Is multidetector CT-based bone mineral density and quantitative bone microstructure assessment at the spine still feasible using ultra-low tube current and sparse sampling?

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Abstract
Objective Osteoporosis diagnosis using multidetector CT (MDCT) is limited to relatively high radiation exposure. We investigated the effect of simulated ultra-low-dose protocols on in-vivo bone mineral density (BMD) and quantitative trabecular bone assessment.

Materials and methods Institutional review board approval was obtained. Twelve subjects with osteoporotic vertebral fractures and 12 age- and gender-matched controls undergoing routine thoracic and abdominal MDCT were included (average effective dose: 10 mSv). Ultra-low radiation examinations were achieved by simulating lower tube currents and sparse samplings at 50%, 25% and 10% of the original dose. BMD and trabecular bone parameters were extracted in T10–L5.

Results Except for BMD measurements in sparse sampling data, absolute values of all parameters derived from ultra-low-dose data were significantly different from those derived from original dose images (p<0.05). BMD, apparent bone fraction and trabecular thickness were still consistently lower in subjects with than in those without fractures (p<0.05).

Conclusion In ultra-low-dose scans, BMD and microstructure parameters were able to differentiate subjects with and without vertebral fractures, suggesting osteoporosis diagnosis is feasible. However, absolute values differed from original values. BMD from sparse sampling appeared to be more robust. This dose-dependency of parameters should be considered for future clinical use.

Key Points
- BMD and quantitative bone parameters are assessable in ultra-low-dose in vivo MDCT scans.
- Bone mineral density does not change significantly when sparse sampling is applied.
- Quantitative trabecular bone microstructure measurements are sensitive to dose reduction.
- Osteoporosis subjects could be differentiated even at 10% of original dose.
- Radiation exposure should be considered when comparing quantitative bone parameters.

Keywords Computed tomography · Radiation dose · Sparse sampling · Osteoporosis · Trabecular microstructure
Introduction

Osteoporosis is a skeletal disorder, leading to an increased risk for fragility fractures [1]. The loss of bone mineral density (BMD) and the deterioration of bone microstructure is typically unnoticed until actual fractures occur. Osteoporotic fractures do not only reduce quality of life, but are also associated with increased mortality [2]. The prevalence of osteoporotic fractures is increasing in our aging society and causing a large burden to healthcare systems [3]. In order to prevent the occurrence of osteoporotic fractures, it is of great importance that patients at risk are identified in order to receive proper treatment in a timely manner.

The current clinical standard method to measure BMD is via dual-energy X-ray absorptiometry (DXA). However, it is partly insufficient in identifying subjects at high risk for osteoporotic fractures: Studies have shown that over half of all non-vertebral fractures occurred in patients with non-pathological BMD values [4, 5]. Quantitative BMD and trabecular bone microstructure analysis based on high-resolution multidetector computer tomography (MDCT) improves the prediction of biomechanical bone strength and fracture risk beyond BMD [6-8]. However, the currently applied radiation dose is clinically not acceptable, particularly for longitudinal assessment of fracture risk and therapy monitoring [9].

Several parameters contribute to the radiation dose of a conventional MDCT, namely tube current, peak kilovoltage (kVp), pitch and gantry cycle time [10]. In this study we considered two approaches to reduce the radiation dose. The first approach was to reduce the X-ray tube current, which can currently be realized with a commercial scanner. Due to the nature of commercially available detectors, lowering the tube current linearly decreases radiation dose, but causes a much lowered signal-to-noise ratio (SNR) at the detector, which reduces the diagnostic quality of the images. The second approach was to acquire fewer projections during the scan, which we refer to as sparse sampling. With the future development of X-ray generator units, it will be possible to switch off the X-ray source in MDCT scanners at certain angles and provide shorter X-ray pulses, thus keeping the SNR but lowering the total radiation dose in practice.

With a reduced radiation dose, it is still possible to generate images with relatively high diagnostic quality by applying advanced reconstruction algorithms, e.g. statistical iterative reconstruction (SIR). The performance of SIR under lower tube current [11-15] or fewer projection angles [16] has been validated. To reduce the resulting noise and artefacts, SIR uses a regularization term to produce smoother images.

