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Original Investigation

Thoracic Quantitative Computed Tomography (QCT) Can Sensitively Monitor Bone Mineral Metabolism: Comparison of Thoracic QCT vs Lumbar QCT and Dual-energy X-ray Absorptiometry in Detection of Age-relative Change in Bone Mineral Density

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Rationale and Objective: Sensitive detection of bone mineral density (BMD) change is a key issue to monitor and evaluate the individual bone health status, as well as bone metabolism and bone mineral status. The ability to use thoracic quantitative computed tomography (QCT) to detect the annual change of BMD remains unclear. We aimed to investigate the sensitivity in detecting age-related bone mineral loss using the thoracic QCT from the electrocardiographically gated heart scans in comparison to whole-body dual-energy X-ray absorptiometry (DXA) and standard lumbar QCT.

Materials and Methods: A total of 121 asymptomatic patients' imaging data, including DXA whole body scan, cardiac CT scan, and abdomen scans were analyzed. The BMD of the thoracolumbar spine, upper, and lower extremities were measured using QCT and DXA, respectively. The age-related annual rate of bone density loss was computed and compared to the thoracic and lumbar QCT, as well DXA measures.

Results: The age-related annual rate of bone loss with QCT was –0.70 mg/mL^3 (–0.75%/y) in women, –0.83 mg/mL^3 (–0.86%/y) in men in the thoracic and the lumbar trabecular QCT, respectively. Compared to the QCT, DXA demonstrates a lower annual rate of bone loss in the area of BMD measurement ($P < .05$ in all, excluding legs of women) in –0.45, –0.42, –0.67, and –0.46 in women, in –0.32, –0.02, –0.12, and –0.08 in men for thoracic, lumbar, leg, and arm, respectively.

Conclusion: We conclude that the thoracic and the lumbar QCT provide a similar and more sensitive method for detecting bone mineral loss when compared to DXA.

Key Words: Quantitative computed tomography (QCT); dual-energy X-ray absorptiometry (DXA); bone mineral density (BMD); osteoporosis; bone density annual loss rate.

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INTRODUCTION

Bone fracture and cardiovascular disease are two of the most common diseases and strongly associated with high morbidity and mortality. Osteoporosis and coronary atherosclerosis are crucial independent risk factors for bone fracture and cardiovascular disease, respectively (1,2), and both can be detected by quantitative computed tomography (QCT) using a low-dose cardiac CT-produced image (3–5). Given that the importance of using QCT to assess bone mineral density (BMD) of the spine may be a potentially diagnostic tool for osteoporosis-related vertebral fractures, several initial studies have indicated that the lumbar QCT is robust for the detection of osteoporosis, and BMD change can be more sensitively detected with serial scans (6,7). As a matter of fact, some preliminary thoracic QCT data from a routine lung or heart scan have indicated its compatibility with the lumbar QCT (3,8,9) even if the sensitivity to detect the annual loss rate of BMD with the thoracic QCT remains unclear. In this study, we aimed to evaluate the ability to detect the age-related annual rate of bone loss by the thoracic QCT with an electrocardiographically gated routine heart scan in comparison to whole-body double-energy densitometry (DXA) and lumbar QCT.

SUBJECT AND METHODS

Study Population

This chart review retrospective study comprises a total of 121 (56, 20–81 years) asymptomatic patients who underwent DXA whole-body and CT heart and abdomen scans on the same day. The aims of the study were the quantification of coronary calcified burden and examination of body composition, including bone mineral content (BMC), BMD, and percentage of the body fat and fat-free mass. The exclusion criteria are patients with metal implement in the thoracolumbar spine (only one case). All patients had optimal CT and DXA images with no significant noise or metal artifact.

CT Scan Technique

The study used a GE 64-detector CT scanner (LightSpeed VCT, General Electric Medical System, Milwaukee, WI) and an electron-beam tomography scanner (C-150, GE-Imatron, South San Francisco, CA) (3,4).

The CT coronary artery calcium scan parameters were 120 kVp, 200–600 mA in current, and 350 ms in gantry per rotation times. The collimation was 0.625 mm × 64 with a reconstruction thickness of 2.5 mm using a standard kernel. Prospective gating was used at 75% of relative risk interval. The radiation dose was 1.1 mSv in average per study.

