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Vertebral morphometry: current methods and recent advances

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Abstract Vertebral fractures are the hallmark of osteoporosis and are associated with increased morbility and mortality. Because a majority of vertebral fractures often occur in absence of specific trauma and are asymptomatic, their identification is radiographic. The two most widely used methods to determine the severity of vertebral fractures are the visual semiquantitative (SQ) assessment and the morphometric quantitative approach, involving the measurements of vertebral body heights. The measurements may be made on conventional spinal radiographs (MRX: morphometric X-ray radiography) or on images obtained from dual X-ray absorptiometry (DXA) scans (MXA: morphometric X-ray absorptiometry). The availability of a rapid, low-dose method for assessment of vertebral fractures, using advanced fan-beam DXA devices, provides a practical method for integrated assessment of BMD and vertebral fracture status. The visual or morphometric assessment of lateral DXA spine images may have a potential role for use as a prescreening tool, excluding normal subjects prior to performing conventional radiographs.

Keywords Osteoporosis · Vertebral fractures · Vertebral heights · Semiquantitative vertebral assessment · Quantitative vertebral morphometry · Morphometric X-ray radiography · Dual X-ray absorptiometry · Morphometric X-ray absorptiometry

Introduction

Vertebral morphometry is a quantitative method to identify osteoporotic vertebral fractures that relies on the measurement of distinct vertebral dimensions, calculating relative changes.

A vertebral fracture appears as an alteration in the shape and size of the vertebral body, with a reduction in vertebral body height, as a *wedge, end-plate (mono-or biconcave), or collapse* vertebral deformity (Fig. 1).

The majority of osteoporotic vertebral fractures are mild vertebral deformities, with a reduction in height of not more than 20–25 percent (according to Genant's semi-quantitative index) [1] without a visible discontinuity of bone architecture. These are often asymptomatic and occur in absence of specific trauma, with a prevalence of 31% in men and 17% in women, but it should be specified that in younger men the prevalence rates are extremely age-dependent, and the large fraction of vertebral fractures is not due to osteoporosis [2]. Even these mild vertebral

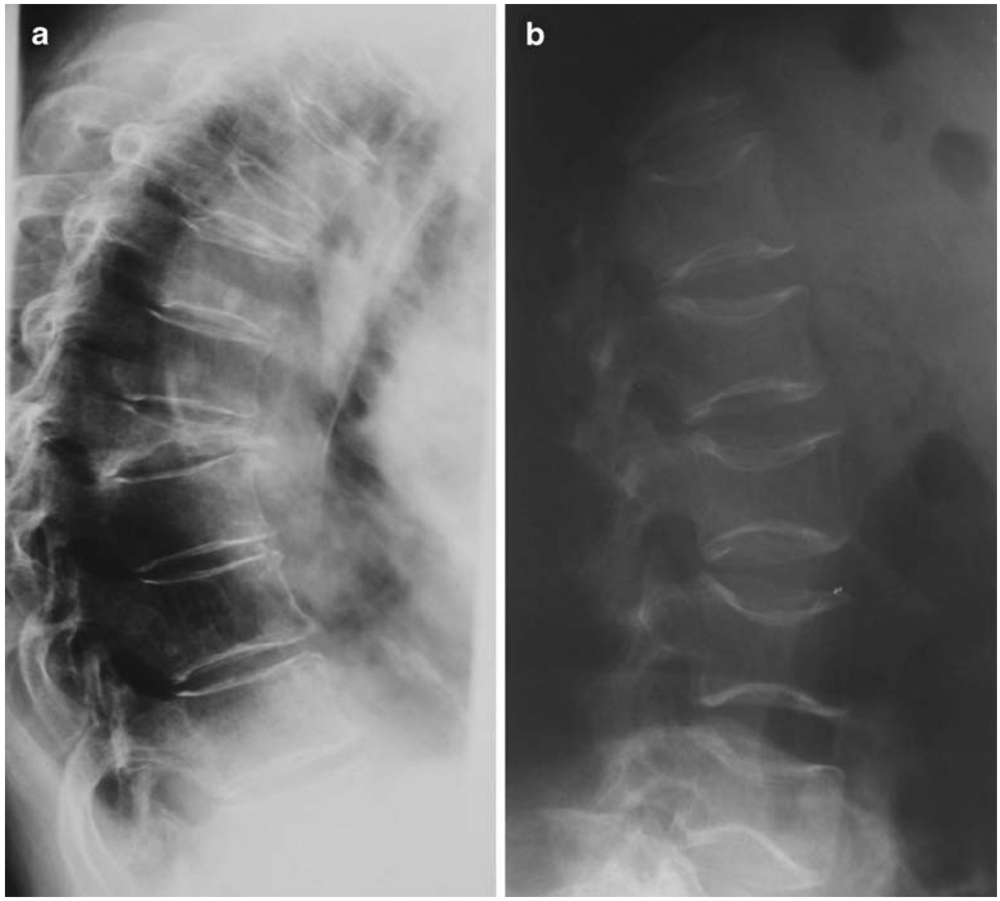

Fig. 1 Multiple vertebral fractures: crushing and wedging at the thoracic spine level (a) and biconcavity at the lumbar level (b)

deformities could have clinical consequences for the patient because of the increased, approximately five fold, risk of future fractures that may be symptomatic [3]. Vertebral fractures are the most common of all osteoporotic fractures [4–9] and are associated with an increased mortality rate [10, 11], loss of independence in elderly patients, and impaired quality of life [12–16]. For these reasons the prevention of future fractures in patients with vertebral fractures has been considered the endpoint in clinical osteoporosis therapy trials [17–23]. It is in the accurate diagnosis of asymptomatic vertebral fractures that radiologists make perhaps the most significant contribution to osteoporotic patient care [24]. In everyday clinical practice, vertebral fractures are usually diagnosed by visual inspection of the patient's spinal radiographs. However, this qualitative approach to identify vertebral fractures is regarded as subjective and therefore may lead to disagreement, especially when performed by inexperienced observers [25]. For epidemiological studies and clinical drug trials in osteoporosis research, objective and reproducible results are required. Therefore more than a decade ago the semiquantitative (SQ) [1] and the quantitative (e.g., vertebral morphometry) [26–28] methods of defining prevalence and incidence of vertebral fractures were proposed.

Standardized visual assessment of vertebral deformities

Using this approach, numeric scores are assigned to vertebral deformities according to their shape or type and their severity in a definable and reproducible manner without making direct measurements. Several standardized methods to assess vertebral deformities have been proposed [29], but the visual semiquantitative (SQ) method previously described by Genant et al. [25] is currently most widely used in multi-centre clinical trials.

The SQ method is based on evaluation of conventional radiographs by radiologists or experienced clinicians in order to identify and then classify vertebral fractures. Vertebrae T4-L4 are graded by visual inspection and without direct vertebral measurement as *normal* (grade 0), *mild* but "definite" fracture (grade 1 with approximately 20–25% reduction in anterior, middle, and/or posterior height, and 10–20% reduction in area), *moderate* fracture (grade 2 with approximately 25–40% reduction in any height and 20–40% reduction in area), and severe fracture (grade 3 with approximately 40% or grater reduction in any height and area) Additionally, a grade 0.5 was used to designate a borderline deformed vertebra that is not considered to be a definite fracture (Fig. 2).

