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► **To cite this version:**

Daphne Guenoun, Pierre Champsaur. Opportunistic Computed Tomography Screening for Osteoporosis and Fracture. *Seminars in Musculoskeletal Radiology*, 2023, 27 (04), pp.451-456. 10.1055/s-0043-1771037 . hal-04483077

HAL Id: hal-04483077

<https://hal.science/hal-04483077>

Submitted on 29 Feb 2024

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Opportunistic Computed Tomography Screening for Osteoporosis and Fracture

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Abstract

Keywords

- ▶ opportunistic computed tomography
- ▶ osteoporosis
- ▶ bone mineral density
- ▶ quantitative computed tomography
- ▶ asynchronous calibration

Osteoporosis is underdiagnosed and undertreated, leading to loss of treatment for the patient and high costs for the health care system. Routine thoracic and/or abdominal computed tomography (CT) performed for other indications can screen opportunistically for osteoporosis with no extra cost, time, or irradiation. Various methods can quantify fracture risk on opportunistic clinical CT: vertebral Hounsfield unit bone mineral density (BMD), usually of L1; BMD measurement with asynchronous or internal calibration; quantitative CT; bone texture assessment; and finite element analysis. Screening for osteoporosis and vertebral fractures on opportunistic CT is a promising approach, providing automated fracture risk scores by means of artificial intelligence, thus enabling earlier management.

The prevalence of osteoporosis and the economic impact of associated fracture due to bone insufficiency are increasing worldwide with the rapid aging of the population.^{1,2} Fracture risk screening most often associates clinical risk factor assessment and dual-energy X-ray absorptiometry (DEXA) to measure bone mineral density (BMD). Occurrence of osteoporotic fracture in distal radius, vertebrae, or proximal femur indicates a diagnosis of osteoporosis. However, despite the known morbidity incurred by osteoporotic fractures and the existence of guidelines for screening, osteoporosis continues to be underdiagnosed and undertreated.³⁻⁵

Routine thoracic and/or abdominal computed tomography (CT) performed for other indications can opportunistically screen for osteoporosis with no extra cost, time, or irradiation.⁶ Routine thoracic, abdominal, or spinal CT for various indications numbered 80 million in 2011 in the United States and 6 million in 2020 in the United Kingdom, 1 million of which were thoracoabdominal. The L1 vertebra is perfectly analyzable on scans obtained for clinical pur-

pose unrelated to osteoporosis and can be seen on both thoracic and abdominal scans.⁷

Detection of osteoporosis on opportunistic CT is different from traditional BMD assessment. Several methods have been described. The one that fits the best with the use of the term “opportunistic” is the direct use of Hounsfield units, consisting of analyzing them in the trabecular part of the vertebral body, generally on axial slices, and in detecting vertebral fracture, visually or automatically on dedicated artificial intelligence (AI) software.^{8,9} However, various inherent CT factors affect measurements: CT manufacturer and model, beam collimation width, and protocol (e.g., voltage, slice thickness, reconstruction algorithm, etc.). Thus these measurements are currently not much used in clinical routine.

Other options for opportunistic BMD assessment on clinical CT are the use of asynchronous calibration, in which the phantom is not measured simultaneously with the subject, or the use of internal calibration, where air and body tissues such as muscle, blood, or subcutaneous adipose tissue are used for BMD calibration.

Quantitative computed tomography (QCT) is challenging in BMD opportunistic screening because it uses an in-scan calibration to convert CT to BMD values, and acquisition and reconstruction parameters are highly standardized.¹⁰

In this article, we describe the various opportunistic CT detection methods for osteoporosis and vertebral fracture.

Opportunistic Computed Tomography Detection of Osteoporosis

We first address measurement of BMD in Hounsfield units (BMD_{HU}) that is the most promising for the opportunistic CT diagnosis of osteoporosis. Then we focus on CT measurements with asynchronous and internal calibration. Finally, we discuss other tools that can be used on opportunistic CT.

