

Opportunistic Osteoporosis Screening at the Spine – Clinical Applications and Diagnostic Value

Opportunistisches Osteoporose-Screening an der Wirbelsäule – Klinische Anwendungen und Diagnostischer Nutzen



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ABSTRACT

Osteoporosis is a systemic skeletal disease with increasing prevalence. In Germany, decisions regarding basic diagnostics and therapy are currently based on the estimation of the 3-year risk for femoral neck and vertebral fractures. Reduced bone density is a measurable risk factor, for which DXA has served as the reference standard for decades. However, DXA has limitations, particularly at the spine, and is only available to a very limited extent in some regions. Many osteoporotic fractures occur in individuals who have never been screened. Vertebral fractures are the most common osteoporotic fractures in both sexes and increase the risk of subsequent fractures by a factor of two to five. In such cases, a differential diagnosis and determination of the treatment threshold should be made quickly, even if no DXA measurement is available. CT-based methods for the automated detection of vertebral fractures, combined with opportunistic bone density measurement, are increasingly used in routine clinical practice for the initial identification of high-risk patients. Here, opportunistic CT-based bone density measurements at the spine are at least equivalent to DXA in predicting vertebral fractures. For longitudinal bone density measurements, such as those used to assess the effectiveness of a therapy, DXA is currently the preferred method due to a higher reproducibility. In a controlled setting of sequential CT examinations with the same hardware and protocols, equivalent reproducibility can be assumed – however, this first must be demonstrated in studies involving bone-healthy populations. To ensure valid and comparable results from opportunistic measurements, scanner-specific calibration and, when applicable, correction for contrast agents must be performed.

ZUSAMMENFASSUNG

Osteoporose ist eine systemische Skeletterkrankung mit steigender Prävalenz. In Deutschland basiert die Entscheidung zur Basisdiagnostik und Therapie derzeit auf der Abschätzung des 3-Jahres-Risiko für Schenkelhals- und Wirbelkörperfrakturen. Bezogen auf die verminderte Knochendichte als messbaren Risikofaktor gilt die DXA seit Jahrzehnten als Referenzstandard. Sie weist jedoch insbesondere an der Wirbelsäule Limitationen auf und ist regional teils nur eingeschränkt verfügbar. Viele osteoporotische Frakturen treten bei Personen auf, die nie gescreent wurden. Wirbelkörperfrakturen sind bei beiden Geschlechtern am häufigsten und erhöhen das Folgefrakturrisiko um das Zwei- bis Fünffache. In solchen Fällen sollte eine Differentialdiagnostik sowie Festlegung der Therapieschwelle rasch erfolgen, auch ohne vorliegende DXA-Messung. CT-basierte Verfahren zur automatisierten Erkennung von Wirbelkörperfrak-

turen in Kombination mit opportunistischer Knochendichtemessung werden zunehmend in der klinischen Routine zur Erstidentifikation von Hochrisikopatienten eingesetzt. Hier ist die opportunistische CT-basierte Knochendichtemessung an der Wirbelsäule der DXA in der Frakturvorhersage von Wirbelkörperfrakturen mindestens gleichwertig. Für longitudinale Knochendichtemessungen, etwa zur Therapiekontrolle, ist die DXA aufgrund der besseren Reproduzierbarkeit derzeit grundsätzlich zu bevorzugen. Im kontrollierten Rahmen sequenzieller CT-Untersuchungen mit gleicher Hardware und Protokollen ist von gleichwertiger Reproduzierbarkeit auszugehen – was jedoch in Studien einer knochengesunden Population zu zeigen ist. Zur Sicherstellung valider und vergleichbarer opportunistischer Messergebnisse muss eine Scanner-spezifische Kalibrierung und gegebenenfalls eine Kontrastmittelkorrektur erfolgen.

Introduction

Osteoporosis presents an increasing challenge for healthcare systems. Vertebral fractures (VFs), the most common clinical manifestations related to osteoporosis in postmenopausal women and men over 50 years, have considerably increased between 2009 and 2019: by 32 % in the thoracic spine and by 21 % in the lumbar spine [1]. Moreover, VFs pose an imminent risk of subsequent fractures [2], are associated with increased mortality [3], and should therefore prompt timely differential diagnostic assessment and decision regarding the initiation of adequate treatment [4]. However, VFs and other indicators of poor bone health are frequently overlooked or not clearly identified as “fractures” in routine radiology reports [5].