The aims of our study were: (i) to assess the feasibility of BMD and trabecular bone microstructure parameter measurements in MDCT examinations when tube current is ultra-low or data is sparsely sampled, (ii) to compare their values with those derived from the original imaging data, and (iii) to investigate the possibility of differentiating subjects with and without prevalent vertebral fractures with the acquired quantitative measurements.

Materials and methods

Subjects and multidetector CT (MDCT) scanning

Institutional review board approval was obtained for this retrospective study. Twelve subjects with osteoporotic vertebral fractures and 12 age- and gender-matched subjects without fractures who all underwent routine thoracic and abdominal MDCT were retrospectively identified and included in this study. The presence of actual fractures was determined by radiologists. Collected scans had no original purpose for osteoporotic screening.

MDCT scans were acquired using a 256-row scanner (iCT, Philips Healthcare, Best, The Netherlands). Clinical thoracic/abdominal protocols after standardized intravenous contrast agent application were used in all subjects. For calibration purposes, a reference phantom (Mindways Osteoporosis Phantom, Austin, TX, USA [17]) was placed in the scanner mat beneath the subjects. The helical pitch was set as 0.91 in 18 subjects and 0.75 in four subjects. The tube voltage was 120 kVp in all cases. Maximum tube currents of the 24 scans ranged between 200 mA and 400 mA, while exact tube current during each scan was modulated implicitly by the scanner. The average of the exposure values recorded in all 24 dose reports was 109 mAs (min: 33 mAs, max: 188 mAs).

Tube current simulation and sparse sampling

For all subjects, we used a simulation tool to generate lower tube current scans. The simulation algorithm was based on raw projection data, as described in detail previously [18]. System parameters of the CT scanner, such as detector gain, were taken into consideration to properly account for
electronic noise. Therefore, the result was accurate especially for ultra-low tube current [19]. Low-dose simulations at 50%, 25% and 10% of the original tube current were generated.

Sparse sampling was applied at levels of 50%, 25% and 10% of the original projection data. This was done by only reading every second, fourth and tenth projection angle and deleting the remaining projections in the sinogram. Thus, only the number of projections per full rotation was reduced, whereas other parameters, such as projection geometry and patient location, were kept the same.

Table 1 provides the average radiation exposure of all scans in this study. Original exposure (mAs) and CT Dose Index

|                   | Mean exposure (mAs) | Mean CTDIvol (mGy) | Effective dose (mSv) | SNR   | CNR   |
|-------------------|---------------------|--------------------|----------------------|-------|-------|
| Original          | 109                 | 7.5                | 10                   | 32.802| 13.682|
| Proj50            | 55                  | 3.8                | 5                    | 21.483| 8.597 |
| Proj25            | 27                  | 1.9                | 3                    | 16.193| 6.336 |
| Proj10            | 11                  | 0.8                | 1                    | 14.208| 5.619 |
| Tube50            | 55                  | 3.8                | 5                    | 18.552| 7.234 |
| Tube25            | 27                  | 1.9                | 3                    | 9.524 | 3.794 |
| Tube10            | 11                  | 0.8                | 1                    | 2.858 | 1.146 |

Proj50, Proj25 and Proj10 represent 50%, 25% and 10% of the sparse sampling, respectively.
Tube50, Tube25 and Tube10 represent 50%, 25% and 10% of the simulated lower tube current, respectively.

Effective dose was estimated for a female from the shoulder to the middle of the thigh.
SNR was estimated within a homogenous region of the material of the highest density in the phantom.
CNR was estimated between the homogenous regions of the materials of the highest and lowest density in the phantom.

Fig. 1  Representative reconstructions of the lumbar spine (L1–L5) of in-vivo spine multidetector CT (MDCT) data at the original dose. The left column depicts a subject with a fracture; the right column displays the matched healthy subject with regard to age and gender. The original dose was at 120 kV, 107 mAs (left) and 114 mAs (right) (exact tube current was modulated). Window level was 300 HU and width was 1,500 HU. Field of view was 180 × 153 mm² for (a) and (b), and 156 × 156 mm² for (c) and (d).
Effective radiation dose (mSv) was approximated for a female shoulder to middle thigh. Both sparse sampling and lowering tube current reduced the radiation dose linearly.