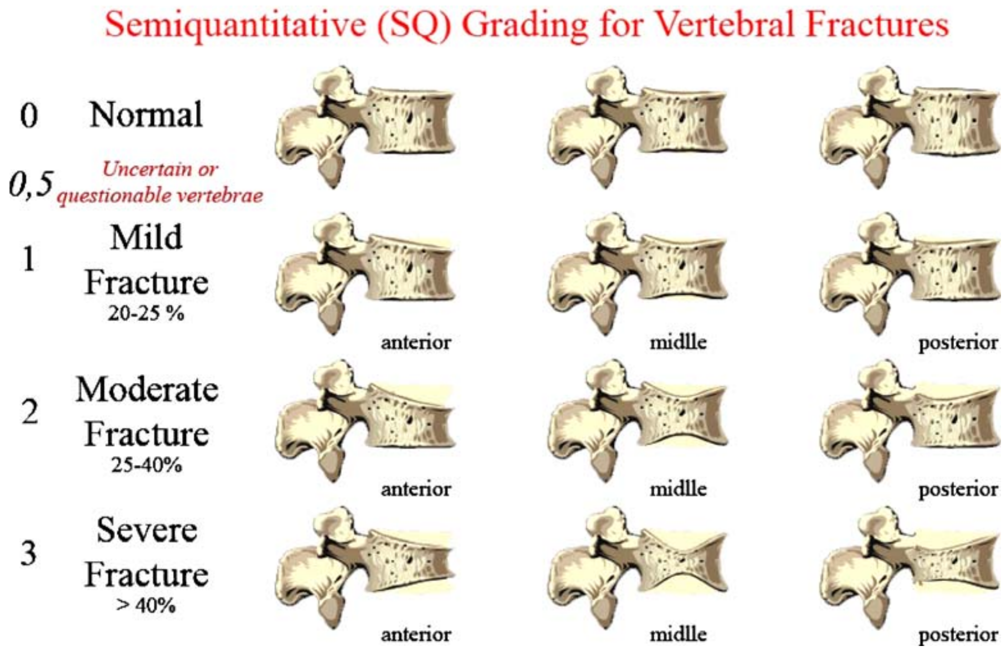

Fig. 2 Semiquantitative (SQ) visual grading scheme for vertebral fractures. Genant's grading scheme for a semi-quantitative evaluation of vertebral fracture. The drawings illustrate normal vertebrae (top row) and mild to severe fractures (respectively in the following rows). The size of the reduction in the anterior, middle, or posterior height is reflected in a corresponding to fracture grade, from 1 (mild) to 3 (severe)

Incident fractures are defined as those vertebrae that show a higher deformity grade on the follow-up radiographs. Because both the number and the severity of prior vertebral fractures are important predictor variables, Genant et al. [30] combined the information into one measure, the so-called spinal deformity index (SDI). For each vertebra, a visual semiquantitative grade of 0, 1, 2, or 3 is assigned for no fracture or mild, moderate, or severe fracture, respectively, and the SDI is calculated by summing the fracture grades of the 13 vertebrae from T4 to L4 (Fig. 3). An increase in SDI could occur either due to a new vertebral fracture or due to worsening of mild or moderate prevalent vertebral fractures. Crans et al. [31] demonstrated the prognostic utility of the SDI for assessing future vertebral fracture risk; patients with greater baseline SDI had the greater future risk for vertebral fractures.

The SQ method represents a simple, but standardized approach that provides reasonable reproducibility, sensitivity, and specificity, allowing excellent agreement for the diagnosis of prevalent and incident vertebral fractures to be achieved among trained observers [32].

However, this method has some limitations. In cases of subtle deformities, such as mild wedge-like deformities in the mid-thoracic region and bowed endplates in the lumbar region, the distinction between borderline deformity (grade 0.5) and definite mild (grade 1) fractures can be difficult and sometimes arbitrary (Fig. 4). Accurate diagnosis of prevalent fractures, which requires assessment of normal variations and degenerative changes and distinguishing them from true fractures, still depends on the experience of the observer. Another limitation of visual SQ assessment is the relatively poor reproducibility in distinguishing the three different grades of vertebral fractures.

Vertebral morphometry

This technique was introduced as early as 1960 by Barnett and Nordin [33], who used a transparent ruler to measure vertebral heights on conventional lateral radiographs of the thoracolumbar spine. Vertebral morphometry may be performed on conventional spinal radiographs (MRX: morphometric X-ray radiography) or on images obtained from dual X-ray absorptiometry (DXA) scans (MXA: morphometric X-ray absorptiometry).

Morphometric X-ray radiography (MRX)

Quantitative vertebral morphometry involves making measurements of vertebral body heights. Before performing the vertebral heights measurement, the radiologist has to identify the vertebral levels; to make this easier, T12 and L1 should be visualized on both the lateral thoracic and lumbar radiographs. Identification of vertebral levels on radiographs of lumbar and thoracic spine may be difficult at times (e.g., anatomic variants of the lumbosacral transition or the thoracolumbar junction). The vertebral bodies should be marked so that they can be more easily identified in other reading sessions or when compared with follow-up radiographs. On lateral radiographs, with six-point placement-the most widely used technique [34]-the four corner points of each vertebral body from T4 to L4 and an additional point in the middle of the upper and lower endplates are manually marked (Fig. 5). The manual point placement is done according to Hurxthal [35], who proposed excluding the uncinate process at the posterosuperior border of the thoracic vertebrae and the Schmorl's

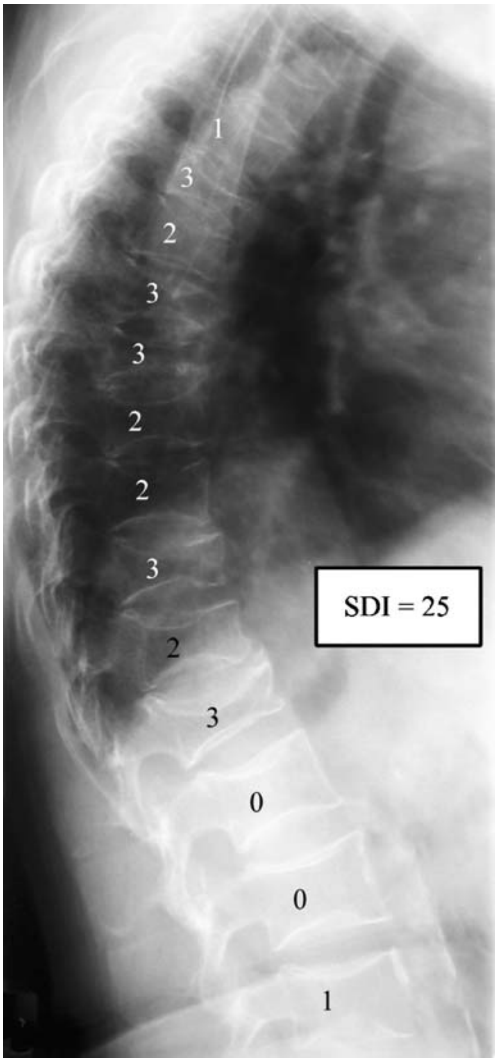

Fig. 3 Spine Deformity Index (SDI) calculated by summarizing the semiquantitative grades of all vertebrae from T4 to L4

nodes and osteophytes from vertebral height measurement. When the outer contours of the endplate are not superimposed (incorrect patient positioning or severe scoliosis), the middle points are placed in the centre between the upper and the lower contour (Fig. 6).

