# **Current imaging techniques in osteoporosis**

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"We need to move beyond standard setting... and make those standards a reality for living people everywhere". Dr Mary Robinson, former U.N. High Commissioner for Human Rights

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#### ABSTRACT

Osteoporosis is a global pandemic affecting children, men and women of all ages and ethnicities. Millions of people suffer fragility fractures each year around the world as a result of this bone disease, which can have devastating consequences for them, including permanent disability and death. Many fractures are preventable by identifying people at high risk for fracture and falls, and diagnosing those who already have osteoporosis, before they fracture. Rheumatologists commonly encounter people with fragile bones, either as an isolated entity, or a co-morbidity to their underlying rheumatic illness or treatment. Imaging in osteoporosis can be used to make a diagnosis, while measurements of bone and body tissues, most commonly bone mineral density, can be used to identify those at risk and monitor them following treatment. Modern densitometry scanners may have multiple new features including measures of hip geometry, trabecular bone score, finite element analysis, fat and muscle mass, and may have additional imaging features including vertebral fracture assessment and atypical femoral fracture screening. When used correctly, these tools provide invaluable information for the assessment of the effectiveness of interventions in clinical studies, and patient management in clinical practice. In this article we review osteoporosis imaging techniques, with an emphasis on dual-energy x-ray absorptiometry. and how to apply and interpret them in modern rheumatology practice.

#### Introduction

Osteoporosis is derived from Greek, which literally means a bone with too many holes. The clinical disease is a spectrum of illness characterised by 'progressive systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture (1, 2). Fragility fractures are the hallmark clinical feature of this disease, which can be life-altering and/or life-threatening. Operationally, a fragility fracture may be defined as one that occurs in a bone from a force that would not be expected to fracture a healthy bone.

Osteoporotic fractures are common in older adults: more than a third of women and more than one quarter of men will experience fragility fractures (3, 4). A report from a study of more than 100,000 postmenopausal women shows the annual risk of fracture is greater than the combined risk of all cardiovascular disease and invasive breast cancer, regardless of ethnicity (5). Fractures increase the risk for future fractures significantly, decrease quality of life and mobility, result in a significant economic burden, and increase mortality (6-17). Almost four million osteoporotic fractures occur each year in the European Union, placing a financial burden of around  $\in 40$ billion on health economies, or around €200 per E.U. citizen (17). Although the entire skeleton is at risk, the most common sites of fracture are the spine, proximal femur, forearm and proximal humerus (16-19). Mortality is increased following all clinical fractures (15), particularly of the hip and spine (9, 14, 20-23).

Risk factors for developing osteoporosis have been studied extensively and are well- documented (19, 24). The major ones are low bone mineral density, advancing age, frailty or self-reported poor health, a family history of osteoporosis (8, 19, 24), but they also include a growing list of other diseases and medications which can contribute to bone loss and skeletal fragility or falls including rheumatic diseases and their treatments (25, 26). Risk factors for fracture also include falls and previous fracture (10, 14, 20, 27). Indeed the highest risk group are older people with low BMD and a prior fracture (28,

29), particularly if they are frail and prone to falling (30).

Glucocorticoid-induced osteoporosis (GIOP) is the most common cause of secondary osteoporosis (31, 32). Up to 50% of patients with chronic glucocorticoid exposure fracture (31-33). Patients with GIOP may fracture at higher BMD than those with postmenopausal osteoporosis (33, 34). The risk is pathophysiological, driven not only by increased bone resorption, as in most forms of osteoporosis but also by decreased osteocyte and osteoblast function (32, 33, 35, 36). Even without glucocorticoid exposure, patients with rheumatic diseases such as rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis have an increase fracture risk. (37-41). Others have suggested this risk is increased in people with any rheumatic disease (25).