**Statistical iterative reconstruction**

Collected subjects were all reconstructed anew with statistical iterative reconstruction (SIR) in a much denser grid focusing on the spine. SIR was applied on the full dose data, the simulated projection data at 50%, 25% and 10% as well as the sparse sampling data at levels of 50%, 25% and 10%. SIR was performed with ordered-subset separable paraboloidal surrogate [20] combining a momentum-based accelerating approach [21].

The objective function of SIR consisted of a likelihood term and a regularization term. The likelihood term was computed with log-converted projection data. A Gaussian noise model was applied. We assumed the reconstruction with a helical path can converge with the selected solver. The iterative reconstruction stopped at a manually given number of iterations. Each small update of image \( u \) was made with a subset of projection data. This required one forward projection and one back projection. The forward and back projectors were implemented with a highly parallel framework [22].

For a non-sparse-sampling scan, the scanner acquired 2,400 projections per full rotation (PPR) and we chose a subset size of 100 projection images in one full rotation. The total number of iterations was 15, which yielded 360 subset updates. For 50%, 25% and 10% sparse sampling data, we kept the subset size as 100 projection images per PPR and increased the iteration number to be 30, 60 and 150, respectively. The selection of projection images was made randomly for each subset.

Regularization was applied between updates of the subsets. The regularization term was based on a Huber penalty. In order to preserve the trabecular bone microstructure as much as possible, regularization with a limited influence was selected [23].

All image slices were reconstructed as 1,152 × 1,152 pixels with a field of view of 450 × 450 mm². All parts of the patient and the table were included in the field of view. Reconstruction slice interval was 0.3 mm. The resulting images had voxel spacing of 0.39, 0.39 and 0.3 mm in three dimensions. The exact voxel size was limited to the collimator width at the detector. Voxel intensities (linear attenuation coefficients) were translated to Hounsfield units (HU) using air/water information from the calibration of the scanner. Patient...
position and table height were incorporated so that all images for each individual were automatically registered.

**Bone mineral density and trabecular microstructure analysis**

Hounsfield units inside the vertebrae were calibrated to BMD values by using the reference phantom [17]. The phantom consisted of five rods of basic materials with known equivalent water and K$_2$HPO$_4$ densities. Transferring coefficients were thus calculated in a least squares manner with all five rods for each subject independently. To eliminate the effect of the intravascular contrast agent, a conversion equation was applied empirically as described previously [24].

Mean BMD and standard deviation were calculated inside regions of interest (ROIs) within the trabecular part of the vertebral bodies of each subject. ROIs were placed inside the ventral part, within the central third of the height of the thoracic vertebrae T10–T12 and lumbar vertebrae L1–L5 similar to standard QCT measurements. All ROIs were cylinders with a diameter of 14–16 mm and a height of 4–6 mm, depending on the individual’s vertebrae size. The same ROIs were applied for original dose images, sparsely-sampled and simulated lower-current images. Vertebrae with fractures were excluded from the ROI selection.

Trabecular bone microstructure within the ROIs was analysed with an in-house developed program based on IDL (Interactive Display Language; ITT Visual Information Solutions, Boulder, CO, USA). Similar to previous studies [25], voxels in ROIs were binarized to be either bone or marrow. A global threshold was chosen as 200 mg/cm$^3$ equivalent K$_2$HPO$_4$, which was optimized visually for the microstructure analysis of the subjects [26]. Four morphometric parameters were estimated: bone volume over total volume as bone fraction (BF), trabecular number (TbN, mm$^{-1}$), trabecular separation (TbSp, mm) and trabecular thickness (TbTh, mm) [9]. Parameters were labeled as apparent (app.) due to the limited spatial resolution. One texture parameter of the trabecular bone microstructure (fractal dimension, FD) was determined using a box counting algorithm [27].

