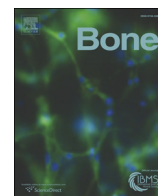




Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Full Length Article

Vertebral fracture assessment: Enhancing the diagnosis, prevention, and treatment of osteoporosis

Meltem Zeytinoglu ^{*}, Rajesh K Jain, Tamara J Vokes

University of Chicago, Department of Medicine, Section of Diabetes, Endocrinology, and Metabolism, United States

ARTICLE INFO

Article history:

Received 19 December 2016

Revised 6 March 2017

Accepted 7 March 2017

Available online xxx

Keywords:

Vertebral fracture assessment

VFA

DXA

Vertebral fractures

ABSTRACT

Osteoporosis is a highly prevalent condition, resulting in significant morbidity and mortality. Nevertheless, it is frequently untreated. Vertebral fractures often do not come to clinical attention, yet, their presence is diagnostic of osteoporosis, helps to predict the risk of future fractures, and may alter the choice of pharmacotherapy. The addition of lateral spine imaging technology to the densitometer, for vertebral fracture assessment (VFA), represented a major advancement in the ability to diagnose vertebral fractures and osteoporosis. VFA is an underutilized and highly effective imaging tool to enhance osteoporosis detection and fracture prevention. Several factors make VFA an ideal technology to evaluate for vertebral fractures. These include: the ability to obtain the image at the same time the bone density is done, with significantly lower radiation exposure than with spine radiography, and at a lower cost. This review provides an overview of the clinical significance of identifying vertebral fractures, the origins of the VFA, its clinical indications, a review of the methods used to diagnose vertebral fracture, an overview on interpreting the VFA, and the strengths and limitations of this technique.

© 2017 Published by Elsevier Inc.

1. Introduction

Osteoporosis is a disease that results in 8.9 million fractures worldwide each year [1]. While bone mineral density (BMD) assessment using dual-energy X-ray absorptiometry (DXA) represented a tremendous leap forward in the diagnosis of osteoporosis, many patients will not have osteoporosis by BMD criteria, but will have already suffered a clinically unrecognized vertebral fracture. Thus, in order to assess vertebral integrity on a lateral image of the spine, vertebral fracture assessment (VFA), which utilizes DXA, was developed. This method, which can be done as a point-of-care service at the time of the BMD assessment, also has the advantage of exposing the patient to significantly lower radiation than with conventional radiography. While it does have these advantages over standard radiography, there are important caveats and limitations to consider in the proper use and interpretation of VFA. This review will provide an overview of the clinical importance of recognizing vertebral fractures, the origins of VFA, its clinical indications, interpretation of VFA, and the strengths and limitations of this technique.

2. Clinical significance of vertebral fractures

VFA technology was designed exclusively to detect vertebral fractures, the diagnosis of which is of paramount importance in the

detection and treatment of osteoporosis. Not only do vertebral fractures often represent the first osteoporotic fracture, but they also establish the diagnosis of osteoporosis, regardless of an individual's bone mineral density. Nevertheless, the majority of vertebral fractures are not clinically apparent. Indeed, it has been estimated that only one out of three individuals affected by a fracture will have a clinical diagnosis [2–5]. It should be noted, however, that undiagnosed fractures are not truly asymptomatic. Instead, they are often associated with back pain and decreased activity, but are usually ignored by patients and their physicians or attributed to other common etiologies such as degenerative joint disease [6].

Vertebral fractures found on imaging are traditionally divided into prevalent (seen for the first time on an image, with no clear knowledge of the time of their occurrence) and incident (new fractures that were not present on a prior image). Vertebral fractures are important to detect, as they portend a significantly increased risk for future osteoporotic fractures and are also associated with increased morbidity and mortality [7,8]. In a large multinational study, the risk of a new vertebral fracture in the year after sustaining an incident vertebral fracture was 5-fold that of women who did not suffer a vertebral fracture the previous year (relative risk, RR, 5.1, 95% CI 3.1–8.4). The overall incidence of a new vertebral fracture in the subsequent year after suffering an initial vertebral fracture was 19.2% (95% CI 13.6–24.8%) [7]. Prevalent fractures, too, are strongly associated with risk of future fracture—in the Study of Osteoporotic Fractures (SOF), prevalent vertebral fracture was associated with increased risk of new vertebral fracture (RR 5.4, 95% CI 4.4–6.6), hip fracture (RR 2.8, 95% CI 2.3–3.4), and non-vertebral fracture (RR

^{*} Corresponding author.

E-mail address: mzeytinoglu@medicine.bsd.uchicago.edu (M. Zeytinoglu).

1.9, 95% 1.7–2.1) [9]. As might be suspected, more severe or greater number of vertebral fractures are associated with higher fracture risk than milder or fewer vertebral fractures [7–11].

Vertebral fractures have also been demonstrated to negatively impact quality of life and functional status. As a consequence of vertebral fracture, loss of height and kyphosis can occur, leading to debilitating limitations in activity. This can include limitations in the ability to extend or reach and flex or bend, leading to the loss of functional independence in some individuals [8,12]. In the Fracture Intervention Trial (FIT), women with an incident clinical vertebral fracture had a relative risk of 6.7 (95% CI 3.6–12.6) of seven or more days of severe or worse back pain, a relative risk of 12.6 (95% CI 8.9–17.7) of seven or more days of limited activity, and a relative risk of 27.7 (95% CI 17.9–42.7) of seven or more days of bed rest [6]. In a different study of 751 osteoporotic women with and without vertebral fractures, quality of life was assessed using the quality of life questionnaire of the European Foundation for Osteoporosis (QUALEFFO), a measure containing questions in the domains of pain, physical function, social function, general health perception, and mental function [13]. Women with vertebral fracture had significantly higher (i.e. worse) QUALEFFO scores, which increased with number of vertebral fractures. Even more alarmingly, vertebral fractures have been associated with increased mortality [2,14], though the pathophysiology of this association is not clear. Vertebral fractures may also contribute to a number of other systemic complications such as reduced pulmonary function and gastrointestinal complaints, including hiatal hernia, reflux, constipation, and bowel obstruction [15,16].

Unfortunately, as has been noted, the majority of individuals with vertebral fractures do not come to clinical attention [3–5]. For example, in patients enrolled in FIT, only 22.6% of 446 incident radiographic vertebral fractures were also clinically diagnosed [4]. Even severe fractures (at least 30% and 4 mm height loss) were only diagnosed clinically 28.4% of the time. Further, even if imaging is obtained for other purposes and vertebral fractures are present, they are often missed or not reported [3, 4,17,18]. In a study of 934 women who had undergone chest X-ray, 132 subjects had vertebral fractures present but it was only commented

upon in 50% of the radiology reports [17]. On CT scan, only 5% of moderate or severe vertebral fractures were reported in a series of 192 subjects [19]. The reasons for the lack of reporting are complex and may relate to the fact that radiologists are focused on the clinical indication for which the radiograph was ordered, particularly for non-spine radiographs. Additionally, the lack of consensus for diagnostic criteria of vertebral fracture by qualitative, quantitative, or semi-quantitative assessment of radiography may also hinder the radiologist from reporting deformities in the vertebral bodies [20]. Finally, ambiguous terminology used to describe abnormal vertebrae (vertebral deformities, fractures, wedging, etc.) also contributes to a lack of clear understanding of how vertebral abnormalities should be interpreted and reported.

