Bone Mineral Densitometry: Measurement and Evaluation Methods

12

M. Özdeş Emer, Semra İnce, and Nuri Arslan

Abstract

Bone mineral density (BMD) is described as the bone mass in a bone mass unit and is found to be lesser than the normal value in patients who have osteoporosis and development of fracture risk. Although indications for measuring BMD have been increasing day by day, using dual-energy X-ray absorptiometry (DXA) method to determine the risk of fracture is still controversial, and there are different approaches in the guidelines prepared by national and international associations. Quantitative computed tomography, quantitative ultrasound, single-photon absorptiometry, dual-photon absorptiometry, and DXA are the most common methods used for measuring BMD. DXA is considered as the gold standard for BMD measurement with its high-resolution power as well as its high image quality and short acquisition time.

Lumbar spine and proximal femur BMD measurement is accepted as the standard examination protocol. While femoral neck and whole hip BMD measurement is performed for determination of fracture risk, whole hip BMD measurement is recommended for monitoring disease progression and response to therapy. On the other hand, forearm BMD measurement is recommended for patients who cannot have hip and/or spine BMD measurement and also for patients being investigated due to hyperparathyroidism-induced osteoporosis.

The World Health Organization Fracture Risk Assessment Working Group on the BMD criteria defined osteoporosis in young adults with a BMD T score below 2.5 standard deviation value. It is sufficient to perform DXA study once in every 1–2 years to monitor the response to treatment, and it is necessary to take into account at least 5 % of BMD change in order to demonstrate the effectiveness of treatment.

In this section, we will discuss these and other indications for the application of DXA with a brief section on the specifications of the used methods.

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Learning Targets

- Describing osteopenia and osteoporosis
- Classifying osteoporosis considering its etiological reasons
- Identifying the groups of people who are at risk
- Identifying the fractures caused by osteoporosis and mortality and morbidity from these fractures
- Apprehending main treatment options used in osteoporosis treatment
- Defining T and Z scores used in the evaluation of bone mineral density (BMD) measurements, as well as the normal and pathological values of these scores
- Learning main indications and measurement methods for BMD measurement
- Apprehending advantages and disadvantages of methods used in BMD measurement and being able to decide on the most suitable method when it is necessary

Osteoporosis is today's most common metabolic bone disease characterized by decreasing bone mass, deteriorating microarchitecture of bone tissue, and increasing bone fragility [1–4]. Osteoporosis differentiates into two main types, namely, primary and secondary, considering its etiological reasons [1]. While primary osteoporosis is characterized by the loss of bone mass by age, secondary osteoporosis has some diseases and drug use in its etiology [1]. Type 1 (primary) osteoporosis is seen often in postmenopausal women and probably caused by the decrease in estrogen secretion. Vertebral and wrist fractures are the most common in primary osteoporosis. On the other hand, senile or Type 2 (secondary) osteoporosis is associated with an increased level of parathyroid gland function in old people. Femoral, proximal humerus, tibial, and pelvic fractures are more common in Type 2 osteoporosis [1]. Steroid use, Cushing disease, sedentary lifestyle, and nutritional disorders (malabsorption syndromes such as celiac disease) may be listed among the reasons of secondary osteoporosis [1, 5, 6].

Bone mass is the most important element contributing to the bone strength. Bone fracturability (or strength) is directly proportional to the bone structure and its mineral (Ca, P) content. Fracture risk increases considerably as the bone mass decreases. Bone mineral mass indicates the amount of minerals in bones in terms of gram.

The most important health problems arising from osteoporosis are the fractures due to decreased bone strength and consequent mortality and morbidity. Mortality in 6 months following femoral neck fractures is reported as 12–20 %. While 20 % of these cases die in 1 year, 50 % face long-term dysmotility, and 20–25 % need nursing for a long period [1, 6, 7]. Vertebral fractures are typically seen in thoracolumbar intersection (T12–L1) and midthoracic area (T7 and T8), while they are multicentric in 20–30 % of the patients [1]. On the other hand, while vertebral fractures are much more common compared to femoral fractures, fortunately they cause less serious health problems.

Bone mineral density (BMD), which means bone mass in mineral grams per unit of bone volume, accounts for 60–70 % of bone strength, and thus, it is the most important determinant of bone fracturability [2, 5]. T and Z scores are used in the evaluation of BMD measurements. T score identifies the difference between the average BMD score of normal young adult (ages 20–30) population of the same sex and ethnic background as the patient and the BMD score of the scanned patient. Z score stands for the difference between the scanned patient's BMD value and the BMD value of a control group of the same age and sex as the patient [1, 5]. World Health Organization (WHO) criteria for the diagnosis of osteopenia and osteoporosis using T scores by BMD measurement are given in Table 12.1.

Table 12.1 World Health Organization (WHO) criteria for BMD measurement

	T score
Normal[a]	At or over −1,0 SD
Osteopenia (low bone mass)[b]	Ranges between −1.0 and −2.5 SD
Osteoporosis[c]	At or below −2.5 SD
Severe or established osteoporosis	The existence of one or more fractures due to a mild trauma (such as a fall while standing up) in addition to a T score below −2.5 SD