The scorecard for osteoporosis in Europe (SCOPE) study illustrated the socio-economic consequences at the European level [6]. On average, the treatment gap, defined as the proportion of women and men at high fracture risk who do not receive treatment, is 71 % [6]. A definitive diagnosis of osteoporosis, including bone mineral density (BMD) results, appears to have high positive impact, with an absolute reduction in the treatment gap of 63 % [7]. Screening for low BMD is typically performed by using dual-energy X-ray absorptiometry (DXA). Specifically, DXA is a two-dimensional (2D) imaging technique that assesses areal BMD. DXA can be negatively affected by factors such as degenerative changes, scoliosis, and arterial calcification – particularly at the spine [8, 9]. Thus, almost half of patients with osteoporotic fractures have normal or only lowered BMD with a spine T-score ≥ -2.5 [10, 11]. More importantly, most women and men who are eligible do not undergo osteoporosis screening, and many osteoporotic fractures occur in individuals who have never been screened.

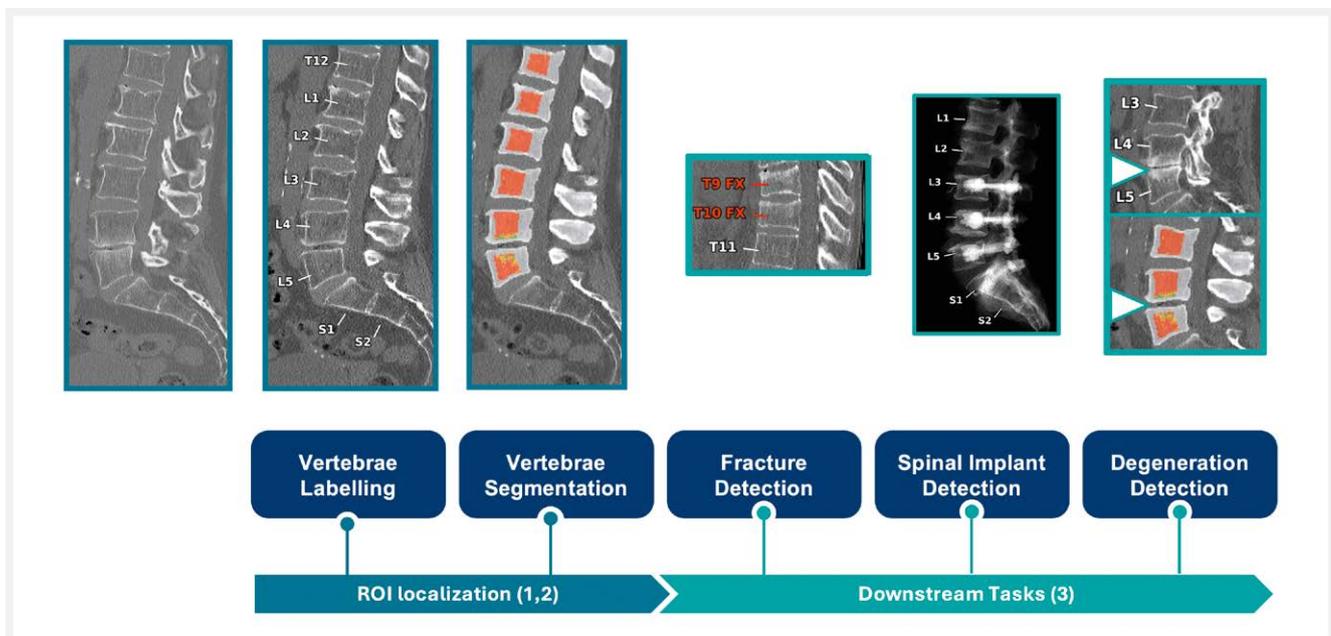
Opportunistic osteoporosis screening using non-dedicated computed tomography (CT) is increasingly used to identify individuals at high risk of osteoporotic fractures [12, 14]. In this context, opportunistic screening refers to the use of clinical routine imaging data that have initially been acquired for other purposes than osteoporosis screening, such as for oncological staging. Advances in computational performance and machine learning (ML), as well as the availability of large datasets, have enabled automat-

ed screening for two major factors related to osteoporosis: BMD and VFs. In addition, CT systems have become increasingly stable in recent years, particularly regarding scanner drift [12]. However, several requirements for effective opportunistic BMD measurements – particularly regarding ML-based software – should be considered to ensure (1) accuracy, (2) reproducibility, (3) comparability, and (4) full automation, all of which are needed for a widespread clinical implementation and adoption beyond research.

