A COMPARISON OF DXA AND RADIOGRAPHIC MORPHOMETRY OF THE SPINE IN OSTEOPOROTIC WOMEN

Elina Reimer

Student thesis

UNIVERSITY OF OSLO
The Faculty of Medicine

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Supervisor: Professor dr. med. Erik Fink Eriksen

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Abstract

Introduction:

Prevalent vertebral fractures indicate a high risk of subsequent fractures, which makes fracture identification play a key role in the management of osteoporosis. Dual-energy X-ray absorptiometry can provide images for assessment of vertebral morphometry (MXA) with a much lower radiaton dose than conventional radiography, but it is still uncertain wether the resolution of MXA is adequate for vertebral morphometry. The aim of the study was to compare the number and level of agreement of quantitative morphometry of the vertebrae on lateral views of the spine using conventional X-ray (MRX) and using a dual X-ray absorbtiometry device (DXA/MXA)) in determining if there is a fracture of the vertebrae, and the degree of fracture in patients with osteoporosis.

Material and methods:

In order to test for concordance between spine fracture identification on conventional lateral X-ray and lateral X-rays obtained from DXA scans we investigated 74 patients with osteoporosis, who underwent DXA to acquire single-energy morphometric X-ray absorptiometry (MXA) scans and conventional lateral radiography (MRX) of the thoracic and lumbar spine. Adequate images were obtained in 99,2 % of the 1258 vertebrae by MRX and 77,7 % by MXA when vertebrae T1 to L5 were counted. Poor image quality was mostly found at T1-T4 and L4-L5 by MXA, and incident fractures of vertebra T5 were excluded from analysis because of poor image quality due to overlap of the ilium. Vertebral anterior and posterior heights were measured and the anterior/posterior (AP)-ratio was calculated.

Results:

MRX and MXA showed concordant results with respect to presence of fracture in 94,9 % of vertebrae examined. Concordance with respect to fracture severity (SQ grade) was 94,1 %. MXA graded 21 vertebrae (2,2 %) to be one SQ level higher than corresponding vertebrae on MRX images, while only 15 vertebrae (1,6 %) were graded as one SQ level higher using MRX. This represents a difference of 6 vertebrae (0,6 %). 7 vertebrae (0,7 %) were graded to be two SQ levels higher in MXA images than for MRX images, while this is the case in 4 vertebrae (0,4 %) in MRX images compared to MXA. This represents a difference of 3 vertebrae (0,3 %). Both MRX and MXA measurement graded one vertebrae (0,1 %) to be three fracture degrees higher.

Conclusions:

In conclusion we have demonstrated acceptable concordance between conventional X-ray readings and readings obtained from lateral X-rays from DXA scanners. Both techniques agreed on the presence of fractures in 95 % of cases and on fracture severity in 94 % of cases. This makes MXA well suited for assessment of spine fracture status in routine clinical practice. As the presence of spine fractures are major determinants of future fracture risk, but clinically silent in 80 % of cases the routine use of MXA should be expanded.

Key Words: Vertebral morphometry; vertebral deformity; osteoporosis; morphometric absorptiometry; MRX; MXA; Dual X-ray Absorptiometry (DXA); women; spine.

Introduction

Osteoporosis is a common disease, in particular in Scandinavian countries. The disease is characterized by excessive loss of bone from the skeleton with aging resulting in fractures after minimal trauma. These fractures, which mainly affect the forearm, spine and hip, do not only cause significant suffering and disability among patients, but also constitute a significant economic burden to society, in particular from treatment and subsequent disability caused by hip fractures in the elderly.

Among the Scandinavian countries, Norway ranks first in terms of number of hip fractures. The hip fracture is, however, a late event in the cascade of osteoporotic fractures. Spine fractures happen earlier. They signify more severe disease, but are far less symptomatic than hip- and forearm fractures. The bone loss in osteoporosis can be monitored with Dual X-ray Absorptiometry (DXA) and a bone mass 2,5 standard deviations or more below the bone mass of normal young women defines osteoporosis. However, as has been shown in several studies, the presence of a spine fracture increases the risk of subsequent fractures multiple times, and provides a better estimate of disease severity[47,72]. Detection of spine fractures is therefore of significant clinical value, but early detection is hampered by the fact that two thirds of spine fractures are asymptomatic. Until recently, therefore, patients had to undergo classical spine x-ray procedures, which are associated with significant radiation exposure (550 µSv for a lateral lumbar spine radiograph and 400 µSv for a thoracic film, estimated by Lewis et al.[51]). However, in recent years, DXA scanners have been equipped with software, which permits the construction of spine X-rays from the scans with far less radiation exposure.

The aim of this thesis was therefore to investigate the utility of a new technique for the assessment of spine fractures from pictures obtained on DXA scanners. Clinical use of this modality would result in less x-ray exposure to patients than conventional X-rays of the spine.

Definition

Osteoporosis is a systemic skeletal disease characterized by low bone density and micro architectural deterioration of bone tissue with a consequent increase in bone fragility and risk of fractures [1,3,27,47].

The World Health Organization (WHO) defines osteoporosis in postmenopausal women as "a BMD value at the spine, hip, or forearm of 2,5 or more SD (standard deviations) below the young adult mean (T-score ≤-2,5), with or without the presence of a fragility fracture" [11].

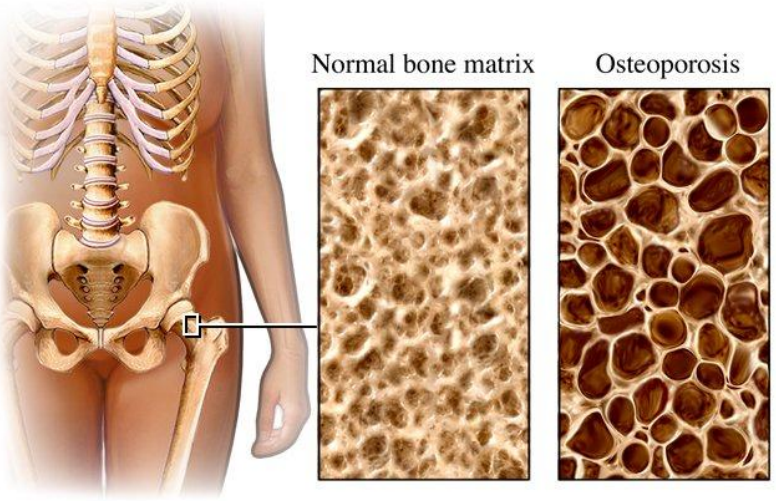

Figure 1: Comparison of normal bone matrix and osteoporosis in the hip.[5]

Epidemiology

Osteoporosis affects more than 75 million people in Europe, Japan and the USA, and each year it causes more than 2,3 million fractures in Europe and the USA alone [3]. The lifetime risk for hip, vertebral and forearm fractures in women has been estimated to be approximately 40 percent, and for men about 15 percent[3]. Vertebral fractures are the most common osteoporotic fracture, occurring in 15 % of women 50 to 59 years old and in 50 % of women 85 years or older, but are frequently undiagnosed, and only one third come to clinical attention[19,21,23,61]. The present of a fragility (low-trauma) fracture, both radiographically detected and clinical vertebral fractures, are associated with significant future fracture risk[47,72], morbidity[54,57,75], and mortality[45,46], and is a better predictor of the risk for subsequent fractures than DXA. Approximately 19 percent of patients who have a vertebral compression fracture will have another fracture within the next year [53,72].