Despite the difficulties in identifying vertebral fractures, their presence substantially alters diagnosis and management. As stated above, a vertebral fracture in the absence of trauma establishes a diagnosis of osteoporosis, even if the BMD is not in osteoporotic range, and increases future fracture risk. This has important clinical implications, including referral of patients to osteoporosis specialists, increased frequency of BMD monitoring, and, most importantly, eligibility for pharmacotherapy. In addition, the identification of vertebral fractures may alter the choice of management. For example, anabolic agents can substantially reduce the risk of future vertebral fractures, and the presence of a prevalent fracture may alter the risk-benefit ratio, both for clinician and patients, of these agents and may aid in the decision to select this therapy [21,22]. Finally, given the substantial concern over rare, but serious side effects of osteoporosis medications, the very presence of a vertebral fracture that has already occurred may provide the impetus for the patient to accept the need for osteoporosis therapy [23].

3. Origins of vertebral fracture assessment

Given that the majority of vertebral fractures are asymptomatic, developing technologies to identify fractures was of paramount importance. Prior to the development of VFA with dual-energy X-ray absorptiometry, conventional radiography was the primary modality

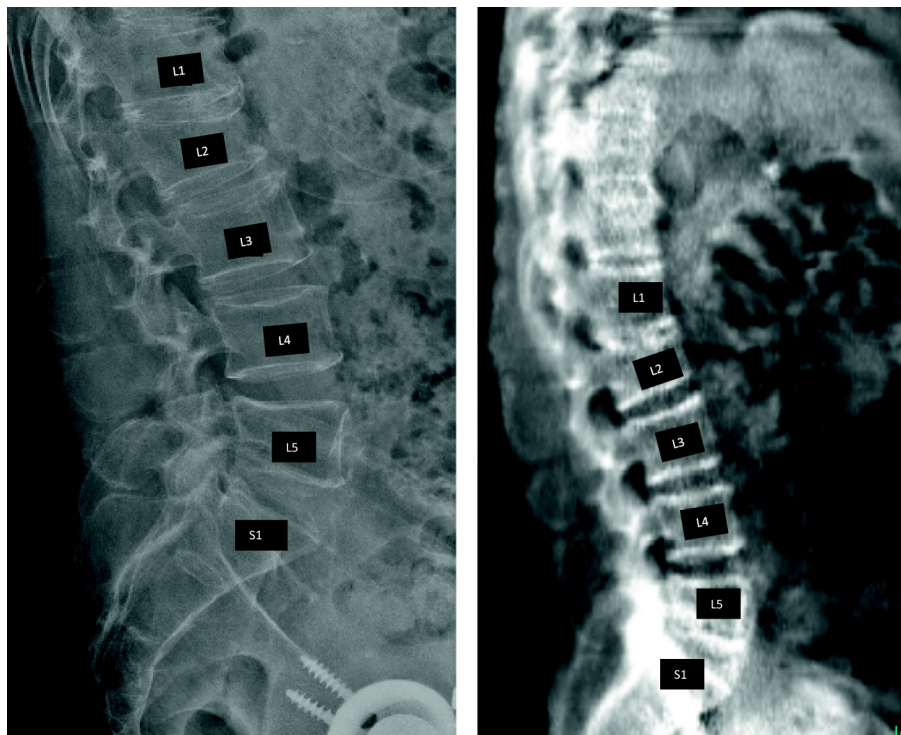


Fig. 1. Obliquity with spine radiography. On the left, a lumbar spine radiograph demonstrates a grade 2 wedge fracture of L2. The cone beams used to create the image hit the spine at an angle, resulting in the appearance of oval, rather than parallel endplates. On the right, VFA obtained on the same patient demonstrates the same L2 fracture but with less obliquity and an enhanced view of the lumbar spine. Also seen on the VFA are hepatobiliary and intestinal shadows.

used to identify vertebral fractures. The radiologist, using lateral lumbar and thoracic spine films can visualize the C7-S1 vertebrae and identify various deformities in the vertebral bodies in order to make the diagnosis of vertebral fracture. The lateral thoracic spine images are centered on T7, while the lateral lumbar spine images, centered on L4, capture T12 to S1. As conventional films became digitalized, the addition of morphometry enabled the quantification of vertebral shape by

measurement of anterior, posterior, and mid-vertebral heights [24]. Using these measurements, changes in ratios of vertebral heights are used to determine the type and severity (degree) of fracture. With the high-resolution of the radiograph, the clinician could appreciate changes in the anatomy of the vertebral endplates and cortices.

Despite its high resolution, there was a need for an additional imaging modality to address some of the limitations of spine radiography

Table 1
Indications for vertebral fracture assessment or with densitometry or lateral spine imaging.

International Society for Clinical Densitometry	National Osteoporosis Foundation	International Osteoporosis Foundation
<p>When T-score is < -1.0 at the spine, total hip, or femoral neck and one or more of the following is present:</p> <ul style="list-style-type: none"> • Women age ≥ 70 years or men ≥ 80 years • Historical height loss > 4 cm (>1.5 inches) • Self-reported but undocumented prior vertebral fracture • Glucocorticoid therapy equivalent to ≥5 mg of prednisone or equivalent per day for >3 months <p><i>Recommendations from the ISCD Official Position Statement 2015</i></p>	<p>All women age ≥ 70, and all men age ≥80 if BMD T-score at the spine, total hip, or femoral neck is ≤ -1.0</p> <p>Women age 65–69 and men age 70–79 if BMD T-score at the spine, total hip, or femoral neck is ≤ -1.5</p> <p>Postmenopausal women and men age ≥50 with specific risk factors:</p> <ul style="list-style-type: none"> • Low-trauma fracture occurring at age ≥50 • Historical height loss of 1.5 inches (4 cm) or more • Prospective height loss of 0.8 inches (2 cm) or more • Recent or ongoing long-term glucocorticoid treatment <p><i>National Osteoporosis Foundation's Clinician's Guide to Prevention and Treatment of Osteoporosis</i></p>	<p>Post-menopausal women with a T-score of -1.5 to -2.4, and:</p> <ul style="list-style-type: none"> • Age 70 or older • Historical height loss > 4 cm (1.5 inches) • Prospective height loss of > 2cm (0.75 inches) • Self-reported history of vertebral fracture* <p>Two or more of the following*:</p> <ul style="list-style-type: none"> • Age 60–69 • Historical height loss of 2–4 cm • Self-reported prior non-vertebral fracture • Chronic systemic diseases associated with increased risk of vertebral fractures <p>Post-menopausal women with a T-score of ≤ -2.5 if documentation of a prevalent vertebral fracture would influence choice of or duration of therapy</p> <p>Women of any age on chronic systemic glucocorticoid therapy (dose equivalent to > 5 mg of prednisone per day)</p> <p>Men with a T-score of -1.5 to -2.4, and:</p> <ul style="list-style-type: none"> • Age 80 or older • Historical height loss > 6 cm (2.4 inches) • Prospective height loss of >3 cm (1.2 inches) • Self-reported history of vertebral fracture* <p>Two or more of the following*:</p> <ul style="list-style-type: none"> • Age 70 to 79 • Historical height loss of 3–6 cm • Self-reported prior non-vertebral fracture • Chronic systemic diseases associated with increased risk of vertebral fractures <p>Men with a T-score of ≤ -2.5 if documentation of a prevalent vertebral fracture would influence choice of or duration of therapy</p> <p>Men of any age on chronic systemic glucocorticoid therapy (dose equivalent to > 5 mg of prednisone per day)</p> <p>*If the documentation of a vertebral fracture would influence choice of therapy.</p>

and enable accurate assessment of vertebral anatomy. This need was met by the manufacturers of densitometers, General Electric (GE Lunar) and Hologic, who added spine imaging and VFA capabilities to the DXA machines. Of note, several other terms have been utilized to describe this technique, including instant vertebral assessment with or without high definition (IVA and IVA-HD), lateral vertebral assessment (LVA), and dual-energy vertebral assessment (DVA). The International Society for Clinical Densitometry (ISCD) has adopted the VFA term to denote densitometric spine imaging performed for the purpose of identifying vertebral fractures, and VFA will be used throughout this review [25].