[a]Figure 12.1
[b]Figure 12.2
[c]Figure 12.3

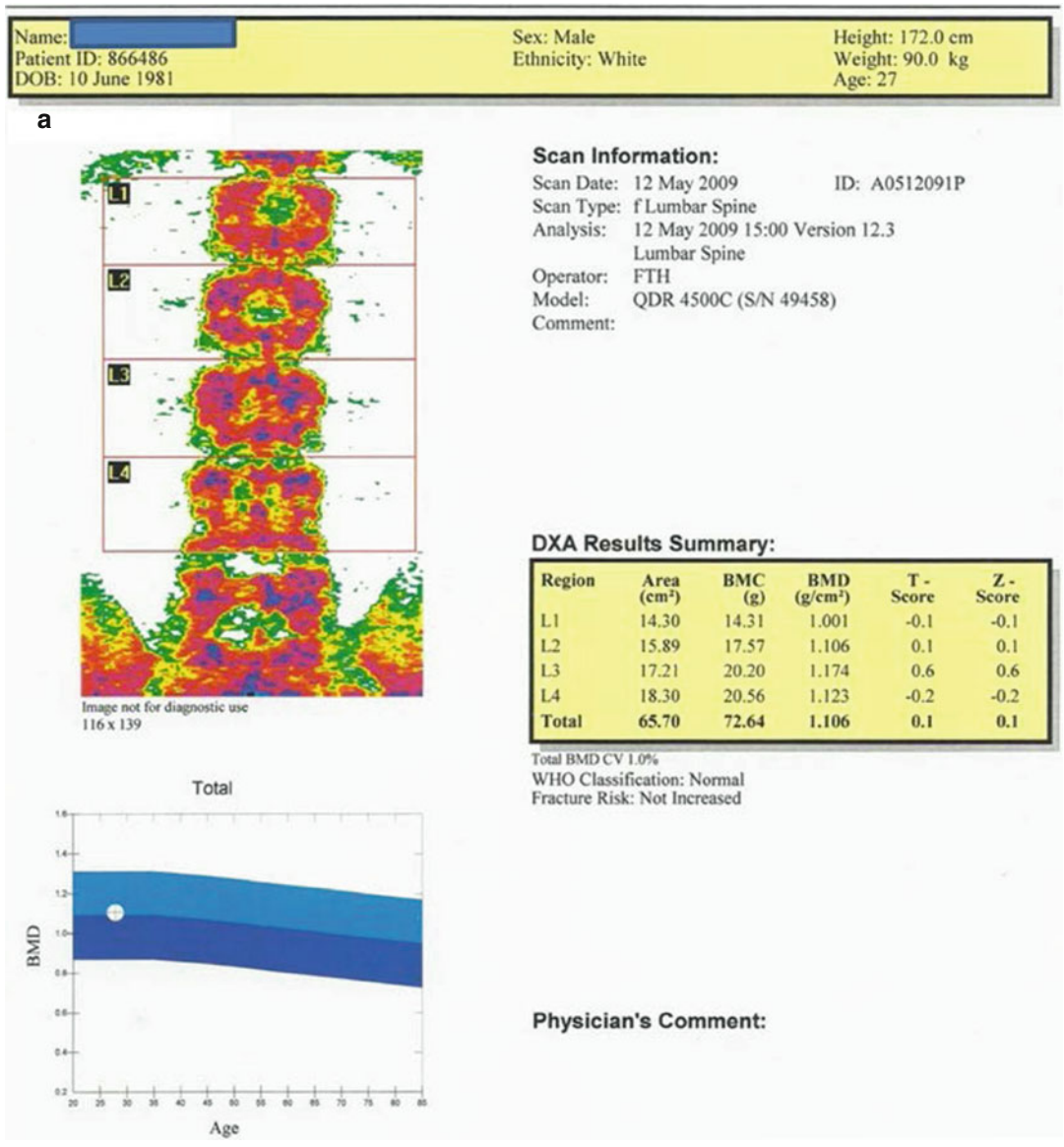


Fig. 12.1 (**a**) 27-year-old male patient suffering from hypogonadism. Average T and Z scores of L1–L4 vertebrae are calculated to be 0.1 and 0.1, respectively. The fracture risk is not increased, and Z score is to be evaluated as "within the expected range for this age" since the case is a male patient below 50 years of age. (**b**) The average T score for proximal femur in the same case is 0.4; Z score is 0.4. Fracture risk is not increased, and Z score is to be described as "within the expected range for this age" since the case is a male patient below 50 years of age

Name: [redacted]
Patient ID: 866486
DOB: 10 June 1981

Sex: Male
Ethnicity: White

Height: 172.0 cm
Weight: 90.0 kg
Age: 27

b

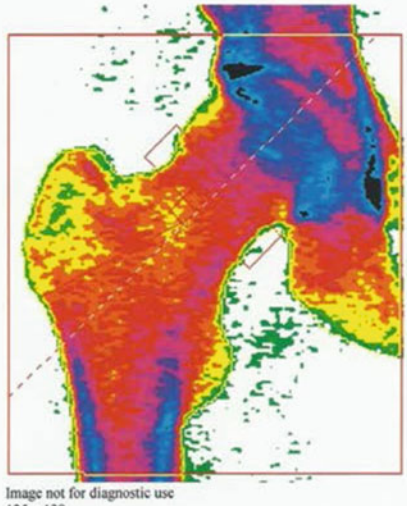


Image not for diagnostic use
125 x 139

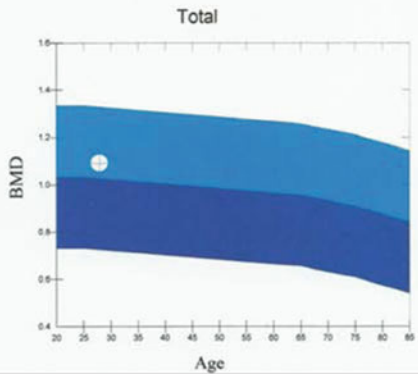
Scan Information:

Scan Date: 12 May 2009 ID: A0512091Q
Scan Type: f Right Hip
Analysis: 12 May 2009 15:01 Version 12.3
Right Hip
Operator: FTH
Model: QDR 4500C (S/N 49458)
Comment:

DXA Results Summary:

Region	Area (cm^2)	BMC (g)	BMD (g/cm^2)	T - Score	Z - Score
Neck	5.85	6.41	1.095	1.2	1.3
Troch	15.23	11.98	0.787	0.1	0.1
Inter	34.18	42.00	1.229	0.2	0.2
Total	**55.26**	**60.39**	**1.093**	**0.4**	**0.4**
Ward's	1.12	1.00	0.895	0.8	0.9

Total BMD CV 1.0%
WHO Classification: Normal
Fracture Risk: Not Increased



Physician's Comment:

Fig. 12.1 (continued)

