



# Bone mineral density differences between femurs of scoliotic patients undergoing quantitative computed tomography analysis

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## Abstract

**Purpose** Scoliosis is a cause of loading imbalance between the lower limbs, which can result in BMD differences between the two femurs. We investigated the discrepancy in BMD values assessed by quantitative computed tomography (QCT) between femurs in patients with and without scoliosis, also assessing if this difference can be related to spine convexity.

**Methods** Abdominal CT examinations were retrospectively reviewed. An “asynchronous” calibration of CT images was performed to obtain BMD values from QCT. Scoliosis was evaluated on the antero-posterior CT localizer to calculate the Cobb angle. Differences between aBMD and vBMD of femurs were assessed in both scoliotic and non-scoliotic subjects.

**Results** Final study cohort consisted of 263 subjects, 225 of them without scoliosis (85.6%) and 38 with scoliosis (14.4%). No significant differences were found in the general population without scoliosis, except for vBMD at the neck. Comparison of femurs in scoliotic patients showed statistically significant differences at neck aBMD  $-0.028 \text{ g/cm}^2$ ,  $p=0.004$ , total femur aBMD  $(-0.032 \text{ g/cm}^2, p=0.008)$  and total femur vBMD  $(-8.9 \text{ mg/cm}^3, p=0.011)$ , with lower BMD values on the convexity side. In 10 cases (26%) a change in the final T-score diagnosis was observed.

**Conclusion** QCT analysis demonstrated a difference in both areal and volumetric BMD between the two femurs of scoliotic patients, in relation to the side of the scoliotic curve. If these data will be confirmed by larger studies, bilateral femoral DXA acquisition may be proposed for these patients.

**Keywords** Osteoporosis · Scoliosis · QCT · T-score · BMD

## Introduction

Osteoporosis is a systemic skeletal disorder characterized a decrease in bone density bone mass and a deterioration of bone microarchitectural, with a consequential increase in the individual's fracture risk. Fragility fractures from osteoporosis commonly occur at the hip, dorsal and lumbar spine, proximal humerus and distal forearm, and they can represent a major cause of morbidity, especially in the elderly population [1].

The definition of osteoporosis on adults is based on the assessment of bone mineral density (BMD) by dual energy X-ray absorptiometry (DXA). Osteoporosis can be diagnosed if a T-score value of  $-2.5$  or less is found at lumbar spine and femoral neck [2].

Bone density differences between the dominant and non-dominant femur are matter of debate [3, 4]. While arm dominance significantly impacts on bone density in the forearm (with reported increased values of 6% to 9% in the dominant

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arm compared to the non-dominant one) [5], a significant difference does not seem to exist between right and left proximal femur in normal individuals [6, 7]. Therefore, the International Society for Clinical Densitometry (ISCD) adult official positions recognize that there is still insufficient evidence to justify the use of mean T-score value from bilateral hip DXA in the general population [8].

Scoliosis and osteoporosis may co-exists, with several reports describing a correlation between the two diseases both in adolescents and adults [9, 10]. The presence of loading imbalance between the two limbs due to scoliosis has been reported [11, 12]. Such imbalance may also result in BMD differences between the two femurs of scoliotic patients, as reported by Hans et al., who found lower femoral BMD values on the side of spinal convexity compared to that of spinal concavity [13]. A more recent study by Bandirali et al. confirmed that about 70% of scoliotic subjects routinely undergoing DXA had lower femoral neck BMD values on the side of scoliosis convexity [14].

Quantitative CT is a cross-sectional technique that is used to obtain measurements of volumetric BMD (vBMD) at lumbar spine and femurs, with the advantage over DXA of providing separate measurements of cortical and trabecular volumes of BMD [15]. Differently from the spine, QCT 3D data at the proximal femur can be used to generate a bi-dimensional projectional image to apply the standard DXA regions of interest (ROIs) and obtain DXA-equivalent CT X-Ray Absorptiometry (CTXA) areal BMD values. Due to the very strong correlations between areal BMD values of the proximal femur from QCT and those obtained using DXA, the WHO T-score classifications can be applied also for QCT [16].