Osteoporosis is three times more common in women than in men, partly because women have a lower peak bone mass and partly because of the hormonal changes that occur at the menopause [3]. Estrogens have an important function in preserving bone mass during adulthood, and bone loss occurs as levels decline, usually from around the age of 50 years [3]. So the majority of postmenopausal women with osteoporosis have bone loss related to oestrogen deficiency and/or age [69]. In addition, women live longer than men[4] and therefore have greater reduction in bone mass.

Among the Scandinavian countries having the highest incidence of hip fractures world wide [40], Norway ranks first, with the highest incidence of osteoporotic fractures [59]. In high prevalence areas like the Nordic countries, every second woman and 1 in 5 males can expect to suffer an osteoporotic fracture[28]. In Norway the incidence of osteoporosis in urban cities is higher than in rural cities, and a lower BMD in urban areas might help explaining this difference [59].

Osteoporosis does not only cause fractures, it also causes people to become bedridden with secondary complications that may be life threatening in the elderly population [3]. At the same time osteoporosis can cause back pain and loss of height, and prevention of the disease and its associated fractures is essential for maintaining health, quality of life, and independence among the elderly [3].

Pathogenesis

Histology studies on bone remodeling as well as other clinical studies in osteoporosis have established that bone in osteoporotic individuals in the majority of cases are characterized by two defects: 1) negative bone balance at each remodeling unit due to impaired osteoblastic function, which results in resorption outweighing bone formation and subsequent bone loss, and 2) a high turnover state with a lot of remodling units, which will tend to exacerbate and accellerate bone loss[25,29].

A slow phase of bone loss begins at the age of 40 years or earlier in both sexes and continues until late in life[25]. In postmenopausal women, an accelerated phase of bone loss is superimposed upon this pattern[25]. The accelerated bone loss begins at the time of the menopause, and decreases exponentially to become asymptotic with the slow phase after about 3-5 years[49,52].

Estrogen inhibits bone resorption and, after the menopause, estrogen deficiency results in increased bone resorption and rapid bone loss[18]. Type I (postmenopausal) osteoporosis occurs predominantly in women within 15-20 years after menopause, and is associated with vertebral crush fractures and fractures of the distal forearm[67].

Bone mass decreases with aging, and this decrease results in an increased incidence of hip and other fractures in elderly men and women (> 70 years of age), a condition called type II (age-related) osteoporosis[67], where vitamin D deficiency and subsequent secondary hyperparathyroidism play a pivotal role.

Age- and menopause-related bone loss are important pathogenetic factors, but their expression varies as there are wide variations in the amount of bone and the amount of "porosity" of bone in older persons of the same age[30].

Twin studies indicate that genetic determinants account for 40 to 80 percent of the differences in peak bone mass, BMD and fracture risk[18]. Skeletal structure and bone turnover are probably also genetically determined, but environmental factors affect bone growth during childhood and adolescence[18]. Thus, increasing calcium intake and physical activity have a small positive effect on peak bone mineral density[18]. Extensive genome wide searches have been unable to identify single genes with major impact on bone mass, all the hot spots identified so far only explain less than 5 % of the variance in fractures of bone mass[74].

Elements that distinguish osteoporosis from other causes of low bone mass, such as hyperparathyroidism and osteomalacia, include normal serum of calcium and phosphorus, and microarchitectural disruption without an increase in unmineralized osteoid[18].

A wide variety of medical conditions can cause secondary osteoporosis. Among the most prominent are: renal disease, celiac disease, thyroxicosis, hyperparathyroidism, hematological disorders, myeloma and other malignancies, alcoholism and hypogonadism.

Diagnosis

Osteoporosis has no clinical manifestations until a fracture occurs[69]. In comparison, pain is common in osteomalacia in the absence of fractures or other bone deformities[69]. The most common clinical manifestation of osteoporosis, is a vertebral compression fracture [35,69,72]. About two-thirds of these fractures are however asymptomatic, and are often incidental findings on chest- or abdominal x-rays[69,72].

Osteoporotic fractures (fragility fractures, low-trauma fractures) are those occurring from a fall from a standing height or less, without major trauma such as a motor vehicle accident [72]. The typical patient presents with acute back pain after sudden bending, coughing, or lifting, and the pain often radiates bilaterally into the anterior abdomen in the distribution of contiguous nerve routes, a so-called "girdle of pain"[72]. Radiation into the legs, as may be seen with a herniated disc, is rare with compression fractures[72].

Bone mass is the most commonly used method for assessment of fracture risk[56]. Even though bone mass estimates not tell anything about trabecular continuity and mechanical properties of the bone studied, a clear correlation between reductions in bone mass and increased

fracture risk exists[27]. Furthermore, the best prediction is achieved by measurements over the site, at which a risk estimate is wanted[56]. For osteoporosis, this happens to be over the hip and vertebrae, since this is where the clinically two most important fractures occur[56].

The most widely used definition of a vertebral fracture is a 20 % decrease in height at either the anterior, median or posterior aspects of vertebrae[27]. If the vertebrae of interest has undergone a total crush fracture, the height is compared to normal vertebrae either above or below the area of interest[27]. Vertebral morphometry is a quantitative method to identify osteoporotic vertebral fractures based on the measurement of vertebral heights[24]. There are two ways of performing vertebral morphometry:[24]

1) MRX: morphometric x-ray radiography,- conventional spinal radiographs
2) MXA: morphometric x-ray absorptiometry,- images obtained from dual x-ray absorptiometry (DXA)

Morphometric X-Ray Radiography

As the diagnosis of osteoporosis rests on the demonstration of a low energy fracture, x-ray studies are mandatory[27]. Fractures are easily demonstrated in long bones, while the assessment of vertebral fractures is more difficult[27].

In 1960 Barnett and Nordin introduced the technique, by using a transparent ruler to measure vertebral heights on conventional lateral radiographs of the thoracolumbar spine[24]. The radiologist has to identify the vertebral levels before performing vertebral heights measurements, but this may be difficult[24].

The accuracy and precision of SQ and morphometric methods are heavily influenced by the quality of the spinal radiographs, and it is therefore important to train x-ray technologists to use a standardized radiographic technique, which includes both patient positioning and the choice of radiographic parameters[24]. The lateral views of the thoracic and lumbar spine are the most important for assessment of osteoporotic deformity, but for the baseline identification of prevalent vertebral fractures, anteroposterior (AP) spinal views are also required to detect nonfracture vertebral deformities and to accurately define the number of vertebrae present[24].

Due to overlap with shoulders and pelvis, there are limitations in visualizing T1 to T3 and L5, and therefore T4 to L4 are routinely used for vertebral morphometry[24]. The vertebral endplates should be superimposed and the intervertebral disc spaces clearly seen throughout the length of the spine, if positioning of the patient and centering of the x-ray beam (eg, T7 and L3) has been correctly performed[24].

The need to reduce operator-dependent errors, such as manual point placement, led to the development of a computer-assisted system[60]. The procedure is based on an algorithm that automatically locates the vertebral body contour in the digitized x-ray image with the 6-point placement, which is then checked by the operator for accuracy[24]. The x- and y-coordinates of each point are stored in the computer, and the posterior, middle, and anterior heights of each vertebra, from T4 to L5, is calculated[24]. There are specific indices derived from height measurements for defining vertebral deformities, and the system also performs geometric calculations, enhancing the diagnostic capability of quantitative vertebral morphometry[24].