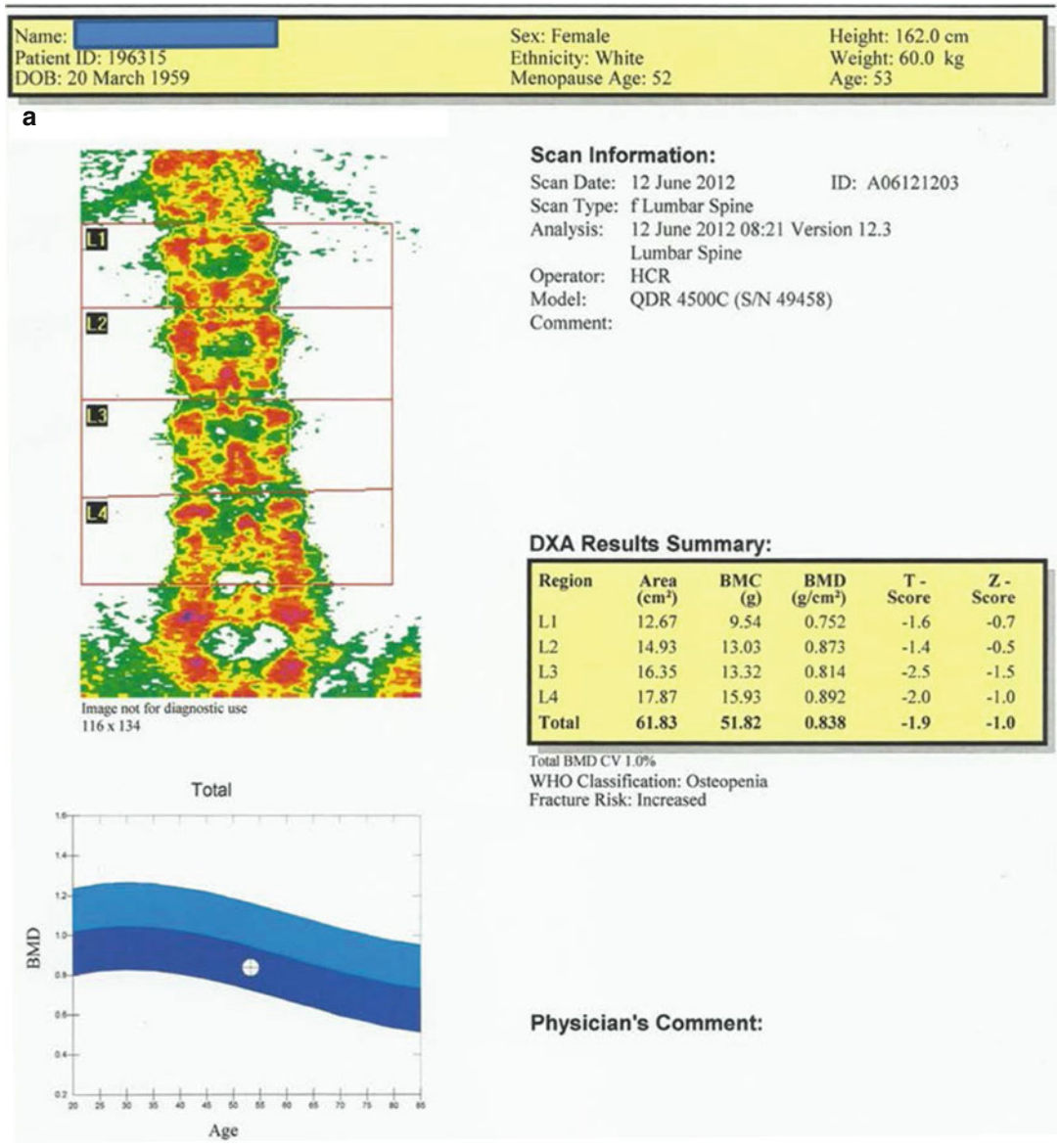


Fig. 12.2 (**a**) 53-year-old female patient. The average T score of L1–L4 vertebrae is −1.9, and Z score is −1.0. The BMD value is consistent with "osteopenia" range by WHO criteria and the fracture risk is increased. (**b**) The average T score for proximal femur in the same case is −1.2; Z score is −0.6. Although BMD value is consistent with "osteopenia" by WHO criteria, the fracture risk is increased

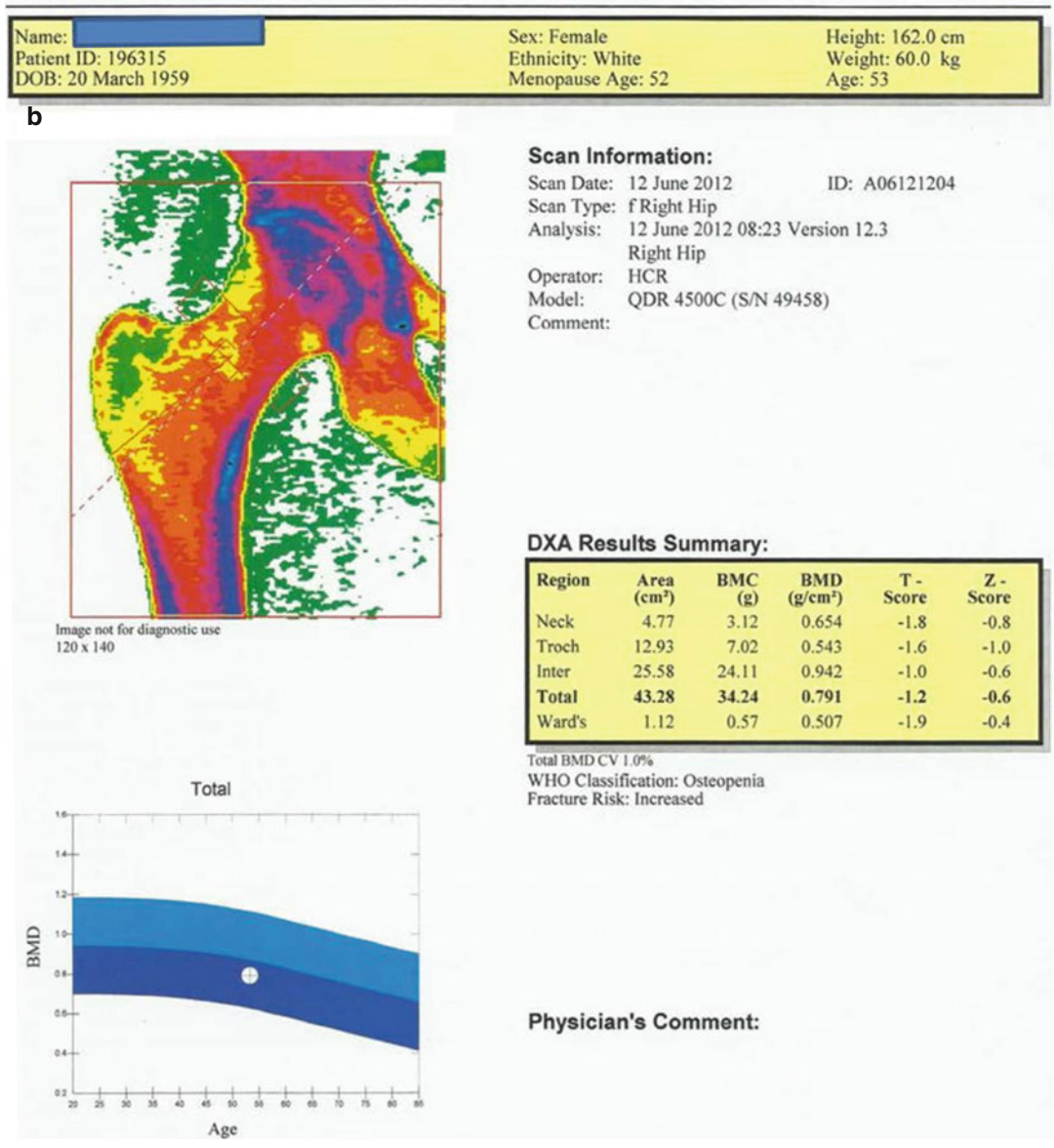


Fig. 12.2 (continued)

