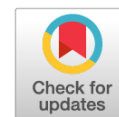


DOI: <https://doi.org/10.17816/DD635014>



# Application of radiomics in osteoporosis detection — current capabilities and future prospects (a review)

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## ABSTRACT

The prevalence of osteoporotic fractures continues to increase as the population ages due to demographic transition. This is particularly relevant for developed countries, including Russia. Radiomics may emerge as a valuable tool for osteoporosis detection.

This review demonstrates the development and application of radiomics in diagnosing oncological and non-oncological diseases including osteoporosis.

A literature search was conducted using the databases PubMed, Google Scholar, and eLibrary over the past 5 years. Data on the prevalence and epidemiology of osteoporosis were obtained from publications in the last 15 years. The search was performed using the following keywords: "radiomic", "osteoporosis", "texture", "magnetic resonance imaging", "computed tomography", "non-oncological radiomics", «магнитно-резонансная томография» ("magnetic resonance imaging"), «компьютерная томография» ("computed tomography"), «радиомика» ("radiomics"), «остеопороз» ("osteoporosis"), «текстуальный анализ» ("texture analysis"), «радиомический анализ» ("radiomic analysis"). Data from original clinical studies were included. In total, 247 articles were found and analyzed. Finally, 59 studies were selected for the review.

The number of studies examining the potential of radiomics in detecting osteoporosis was limited. Further research is required to explore the potential of radiomic analysis using computed tomography and magnetic resonance imaging for detecting osteoporosis compared to established methods such as dual-energy X-ray absorptiometry and the FRAX (Fracture Risk Assessment Tool) algorithm.

**Keywords:** radiomics; osteoporosis; review; osteoporotic fractures; radiomic analysis; texture analysis.

## To cite this article:

Chugaev AI, Vasilev YuA, Petraikin AV, Blokhin IA, Vladzimirskyy AV, Omelyanskaya OV. Application of radiomics in osteoporosis detection — current capabilities and future prospects (a review). *Digital Diagnostics*. 2025;6(1):63–77. DOI: <https://doi.org/10.17816/DD635014>

DOI: <https://doi.org/10.17816/DD635014>

# Применение радиомики для выявления остеопороза — текущие возможности и перспективы (научный обзор)

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## АННОТАЦИЯ

Распространённость остеопоротических переломов продолжает увеличиваться по мере старения населения, происходящего по причине демографического перехода. Данная проблема актуальна для развитых стран, включая Российскую Федерацию. Радиомика в перспективе может стать хорошим инструментом для выявления остеопороза.

В обзоре продемонстрировано развитие и применение радиомического анализа в диагностике онкологических и не-онкологических заболеваний, в частности — остеопороза.

Поиск литературы, соответствующий теме обзора, осуществляли с использованием поисковых систем, таких как PubMed, Google Scholar и eLibrary, за последние пять лет. Данные о распространённости и эпидемиологии остеопороза взяты из публикаций за последние пятнадцать лет. Поиск выполняли с использованием ключевых слов: «radiomic», «osteoporosis», «texture», «magnetic resonance imaging», «computed tomography», «non-oncological radiomics», «магнитно-резонансная томография», «компьютерная томография», «радиомика», «остеопороз», «текстурный анализ», «радиомический анализ». В обзор включены данные оригинальных клинических исследований. В результате найдено 247 статей, из которых в обзор после анализа публикаций отобрано 59 исследований.

Отмечено ограниченное количество работ, изучающих возможности радиомического анализа в отношении выявления остеопороза. Необходимо дальнейшее проведение исследований в области изучения потенциала радиомического анализа с использованием изображений компьютерной и магнитно-резонансной томографии в выявлении остеопороза в сравнении с признанными методиками — двухэнергетической рентгеновской абсорбциометрией и алгоритмом FRAX (Fracture Risk Assessment Tool).

**Ключевые слова:** радиомика; остеопороз; научный обзор; остеопоротические переломы; радиомический анализ; текстурный анализ.

## Как цитировать:

Чугаев А.И., Васильев Ю.А., Петрайкин А.В., Блохин И.А., Владзимирский А.В., Омелянская О.В. Применение радиомики для выявления остеопороза — текущие возможности и перспективы (научный обзор) // Digital Diagnostics. 2025. Т. 6, № 1. С. 63–77. DOI: <https://doi.org/10.17816/DD635014>