**Statistical analysis**

The statistical analysis was performed with SPSS software package (SPSS, Chicago, IL, USA). All tests were done using a two-sided 0.05 level of significance. Mean and standard deviation of BMD and trabecular bone microstructure parameters were calculated. The Kolmogorov-Smirnov test showed for most parameters no significant difference from normal distribution ($p < 0.05$). Therefore, paired t-tests were used to
evaluate the differences between BMD and trabecular bone microstructure parameters derived from the different sparse sampled and low-dose simulated data in all subjects. Differences in BMD and trabecular bone microstructure parameters derived from the different sparse sampled and low-dose simulated data between the matched groups of subjects with and without osteoporotic vertebral fractures were evaluated with paired tests and area under the receiver-operating characteristic (ROC) curves.

**Results**

At 10% of the original dose, estimated SNR and CNR were five times better with sparse sampling than with simulated lower tube current images (Table 1). For sparsely sampled data, artefact patterns slowly became obvious when fewer projections were used. For simulated lower tube current images, streaking artefacts emerged with the decrease of tube current and image quality dropped rapidly. A representative
A matched subject pair with and without osteoporotic vertebral fracture at original dose is depicted in Fig. 1. Sparse sampling and simulated lower current images are depicted in Figs. 2, 3 and 4 and in the Appendix in Figs. A1 and A2.

We observed no significant change in BMD when analysing the reduced projections even at 10% sampling rate \((p > 0.05)\), whereas lowering tube current to 10% resulted in on average 38% higher BMD values (Fig. 5). For all trabecular parameters, both sparse sampling and lowering tube current affected the measurements in various degrees. BF, TbN and FD tended to increase when dose was lowered, while TbSp and TbTh decreased. TbN and TbSp were most sensitive to the dose reduction \((p < 0.001)\) around changes of 20–40% (Fig. 6). All changes in BMD and trabecular bone microstructure parameters from the different reconstructions are shown in Table 2 and in the Appendix in Fig. A3 and Table A1.

For BMD, BF and TbTh, subjects without osteoporotic fractures still had greater values as compared to the matched subjects with osteoporotic fractures in both dose-reducing approaches. The two groups could still be differentiated, as differences were statistically significant \((p < 0.05)\) even at 10% of the original dose level. For TbSp and FD, the differences between the two groups were significant only when the original dose was used, but was not significant when either data were sparsely sampled or tube current was reduced \((p > 0.05)\). The differences in TbN between the two groups was not significant at any dose level. The mean, standard deviation, \(p\)-value and area under ROC curves of all parameters for differentiating the two groups are listed separately in Tables 3 and 4.

**Discussion**

To the best of our knowledge, this is the very first study of in-vivo data comparing reduced tube current and projection...
angles with statistical iterative reconstruction with regard to BMD and trabecular bone microstructure analysis. Our results demonstrated that it is computationally possible to assess the bone microstructure quantitatively with half or less of the dose in non-dedicated routine MDCT. BMD, BF and TbTh, were robust to dose changes and still differentiated between subject with and without osteoporotic vertebral fractures, while TbSp and FD were dose-sensitive.

For sparse sampling, we observed that vertebral BMD did not change on a statistically significant level when less projection angles (down to only 10%) were used. This may allow BMD measurements with much lower radiation exposure in the future. However, it is not yet possible to apply sparse sampling to lower radiation exposure at commercial CT scanners. In current systems, the X-ray source is constantly delivering X-rays during the entire examination. However, precise and fast grid-switching units are reported to be introduced to control the X-ray source on and off in the future. On the other hand, tube current reduction, or modulation, is relatively easy to realize and has been intensively studied [10]. Current detectors are more suspended to electronic noise, especially when the tube current is lowered. Electronic noise can destroy the signal or can cause a bias to R1.4 quantitative values. For this reason, we observed significant changes in absolute BMD values when tube current was lowered, compared to the data from sparse sampling. This suggests that values from sparse sampling seem to be more robust than values from lower tube currents for BMD measurement. However, the computed parameters at ultra-low-dose levels from both approaches still adequately differentiated subjects with and without osteoporotic fractures.