Several additional limitations of spine radiography were addressed by VFA technology. Among the most important of these is that spine radiographs are often obtained at distinct sites from the clinic. The introduction of VFA enabled the clinician to perform the study as part of a

point of care service, in the same clinic and even at the same time as the DXA evaluation, and at a lower cost than with spine radiography [26]. VFA is also associated with <1% of the radiation associated with an analogous spine radiograph [27]. Additionally, obliquity, which at times complicates the interpretation of spine radiography, is less common with VFA. The direction of the cone beam used in spinal radiographs lends itself to more obliquity—occurring as a result of the beams hitting the spine at an angle, and thereby resulting in oval endplates, instead of a single line. VFA, which utilizes a parallel beam, enables the beam to hit the vertebral bodies in parallel and thereby creates an image of the endplates as a single line with less parallax effect and obliquity. Fig. 1 demonstrates obliquity occurring with a lumbar spine radiograph and the corresponding VFA, where endplates are parallel. Please note that the figures included in this review were obtained with iDXA on GE Lunar densitometers. The iDXA utilizes higher energy to generate images with even greater resolution. Finally, while surrounding soft tissue, ribs, and the scapula limit visualization of vertebrae above T7 with VFA, as compared to spine radiographs, visualization of the lumbar spine is often enhanced in VFA [28].

Several studies have compared the ability to detect vertebral fractures by VFA by densitometry compared to spine radiography [25, 29–32]. In one more recent study, 269 females and 81 males underwent



Fig. 2. Obliquity of the lumbar spine occurring in this patient with scoliosis. Noted also is the presence of calcified aorta.



Fig. 3. Image quality is reduced by poor rotation, which may be in part due to increased adipose tissue from obesity. Please note an incidental finding of calcified abdominal aorta.

both conventional spine radiography and VFA evaluation of T4-L4 [32]. Among 4550 vertebrae studied, they reported 98.4% as adequately visualized by VFA images. They found that 36.0% (126) of subjects were found to have vertebral fractures by radiography compared with 35.7% (125) by VFA. The authors found that on both a per-vertebra and per-patient basis, there was significant agreement between the two techniques, even among mild fractures. However, sensitivity to detect fractures among older models of densitometers was lower than with the newer models. Prior studies have shown that agreement between spine radiography and VFA for mild fractures (grade 1) is lower than that seen for more moderate or severe (grade 2 and 3) fractures, with VFA having lower sensitivity to detect milder fractures [29,31]. Of note, however, grade 1 fractures may be less clinically relevant, as they are more likely to represent non-fracture deformities and are less predictive of future fractures compared to grade 2 and 3 fractures [10].

Despite their differences, VFA and spine radiography both rely heavily upon the experience of the technician performing the study and the expert interpreting it. For both techniques, the ability to detect mild vertebral fractures is reduced compared to more moderate or severe fractures. Other imaging modalities, including MRI, CT, and nuclear bone scans, may also be used to identify vertebral fractures. CT and MRI

provide improved resolution, a better picture of overall anatomy, the ability to evaluate the acuity of the fracture, and to differentiate between osteoporotic and non-osteoporotic (e.g. malignant) fracture. Unfortunately, these modalities require a separate location to perform the study and, most problematically, result in significantly higher radiation exposure and/or cost. Given all of these limitations, VFA can be considered the optimal screening technology for the detection of vertebral fractures. Nevertheless, while VFA may be considered ideally suited for the initial evaluation for vertebral fracture, there are some limitations. Determining the acuity of the fracture and whether the etiology is related to non-osteoporotic pathology such as malignancy is not feasible by VFA alone. Therefore, in combination with the patient's clinical presentation, the ISCD recommends that additional imaging modalities may be considered when there are two or more mild (grade 1) deformities without any moderate or severe (grade 2 or 3) deformities, when there is an equivocal fracture, when there are lesions in the vertebrae which cannot be attributed to benign causes, or if the patient has a vertebral deformity and a known history of malignancy [25]. Additional imaging is also indicated when vertebrae between T7-L4 are unidentifiable on VFA or in the presence of sclerotic or lytic changes not usually seen in osteoporosis.

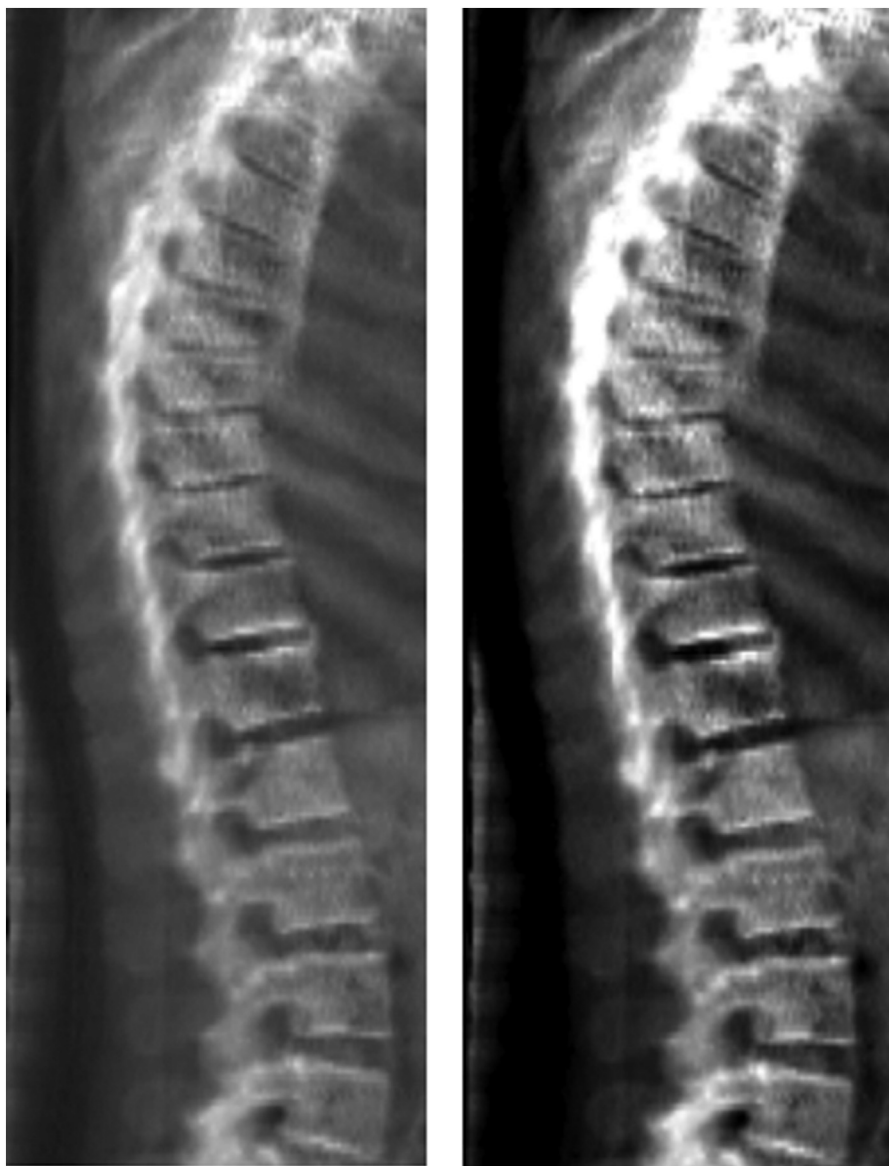


Fig. 4. Rib shadows. Manipulation of image contrast enables a clearer distinction of the rib and vertebral borders.