There are many advantages in performing digital morphometry, first and foremost convenience for the patient and lower radiation exposure, which permits more frequent use of

the technique. Lewis et al. estimated an average effective dose to female subjects of 550 µSv for a lateral lumbar spine radiograph and 400 µSv for a thoracic film[51]. A set of films for radiographic morphometry (MRX) therefore delivers an effective dose around 40 times greater than a MXA study[51].

Morphometric X-Ray Absorptiometry – vertebral fracture assessment by dual-energy x-ray absorptiometry (DXA)

Several studies have examined the concordance of VFA and lateral radiographs and found moderately good agreement[17,22,66,71]. There are two major manufacturers of new-generation densiometers:[24]

1) Hologic, Inc (Bedford, MA, USA)
2) GE Medical Systems (Lunar, Madison, WI, USA)

Figure 2: Bone Density Scan (DXA) used for osteoporotic screening and monitoring[9].

DXA scan of the spine is performed either by using a rotating arm (Hologic QDR 4500A, QDR Delphi, GE-Lunar Expert) with the patient lying in the supine position (Figure 2), or by placing the patient on in the left decubitus position similar to standard spinal radiographs (GE-Lunar Progidy and i-DXA)[24]. There are no significant differences between the lateral decubitus (Prodigy) and supine position (Expert) in measuring vertebral dimensions and in identifying vertebral fractures[64].

The program can automatically perform vertebral morphometry (MXA), after the scan, and the software places 6 points in each vertebra from L4 to T4 to calculate the vertebral heights, their ratios, and average height[24].

A final report is displayed after the analysis is finished, and it gives information on the measured vertebral heights and their ratios[24]. It also includes an assessment of the patient's fracture status based on normative data and different models for fracture assessment using quantitative morphometry[24].

In a population cohort of elderly women, VFA can frequently detect vertebral fractures, and these fractures predict future clinical fractures independent of age, weight and BMD[58].

Comparison between conventional radiography (MRX) and DXA images (MXA)

The accuracy and precision of radiographic morphometry (MRX) are limited by geometrical distortion due to projection effects and variable magnification in the X-ray cone beam[73]. Although MXA image definition is poorer than with MRX, the studies are acquired with a single scan of the spine from L4 to T4 and are undistorted in the cranio-caudal axis[51]. This difference is demonstrated in Figure 10, where the two MRX images have been merged.

On the other hand, a low radiation dose in MXA compared to radiographic morphometry (MRX), also means that MXA images constitute a lower geometric resolution, and may be more difficult to evaluate than MRX images.

A further advantage of MXA is the elimitation of the need for repeat films to obtain a technically adequate study[51].

However, further studies are required to document the ability of MXA to detect prevalent and incident vertebral deformities compared with radiographic morphometry (MRX)[51,73]

Treatment/management

Initial management of osteoporotic vertebral compression fractures should include pain control, with resumption of activity as quickly as possible and physical therapy [10,72]. The prevention and treatment of osteoporosis consists roughly of non-drug and hormonal therapy [2,28,68,70].

Nonpharmacologic therapy

Smoking is a significant risk factor for fracture[15,20,62], anorexia nervosa in young women demonstrates the influence of poor nutrition on skeletal health[28], while as exercise can slow down bone loss after menopause and is also important for muscular strength and coordination in elderly[20]. Therefore general changes in life style like smoking cessation, optimization of nutrition and regular exercise should be implemented in all osteoporotic patients at increased risk of fractures[28].

Over 90 % of hip fractures and all forearm fractures are caused by falls, mostly indoors, and preventive measures against falls can also be considered as lifestyle changes[28]. Yet there are no data showing that fall prevention decreases the risk of fracture[28], but some examples which may reduce the risk of falls in elderly include removing loose carpets, reduce the use of sleep medicine and other tranquilizers and correct visual impairment[28,38].

Supplementation with calcium and vitamin D has long been considered pivotal in the treatment of postmenopausal osteoporosis[28]. The current recommendations are that all osteoporosis treatments should be supplemented with 1000-1200 mg of calcium and 800 IU of vitamin D[16]. New studies have, however, raised questions about the efficacy and safety of calcium in fracture prevention, one of the first being The Women's Health Initiative (WHI) study[28]. Meta-analyses indicate that correction of vitamin D deficiency results in a decreased fall and fracture risk[13,14], but the effects depend on the target population and the dose of vitamin D, where high dose vitamin D may be effective in institutionalised persons eith severe vitamin D deficiency but may not be effective in the general population[44].

There is still much uncertainty regarding nutrition and bone health, especially when it comes to supplementation of osteoporosis treatment other than vitamin D and calcium[28].

Finally it is desirable to avoid, if possible, drugs that increase bone loss, such as glucocorticoids[70].

Pharmacologic therapy

- Bisphosphonates
- Selective estrogen receptor modulator (SERM) - *raloxifene*
- Estrogen/progestin therapy
- Parathyroid hormone (PTH)
- Denosumab (RANKL)
- Calcitonin
- Calcitriol
- Other therapies (vitamin K, folate/vitamin B12, growth factors o.l.)

Figure 3: Pharmacologic treatment of osteoporosis[6].

In a systemic review, MacLean et al. compared the effectiveness of treatments to prevent fractures in men and women with osteoporosis. The agens evaluated were bisphosphonates (alendronate, etidronate, ibandronate, pamidronate, siredronate and zoledronic acid), calcitonin, estrogen, teriparatide, selective estrogen receptor modulators (raloxifene and tamoxifen), testosterone, and vitamin D and calcium. They could not identify any head to head studies that demonstrated superiority of 1 agent over another in preventing fractures. Studies on postmenopausal osteoporotic women, however, provided good evidence that the bisphosphonates alendronate, etidronate, ibandronate and risedronate, as well as the hormones calcitonin and teriparatide, and the selective estrogen receptor modulator raloxifene, prevent fractures in the high-risk group. Effects of these agents on the different osteoporotic fractures: vertebral, hip and non-vertebral, however, differ.[55]

Materials and methods

Study Participants

The study group consisted of 74 postmenopausal osteoporotic women aged from 64-84 years (mean 72 ± 5 years), as illustrated in Figure 4 and Table 1. They were initially selected for a phase III osteoporosis trial, the main study and basis for this trial. On the basis of archive data in an osteoporotic specialist centre, 454 female patients were invited to DXA-scanning, and 86 patients were included in the main study, and both MXA- and MRX-images were captured. To be included in the study, the patients had to be ≥ 65 years on the day of randomization, postmenopausal for at least 5 years, and not having attended any previous osteoporosis treatment. Some of the patients from the main study are missing because they could not be found in the computer system for MXA measurements or MRX measurements.

For the women in this trial, mean bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (DXA), was 0,945 ± 0,125 g/cm^2 for vertebrae L1-L4 calculated on 73 of 74 participants (one patient's data missing due to computer error). The characteristics of this group are shown in Table 1.