In our study, the mean CTDIvol value was 7.5 mGy (max. 13.7 mGy, min. 5.1 mGy, among abdomen scans) in the original scans. The approximated effective dose was about 2.6 mSv per person (estimation of T12–L5 coverage [28]).

| Table 2 | Changes in bone mineral density (BMD) and trabecular bone microstructure parameters at reduced dose levels |
|---------|---------------------------------------------------------------------------------------------------|
| BMD, mg/cm³ | Mean | SD | p-value | vs. original dose |
| Proj50 | +0.216 | 0.797 | .197 | Proj50 | +0.024 | 0.034 | .002 |
| Proj25 | +0.145 | 1.547 | .650 | Proj25 | +0.036 | 0.052 | .003 |
| Proj10 | +0.233 | 1.978 | .569 | Proj10 | +0.035 | 0.055 | .004 |
| Tube50 | +2.900 | 1.863 | .000 | Tube50 | +0.037 | 0.032 | .000 |
| Tube25 | +7.546 | 11.040 | .003 | Tube25 | +0.057 | 0.072 | .001 |
| Tube10 | +41.32 | 67.131 | .006 | Tube10 | +0.094 | 0.120 | .001 |
| App. TbN, mm⁻¹ | Mean | SD | p-value | vs. original dose |
| Proj50 | +0.058 | 0.025 | .000 | Proj50 | -0.675 | 0.555 | .000 |
| Proj25 | +0.089 | 0.066 | .000 | Proj25 | -0.849 | 0.690 | .000 |
| Proj10 | +0.038 | 0.047 | .001 | Proj10 | -0.648 | 0.678 | .000 |
| Tube50 | +0.046 | 0.027 | .000 | Tube50 | -0.685 | 0.650 | .000 |
| Tube25 | +0.082 | 0.048 | .000 | Tube25 | -1.000 | 0.865 | .000 |
| Tube10 | +0.104 | 0.091 | .000 | Tube10 | -1.200 | 1.119 | .000 |
| App. TbTh, mm | Mean | SD | p-value | vs. original dose |
| Proj50 | -0.304 | 0.402 | .001 | Proj50 | +0.059 | 0.045 | .000 |
| Proj25 | -0.372 | 0.520 | .002 | Proj25 | +0.081 | 0.062 | .000 |
| Proj10 | -0.232 | 0.527 | .042 | Proj10 | +0.067 | 0.061 | .000 |
| Tube50 | -0.234 | 0.377 | .006 | Tube50 | +0.063 | 0.051 | .000 |
| Tube25 | -0.379 | 0.642 | .008 | Tube25 | +0.103 | 0.083 | .000 |
| Tube10 | -0.370 | 0.797 | .033 | Tube10 | +0.137 | 0.133 | .000 |

Values are shown as compared to the original dose in all subjects (n=24) with respective p-values
Proj50, Proj25 and Proj10 indicate sparse sampling of 50%, 25% and 10% projection data, respectively
Tube50, Tube25 and Tube10 indicate simulation of 50%, 25% and 10% of the original tube current, respectively
Displayed means and standard deviations (SD) are given in absolute values
App. apparent, BF bone fraction, BMD bone mineral density, FD fractal dimension, TbN trabecular number, TbSp trabecular separation, TbTh trabecular thickness
Our results showed that further dose reduction was still adequate to approximate quantitative bone parameters; this was actually much lower than previously reported (1.5 mSv for L1 and L2 only [29]).

We used statistical iterative reconstruction (SIR) in this study. Compared to the reconstruction process based on traditional methods like FBP, an iterative-based algorithm is considered more suitable handling noise and streaking artefacts, because it integrates physics modeling, providing better performances for missing data, irregular sampling and tube current reduction [30]. A higher level of the modelling provides greater image quality improvement, but also at a greater price of computational complexity. Because the image quality generated by traditional algorithms is still acceptable for most diagnostic purposes, additional algorithms with higher modelling complexity are often used in academics and avoided by manufacturers for clinical routine [31]. However, with the vast development of graphic units and computational power, SIR will become much more widely available [32]. The image noise in SIR is mainly handled with a regularization term. A previous study [23] investigated the effect of different models of regularization on trabecular bone microstructure at the spine in-vitro. These investigators observed that a minimum of regularization is best suited for quantitative bone microstructure analysis. For this reason, we also used a low regularization term in this study.