DOI: <https://doi.org/10.17816/DD635014>

# 应用放射组学识别骨质疏松症—当前的可能性和前景： 科学综述

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## 摘要

随着人口的老齡化，骨质疏松性骨折的发生率持续增加，这与人口转变有关。这个问题在包括俄罗斯联邦在内的发达国家尤为重要。放射组学有望成为识别骨质疏松症的有效工具。

本文综述了放射组学分析在肿瘤性和非肿瘤性疾病诊断中的发展和应用，特别是在骨质疏松症方面。

文献检索工作使用了PubMed、Google Scholar和eLibrary等搜索引擎，涵盖了过去五年的相关文献。有关骨质疏松症的流行病学和流行率数据来自过去十五年的出版物。检索使用了以下关键词：“radiomic”（放射组学）、“osteoporosis”（骨质疏松症）、“texture”（纹理分析）、“magnetic resonance imaging”（磁共振成像）、“computed tomography”（计算机断层扫描）、“non-oncological radiomics”（非肿瘤学放射混合疗法）、“магнитно-резонансная томография”（磁共振成像）、“компьютерная томография”（计算机断层扫描）、“радиомика”（放射组学）、“остеопороз”（骨质疏松症）、“текстуальный анализ”（纹理分析）和“радиомический анализ”（放射组学分析）。本文包括了原始临床研究的数据。最终，找到了247篇文章，其中经过分析后，选出了59项研究。

研究发现，关于放射组学分析在识别骨质疏松症中的应用研究相对较少。未来需要进一步研究放射组学分析在使用计算机断层扫描和磁共振成像图像识别骨质疏松症的潜力，并与公认的方法进行比较——例如双能X射线吸收法和FRAX（Fracture Risk Assessment Tool）算法。

**关键词：**放射组学；骨质疏松症；科学综述；骨质疏松性骨折；放射组学分析；纹理分析。

## 引用本文：

Chugaev AI, Vasilev YuA, Petraikin AV, Blokhin IA, Vladzmyrskyy AV, Omelyanskaya OV. 应用放射组学识别骨质疏松症—当前的可能性和前景：科学综述. *Digital Diagnostics*. 2025;6(1):63–77. DOI: <https://doi.org/10.17816/DD635014>

收到: 08.08.2024

接受: 10.10.2024

发布日期: 22.01.2025

## INTRODUCTION

Osteoporosis is a progressive systemic skeletal disease characterized by reduced bone mineral density (BMD) and disrupted bone microarchitecture, which cause increased bone fragility and susceptibility to fractures [1]. This disorder manifests as low-energy fractures that occur even with minimal trauma. Although osteoporosis is systemic, the most common fracture sites are the vertebrae, proximal femur, distal forearm, and proximal humerus. Osteoporotic fractures, particularly proximal femur fractures, significantly impair quality of life and increase mortality [2, 3]. Individuals with lower BMD are most susceptible to osteoporotic fractures; however, most fractures occur in patients with T-scores above  $-2.5$  standard deviations (SD) [4–8]. Several vertebral fractures remain undiagnosed, as patients often do not seek medical care [9]. The prevalence of fractures continues to increase as the population ages owing to demographic transition. This is particularly relevant for developed countries, including Russia [10]. Appropriate and prompt treatment allows for disrupting the cycle of repeated fractures, disability, and premature death among elderly patients [11]. Radiomics may become a valuable clinical decision-support tool, as it involves extracting digital features from diagnostic images to correlate with tissue and organ characteristics [12].

This review evaluated the development and application of radiomics in diagnosing oncological and non-oncological diseases, including osteoporosis. Intermediate stages, variables related to radiomic analysis, and advances in this field are discussed. Additionally, the importance of osteoporosis detection and instrumental diagnostic methods used in radiomics are assessed.

## SEARCH METHODOLOGY

This review included a search using the databases PubMed, Google Scholar, and eLibrary over the past 5 years. Data on the prevalence and epidemiology of osteoporosis were obtained from publications in the last 15 years. The search was performed using the following keywords in English and Russian: *radiomics / радиомика, osteoporosis / остеопороз, texture / текстурный анализ, magnetic resonance imaging / магнитно-резонансная томография, computed tomography / компьютерная томография, non-oncological radiomics, and радиомический анализ (radiomic analysis)*. Data from original clinical studies were included, and 247 articles were found and analyzed; 64 studies were selected for the review.

## DIAGNOSING OSTEOPOROSIS AND CHALLENGES FACED BY CLINICIANS

According to international and Russian clinical guidelines, currently, there are no reliable physical examination methods

or laboratory tests for diagnosing osteoporosis. This distinguishes osteoporosis from other metabolic diseases, which are typically diagnosed using laboratory-based approaches. Primarily, bone resorption markers are used for early evaluation of treatment efficacy and patient adherence, rather than for diagnosis.

The 2021 Russian Federal Clinical Guidelines reveal that osteoporosis diagnosis is based on:

- Confirmed low-energy fracture;
- A decrease in BMD according to T-score  $\leq -2.5$  SD in the proximal femur and/or spine by dual-energy X-ray absorptiometry (DXA);
- High fracture risk assessed using the Fracture Risk Assessment Tool (FRAX) [13].