To our knowledge, no study investigated if a difference in terms BMD by QCT exists between the two femurs in scoliotic subjects. Therefore, the aim of the present study is to analyze the possible discrepancy of BMD values assessed by QCT between femurs in patients with scoliosis, also assessing if this difference can be related to spine convexity. The possible difference between QCT-based BMD values was also compared in the general population without scoliosis.

## Materials and methods

### Study population

This retrospective study was approved by the local ethics committee (RETRORAD, approved by the Local Ethical Committee of San Raffaele Hospital). Patients who underwent a CT scan at IRCCS Istituto Ortopedico Galeazzi in Milan, Italy from January 2018 to May 2019 were evaluated, according to the following inclusion criteria: non-enhanced CT scan of the chest and abdomen; presence of

a CT localizer scan that included the thoraco-lumbar spine for scoliosis evaluation; CT scan performed with patient positioned with his/her arms up; scan had to include the proximal femur (at least 1 cm below the lesser trochanter). Exclusion criteria were the history of previous surgery at the spine or at the lower limb joints and the presence of technical limitations (motion artifacts, inadequate technical CT parameters).

### Multi-detector computed tomography (MDCT) acquisition

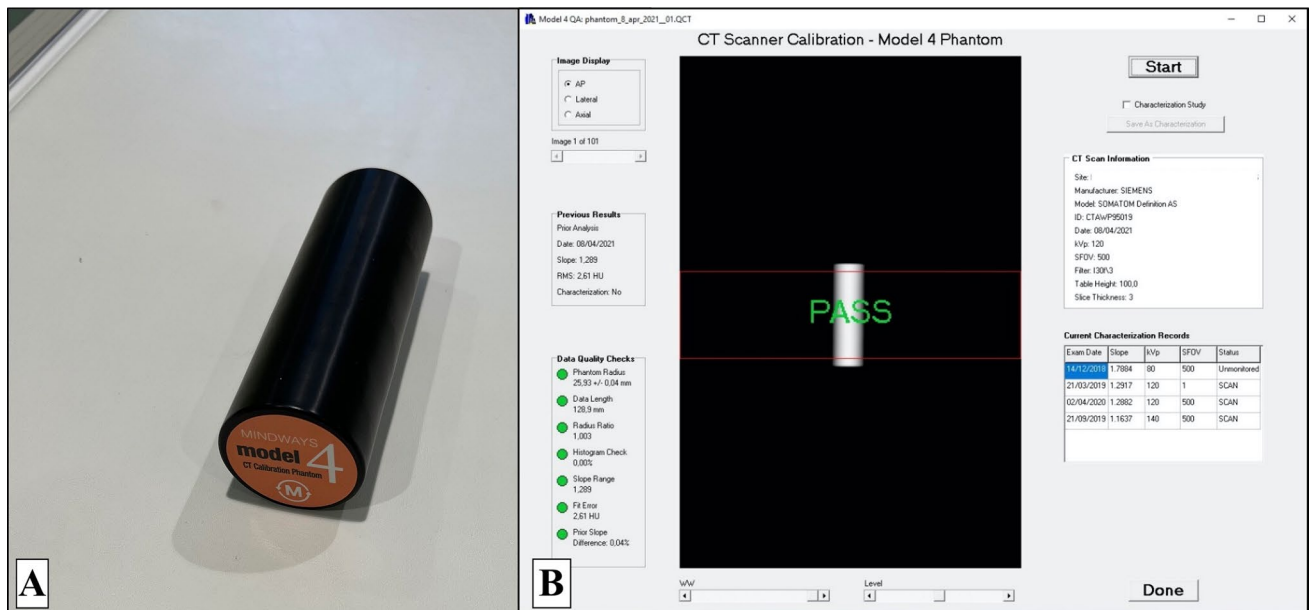
All MDCT scans were acquired with the patient supine using a 64 slice Somatom Emotion CT (Siemens Medical Solutions, Erlangen, Germany). Tube voltage ranged between 120 and 140 kV, and tube current ranged between 220 and 260 mA. Images were reconstructed using a standard soft tissue algorithm with 3-mm slice thickness at 1-mm intervals. The MDCT scanner used in this study is calibrated daily to ensure accurate CT attenuation numbers, measured in Hounsfield units (HU).