Vertebral Trabecular Bone Mineral Density in Hounsfield Units

Measurement Technique

BMD_{HU} measurement consists of measuring vertebral density in Hounsfield units on opportunistic CTs, with or without contrast enhancement, in a region of interest (ROI). Most studies have focused on L1, which conveniently is explored on all thoracic, abdominal, and spine CTs. It is also easy to identify, as the first vertebra without ribs, if only thoracic CT is available, has fewer degenerative changes than other lumbar vertebrae, and extrapolated BMD from its Hounsfield units is more closely related to BMD obtained by DEXA than from the other vertebrae.⁶ Although most studies on opportunistic screening have used results from a single vertebra, most often L1, an average of at least two nonfractured vertebrae, typically L1 and L2, is recommended to increase accuracy.¹⁰

For manual measurement, an oval ROI is positioned at the anterior part of L1, in the trabecular space, ideally on a native axial slice (→ Fig. 1). The sagittal plane can also be used but has been less widely reported.¹¹ Cortical bone, abnormalities and focal lesions, and artifacts should be excluded from the

ROI. Avoiding the center of the vertebra is also recommended because it may show excessive density on sagittal slices and excluding the basivertebral vein. An axial slice midway between the superior vertebral plate and the midline is generally used for measurement (→ Fig. 1). This method requires no specific experience and has good interobserver reproducibility.¹²

If fracture, tumor, cementoplasty, or fusion preclude measurement at L1, the ROI may be positioned above or below, at T12 or L2. AI software can sometimes make these BMD_{HU} measurements automatically.^{7,9,13}

Interpretation of Measurements

Interpreting BMD_{HU} results depends on several parameters:

- Make and model of CT scanner⁷;
- Acquisition technique, and notably voltage: In a given patient, the higher the voltage, the lower the BMD in Hounsfield units; studies tend to use 120 kV,^{6,7} and their thresholds cannot be extrapolated to scans using other tube voltages¹⁴;
- ROI position: Automatic positioning tends to increase BMD_{HU} by ~ 20 HU compared with manual positioning⁷;
- Contrast enhancement: Depending on the study, BMD_{HU} was unaffected by contrast medium injection in patients > 30 years of age⁷ or increased by ~ 20 HU,^{9,15} depending on time postinjection and the concentration of the contrast medium (→ Fig. 2)¹⁶;
- Age and sex: L1 BMD_{HU} decreases linearly with age; > 60 years of age, it is comparable between men and women.⁷

The threshold value to classify patients with or without fracture (vertebral or proximal end of femur) is 90 to 100 HU.^{6,11,17,18} L1 values < 90 HU indicate significantly greater fracture risk and the need to manage osteoporosis.¹⁷ Between 110 and 135 HU, patients may be considered osteopenic.¹⁷ Generally, the lower the Hounsfield unit density, the more severe the osteoporosis or at least the higher risk of a fracture cascade.¹⁹

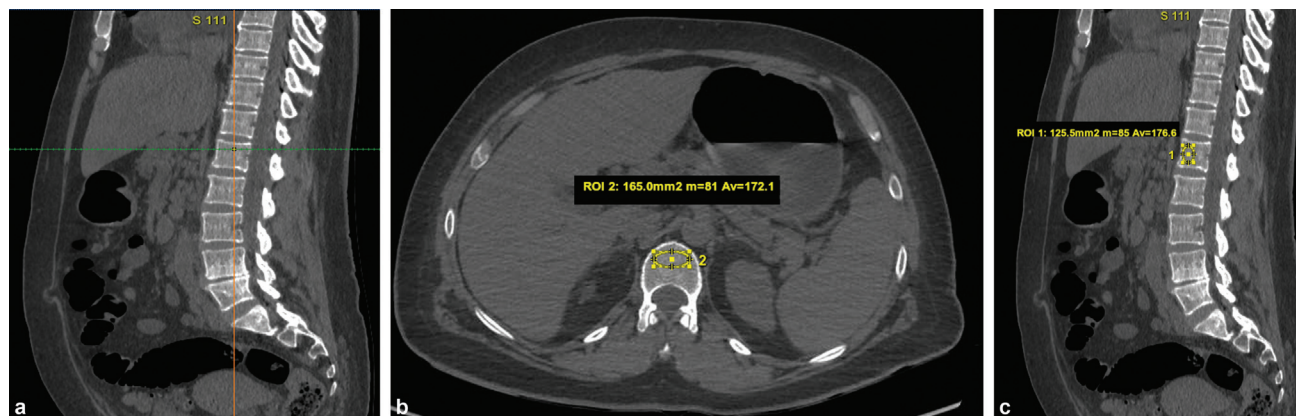


Fig. 1 Vertebral bone mineral density in Hounsfield units (BMD_{HU}) on opportunistic abdominal computed tomography without contrast enhancement in a 56-year-old woman. (a) Sagittal reconstruction: no fracture; the axial slice midway between the superior plate, and the midline locates L1. (b) L1 BMD_{HU} on native axial slice. At 172 HU, the patient is at very low risk of fracture. (c) BMD_{HU} can also be measured on sagittal reconstruction. ROI, region of interest.