Imaging has an important role in the diagnosis and management of osteoporosis. Fractures can be diagnosed clinically, but radiographs and more sophisticated techniques such as computerised tomography (CT) and magnetic resonance imaging (MRI) usually are used for confirmation when there is a clinical suspicion. The presence of one or more fragility fractures should arouse the suspicion for osteoporosis, as the diagnosis can be made in the presence of a fragility fracture, particularly of the spine and hip. Examples are shown in Figure 1, with a left hip fragility fracture in a person who did not fall but experienced acute severe pain while walking, and another person who presented with two years of low back pain and height loss. Modern imaging and technology enables imaging of far greater detail to be seen than ever was available previously. Micro-CT imaging shows detailed bone structure including trabecular size, spacing and number, but even usual clinical images such as those shown in Figure 2 can detect fractures, and show frank osteoporosis.

Measurement of bone mineral density (BMD) has been possible using a variety of techniques for more than a century, including quantitative radiography, and more recently single-photon absorptiometry (42). Subsequent developments included use of two x-ray





Fig. 1. Radiographs showing a left hip (A) and multiple vertebral fractures (B).

beams, which led to the production of Dual x-ray absorptiometry (DXA) just over 30 years ago (42, 43). This concept enabled much greater distinction between bone and soft tissue, and later became the gold standard for the noninvasive measurement of BMD (7, 43, 44). Shortly thereafter, a society was formed whose mission has been to train and certify professionals around the world in the acquisition and interpretation of these measurements (43). Measurement of BMD remains an essential procedure for the identification of people (or patients) at risk for, the diagnosis and monitoring of osteoporosis treatment (42-44), based on quality technical considerations and their interpretation (45, 46).

In 1994 criteria for establishing the prevalence of osteoporosis in postmenopausal women were proposed by the World Health Organization using DXA measurement of BMD (1, 2). The criteria use DXA 'T-scores' (Fig. 2a) which are derived from measuring BMD in g/cm<sup>2</sup> at the proximal femur, and comparing this value to the mean BMD of a 'young adult' reference population on a standard deviation scale. A 'T-score' is calculated as follows:

# $T-score = \frac{Patient BMD - Mean Young Adult BMD}{Standard Deviation of Young Adult BMD}$

This definition came with several caveats, and has been clarified, ratified and modified over time by other organisations such as the International Soci-

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ety for Clinical Densitometry (https:// www.iscd.org/official-positions/2015iscd-official-positions-adult/), and The International Osteoporosis Foundation to enhance clinical use in individual patients, and other populations including men, younger adults and children (45, 47). Today DXA can be used to diagnose osteoporosis in postmenopausal women and men aged 50 years and older using modified 1994 criteria by measuring BMD at the spine, femoral neck or total hip, and in some circumstances the 1/3 distal radius (48). The recommended T-score reference population is NHANES III white female (49) at the hip for all genders (47, 48, 50). and manufacturer reference at the lumbar spine (50).

BMD is also converted to a 'Z-score' (Fig. 2a) which compares measured BMD to an age-matched reference population on a standard deviation scale:

#### Z- score = <u>Patient BMD - Mean Young Adult BMD</u> <u>Standard Deviation of Age matched</u> population BMD

In younger men (<50 years of age), premenopausal women, and children (<20 years of age) a diagnosis of osteoporosis should not be made on the basis of densitometric criteria alone (51, 52). In these populations 'Z-scores' are preferred to T-scores. The recommended term is that of "low BMD for age" if the Z-score is <-2.0 (51, 52). The recommended skeletal sites are the same for all adults, but in children the spine and whole body not including the head are preferred (51). Normative reference data may be localised if they exist (50-52).