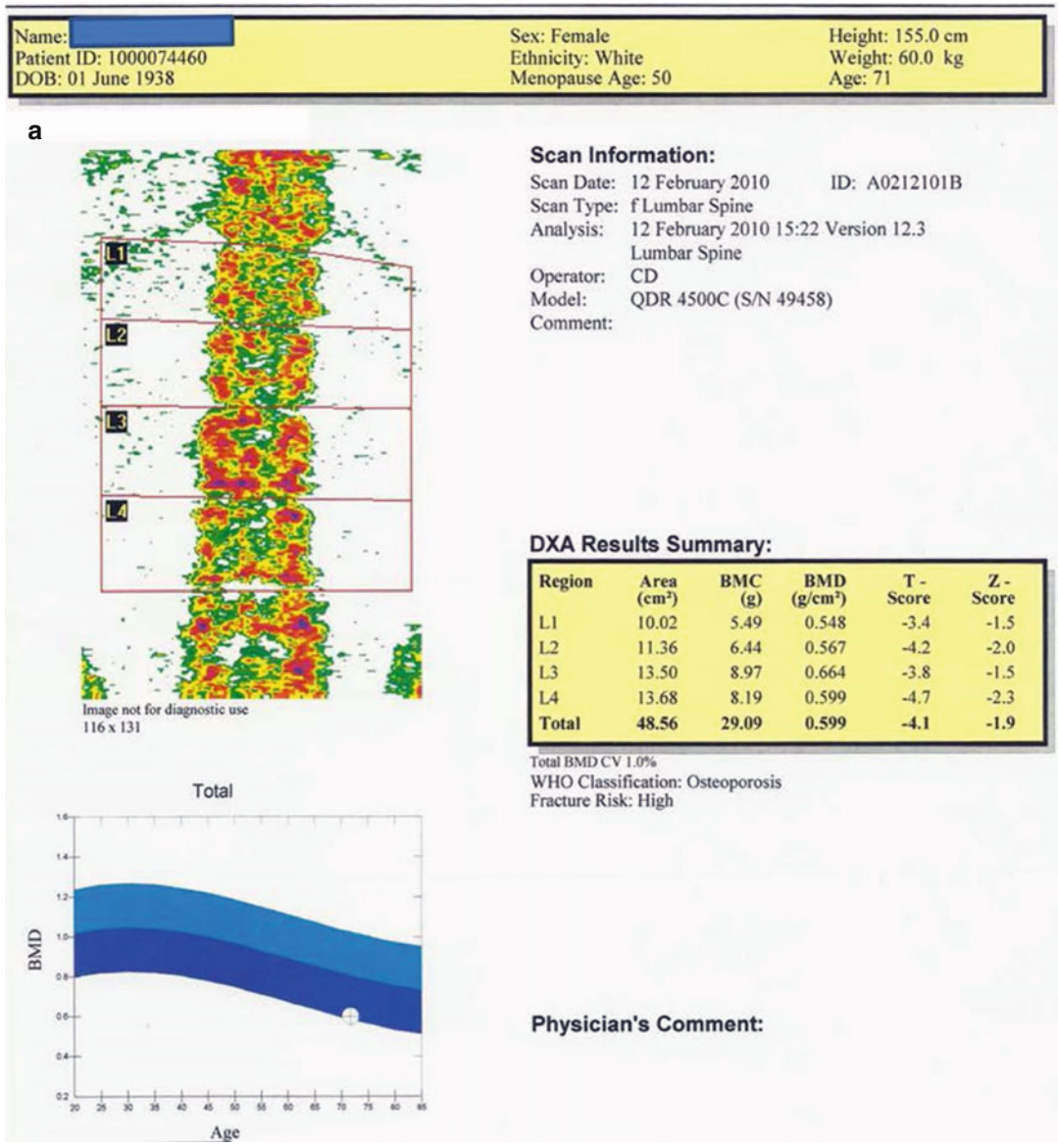


Fig. 12.3 (**a**) 71-year-old female patient. The average T and Z scores of L1–L4 vertebrae are −4.1 and −1.9, respectively. The BMD value of this case is consistent with "osteoporosis" by WHO criteria and the fracture risk is high. (**b**) The average T and Z scores for the proximal femur in the same case are −2.9 and −1.3, respectively. The BMD value is consistent with "osteoporosis" by WHO criteria, and the fracture risk is high