4. Indications for vertebral fracture assessment

The ISCD has provided recommendations on defining and reporting fractures on VFA in its official position statements [25]. The National Osteoporosis Foundation and International Osteoporosis Foundation recommendations are generally in accordance with the ISCD, with a few additions [33,34]. The recommendations of all three are summarized in Table 1. The ISCD has noted that the methodology used for identification of vertebral fractures should be similar to standard radiological approaches and should be described in the report. Further, fracture diagnosis should be based upon visual evaluation, include an assessment of grade and severity, and not be based upon morphometry alone—although morphometric analysis may be used to confirm the severity of a deformity. Finally, at this time, the ISCD endorses the Genant visual semi-quantitative method as the clinical technique of choice when diagnosing vertebral fractures by VFA [25]. In our experience, the algorithm based qualitative (ABQ) method, with its attention to the endplates can also be used to enhance diagnoses made using the Genant semi-quantitative method.

5. Interpretation of VFA

In order to adequately interpret the VFA study, as with all DXA evaluations, the proper positioning of the patient is very important. On GE Medical Systems instruments, the patient is placed in the left lateral decubitus position and stabilized with a special positioning apparatus that helps to ensure that the spine is parallel to the table. Of note, the

Hologic C and W series also rely on the lateral decubitus position (right), but the majority of Hologic scanners provide a lateral image obtained with a rotating C-arm while the patient remains in the supine position. With both systems, a posteroanterior (PA) and lateral view is available, with the former useful for determining landmarks and vertebral numbering and the latter for visualization of the vertebral anatomy. Using the PA view, L4–L5 is usually visualized at or near the pelvic crest and the lowest rib is usually seen at the anterior aspect of L1. Several scenarios can limit the ability of the VFA to provide optimal visualization of the vertebrae. Among these is shoulder rotation, which can impede visualization of the upper thoracic vertebra by overlapping the scapula and ribs over the thoracic spine. Although occurring less than with spine radiography, obliquity and parallax distortion may also occur with VFA. An example of this is seen in Fig. 2, where the patient's scoliosis creates obliquity and makes assessing vertebral anatomy in the lumbar spine more challenging. In the case of excess adiposity with obesity, visualization of the vertebrae can also be impaired. Fig. 3 demonstrates poor rotation of the patient, which may have been difficult due to the patient's excess adipose tissue, and makes the VFA more difficult to interpret. In such cases, the interpreter should comment on any vertebrae that are uninterpretable. Additionally, the diaphragmatic shadow may change with inspiration/expiration and obscure the vertebral borders, thereby making it more difficult to identify a fracture (this is more of a problem when evaluating a single energy image). Rib shadows can also obscure vertebral outlines. Fig. 4 demonstrates how a rib shadow obscures the vertebral body, and how adjusting the contrast can enable the interpreter to more easily distinguish between the rib and vertebral



Fig. 5. Reverse VFA. VFA is visualized from T4 to L5. The image on the left was obtained in the left decubitus position. The image on the right was obtained with the patient in the right decubitus position and is considered a “reverse VFA”. Note the improvement in visualization of the thoracic vertebrae on the reverse VFA and the loss of height at T5–T7—consistent with a grade 2 wedge fracture at T5 and a grade 2 crush fracture at T6.

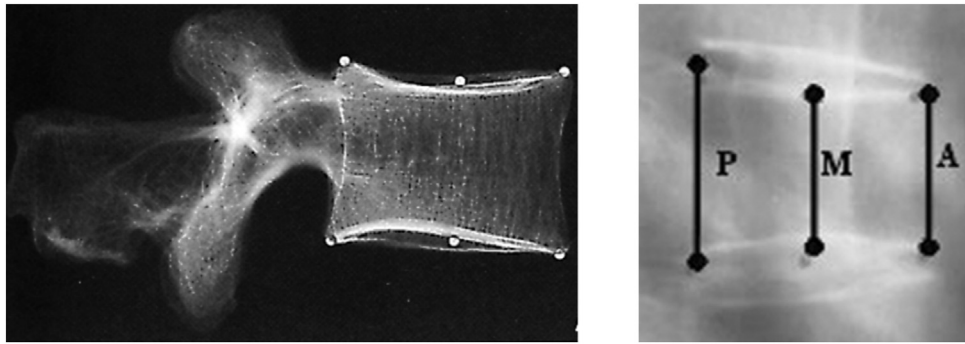


Fig. 6. Six-point morphometry. Six points are placed on the superior and inferior anterior (A), middle (M), and posterior (P) margins of the endplates. Using these points, vertebral heights and changes in height ratios can be used to assess for vertebral fracture. Note that when there is more obliquity, and the endplates are not parallel, point placement becomes more subjective.

Adapted from Vertebral Fracture Teaching Program|International Osteoporosis Foundation, (n.d.). <https://www.iofbonehealth.org/what-we-do/training-and-education/educational-slide-kits/vertebral-fracture-teaching-program> (accessed December 8, 2016).

shadows. Finally, the interpreter should ensure that there are no other foreign shadows occurring from accessories and undergarments that may interfere with visualization of vertebral anatomy.

One can use a variety of strategies to enhance visualization of the vertebrae. One such technique to address the limited visualization of vertebrae in the left lateral decubitus position is to perform a “reverse VFA”, where the patient is repositioned in the right decubitus position. Fig. 5 demonstrates a VFA obtained from the right decubitus position. A variety of other image manipulations, including magnification of the individual vertebra, inverting the image, and adjustment of the contrast

and brightness of the image can also enhance visualization and interpretation and underscore the importance of viewing images on-screen, with low-ambient lighting, whenever possible.

Unlike other fractures, distinguishing fractured vertebrae from normal can be quite challenging. Vertebral fractures are often not precipitated by a single traumatic event, and, anatomically, there appears to be a progressive continuum through which the vertebral body undergoes changes leading to a fracture. This makes radiologic diagnosis of vertebral fracture difficult and has resulted in a lack of clear consensus on the best method for evaluation of spine images. Commonly,