The purpose of this work was to review the current evidence and clinical value of opportunistic CT-based screening for evaluating the osteoporotic spine. We discuss the technical requirements, strengths, and limitations of this approach, as well as how guideline-based therapies can be derived from its results. Relevant studies were identified via a PubMed literature search (<http://www.ncbi.nlm.gov/pubmed>).

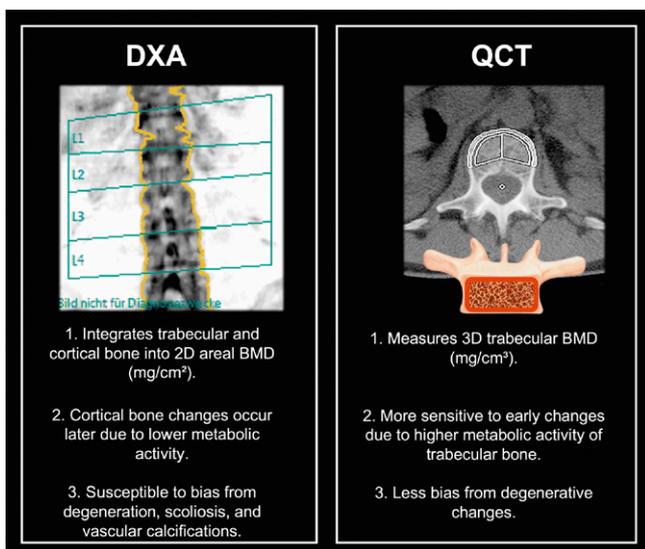
The Principles Of Opportunistic Screening And Advances In Machine Learning

In recent years, a considerable number of software tools – approved by the US Food and Drug Administration (FDA) or bearing CE-marking in the European Union – have been developed using automated or semi-automated approaches for osteoporosis screening [15]. For a fully automated analysis of the spine, three tasks are fundamental: (1) precise spine segmentation, (2) vertebral labelling, and (3) automated selection of appropriate vertebrae for measurements of BMD (► Fig. 1). Considerable progress has been made in tasks (1) and (2), facilitated by the availability of large datasets that can support the training of segmentation algorithms capable of reliably handling complex spinal morphologies, including developmental and degenerative changes, as well as anatomical variants (such as a sixth lumbar vertebral body / L6) [16, 18]. Task (3) is a critical filtering step to avoid erroneous BMD measurements. It requires not only the correct identification of standard vertebral levels (e. g., L1 through L3) but especially the exclusion of vertebrae that should not be measured due to findings such as VFs (Genant Grades 1–3), severe degenerations, or the presence of spinal instrumentation.



► **Fig. 1** Overview of steps for an exemplary spine processing pipeline based on computed tomography (CT). First, correct labelling of vertebral bodies and segmentation is performed (1,2). In downstream tasks, vertebrae that should not be measured are excluded (3). In a final step, trabecular volumetric bone mineral density (vBMD) values is extracted for measurable vertebrae (usually L1 through L3) using regions of interest (ROIs).

► **Abb. 1** Schematische Darstellung einer beispielhaften Pipeline zur Wirbelsäulenanalyse mittels Computertomographie (CT). Zunächst werden die Wirbelkörper korrekt beschriftet und segmentiert (1,2). In den nachfolgenden Schritten werden Wirbelkörper, die nicht gemessen werden sollen, ausgeschlossen (3). Im letzten Schritt wird die trabekuläre volumetrische Knochenmineraldichte (vBMD) in messbaren Wirbelkörpern (in der Regel LWK1 bis LWK3) anhand definierter Regions of Interest (ROIs) extrahiert.



► **Fig. 2** Comparison of measurement principles between dual-energy X-ray absorptiometry (DXA) and quantitative computed tomography (QCT).

► **Abb. 2** Vergleich der Messprinzipien zwischen dualer Röntgen-Absorptiometrie (DXA) und quantitativer Computertomographie (QCT).

The Current Evidence and Requirements for Reliable Clinical Application

A Foreword About 3D CT-Based BMD Values And 2D DXA T-Scores At The Spine

There still seems to be confusion on how to interpret and report spine BMD values obtained using CT. While CT and DXA metrics may appear similar at first glance, a closer look reveals that each technology produces results that must be interpreted independently. Specifically, 3D volumetric BMD derived from CT allows dedicated assessment of trabecular bone, while DXA as a 2D method summarizes cortical and trabecular bone based on areal BMD (► **Fig. 2**). Trabecular bone is more metabolically active than cortical bone and is therefore more susceptible to early changes in bone mass [19]. Furthermore, overestimation of BMD due to large vertebrae in tall people and spinal degenerative changes such as osteophytes can be avoided using 3D volumetric BMD from CT [20].