DXA diagnosis comes with several important caveats, and has important limitations such as specificity and sensitivity. The Study of Osteoporotic Fractures followed more than 8,000 women aged 65 years and older following measurement of hip BMD. 17% had "osteoporosis" based on a T-score <-2.5 at baseline. Over the next 5 years 243 (3%) experienced a hip fracture: 112 (8%) subjects with DXA-defined "osteoporosis" suffered incident hip fracture, while 131 (2%) of those without "osteoporosis" experienced a hip fracture over that time period. Thus 54% of women who experienced a hip fracture, presumably due to osteoporosis, were not "osteoporotic" by DXA criteria (53). These data give a sensitivity of <50% and a specificity of >80% but importantly a positive predictive value of <10% and a negative predictive value of >98% (54). Furthermore the expert panel recommended not applying these criteria in the setting of vitamin D deficiency (2). Choosing different reference populations for calculating T-scores and Zscores will change the value obtained (55), since BMD varies by age, gender and ethnicity (49). Today national and international clinical guidelines for osteoporosis are based on measurement of BMD, in particular T-scores and Zscores (19, 50, 55-57).

Clearly DXA has limitations as a diagnostic test, and such testing is not always available. Studies show the presence of multiple additional risk factors enhances fracture risk prediction (7, 8, 19, 24, 58). Recent attention has focused on overall fracture risk which includes additional risk factors beyond simply measuring BMD. While BMD remains the most important risk factor in older women and men in the absence of a prior fracture (24, 47), there is no threshold value above or below which a patient will or will not fracture. This paradigm shift occurred because prospective studies documented that in absolute numbers. more adults who did not meet the BMD criteria for osteoporosis had fractures compared to those who met the criteria (53). Furthermore, measurement of BMD is not always possible.

DXA measured BMD is thus no longer viewed as the sole way of defining and estimating fracture risk (58-63). Fracture risk calculators have been developed that combine BMD and clinical risk factors, which enhance prediction (58, 63). A comprehensive global taskforce of experts reviewed and clarified how best to estimate fracture risk in

2010, and produced a comprehensive set of recommendations which have global validity and applicability (64). Such tools are not a panacea, and published data indicate that despite providing a reasonable estimate of risk, there is a wide confidence limit (19) and further refinements and improvements are needed.

Since its introduction more than 20 years ago, DXA has become the most widely used tool to measure BMD. New developments have been incorporated into DXA technology which have advanced the capabilities for risk assessment, diagnosis and monitoring patients over time. One example is DXA vertebral fracture assessment (VFA), which can identify vertebral fractures in the thoracic and lumbar spine. Many osteoporotic vertebral fractures are clinically silent (23, 65), i.e. they do not cause enough pain to arouse suspicion of a fracture or request imaging, and height loss may be attributed to getting older, poor posture or degenerative changes. However these 'silent' vertebral fractures increase the risk of future fracture by an order of magnitude similar to those that were detected (19, 23). The more severe the fracture, the greater the risk (23, 29, 66). As such, an effective efficient tool such as DXA VFA can quickly ascertain the presence and severity of vertebral fractures at much lower radiation levels than plain radiographs, and often is very useful.

Another new application of DXA is the trabecular bone score (TBS), which has been introduced into clinical practice as a method to estimate trabecular microarchitecture based on DXA imaging used to estimate the lumbar spine BMD (67, 68). TBS can predict future fractures independent of BMD and divides an additional tool to improve fracture risk calculation (69-71). A third application beyond simple measurement of BMD is the use of DXA to measure appendicular lean mass as a surrogate parameter for muscle mass, which in combination with muscle function can be used to assess fall risk (72-74). This is important for osteoporosis management because 90% of non-vertebral fractures occur after a fall (27, 72, 75, 76). Decreased muscle mass and function, now often called sarcopenia, and falls are independent risk factors for osteoporotic fractures (77-80).

DXA is not the only imaging tool used to assess bone mineral density, bone microarchitecture and bone strength. Other imaging modalities have been tested and validated including CT and advanced CT imaging, MRI and ultrasound (81, 82). Space limitations do not allow a broad overview on all imaging techniques used to image osteoporosis, so we have focused on DXA technology for several reasons: a) DXA remains the most commonly used technology to assess bone mineral density clinically. b) DXA-measured BMD is used in the WHO T-score definition of osteoporosis and most tools to calculate absolute fracture risk, c) DXA is well validated and reproducible, d) Guidelines and recommendations exist how to perform, standardise, analyse and report DXA BMD results, e) new applications of DXA are emerging, either using new software analyses of images used to calculate BMD (like TBS, hip angle/axis analysis or 3D-DXA (83, 84)) or imaging other tissues or regions (like VFA, body composition, aortic calcification assessment or screening for atypical femur fractures). An entire issue was recently published for the 30th anniversary of DXA (42). We refer the interested reader to the detailed articles on many of the topics just listed.