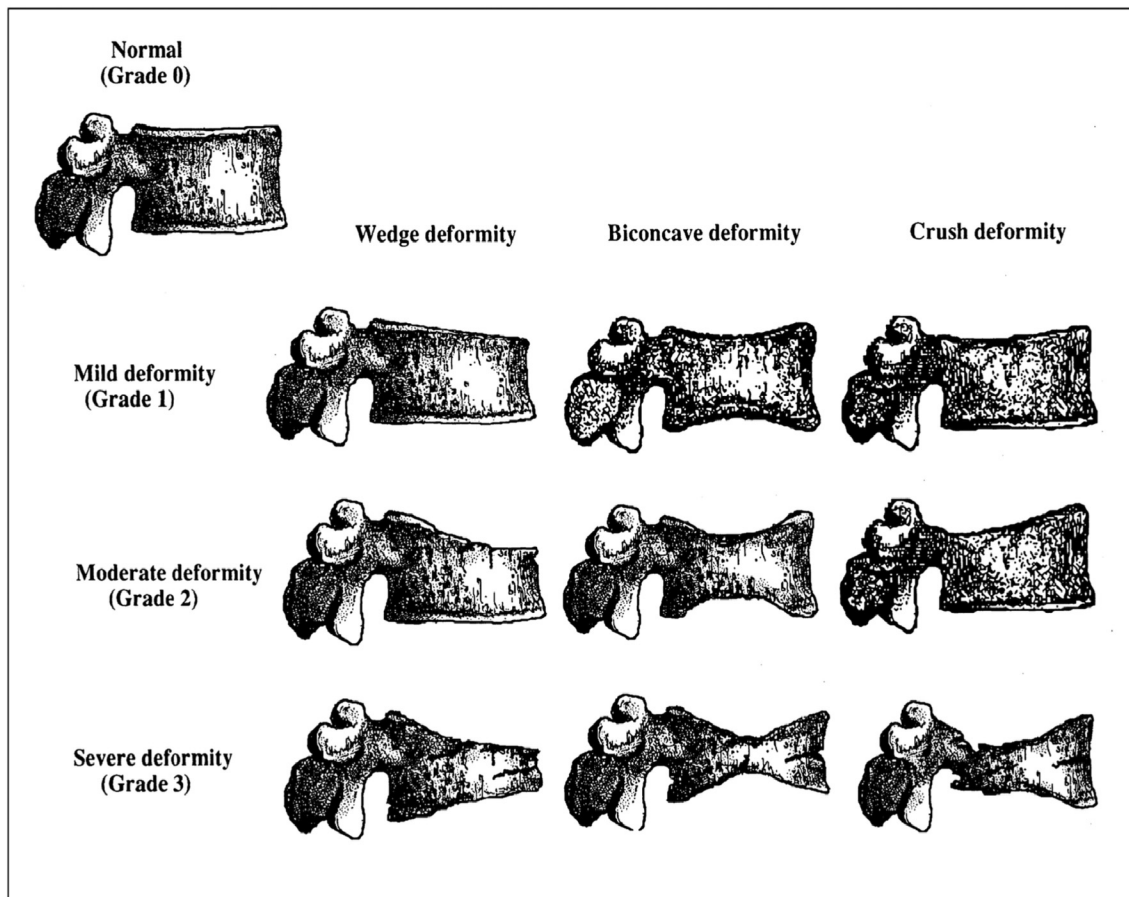


Fig. 7. Genant Semi-Quantitative Method.

Adapted from H.K. Genant, C.Y. Wu, C. van Kuijk, M.C. Nevitt, Vertebral fracture assessment using a semiquantitative technique, *J. Bone Miner. Res.* 8 (1993) 1137–1148. doi:10.1002/jbmr.5650080915.

anterior, middle, and posterior heights are measured, and the reduction in any of these heights, or their ratios, represents a vertebral deformity, which often, but not always, identifies a vertebral fracture. Several methods for radiographic and densitometric diagnosis of vertebral fracture have been utilized. These methods rely on either visual assessment for vertebral deformity, morphometric measurement of the change in vertebral height, or some combination of both. The four methodologies currently used are the qualitative visual, quantitative morphometric (QM), semiquantitative (SQ) visual method of Genant, and algorithm-based qualitative assessment (ABQ). The lack of consensus on which method is best to define and identify a vertebral fracture may contribute to underreporting of fracture on radiographic studies. The ISCD has recommended that the Genant semi-quantitative method be used as the method of choice for diagnosis of vertebral fracture with VFA. If the severity of the deformity needs to be confirmed, morphometric



Fig. 8. Using the Genant semi-quantitative method of interpretation, one can identify a grade 2 wedge fracture of L3, with an estimated height loss of between 25 and 40%, and a grade 3 biconcave fracture of L1 where there is an estimated mid-vertebral height loss of at least 40%.



Fig. 9. Kyphosis and multiple vertebral fractures are present in this patient. VFA is visualized from T2 to L4 and the importance of not missing vertebral fractures by counting all vertebrae can be seen here. There is a grade 2 biconcave fracture at L3, grade 3 biconcave fracture at L1, grade 2 biconcave fracture at T11 and a grade 3 crush fracture T7. Note also the presence of artifact from bra clips adjacent to T10 and T11 and the calcification of the aorta.

measurement can then be used, but morphometry alone is not recommended [25].

With qualitative visual assessment, a trained interpreter (e.g. radiologist) reports a vertebra as being normal or fractured without describing the type or severity of the fracture. The elements that are assessed to decide that the vertebra is fractured include lack of self-similarity (anatomic discordance between adjacent vertebrae); disruption of the endplate with an impression into the vertebral body (endplate deformities—horizontal edge irregularity); end-plates are no longer parallel (loss of parallelism); and cortical buckling (vertical edge irregularity) [20,35]. Limitations of this methodology include subjectivity and the need to have an experienced interpreting clinician. Another limitation is the lack of assessment of the type or severity of the fracture—both of which have been shown to influence the risk of future fractures [10, 36].

On the other end of the spectrum is pure morphometric analysis using measurement of vertebral heights. The provider or technician places 6 morphometric points to define the anterior, middle, and posterior vertebral heights as demonstrated in Fig. 6. The placement of morphometric points is automated by the VFA software, but is not always accurate and should always be verified by a reading clinician. Thus, morphometry is not truly an objective method since the point placement is subjective—inaccurate point placement can significantly alter the ratios of vertebral heights and diagnosis of the severity of the fracture. A certain change in the ratio of anterior, middle, and/or posterior heights is commonly used to signify a vertebral deformity, although the exact amount of change necessary is a matter of debate. Alternative methods for quantifying change in vertebral height are the Eastell-Melton and McCloskey methods, where reductions of 3 standard deviations or more from the mean vertebral heights in a normative population



Fig. 10. Not all vertebra deformities are fractures. Here, there is a short vertebral height at T12, and degenerative changes.



Fig. 11. Schmorl's Node. VFA visualized from T2 to L4 demonstrates grade 2 wedge fractures of L2, T12, and T6. Note the presence of a Schmorl's nodules on T12 where a focal depression in the middle of upper and lower endplate is seen. In this case there is co-occurrence of vertebral fracture and Schmorl's nodules on the same vertebra.

comprise a vertebral fracture [37,38]. Pure morphometric analysis has its limitations, as several common conditions, including degenerative disc disease, osteophytes, scoliosis, the presence of hardware, or prior vertebroplasty or kyphoplasty, can result in incorrect point placement and changes in vertebral heights that hinder the ability to define a fracture. The interpreting clinician plays a critical role in differentiating non-fracture deformities from true vertebral fractures [36].

The ABQ method is an algorithm-based qualitative tool where the diagnosis of vertebral fracture requires a disruption of vertebral endplates [34,39]. Vertebral bodies are evaluated for features of non-fracture deformities. The clinician begins by assessing for depression of the endplate. In the absence of a depressed endplate, evidence of short vertebral height points to physiologic variants such as Scheuermann's, scoliosis, a prior childhood fracture, or other variants. If the endplate is depressed, the location and length of the depression is next assessed. If the depression is concave, but occurs in a focused area of the endplate, a Schmorl's node should be considered. If the entire endplate is depressed within the ring, and there is no evidence of trauma, tumor, or other metabolic disease that could be contributing, then the diagnosis of osteoporotic fracture can be made. This method may be particularly useful with mild, grade 1 fractures [20].