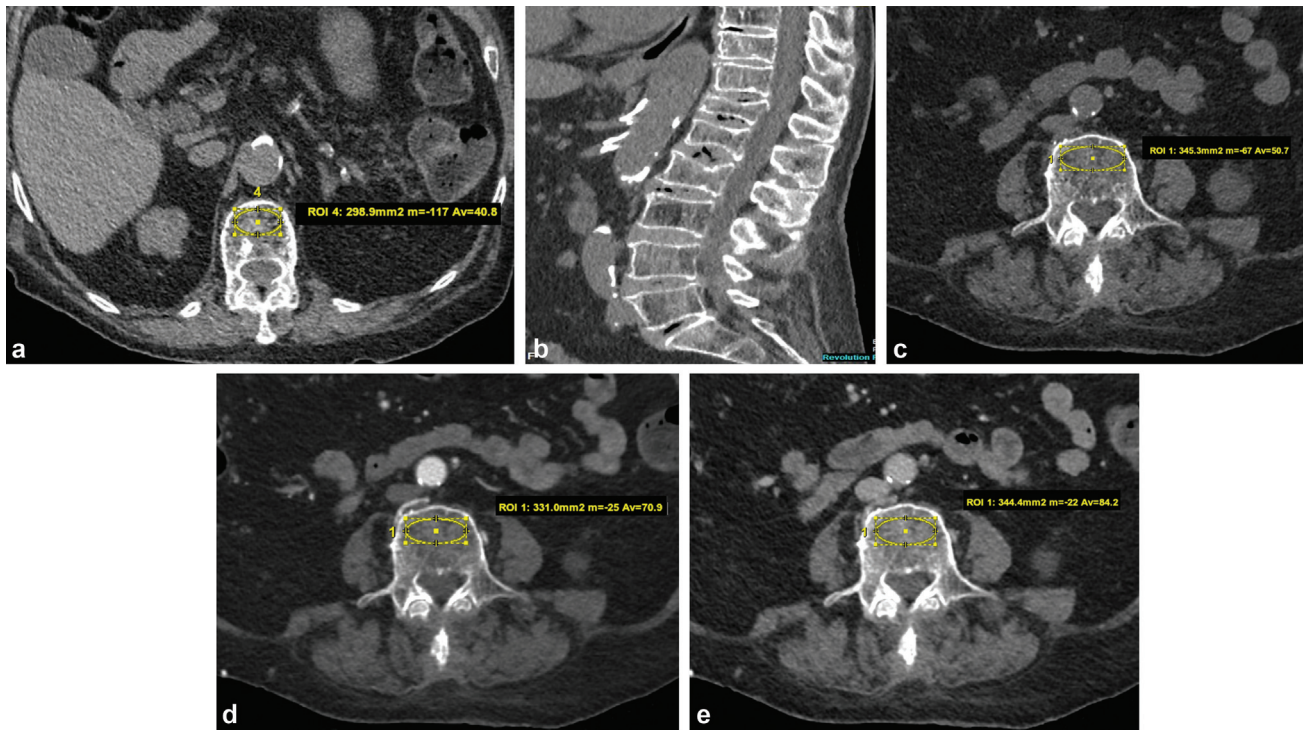


Fig. 2 Vertebral bone mineral density in Hounsfield units (BMD_{HU}) in opportunistic abdominal computed tomography with and without contrast enhancement in a 96-year-old woman. (a) Native axial slice. L1 BMD_{HU} , 40 HU: that is, high risk of fracture. (b) Sagittal reconstructions show fractures in T12, L1, L2, and angioma in L3. The vertebral fractures indicate osteoporosis. BMD_{HU} must be measured in unfractured vertebrae. (c) L4 BMD_{HU} without contrast enhancement: 50 HU. (d) L4 BMD_{HU} with contrast enhancement in the arterial phase: 70 HU. (e) L4 BMD_{HU} with contrast enhancement in the portal phase: 84 HU. BMD_{HU} increased after contrast medium injection and according to time after injection. ROI, region of interest.