For lumbar QCT scan, the helical technique was used with 2.5 mm reconstruction slice thickness, automatic changeable current from 200 to 700 mA (dose modulation), the pitch of 1.375 and 500 ms in gantry per rotation speed. At least three lumbar (L1–L3) vertebrae were covered in all these scans. The radiation dose was 4.8 mSv in average. The imaging reconstruction field of view was 35–40 cm in range. A CT calibration phantom (Image Analysis, Inc, Columbia, KY) was used for all scans. The phantom has four rods with calcium hydroxyapatite in 0, 50, 100, 200 mg/cm^3, respectively.

QCT BMD Measurement, Coronary Calcium Burden Quantification, and Investigation in Spine Degenerative Change

The trabecular BMD of the three consecutive thoracic (from left main coronary level) and lumbar (L1–L3) vertebrae were measured using a Q5000 workstation (Image Analysis, Inc) described by the prior studies (3–5). The thickness of a region of interest used by the computer was 10 mm. After clicking the center of a given vertebra, the value of bone density (mg/cm^3) for the individual vertebra can be displayed automatically. In the cortical bone, an area with island bone, a fractured spine was excluded as much as possible from the region of interest by using the manual free tracing protocol (Fig 1a and 1b).

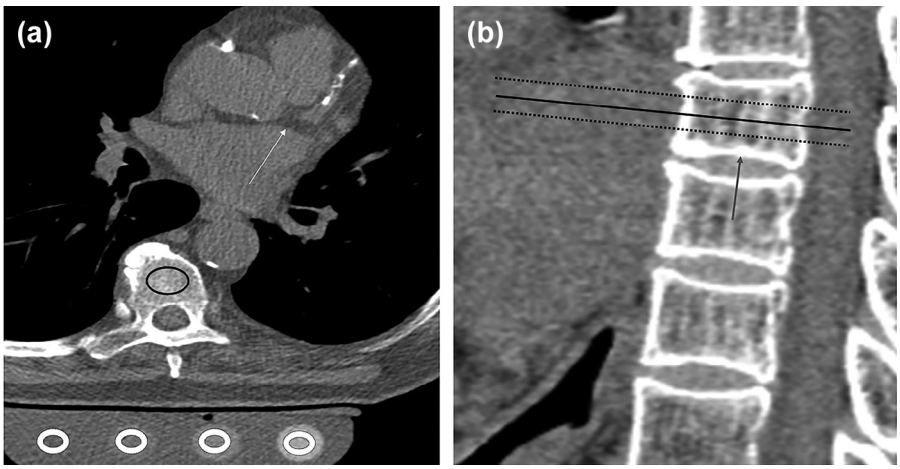

Figure 1. QCT BMD measurement. **(a)** (Panel 1) and **(b)** (Panel 2) are axial and sagittal chest images with a four-rods calibration phantom (bottom of the panel 1, *white circles*). The three consecutive thoracic trabecular tracing was performed from the slice level of left main coronary artery caudally (*white arrow* on panel 1, or *black* line and *arrow* on panel 2) from a CT heart scan of a 60-year-old man. After selection of a spine level, the segmentation of phantom rods and trabeculae were completed automatically by computer. The calibrated thoracic BMD (mg/cm^3) can be displayed automatically. The Q5000 system was used in this measurement. BMD, bone mineral density; CT, computed tomography; QCT, quantitative computed tomography.

The calcium burden quantification of coronaries and aorta was evaluated by using the Agatston score method. The degenerative change of the spine and relative tissue was observed and recorded, including osteophyte, disc, and ligament calcification. All assessments were performed by two skilled physicians with 10 years of cardiac CT experience (YLG and SSM) described by the prior studies using an Advantage Workstation system (version 4.6, GE Medical Systems, Milwaukee, WI).

Whole-body DXA Scans and BMD Measurement

A whole-body DXA scan was performed by using a fan beam scanner with a posterior-anterior projection (QDR 4500, Hologic Inc, Waltham, MA; enhanced whole-body, software version 11.2). The DXA scanner was maintained according to the manufacturer's recommendations, including the performance of daily quality control calibrations. The scan procedure included an auto-centering routine to ensure the spine was centered and straight in the scan area. A standard whole-body composition examination was completed in all cases with a radiation dose less <0.01 mSv. The DXA scans provided the values of the body composition and bone density measures for the arms, legs, ribs, pelvis, thoracic and lumbar spine, head, subtotal regions, and total body.