The detection of vertebral compression fractures indicates initiating pharmacologic osteoporosis treatment to reduce further fracture risk [1]. The patient's condition is assessed by lateral thoracolumbar X-ray using standard X-ray equipment. Vertebral compression fractures are characterized by a  $\geq 20\%$  decrease in vertebral body height in anterior, middle, or posterior sections compared with adjacent sections of the same vertebra [14]. Clinicians are discouraged from diagnosing osteoporosis solely based on indirect signs of increased skeletal radiolucency in patients without compression fractures. Computed tomography (CT) and magnetic resonance imaging (MRI) are primarily used for differential diagnosis.

Russian and international guidelines (the World Health Organization and International Osteoporosis Foundation) indicated DXA as the gold standard for measuring BMD [13]. In this study, the primary diagnostic criterion for osteoporosis was a decrease in BMD according to T-score  $\leq -2.5$  SD in the proximal femur and/or spine.

In Russia, the use of DXA-based screening has limitations, including insufficient availability of densitometry equipment [15]. DXA measures are two-dimensional and do not differentiate between degenerative changes in cortical and trabecular bone and cannot evaluate three-dimensional vertebral geometry. Moreover, DXA tends to overestimate BMD in patients with obesity [16]. Epidemiologic studies of osteoporosis indicated that most osteoporotic fractures occur at T-scores corresponding to osteopenia (from  $-1.0$  to  $-2.5$  SD) [4–8]. A large-scale prospective study including over 7000 participants revealed that in some cohorts, two-thirds of fractures occurred at BMD values  $> -2.5$  SD according to DXA data, which corresponds to osteopenia or normal BMD. This demonstrates limitations of DXA as an osteoporotic fracture predictor [17].

Quantitative computed tomography (QCT) shows the same mineral components as DXA and measures volumetric BMD, independent of soft tissues. Thus, QCT is not influenced by obesity and degenerative changes that can falsely increase DXA measurements. QCT separately assesses cortical and trabecular bone and predicts overall bone strength. Furthermore, it evaluates cortical bone structure, dimensions,

and shape. The guidelines for opportunistic osteoporosis screening using automated volumetric BMD assessments via artificial intelligence and phantom modeling have been developed [18].

Receiver operating characteristic (ROC) analyses comparing QCT and DXA indicated slightly superior performance of QCT in patients with vertebral fractures (AUC = 0.802 vs 0.76). Similar outcomes occurred in women (AUC = 0.798 vs 0.748), but not in elderly men (AUC = 0.779 vs 0.780) [19].

Despite its benefits in fracture risk assessment, QCT is more expensive and involves higher radiation exposure compared with DXA, limiting repeated assessments. QCT requires calibration with an external phantom or body tissues. Phantom-based QCT (PB-QCT) uses an external phantom placed beneath the patient, whereas phantom-less QCT (PL-QCT) calibrates using patient tissues, such as muscle and fat [20]. Contrast-enhanced templates were developed to standardize densitometric measurements for cone-beam and multislice CT scanners, reducing calibration variability tenfold and allowing for classification in Hounsfield units according to the Misch classification [21]. Notably, like DXA, QCT is not sensitive to changes in the collagen matrix of bone. However, it is considered more useful than DXA, particularly micro-CT, for assessing bone quality. Nevertheless, owing to the abovementioned limitations, both methods, when used alone to measure BMD without adjustments for specific structural degradation, have substantial limitations in predicting fracture risk [22].

Additionally, FRAX is used to diagnose osteoporosis in postmenopausal women and men aged  $\geq 50$  years by estimating 10-year fracture probability. The result of the calculation is the 10-year probability of major osteoporotic fractures, particularly proximal femur fractures. FRAX accounts for age, sex, weight, height, and additional fracture risk factors, including:

- Presence or absence of a fracture;
- Parental history of hip fracture;
- Smoking and alcohol consumption;
- Glucocorticoid use;
- Confirmed rheumatoid arthritis, a condition associated with osteoporosis.

Moreover, clinicians should consider BMD values at the femoral neck and trabecular bone scores. FRAX models were developed based on population studies from Europe, North America, Asia, and Australia. An advanced, computerized version of FRAX is publicly available online (<https://fraxplus.org/>). It is recommended to diagnose osteoporosis and initiate treatment for patients with a high individual 10-year probability of major osteoporotic fractures based on FRAX results, regardless of lumbar spine or proximal femur DXA findings [13]. Although FRAX is a useful tool for osteoporosis identification, it lacks detailed information on bone composition [23].

The effectiveness of FRAX for assessing osteoporotic fracture risk considerably varies. In a systematic review of 40 publications in the final group [24], AUC for predicting major osteoporotic fractures with FRAX was 57–88 (95% CI: 41–88) when including BMD and 55–81 (95% CI: 55–85) without BMD data. The Russian FRAX model demonstrated lower sensitivity (42%) and specificity (74%). When incorporating BMD, sensitivity decreased to 28%, and specificity increased to 84% [25].