### QCT calibration

To obtain BMD values from HU the CT scanner needs to be calibrated, which is generally done using an external phantom containing a reference set of known BMD. The external calibration has been traditionally performed using a phantom placed within the CT table under the patient during the CT acquisition, a method called “synchronous calibration” [17]. For this study we used the “asynchronous” calibration of the MDTC images by performing calibration studies with quality assurance (QA) on the CT scanner, in the absence of patient. For each calibration/QA study, the Mindways QA phantom was scanned using the same technical protocol of CT acquisitions (see Fig. 1). Then, each CT scan is associated to the specific calibration data, allowing for a retrospective evaluation of patients’ BMD in scan previously acquired.

### QCT images analysis

All QCT measurements were performed by an operator with ten years of experience in osteoporosis imaging (CM). The QCT Pro CXTA analysis software (Mindways Software Inc., Austin, TX) was used to perform the QCT analysis on both hips. First, we used the antero-posterior CT “localizer” of patient to select the specific volume of analysis from the top of the acetabulum to the lesser trochanter. Then, the software automatically identifies the different ROIs on the projected hip image: femoral neck (FN), total hip (TH), intertrochanter, trochanter. ROIs positioning by the software is generally accurate, but they



**Fig. 1** Example of the asynchronous calibration. Image A shows the Mindways QA phantom on the CT table during the calibration process, in which a CT scan of the whole phantom is acquired. Then,

the acquired phantom (with its specific technical parameters) is analyzed and processed with the QA analysis software, as showed in image B

were adjusted when necessary by the same operator. Once the analysis was completed, the software provides areal BMD (aBMD,  $\text{g}/\text{cm}^2$ ) and volumetric BMD (vBMD,  $\text{g}/\text{cm}^3$ ) for the specific regions. In our study, we considered the TF and FN regions, due to their clinical relevance over the remaining variables. FN T-scores values were automatically calculated using the CTXA reference database of manufacturer. An example of the QCT analysis process is reported in Fig. 2.

Diagnosis of osteoporosis and osteopenia was based on the lower femoral T-score, according to the World Health of Organization (WHO) criteria: T-score values equal or lower than  $-2.5$  for osteoporosis,  $T\text{-score} < -1$  and  $> -2.5$  for osteopenia.

## Scoliosis evaluation

To identify the presence of scoliosis and the side of convexity, we evaluated the antero-posterior CT localizer scan or coronal multiplanar reformation (MPR) that included the whole thoraco-lumbar spine to calculate the Cobb angle [18]. Scoliosis in adults is defined as a spinal deformity in a skeletally mature patient with a Cobb angle of more than  $10^\circ$  in the coronal plain [18]. Lines were then drawn along the endplates, the angle between intersecting lines drawn perpendicular to the top of the top vertebrae and the bottom of the bottom vertebrae is the Cobb angle (see Fig. 3).