If a T-score is calculated on trabecular BMD alone, this may lead to an overestimation of fracture risk [21]. Instead, classification thresholds for absolute BMD values established by the American College of Radiology (ACR) should be used (► **Fig. 3**) [22]. Consequently, efforts to directly correlate DXA T-scores with CT-based BMD values at the spine are not meaningful, as the measurements are inherently different and are therefore only moderately correlated [23].

Discrepant results between opportunistic QCT and DXA are therefore not uncommon and should not be automatically interpreted as methodological errors. Rather, both methods should be

evaluated based on their differing associations with the relative risk of fractures, and this risk should then be integrated into the individual assessment of a patient.

Accuracy

To determine whether opportunistic BMD measurements from CT are accurate, conventional quantitative CT (QCT) and not DXA must serve as the reference method. To establish accurate BMD estimates from CT images, several technical considerations must be respected [24].

First, CT scanners made by different manufacturers but also different model series from the same manufacturer can show systematic offsets in mean attenuation (HU) values that form the foundation of subsequent BMD calculations [25, 27]. Second, (peak) tube voltage, which may vary between protocols, significantly influences HU measurements, with deviations exceeding 50 % [25, 28]. Third, the widespread application of iodinated contrast agent results in a bias for various tissues, including trabecular bone [29, 30]. This bias arises not only from the contrast agent itself, but also from differences in the respective contrast phases [31, 33]. In this context, HU values can vary considerably, and attenuation values are significantly higher in both contrast-enhanced phases compared to the unenhanced phase, with measurements in the arterial and portal phase resulting in 7 to 25 % false negatives with different thresholds to define osteoporosis [34]. Given these well-known limitations, it is unlikely that any uncalibrated HU thresholds will achieve a broad clinical adoption, as comparability between scanners, protocols, institutions, and patient groups cannot be ensured [35, 36].

Instead, to reach an adequate level of accuracy, a scanner- and protocol-specific calibration is required [27]. This can be achieved either through asynchronous phantom-based calibration or via phantom-less calibration methods, such as material-decomposition in dual-energy CT (DECT) or internal calibration using certain tissues [12, 23, 37, 38].

In a recent experimental study, DECT-based BMD values were found to precisely reflect the calcium hydroxyapatite (HA) concentrations in the quality reference European Spine Phantom (ESP) [37]. In a clinical multi-scanner study with asynchronous calibration, opportunistic BMD correlated well with conventional QCT in a common clinical environment with different imaging protocols and contrast-enhanced scans [39]. In this study, opportunistic BMD better discriminated between patients with and without prevalent VFs (area under the curve [AUC] = 0.86) than conventional QCT (AUC = 0.82) [39]. The intraclass correlation coefficient (ICC) indicated high agreement between both methods (ICC = 0.91), while the overall root mean square coefficient of variation (RMSCV %) was < 15 % across all protocols and scanners [39]. This high agreement between both methods was replicated in an ex-vivo study, which reported an ICC of 0.992 using the same algorithm in cadaver scans of two female donors [40]. In another study comparing the ability of DXA and opportunistic QCT to discriminate patients with and without VFs, opportunistic QCT demonstrated a similar AUC of 0.88, thereby highly outperforming DXA (AUC = 0.66) [41].

It should be noted that the absolute difference between conventional QCT and opportunistic QCT can be quite pronounced in some subjects, even when exactly the same vertebrae were select-

QCT Trabecular Spine BMD	Equivalent WHO Diagnostic Category
BMD > 120 mg/cm ³	Normal BMD
80 mg/cm ³ ≥ BMD ≤ 120 mg/cm ³	Osteopenia or low BMD
BMD < 80 mg/cm ³	Osteoporosis