This review will address the scientific background on the following topics: 1) the importance of performing high quality DXA measurements and reports, using standardised quality assurance tools, performing standardised analyses, and certifying DXA technologists and readers, 2) vertebral fracture detection through DXA VFA, 3) improving fracture risk prediction through the TBS, 4) using DXA body composition to measure lean mass as a surrogate for muscle mass, 5) calculating absolute fracture risk by integrating various risk factors using validated tools.

### The importance of DXA quality

The importance of obtaining a quality BMD measurement cannot be overemphasised (43, 46, 85). Quality DXA is essential for any quality osteoporosis

service, not optional, and dedicated time needs to go into training and educating the personnel performing and interpreting the results (46, 85, 86). In order to be valid, a measure must be accurate and reliable (46). Manufacturers provide some hands-on service training for those using their equipment, many manuals, articles and books have been published, and online tools are available for practitioners. A working knowledge of who should be studied in a scan, how the scan should be performed, and proper interpretation of the results, is essential for people managing patients with or at risk for osteoporosis.

A basic guide to quality densitometry is available without cost through the ISCD website and journal, and a summary of the minimum requirements for providing a quality densitometry service was published recently (45). Seven recommendations are included for scan acquisition and seven for interpretation. Some emphasise the need for formal training and certification, at least by a national, but ideally an internationally recognised accredited body (45). A basic 12 hour course is available through a global collaboration between The International Society for Clinical Densitometry (ISCD) and The International Osteoporosis Foundation, details of which can be found on a joint course website (www.osteoporosisessentials. org). Advanced DXA courses are also conducted by the ISCD on body composition, vertebral fractures and pediatric densitometry.

Medical errors are an inevitable part of practice, and may be one of the leading causes of death (87), and studies show DXA errors are not uncommon (85, 86, 88). A previous study shows 1 in 4 clinicians and 1 in 3 technologists reported poor quality DXA results in major harm to patients, while a further 73% and 50% respectively reported moderate or occasional harm (85). Much greater support and recognition is required by governing bodies and payers emphasising not only the essential role, but also the critical importance of quality DXA. Training and education in quality densitometry will reduce the frequency and magnitude of occurrence (85, 86, 89). However no amount of adjustment can overcome

poor scan acquisition, and conversely a poor report of a high quality scan does little for the patient or the service. Many practitioners do excellent work in producing accurate and reliable results every day. Support for the training, certification and accreditation of those involved in the performance or management of DXA services must be seen as essential, established and maintained.

## Vertebral fracture assessment (VFA)

The vertebrae are the most common site of fracture, particularly between T5 and L5. Unlike non-spine fractures the majority are not preceded by a fall (18). Recent USA data from a nationally representative sample of men and women shows a similar prevalence across genders, a clear age-related increase rising to almost 20% of those aged >80 years, and the prevalence varies within and between countries (90).

The majority of patients were unaware of the presence of vertebral fractures (91). This finding is consistent with clinical trial data suggesting approximately 2 in 3 are "clinically silent". Importantly, not only are patients unaware, but their doctors are too, as these fractures are commonly not reported (92), likely due to "inattentional blindness" (93). A study of people with spine fractures aged 65 years and older shows they have a much higher mortality than those who had no spine fracture, with survival rates of 50% at 3 years, 30% at 5 years and only 10% at 7 years (21). Such figures are stark, but likely partly explained by co-morbidities including cancer, rheumatoid arthritis and cardiovascular disease. Finally, as noted earlier, the presence of spine fractures may be diagnostic of osteoporosis, and the presence predicts a higher risk of future fracture (6, 28, 29). Thus mechanisms to identify them are of paramount importance for diagnosis and monitoring.