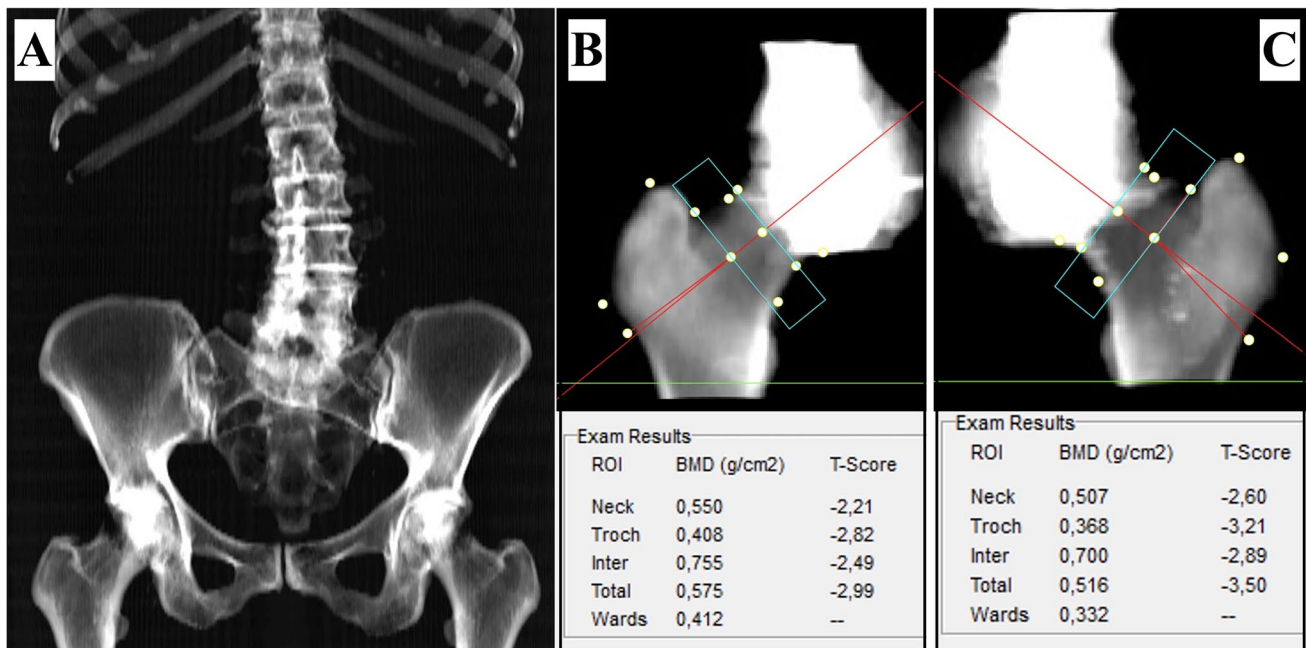
## Statistical analysis

Differences between aBMD and vBMD of femurs were assessed in both scoliotic and non-scoliotic subjects. Normal distribution of continuous variables was assessed through the Kolmogorov–Smirnov or Shapiro–Wilk tests, according to the sample size. For normally distributed values, data were presented as mean  $\pm$  standard deviation (SD), and variables were compared by using dependent sample t test. When normality was not satisfied, data were presented as median with interquartile range (IQR) and the comparison between groups was performed using Wilcoxon signed rank test. Significance was considered for p values lower than 0.05 in all the tests. Statistical analysis was performed using SPSS v25 (SPSS Inc., Chicago, IL, USA).

## Results

The initial cohort was composed by 404 subjects. After applying exclusion criteria,  $n = 141$  (34.9%) subjects were excluded, and the final sample size consisted of  $n = 263$  subjects. The reasons for exclusion were: distal scan too short to include both femurs ( $n = 89$ , 63.1%); previous spinal surgery ( $n = 25$ , 17.8%); previous hip replacement ( $n = 12$ , 8.5%); absence of non-contrast scan ( $n = 7$ , 5%); technical limitations ( $n = 6$ , 4.2%); previous knee surgery ( $n = 2$ , 1.4%).

The final cohort consisted of 145 males (55.1%) and 118 females (44.9%), with a mean age of 64 years ( $\pm 16.3$ ).