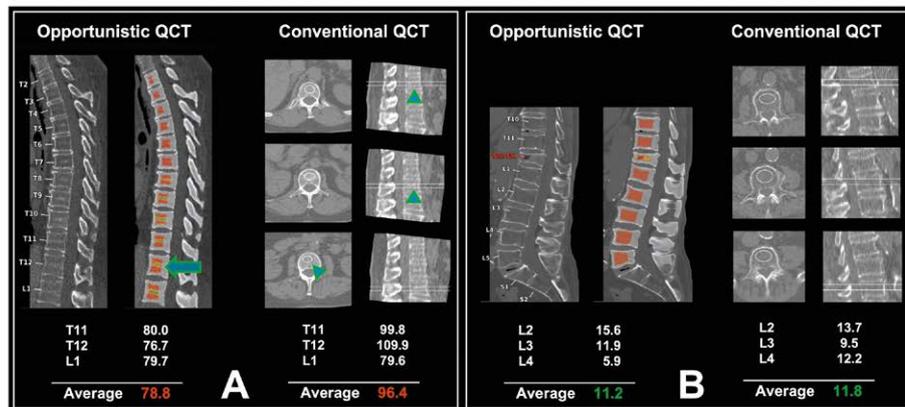
► **Fig. 3** Diagnostic thresholds for (opportunistic) quantitative computed tomography (QCT) that are approximately equivalent to the World Health Organization (WHO) DXA-based definition of osteoporosis [22]. According to the American College of Radiology (ACR), the interpretation at the spine should rely on absolute bone mineral density (BMD) values (left column) [22].

► **Abb. 3** Diagnostische Grenzwerte für die (opportunistische) quantitative Computertomographie (QCT), die annähernd äquivalent zur DXA-basierten Definition der Weltgesundheitsorganisation (WHO) für Osteoporose sind [22]. Gemäß dem American College of Radiology (ACR) sollte die Beurteilung an der Wirbelsäule auf den absoluten Werten der Knochenmineraldichte (BMD) basieren (linke Spalte) [22].

ed for measurements [39]. The most likely explanation for differences lies in the divergent definition and extraction of regions of interest (ROIs) (► **Fig. 4**). Conventional QCT software typically relies on manually placed circular ROIs in the mid-portion of the trabecular compartment, resulting in non-standardized ROI placement that can cause variability. In contrast, semi-automatic [42] or fully automatic approaches [18] allow for user-independent ROI selection which enables the analysis of larger volumes compared to planar or small volumetric ROIs. Such an approach can capture the entire structural information of the trabecular compartment of a vertebral body without additional manual work. Full coverage of the trabecular area may be particularly relevant in patients with focal variations in bone loss. In such patients, depending on placement of the ROI, manually extracted BMD values can differ substantially even between single vertebrae (► **Fig. 4A**). Which method provides better predictive power for fracture risk, or whether there is a clinically significant difference at all, remains to be carefully determined. Yet, the current body of evidence indicates that opportunistic QCT could be a non-inferior alternative to conventional QCT, at least for assessment of BMD at one time point [37, 39–41].

Precision and Reproducibility

Precision refers to consistency of results in repeated measurements under the same conditions. Of note, short-term precision is commonly defined as measurements performed on the same day [43]. This condition is rarely met in opportunistic CT and thus can hardly be tested. For DXA measurements at the spine, the short-term precision is considered good, with a low RMSCV of around 1.3 % in immediately repeated measurements with correct patient repositioning between scans and consistent image analysis [13, 44]. In a study investigating opportunistic QCT, a similar RMSCV of 1.3 % (equal to 3 mg/cm³) was reported for different reconstruction kernels [45]. For repeated measurements conducted within less than one month on a single calibrated scanner, the short-term precision



► **Fig. 4** Two example cases illustrating differences in region of interest (ROI) definitions between separately performed conventional and opportunistic quantitative computed tomography (QCT). A Female patient (68 years old) with focal variations in bone loss (i. e., relatively preserved trabecular bone centrally within the vertebra at T8-L1, see heatmap & arrow). In conventional QCT, manual two-dimensional (2D) ROI placement in the vertebral midplane (arrowheads) resulted in higher bone mineral density (BMD) values at T11 and T12 and notable variability for vertebrae. The average BMD was 96.4 mg/cm³. In contrast, opportunistic QCT, which analysed the entire trabecular volume, yielded more consistent BMD values. The absolute difference between the two methods was 17.6 mg/cm³ – conventional QCT indicated low BMD, while opportunistic QCT indicated osteoporotic BMD. Notably, the patient sustained two vertebral fractures (VFs), confirmed at follow-up examinations: the first at T5 after 6 months, the second at T6 after 12 months. B Male patient (88 years old) with relatively uniform trabecular bone loss (see heatmap). Both conventional and opportunistic QCT show high agreement, with a difference of 0.6 mg/cm³ between the two measurements.