The values of the BMD included the bone area (cm^2), BMC (g), and aBMD (g/cm^2). The mean value of both symmetric structures (arm and leg) was used in this study. The T-scores of all individual sites and subtotal regions were calculated by using the National Health and Nutrition Examination Survey II (NHANES II) reference values (10). This retrospective chart review studied no more than minimal risk to the subject. This study received a local Institutional Review Board waiver of the consent process.

ANALYSIS

All parameters were represented as mean values. The age-relative annual rate of bone loss was defined as difference per year with the reference value at age of 20–29 years by NHANES (10), Budoff et al. (3) for thoracic QCT (215 mg/cm^3 in men and 220 mg/cm^3 in women), and was computed using the following formula: (individual BMD or aBMD − reference BMD or aBMD)/reference BMD or aBMD/y interval to 29 years × 100%). The individual T-score in DXA or QCT was calculated using same reference values described earlier (3,10). Because high association exists between the BMD values of thoracic and lumbar QCT in both genders ($r > 0.95$, $P < .001$), the thoracic reference value of Budoff et al.'s data (3) was used to calculate the loss rate for the lumbar QCT, using the thoracic equivalent values with the following formulas: $Y = 1.0494 \times \text{lumbar BMD} + 28.0\ mg/cm^3$ in women, $Y = 1.2364 \times \text{lumbar BMD} - 7.9\ mg/cm^3$ in men. The formulas were obtained from the progression analysis based on data from this study. Parameters of DXA measures, which were used more commonly, are investigated in this study, including thoracic, lumbar, leg, and arm measurement.

The gender-specific three subgroups (<50, 50–64, and ≥65years) were divided. The analysis of variance and Student *t* test were used to estimate the difference within groups in BMD and within thoracic QCT and DXA or lumbar QCT in the loss rate. The patient's weight was adjusted to test the difference in BMD assessment within age groups. The Pearson correlations were used to estimate the association between age or patient's weight and individual BMD assessments. All data analyses were conducted with SAS software, version 9.4 (SAS Inc., Cary, NC), and statistical significance levels for all tests were set at a two-tailed *P* value <.05.

RESULTS

Table 1 shows the demographic characteristics over genders, including coronary calcium score, percentage of BMC, body fat, and fat-free mass. The age-related annual rate of BMD loss with the QCT was −0.70 and −0.75%/y ($P < .01$) in women, −0.83 and −0.86 ($P < .01$) in men in the thoracic and lumbar QCT, respectively. Compared to the QCT, the DXA demonstrates a lower annual rate of BMD loss ($P < .05$ in all, excluding leg in women) in −0.45, −0.42, −0.67, and −0.46 in women, in −0.32, −0.02, −0.12, and −0.08 in men for thoracic, lumbar, leg, and arm measurements, respectively (shown in Table 2).

A significant reverse linear correlation between BMD and age was found in both thoracic and lumbar QCT (r value from −0.45 to −0.62, $P < .01$) in both genders, but not in the DXA, excepting the legs in women ($r = -0.27$, $P < .05$). A significant positive association was shown between patient's weight and BMD accessed from DXA in all measures (excepting arms of women), but not in the QCT, except in the thoracic measure in women ($r = 0.26$, $P < .05$) (shown in Table 3).

A significantly lower bone density exists in the aging population of both genders with both thoracic and lumbar QCT

TABLE 1. Demographic Characteristics Over Genders

	Female (*n* = 60)	Male (*n* = 61)
Age (y)	57.7 ± 11.8	55.7 ± 11.9
Race, %		
Caucasian	4.5	5.5
Hispanic	34.1	34.5
African-American	52.3	47.3
Asian	9.1	12.7
Height (cm)	158.5 ± 9.5	170.4 ± 11.0
Weight (kg)	71.4 ± 17.2	86.5 ± 20.1
Body mass index (kg/m^2)	28.1 ± 5.4	26.8 ± 5.2
Agatston score	109 ± 313	377 ± 512
Total fat percentage (%)	36.2 ± 7.9	25.0 ± 7.9
Total free-rat mass (%)	61.0 ± 7.6	71.9 ± 7.6
Total bone mineral content (%)	2.7 ± 0.5	3.0 ± 0.5