**Fig. 2** Example of an analysis of an 81-year-old female subject affected by left-side degenerative lumbar scoliosis. In A the QCT Pro CTXA software enables a preview of the whole scan area by means of coronal reformation. Image B and C show the resulting QCT analysis at the right and left femur, respectively, with the corresponding

BMD and T-score data reported below. T-score values are lower at the left hip, which is the one on the convex scoliosis side, with a different final diagnosis between the right (osteopenia) and left (osteoporosis) femur



**Fig. 3** Example of the two methods we used to measure the Cobb angle for evaluating the degree of scoliosis. In A, the Cobb angle was measured on the antero-posterior CT scout (14.2° of scoliosis). In B,

we used coronal multiplanar reformation (in this case a Maximum Intensity Projection, MIP) to identify the upper and lower vertebrae (21.6° of scoliosis)

**Table 1** Summary of patients' characteristics with sub-analysis according to the presence of scoliosis

	Subjects with-out scoliosis (n=225)	Subjects with scoliosis (n=38)	Total (n=263)
Age	62.9 ± 16.2	70.1 ± 16.3	64.0 ± 16.3
Gender	M: 127 (56%) F: 98 (44%)	M: 18 (47%) F: 20 (53%)	M: 145 (55%) F: 118 (45%)
Normal BMD	79 (35%)	9 (23.5%)	88 (33%)
Osteopenia	109 (48.5%)	20 (53%)	129 (49%)
Osteoporosis	37 (16.5%)	9 (23.5%)	46 (18%)
Scoliosis degree	–	15.1° ± 9.0°	–

Age and scoliosis degree are reported as mean ± standard deviation. *BMD* bone mineral density

Subjects with scoliosis 38/263 (14.4%), with a mean age of 70.1 ± 16.3. Sub-analysis of the non-scoliosis group revealed that 98/225 (43%) were females, while 127/225 (56.4%) were males. Among the 38 subjects with scoliosis, there were n = 20 (52.6%) females and n = 18 (47.4%) males. The mean value of scoliosis degree was 15.1° ± 9.0° (mean ± SD).

Osteoporosis was diagnosed in 16.5% of patients without scoliosis and in 23.5% of patients with scoliosis. A detailed summary of patients' characteristics according to the presence of scoliosis, and BMD T-score diagnosis are reported in Table 1.

### Analysis in the non-scoliotic subgroup

When comparing aBMD and vBMD values of left and right femurs in patients without scoliosis, we only found a statistically significant difference for FN vBMD, with a mean difference of + 5.3 mg/cm<sup>3</sup> (p=0.013). No significant differences were found for TF vBMD femur, neither for FN nor TF aBMD (Table 2).

### Analysis in the scoliotic subgroup

When comparing aBMD and vBMD values of left and right femurs in patients without scoliosis, regardless the spine convexity, we found no statistically significant differences both for aBMD and vBMD at all sites (Table 3).

When we compared femoral BMD values of scoliotic patients in relation to scoliotic curve, we found statistically significant lower values on the side of convexity at all

**Table 2** Comparison of areal BMD and volumetric BMD values between left and right femurs in patients without scoliosis

	Left femur		Right femur		Difference	
	Mean/median	Distribution	Mean/median	Distribution	Δ L-R	P-value
Areal BMD NECK* (g/cm <sup>2</sup> )	0.666	0,579–0,760	0.662	0,572–0,746	+ 0.002	0.705
Areal BMD TOTAL* (g/cm <sup>2</sup> )	0.755	0,639–0,845	0.748	0,656–0,851	– 0.002	0.836
Volumetric BMD NECK# (mg/cm <sup>3</sup> )	259.7	61.3	254.4	63.1	<b>+ 5.3</b>	<b>0.013</b>
Volumetric BMD TOTAL# (mg/cm <sup>3</sup> )	253.4	57.8	250.9	56.7	+ 2.48	0.088