► **Abb. 4** Zwei Fallbeispiele, welche die unterschiedliche Definition der Region of Interest (ROI) zwischen separat durchgeführter konventioneller und opportunistischer quantitativer Computertomographie (QCT) veranschaulichen. A Eine weibliche Patientin (68 Jahre), mit fokalen Schwankungen der trabekulären Knochendichte (d.h. relativ gut erhaltenem Trabekelknochen im Zentrum der Wirbelkörper BWK8-LWK1, siehe Heatmap & Pfeil). Bei der konventionellen QCT führte die manuelle, zweidimensionale (2D) ROI-Platzierung in der Mitte der Wirbelkörper (Pfeilspitzen) zu höheren Knochenmineraldichtewerten (BMD) bei BWK11 und BWK12, und zu einer merklichen Variabilität zwischen den einzelnen Wirbelkörpern. Die durchschnittliche BMD betrug 96,4 mg/cm³. Im Gegensatz dazu ergab die opportunistische QCT, bei der das gesamte trabekuläre Volumen analysiert wurde, konsistentere BMD-Werte. Die absolute Messdifferenz zwischen den beiden Methoden betrug 17,6 mg/cm³ – die konventionelle QCT zeigte eine erniedrigte BMD an, während die opportunistische QCT eine osteoporotische BMD anzeigte. Bei der Patientin traten in den Nachuntersuchungen zwei Wirbelkörperfrakturen auf: die erste nach 6 Monaten auf Höhe von BWK5, die zweite nach 12 Monaten auf Höhe von BWK6. B Männlicher Patient (88 Jahre), mit relativ gleichmäßiger trabekulären Knochendichte (siehe Heatmap). Sowohl die konventionelle als auch die opportunistische QCT zeigen eine hohe Übereinstimmung, mit einer Differenz von 0,6 mg/cm³ zwischen den beiden Messungen.

error increased to 4.7% [45]. Notably, significant outliers in patients that showed signs of hydropic decompensation have been reported, which should be recognized as a clinical contraindication [45].

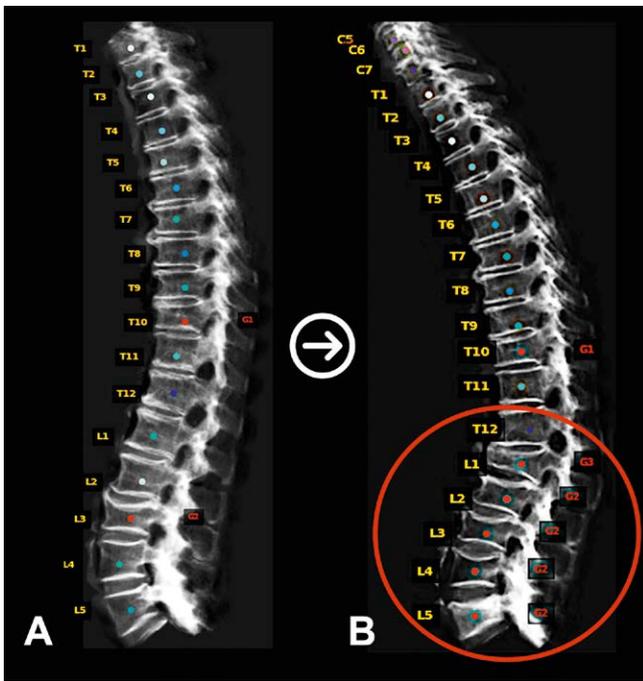
For longitudinal measurements, the least significant change (LSC), which is the smallest difference between two measurements that can be attributed to physiological changes in bone mass, is essential for distinguishing true biological change from measurement variability. In DXA, the LSC is considered small, as the LSC directly depends on the short-term precision error [46]. When the patient is scanned on the same DXA scanner, a change in BMD of approximately $\geq 5\%$ is typically regarded as a true (therapy-related) change [13]. In conventional QCT, LSC values are comparable to DXA, meaning conventional QCT can also be reliably used to monitor BMD [47]. However, the radiation dose is significantly higher compared to DXA. In opportunistic QCT, where scanner types, protocols, and patient positioning may vary, the measurement error is naturally higher. On the other hand, opportunistic QCT offers a cost-effective option [48], without additional examinations or radiation exposure. In controlled settings including sequential CT examinations using the same hardware and protocols, a reproducibility error comparable to that of DXA is likely achievable. However, such studies in bone-healthy populations are still lacking.

Thus, while DXA may be preferred for longitudinal follow-up due to its lower radiation dose and currently more standardized acquisition protocols, opportunistic QCT may also play an important role in the future, provided appropriate conditions are met.