TABLE 2. The Age-related Annual Rate of Bone Loses (%/y) Over Genders with QCT and DXA

	Female (n = 60)		Male (n = 61)	
	β	95% CI	β	95% CI
QCT Thoracic TRAB, %/y	–0.70	–2.50,1.11	–0.83	–3.12,1.47
QCT Lumbar TRAB,%/y	–0.75	–2.22,0.74	–0.86	–2.7,0.97
DXA Thoracic, %/y	–0.45*	–1.67,0.92	–0.32†	–2.41,1.77
DXA Lumbar, %/y	–0.42*	–1.45,0.75	–0.02†	–0.24,0.19
DXA Legs, %/y	–0.67	–1.90,0.56	–0.12†	–0.31,0.08
DXA Arms, %/y	–0.46*	–0.57,0.65	–0.08†	–0.24,0.07

CI, confidence interval; DXA, dual-energy X-ray absorptiometry; QCT, quantitative computed tomography; TQCT, thoracic quantitative computed tomography; TRAB, trabecular bone.

* $P < .05$.

† $P < .01$, in comparing the annual rate of bone loss to TQCT.

TABLE 3. The Correlation Between BMD Assessment and Weight or Age

	Female		Male	
	Weight	Age	Weight	Age
QCT Thoracic TRAB	0.26*	–0.55†	0.07	–0.47†
QCT Lumbar TRAB	0.02	–0.62†	0.08	–0.45†
DXA Thoracic	0.50†	–0.13	0.41†	0.27*
DXA Lumbar	0.55†	–0.25	0.34†	0.30*
DXA Legs	0.34†	–0.27*	0.36†	0.04
DXA Arms	0.23	–0.19	0.32†	0.14

BMD, bone mineral densaity; DXA, dual-energy X-ray absorptiometry; QCT, quantitative computed tomography; TRAB, trabecular bone.

* $P < .05$.

† $P < .01$.

($P < .05$), but not in all DXA, excepting the lumbar measure in women ($P = .046$) (shown in Tables 4 and 5).

Compared to lumbar spine, a significant higher BMD was noted in thoracic QCT, but reversely in DXA measures ($P < .001$, shown in Tables 4 and 5).

Overall, the thoracic QCT displays a significantly higher age-based annual change of BMD than most sites of DXA ($P < .01$), and a similar result in comparison to the lumbar QCT (Fig 2).

With the CT observation, 63.9% of women and 75.3% of men has a calcification of coronary arteries, aorta, or other organs within the chest or abdomen, and 17.3% of women and 29.5% of men have an osteophyte in the thoracolumbar spine, known confounds to measures of aBMD with DXA. The subjects over 60 years have over two fords of calcification or osteophyte compared to cases of less than 50 years.

DISCUSSION

At present, hip and lumbar central DXA is a major technique in BMD assessment. The lumbar QCT has been generally recommended as analogous to central DXA technologies in assessing or monitoring ages, disease- and treatment-related BMD changes (11). The thoracic QCT from a no BMD-aimed CT scan was also used in bone mineral assessment as an additional application (3,4). The sensitivity to detect the age-related bone density change associated strongly with the ability to evaluate the bone status in patients with mineral metabolites disorders. It is also relative to the management of bone health in aging populations. Studies on the ability to detect the annual rate of BMD loss have been reported with DXA, lumbar QCT, and peripheral QCT (6,7,12). Results of investigations indicated that the lumbar spine contains an abundance of trabecular tissue, consisting of 66%–99% of total bone. The trabeculae is a more sensitive structure in the bone