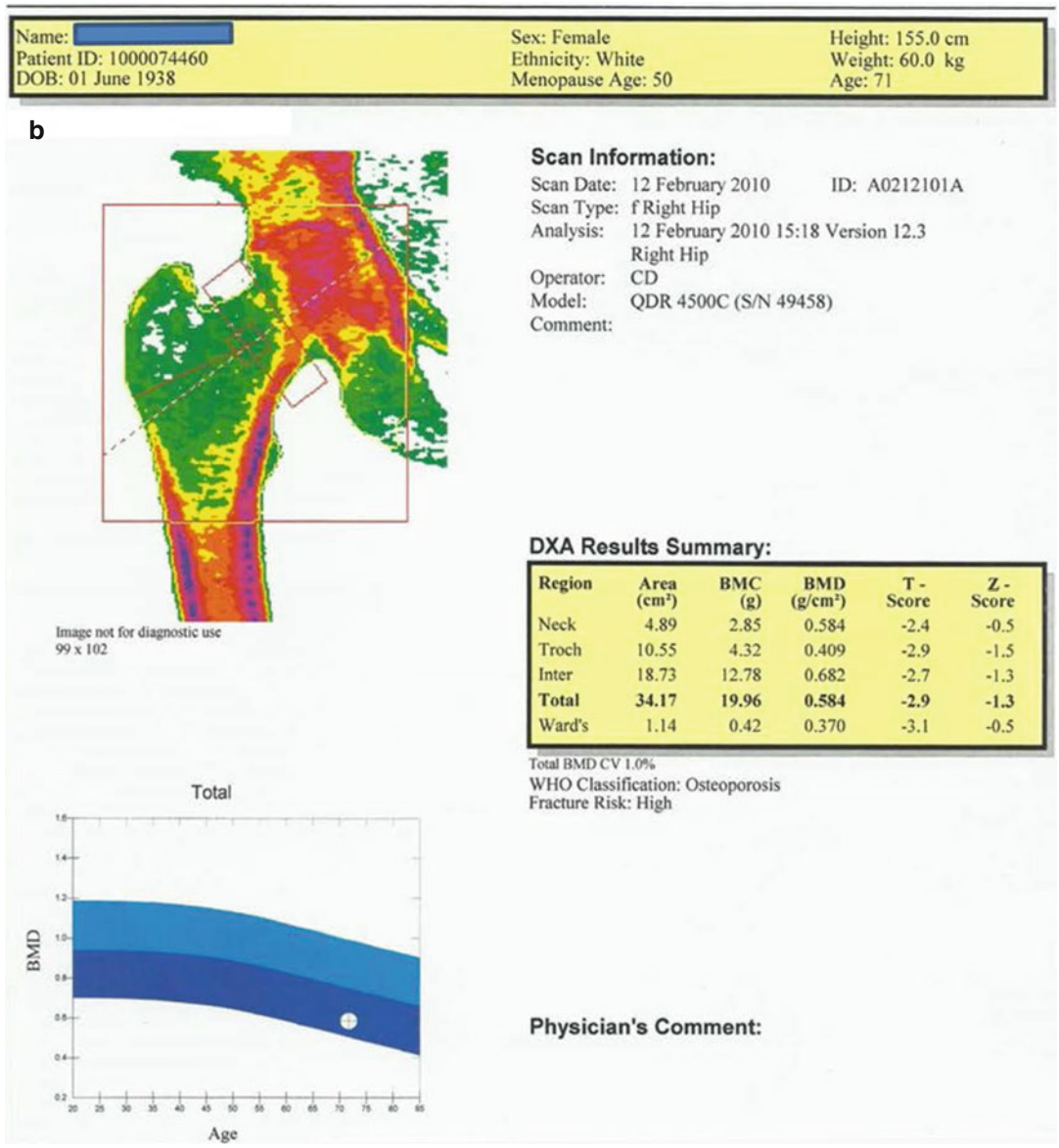


Fig. 12.3 (continued)

T score should be used for the diagnosis of osteoporosis in postmenopausal women and men over 50 years of age.

Z score should be used in premenopausal women, men under 50 years of age, and children.

The International Society for Clinical Densitometry (ISCD) states that:

Z score under −2 SD should be defined as "low bone mineral density below the expected range for chronological age."

Z score over −2 SD should be defined as "bone mineral density within the expected range for chronological age."

Z score is also especially important for the patients aged 75 years and over. ISCD also states that these populations cannot be diagnosed with osteoporosis only by using dual-energy X-ray absorptiometry (DXA) [1, 5, 8].

The proximal femur is not a reliable measurement location in pediatric patient group because of the variations in the development of skeletal system and a low level of repeatability in locating the field of interest. Lumbar vertebras (PA) and whole-body measurement excluding the head are the recommended locations for BMD measurement in children. Z score should be used instead of T score in the reports of pediatric patients. Besides that, the term "osteopenia" and, as long as there is no clinical history of fracture, the term "osteoporosis" should not be used in the pediatric patient group [9].

Patients with either osteoporosis or under the risk of developing fractures constitute the most important patient group for BMD measurement. BMD results must be comparatively evaluated in terms of age and sex for a more precise assessment. The fracture threshold for any individual is defined as 2.5 standard deviation (SD) below the BMD value of a young adult. While the fracture risk is almost nonexisting in an osteopenic patient with a T value of −1.1 SD, it is almost as much as an osteoporotic patient's risk in a person with a T value of −2.4 SD [2]. On the other hand, every unit of decrease in standard deviation increases the risk of femoral fracture 1.5–2 times [1, 5]. In addition to a low BMD value, the existence of femoral fracture or osteoporosis in the family, a low level of bone mass, use of steroids, smoking and alcohol habits, low calcium and vitamin D intake, and environmental factors increasing the risk of falling are defined as the risk factors for fractures [2]. Although the loss of BMD is related to the whole skeleton, it is more explicit in bones with higher trabecular density such as vertebras, femoral neck (Ward's triangle), and distal radius. BMD does not range in the same interval for the whole lifetime. It decreases in parallel with aging after the young adult age period. For example, BMD in the femoral neck decreases about 0.3 % every year in the third to fifth decades of a person's lifetime which means that a person's BMD value may decrease below the osteoporotic level due to age-associated bone loss even with no additional reason [2].

The main target in the treatment of low BMD is to get increase in bone mass to prevent fractures. Calcium and vitamin D should be taken both with diet and from sources external to diet. For the treatment of patients at the age of 80 and over, 1,500 mg calcium and 800 units of vitamin D intake is advised on a daily basis [2]. Bisphosphonates (alendronate, risedronate, ibandronate, and zoledronic acid) are also suggested in order to limit bone resorption and increase bone mass [2].

BMD measurement is advised for all menopausal women at the age of 65 and over and for all men over 70 years old regardless of risk factors, as well as for menopausal women aged below 65 years old with at least one risk factor, for premenopausal women over 40 years old with at least one history of a fracture associated with light trauma, and for all patients on osteoporosis treatment and on long-term steroid use [2]. In young people and in children, BMD should be measured if causes for secondary osteoporosis exist [9]. Main indications for BMD measurement are summarized in Table 12.2 [8, 10–13].

Table 12.2 Main indications in BMD measurement

Women aged 65 and older and men aged 70 and older, regardless of clinical risk factors
Younger postmenopausal women and men aged 50–69 with clinical risk factors listed below for fracture
Existence of osteopenia and/or vertebral pathology in radiology
History of fragility fracture (hip, vertebra, radius, proximal humerus fractures)
Smoking and increased alcohol consumption
History of osteoporotic fracture in family
Existence of significant shortening and thoracic kyphosis
Premature menopause (<45)
Prolonged secondary amenorrhea
Primary hypogonadism
Corticosteroid treatment (>5 mg/day or equivalent for ≥3 months)
Anorexia nervosa and malabsorption
Primary hyperparathyroidism

(continued)

Table 12.2 (continued)

Osteogenesis imperfecta
Hyperthyroidism
Long-term immobility
Cushing syndrome
Neoplasia (multiple myeloma and others)
Follow-up of treatment efficiency in patients being treated for osteoporosis
Cases that are not being treated but with possibility of bone loss that would require treatment
Women and men before 50 years of age with causes of secondary osteoporosis

Table 12.3 Commonly used BMD measurement methods

General classification	Method
Radiological methods:	Standard conventional radiography
	Bone radiometry
	Radiologic photodensitometry
	Digital image processing (DIP)
	Quantitative computed tomography (QCT)
Photon absorption techniques:	Single-photon absorptiometry (SPA)
	Dual-photon absorptiometry (DPA)
	Single-energy X-ray absorptiometry
	Dual X-ray absorptiometry (DXA)
Other methods:	Quantitative ultrasonography (QUS)
	Neuron activation analysis
	Magnetic resonance imaging
	Slit screening flography
	Bone biopsy

BMD Measurement Methods

The method of BMD measurement should be easy, cheap, reproducible, and specific, and it should provide sufficient and accurate information on the risk of fracture in advance. Other qualifications desired in the method are a low dose of radiation and comparability of the test to the standards of race, age, sex, and region in which the test is performed, providing sufficient and fast information for treatment follow-up and compatibility with other diagnostic tests (biochemical tests, biopsy, etc.) used for osteoporosis [14].