Opportunistic Quantitative Computed Tomography and Asynchronous or Internal Calibration

QCT uses standard calibration to convert Hounsfield units into BMD (mg/cm^3). An in-scan calibration phantom is placed beneath the patient during acquisition, for calibration, containing materials representing various BMD values. Hydroxyapatite or potassium phosphate are often used as standards of reference. Based on three-dimensional (3D) acquisition, QCT has the advantage of being unaffected by bone degeneration and distinguishes trabecular from cortical bone, but it is only available in a few centers in France. It is costly and comes with additional radiation because a separate CT is needed to obtain BMD.⁸

BMD can be measured on QCT in the lumbar region (L1–L4) or in the proximal femur. On QCT, osteoporosis is defined by $BMD < 80 mg/cm^3$ and osteopenia by BMD between 80 and $\leq 120 mg/cm^3$.⁸ Unfortunately, in opportunistic screening, most QCT conditions (in-scan calibration phantom, acquisition and reconstruction standardization, absence of contrast agent) cannot be respected. Thus to use routine CT for risk assessment in osteoporosis, several new techniques were developed without a calibration phantom measured simultaneously with the subject, such as asynchronous calibration and internal calibration.

In asynchronous calibration, a calibration phantom is measured separately from the subject, for example once a week or once a month.¹⁹ The CT value-to-BMD calibration procedure is the same as for simultaneous calibration.¹⁰ The

main factors to consider for calibration are the tube voltage and the scanner model.²⁰ Löffler et al, in a cohort of 84 patients aged > 50 years, showed that volumetric BMD (vBMD) on opportunistic CT using asynchronous calibration was associated with a risk of vertebral fracture, whereas BMD on DEXA was not.²¹

Leonhardt et al (2020), in a cohort of 58 patients, reported that opportunistic CT based on BMD measurements with asynchronous calibration was a valid tool to predict osteoporotic fractures during a 3-year follow-up.²² Dieckmeyer et al performed an HU-to-vBMD conversion using asynchronous calibration based on kilovolt (peak) and scanner-specific equations. Automated detection and correction of the presence of contrast agent and the contrast phase was implemented.²³ They found that automated opportunistic osteoporosis screening of vBMD along the entire thoracolumbar spine allows for risk assessment of imminent vertebral fracture and proposed a level-specific vBMD threshold at the thoracolumbar spine to identify individuals at high fracture risk.²³

Internal calibration, also called patient-specific phantom-less calibration, uses the patient's own internal tissues as a calibrating reference material.²⁴ Internal density calibration uses in-scan ROIs to determine a voxel-specific density calibration. Different techniques to calculate the linear calibration equation from CT values to BMD exist: ROIs of air and blood or fat have been paired with developed reference values of equivalent BMD to determine a scan-specific density calibration.²⁴ A regression model for the phantom-less

HU-to-BMD conversion including patient physical factors has been proposed.²⁵

BMD calibration based on the linear correlation between measured CT values of internal tissues and their known density absorption coefficients have been evaluated.²⁶ Internal calibration has the advantages of eliminating the requirement of additional clinical resources and time for performing calibration scans, and it is less affected by patient size than simultaneous calibration and by X-ray field inhomogeneity.

Nevertheless, workflow is not yet implemented in clinical routine that limits the use of asynchronous and internal calibration.

Other Potential Tools for Opportunistic Screening: Bone Texture and Finite Element

Bone texture provides information on trabecular bone quality via mathematical formulations and algorithms.²⁶ It is an indirect representation of bone microarchitecture.

Image texture corresponds to the spatial distribution of intensity, enabling analysis of pixel distribution. There are first-order and second-order parameters.²⁷ With a ROI in the vertebral body as for BMD_{HU} ,¹⁸ or in the proximal femur in the trochanteric or neck region,²⁸ the software calculates the bone texture elements degraded by osteoporosis. Texture parameters associated with BMD_{HU} differentiate between patients with and without vertebral fracture in opportunistic magnetic resonance imaging and CT.¹⁸ Texture can also be assessed automatically in vertebrae.^{29,30} Bone texture is a useful way to improve detection of osteoporosis on opportunistic CT, but it is not yet widely used outside research because it requires dedicated software.

It is also possible to simulate biomechanical tests on 3D CT volumes, using finite element (FE) models. This method is widely used in biomechanics and derived from mathematics and information theory. FE allows access to the biomechanical properties of bone noninvasively and in vivo, and it can help identify patients at risk of proximal femoral fracture.³¹ Vertebral FE on opportunistic abdominal CT can also assess fracture risk.³² However, FE requires dedicated hardware and software, limiting its routine application.

Opportunistic CT and Detection of Fracture by Bone Fragility

In reading thoracic and abdominal CTs, radiologists almost always use 3D reconstruction with a bone window to screen for associated bone lesions. This technique can detect vertebral fractures that were clinically overlooked because they are painless and not associated with any trauma. Without reconstruction, these vertebral fractures cannot be detected. Other osteoporotic fractures, in the hip or distal radius, are painful and/or cause functional impairment, and they are thus easily diagnosed clinically and radiologically. The aim is thus to enhance detection of vertebral fractures that were overlooked on CT performed for another indication, to improve early diagnosis of osteoporosis, initiate treatment, and avoid future fractures.