TABLE 4. Bone Mineral Density and T-score of Women Across Age Categories

		Age (Y)			
	Total (n = 60)	<50 (n = 14)	50–64 (n = 24)	≥65 (n = 22)	Trend P Value
QCT Thoracic TRAB (mg/cc)	172.1 ± 53.2	216.4 ± 41.3	178.4 ± 52.6	137.0 ± 33.1	<.001
QCT Thoracic T-score	–1.2 ± 1.7	0.0 ± 1.5	–1.1 ± 1.5	–2.4 ± 0.9	<.001
QCT Lumbar TRAB (mg/cc)	133.9 ± 42.5	174.8 ± 31.8	139.5 ± 31.0	108.4 ± 38.5	<.001
QCT Lumbar T-score	–1.2 ± 1.7	–0.2 ± 1.6	–1.3 ± 1.0	–2.2 ± 1.3	<.001
DXA Thoracic (g/cm^2)	0.75 ± 0.12	0.75 ± 0.12	0.78 ± 0.12	0.72 ± 0.09	.462
DXA Thoracic T-score	–1.1 ± 1.2	–1.0 ± 1.3	–0.9 ± 1.3	–1.5 ± 0.8	.231
DXA Lumbar (g/cm^2)	0.98 ± 0.16	1.00 ± 0.15	1.02 ± 0.14	0.91 ± 0.12	.046
DXA Lumbar T-score	–0.8 ± 1.2	–0.6 ± 1.2	–0.6 ± 1.3	–1.3 ± 1.3	.062
DXA Legs (g/cm^2)	0.95 ± 0.15	0.99 ± 0.15	0.97 ± 0.13	0.92 ± 0.15	.193
DXA Legs T-score	–1.8 ± 1.4	–1.6 ± 1.4	–1.7 ± 1.4	–2.1 ± 1.3	.363
DXA Arms (g/cm^2)	0.64 ± 0.10	0.67 ± 0.08	0.65 ± 0.08	0.62 ± 0.1.2	.222
DXA Arms T-score	–1.5 ± 1.2	–1.0 ± 1.3	–1.4 ± 1.1	–1.9 ± 1.1	.052

DXA, dual-energy X-ray absorptiometry; QCT, quantitative computed tomography; TRAB, trabecular bone.
The patient's weight was adjusted when the difference within groups was tested.

TABLE 5. Bone Mineral Density and T-score of Men Across Age Categories

		Age (Y)			
	Total (n = 61)	<50 (n = 23)	50–64 (n = 25)	≥65 (n = 13)	Trend P Value
QCT Thoracic TRAB (mg/mL^3)	174.3 ± 55.3	198.8 ± 54.9	168.0 ± 51.5	143.3 ± 42.0	.003
QCT Thoracic T-score	–1.2 ± 1.5	–0.2 ± 1.4	–1.4 ± 1.3	–2.2 ± 0.9	<.001
QCT Lumbar TRAB (mg/mL^3)	131.9 ± 39.4	142.7 ± 40.3	138.7 ± 41.9	116.4 ± 34.4	.042
QCT Lumbar T-score	–1.4 ± 1.0	–0.1 ± 1.3	–1.1 ± 0.8	–2.0 ± 0.7	<.001
DXA Thoracic (g/cm^2)	0.84 ± 0.12	0.82 ± 0.09	0.84 ± 0.14	0.88 ± 0.16	.242
DXA Thoracic T-score	–0.4 ± 1.3	–0.7 ± 1.0	–0.3 ± 1.2	0.0 ± 1.6	.014
DXA Lumbar (g/cm^2)	1.04 ± 0.16	1.03 ± 0.14	1.01 ± 0.17	1.10 ± 0.15	.213
DXA Lumbar T-score	–0.2 ± 1.2	–0.4 ± 1.0	–0.3 ± 1.3	0.2 ± 1.1	.113
DXA Legs (g/cm^2)	1.12 ± 0.14	1.13 ± 0.12	1.10 ± 0.15	1.09 ± 0.13	.737
DXA Legs T-score	–1.5 ± 1.0	–1.4 ± 0.8	–1.6 ± 1.1	–1.6 ± 1.0	.655
DXA Arms (g/cm^2)	0.78 ± 0.08	0.78 ± 0.08	0.76 ± 0.09	0.76 ± 0.07	.315
DXA Arms T-score	–1.4 ± 1.0	–1.2 ± 1.1	–1.5 ± 1.0	–1.5 ± 1.0	.421

DXA, dual-energy X-ray absorptiometry; QCT, quantitative computed tomography; TRAB, trabecular bone.
The patient's weight was adjusted when the difference within groups was tested.