Thus, using DXA and FRAX alone to accurately predict the risk of low-energy fractures is challenging for clinicians. Refining these methods by incorporating additional structural bone data could improve prediction accuracy. An approach in this direction is radiomic analysis.

## WHAT IS RADIOMICS?

Radiomics is an emerging medical research area involving the transformation of digital medical images into quantifiable metrics based on signal intensity, shape, volume, and textural features [12]. These quantitative metrics, called radiomic features or patterns, reflect tissue characteristics such as heterogeneity and shape. They may be used individually or in combination with demographic, histologic, genomic, or proteomic data for clinical decision-making.

X-ray image interpretation involves qualitative assessment, which is experience-based and prone to subjectivity, or simplified summary measures such as lesion diameter and metabolic activity. Diagnostic studies extract a fraction of quantitative image information. Radiomics focuses on extracting quantitative features from digital images, making them accessible for further analysis. The primary hypothesis is that these features reveal biological characteristics undetectable by traditional visual inspection [26].

Initially, radiomics was developed for aerial photography analysis before becoming widely applied in medical image processing [27]. Although early radiomic studies explored rheumatic heart diseases and pulmonary disease classification using chest radiographs [28], most recent radiomic models have been utilized in oncology [12]. Moreover, radiomics was developed as part of molecular biology. However, with the advent of high-throughput computational technology, machine learning, artificial intelligence, and increased computational capabilities, complex structured data from deoxyribonucleic acid, ribonucleic acid-associated proteins, and specific biochemical processes can now be analyzed. Unlike other methods, radiomics relies on radiologic imaging and identifying unique patterns from digital images rather than invasive biopsy and molecular analysis. Radiomic analysis is performed using standard imaging equipment at one or multiple time points during routine diagnostic evaluation. No additional imaging is required, as radiomics captures all visual disease characteristics, considering lesion differences or heterogeneity. Radiomics achieves optimal

effectiveness when integrated with other disease-specific data. Models combining radiomic features with genomic and clinicopathological data have demonstrated improved predictive accuracy [29].

Radiomic image analysis involves several stages (Fig. 1). It can be performed using images acquired through various modalities. However, the majority of studies utilized images obtained through CT or MRI. One study involved a comparative analysis of radiomic nomograms generated from dual-energy CT and DXA [30]. Several factors associated with image acquisition influence extracted radiomic features, including hardware (scanner brand and model), equipment settings (tube voltage and current for CT; magnetic field strength, pulse sequences, and contrast agent use for MRI), and reconstruction parameters (filters and voxel size). These are recognized as method limitations [31].

Before analysis, images should undergo segmentation, which involves delineating regions from which radiomic features will be extracted. Regions of interest depend on the study goal, such as tumors on CT or MRI images or abnormalities on X-rays. Manual segmentation by radiologists is time-consuming and a critical limitation. There is increasing interest in using artificial intelligence (AI)-based automated or semi-automated segmentation with manual adjustments [32]. However, AI-based segmentation tools may be less accurate due to tumor heterogeneity, image noise, and artifacts [33]. Various open-source and proprietary software packages for segmentation and radiomic feature extraction are available, including 3D Slicer (3D Slicer community, <https://www.slicer.org/>), Microsoft Advanced Image Labeler (project InnerEye, Microsoft, Redmond, WA, USA), and MIM Software (MIM Software, Cleveland, OH, USA).

Radiomics quantitatively assesses lesion size, shape, and contrast and mathematically identifies subtle “agnostic” features invisible to human observers, including histogram characteristics and texture analysis. Shape analysis ranges from basic size measurements to more complex topological characteristics such as roundness, compactness, sharpness, and convexity. Texture features describe statistical relationships between voxel intensity values within a defined region of interest [34].

Several radiomic features can be identified, although relatively few of them significantly contribute to a radiomic model. The most relevant radiomic patterns are identified by dimensionality reduction. This step is crucial to retain only diagnostically meaningful features and eliminate the rest as noise [35]. Pattern selection mechanisms commonly used for this purpose include ranking based on mathematical criteria (e.g., intraclass correlation coefficients) or importance scores.