The Genant semiquantitative method combines a qualitative approach of inspecting the vertebral bodies to decide whether a vertebra is fractured with a quantitative assessment of grade and type of fracture by a comparison to a chart (Fig. 7) [40]. Fractures are defined as either wedge (a reduction in the anterior to posterior height ratio), biconcave (a reduction of the mid- to posterior vertebral height ratio), or a crush fracture (a reduction of the anterior, mid, and posterior heights compared to that of the vertebrae above or below). Of note, fractures may have a combination of these deformities. The fracture is also graded in severity—grade 1 or mild fracture defined as a reduction in anterior, middle, and/or posterior vertebral height of 20–25%, grade 2, or moderate fracture with a reduction in height of 25–40%, and grade 3, or severe, where vertebral height loss is >40%. As has been described, this is the preferred method of the ISCD for identifying and classification of vertebral fractures. One limitation of this method is that physiologic wedging in the thoracic spine can lead to over-diagnosis of wedge vertebral fractures. Fig. 8 demonstrates grade 2 and grade 3 fractures identified using the Genant method.

After verifying the correct patient, assessing for proper positioning, and adjusting image quality (brightness, contrast, etc.) as needed, there are several other important considerations when interpreting the VFA. The interpreting clinician should examine all vertebrae from bottom to top and assess for similarity between adjacent vertebrae. Fig. 9 demonstrates multiple vertebral fractures in both the lumbar and thoracic spine. Although the presence of any vertebral fracture defines osteoporosis, independently of BMD, the number and severity of fractures help predict future fracture risk, and therefore interrogating all vertebrae for evidence of fracture is critical [7,9,10,41]. While grade 2 and 3 fractures can be easier to identify, milder grade 1 (<25% height loss) fractures can be more difficult to detect and interpret. These fractures correlate less with radiographic spine images and are less predictive value for future fracture than grade 2 and 3 fractures. The provider should use caution in over-interpreting mild fractures since the diagnosis of osteoporosis occurring with vertebral fracture can significantly alter the course of treatment. Radiographic, CT, or MR imaging may help to further characterize suspected deformities and differentiate a true fracture from non-fracture deformities.

Several non-fracture deformities can confound the interpretation and assessment for vertebral fractures. Shortened vertebral height, as seen in Fig. 10, is seen with aging and degenerative changes including anterior osteophytes and narrowing of the disc space. Schmorl's nodes, which occur when the nucleus pulposus herniates into the vertebral body, often represent a developmental abnormality or can be seen in adolescent males, particularly those who engage in contact sports. They may additionally be seen in situations where there is endplate weakness

such as with trauma, malignancy, infection, and in hyperparathyroidism. While the impaction of the endplate into the vertebral body can give the impression of a fracture, it should be noted that these are localized herniations of the endplate, rather than those that are seen with fracture and which extend from end to end [35]. Fig. 11 demonstrates a Schmorl's node, degenerative changes, and physiologic wedging. One can also assess for the presence of prior vertebral augmentation, as seen in Fig. 12 to determine the presence of prior vertebral fractures.

Finally, it is also important to look at all prior VFA or other radiologic studies to identify incident vertebral fractures occurring between studies. In addition to helping predict risk of subsequent fractures, this will also enable the provider to assess for response to osteoporosis therapies. Fig. 13 shows serial scans demonstrating a new fracture and progression of kyphosis in follow-up scan in a patient with prior vertebral fractures.

6. Conclusion

Osteoporosis is highly prevalent, yet often untreated. Identifying vertebral fractures, which are often not clinically apparent, is paramount to

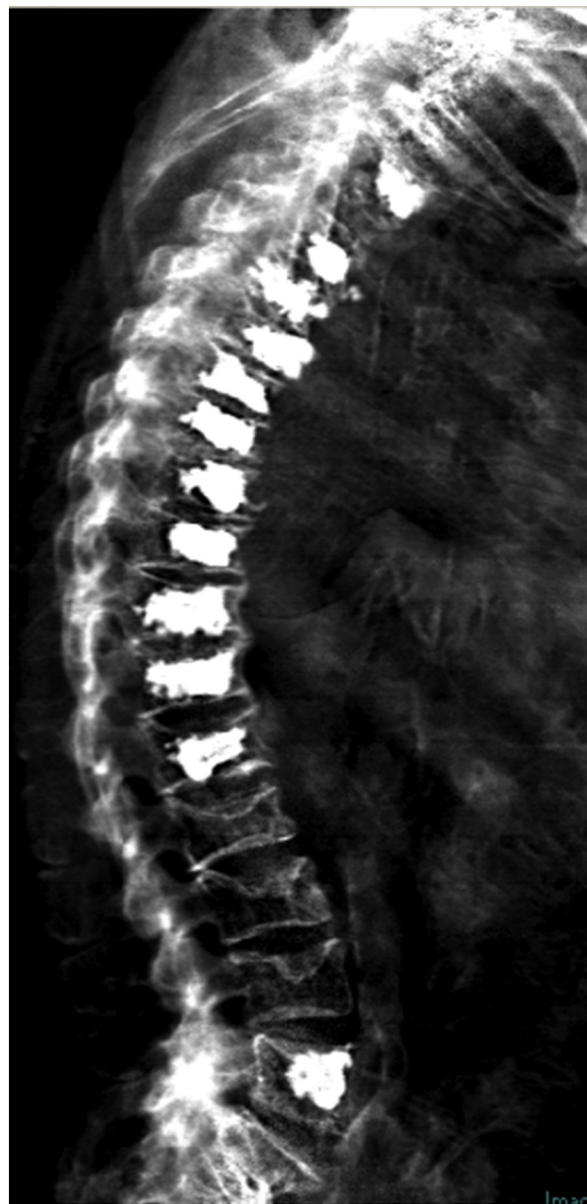


Fig. 12. Fractures are seen in all vertebrae from T3-L5 with the patient having gone vertebral augmentation in multiple vertebrae.