Admittedly our study had limitations. Firstly, the number of the investigated subjects was relatively small due to the pilot character of this study. Secondly, the decisions of osteoporotic or control subjects were determined merely by the presentation of actual vertebral fractures. Thirdly, MDCT imaging was performed with application of an intravenous contrast agent due to the clinical indication of the examinations, which affects quantitative bone measurements. However, a BMD conversion

| Fracture | No fracture | Fracture | No fracture |
|----------|-------------|----------|-------------|
| BMD      |             |          |             |
| SIR      | 90.236      | 17.455   | 125.228     | 33.868      |
| Proj50   | 90.447      | 17.668   | 125.449     | 33.404      |
| Proj25   | 89.671      | 17.477   | 126.083     | 34.116      |
| Proj10   | 90.189      | 17.262   | 125.742     | 33.951      |
| Tube50   | 92.439      | 17.513   | 128.824     | 34.078      |
| Tube25   | 94.938      | 17.883   | 135.619     | 42.176      |
| Tube10   | 110.210     | 21.069   | 187.904     | 104.438     |
| App. BF  |             |          |             |
| SIR      | 0.311       | 0.095    | 0.500       | 0.160       |
| Proj50   | 0.356       | 0.082    | 0.503       | 0.127       |
| Proj25   | 0.378       | 0.074    | 0.505       | 0.107       |
| Proj10   | 0.375       | 0.072    | 0.507       | 0.103       |
| Tube50   | 0.362       | 0.083    | 0.523       | 0.138       |
| Tube25   | 0.406       | 0.065    | 0.519       | 0.082       |
| Tube10   | 0.472       | 0.035    | 0.526       | 0.037       |
| App. TbN |             |          |             |
| SIR      | 0.284       | 0.108    | 0.269       | 0.080       |
| Proj50   | 0.352       | 0.106    | 0.316       | 0.084       |
| Proj25   | 0.377       | 0.108    | 0.353       | 0.109       |
| Proj10   | 0.331       | 0.074    | 0.298       | 0.069       |
| Tube50   | 0.341       | 0.091    | 0.306       | 0.071       |
| Tube25   | 0.378       | 0.080    | 0.339       | 0.065       |
| Tube10   | 0.412       | 0.073    | 0.350       | 0.060       |
| App. TbTh|             |          |             |
| SIR      | 1.301       | 0.609    | 2.483       | 1.100       |
| Proj50   | 1.171       | 0.477    | 2.006       | 0.706       |
| Proj25   | 1.165       | 0.477    | 1.876       | 0.579       |
| Proj10   | 1.282       | 0.441    | 2.038       | 0.611       |
| Tube50   | 1.234       | 0.510    | 2.083       | 0.728       |
| Tube25   | 1.218       | 0.369    | 1.808       | 0.485       |
| Tube10   | 1.284       | 0.308    | 1.761       | 0.352       |

Parameters are shown as matched groups with (n=12) and without vertebral fracture (n=12) for the different dose levels

SIR indicates iterative reconstruction of the original dose
Proj50, Proj25 and Proj10 indicate sparse sampling of 50%, 25% and 10% projection data, respectively
Tube50, Tube25 and Tube10 indicate simulation of 50%, 25% and 10% of the original tube current, respectively
App. apparent, BF bone fraction, BMD bone mineral density, FD fractal dimension, TbN trabecular number, TbSp trabecular separation, TbTh trabecular thickness
Table 4  P-values and area under the receiver-operating characteristic (ROC) curve for the fracture and no-fracture groups, observed at different dose levels

