

# BONE MINERAL DENSITOMETRY. THE IMPORTANCE OF BMD IN ENDOCRINOLOGIST PRACTICE

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## REZUMAT

Osteoporoza este o boală endocrină. Indiferent de tipul de osteoporoză, implicarea sistemului endocrin este major. Endocrinologul clinician trebuie să facă parte în mod obligatoriu din echipa de specialiști care se ocupă de bolnavul osteoporotic.

Autorii trec în revistă principalele metode de determinare a densității minerale osoase, element major al diagnosticului osteoporozei.

Sunt prezentate indicațiile BMD, metodele, locurile scheletale unde trebuie făcute măsurătorile, date privind riscurile, performanțele aparatelor, reproductibilitatea măsurătorilor, controlul de calitate, standardizarea. Se prezintă date personale ale determinărilor DXA vs. QUS.

## ABSTRACT

Osteoporosis is an endocrine disease. Endocrine factors have a major impact in all types of osteoporosis. The endocrinologist has to be part of specialists' team taking care of osteoporotic patient.

The authors review the main methods for the assessment of bone mineral density, a key element in the diagnosis of osteoporosis.

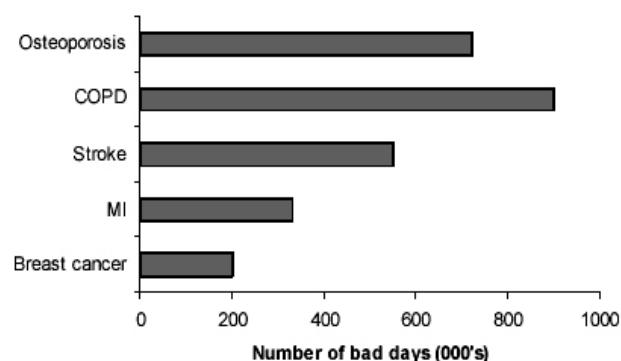
Several aspects are presented: BMD indications, methods, bone sites to be measured, risk prediction, instruments quality, reproductibility, quality control. Personal data concerning DXA vs. QUS comparison are presented.

## INTRODUCTION

Osteoporosis is "a skeletal disorder characterized by a low bone mass and microarchitectural deterioration of bone tissue, with a subsequent increase in bone fragility and susceptibility to fracture" (WHO definition – 1994).

After the age of 50 years one out of eight men and one out of three women of three will develop osteoporosis.<sup>1</sup> Chronic pain, deformities, reduced mobility and disability due to osteoporosis will alter the quality of life. Social costs of osteoporosis are comparable with those of chronic obstructive pulmonary diseases (COPD), myocardial infarction, stroke or breast cancer. When comparing osteoporosis economic costs only COPD are more expensive while myocardial infarct and breast cancer are twice or

respectively three times less expensive. (Fig. 1) Osteoporosis fractures have at least the same prevalence as myocardial infarction, stroke or breast cancer. The lifetime risk of an osteoporotic fracture is 40% for women at the age of 50 years and 13% for men.<sup>2</sup> The risk of a woman dying from a hip fracture is equal to that of dying from breast cancer and four-fold greater than that for endometrial cancer.<sup>3,4</sup> Around 20% of patients die in the year following a hip fracture.<sup>5</sup>



**Figure 1.** The economic costs of osteoporosis (Ref. 2, modified)

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Compared with the normal ageing process, osteoporosis is associated with reduced quality of life and functional impairment. This is unacceptable, since well-established diagnostic techniques and effective therapies for the prevention and treatment of osteoporosis are available.<sup>2</sup>

There are two main subgroups of osteoporosis: primary (postmenopausal – type I and involutional type II) and secondary osteoporosis. Most cases of primary osteoporosis (postmenopausal) and many of those secondary (osteoporosis from endocrine disorders: Cushing disease, hypogonadism, hypopituitarism, diabetes mellitus) “belong” to endocrinology.

The endocrinologist is the first who has to identify and treat a patient with osteoporosis. Moreover, the endocrinologist has the priority in applying hormonal therapy, a major part of osteoporosis treatment.

## OSTEOPOROSIS: DIAGNOSIS STEPS

Osteoporosis diagnosis includes several steps: clinical investigation, bone mineral density measurement, bone turnover evaluation.

The skeleton acquires the maximal bone density - “peak bone mass” – at 25-30 years. Peak bone mass is a strong predictor of later osteoporotic fractures. When we are born, our skeleton contains approximately 25 g of calcium. At the age 30, when our bone mass reaches its peak, our skeleton harbors about 1000 g of calcium. Thereafter at about 30 years, a negative bone balance sets in, so that on average 1% of bone is lost every year, independent of sex. Measurement of trabecular bone density between ages 20 and 80 have shown a reduction of approximately 50% in density. This bone loss is apparently genetically programmed. In postmenopausal women, the decline in estrogen is accompanied by an increased of bone loss of up to 4% annually. This implies that women may lose 40% of their bone mass from age 40 to 70 years. During the same period men lose only about 12%.<sup>6</sup> (Fig. 2)