Supervised and unsupervised dimensionality reduction approaches can be applied in radiomic analysis. Unsupervised methods eliminate features based on their correlations with other features, independent of predictive value [36]. Conversely, in supervised approaches, models

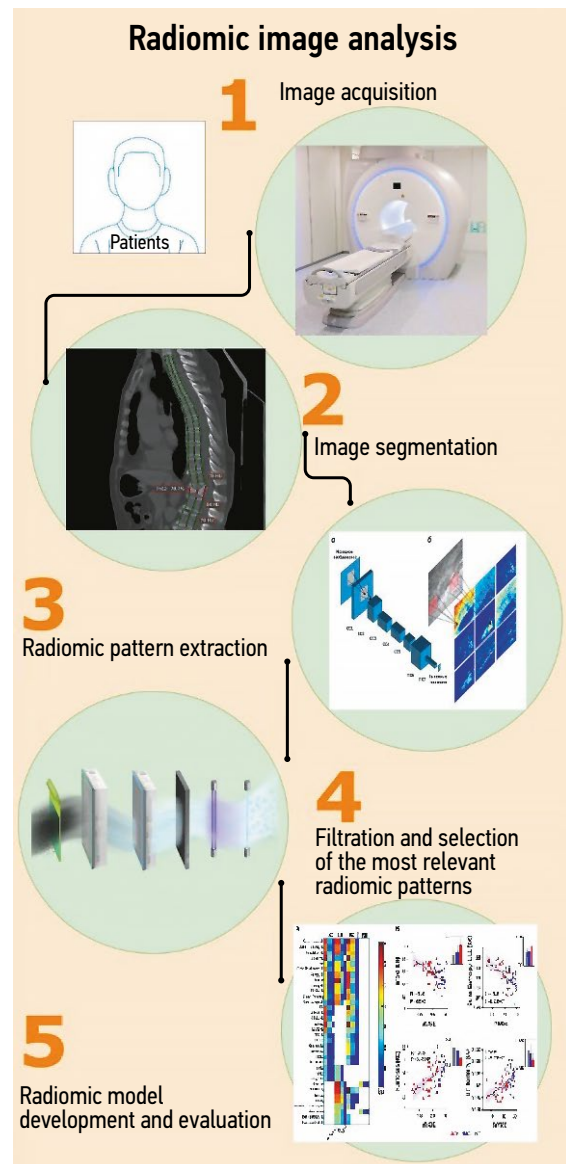


Fig. 1. Main stages of radiomic image analysis.

are fitted to a target variable or study endpoint, such as tumor histology and disease progression, typically selecting the most predictive radiomic features [37].

Supervised models are trained on datasets called training data, after which model accuracy and generalizability are assessed using validation testing. Two validation approaches exist. The first approach, namely, internal validation, uses data similar to those on which the model was originally developed. A common example is cross-validation. The original dataset is divided into two parts; the model is developed on the training subset and tested on the remaining data. For smaller sample sizes, cross-validation is performed by partitioning the data into several subsets, which are then sequentially used for training and validating the model [38]. The second approach is external validation, wherein the data used to evaluate model performance are structurally different from those used to train the model and are obtained from a separate institution in another region [39].

## WHICH CLINICAL FIELDS MOST COMMONLY USE RADIOMIC IMAGE ANALYSIS?

Radiomic methods are predominantly employed in oncology research. Radiomic tools have been applied in studies addressing screening, detection, diagnosis, staging, and disease outcomes and identifying and predicting biological correlations and responses to treatment and in research on key oncogenic processes [40].

Accurate identification of tumor biological subtypes is crucial for oncology treatment decisions, but can be limited by tissue availability and tumor heterogeneity. Radiomics has been widely investigated for predicting critical histotypes across various tumor types [41].

Recently, radiomic studies aiming to predict molecular biomarkers associated with immune checkpoint inhibitor responses have significantly increased, owing to the increasing clinical use of these therapies [42].

Preoperative staging is another promising area of radiomics application. MRI-based radiomics has successfully staged head and neck cancers [43], whereas CT texture analysis has demonstrated a significant correlation with overall tumor staging in primary lung cancer [44].

Research into the clinical use of radiomics has expanded to predicting treatment responses in oncology. MRI-based radiomics have extensively predicted pathological and/or radiological responses to neoadjuvant chemotherapy or chemoradiotherapy in breast [45], rectal [46], cervical [47], and head and neck cancers [48]. CT-based radiomics have been utilized for predicting responses to first-line chemotherapy in gastric, bladder, lung, and ovarian cancers and responses to neoadjuvant chemoradiotherapy in esophageal and lung cancers.

Delta radiomics, which measures imaging feature changes over time (usually pre- and post-treatment), has become increasingly popular for evaluating treatment effectiveness. It identifies subtle early tumor changes preceding measurable size variations. Thus, delta radiomics is considered a valuable adjunctive tool for reassessing disease progression or regression. Delta radiomics has been used to assess treatment efficacy in brain tumors, head and neck cancers, lung cancers, gastrointestinal malignancies, colorectal cancer, breast and prostate cancers, renal cancers, and various other malignant neoplasms [49].