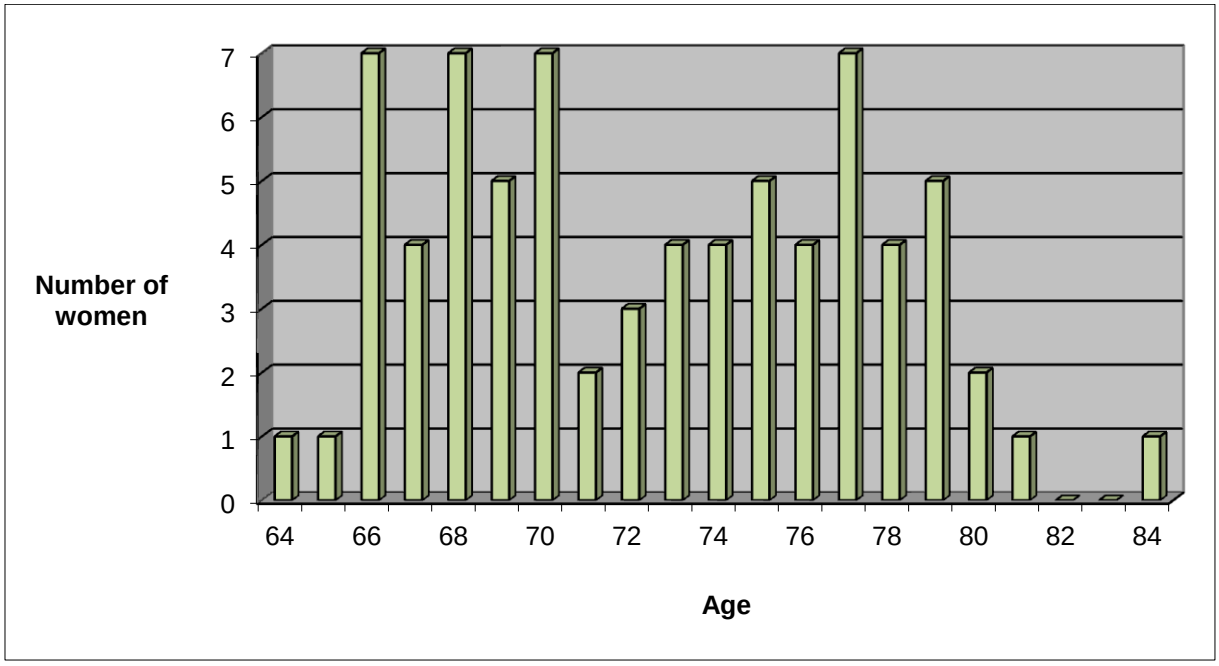

Figure 4: Age distribution in the patient material.

A total of 1258 vertebrae were examined. Of these 290 were excluded because of inadequate images. The participants went trough both classical spine X-ray procedures (MRX) and dual-energy X-ray absorbtiometry (DXA/MXA), and we analysed the level of agreement for vertebral compression fracture between MRX and MXA.

Vertebral morphometry

Lateral conventional spinal radiographs (MRX), and lateral images obtained from dual X-ray absorbtiometry (DXA/MXA) were obtained in each patient. The MRX images were captured under highly standardized guidelines to free project vertebrae in lateral view (patient lying on her side with knees bent), in order to achieve exact positioning of the vertebrae and avoid rotation of the vertebral corpuses. Furthermore the images were sentered in the middle of the thoracic and lumbar spine, producing two radiographic images of the spine. The MXA assessment was performed using GE-Lunar Progidy advance and Lunar i-DXA, both provided

with en CORE 2007 Software GE Healthcare. The patient was placed in the left lateral decubitus position similar to standard spinal radiographs. Adequate images were obtained in 99,2 % of the 1258 vertebrae by MRX and 77,7 % by MXA when vertebrae T1 to L5 were counted. Poor image quality was mostly at T1-T4 and L4-L5 by MXA, and an incident fracture of vertebrae T5 was excluded from analysis because of poor imgae quality.

Descriptive Data on Study Subjects			
Variable	Mean	SD	Range
Age (yr)	71,8	4,9	64-84
Weight (kg)	66,6	10,7	47,0-91,0
Height (cm)	161,6	5,6	151,6-178,0
BMI (kg/m^2)	24,8	3,7	17,2-38,3
Lumbar spine BMD (g/cm^2)	0,95	0,13	0,75-1,35

Table 1: Descriptive Data on Study Subjects. N = 74, all subjects were postmenopausal women. BMD, bone mineral density; BMI, body mass index.

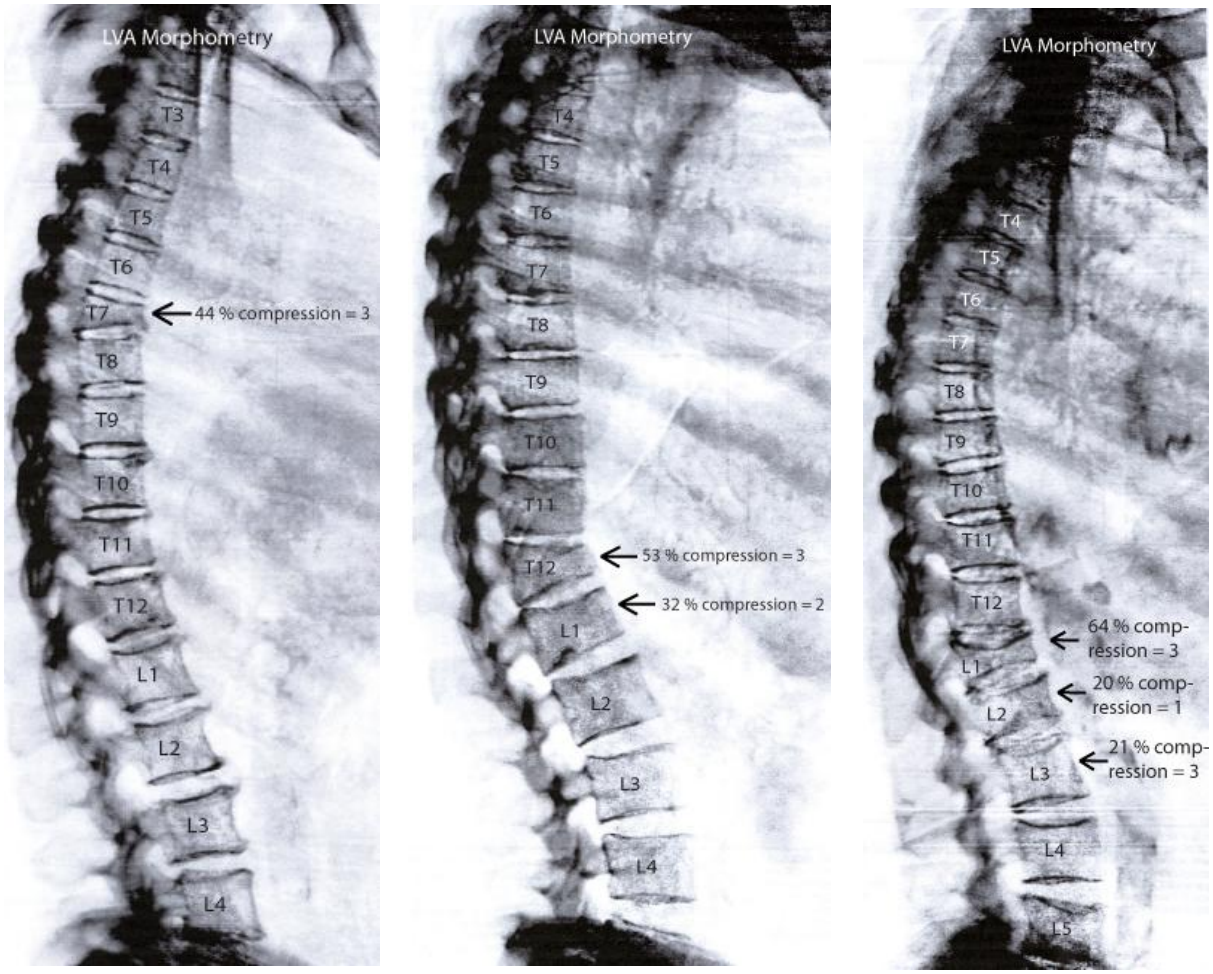

Figure 5: In this figure you can see MXA images where the vertebrae compression fractures are graded after a semi-quantitative (SQ) vertebral deformity score, from ”0” to ”3”.