| BMD         | p-value | ROC  | App. BF | p-value | ROC  |
|-------------|---------|------|---------|---------|------|
| SIR         | .002*   | .875 | SIR     | .002*   | .861 |
| Proj50      | .002*   | .875 | Proj50  | .002*   | .840 |
| Proj25      | .002*   | .875 | Proj25  | .002*   | .833 |
| Proj10      | .002*   | .868 | Proj10  | .001*   | .854 |
| Tube50      | .002*   | .875 | Tube50  | .003*   | .878 |
| Tube25      | .002*   | .882 | Tube25  | .001*   | .868 |
| Tube10      | .023*   | .896 | Tube10  | .001*   | .878 |
| App. TbN    | p-value | ROC  | App. TbSp | p-value | ROC  |
| SIR         | .699    | .458 | SIR     | .028*   | .319 |
| Proj50      | .371    | .375 | Proj50  | .279    | .396 |
| Proj25      | .601    | .417 | Proj25  | .640    | .458 |
| Proj10      | .285    | .368 | Proj10  | .347    | .417 |
| Tube50      | .351    | .372 | Tube50  | .201    | .382 |
| Tube25      | .253    | .361 | Tube25  | .459    | .424 |
| Tube10      | .033*   | .236 | Tube10  | .079    | .656 |
| App. TbTh   | p-value | ROC  | FD      | p-value | ROC  |
| SIR         | .004*   | .861 | SIR     | .087    | .694 |
| Proj50      | .003*   | .854 | Proj50  | .385    | .618 |
| Proj25      | .005*   | .861 | Proj25  | .650    | .587 |
| Proj10      | .004*   | .896 | Proj10  | .447    | .597 |
| Tube50      | .006*   | .868 | Tube50  | .378    | .618 |
| Tube25      | .010*   | .875 | Tube25  | .808    | .556 |
| Tube10      | .002*   | .833 | Tube10  | .381    | .417 |

Parameters are shown as matched groups with (n=12) and without vertebral fracture (n=12) for the different dose levels. ROC denotes area under the ROC curve. SIR indicates iterative reconstruction of the original dose. Proj50, Proj25 and Proj10 indicate sparse sampling of 50%, 25% and 10% projection data. Tube50, Tube25 and Tube10 indicate simulation of 50%, 25% and 10% of the original tube current. * indicates p-values with statistically significant differences between the two groups (p<0.05).

App., apparent; BF, bone factor; BMD, bone mineral density; FD, fractal dimension; TbN, trabecular number; TbSp, trabecular separation; TbTh, trabecular thickness.

equation was applied as reported previously [24]. Lastly, low-dose scans in this study were simulated retrospectively and were not acquired prospectively due to radiation protection regulations. However, the validity of the low-dose simulation tool has been demonstrated previously both by the industrial manufacturers’ laboratory [18] and clinical research institution [19]. Further studies have to be performed in the future to validate the potential of dose reduction approaches for CT-based osteoporosis diagnostics and therapy monitoring.

In conclusion, we investigated the effect of sparse sampling and simulated lower tube current in non-dedicated MDCT scans combined with SIR on BMD and quantitative bone microstructure assessment. Our findings indicate that BMD and trabecular bone microstructure are still assessable at ultra-low dose levels. BMD, apparent bone factor and trabecular thickness were able to differentiate between subjects with and without osteoporotic fractures based on both approaches for dose reduction, sparse sampling and lower tube currents. This suggests that fracture risk prediction with low-dose protocols is feasible. However, absolute parameter values at reduced dose levels significantly differed from original values. BMD measurements derived from sparse sampling showing less changes compared to values acquired with lower tube currents, suggesting sparse sampling to be a more robust dose reduction approach for BMD measurements. These changes in parameters should be considered for future studies and clinical use.

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Dr Peter B. Noël.

Conflict of interest The authors of this manuscript declare relationships with Philips Research Hamburg.

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Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Methodology

• retrospective
• retrospective
• case-control study
• performed at one institution