## RADIOMIC ANALYSIS FOR EVALUATING VERTEBRAL FRACTURE RISK

Furthermore, radiomics has also been applied to identify patients at high risk of pathological fractures based on image-derived texture features [50–54]. Preliminary data indicate that the use of radiomic features from CT and MRI images may improve bone structural assessment, providing

fracture risk predictions independently and more accurately than DXA-derived BMD.

Radiomic analysis has enhanced CT accuracy in predicting osteoporosis-related fracture risk. An automated CT image-processing pipeline improved identification of patients with osteoporotic vertebral fractures (AUC = 0.88 using volumetric BMD data combined with five texture features vs AUC = 0.64 using BMD alone) [52]. In this study, five texture features were initially analyzed in 154 patients with cancer without vertebral metastases, among whom 51 had compression fractures.

Another study identified 12 distinct texture-based radiomic features from an initial set of 1040 features [55]. A specific combination of these features significantly improved the classification accuracy of 386 individual vertebrae from 99 patients, 34 of whom had DXA-confirmed osteoporosis, with AUC increasing from 0.84 to 0.92 in the test set (116/386 vertebrae). Notably, this study utilized the 3D Slicer Pyradiomics software [56].

Recently, an original radiomic analysis method for metastatic vertebral lesions was proposed in a joint Russian–German study [57]. MRI-based radiomic analysis identified stable texture features associated with morphological vertebral changes during the treatment of patients with breast cancer with spinal metastases. The radiomic analysis, based on three patient cases, included the following steps:

- Native-image texture analysis;
- Contrast-enhanced image analysis;
- Analysis of microfoci or microlesions (calderas).

## RADIOMIC ANALYSIS FOR OSTEOPOROSIS DETECTION

One of the largest studies on the use of texture analysis for osteoporosis detection was conducted by Kim et al. [58] and was published in 2022. A radiomic model employing machine learning was developed using 4924 hip X-rays from 4308 patients (3632 women; mean age:  $62 \pm 13$  years). The study was conducted in a large South Korean hospital from September 2009 to April 2020. The DXA-derived T-score was the reference standard for osteoporosis diagnosis. Seven radiomic models incorporating various feature types were developed. Independent testing involved 444 hip X-rays obtained between January 2019 and April 2020 from a different institution. Diagnostic effectiveness was evaluated by calculating AUC. Among the seven models, the radiomic model combining clinical and texture features showed the highest diagnostic performance during external independent testing (AUC = 0.95). Results demonstrated that radiomic models based on hip X-rays using machine learning can be used to diagnose osteoporosis. Kim et al. reported that their radiomic model had excellent diagnostic performance and can be an alternative tool for identifying patients at risk of osteoporosis for subsequent confirmatory

testing, including DXA. Based on the test dataset, its sensitivity was 89% (66/74), with most false-positive results occurring in the osteopenia group (61/64). Among patients with normal BMD, the false-positive rate was 2% (3/143). Furthermore, the study confirmed that the machine learning-based radiomic model exhibited good generalizability regarding external validation. However, the authors noted limitations. Radiomic features were extracted from a bounding box containing the proximal femur and adjacent soft tissues, which is a significant constraint when projecting three-dimensional anatomical structures onto a two-dimensional plane. This makes it challenging to eliminate overlapping soft tissues in front of and behind the area of interest, namely, the bone.

Scientific studies describing the application of radiomic analysis of CT images for osteoporosis detection were conducted by researchers from China. Wang et al. [59] developed and validated a clinical–radiomic model based on monochromatic imaging obtained from single-source dual-energy CT for osteoporosis prediction. Overall, 164 patients underwent both single-source dual-energy CT and QCT of the lumbar spine and were divided into two groups:

- Group 1: training cohort,  $n = 114$ ; 30 patients with osteoporosis and 84 without osteoporosis;
- Group 2: validation cohort,  $n = 50$ ; 12 patients with osteoporosis and 38 without osteoporosis.

A total of 107 radiomic features were extracted from monochromatic CT images. Using QCT as the reference standard, a radiomic signature was created with the least absolute shrinkage and selection operator (LASSO) regression method based on reproducible features. The clinical–radiomic model incorporated the radiomic signature and a significant clinical predictor (i.e., age) via multivariate logistic regression. This model's effectiveness was evaluated by calibration, discrimination, and clinical utility analyses. The radiomic signature demonstrated good calibration and discrimination in the training and validation cohorts. The clinical–radiomic model, combining radiomic features with age as a clinical–demographic predictor, showed high discriminative ability, with an AUC of 0.938 (95% CI: 0.903–0.952) in the training cohort and 0.988 (95% CI: 0.967–0.998) in the validation cohort.