Modern DXA scanners usually are equipped with adaptions to enable the user to record an image of the mid and lower spine to assess for the presence of spine fractures and other abnormalities at the time of DXA testing, VFA. Official positions on who should have, how to perform and how to interpret such images is provided by the ISCD and many



**Fig. 3.** CT scan of 2 patients showing osteoporosis (yellow arrows) and spine fracture (red arrow) (Fig. 3a) and of a foot (Fig. 3b) in patient who first presented with bilateral tibial fractures secondary to arthritis (No fall, no treatment prior to presentation) showing osteoporosis (yellow arrows) and multiple erosions (blue arrows).

publications (94, 95). These studies are particularly helpful for augmenting the diagnosis where the BMD measurement does not cross a diagnostic threshold for osteoporosis or low BMD, and to monitor people receiving therapy for incident fractures and treatment failure (95). VFA studies may be particularly useful in people with rheumatic diseases, particularly in rheumatoid arthritis and ankylosing spondylitis, in whom the presence of vertebral fractures and osteoporosis is surprisingly high (96, 97). Special consideration should be given to perform such scans amongst those with more severe, active or prolonged disease, and those with a history of prolonged high dose glucocorticoid use (96, 97). In practical terms, these data may be very informative in arthritis patients in whom the presence of severe arthritic changes or prior surgery may preclude the accuracy of BMD measurement. VFA scans may show other

abnormalities, such as the presence of aortic calcification. The degree of calcification may be quantified to provide an important marker of prevalent cardiovascular disease (98), which predicts future cardiovascular events (99, 100).

### Trabecular bone score (TBS)

Bone strength is determined not only by bone mineral density, a marker of bone composition, particularly the degree of mineralisation, but also by other factors such as bone cell function (e.g. osteocytes, osteoblasts and osteoclasts), accumulation of microdamage and its repair, bone geometry (for example the diameter of the bone or the hip axis length) and bone microarchitecture (e.g. cortical thickness or trabecular volume) (101). The spatial resolution and 2-dimensional nature of DXA imaging does not allow direct measurement of microarchitectural parameters such as trabecular volume. However, statistical modelling (grey-level textural metrics) from routine anteroposterior DXA BMD images of the lumbar spine the Trabecular Bone Score has been proposed to provide a surrogate marker for vertebral body microarchitecture.

Conceptually, this approach examines differences in grey levels within the vertebral body. Large differences of grey levels in adjacent areas suggest decreased trabecular density, decreased trabecular volume, more "rod-like" rather than "plate-like" trabecular shape and decreased trabecular connectivity. In lay words, TBS using DXA imaging "might not be able to detect each individual tree but can find the clearings within a forest". The "more clearings and less areas of thick woods", the larger and more frequent the differences in grey level and the poorer the microarchitecture. Examples of a normal TBS and a very low TBS are shown in Figures 4a and 4b. Several studies have documented that TBS is correlated significantly with high resolution imaging of the trabecular microarchitecture such as quantitative CT (67, 68, 102-104). Since its introduction, several groups

have examined the capacity of TBS to predict future fracture risk and proven that it is an independent factor (67, 69, 71, 105-107). As with BMD, ongoing



**Fig. 4.** Images of a normal TBS (**a**) and very low TBS (**b**). The male in image a) had a DXA bone assessment because of a possible endocrine disorder but had normal BMD for his age (Z-scores around 0.0). The male in image b) is multi-morbid with renal, cardiac and rheumatologic diseases and has severe secondary osteoporosis (lowest Z-score -3.5). The individual in image a) has TBS of 1.551, well above the cut-off of 1.31 for normal trabecular microarchitecture. The individual in image b) has a TBS of 0.734, well below the cut-off of 1.23 for degraded microarchitecture. Similar to the term "osteopenia" the term "partially degraded microarchitecture exist for TBS between 1.31 and 1.23.