Digital morphometry

More than a decade ago, some investigators [36, 37] developed a system for vertebral morphometry that is based on digital images displayed on a high-resolution workstation. Post-processing of the digital images can highlight the endplate and the four corners of vertebral bodies allowing points to be placed more precisely. The software automatically determines the midpoints between anterior and posterior corner points of the upper and lower endplates. Then the operator selects the true midpoints moving the calipers along a vertical line joining the vertebral endplates. The *x* and *y* coordinates of each point are stored in the computer, which calculates the posterior, middle, and anterior heights (Hp, Hm, Ha) of each vertebra, from T4 to L5, and specific indices derived from height measurements for defining vertebral deformities. There are many advantages in performing digital morphometry: magnification of the images to a specific level; selection of the contrast and brightness levels for optimum visibility of the cortical bone, a capability that is especially valuable when the film is of less than optimal quality; the images may be stored on optical disks, CD or DVD and can be re-measured on multiple occasions. Finally, measurement data can be captured directly from the images into a database, eliminating the need for data entry. The manual placement of the six measuring points represents a source of error in the measurement of the vertebral body because the placement can vary widely among various operators. The need to reduce these operator-dependent errors led to the development of a computer-assisted system [38, 39]. The procedure is based on an algorithm that automatically locates the vertebral body contour in the digitized X-ray

Fig. 4 Limits of the visual SQ method in subtle deformities: “borderline” deformity of T7 defined as grade 0.5

Fig. 5 MRX: measurement of vertebral heights shows mild wedging of T7 with 20–25% reduction in anterior height

image and then is checked by the operator for accuracy. Correction is possible through operator intervention at any time. The system also performs additional geometric calculations, enhancing the diagnostic capability of quantitative vertebral morphometry. This algorithm was used in the European Vertebral Osteoporosis Study (EVOS), but the reproducibility was worse than that with the manual placement technique [40]. Because the six-point placement technique might not completely describe vertebral shape, Smyth et al. [41] developed a technique based on use of an active shape model (ASM). An ASM is a statistical model to locate and measure the shapes of variable objects in images. It was applied to the measurement of vertebral shape on lateral spine DXA scans. The ASM technique obtained entire shape information, with accuracy as good as that with manual methods, but it can be performed more easily and rapidly [41, 42]. Therefore, digital morphometry with computer assistance and hierarchical segmentation of vertebrae from X-ray images [43–45] represent useful tools to evaluate a large number of cases, allowing centralization of images for a large-scale clinical trial.

Recently a new digital technique for vertebral morphometry has been introduced in clinical practice using an instrument called MorphoXpress. MorphoXpress (Procter & Gamble Pharmaceuticals, Rusham Park, Egham, UK) is a statistical model-based vision system to digitise and analyse plain film vertebral X-rays for semi-automated morphometric assessment. This system is based on a new technology that represents the next generation of statistical model-based techniques. To our knowledge, MorphoXpress is the first automated six-point morphometric system to operate on digitised plain film X-ray images, as opposed to DXA. Furthermore, unlike DXA, X-rays of the spine are still the only approved modality for diagnosis of vertebral fracture by the US Food and Drug Administration (FDA).

This system works as follows: having defined a patient record, original lateral spine X-rays are digitised using a flatbed scanner connect to the personal computer that hosts the MorphoXpress software application, and analysis is initialised by the manual indication of the centres of the upper and lower vertebrae to be analysed. The software then automatically finds the positions of the contours of the vertebrae, including the double endplate contours and part of vertebral process. This annotation is then used to determine landmarks for a standard six-point morphometry measurement, providing an optional confidence measure of correct registration for each vertebra. The software allows these points to be moved by the operator, if necessary, before the points are confirmed as being in correctly positioned. The positions of the confirmed points are then used by the software to calculate anterior, medial, and posterior vertebral heights, and these heights may also be used for the determination of a deformity metric. Finally, another advantage of this approach is given by the improvement of the workflow and in the overall positive results in terms of diagnostic accuracy (2.1% CV) and precision (1.68% CV) [46, 47].

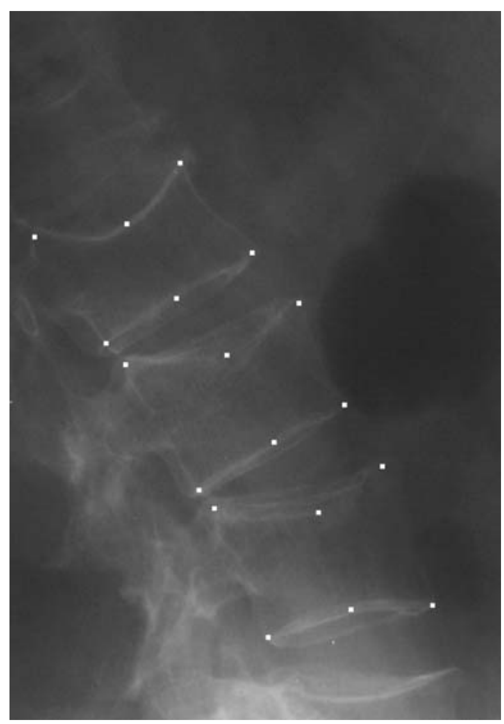

Fig. 6 Manual placement of six vertebral points in MRX

Consideration of radiographic technique

The accuracy and precision of semiquantitative and morphometric methods are heavily influenced by the quality of the spinal radiographs. Optimal radiographs can be achieved by training X-ray technologists and making sure that they are aware of the difference between radiographs for osteoporotic vertebral assessment and those for routine clinical practice, by using a standardized radiographic technique [48], which includes both patient positioning and the choice of radiographic parameters. Because the lateral views of the thoracic and lumbar spine are the most important views for the assessment of osteoporotic deformity, time and attention should be taken in correctly positioning the patient and in properly exposing the films.

However, for the baseline identification of vertebral fractures, also antero-posterior (AP) spinal views are required to accurately define the number of vertebrae present and thus to allow accurate identification of the vertebral levels on the lateral spine views. Currently, T4 to L4 are routinely used for vertebral morphometry, because of limitations in visualizing T1-T3 due to overlying of the shoulders and L5 due to overlying pelvis. In a patient with marked scoliosis of the thoracic or lumbar spine (Cobb angle >15 degrees on the AP view), it is unlikely that vertebral morphometry can be performed because of the difficulty of positioning the spine parallel to the X-ray table. If positioning of the patient and centering of the X-ray beam (e.g., T7 and L3) has been correctly performed, the vertebral endplates should be superimposed, and the intervertebral disc spaces can be clearly seen throughout the length of the spine. The obliquity could cause false appearance of biconcavity, thus affecting the diagnosis of vertebral deformity. The obliquity of the vertebrae can also be observed at the periphery of the radiographs due to the effect of parallax, which is caused by the divergence of the cone-beam of X-rays.

In the case of serial X-rays, it is important to use the same focus to film distance to avoid the apparent decrement of vertebral heights. In fact, a 10.2-cm increase in tube-to-film distance results in a 6.4% decrease in the measured posterior height, a 5.5% decrease in the measured anterior height, and a 3.5% decrease in measured vertebral area [49].