We will now examine briefly today's most commonly used BMD measurement methods listed in Table 12.3.

Quantitative Computed Tomography (QCT)

Computed tomography (CT) measures BMD in Hounsfield units as mg/cm^3 using single or dual energy [6]. One of the most important problems in QCT is that bone mineral content can be measured 15–20 % lower than its real value because of the increasing fat content in the bone marrow by age. Use of dual-energy technique provides more accurate results due to the capacity to correct the effect of fat in the bone marrow. Besides, this error associated with fat content is accepted as clinically insignificant since age is used to determine the risk of fracture [6].

It is important to be able to measure the BMD value of trabecular bone separately in patients with osteoporosis, since it is more sensitive in monitoring the changes in the course of disease and evaluation of response to the treatment [1, 5]. The overall sensitivity of QCT as an effective method in the estimation of vertebral fractures and in the measurement of bone loss with the capability of measuring trabecular and cortical bone density separately is higher than the overall sensitivity of DXA. The front part of the trabecular bone in vertebral corpus is used for analysis with QCT. It is also possible to measure trabecular bone selectively by excluding concentrations that can lead to a higher BMD value inaccurately, such as aortic calcification in the field of measurement [1]. Despite all these advantages, QCT is not often used in BMD measurement because of its high cost and higher radiation exposure (1.5–2.9 mSv) compared to other methods [5].

Quantitative Ultrasonography (QUS)

It is a method developed on the basis of physical changes that ultrasonic waves undergo while they pass through bone mass. Bone elasticity and hardness could be demonstrated by QUS. No radiation exposure, low cost, and ease of application are the advantages of QUS. The most important limit of QUS is that it can be used on superficial bones such as the patella, tibia, and calcaneus [15].

Single-Photon Absorptiometry (SPA)

One hundred fifty to 800 millicurie (mCi) I-125 (Iodine-125) source and 27–35 keV collimated X-rays photons are used for SPA. Similar to QUS, SPA is suitable for the measurement of superficially located bones with very few neighboring soft tissue [16]. Radiation dose to skin in SPA varies between 15 and 100 μSv [17]. It is most commonly used for the middle and distal section of radius and calcaneus. The most important disadvantage of this technique is the possibility of false measurement in the existence of prevailing soft tissue. On the other hand, although SPA can measure both cortical and trabecular bone density, the measurement results do not reflect accurately the vertebral and femoral density where the risk of fracture is the highest [16].

Dual-Photon Absorptiometry (DPA)

Gadolinium-153 (Gd-153) having 44 and 100 keV photons with 242 days physical half-life is used as a radioactive source in DPA. The basis of BMD measurement is the fact that the attenuation of each photon in soft tissue and bone is different. For this reason, it should be considered that false low BMD measurements could come up in the cases of laminectomy or lytic bone lesions, and false high BMD measurements could come up in the cases of pressure-related fractures, serious aortic calcification, myelographic contrast material use, and degenerative sclerotic changes [18]. The average dose being exposed in DPA is 12 mR. On the other hand, while both cortical and trabecular bone density can be measured by DPA in the vertebra and proximal femur, DPA of vertebra reflects mainly trabecular bone density.

Dual X-Ray Absorptiometry (DXA)

DXA is today's most commonly used method, and it is accepted as the golden standard in BMD measurement. X-ray tube radiating X-rays of two different energy levels, that is, 70 and 140 keV, is used as the radiation source in DXA. Patients are located between X-ray tube and detector. X-rays, after passing through the collimator system that helps their orientation to the selected field of interest, are absorbed at varying levels because of varying densities of the bone and soft tissue in the field of interest, and they reach to the detector on the patient (Fig. 12.4). Attenuation difference between the bone and soft tissue becomes more evident at low energy level. By entering the bone and soft tissue attenuation values in the system, it is possible to exclude the attenuation of soft tissues in the field of interest and to develop the attenuation profile of the interested bone [1, 5]. Radiation dose being exposed in the DXA technique (50 μSv) is 1/1,000 of conventional vertebral X-ray graphy [19]. High resolution and image quality as well as the short test duration (2–5 min) are the other advantages of this technique [5].

The loss of bone mineral is not the same in different parts of the body. Therefore, although the most suitable skeleton part to be used for measurement is not specified in diagnosing osteoporosis, lumbar spine and proximal femoral measurements are used in DXA as standard protocol [20, 21]. Routine DXA analysis of the femur (Fig. 12.5) gives us information about the BMD value of the femoral neck, trochanter, and Ward's triangle. Ward's triangle is defined as the lowest density area in the midpoint of the bottom edge of the triangle in the femoral neck. Whereas whole hip and femoral neck measurements provide the most valuable information in determining the fracture risk, total hip measurement is used for monitoring the course of disease and for the evaluation of the response to treatment since it provides a broader sampling area [6].

Use of peripheral skeleton areas for the diagnosis of osteoporosis has limited value. Among the peripheral measurements, only distal one third of the radius is valid according to World Health Organization's (WHO) criteria for diagnosing osteoporosis and osteopenia [22]. BMD measurement of the forearm may be preferred in cases where hip and/or vertebral measurements cannot be conducted or where results of the analysis cannot be evaluated. Besides that, forearm BMD measurement can also be performed in patients with acidic cirrhosis, in patients with hyperparathyroidism-associated osteoporosis,