Diagnostic Value of Opportunistic Osteoporosis Screening

Fracture Detection and Prediction of Fracture Risk

Prevalent VFs, particularly those of grade 2 or higher, represent one of the strongest risk gradients for predicting hip fractures and VFs over the subsequent three years [36]. Specifically, VFs can cause a change in spinal alignment and balance [49], which may impair coordination and lead to reduced mobility and, in turn, further increase the risk of falls [50, 51]. This substantially increased risk of subsequent fractures, particularly within the first year following the initial fracture [2], is recognized as an imminent risk factor in guidelines [4]. However, even in routine imaging at tertiary care hospitals, this clear indicator of poor bone health seems drastically underreported (► **Fig. 5**) [52]. Underreporting of VFs in routine clinical practice is most likely not primarily due to insufficient radi-



▶ **Fig. 5** Example case of a 69-year-old female patient with an oncological disease, who underwent computed tomography (CT) staging at baseline and follow-up, two years apart. **A** Retrospective analysis revealed two vertebral fractures (VFs) at T10 and L3 that were already present at baseline but were neither reported in the radiology reports nor documented in any medical records. No diagnosis of osteoporosis was made at that time. **B** Two years later, the patient had sustained multiple additional VFs at the lumbar spine, including a VF at L1 (Genant grade 3).

▶ **Abb. 5** Fallbeispiel einer 69-jährigen Patientin mit einer onkologischen Grunderkrankung, bei der im Abstand von zwei Jahren eine Staging-CT durchgeführt wurde. **A** Die retrospektive Analyse ergab zwei Wirbelkörperfrakturen auf Höhe von BWK10 und LWK3, die bereits in der initialen Untersuchung vorhanden waren, jedoch weder in den radiologischen Befunden erwähnt noch in den medizinischen Unterlagen dokumentiert wurden. Zu diesem Zeitpunkt wurde keine Osteoporose diagnostiziert. **B** Zwei Jahre später waren bei der Patientin bereits mehrere zusätzliche Wirbelkörperfrakturen an der Lendenwirbelsäule aufgetreten, darunter eine LWK1-Fraktur (Genant Grad 3).

ologist training or overlooked findings. Rather, osteoporosis has remained a niche topic within radiology and has not received widespread attention to date. Mild to moderate VFs are therefore frequently and incorrectly summarized as degenerative changes or not given adequate attention. Given the increasing workload, accelerated scan times, and the growing number of images per examination, a significant shift towards more consistent reporting of osteoporotic VFs appears unlikely. To improve the detection and reporting of VFs, automated fracture detection tools have been developed to assist in the systematic evaluation of the entire spine [15]. In a recent validation study, a CE-marked algorithm demonstrated good sensitivity (0.86) and high specificity (0.99) for detecting thoracolumbar VFs in 246 CT scans [53]. However, this study was limited to moderate to severe fractures (Genant grades 2 and 3) [53]. Another comparison study evaluated algorithm performance versus human raters including all fracture grades in 331

patients. Here, a CE-marked tool outperformed both residents and attending physicians in detecting any VF, as well as moderate to severe VFs, across vertebral-, regional-, and patient-level analyses [unpublished data].

Even more important than fracture detection is the prevention of fractures by risk assessment including BMD screening. Prospective studies in both sexes such as the Age Gene/Environment Susceptibility (AGES) Reykjavik Study and the Osteoporotic Fractures in Men Study (MrOS) have demonstrated that conventional QCT at the spine is at least equivalent to DXA in predicting VFs and may even offer superior predictive performance [54, 56]. As previously noted, comparing the consistency of diagnostic category classification between CT and DXA is not meaningful. Rather, the predictive performance of each modality should be directly evaluated. In a retrospective study, opportunistic QCT outperformed DXA in predicting incident VFs, with an AUC of 0.76 compared to a non-significant result based on DXA T-scores, in a cohort of 84 patients undergoing CT for indications unrelated to osteoporosis assessment [57]. In a larger prospective case-control study of AGES participants, opportunistically assessed BMD predicted incident VFs with a sensitivity of 0.79 and a specificity of 0.47 (for lumbar BMD $\leq 80 \text{ mg/cm}^3$) over an average follow-up period of five years [58]. Notably, the predictive performance remained nearly unchanged when lumbar BMD values were estimated from thoracic spine measurements (T8) via linear regression (sensitivity: 0.76, specificity: 0.44) [58]. A prospective cohort study in 1,487 patients undergoing cardiac CT found that age- and sex-adjusted thoracic BMD was independently associated with any osteoporotic-related fracture (hazard ratio = 4.0; 95% confidence interval [CI]: 1.1–14.6) [59]. In retrospective analyses, linear regression models applied to cervico-thoracic BMD also reliably predicted osteoporosis (as defined by lumbar BMD in the same patient) and the presence of prevalent VFs [60, 61]. In an analysis including over 22,000 participants of the National Lung Screening Trial (NLST), baseline BMD and baseline fractures were significantly and independently associated with incident VFs after one year. The relative risk (RR) for incident VFs after 2 years was 2.06 (CI: 1.70–2.52) for low bone mass and 3.52 (CI: 2.79–4.44) for osteoporotic BMD after adjusting for clinical risk factors (age, sex, body mass index, race, smoking status, alcohol consumption, comorbidities) and baseline vertebral fractures [unpublished data]. Thus, opportunistic BMD assessment in thoracic CT appears to be clinically meaningful and could potentially be integrated into routine workflows and other screening programs, such as low-dose lung cancer screening.