Xie et al. [60] developed and validated a radiomic model based on quantitative CT data for the detection of osteoporosis and osteopenia. In total, 635 patients who underwent quantitative CT were retrospectively analyzed. Patients with osteopenia or osteoporosis ( $n = 590$ ) were divided into the training ( $n = 414$ ) and test ( $n = 176$ ) cohorts. Radiomic features were extracted from the quantitative CT images of the L3 vertebra. In developing a combined clinical–radiomic model for diagnosing osteoporosis and osteopenia, six predictive radiomic features were selected, along with clinical risk factors such as age, alkaline phosphatase activity, and homocysteine levels. The AUC of the combined

clinical–radiomic model was 0.96 [95% CI: 0.95–0.98] and 0.96 [95% CI: 0.92–1.00] in the training and test cohorts, respectively.

Another study demonstrated that radiomic features can be extracted from MRI images to indicate the presence of osteoporosis. Martel et al. [61] assessed bone status using the radiomic analysis of proximal femur MRI scans. MRI was performed on 45 women with osteoporosis (15 with a history of fractures and 30 without) using high-resolution 3D sequences and 3-T magnetic field strength. Radiomic features in the trabecular region of the proximal femur were obtained from T1-weighted images in the provided dataset. The predictive value of each feature was evaluated using the Wilcoxon test and ROC analysis. These features were compared with DXA results and FRAX scores. The study aimed to reveal key radiomic patterns that play a critical role in the assessment of osteoporotic fracture risk. The analysis and individual prediction accuracy of specific features enable more effective use of the dataset without the need to develop a multiparametric machine learning model. The correlation between radiomic patterns and values derived from DXA and FRAX ranged from weak to moderate; however, the authors concluded that radiomic features allow for the evaluation of bone status from MRI scans of the proximal femur and potentially predict fracture risk.

Zhen et al. [62] conducted a retrospective radiomic analysis of lumbar spine images obtained from 160 patients using DXA and MRI. Among the patients, 86 were diagnosed with low BMD consistent with osteoporosis, whereas 74 had normal BMD. Sagittal T1- and T2-weighted images of all patients were imported into the United Imaging Intelligence platform for boundary delineation and radiomic analysis, which yielded various radiomic patterns. Radiomic models were developed based on T1-WI, T2-WI, and combined T1 + T2-WI sequences using features selected by LASSO regression. ROC curve analysis was performed to evaluate the predictive performance of each model in identifying bone abnormalities, and decision curve analysis (DCA) was used to assess the effectiveness of each model. The model was tested on an external validation set of 35 patients from different medical institutions. Based on combined T1 + T2-WI features, the radiomic model showed the highest screening performance for identifying patients with low BMD. In the training cohort, the sensitivity and specificity were 0.758 and 0.78, respectively, with an accuracy of 0.768 (AUC = 0.839 [95% CI: 0.757–0.901]). In the test cohort, sensitivity and specificity reached 0.792 and 0.875, respectively, with an accuracy of 0.833 (AUC = 0.86 [95% CI: 0.73–0.943]). Furthermore, DCA demonstrated that the combined model exhibited better predictive utility. In the external validation cohort, sensitivity and specificity were 0.764 and 0.833, respectively, with an accuracy of 0.8 (AUC = 0.824 [95% CI: 0.678–0.969]). Thus, radiomic analysis can be used to quantitatively assess MRI data and accurately screen patients with low BMD.

**Table 1.** Summary of publications on the use of radiomic analysis in osteoporosis diagnosis included in the review

Authors	Year	Country	Aim	Modality	No. of patients	Accuracy
Kim et al. [58]	2022	South Korea	To develop and validate radiomic models for osteoporosis diagnosis using hip X-rays	X-ray	4308	• AUC = 0.95
Wang et al. [59]	2023	China	To develop and validate a clinical–radiomic model based on CT data for osteoporosis prediction	CT	164	• AUC = 0.938; • AUC = 0.988
Xie et al. [60]	2022	China	To develop and validate a radiomic model based on quantitative CT data for the identification of osteoporosis and osteopenia	CT	635	• AUC = 0.95
Martel et al. [61]	2023	USA	To analyze radiomic features and their extractability in patients with and without osteoporotic fractures	MRI	45	• AUC DNU = 0.751, $p < 0.05$ ; • AUC LGLE = 0.729, $p < 0.05$ ; • AUC Kurtosis = 0.718, $p < 0.05$
Zhen et al. [62]	2024	China	To compare the effectiveness of radiomic features extracted from MRI images acquired using different sequences (T1-weighted, T2-weighted, and combined T1- and T2-weighted) for osteoporosis detection in patients	MRI	160	• AUC = 0.839; • AUC = 0.86; • AUC = 0.824

Note. AUC, area under the curve; CT, computed tomography; DNU, dependence nonuniformity; LGLE, low gray-level emphasis; MRI, magnetic resonance imaging; USA, United States of America; WI, weighted image.