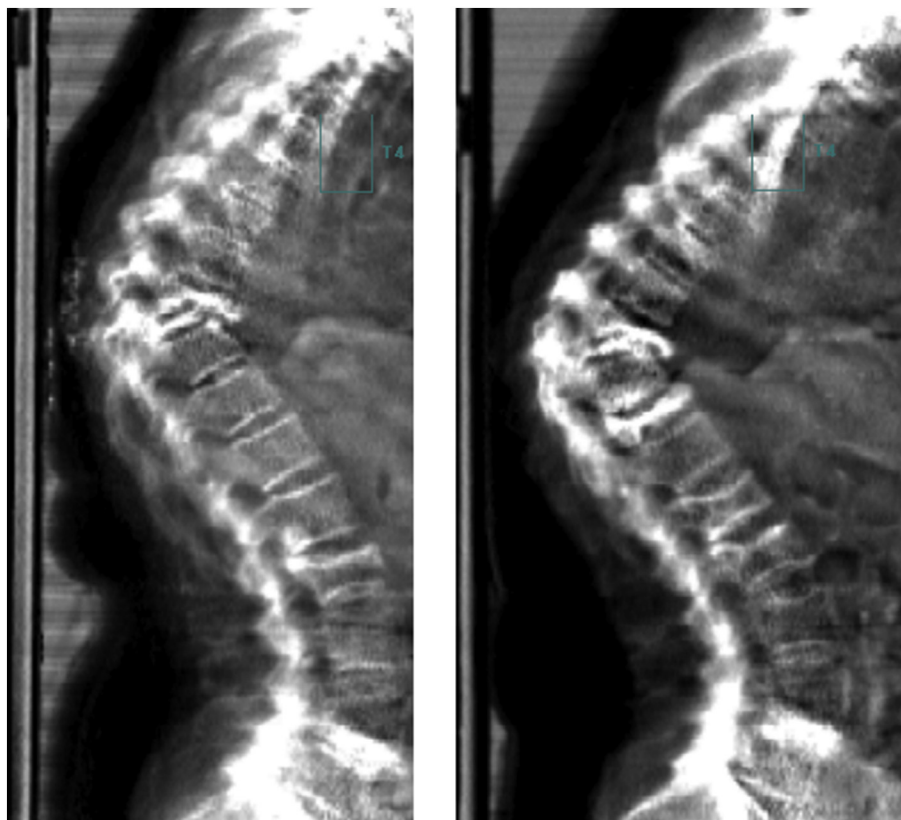


Fig. 13. Monitoring for incident fractures. Serial VFA studies in this patient demonstrate progression of marked kyphosis from incident vertebral fractures occurring between scans. The image on the left demonstrates multiple fractures including grade 2 wedge fractures of L2 and L3, and grade 3 crush fracture of T9. A follow-up scan done on a subsequent encounter shows a new grade 2 biconcave fracture of L1 and grade 3 crush fracture of T11.

diagnosing osteoporosis. In doing so, the clinician can risk stratify the patient and treat to prevent future osteoporotic fractures and their associated morbidity and mortality. The addition of lateral spine imaging technology to the densitometer, VFA, was a major advancement in the ability to diagnose osteoporosis and vertebral fractures. The ability to obtain the image at the same time as the DXA is performed, at a lower cost, and significantly lower radiation dose than with spine radiography make VFA the optimal initial imaging modality to screen for and identify vertebral fractures. Prior to assessing the VFA for fractures, the image should be reviewed to verify the correct patient, ensure proper positioning was used, and to identify any uninterpretable vertebrae or artifacts. While multiple methods such as qualitative, quantitative morphometric, and ABQ assessment can all be used to diagnose vertebral fractures, the Genant semi-quantitative method is the preferred initial method with a possible addition of ABQ for grade 1 fractures. Given the potential to predict future fractures and fracture-related morbidity, all vertebrae should be analyzed to avoid missing any fractures. Serial VFA images can be used to diagnose incident vertebral fractures and assess response to therapy when applicable. As has been described in this review, the clinician can follow guidelines for when VFA is indicated to assist in optimizing use of this technology. Finally, in cases of equivocal fractures, or multiple mild vertebral deformities, when there is a history of or suspicion for malignancy, and when the acuity of the fracture needs to be determined, the provider can consider an additional imaging modality to better evaluate vertebral anatomy.

References

- [1] Facts and Statistics|International Osteoporosis Foundation, (n.d.). <https://www.iofbonehealth.org/facts-statistics> (accessed December 12, 2016).
- [2] C. Cooper, E.J. Atkinson, S.J. Jacobsen, W.M. O'Fallon, L.J. Melton, Population-based study of survival after osteoporotic fractures, *Am. J. Epidemiol.* 137 (1993) 1001–1005.
- [3] T.J. Vokes, L.B. Dixon, M.J. Favus, Clinical utility of dual-energy vertebral assessment (DVA), *Osteoporos. Int.* 14 (2003) 871–878.
- [4] H.A. Fink, D.L. Milavetz, L. Palermo, M.C. Nevitt, J.A. Cauley, H.K. Genant, D.M. Black, K.E. Ensrud, What proportion of incident radiographic vertebral deformities is clinically diagnosed and vice versa? *J. Bone Miner. Res.* 20 (2005) 1216–1222.
- [5] E.T. Middleton, S.A. Steel, Routine versus targeted vertebral fracture assessment for the detection of vertebral fractures, *Osteoporos. Int.* 19 (2008) 1167–1173.
- [6] M.C. Nevitt, D.E. Thompson, D.M. Black, S.R. Rubin, K. Ensrud, A.J. Yates, S.R. Cummings, Effect of alendronate on limited-activity days and bed-disability days caused by back pain in postmenopausal women with existing vertebral fractures, *Arch. Intern. Med.* 160 (2000) 77–85.
- [7] R. Lindsay, S.L. Silverman, C. Cooper, D.A. Hanley, I. Barton, S.B. Broy, A. Licata, L. Benhamou, P. Geusens, K. Flowers, et al., Risk of new vertebral fracture in the year following a fracture, *JAMA* 285 (2001) 320–323.
- [8] L.J. Melton, Adverse outcomes of osteoporotic fractures in the general population, *J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res.* 18 (2003) 1139–1141, <http://dx.doi.org/10.1359/jbmr.2003.18.6.1139>.
- [9] D.M. Black, N.K. Arden, L. Palermo, J. Pearson, S.R. Cummings, Prevalent vertebral deformities predict hip fractures and new vertebral deformities but not wrist fractures, *J. Bone Miner. Res.* 14 (1999) 821–828.
- [10] P.D. Delmas, H.K. Genant, G.G. Crans, J.L. Stock, M. Wong, E. Siris, J.D. Adachi, Severity of prevalent vertebral fractures and the risk of subsequent vertebral and nonvertebral fractures: results from the MORE trial, *Bone* 33 (2003) 522–532.
- [11] E.S. Siris, H.K. Genant, A.J. Laster, P. Chen, D.A. Misurski, J.H. Krege, Enhanced prediction of fracture risk combining vertebral fracture status and BMD, *Osteoporos. Int.* 18 (2007) 761–770, <http://dx.doi.org/10.1007/s00198-006-0306-8>.
- [12] H.K. Svensson, E.H. Olofsson, J. Karlsson, T. Hansson, L.-E. Olsson, A painful, never ending story: older women's experiences of living with an osteoporotic vertebral compression fracture, *Osteoporos. Int.* 27 (2016) 1729–1736.
- [13] A. Oleksik, P. Lips, A. Dawson, M.E. Minshall, W. Shen, C. Cooper, J. Kanis, Health-related quality of life in postmenopausal women with low BMD with or without prevalent vertebral fractures, *J. Bone Miner. Res.* 15 (2000) 1384–1392.
- [14] D.M. Kado, W.S. Browner, L. Palermo, M.C. Nevitt, H.K. Genant, S.R. Cummings, Vertebral fractures and mortality in older women: a prospective study, *Arch. Intern. Med.* 159 (1999) 1215–1220.
- [15] T. Yamaguchi, T. Sugimoto, M. Yamauchi, Y. Matsumori, M. Tsutsumi, K. Chihara, Multiple vertebral fractures are associated with refractory reflux esophagitis in postmenopausal women, *J. Bone Miner. Metab.* 23 (2005) 36–40.
- [16] Leech, et al., Relationship of lung function to severity of osteoporosis in women, *Am. Rev. Respir. Dis.* 141 (1990) 68–71 Google Search, (n.d.) <https://www.google.com/search?q=Leech+et+al.+Relationship+of+lung+function+to+severity+of+osteoporosis+in+women>.