Morphometric X-ray absorptiometry (MXA)

To overcome some limitations of MRX, another method called morphometric X-ray absorptiometry (MXA) has been developed by the two major manufacturers of DXA

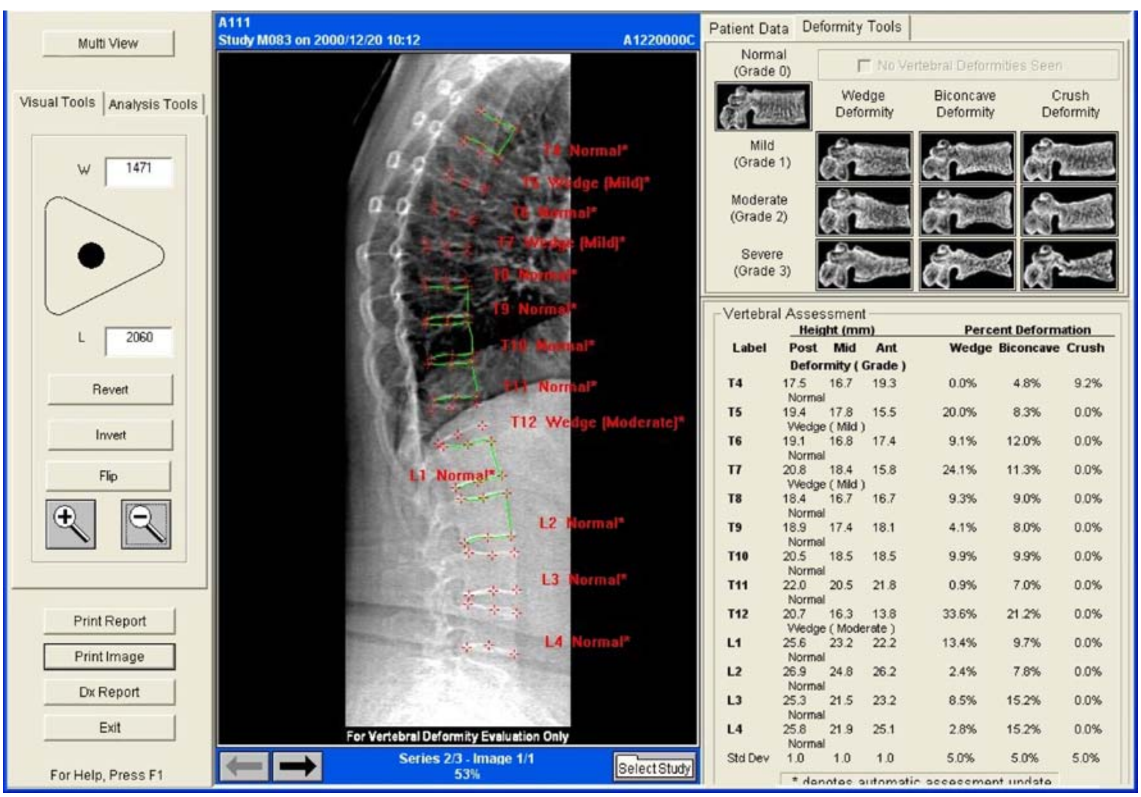

Fig. 7 MXA scan analysis with six vertebral points on T4-L4 vertebrae in a 65-year-old osteoporotic female. Results show two vertebral fractures: mild wedging of T5 and moderate wedging of T12

equipment-Hologic, Inc. (Waltham, MA) and General Electric/Lunar (Madison, WI) [50, 51]. In Hologic systems, two views of the thoracic and lumbar spine are acquired: a posteroanterior (PA) scan and a lateral scan. The PA image is acquired in order to visualize spinal anatomy, such as scoliosis, to determine the centre line of the spine. This information is used in subsequent lateral scans to maintain a constant distance between the centre of the spine and the X-ray tube for all subjects at all visits, regardless of patient position or degree of scoliosis, thus eliminating the geometric distortion [52]. Each lateral scan covers a distance of 46 cm, imaging the vertebrae from L4 to T4. The GE /Lunar scanner determines the starting position of the lateral morphometry scan by positioning a laser spot 1 cm above the iliac crest. The scan range for the GE-Lunar systems is determined by measuring the length between the iliac crest and the armpit. The lateral scan can be acquired using a single-energy X-ray beam with a very short scan time (12 s). However, the analysis may be affected by soft tissue artefacts in the image caused by prominent lung structures. These artefacts are absent in the dual-energy scans, which, however, take between 6 min (array mode) and 12 min (fast and high-definition modes). After the scan, the programme automatically identifies vertebral levels and indicates the centres of the vertebrae. The six-point placement for the determination of the vertebral heights is semiautomated. The operator uses a mouse pointing device to specify the 13 locations of the anterior inferior corner of the vertebrae from L4 to T4. Then the MXA software computes the positions of the remaining five vertebral points for each. To guide the operator during image analysis of follow-up scans, the vertebral endplate markers from the previous scan are superimposed on the current scan, improving long-term precision. After the analysis is finished, a final report is displayed. It gives information on the measured vertebral body heights and their ratios, and includes an assessment of the patient's fracture status based on normative data and different models for fracture assessment using quantitative morphometry (Fig. 7).

Comparison between MRX and MXA

Vertebral morphometry should be performed by trained observers resulting in good inter-observer measurement precision [53].

Both MRX and MXA have a good precision, the intraoperator CV ranging from 1.2% for MXR to 3.4% for MXA, while the interoperator CV from 1.9% to 5.3 according to various authors [50, 54, 55]. For MXA the precision obtained with two systems, Hologic and GE/Lunar, is similar [56, 57].

MXA overcomes some of the patient-positioning and exposure factor problems inherent in conventional radiography. In fact, the scanner arm of some models of densitometers can be rotated 90°, so that lateral scans can be obtained with the patient in the supine position without repositioning. A further advantage of MXA when using the scanning fan-beam geometry of DXA devices is the absence of distortions and magnification effects inherent in the standard X-ray technique [58]. The main attraction of MXA is that the effective dose-equivalent to the patient is considerably lower than for conventional radiography [59, 60]. While MXA is able to assess the entire spine in a single image, in conventional radiography, radiographs of the lumbar and thoracic spine have to be performed separately, so the identification of the vertebral levels to perform MRX may be difficult at times. Furthermore, the improved image spatial resolution of the new DXA scanners (Fig. 8) allows a better visualization of the upper thoracic vertebrae [61]. So far, various comparative studies exist [62–64] that have found excellent agreement between qualitative and quantitative radiographic assessment using fan-beam dual-energy DXA images, particularly for moderate and severe deformities in osteoporotic populations**.** A large proportion of vertebrae are not visualized sufficiently for analysis on MXA scans, and this reduces the number of vertebral fractures identified, particularly in the upper thoracic spine (T4-T5). However, other authors [61] have shown that high-speed fan-beam DXA imaging was feasible in a clinical population, allowing visualization of a substantial proportion of the vertebrae, using a rapid (10-s) single-energy imaging mode during suspended respiration.

Morphometric definition of vertebral fractures

Because there is no gold standard for osteoporotic fracture, it may sometimes be difficult to discriminate the osteoporotic vertebral fracture from a normal variant of vertebral shape or from a vertebral deformation that may have occurred long ago [29]. Furthermore, there is variation in vertebral size and shape at different levels of the spine; the anterior and posterior vertebral height increases from T3 to L2, but for L3-L5 the posterior height is lower than the anterior height [65]. Vertebral size also varies between individuals: large people tend to have larger vertebrae [66]. For this reason reference ranges should be established in the population under study, using the same technique, and derived from “normal” subjects or by “data trimming” of a population-based-sample. To determine the reference values of vertebral body heights, some authors have used a sample of premenopausal women, assuming that the prevalence of vertebral fractures is very low in this population [67]. This approach may not be feasible for many studies because it involves radiation exposure for fertile women. Moreover, it has been demonstrated that vertebral heights change significantly with age, showing rates of loss of 1.2–1.3 mm/year [68–70]. Age-related decrease of vertebral heights influences the definition of the normal range of vertebral shape, since a deformity that may be in excess of 2 SD from the mean in younger subjects may be well within this limit 20 years later. Other authors [71, 72] have selected a subsample of postmenopausal women in which all vertebrae have been judged to be normal (un-fractured) on the radiographs by an expert reader. A third approach for defining normal vertebral dimensions uses the values of a population that includes postmenopausal women with and without vertebral fractures [73].