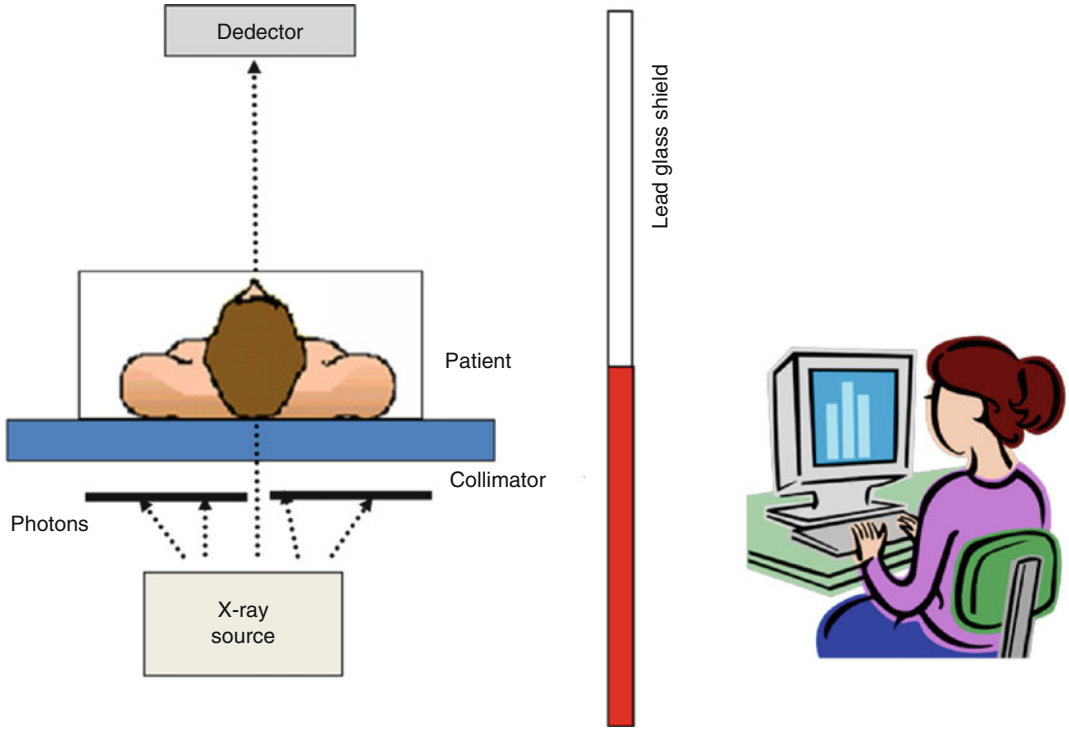


Fig. 12.4 DXA system composed of X-ray source and collimator system with the capacity to choose appropriate photons and detector

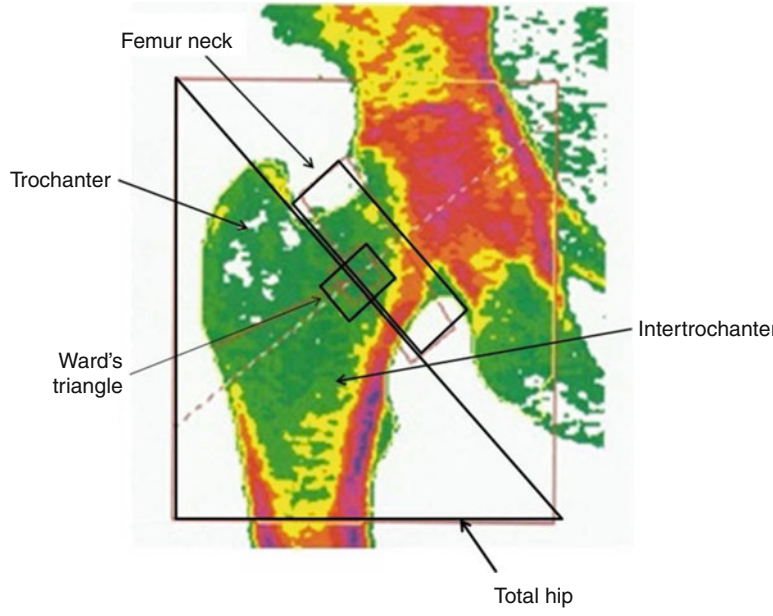


Fig. 12.5 Fields of interest in BMD measurement of the femoral neck

and in patients with extreme obesity who are over the limit of carrying capacity of DXA [22, 23].

BMD measurement should not be based upon the evaluation of only one or two vertebral corpus. The lesser the number of vertebral corpus analyzed, the higher the risk of false measurement. For this reason, the BMD value of lumbar vertebrae should be determined by tak-