Δ L-R = mean or median areal of volumetric BMD difference between left and right side. *BMD* bone mineral density. Statistically significant differences are in bold. \*Data presented as median with interquartile range (IQR 25–75), and the comparison between groups was performed using Wilcoxon signed rank test. #Normally distributed values, data were presented as mean ± standard deviation, and variables were compared by using dependent sample t-test

**Table 3** Comparison of areal BMD and volumetric BMD values between left and right femurs in patients with scoliosis

	Left femur		Right femur		Difference	
	Mean/median	Distribution	Mean/median	Distribution	Δ L-R	P-value
Areal BMD NECK* (g/cm <sup>2</sup> )	0.634	(0,557–0,673)	0.641	(0,546–0,767)	– 0,013	0.128
Areal BMD TOTAL# (g/cm <sup>2</sup> )	0.692	0.140	0.709	0.166	– 0,017	0.167
Volumetric BMD NECK# (mg/cm <sup>3</sup> )	235.0	50.6	232.3	50.2	+ 2,7	0.508
Volumetric BMD TOTAL# (mg/cm <sup>3</sup> )	229.1	47.5	229.5	52.5	– 0,4	0.916

Δ L-R = mean or median areal of volumetric BMD difference between left and right side. *BMD* bone mineral density. \* Data presented as median with interquartile range (IQR 25–75) and the comparison between groups was performed using Wilcoxon signed rank test #Normally distributed values, data were presented as mean ± standard deviation, and variables were compared by using dependent sample t test

regions, with the exception of FN vBMD. The mean/median difference was  $-0.028 \text{ g/cm}^2$  at FN aBMD ( $p=0.004$ ),  $-0.032 \text{ g/cm}^2$  at TF aBMD ( $p=0.008$ ) and  $-8.9 \text{ mg/cm}^3$  at TF vBMD ( $p=0.011$ ), with lower BMD values for the femur on the side of convexity (Table 4).

When considering the WHO diagnostic criteria using femoral neck T-score, in the majority of cases (28/38, 74%) there was no change in the final diagnosis between the femur on the convex and concave scoliotic side. In 3 cases the diagnosis changed from normality (concavity) to osteopenia (convexity), while in 5 cases the diagnosis changed from osteopenia (concavity) to osteoporosis (convexity). Curiously, in two patients there was an opposite change of diagnosis, with the lower T-score value being found on the concave side.

## Discussion

The main finding of our study is that, in scoliotic patients, significant lower values of femoral BMD were found on the side of scoliosis convexity, except for FN vBMD. No significant differences were found in the general population without scoliosis, except for FN vBMD. The present study is the first one focusing on BMD differences between femurs evaluated using QCT, further enriching the evidence about the possible differences of bone density between the two femurs, which remains a debated topic [6, 7, 13, 14].

Regarding the general population there are conflicting results about the need for bilateral femoral BMD assessment using DXA. A paper by Rao et al. in 2000 found high correlation between the BMD measured by DXA at the two hips, without the evidence of a dominant hip as found in the forearm [6]. Petley et al. evaluated more than 2,300 Caucasian women, showing that only in 51 subjects (about the 2%) measuring BMD at both femurs would have changed the final classification of the lowest site assessed (including spine) to osteoporotic [7]. Therefore, both papers conclude

that there is little justification to perform bilateral hip BMD assessment due to the very small benefit in terms of patient's management. At the same time, a recent paper showed that assessing BMD at only one femur would lead to up to 15.8% of failure in identifying subjects with osteoporosis [19]. The results of our study align with those that do not show a difference between femurs in the general population.