An experienced radiologist graded the conventional spinal radiographs (MRX-images), while the DXA-images (MXA-images) were graded by the author. Both used a semi-quantitative

(SQ) vertebral deformity score as seen in Figure 6. On both scans and radiographs anterior (Ha) and posterior (Hp) vertebral heights were measured, alternatively mid (Hm) heights where it visually appeared to be a deformity, and wedge (Ha/Hp) and mid-wedge (Hm/Hp) ratios were calculated in percentage for the vertebral bodies. Equation used for estimation of compression degree in percentage:

$$100 - ((\frac{compression}{no\ compression}) \times 100)$$

Where *compression* was vertebral hight measured in millimeter at the site of compression, while *no compression* was vertebral hight measured in millimeter at the site of no compression.

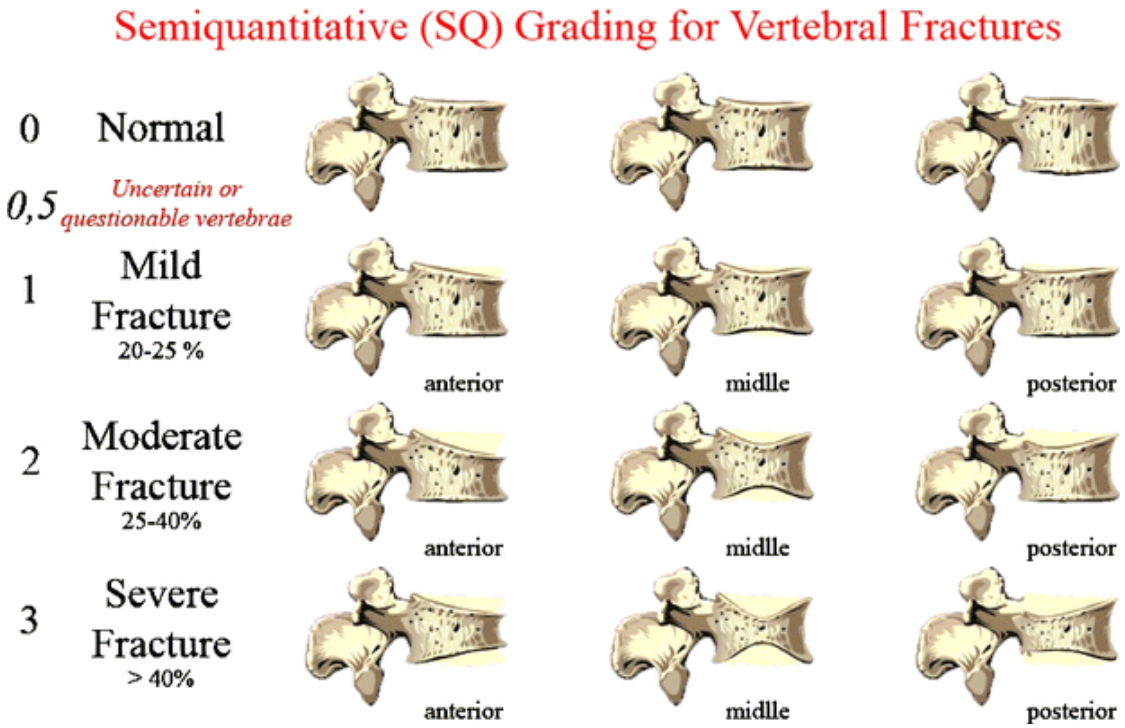

Figure 6: Semiquantitative (SQ) visual grading scheme for vertebral fractures. Genant's grading scheme for a semiquantitative evaluation of vertebral fracture. The drawings illustrate normal vertebrae (top row) and mild to severe fractures (respectively in the following rows). The size of the reduction in the anterior, middle, or posterior height is reflected in a corresponding to fracture grade, from 1 (mild) to 3 (severe).[41]

Both quantitative morphometry (QM) and semi-quantitative (SQ) methods are designed for the assessment of prevalent and incident fractures, but compared to QM, the SQ method is more convenient and reproducible, as well as better in the assessment of the risk of future fractures[43]. In this study we therefore chose to use the SQ score (Figure 6), which has been tested and applied in many clinical trials and epidemiological studies, and has been shown to represent an accurate and reproducible method of assessing fracture severity[36,37,39,42]. One should, however, be aware of that untrained SQ readers might produce a high number of false negative fractures of grade 1 (mild fracture)[43].

Vertebrae were assigned a SQ score of "0" if no fracture was present, "1" for a mild deformity (20-25% compression), "2" for a moderate deformity (26-40% compression), and "3" for a severe deformity (> 40% compression)[48]. Some examples from MXA images are given in Figure 5.

Results

In Table 2 we see the comparison of fracture severity based on SQ scoring obtained with the two methods. In the 74 subjects, nine hundred and sixty-eight vertebrae were available for analysis. Due to poor quality in MXA images mostly at the level from T1-T4 and L4-L5, 290 vertebrae (23,1 %) were defined as "not comparable" and were excluded from the analysis.

Not comparable		289		1	
MRX	3	1		2	4
	2	4	3	15	1
	1	12	9	4	
	0	889	16	7	1
		0	1	2	3
		MXA			

Table 2: Comparison of fracture severity in each vertebra. The green marked numbers in the middle show totally agreement between MXA- and MRX-images.

By eliminating the "not comparable" vertebrae, one can compare fracture and no fracture readings detected by MRX- and MXA measurements. This can be done at the level of individual vertebrae as seen in Table 3, or at the level of individual patients, as illustrated in Table 4, where each patient was counted once irrespective of how many fractures were present in each patient. Due to a poor quality MXA image it was not possible to compare the vertebrae in one of the patients, and therefore one patient is missing in Table 4.

		MXA		
		Fracture	No fracture	Total
MRX	Fracture	38	17	55
	No fracture	24	889	913
	Total	62	906	968

Table 3: Comparison of fracture versus no fracture in MRX- and MXA measurements on vertebrae level.

		MXA		
		Fracture	No fracture	Total
MRX	Fracture	26	5	31
	No fracture	10	32	42
	Total	36	37	73

Table 4: Comparison of fracture versus no fracture in MRX- and MXA measurements on patient level.

Another way of illustrating the degree of concordance is demonstrated in Figure 7. MRX and MXA measurements showed concordant results in 917 vertebrae (94,9 %) in terms of whether a fracture was present or not. MXA measurements graded 21 vertebrae (2,2 %) to be one SQ level higher than corresponding vertebrae on MRX images, while only 15 vertebrae (1,6 %) are graded as one SQ level higher for MRX images compared to MXA images. This represents a difference of 6 vertebrae (0,6 %). 7 vertebrae (0,7 %) are graded to be two SQ levels higher in MXA images than for MRX images, while this is the case in 4 vertebrae (0,4 %) in MRX images compared to MXA. This represents a difference of 3 vertebrae (0,3 %). Both MRX and MXA measurement have graded one vertebrae (0,1 %) to be three fracture degrees higher. Thus, both techniques agreed on the presence of fractures in 95 % of cases and on fracture severity in 94 % of cases.