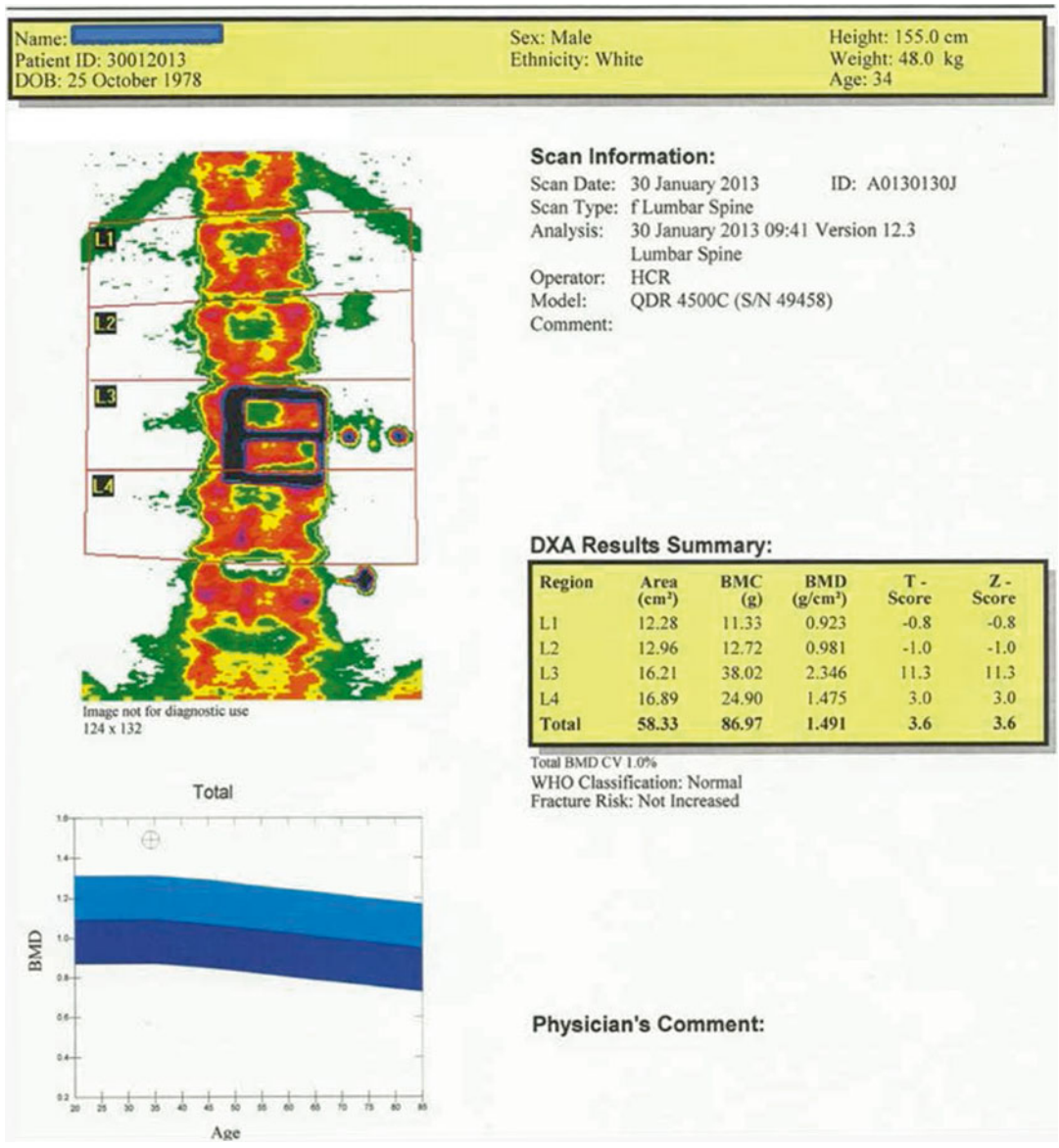


Fig. 12.6 The metal artifact and artificial increase in the BMD due to a belt buckle in a 34-year-old male patient

ing the average of the BMD values of L1–L4 vertebrae [6, 13].

BMD measurement of lumbar spine may score higher than its real value in the existence of morphological changes such as osteophytes overlapping with the vertebrae in the field of interest, severe scoliosis, old fractures and vertebral deformities, aortic calcification, reactive bone changes associated with degenerative facet, and disk, metallic, and radiopaque implants (Fig. 12.6) which may cause underestimation of the fracture risk [6, 14, 24]. Similarly, in obese patients, the excess of superimposed soft tissue would result in a BMD measurement value higher than actual since it would increase the amount of X-rays attenuated [5]. For these reasons, slower imaging speed should be preferred in obese patients or in the existence of very low BMD [6]. On the other hand, pressure fractures limit the vertebra field being measured and thus may cause false high BMD value often [6]. Also the existence of intestinal barium or recent injection of

radiopharmaceutical agent may end up with an incorrect BMD measurement [6].

In cases which scintigraphic scanning or radiopharmaceutical agent injection with the purpose of radionuclide treatment is delivered, BMD measurement should be postponed until ten physical half-life of used radionuclide passes.

It is also possible to evaluate vertebral corpus in lateral position for determining and fixing artifacts formed in anterior and posterior projection by degenerative changes and vascular calcifications. However, in this method, only L3 and L4 vertebrae could be evaluated because of the superimposition of the ribs and iliac crest [6].

One of the most important disadvantages of DXA is that it cannot differentiate between cortical and trabecular bones and it cannot distinguish the changes associated with bone geometry since it is a two-dimensional technique [1].

BMD measurement should be performed on the healthy side in patients with femoral prosthesis and on the forearm in patients with bilateral prosthesis.

While DXA can only measure the density in a defined area (g/cm^2) as it is a two-dimensional measurement, QCT is capable of volumetric measurement (mg/cm^3).

Although BMD measurement by DXA could be conducted every 1–2 years for monitoring the response to treatment, the frequency of measurement should be decided according to the patient's clinical symptoms. Follow-up could be conducted in postmenopausal women and men over 70 years of age once in 1–2 years for the evaluation of treatment efficiency and in longer intervals in clinically stable cases. However, closer follow-up (6-month intervals) is more suitable in patients who have secondary osteoporosis and who are on medications speeding up bone mineral loss such as corticosteroids. On the other hand, follow-up periods should be once in a year and twice in a year in patients who are on bisphosphonate and teriparatide therapy, respectively. The minimum follow-up interval for BMD measurements in children and adolescents should be at least 6 months [13].

DXA alone is not sufficient to determine fracture risk in patients with osteopenia. Therefore, other risk factors are needed to be determined to make a conclusion about fracture risk. The most important recent development about this issue is FRAX (WHO Fracture Assessment Tool). FRAX is an Internet software published by World Health Organization (WHO) which is used to identify the fracture risk in osteopenic cases. The hip is used for BMD measurement in FRAX as the best indicator for the fracture risk. The risk of hip fracture in 10 years and the risk of a major osteoporotic fracture could be calculated according to FRAX by answering the questionnaire. Its disadvantages are that it cannot evaluate risk depending on other body parts other than hips and it cannot be used in previously treated patients. FRAX should be considered in patients for whom DEXA T score is smaller than −2.5 SD and in the existence of fragility fracture [25].

The test's accuracy and its reproducibility are very important in clinicians determining the change and stability in the patient's BMD value. A crucial aspect in BMD measurement by DXA is accuracy [7]. Accuracy tells us about how close are the measurements to the real values. In the evaluation of measurements by DXA, for the difference to be significant, the least significant change (LSC) should be considered. LSC means that the difference between two measurements is significant with a 95 % possibility. In order to be able to talk about treatment efficiency in general, at least 5 % change in BMD is required. Vertebral measurement should be used in the evaluation of response to treatment. Peripheral measurements are not suitable for follow-up and response evaluation [26].

T score is not used in the follow-up; instead, definitely, change in g/cm^2 should be calculated.

In order to calculate LSC, first of all the coefficient of variation (CV) should be determined. CV is the criterion of reproducibility (precision), and it is the expression in percentage of the difference coming up in repeating measurements. For the calculation of CV, BMD measurements are conducted in 30 patients in maximum of 1-month intervals. This group is composed of 30 people and should be compatible with the patient group to be tested in terms of age and weight.

LSC is calculated by the equation below after CV in vivo is determined:

$$\mathrm{LSC}(\%) = \mathrm{Coefficient\ of\ Variation}(\mathrm{in\ vivo}) \times 2.77[7].$$

Higher reproducibility of DXA machine means that the possibility of obtaining the same results in repeating measurements conducted under the same conditions will be high. CVs of the DXA machines should be monitored for a healthy and reliable measurement. If the machine requires daily calibration, calibration steps should be followed precisely by the phantom provided by the producer company. Calibration should be carried out again by the phantom provided by the producer company when the BMD measurement machine is moved to a new location and also in cases of hardware/software updates or when a dramatic change occurs in the environment (temperature, humidity, etc.) [7].

Accuracy and reproducibility depend on several factors. Besides calibration of the scanner, the patient population and the region in which the measurement is made and the talent of the technician in patient positioning and in analyzing the test may affect the test results. Although it seems like a minor detail, it is recommended that the measurements are made in the same season because of small seasonal variations in BMD. Moreover, although both right and left femurs could be used for BMD measurement, the same side body site should be measured for reproducibility [27]. Results of BMD measurements by DXA are correlated with total body fat mass; therefore, it should be considered that the BMD measurements could be influenced by weight gain or weight loss [5, 6].

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