Table 1 summarizes the key characteristics of the studies included in this review concerning the use of structural analysis in diagnosing osteoporosis. Although most radiomic research has focused on oncology, interest in its application to non-oncologic conditions, particularly osteoporosis, has emerged only recently, with the earliest study in this area published in 2022 (see Table 1). The study with the largest patient cohort involved the radiomic analysis of X-rays; however, the most recent studies explored its use for diagnosing osteoporosis using CT and MRI images. The studies (see Table 1) revealed that radiomic analysis for the detection of osteoporosis has greater potential than the use of the texture analysis for diagnosing oncological diseases.

## LIMITATIONS AND FUTURE DIRECTIONS

Studies on radiomic image analysis primarily focused on oncology. However, there is an increasing number of studies on the use of the texture analysis in the assessment of non-oncological diseases, including screening and diagnosing osteoporosis. This is a promising direction. Before the occurrence of severe clinical manifestations, namely, osteoporotic fractures, diagnosing osteoporosis is challenging for clinicians. Unlike other metabolic disorders (e.g., a suspected case of diabetes mellitus can be evaluated with a relatively simple plasma glucose test), there are no laboratory tests or pathognomonic clinical signs

for osteoporosis. In oncology, radiomic analysis is used to extract quantitative data, often in addition to qualitative findings. Typically, clinicians dealing with osteoporosis lack quantitative and qualitative information. A radiologist or oncologist can visually identify the presence, progression, or regression of a tumor on MRI or CT scans. However, in cases of osteoporosis without fractures, such visual confirmation is not feasible.

Nevertheless, DXA is considered the gold standard for diagnosing osteoporosis. It confirms the diagnosis if a T-score of  $\leq -2.5$  SD is determined. However, DXA results represent calculated estimates, and most osteoporotic fractures occur in patients with osteopenia: T-scores from  $-1.0$  to  $-2.5$  SD [4–8].

Moreover, DXA is an expensive diagnostic method, and limited access to the required imaging equipment has been reported in Russia and in developed countries, including the United States [15]. This has led to increased interest in radiomics as a potential alternative for osteoporosis detection and for generating quantitative data.

A database containing 120 CT scans<sup>1</sup> with and without signs of spinal osteoporosis has been developed to evaluate the accuracy of automated image analysis systems. The recent proliferation of AI technologies in healthcare has led to a surge in medical data collection, including data from radiologic and instrumental diagnostic data, which support the development of machine learning models. As more datasets are created for various digital health technology applications, issues of systematization, standardization,

<sup>1</sup> Vasiliev Yu.A., Turavilova E.V., Vladzimirskiy A.V., et al. Certificate of State Registration of Database No. 2023621171 Russian Federation. MosMedData: CT Scans with Signs of Spinal Osteoporosis: No. 2023620784. Application Date: March 24, 2023. Publication Date: April 11, 2023. EDN: SHLWTC.

storage, access, and the safe and efficient use of such data become increasingly relevant [63]. However, high-quality data are critical for the development and validation of radiomics-based osteoporosis detection systems.

## CONCLUSION

Studies of the potential of radiomic analysis for the detection of osteoporosis are limited. Some large-scale studies demonstrated that radiomic models can achieve diagnostic accuracy comparable to the T-score obtained via DXA, which serves as the reference standard. Within the current healthcare infrastructure, the practical application of radiomic analysis is promising, as vast repositories of raw CT and MRI images are available. With sufficient automation, these datasets can be used to generate novel insights and enhance osteoporosis detection methods. Further study is warranted to explore the full potential of radiomic analysis using CT and MRI images in comparison with established techniques such as DXA and the FRAX algorithm. Additionally, radiomics holds considerable promise for predicting osteoporotic fractures, particularly when integrated with trabecular bone score metrics.

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## ADDITIONAL INFORMATION

**Funding source.** This article was prepared by a group of authors as a part of the research and development effort titled "Scientific evidence for using radiomics-guided medical imaging to diagnose cancer" (USIS No. 123031500005-2) in accordance with the Order of the Moscow Health Care Department No. 1196 dated December 21, 2022 "On approval of state assignments funded by means of allocations from the budget of the city of Moscow to the state budgetary (autonomous) institutions subordinate to the Moscow Health Care Department, for 2023 and the planned period of 2024 and 2025".

**Disclosure of interests.** The authors declare that they have no relationships, activities or interests (personal, professional or financial) with third parties (commercial, non-commercial, private) whose interests may be affected by the content of the article, as well as no other relationships, activities or interests over the past three years that must be reported.

**Authors' contribution.** A.I. Chugaev: literature review, collection and analysis of literature data, writing and editing the article; A.V. Petryaikin, I.A. Blokhin: collection and analysis of literature data, writing the text of the article; Yu.A. Vasilev, A.V. Vladzmyrskyy, O.V. Omelyanskaya editing the article. Thereby, all authors provided approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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