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References

1. Consensus NI (2001) Development panel on osteoporosis: prevention, diagnosis and therapy. Jama 285(6):785–795
2. Ioannidis G, Papaioannou A, Hopman WM et al (2009) Relation between fractures and mortality: results from the Canadian Multicentre Osteoporosis Study. CMAJ 181(5):265–271
3. Burge R, Dawson-Hughes B, Solomon DH et al (2007) Incidence and economic burden of osteoporosis-related fractures in the United States, 2005–2025. J Bone Miner Res 22(3):465–475
4. Schuit SC, Van der Klift M, Weel AE et al (2009) Low-tube-voltage, high-tube-current multidetector abdominal CT: Improved image quality and decreased radiation dose with adaptive statistical iterative reconstruction algorithm. Am J Roentgenol 197(6):1404–1408
5. Graeff C, Timm W, Nickelsen TN et al (2007) Monitoring Teriparatide-Associated Changes in Vertebral Microstructure by High-Resolution CT In Vivo: Results From the EUROFORS Study. J Bone Miner Res 22(9):1426–1433
6. Coursey CA, Frush DP (2008) CT and radiation: What radiologists should know. Appl Radiol 37(3):22
7. Link TM (2012) Osteoporosis imaging: state of the art and advanced imaging. Radiology 263(1):3–17
8. Baum T (2013) C Karampinos D, Liebl H, et al. High-resolution bone imaging for osteoporosis diagnostics and therapy monitoring using clinical MDCT and MRI. Curr Med Chem 20(35):4844–4852
9. Noël PB, Renger B, Fiebich M et al (2013) Does iterative reconstruction lower CT radiation dose: evaluation of 15,000 examinations. PLoS One 8(11), e81141
10. Sauter A, Koehler T, Fingerle AA et al (2016) BMD measurements of the spine derived from sagittal reformations of contrast-enhanced MDCT without dedicated software. EJR 80(2):e140–e145
11. Majumdar S, Genant HK, Grampp S et al (1997) Correlation of trabecular bone structure with age, bone mineral density, and osteoporotic status: in vivo studies in the distal radius using high resolution magnetic resonance imaging. J Bone Miner Res 12(1):111–118
12. Stamm G, Nagel HD (2002) CT-expo, a new program for dose evaluation in CT. RoFo. Fortschr Geb Rontgenstr Nuklearmed 174(12):1570–1576
13. Damilakis J, Adams JE, Guglielmi G et al (2010) Radiation exposure in X-ray-based imaging techniques used in osteoporosis. Euro Radiol 20(11):2707–2714
14. Hara AK, Paden RG, Silva AC et al (2009) Iterative reconstruction technique for reducing body radiation dose at CT: feasibility study. Am J Roentgenol 193(9):764–771
15. Siris ES, Chen YT, Abbott TA et al (2004) Bone mineral density thresholds for pharmacological intervention to prevent fractures. Arch Intern Med 164(10):1108–1112
16. Ito M, Ikeda K, Nishiguchi M et al (2005) Multi-detector row CT imaging of vertebral microstructure for evaluation of fracture risk. J Bone Miner Res 20(10):1828–1836
17. C Karampinos D, Liebl H, et al. High-resolution CT In Vivo: Results From the EUROFORS Study. J Bone Miner Res 22(9):1553–1564
18. Baum T, Müller D, Dobritz M et al (2011) BMD measurements of the spine derived from sagittal reformations of contrast-enhanced MDCT without dedicated software. Eur J Radiol 80(2):e140–e145
19. Fessler JA (2000) Statistical image reconstruction methods for transmission tomography. Handb Med Imaging 2:1–70
20. Fehring A, Lasser T, Zanette I, et al. A versatile tomographic forward- and back-projection approach on multi-GPUs. SPIE Medical Imaging 2014. International Society for Optics and Photonics.
21. Kopp FK, Holzapfel K, Baum T et al (2016) Effect of low-dose MDCT and iterative reconstruction on trabecular bone microstructure assessment. PLoS One 11(7), e0159903
22. Baum T, Müller D, Dobritz M et al (2011) BMD measurements of the spine derived from sagittal reformations of contrast-enhanced MDCT without dedicated software. EJR 80(2):e140–e145
23. Majumdar S, Genant HK, Grampp S et al (1997) Correlation of trabecular bone structure with age, bone mineral density, and osteoporotic status: in vivo studies in the distal radius using high resolution magnetic resonance imaging. J Bone Miner Res 12(1):111–118
24. Stamm G, Nagel HD (2002) CT-expo—a novel program for dose evaluation in CT. RoFo. Fortschr Geb Rontgenstr Nuklearmed 174(12):1570–1576
25. Damilakis J, Adams JE, Guglielmi G et al (2010) Radiation exposure in X-ray-based imaging techniques used in osteoporosis. Euro Radiol 20(11):2707–2714
26. Beister M, Kolditz D, Kalender WA (2012) Iterative reconstruction methods in X-ray CT. Phys Med 28(2):94–108
27. Pan X, Sidky EY, Vannier M (2009) Why do commercial CT scan-...tion? Inverse Prob 25(9), 1540–1558
28. Eklund A, Dufort P, Forsberg D et al (2013) Medical image processing on the GPU—Past, present and future. Med Image Anal 17(8):1073–1094