Burns et al reported an AI package for automatic detection of vertebral fractures on spinal CT, with very good sensitivity (98.7%) and good specificity (77.3%), in a cohort of 150 patients.³³ The software also classifies fractures according to Genant's scheme or a score for semiquantitative fracture assessment.³³ It allows automatic segmentation of the spine and detects the superior and inferior plates of each vertebra and calculates height compared with adjacent vertebrae. The drawback is that it does not extend to thoracic and abdominal scans, which are of prime interest for opportunistic detection of vertebral fractures.

Tomita et al used a deep convolutional neural network to extract CT data slice by slice after training on 1,432 opportunistic thoraco-abdominopelvic (TAP) scans with sagittal reconstructions; 713 showed fractures and 719 did not (sensitivity: 85.2%; specificity: 95.8%).³⁴ The system does not require vertebral segmentation and uses all slices (useful in spinal deformity such as scoliosis) with a very short

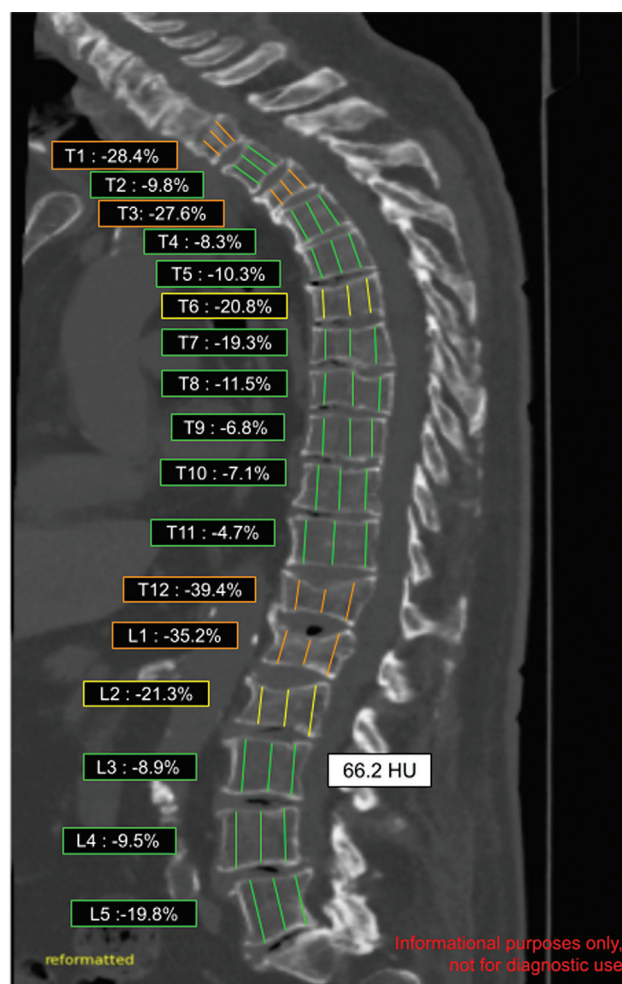


Fig. 3 Automatic detection in opportunistic thoracoabdominal computed tomography. Automatic segmentation and sagittal measurement of vertebral height in the anterior, middle, and posterior parts of the vertebral body. The three measurements were compared within the vertebra and with adjacent vertebrae. Percentage height loss was reported. Density in Hounsfield units was measured in L3 because L1 and L2 were fractured. (Note: Image derived from Avicenna Medical Systems' posttreatment software, not yet on the market.)

acquisition time of 0.02 seconds. It can only use TAP scans and, to our knowledge, cannot be applied to opportunistic thoracic- or abdominal-only scans. Other tools are under development for application not only with TAP but also thoracic, abdominal, and lumbar scans (►Fig. 3).

Conclusion

Osteoporosis is underdiagnosed and undertreated; lack of diagnosis and treatment constitutes a loss of treatment for the patient and high costs for the health system. Screening for osteoporosis and vertebral fracture on opportunistic CT is a promising approach that could offer risk scores automatically in the imaging report. AI has an integral part to play in this screening strategy. Now a plan should be established. The detection of osteoporosis and vertebral fractures is just the beginning of a long process to the appropriate treatment, and currently there is no (or only a few) organized processes. However, there is a lack of evidence that opportunistic screening significantly reduces the rate of fracture, and economic studies are needed.

Conflict of Interest

None declared.

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