Also, in a large study [63] the authors have shown that reference ranges of vertebral heights derived from MRX studies may not be applicable to MXA, in view of the observed differences between their MXA mean values when compared with MRX values reported in the earlier studies [49, 74]. The differences observed led to a tendency for lower MXA critical values for detection of vertebral deformities, suggesting the use of technique-specific reference ranges. The preliminary report of an Italian multi-centre study [75] showed that vertebral heights of 569 Italian normal women measured from T4-L4 using vertebral fracture assessment (VFA) on Lunar Prodigy (GE Healthcare) densitometers in all vertebrae were significantly smaller than the existing values collected from American normal women.

Fig. 8 Lateral spine DXA image obtained in high detail mode. The improved image spatial resolution of the new DXA scanners allows a good visualization of the entire spine

There is still disagreement about establishing a threshold of height reduction that would allow unequivocal discrimination among vertebral fractures, deformities, and normal shape [76]. Various morphometric algorithms to define vertebral fractures have therefore been developed [26, 27, 72]. Thus, it is not possible to measure accurately the true- and false-positive rates of various morphometric definitions of vertebral fractures because there is no gold standard for defining a vertebral fracture. In fact, wide discordances in results among studies on the prevalence of vertebral fractures, ranging from 33% to 85% [67, 77], have been found. Clinical trials have also shown that the estimated incidence of new vertebral fractures in postmenopausal osteoporosis varies markedly, from 6 to 83 fractures per 100 patient-years [78–80]. In particular, less stringent criteria (e.g., –2 SD) result in too many false-positive results, because they identify as fractures some deformities that may represent developmental abnormalities. By contrast, a more stringent cutoff level, such as 4 SD, results in a lower false-positive rate [81].

The number of vertebral fractures may not be representative of the severity of spinal osteoporosis, especially in the case of biconcavity fractures, which represent deformations of only the endplate. For this reason, some methods have been developed to estimate the deformity of the overall thoracic and lumbar spine. Minne et al. [28] and Sauer et al. [82] developed the Spine Deformity Index to quantify spinal deformity and assess progression of vertebral deformation during follow-up. Other authors [36] introduced new morphometric indices to quantify the spinal deformity, namely, sums of anterior, middle, and posterior heights (AHS, MHS, PHS) of the respective 14 vertebral body heights from T4 to L5. A strong correlation between these indices and the lumbar bone mineral density (L-BMD) has been found, suggesting their use as fracture risk indices [83].

Irregularity in the curvature of the spine can be quantified as the integrated average of the ratios of the anterior to posterior vertebral heights of adjacent vertebrae. This Spinal Curvature Irregularity Index (SCII) is a measure of the ‘smoothness’ of the spinal curvature, and a large SCII is correlated with the presence of vertebral deformities [84].

Comparison of semiquantitative (SQ) visual and quantitative morphometric assessment of vertebral fractures

A vertebral deformity is not always a vertebral fracture, but a vertebral fracture is always a vertebral deformity. Some comparative studies [32, 85, 86] found a high concordance between different quantitative morphometric approaches and visual semiquantitative evaluation for prevalent vertebral fractures defined as moderate or severe. In these cases there was a strong association with clinical parameters (bone mineral density, height loss, back pain, incidence of subsequent deformities).

There are many causes of vertebral deformities, and the correct differential diagnoses for them can be achieved only by visual inspection and expert interpretation of a radiograph. In fact, there is a list of potential differential diagnoses for vertebral deformities, such as osteoporosis, trauma, degenerative disease, Scheuermann's disease, congenital anomaly, neoplastic disease, and haematopoietic disorders, infectious disease and Paget's disease, that should be taken into consideration, and the correct classification of vertebral deformities can be achieved only by expert interpretation of the radiograph [6, 87]. The quantitative morphometry is unable to distinguish osteoporotic vertebral fractures by vertebral deformities due to other factors, such as degenerative spine and disc disease. This limitation is a characteristic of any method of quantitative morphometry, but the limited spatial resolution of the DXA images in MXA may increase this problem [88]. On the other hand, MRX, with its superior image quality, has the potential for qualitative reading of the radiographs to aid the differential diagnosis. In fact, although it is recognized that the visual interpretation of radiographs is subjective, it is also true that an expert eye can better distinguish between true fractures and vertebral anomalies than can quantitative morphometry. For example, the distinction between a fractured endplate and the deformity associated with Schmorl's nodes can only be made visually by an experienced observer, as is the case for the diagnosis of the wedge-shaped appearance caused by remodelling of the vertebral bodies in degenerative disc disease [89, 90]. Recently, a new algorithm-based approach for the qualitative (ABQ) assessment of vertebral fracture has been developed [91]. The ABQ assumes that in every vertebral fracture, fracture of the endplate within the vertebral ring is always involved. Thus, by definition, wedge and crush fractures are also concave fractures, because they involve central depression of the endplate. Comparing the ABQ approach, semiquantitative method (SQ) and quantitative morphometry (QM) for the identification of vertebral fracture in a population of elderly men showed that most of the men with vertebral fractures identified by SQ or QM, but not by ABQ were classified as having non-osteoporotic short vertebral height (SVH) by ABQ. These men did not have low BMD [92]. The authors conclude that the exclusion of SVH could reduce false positives.

Assessment of vertebral fractures on DXA images

Recently, the visual semiquantitative (SQ) method for identification of vertebral fractures has been applied to images of the spine acquired by fan-beam DXA devices. This method is called "instant vertebral assessment" (IVA) by Hologic or "vertebral fracture assessment" (VFA) by GE/Lunar. IVA has been compared with SQ evaluation of spinal radiographs demonstrating good agreement (96.3%, k=0.79) in classifying vertebrae as normal or deformed in the 1,978 of 2,093 vertebrae deemed analyzable on both the DXA scans and conventional radiographs [63]. IVA showed good sensitivity (91.9%) in the identification of moderate/severe SQ deformities and an excellent negative predictive value (98%) to distinguish subjects with very low risk of vertebral fractures from those with possible fractures. The disagreement between the IVA and SQ methods resulted from the poor image quality, particularly in the upper thoracic vertebrae that were not visualized sufficiently for analysis. Although some vertebral fractures were missed by IVA, all patients with prevalent vertebral fractures were identified; therefore, for the identification of patients with fracture, visual assessment of DXA scans had 100% sensitivity and specificity [57]. This means that if IVA had been used as a diagnostic pre-screening tool at the first assessment, all the patients with prevalent vertebral fracture would have been correctly referred for radiography to confirm the diagnosis (Fig. 9). Also the "normal" subjects can then be excluded prior to performing conventional radiographs and further time-consuming and costly methods of vertebral deformity assessment such as SQ by an experienced radiologist and/or quantitative morphometry. Also, with its low radiation and good precision, IVA could be utilized to identify vertebral fractures in populations affected by conditions different from osteoporosis, but with high vertebral fracture risk, i.e., liver or kidney transplant patients [93, 94].

