[27,254] Challenges related to data imbalance, and potential selection bias further highlight the need for standardized reporting frameworks and multicenter collaborative research to promote safe clinical adoption of AI technologies in osteoporosis management.[25,255]

Summary

The application of AI in OP research has emerged as a rapidly evolving and interdisciplinary field. This review provides a comprehensive overview of AI technologies currently utilized in OP, categorizing existing studies into four main areas: diagnosis, genomic and bioinformatics research, risk prediction and prognosis assessment, and treatment. By understanding the current progress across these domains, clinicians and researchers can better integrate AI to achieve more intelligent, efficient, and precise management of OP.

Future research should prioritize the development of multimodal AI models that integrate imaging features with genomic and molecular data, which may improve disease characterization and address limitations in the sensitivity of certain imaging modalities, such as MRI. In addition, the use of large-scale, real-world imaging datasets for opportunistic screening represents a promising avenue for early OP detection. Emerging evidence also suggests that AI may facilitate the translation of advanced biomaterials, including metal–organic framework–based nanomedicine, enable personalized multimodal imaging and image-guided therapy through integration with nanomaterial-based contrast platforms, as well as provide comprehensive clinical support thereby expanding future therapeutic strategies for OP. Future investigations may further extend AI applications from diagnosis and drug discovery to personalized treatment planning, rehabilitation optimization, and precision therapeutic intervention. Despite these promising developments, several important limitations remain. Considerable heterogeneity exists among published studies which limit direct comparison and interpretation of reported outcomes. Moreover, insufficient external validation continues to raise concerns regarding model generalizability. Challenges related to data imbalance and potential selection bias further highlight the need for standardized reporting frameworks and multicenter collaborative research.

In conclusion, while AI has already transformed many aspects of OP research—from automated imaging analysis to biomarker discovery—its full potential in treatment personalization, biomaterials translation, and multimodal integration remains to be fully realized. Continued advances in data integration, algorithm transparency, rigorous clinical validation, and interdisciplinary collaboration will be essential for harnessing the full power of AI in the prevention and management of OP.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Zhaochen Zhang, Zhanhao Mo, Yuxi He, Peng Zhang, Zhenya Tian and Lanfeng Huang declare that they have no conflict of interest.

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