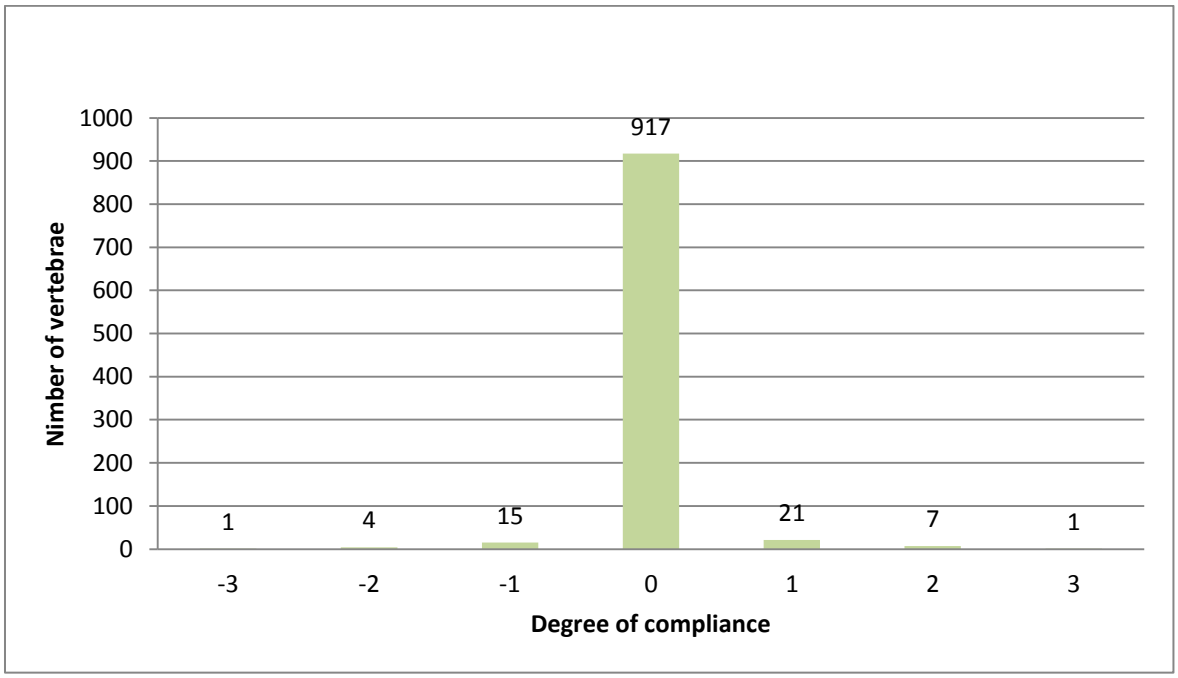

Figure 7: This figure shows the degree of compliance in relation to the grading system of vertebrae fracture (Figure 6). "0" meaning total compliance between MRX- and MXA images. "1": MXA images where the degree of fracture was estimated to be one level higher than in the MRX images. "2": MXA images where the degree of fracture was estimated to be two levels higher than in the MRX. "3": MXA images where the degree of fracture was estimated to be three levels higher than in the MRX images. "-1": MRX images where the degree of fracture was estimated to be one level higher than in the MXA images. "-2": MRX images where the degree of fracture was estimated to be two levels higher than in the MXA images. "-3": MRX images where the degree of fracture was estimated to be three levels higher than in the MXA images.

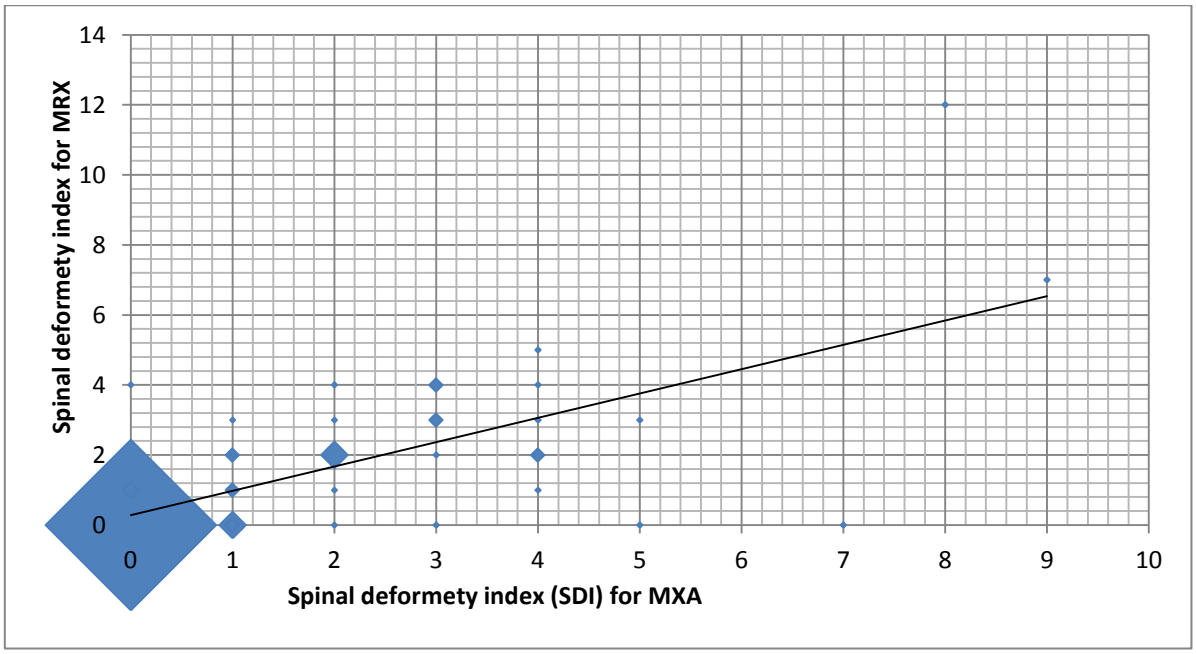

Figure 8: Comparison of Spinal Deformity Index (SDI). Plot (0,1) and (0,2) are covered by plot (0,0) in the diagram, and count for 3 and 2 patients respectively. The size of the plot reflects the number of patients with the same SDI-value.

The Bland-Altman plot is a graphical method to compare two measurements techniques, where the differences between the two techniques are plotted against the average of the two techniques[8]. For spinal deformity index in this paper, the Bland-Altman plot (Figure 9) showed no systematic difference between the 2 methods as the line representing the mean of differences is situated at -0,1 with 95 confidence intervals encompassing the line of identity. The 95 % confidence interval for the mean of differences was between -3,2 to + 2,9.