Conclusion

A combination of semiquantitative visual and quantitative morphometric methods may be the best approach to fracture definition, as suggested by the National Osteoporosis Foundation [95], by Kanis et al. [96], and by the International Osteoporosis Foundation (IOF) [97]. Currently, there is no consensus on which morphometric technique should be used, or how, to evaluate patients at risk of osteoporosis. MRX, based upon assessment of conventional radiographs, has, unlike MXA, the potential for qualitative reading of the radiographs by a trained

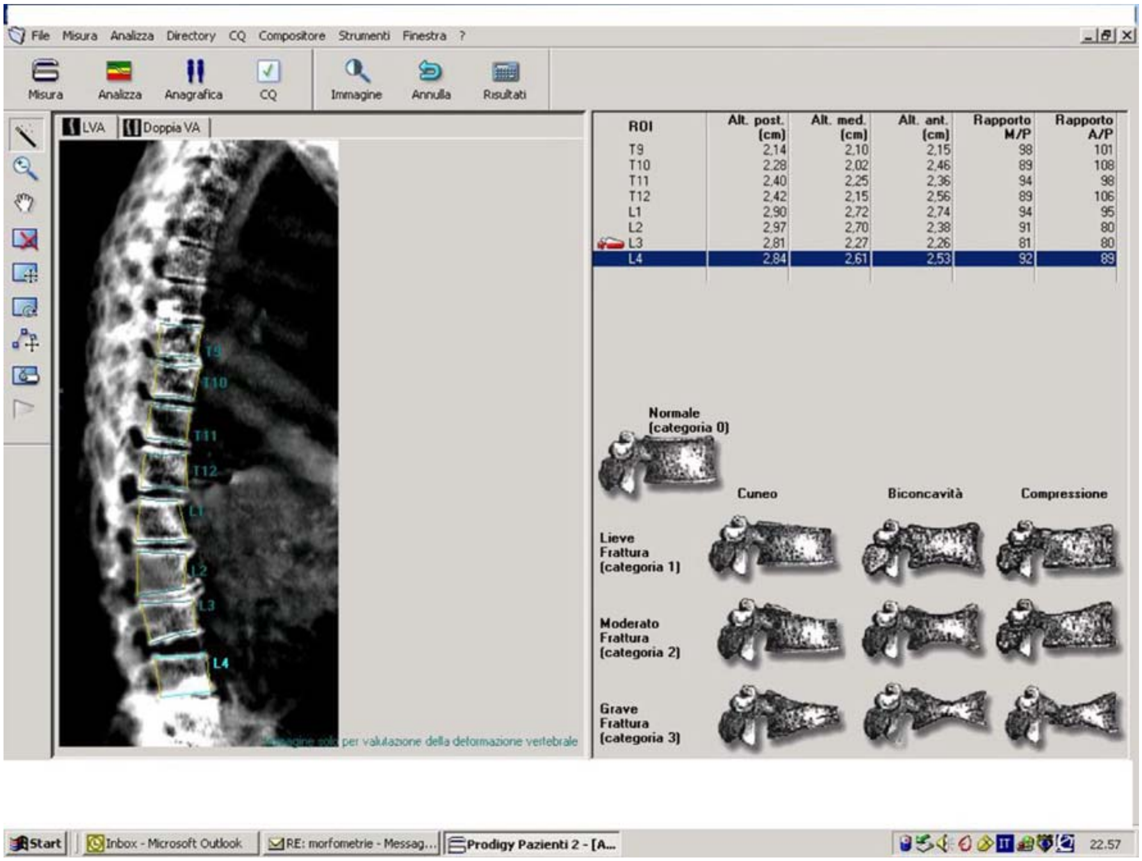

Fig. 9 IVA with vertebral fracture: 57-year-old female with normal BMD (lumbar spine T-score –0.7 and proximal femur T-score –0.8), and severe wedge deformity of L3

radiologist or highly experienced clinician who can distinguish between vertebral anomalies and true fractures and detect technical artefacts on the films, which might increase the errors on quantitative morphometry.

However, in view of the relatively low radiation dose to the patient and the excellent agreement with the visual SQ method for the identification of vertebral deformities, the visual or morphometric assessment of lateral DXA spine images may have the potential for use as a prescreening tool. If all vertebrae are visualized adequately by lateral DXA images and classified as normal by IVA or MXA, the patient could be classified as normal. If all vertebrae are not visualized by DXA and if one or more deformities are detected by IVA or MXA, it will be necessary to acquire conventional radiography to check for further prevalent deformities and to identify the nature of the deformity. The availability of a rapid, low-dose method for assessment of vertebral fractures, using advanced fan-beam DXA devices, provides a practical means for integrated assessment of BMD and vertebral fracture status. This approach allows the identification of most osteoporotic vertebral fractures, even those that are asymptomatic, in patients with low BMD, improving the selection of candidates for therapeutic intervention.

References

1. Genant HK, Wu CY, van Kuijk C et al (1993) Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res 8:1137–1148
2. Pongchaiyakul C, Nguyen ND, Jones G et al (2005) Asymptomatic vertebral deformity as a major risk factor for subsequent fractures and mortality: a long-term prospective study. J Bone Miner Res 20:1349–1355
3. Lindsay R, Pack S, Li Z (2005) Longitudinal progression of fracture prevalence through a population of postmenopausal women with osteoporosis. Osteoporosis Int 16:306–312