debate is seen concerning whether serial monitoring of TBS is of value in everyday clinical care. The effects of osteoporosis therapy (both anti-resorptive and osteoanabolic) on TBS are less robust than the evidence concerning prediction of fracture risk. Although TBS does increase with therapy, the degree of the increase appears to be smaller than that of BMD; furthermore, it is not clear whether this increase (or a lack thereof) results in changes in future fracture risk. While the authors feel that monitoring of DXA BMD is clinically useful if performed correctly and in the right patient and recommend its use, a recommendation cannot be made for TBS until more data are available, other than in selected patients as discussed below. In 2015 The ISCD recommended against routine TBS monitoring based on the limited available published data at the time (57). However as more data emerge, this position may change; it will be reviewed in full at the Official International Position Development Conference in 2019.

From a rheumatologic standpoint, data are emerging that indicate that TBS in patients treated with glucocorticoids and/or with rheumatic diseases can provide additional, incremental information concerning bone health beyond BMD. These studies found consistent evidence that TBS was lower in patients with glucocorticoid exposure than in patients not exposed to glucocorticoids. Rheumatoid arthritis also independently decreased TBS. Interestingly, several studies observed that lumbar spine BMD did not differ to control groups whereas TBS was lower. This observation suggests TBS might be particularly useful in these patient groups because it potentially identifies individuals at higher fracture risk better than BMD alone (56, 108-114). Saag and colleagues reported that TBS improved under teriparatide therapy but not under alendronate in patients with GIOP (115).

In summary, TBS is an easily-applied software tool that provides information concerning vertebral trabecular microarchitecture using traditional lumbar spine DXA images to determine BMD. Published data indicate TBS to be independent risk factor for fracture risk that might be particularly helpful in GIOP and patients with rheumatic diseases. However, how to best apply the information TBS provides to clinical decision making still needs to be established. TBS can be used in fracture risk calculators and algorisms such as FRAX, but places only a modest number individuals across a treatment threshold (either increasing absolute fracture risk enough that treatment is recommended or decreasing it that treatment might not be necessary) (70).

# Lean mass assessment using DXA body composition imaging

Sarcopenia, defined as the age-related loss of muscle mass and function, has gained growing attention in recent years because it has been identified as an important risk factor for decreased mobility, loss of ADLs, frailty increased risk for hospitalisation, and death (83, 84, 116-121). Some experts separate primary (i.e. age-related) from secondary sarcopenia, similar to other diseases such as osteoporosis or hypertension (73, 74). One form of secondary sarcopenia is inflammation-related and several studies suggest that sarcopenia affects patients with rheumatic diseases (122-126). Apart from the systemic inflammation leading to loss of muscle mass and function, medications (such as glucocorticoids) and certain rheumatic diseases themselves (in the form of myositis) can directly affect muscle.

Several consensus definitions for sarcopenia exist. Although they differ in the criteria and cut-points, all include a measure of muscle mass and function (73, 74, 127-130). Various tools can measure muscle mass, each having advantages and limitations (82, 131, 132). All consensus definitions use DXA appendicular lean mass (ALM) rather than whole body lean mass for sarcopenia assessment and either correct for height (kg/m<sup>2</sup>, similar to BMI) or body size (using BMI – ALM/BMI). Some definitions have also corrected for fat mass (130, 133).

DXA technology can separate bone tissue from fat tissue and lean mass through its dual energy approach. The low radiation exposure, good precision, fast scan time, wide availability and low cost has resulted in widespread adoption of DXA technology for this purpose. The ISCD has published comprehensive guidelines on when and how to appropriately perform and report DXA body composition including lean mass assessment (134). DXAmeasured lean mass provides a good estimate of true muscle mass and is correlated significantly with other methods such as whole body MRI. This measure is influenced by several factors, particularly hydration status and oedema, as DXA cannot differentiate between

intracellular and extra-cellular water. In situations in which the ratio of intracellular (representing the muscle tissue) and extracellular water is altered (as in the setting of dehydration or soft tissue oedema) DXA will over or underestimate muscle mass (135-137).