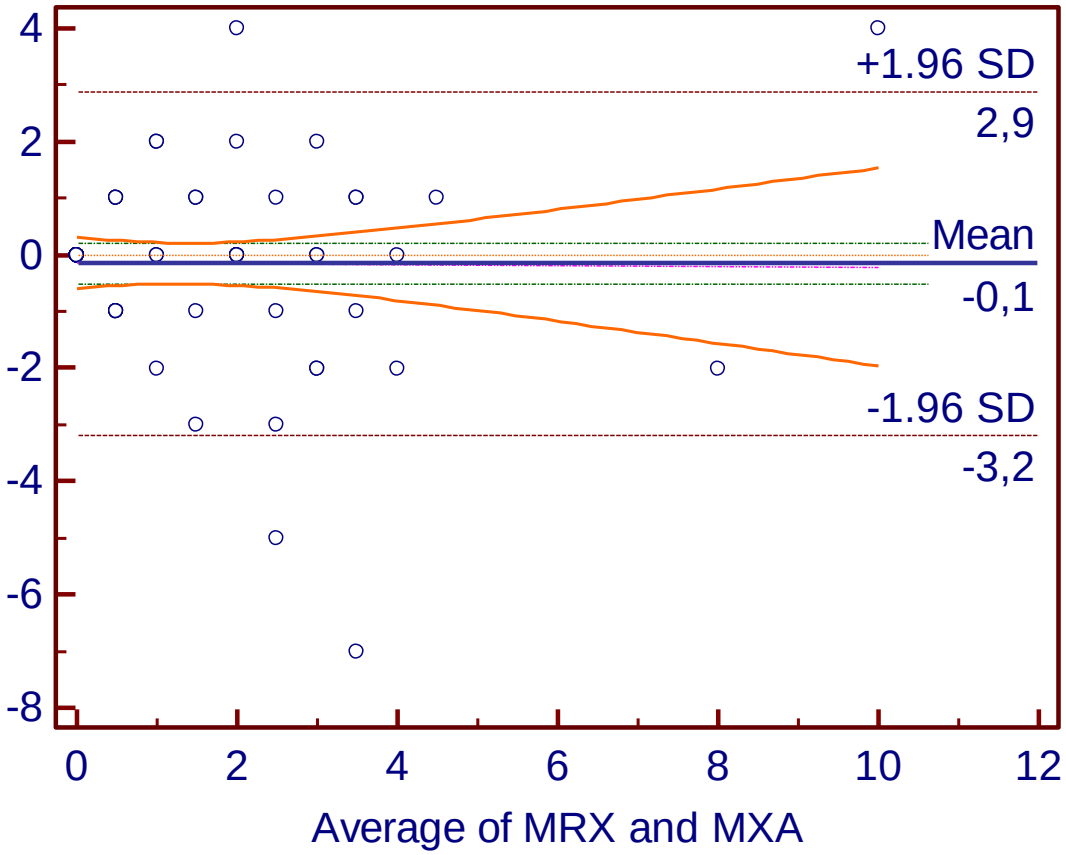

Figure 9: Bland-Altman plot where the average of DXA and Radiography Spinal Deformity Index (SDI) results are plotted against each other. Horizontal lines are drawn at the mean difference, and at the limits of agreement, which are defined as the mean difference plus and minus 1,96 times the standard deviation of the differences. Furthermore lines for 95 % CI of mean difference (-3,2 to + 2,9), the line for 95 % CI of differences (to help detect proportional difference), and the line of equality (difference = 0) is drawn. [7]

Discussion

In the past, different studies have been undertaken to compare the methods morphometric X-ray radiography (MRX) and morphometric X-ray absorptiometry (MXA) to detect osteoporotic fractures. Results vary but conventional radiography is still held as the golden standard.

The concordance between the 2 methods in terms of fracture identification was 94,9 %. This is reassuring because the absence or presence of fracture is one of the most important risk factors for subsequent fracture. The two methods differed more with respect to concordance for fracture severity, but no systematic differences were demonstrable. This is consistent with the results of Pavlov et al., where the 2 techniques found similar numbers of patients to have vertebral deformities, and a concordance in classification of individual vertebrae of 94 % with a 3 standard deviation (SD) criterion[63].

The Bland-Altman plots revealed that no systematic bias was detectable between the 2 methods in this paper (Figure 9), as the differences are symmetrical around zero[8]. This is also shown for the H_a/H_p ratio by Pavlov et al. who used the Bland-Altman plot to compare vertebral heights measured by MRX and MXA[63]. They found, however, that MXA values for H_m/H_p ratio were significantly less than corresponding MRX values, resulting in differences beeing symmetrical around approximately -0,1.

The fraction of discordant readings for fracture severity in this paper were a total of 5,9 %, with differences of 1 SQ grade constituting 3,8 % and differences exceeding 1 SQ grade amounting to 2,1 %. MRX graded one vertebrae to be three degrees of fracture higher than the corresponding vertebrae in the MXA image. This was due to a misjudgment by the radiologist. MXA also graded one vertebra to be three degrees of fracture higher than the corresponding vertebra in the MRX image, which was due to more difficult assessment because of rotation of the image. In retrospect this vertebra should have been classified as "not comparable". It was, however, possible to detect a compression fracture if one compared the anterior part of the current vertebrae with the anterior part of the vertebraes lying caudally and cranially.

Deformed vertebrae can be caused by a compression fracture, degenerative changes and Scheuermann's disease. The latter seemed the major cause for differences between the 2 techniques. What seems like a compression fracture at first, may instead be a deformation caused by for example Scheuermann's disease (as seen in Figure 10), and not be caused by osteoporosis. This leads us to another consideration. Even though the SQ method is easy to use, the results of the analysis depend a great deal on the performer's experience since there are factors that could be misleading. This might help explain the relatively high number of fractures in DXA images compared to radiographic images as seen in Table 3.

Guglielmi et al. and Francucci et al. also came to the conclusion that a trained radiologist or a highly experienced clinician would be necessary to analyse the data correctly. However, they also conclude that it is only the MRX (Radiographic images) that has the potential for qualitative reading, inlike the MXA (DXA images)[33,41].

Furthermore Guglielmi et al., Ferrar et al. and Francucci et al. come to the conclusion that the visual or morphometric assessment of lateral MXA spine images may have the potential for use as a prescreening tool, due to the relatively low radiation dose to the patient and the

excellent agreement with the visual SQ method for the identification of vertebral deformeties[32,33,41]. Guglielmi et al. thus conclude that if one or more deformities are detected by IVA or MXA, it will be necessary to acquire conventional radiography to identify the nature of the deformity and to investigate for possibly further prevalent deformities. In this paper we do agree that MXA may be used as a screening tool, but our results point in the direction that MXA also is well suited for assessment of spinal fracture status in routine clinical practice.