4. Cummings SR, Melton LJ (2002) Epidemiology and outcomes of osteoporotic fractures. Lancet 359:1761–1767
5. Finnern HW, Sykes DP (2003) The hospital cost of vertebral fractures in the EU: estimates using national datasets. Osteoporos Int 14:429–436
6. Link TM, Guglielmi G, van Kuijk C, Adams JE (2003) The hospital cost of vertebral fractures in the EU: estimates using national datasets. Eur Radiol 15:1521–1532
7. Jackson SA, Tenenhouse A, Robertson L, the CaMos Study Group (2000) Vertebral fracture definition from population-based data: preliminary results from the Canadian Multicenter Osteoporosis Study (CaMos). Osteoporos Int 11:680–687
8. Melton LJ III (1997) Epidemiology of spinal osteoporosis. Spine 22(Suppl 1):2S–11S
9. Roy DK, O'Neill TW, Finn JD, Lunt M, Silman AJ et al (2003) Determinants of incident vertebral fracture in men and women: results from the European prospective Osteoporosis Study (EPOS). Osteoporos Int 14:19–26
10. Center JR, Nguyen TV, Schneider D et al (1999) Mortality after all major types of osteoporotic fractures in men and women: an observational study. Lancet 353:878–882
11. Kado DM, Browner WS, Palermo L et al (1999) Vertebral fractures and mortality in older women: study of Osteoporotic Fractures Research Group. Arch Intern Med 159:1215–1220
12. Burger H, Van Daele PLA, Gashuis K et al (1997) Vertebral deformities and functional impairment in men and women. J Bone Miner Res 12:152–157
13. Fink HA, Ensrud KE, Nelson DB et al (2003) Disability after clinical fracture in postmenopausal women with low bone density: The Fracture Intervention Trial (FIT). Osteoporos Int 14:69–76
14. Hasserius R, Karlsson MK, Jonsson B et al (2005) Long-term morbidity and mortality after a clinically diagnosed vertebral fracture in the elderly-a 12- and 22-year follow-up of 257 patients. Calcif Tissue Int 76:235–242
15. Nevitt MC, Ettinger B, Black DM et al (1998) The association of radiographically detected vertebral fractures with back pain and function: a prospective study. Ann Intern Med 128:793–800
16. Schlaich C, Minne HW, Bruckner T et al (1998) Reduced pulmonary function in patient with spinal osteoporotic fractures. Osteoporos Int 8:261–267
17. Delmas PD, Genant HK, Crans GG et al (2003) Severity of prevalent vertebral fractures and the risk of subsequent vertebral and nonvertebral fractures: results from MORE trial. Bone 33:522–532
18. Chesnut CH III, Skag A, Christiansen C et al (2004) Effects of oral ibandronate administered daily or intermittently on fracture risk in postmenopausal osteoporosis. J Bone Miner Res 19:1241–1249
19. Ettinger B, Black DM, Mitlak BH et al (1999) Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomised clinical trial- Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. JAMA 282:637–645
20. Liberman UA, Weiss SR, Broll J et al (1995) Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis. N Engl J Med 333:1437–1443
21. Mc Closkey E, Selby P, de Takats D et al (2001) Effects of clodronate on vertebral fracture risk in osteoporosis: a 1-year interim analysis. Bone 28 (3):310–315 2001
22. Neer RM, Arnaud CD, Zanchetta JR et al (2001) Effect of parathyroid hormone (1–34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med 344:1434–1441
23. Reid DM, Hughes RA, Laan RFJM et al (2000) Efficacy and safety of daily risedronate in the treatment of corticosteroid-induced osteoporosis in men and women: a randomized trial. European Corticosteroid-Induced Osteoporosis Treatment Study. J Bone Miner Res 15:1006–1013
24. Fink AH, Milavetz DL, Palermo L et al (2005) What proportion of incident radiographic vertebral deformities is clinically diagnosed and vice versa? J Bone Miner Res 20:1216–1222
25. Hedlund LR, Gallagher JC (1988) Vertebral morphometry in diagnosis of spinal fractures. Bone Miner 5:59–67
26. Eastell R, Cedel SL, Wahner H et al (1991) Classification of vertebral fractures. J Bone Miner Res 6:207–215
27. Mc Closkey EV, Spector TD, Eyres KS et al (1993) The assessment of vertebral deformity: a method for use in population studies and clinical trials. Osteoporos Int 3:138–147
28. Minne HW, Leidig C, Wuster CHR et al (1988) A newly developed spine deformity index (SDI) to quantitative vertebral crush fractures in patients with osteoporosis. Bone Miner 3:335–349
29. Kleerekoper M, Nelson DA (1992) Vertebral fracture or vertebral deformity? Calcif Tissue Int 50:5–6
30. Genant HK, Siris E, Crans GG et al (2005) Reduction in vertebral fracture risk in teriaparatide-treated postmenopausal women as assessed by spinal deformity index. Bone 37:170–174
31. Crans GG, Genant HK, Krege JH (2005) Measurement of vertebral heights. Bone 37:175–179
32. Genant HK, Jergas M, Palermo L et al (1996) Comparison of semiquantitative visual and quantitative morphometric assessment of prevalent and incident vertebral fractures in osteoporosis. J Bone Miner Res 11:984–996
33. Barnett E, Nordin BEC (1960) Radiographic diagnosis of osteoporosis: new approach. Clin Radiol 11:166–174
34. Jergas M, San Valentin R (1995) Techniques for the assessment of vertebral dimensions in quantitative morphometry. In: Genant HK, Jergas M, van Juijk C (eds) Vertebral Fracture In Osteoporosis. University of California Osteoporosis Research Group, San Francisco, pp 163–188
35. Hurxthal LM (1968) Measurement of vertebral heights. AJR 103:635–644
36. Diacinti D, Acca M, Tomei E (1995) Metodica di'radiologia digitale per la valutazione dell'osteoporosi vertebrale. Radiol Med 91:1–5
37. Nelson D, Peterson E, Tilley B et al (1990) Measurement of vertebral area on spine X-rays in osteoporosis: reliability of digitizing techniques. J Bone Miner Res; 5:707–716
38. Kalidis L, Felsenberg D, Kalender WA et al (1992) Morphometric analysis of digitized radiographs: descrption of automatic evaluation. In: Ring EFJ (ed) Current research in osteoporosis and bone mineral measurement II. British Institute of Radiology, London, pp 14–16
39. Nicholson PHF, Haddaway MJ, Davie MWJ et al (1993) A computerized technique for vertebral morphometry. Physiol Meas 14:195–204
40. O'Neill TW, Felsenberg D, Varlow J et al (1996) The prevalence of vertebral deformity in European men and women: The European Vertebral Osteoporosis Study. J Bone Miner Res 11:1010–1018
41. Smyth PP, Taylor CJ, Adams JE (1999) Vertebral shape: automatic measurement with active shape models. Radiology 211:571–578

42. Roberts M, Cootes TF, Adams JE (2006) Vertebral morphometry: semi-automatic determination of detailed shape from dual-energy X-ray absorptiometry images using active appearance models. Invest Radiol 41 (12):849–859
43. Zamora G, Sari-Sarraf H, Long LR (2003) Hierarchical segmentation of vertebrae from X-ray images. In Proc. of SPIE Medical Imaging 5032:631–642
44. Howe B, Gururajan A, Sari-Sarraf H, Long LR (2004) Hierarchical segmentation of cervical and lumbar vertebrae using a customized generalized Hough transform and extensions to active appearance models. In: Proc IEEE 6th SSIAI; 182–186
45. de Bruijne M and Nielsen M (2004) Image segmentation by shape particle filtering. In: Proc. 17th International Conference on Pattern Recognition 2004;722–725
46. Guglielmi G, Palmieri F, Placentino MG et al (2008) Assessment of osteoporotic vertebral fractures using specialized workflow software for six point morphometry. Eur J Radiol Jan 31 [Epub ahead of print] DOI 10.1016/j.ejrad.2007.12.001
47. Guglielmi G, Stoppino LP, Placentino MG et al (2007) Reproducibility of a Semi-Automatic Method for 6-Point Vertebral Morphometry in a Multi-Centre Trial. Eur J Radiol Dec 8 [Epub ahead of print] DOI 10.1016/j.ejrad.2007.09.040
48. Banks LM, van Juijk C, Genant HK (1995) Radiographic technique for assessing osteoporotic vertebral fracture. In: Genant, Jergas M, van Juijk C (eds) Vertebral Fracture In Osteoporosis. University of California Osteoporosis Research Group, San Francisco, pp 131–147
49. Gallagher JC, Hedlund LR, Stoner S et al (1988) Vertebral morphometry: normative data. Bone Miner 4:189–196
50. Adams JE (1997) Single and dual energy X-ray absorptiometry. In: Guglielmi G, Passariello R,Genant HK (eds) Bone Densitometry: an update. Eur Radiol 7(Suppl 2):S20–S31
51. Steiger P, Cummings SR, Genant HK, Weiss H, the Study of Osteoporotic Fractures Research Group (1994) Morphometric X-ray absorptiometry of the spine: correlation in vivo with morphometric radiography. Osteoporos Int 4:238–244
52. Blake JM, Jagathesan T, Herd RJM, Fogelman I (1994) Dual X-ray absorptiometry of the lumbar spine: the precision of paired anteroposterior/lateral studies. Br J Radiol 67:624–630
53. Gardner JC, von Ingersleben G, Heyano SL et al (2001) An interactive tutorial-based training technique for vertebral morphometry. Osteoporosis Int 12:63–70
54. Blake GM, Rea JA, Fogelman I (1997) Vertebral morphometry studies using dual-energy X-ray absorptiometry. Semin Nucl Med 27:276–290
55. Harvey SB, Hutchinson KM, Rennie EC et al (1998) Comparison of the precision of two vertebral morphometry programs for the Lunar Expert-XL imaging densitometer. Br J Radiol 71:388–398
56. Crabtree N, Wright J, Walgrove A et al (2000) Vertebral morphometry: repeat scan precision using the Lunar Expert-XL and the Hologic 4500A. A study for the 'WISDOM' RCT of hormone replacement therapy. Osteoporos Int 11:537–543
57. Ferrar L, Jiang G, Eastell R et al (2003) Visual identification of vertebral fractures in osteoporosis using morphometric X-ray absorptiometry. J Bone Miner Res 18:933–938
58. Kalender WA, Eidloth H (1991) Determination of geometric parameters and osteoporosis indices for lumbar vertebrae from lateral QCT localizer radiographs. Osteoporos Int 1:197–200
59. Lewis MK, Blake GM (1995) Patient dose in morphometric X-ray absorptiometry (letter). Osteoporos Int 5:281–282
60. Njeh CF, Fuerst T, Hans D et al (1999) Radiation exposure in bone mineral density assessment. Appl Radiat Isot 50:215–236
61. Rea JA, Li J, Blake GM et al (2000) Visual assessment of vertebral deformity by X-ray absorptiometry: a highly predictive method to exclude vertebral deformity. Osteoporos Int 11:660–668
62. Edmondston SJ, Price RI, Valente B et al (1999) Measurement of vertebral body height: ex vivo comparison between morphometric X-ray absorptiometry, morphometric radiography and direct measurements. Osteoporosis Int 10:7–13
63. Rea JA, Chen MB, Li J et al (2000) Morphometry X-ray absorptiometry and morphometric radiography of the spine: a comparison of prevalent vertebral deformity identification. J Bone Miner Res 15:564–574
64. Steiger P, Wahner H (1994) Instruments using fan-beam geometry. In: Wahner, Fogelman I (eds) The Evaluation of Osteoporosis. Dual Energy X-Ray Absorptiometry in Clinical Practice. Martin Dunitz, Ltd., London, pp 281–288
65. Djoumessi RMZ, Maalouf G, Wehbe J et al (2004) The varying distribution of intra-and intervertebral height ratios determines the prevalence of vertebral fractures. Bone 35:348–356
66. O'Neill TW, Varlow J, Felsenberg D et al (1994) Variation in vertebral heights ratios in population studies. J Bone Miner Res 9:1895–1907
67. Smith-Bindman R, Cummings SR, Steiger P et al (1991) A comparison of morphometric definitions of vertebral fracture. J Bone Miner Res 6:25–34
68. Cline MG, Meredith KE, Boyer JT et al (1989) Decline in height with age in adults in a general population sample: estimating maximum height and distinguishing birth cohort effect from actual loss of stature with aging. Hum Biol 61:415–425
69. Diacinti D, Acca M, D'Erasmo E et al (1995) Aging changes in vertebral morphometry. Calcif Tissue Int 57:426–429
70. Nicholson PHF, Haddaway MJ, Davie MWJ et al (1993) Vertebral deformity, bone mineral density, back pain and height loss in unscreened women over 50 years. Osteoporos Int 3:300–307
71. Evans SF, Nicholson PHF, Haddaway MJ et al (1993) Vertebral morphometry in women aged 50–81 years. Bone Miner 21:29–40
72. Melton LJ III, Kan SH, Frye MA et al (1989) Epidemiology of vertebral fractures in women. Am J Epidemiol 129:1000–1010
73. Black DM, Cummings SR, Stone K et al (1991) A new approach to defining normal vertebral dimensions. J Bone Miner Res 6:883–892
74. Hermann AP, Brixen K, Andersen J et al (1993) Reference values for vertebral heights in Scandinavian females and males. Acta Radiologica 34:48–52
75. Diacinti D, Francucci C, Fiore C et al (2005) Italian preliminary reference data of normal vertebral dimensions for morphometric X-ray absorptiometry (MXA): Normal morphometric Dexa (NORMODEXA) Study. Bone 36 (Suppl.2):S351
76. Ziegler R, Scheidt-Nave C, Leidig-Bruckner G (1996) What is a vertebral fracture? Bone 18:169–177