Regarding the scoliotic subjects, our study confirmed that a significant difference between the two femurs exists. Very few papers dealt with a specific analysis of bilateral BMD at the hip of scoliotic patients, and are in line with our results, reporting lower BMD values at the femurs on the convex side [13, 14]. Our study differs from those published so far because we used QCT instead of DXA, therefore providing not only aBMD values but also volumetric bone density measurements. This increases the accuracy of our measurements [15], but at the same time deserve some considerations. The study of Bandirali et al. included a larger sample of patients, but the evaluation of scoliosis degree was done on DXA lumbar spine images [14]. Thus, knowledge of only the lumbar spine makes the distinction between convex and concave side quite arbitrary, as no information is available about a possible second wider curvature in the dorsal spine. Conversely, we evaluated a wider portion of the spine, allowing for a more accurate analysis of the real degree of scoliosis and possible dorsal curves. Second, they evaluated only the femoral neck areal BMD by DXA, while in our study we evaluated both areal and volumetric BMD at femoral neck and total femur. Including the total femoral region allows us to get a more accurate analysis of the real impact of scoliotic curvature in our subjects. In fact, despite the neck region is used for the WHO diagnosis, this ROI is smaller and may be subjected to higher variability. Usually, the smaller the ROI, the greater the BMD variability [20]. Therefore, the fact we showed a significant difference also at the total BMD is even more important and more reflective of the overall femoral density, as these ROI are larger and include a bigger part of the femur.

**Table 4** Comparison of areal BMD and volumetric BMD values between femurs on the convexity and concavity side

	Femur on convexity side		Femur on concavity side		Difference	
	Mean/median	Distribution	Mean/median	Distribution	$\Delta \text{ Cv-Cc}$	<i>P</i> -value
	Patients with scoliosis ( $n=38$ )					
Areal BMD NECK* ( $\text{g/cm}^2$ )	0.629	(0,5377–0,747)	0.641	(0,5665–0,694)	$-0.028$	<b>0.004</b>
Areal BMD TOTAL# ( $\text{g/cm}^2$ )	0.684	0.158	0.716	0.147	$-0.032$	<b>0.008</b>
Volumetric BMD NECK# ( $\text{mg/cm}^3$ )	234.3	50.7	233.0	50.1	1,3	0.749
Volumetric BMD TOTAL# ( $\text{mg/cm}^3$ )	224.9	51.3	233.8	48.4	$-8.9$	<b>0.011</b>

Bold indicates statistically significant *P*-values

$\Delta \text{ Cv-Cc}$  = mean or median areal or volumetric BMD difference between convex (Cv) and concave (Cc) side. BMD bone mineral density. \*Data presented as median with interquartile range (IQR 25–75), and the comparison between groups was performed using Wilcoxon signed rank test # Normally distributed values, data were presented as mean  $\pm$  standard deviation, and variables were compared by using dependent sample *t*-test

In the majority of scoliotic subjects the BMD difference between femurs did not result in a change of final WHO diagnosis, despite about 25% of subjects had a worst diagnosis on the convex side. Nevertheless, the use of femoral neck BMD for the final diagnosis may not be reflected in a change of final diagnosis despite lower BMD values, as the specific threshold are not reached. This can also explain the opposite change of diagnosis in those two patients there was an opposite change in diagnosis, with lower T-score value being found on the concave side. Finally, the implication of the discordance between aBMD and vBMD at the neck deserve future studies for further investigation.

Our work has limitations. First, the study is retrospective therefore we lack various information of the osteo-metabolic status of our subjects. Nevertheless, as the study focuses on intra-subject variability, the lack of previous history knowledge is not expected to significantly impact on our analysis. Second, the sample size related to scoliotic patients is relatively small, therefore future studies with larger sample size are warranted to better investigate scoliotic curvature impacts on the BMD of the two femurs using QCT.

In conclusion, the present study demonstrated that a difference in femoral BMD exists between the two femurs of scoliotic patients undergoing QCT analysis of the hip. If these data are confirmed by larger study, dual hip DXA may be recommended at least in these patients as best practice.

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## Declarations

**Conflict of interest** The authors declare no conflict of interest.

**Ethics approval** This study was approved by the local ethics committee (RETRORAD, approved by the Local Ethical Committee of San Raffaele Hospital) and informed consent waived, since all patients had given written informed consent for the potential use of results of their examination for scientific purposes.

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