Most notably, a recent meta-analysis reported a pooled AUC of 0.76 (95% CI: 0.71–0.81) for opportunistically assessed BMD in predicting osteoporotic fractures (including hip fractures and VFs), which was significantly higher than the reported AUC for areal BMD (AUC = 0.73; 95% CI: 0.71–0.75; $p < 0.01$) [62].

Thus, with respect to fracture prediction at the spine, opportunistic BMD is at least non-inferior to DXA and may even provide advantages for VFs.

Other Practical use Applications with Clinical Value

Prevalence of osteoporosis is also high among elderly patients undergoing spine surgery [63, 65]. However, DXA is often not readily accessible prior to surgery, and a survey conducted among spine

surgeons showed that merely 44% of the queried surgeons opted for DXA examinations when osteoporosis was suspected prior to instrumented spinal fusion [66]. Lowered BMD is a risk factor for postoperative complications, including hardware failure, screw loosening, and adjacent segment disease (ASD) [67, 69]. Importantly, when osteoporosis is identified preoperatively, several risk mitigation strategies are available. For example, cement augmentation with polymethylmethacrylate (PMMA) or the use of extended instrumentation can be considered [70, 72]. Biomechanical ex-vivo studies have consistently demonstrated correlations between conventional QCT-based BMD and screw stability [73, 75]. In-vivo studies have correlated volumetric BMD from preoperative CT scans with the endpoint of postoperative screw loosening, concluding that opportunistic BMD measurements can also reliably predict between patients with and without this postoperative complication [76]. In a retrospective study involving 93 patients, opportunistically assessed BMD in preoperative CT was the most significant risk factor for loosened implants [77]. Notably, both the ex-vivo and in-vivo results closely matched the QCT threshold for osteoporosis according to the ACR criteria ($<80 \text{ mg/cm}^3$) [73, 76]. These findings highlight the potential of preoperative opportunistic QCT as a clinically valuable approach for surgical risk assessment and planning in osteoporotic patients.

Perspectives

Osteoporosis is an asymptomatic and, thus, challenging disease with the primary and only clinically noticeable endpoint of fractures that are associated with excess mortality [3]. Given that effective antiresorptive and osteoanabolic medications exist, primary and secondary prevention are major targets in osteoporosis management. The umbrella organization of the German-speaking Scientific Societies for Osteology (DVO) recommends a stepwise approach to osteoporosis diagnosis, where DXA-based screening is recommended if risk factors are present in postmenopausal women or men aged 50 or above [4]. On step further, the US Preventive Services Task Force (USPSTF) recommends universal screening in women 65 years or older using DXA BMD at central sites (hip or lumbar spine) and a 2-step approach to identify younger postmenopausal women eligible for screening [78]. While these updated recommendations present a clear commitment to X-ray based bone densitometry, they currently mention only DXA. Growing evidence supports reliable fracture prediction through calibrated opportunistic CT. Larger studies on heterogeneous populations with fracture endpoints and, potentially, treatment interventions could provide sufficient evidence for opportunistic bone densitometry to be included in clinical practice guidelines as an alternative screening test.

Conclusions

Opportunistic CT-based osteoporosis screening is feasible and can provide reliable bone mineral density measurements when technical standards are respected. Clinical validation studies have demonstrated successful integrations into routine care. The current evidence indicates that opportunistic CT-derived bone mineral density is at least non-inferior to DXA for the prediction of ver-

tebral fractures. Future practice guidelines should recognize and summarize best standard practices on opportunistic CT measurements of bone as an independent indication and alternative to DXA.

Fundref Information

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Conflict of Interest

JK and SR are co-founders of Bonescreen GmbH. All other authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Unpublished Data

Citations marked as unpublished data refer to data that have been submitted to peer-reviewed journals and are currently under review at the time of publication of this manuscript.

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