77. Grados F, Roux C, de Vernejoul MC et al (2001) Comparison of four morphometric definitions and a semiquantitative consensus reading for assessing prevalent vertebral fractures. Osteoporos Int 12:716–722
78. Nevitt MC, Ross PD, Palermo L et al (1999) Association of prevalent vertebral fractures, bone density, and alendronate treatment with incident vertebral fractures: effect of number and spinal location of fractures. Bone 25:613–619
79. Lunt M, Ismail AA, Felsenberg D et al (2002) Defining incident vertebral deformities in population studies: a comparison of morphometric criteria. Osteoporos Int 13:809–815
80. Hochberg MC, Ross PD, Black D et al (1999) Larger increases in bone mineral density during alendronate therapy are associated with a lower risk of new vertebral fractures in women with postmenopausal osteoporosis. Fracture Inteventional Trial Research Group. Arthritis Rheum 42:1246–1254
81. Melton LJ III, Egan KS, O'Fallon WM et al (1998) Influence of fracture criteria on the outcome of a randomized trial of therapy. Osteoporos Int 8:184–191
82. Sauer P, Leidig G, Minne HW et al (1991) Spine Deformity Index (SDI) versus other objective procedures of vertebral fracture identification in patients with osteoporosis: a comparative study. J Bone Miner Res 6:227–238
83. Mazzuoli GF, Diacinti D, Acca M et al (1998) Relationship between spine bone mineral density and vertebral body heights. Calcif Tissue Int 62:486–490
84. Zebaze R, Maalouf G, Maalouf N, Seeman E (2004) Loss of regularity in the curvature of the thoracolumbar spine: a measure of structural failure. J Bone Miner Res 19:1099–1104
85. Black DM, Palermo L, Nevitt MC et al (1995) Comparison of methods for defining prevalent vertebral deformities: the study of osteoporotic fractures. J Bone Miner Res 10:890–902
86. Wu C, van Kuijk C, Jiang Y et al (2000) Comparison of digitized images with original radiography for semi-quantitative assessment of osteoporotic fractures. Osteoporos Int 11:25–30
87. Ferrar L, Jiang G, Armbrecht G et al (2007) Is short vertebral height always an osteoporotic fracture? The Osteoporosis and Ultrasound Study (OPUS). Bone 41(1):5–12
88. Genant HK, Jergas M (2003) Assessment of prevalent and incident vertebral fractures in osteoporosis research. Osteoporos Int 14(Suppl 3):S43–S55
89. Lenchik LL, Rogers LF, Delmas PD et al (2004) Diagnosis of osteoporotic vertebral fractures: importance of recognition and description by radiologists. AJR 183:949–958
90. Jiang G, Ferrar L, Barrington NA, Eastell R (2007) Standardised quantitative morphometry: a modified approach for quantitative identification of prevalent vertebral deformities. Osteoporos Int 18(10):1411–1419
91. Jiang G, Eastell R, Barrington NA, Ferrar L (2004) Comparison of methods for the visual identification of prevalent vertebral fracture in osteoporosis. Osteoporos Int 15:887–896
92. Ferrar L, Jiang G, Cawthon PM et al (2007) Identification of vertebral fracture and non–osteoporotic short vertebral height in men: the MrOS study. J Bone Miner Res 22:1434–1441
93. Giannini S, Nobile M, Dalle Carbonare L et al (2001) Vertebral morphometry by X-ray absorptiometry before and after liver transplant: a cross-sectional study. Eur J Gastroenterol Hepatol 13:1201–1207
94. Mazzaferro S, Diacinti D, Proietti E et al (2006) Morphometric X-ray absorptiometry in the assessment of vertebral fractures in renal transplant patients. Nephrol Dial Transplant 21:466–471
95. National Osteoporosis Foundation (1998) Osteoporosis: review of the evidence for prevention, diagnosis and treatment and cost-effectiveness analysis. Osteoporos Int 8(Suppl 4):S1–S85
96. Kanis JA, Black D, Cooper C et al (2002) A new approach to the development of assessment guidelines for osteoporosis. Osteoporos Int 13:527–536
97. International Osteoporosis Foundation and European Society of Musculoskeletal Radiology (2003) Vertebral Fracture Initiative Resource Document. Available from URL: http://www.iofbonehealth.org/vfi/assets/resources/Resource-Document.pdf [accessed October 29, 2007]