- ++ Am+ Rev+ Respir+ Dis+ 1990%3B141%3A68-71&ie=utf-8&oe=utf-8 (accessed December 19, 2016).
- [17] S.H. Gehlbach, C. Bigelow, M. Heimisdottir, S. May, M. Walker, J.R. Kirkwood, Recognition of vertebral fracture in a clinical setting, *Osteoporos. Int.* 11 (2000) 577–582.
- [18] D. Lansdown, B. Bennet, S. Thiel, O. Ahmed, L. Dixon, T.J. Vokes, Prevalence of vertebral fractures on chest radiographs of elderly African American and Caucasian women, *Osteoporos. Int.* 22 (2011) 2365–2371, <http://dx.doi.org/10.1007/s00198-010-1452-6>.
- [19] A.L. Williams, A. Al-Busaidi, P.J. Sparrow, J.E. Adams, R.W. Whitehouse, Under-reporting of osteoporotic vertebral fractures on computed tomography, *Eur. J. Radiol.* 69 (2009) 179–183.
- [20] T. Vokes, Utility of vertebral fracture recognition in osteoporosis, *Clin. Rev. Bone Miner. Metab.* 14 (2016) 4–13.
- [21] P. Chen, P.D. Miller, P.D. Delmas, D.A. Misurski, J.H. Kregge, Change in lumbar spine BMD and vertebral fracture risk reduction in teriparatide-treated postmenopausal women with osteoporosis, *J. Bone Miner. Res.* 21 (2006) 1785–1790.
- [22] P.D. Miller, G. Hattersley, B.J. Riis, G.C. Williams, E. Lau, L.A. Russo, P. Alexandersen, C.A. Zerbini, M. Hu, A.G. Harris, et al., Effect of abaloparatide vs placebo on new vertebral fractures in postmenopausal women with osteoporosis: a randomized clinical trial, *JAMA* 316 (2016) 722–733.
- [23] R.A. Adler, G.E.-H. Fuleihan, D.C. Bauer, P.M. Camacho, B.L. Clarke, G.A. Clines, J.E. Compston, M.T. Drake, B.J. Edwards, M.J. Favus, et al., Managing osteoporosis in patients on long-term bisphosphonate treatment: report of a task force of the American Society for Bone and Mineral Research, *J. Bone Miner. Res.* 31 (2016) 16–35.
- [24] J.A. Rea, P. Steiger, G.M. Blake, E. Potts, I.G. Smith, I. Fogelman, Morphometric X-ray absorptiometry: reference data for vertebral dimensions, *J. Bone Miner. Res.* 13 (1998) 464–474.
- [25] H.N. Rosen, T.J. Vokes, A.O. Malabanan, C.L. Deal, J.D. Alele, T.P. Olingenski, J.T. Schousboe, The official positions of the International Society for Clinical Densitometry: vertebral fracture assessment, *J. Clin. Densitom.* 16 (2013) 482–488.
- [26] 2017 Medicare Physician Fee Schedule Final Rule—American College of Radiology, 2016. <https://www.acr.org/Advocacy/Economics-Health-Policy/Medicare-Payment-Systems/MPPFS/2017-Final-Rule> (accessed December 7, 2016).
- [27] P.L. Jager, S. Jonkman, W. Koolhaas, A. Stiekema, B.H.R. Wolffenbuttel, R.H.J.A. Slart, Combined vertebral fracture assessment and bone mineral density measurement: a new standard in the diagnosis of osteoporosis in academic populations, *Osteoporos. Int.* 22 (2011) 1059–1068, <http://dx.doi.org/10.1007/s00198-010-1293-3>.
- [28] R.D. Chapurlat, F. Duboeuf, H.O. Marion-Audibert, B. Kalpakcioglu, B.H. Mitlak, P.D. Delmas, Effectiveness of instant vertebral assessment to detect prevalent vertebral fracture, *Osteoporos. Int.* 17 (2006) 1189–1195.
- [29] N. Binkley, D. Krueger, R. Gangnon, H.K. Genant, M.K. Drezner, Lateral vertebral assessment: a valuable technique to detect clinically significant vertebral fractures, *Osteoporos. Int.* 16 (2005) 1513–1518.
- [30] J.T. Schousboe, C.R. DeBold, Reliability and accuracy of vertebral fracture assessment with densitometry compared to radiography in clinical practice, *Osteoporos. Int.* 17 (2006) 281–289.
- [31] T. Fuerst, C. Wu, H.K. Genant, G. Von Ingersleben, Y. Chen, C. Johnston, M.J. Econs, N. Binkley, T.J. Vokes, G. Crans, et al., Evaluation of vertebral fracture assessment by dual X-ray absorptiometry in a multicenter setting, *Osteoporos. Int.* 20 (2009) 1199–1205.
- [32] D. Diacinti, R. Del Fiacco, D. Pisani, F. Todde, M.S. Cattaruzza, D. Diacinti, S. Arima, E. Romagnoli, J. Pepe, C. Cipriani, et al., Diagnostic performance of vertebral fracture assessment by the lunar iDXA scanner compared to conventional radiography, *Calcif. Tissue Int.* 91 (2012) 335–342.
- [33] F. Cosman, S.J. De Beur, M.S. LeBoff, E.M. Lewiecki, B. Tanner, S. Randall, R. Lindsay, Clinician's guide to prevention and treatment of osteoporosis, *Osteoporos. Int.* 25 (2014) 2359–2381.
- [34] Vertebral Fracture Teaching Program|International Osteoporosis Foundation, 2011. <https://www.iofbonehealth.org/what-we-do/training-and-education/educational-slide-kits/vertebral-fracture-teaching-program> (accessed December 8, 2016).
- [35] B. Lentle, J. Trollip, K. Lian, The radiology of osteoporotic vertebral fractures redux, *J. Clin. Densitom.* 19 (2016) 40–47, <http://dx.doi.org/10.1016/j.jocd.2015.08.009>.
- [36] S.H. Chou, T. Vokes, Vertebral morphometry, *J. Clin. Densitom.* 19 (2016) 48–53.
- [37] R. Eastell, S.L. Cedel, H.W. Wahner, B.L. Riggs, L.J. Melton, Classification of vertebral fractures, *J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res.* 6 (1991) 207–215, <http://dx.doi.org/10.1002/jbmr.5650060302>.
- [38] E.V. McCloskey, T.D. Spector, K.S. Eyres, E.D. Fern, N. O'Rourke, S. Vasikaran, J.A. Kanis, The assessment of vertebral deformity: a method for use in population studies and clinical trials, *Osteoporos. Int.* 3 (1993) 138–147, <http://dx.doi.org/10.1007/BF01623275>.
- [39] L. Ferrar, G. Jiang, J.T. Schousboe, C.R. DeBold, R. Eastell, Algorithm-based qualitative and semiquantitative identification of prevalent vertebral fracture: agreement between different readers, imaging modalities, and diagnostic approaches, *J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res.* 23 (2008) 417–424, <http://dx.doi.org/10.1359/jbmr.071032>.
- [40] H.K. Genant, C.Y. Wu, C. van Kuijk, M.C. Nevitt, Vertebral fracture assessment using a semiquantitative technique, *J. Bone Miner. Res.* 8 (1993) 1137–1148, <http://dx.doi.org/10.1002/jbmr.5650080915>.
- [41] H. Hagino, M. Shiraki, M. Fukunaga, T. Nakano, K. Takaoka, Y. Ohashi, T. Nakamura, T. Matsumoto, Number and severity of prevalent vertebral fractures and the risk of subsequent vertebral fractures in Japanese women with osteoporosis: results from the minodronate trial, *J. Bone Miner. Metab.* 31 (2013) 544–550, <http://dx.doi.org/10.1007/s00774-013-0439-8>.