Muscle mass imaging alone is not sufficient to assess muscle health, and functional testing is required. These include common metrics as usual gait speed, grip strength and chair-rise time. Both mass and function are needed to assess the "quality" of the muscle, and to diagnose sarcopenia.

Some health outcomes such as hospitalisation are predicted more significantly by muscle function tests than by muscle mass (138-140). Active research is ongoing concerning which muscle parameters best predict specific outcomes, and how they should be defined, examined and validated. Although the management of sarcopenia is not the topic of this review, and currently no medication is approved for treatment, exercise and nutritional interventions can be used (141-144).

In summary, the additional information provided by DXA body composition analysis to a BMD measurement and VFA assessment can provide helpful information on muscle tissue when combined with muscle function tests. This knowledge may be of clinical importance, as sarcopenia increases the risk for negative health outcomes, and can be addressed with simple interventions such as exercise and nutrition.

#### A clinical case

A 70-year-old female with rheumatoid arthritis for more than 10 years was seen in clinic to evaluate for osteoporosis because of chronic glucocorticoid use. Her current treatment includes methotrexate, tocilizumab and 5mg of Prednisone. She has ongoing polyarthritis (MCPs, PIPs and ankle joints), and complains of pain in her thoracic and lumbar areas which is exacerbated by standing for longer periods. She has not fallen in the last 12 months.

Physical examination indicates tenderness in the thoracic and lumbar spine, no hyperkyphosis. Grip strength was 22 kg in her left hand and 24kg in her right hand, her total short physical performance (SBBP – combination of usual gait speed, chair-rise time and static balance assessment ) score was 9 (0-12), with normal gait speed but impairment in chair rise and balance. As described in Figure 5 the patient has a low T-score of -2.8 (osteoporotic range), a T8 vertebral fracture on VFA, degraded microarchitecture on TBS and obesity on body composition. Her muscle function assessment and DXA lean mass measurement are reduced but she does not meet the official definition for sarcopenia.

Clinically the patient is obviously at increased fracture risk, but with her multiple risk factors it is hard to "guesstimate" how high her overall fracture risk is. However, using the fracture risk calculation tool FRAX® (https:// www.sheffield.ac.uk/FRAX/), we can combine DXA BMD with her clinical risk factors and calculate her 10-year absolute fracture risk for hip and major osteoporotic fracture (hip, clinical spine, forearm and humerus) as shown in Figure 6 (58, 64). Her 10-year risk for major fractures is now several fold higher than a 50 year old woman with the same BMD and none of the other clinical risk factors.

Discussion of osteoporosis care in terms of absolute fracture risk has many advantages, among them the capacity to compare the absolute fracture risk to other diseases or accidents (for example heart attacks, breast cancer or motor vehicle accidents), to put in relation the fracture risk to potential side effects (which is very relevant for bisphosphonate therapy as the often quoted serious side effects of osteonecrosis of the jaw and atypical femur fractures are exceedingly rare compared to the fracture risk of the patient described here) and to highlight how effective osteoporosis therapy is (it reduces the fracture risk by 30-70% depending on medication and fracture type). Concretely, this patient has a 1 in 2.5 risk of suffering a major osteoporotic fracture (hip, Tspine, L-spine, humerus, wrist) and a 1 in 5 risk of experiencing a hip fracture in the next 10 years, perhaps even higher. On the other hand the patient's risk of developing osteonecrosis of the jaw is <1:10000, the risk of an atypi-