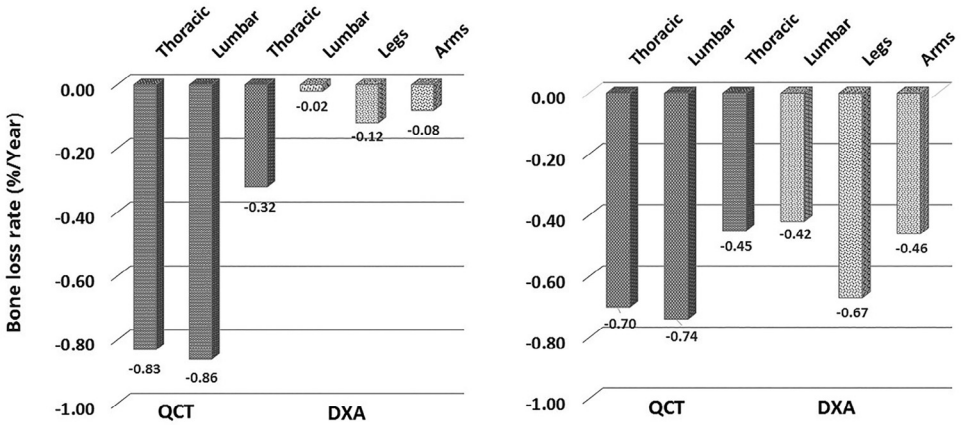

Figure 2. Comparison of QCT and DXA in the age-related annual loss rate of bone in women (left panel) and men (right panel). DXA, dual-energy X-ray absorptiometry; QCT, quantitative computed tomography.

metabolism and an optimal site to monitor the bone status (13). QCT is a unique ability to distinguish the trabecular and the cortical bone, and the lumbar QCT is of high sensitivity to detect bone mineral loss when compared to the DXA (6,7,12,13). With this thoracolumbar QCT and DXA study, the authors investigated the relationship between BMD and age, and bone loss rate with aging in multiple sites. The present study's results are similar to those of previous studies in lumbar QCT (6,7,12,13) and thoracic measures (14) in which authors reviewed a population-based data by Budoff et al. (3) and NHANES III (10) and found that that there is a higher loss rate in thoracic bone by QCT than DXA. Also, the study result validates that the thoracic QCT, with an electrocardiographically gated heart scan, has a similar ability to routine lumbar QCT in assessing bone loss rate.

The whole-body DXA scan is commonly used to examine the composition of lean and fat tissue, as well as bone in individual sites, and is also used for subregional analyses and total body assessments (11). When the regional DXA is used, a significant correlation, mild decrease precision, and underestimation in the BMD assessment was noted compared to when the whole-body DXA is used (15–18). Therefore, it is reasonable to obtain a comparable annual loss rate using both the regional and whole-body DXA assessments and to derive this validation study for the thoracic QCT.

The study results show that a significant association existed between patient's weight and BMD in DXA measures, and only a weak correlation in thoracic QCT in women. Therefore, change of patient's weight may be a factor affecting the estimation of bone loss rate.

Even after adjusting the patient's weight, no significant decrease of BMD was found in most aging groups with DXA. Hypothetically, the high degree of calcification of organs and vessels, and osteophyte of spines in aging subjects, may falsely elevate DXA results in the elderly, excepting patient's weight. This result is similar to prior studies (19,20). This result implies that given the environmental condition of the spine, the QCT is a effective method of monitoring BMD. The patient's weight,

the girth of the abdomen, and the degenerative change must be considered with DXA BMD assessment.

LIMITATION

First, the age-related annual rate of bone loss with DXA is affected by numerous confounding factors, such as a degenerative change in the spine and organs, and a variation in body size. In the cross-sectional study, these factors cannot be adjusted effectively. This is an important reason in reducing bone loss rate with DXA. The effect of these artifacts may be decreased if longitudinal measures are used in place of cross-sectional measures. Again, no scan of a regional hip and lumbar DXA was available for our study. The results may be improved when high-resolution regional DXA images are used. This is another limitation of the study.

CONCLUSION

With this validation study, the age-related annual rate of BMD loss was evaluated using the thoracic QCT with a heart scan, and was compared to the whole-body DXA and the lumbar QCT. We conclude that thoracic and the lumbar QCT provide a similar and more sensitive method for detecting bone mineral loss when compared to whole-body DXA. The thoracic QCT may be recommended as a method to assess and monitor bone mineral metabolism using routine chest CT scan.

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