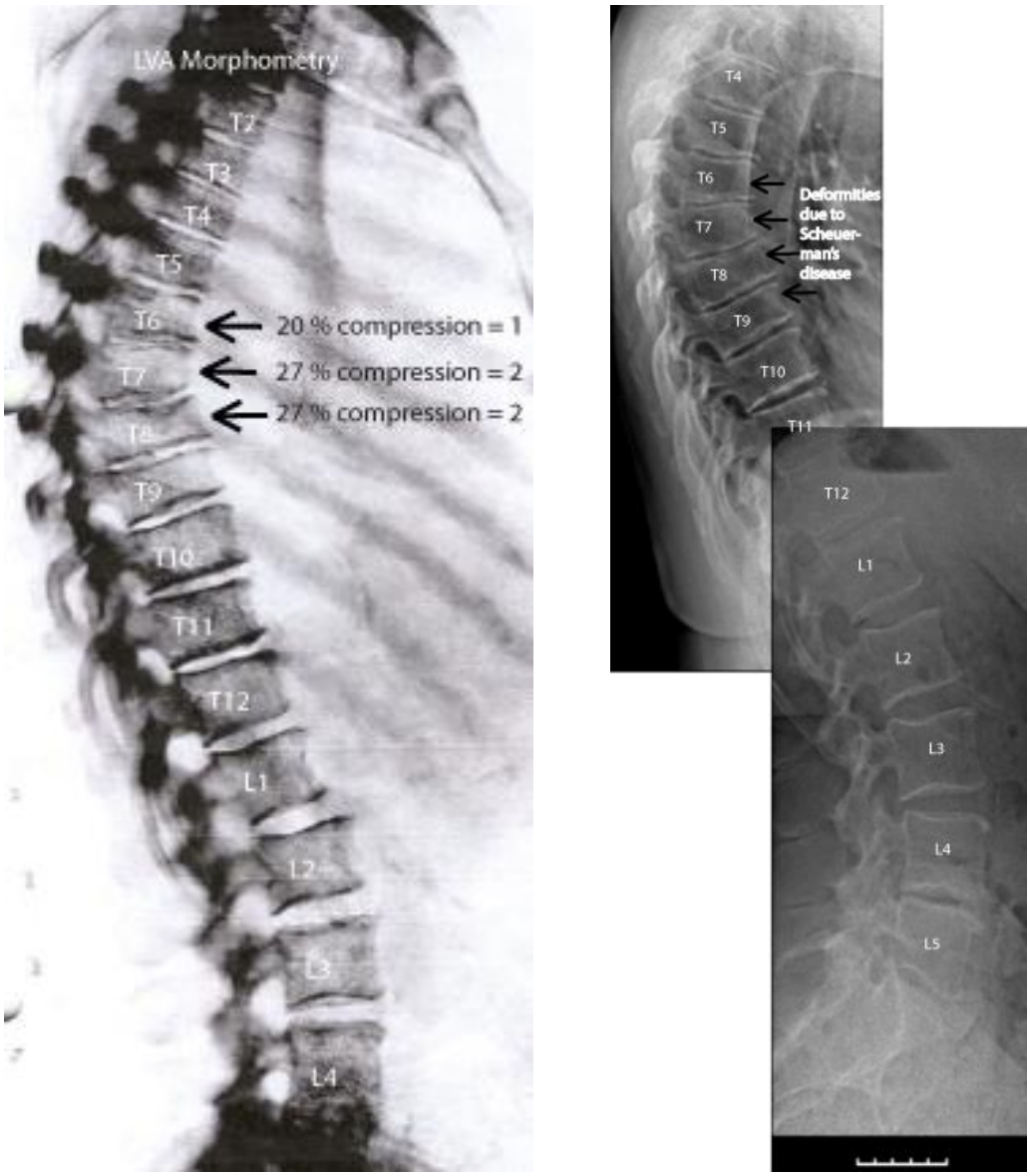

Figure 10: Deformed vertebrae due to Scheuermann's disease. The left picture is a DXA image, and deformed vertebrae are interpreted as compression fractures. This is however mistaken, and in the right picture taken by conventional radiography, the radiologist has evaluated these deformed vertebrae to be caused by Scheuerman's disease.

Our results therefore match better with Pavlov et. al., Fuerst et al. and Ferrar et al., who compared MXA with MRX in detecting vertebral deformities in an osteoporotic population, and found good agreement between the technique[31,34,63]. In the study by Pavlov et al., MXA also showed acceptable performance for clinical use in diagnosing vertebral deformities, as

long as cut-offs of > or = 3 SDs were used, although a few percent of vertebrae in the upper thoracic region could not be imaged adequately by using the MXA technique[63]. Other studies have shown that MXA is comparing favorably with MRX in detecting vertebral fractures using the Genant SQ method[12,50,66,71,76], and in accordance with this paper Lewiecki et al. found MXA to be reliable and accurate at diagnosing vertebral fractures, as well as it showed greater patient convenience, lower cost for the patient and lower radiation exposure compared to MRX[50].

In a study that examined the measurements of vertebral body heights, Edmondston et al. compared morphometric X-ray absorbtiometry, morphometric radiography and direct measurements of vertebral body heights[26]. The study showed that both quantitative morphometry (QM) and MXA measurements were strongly correlated with the direct measurements, and where QM tended to overestimate the true height, MXA tended towards underestimation[26]. They concluded that MXA is comparable to spinal radiography for the assessment of vertebral height under optimal scanning conditions[26].

According to Francucci et al., the reliability of MXA measurements depends on the precision of the technique, which is influenced by system error, variability associated with morphometric analysis, and variability within study populations[33]. Francucci et al. conclude that technological improvements are necessary to improve image quality[33]. Ferrar et al. do not completely agree, but mean that MXA is comparable to MRX for the identification of incident deformities when scans are analyzed with the compare facility, as well as it has good long-term precision[31]. Pavlov et al. even found that the long-term precision was better for MXA than for MRX[63]. In line with this study, however, numerous studies point out that MXA is limited compared to MRX, by the exclution of vertebrae that are not clearly imaged[31,33,34,50,63].

Except for a few vertebrae in the radiographic images, the “not comparable” vertebrae, as listed in Table 2, were mostly due to poor quality MXA images (also experienced by Pavlov et. al., Lewiecki et al. and Fuerst et al.[34,50,63]), and are mostly located from the vertebral level Th1 to Th4 and L4 to L5. In this case this does not affect the outcome of fracture number and degree much, since in all cases except for one, the radiographic images did not show any fractures on corresponding vertebrae. Still, not being able to get good quality images of the whole spine is a disadvantage for the MXA method which could lead to incomplete readings in a limited number of subjects.

When it comes to SQ grading of vertebrae deformities (Table 2), some of the differences between the degrees of deformity might be explained by small differences in fracture percentage. For instance, if a vertebral compression fracture is calculated to be 40 % in MXA-images, and 41 % in radiographic images, the semiquantitative (SQ) score will be respectively 2 and 3. Another aspect of the 0-3 SQ grading is that several values plot together in the Bland Altman plot (Figure 9). These plots would be more accurate if they had some way to express how many cases got the same value.

Intra- and inter-observer precision errors must also be taken into account, and Rea et al. find that these are larger for MXA than for MRX in both normal subjects and those with vertebral deformities[65]. When compared with MRX, this might of course increase the risk of the erroneous classification of vertebrae as either normal or deformed. The difference in precision of these methods could be explained by the difference in image quality, the better quality image in MRX gives less uncertainty and will most probably lead to better intra- and inter-observer precision. In addition, MRX being a well established method, most likely with

experienced personell would probably be a more precise method than MXA which is more recent and thus less established. However, these advantages of MRX are offset by the higher radiation dose and inconvenience for the patients having to go to another facility for examination.

In conclusion we have demonstrated acceptable concordance between conventional X-ray readings and readings obtained from lateral X-rays from DXA scanners. Both techniques agreed on the presence of fractures in 95 % of cases and on fracture severity in 94 % of cases. Discordant results were thus only seen in 5-6 % of patients, which makes MXA well suited for assessment of spinal fracture status in routine clinical practice. As the presence of spine fractures are major determinants of future fracture risk, but clinically silent in 80 % of cases the routine use of MXA should be expanded. Conventional X-ray of the spine is still needed, however, in cases of suspected malignancy, and other indeterminate changes on MXA, but expanded use of MXA would reduce the number of such examinations, thus reducing overall radiation dose administered, as well as reducing inconvenience and cost to the patient.

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