**Fig. 5.** DXA Image series of patient described in clinical case showing: (a), VFA (b), TBS (c) and body composition (d). This approximately 70 year old female has osteoporosis with a lowest T-score of -2.8 at the lumbar spine (L1-L2). It is important to note that she has marked degenerative changes in the lumbar spine (L2-L4) falsely elevating her BMD in this region. The L1-L4 region would have a T-score of only -1.9. This is because the L1 vertebral body has a T-score of -3.4 whereas L2 through L4 have T-scores of -2.3, -1.1 and -1.4 respectively. Since the T-score from 1 vertebral body alone cannot be used (according to ISCD guidance) the L1-L2 region should be reported (T-score -2.8). The patient has a T8 vertebral fracture (Grade 2 according to Genant) on her VFA. Her TBS is score of 1.133 is low and it is noteworthy that the score is not impacted by the degenerative changes present as the scores are similar between L1-L4 whereas the BMD T-scores are not, as outlined above. The patient has a BMI of 27 but her total % body fat is 49% putting her above the 90th percentile. Her ALM/height<sup>2</sup> ratio is  $6.20 \text{ kg/m}^2$  which is on the low side of normal (normal above  $5.45 \text{ kg/m}^2$ ). This exemplifies how a slightly elevated BMI can underestimate the degree of obesity because of lower muscle mass.

Country: Germany	Name/ID:	About the risk factors	
Questionnaire:		10. Secondary osteoporosis	ONO ○Yes
1. Age (between 40 and 90 years) or Date of Birth Age: Date of Birth:		11. Alcohol 3 or more units/day	● No ○ Yes
71 Y:	M: D:	12. Femoral neck BMD (g/cm <sup>2</sup> )	
2. Sex	Male • Female	GE-Lunar \$ 0.653 T-score: -2.8	
3. Weight (kg)	75	Clear Calculate	)
ł. Height (cm)	166		
5. Previous Fracture	🗌 No 💿 Yes	BMI: 27.2 The ten year probability of fracture (%)	) 😑
5. Parent Fractured Hip	ONO ○Yes	with BMD	
. Current Smoking	ONO ○Yes	Major osteoporotic	40
B. Glucocorticoids	No •Yes	Hip Fracture	20
. Rheumatoid arthritis	No Ves	If you have a TBS value, click here:	Adjust with TBS

- (a)
- (b)

Clinical risk factors	Hip Fracture (%)	Major Osteoporotic (%) 7.2	
Risk at 50 years, T-score -2.8, 166cm, 75kg	2.8		
Risk at 71 years, same height, weight & BMD	5.7	14	
+ Rheumatoid arthritis	8	18	
+ Glucocorticoids	14	28	
+ prior fracture	20	40	
+ TBS	22	42	

**Fig. 6.** An example of the value of using the FRAX<sup>®</sup> calculator (**a**) and how the addition of additional clinical risk factors result in a substantial increase in the absolute risk of both hip and other osteoporotic fractures (**b**).

cal femur fracture <1:2000 (145-148). Alendronate has been shown to reduce the risk of vertebral fractures by approximately 50% (145, 146). The numbers highlight the favourable benefit/ risk – ratio of osteoporosis therapy in patient at high fracture risk.

Various guidelines are available on how to apply FRAX® and which cutoffs should be used to initiate treatment (145, 149-155). Regardless of which guideline one would choose, this patient would always meet the criteria for treatment. Treatment should also consist of adequate calcium and vitamin D intake, falls prevention strategies, use of walking aids and hip protectors when appropriate, regular physical activity, risk factor reduction (such as smoking cessation) and osteoporosis medication. This patient was begun on treatment with alendronate. It is worth noting that some guidelines such as the 2016 AACE/ACE treatment algorithm recommend initiating treatment with

denosumab, teriparatide or zoledronic acid in patients with high fracture risk such as this patient (145, 146).

#### Conclusion

Today osteoporosis is a global pandemic affecting millions of children, women and men around the world. Some populations are at greater risk, including those with rheumatic disease. Recent advances in imaging and measurement technology, particularly DXA scanning, has changed the field, such that modern imaging includes several excellent tools for identification of fractures, fracture risk prediction, diagnosis and monitoring therapy. Despite these great advances, access to, and the quality of the service provided remain global challenges, even in Europe and North America. Where access does exist, the application of training, standards and best-practice performance for image acquisition and interpretation remains unfulfilled. Bridging the gap between best practice

and best evidence, and the quality of care provided for patients everywhere is our biggest challenge moving forward.

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