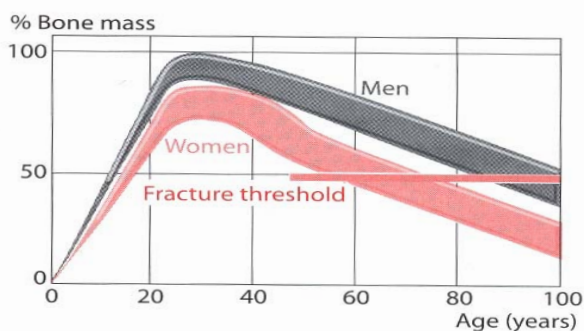


Figure 2. Age-related changes in bone mass<sup>6</sup>

Clinical history and a careful physical examination are essential in diagnosis of osteoporosis. Medical history will include aspects of reproductive function (menarche, quality of menstrual cycles, menopause), previous diseases (renal, GI, endocrine, rheumatic, etc), surgery antecedents (gastrectomy, organ transplants), drugs (glucocorticoids, anticonvulsivants, cytotoxic agents, heparin, etc), lifestyle (smoking, poor nutrition and exercise, alcohol), diet and supplements (frequent dieting, coffee, Ca, vitamins intake, etc). Physical examination will evaluate weight, height, muscular strength, etc.

It is extremely important to detect and evaluate stature modifications and posture. Loss of height, posture and bearing modification, pain on percussion on spinal processes are relevant signs.<sup>6</sup> (Table 1)

Table 1. Medical history and physical examination in osteoporosis (From Ref. 6, modified)

Skeletal history	Fractures, pain, deformity, reduced mobility, height loss
<b>Risk factor assessment</b> <b>Family history</b>	Osteoporosis, fractures, renal stones Age, ethnicity, weight, SGA
<b>Medical history</b> Reproductive Diseases Surgery Drugs	Menarche > age 15 years, oligo/amenorrhoe, menopause Renal, GI, endocrine, rheumatic, neurologic, eating, depression Gastrectomy, organ transplant, intestinal resection or bypass  Glucocorticoids, anticonvulsants, cytotoxic agents, heparin, warfarin, GnRH agonists, lithium, sedatives, hypertensives, diuretics
<b>Lifestyle and exercise</b> <b>Diet and supplements</b>	Smoking, poor nutrition and exercise Frequent dieting, alcohol, calcium, vitamin D, caffeine, protein
<b>Physical examination</b> Weight loss, diarrhea Weight gain, hirsutism Muscle weakness Bone pain Tooth loss Skin pigmentation, stria Nephrolithiasis	Malabsorption, thyrotoxicosis Cushing's syndrome Osteomalacia, Cushing's syndrome Osteomalacia, fracture, malignancy, hyperparathyroidism Hypophosphatasia Mastocytosis, Cushing's syndrome Hypercalciuria, primary hyperparathyroidism

### Bone mineral density (BMD)

The assessment of BMD is the next step in osteoporosis diagnosis. BMD predicts the risk of fracture similar to how blood pressure predicts the risk of stroke or cholesterol predicts the risk of myocardial infarction.

The decision to perform a BMD assessment has to take into account two elements:

- who has or has not an indication for BMD assessment; who has a contraindication to perform BMD measurement; (Table 2)<sup>7</sup>

- what method of measurement has to be chosen.

The final diagnosis step, once BMD is found to be decreased, implies the determination of blood and urinary markers of bone turnover.

**Table 2.** Who has or not an indication for a BMD assessment? (from Ref. 7, modified)

**A. Who should not have a BMD study?**

- Healthy children and adolescents
- Healthy premenopausal women
- Healthy men > 65 years old

**B. Who should have a BMD study?**

- Premenopausal adult women with clinical evidence of hypogestrogenemia: anorexia/bulimia, Athletic amenorrhea, prolactinoma, therapy with GnRH agonist; Depo-Provera
- All women at menopause who do not elect to begin ERT/HRT for non-skeletal reasons
- All women over age 65
- All patients with malabsorption or inflammatory bowel disease
- All patients about to begin chronic (> 3 months) corticosteroid therapy or on chronic corticosteroid therapy
- All men with hypogonadism
- All patients with an unexplained fragility fracture
- All patients with primary hyperparathyroidism
- All patients anticipating organ transplantation

**C. Who might benefit from a BMD study?**

- Patients with recurrent stress fractures, nephrolithiasis or on chronic therapy with: anticonvulsants, Anticoagulants, thyroxine.
- Patients with chronic alcoholism
- All postmenopausal women regardless of their initial decision about ERT/HRT
- All men over age 65

**What method of measurement has to be chose?**

Before the advent of bone densitometry osteoporosis was evaluated by other imagistic techniques. We will not insist over the conventional X-ray imaging of osteoporosis. However it has to be mentioned that skeletal X-rays indicate bone loss only when the density has been reduced by 30%-40%; therefore X-rays are not appropriate for early diagnosis. But they are very useful to reveal previous fractures or compressions. Spinal X-ray is the method of choice for clarification of equivocal results of BMD measurements and for the demonstration of numerous conditions responsible for secondary osteoporosis.

There are also other useful imaging techniques:

-Morphometry (morphometric X-ray absorptiometry, MXA) of the vertebral bodies; “Singh-Index” evaluates the modifications of the proximal femur trabeculae;

-Microradioscopy (radiogrammetry of the metacarpals is a reproducible method of determining the cortical thickness of the bone. This method is inexpensive and readily carried out but does not detect early osteoporosis;

-Bone scan (<sup>99m</sup>Tc bisphosphonates), computed tomography (very good method but high exposure to irradiation), magnetic resonance imaging (MRI).

**Bone mineral density (BMD). Crucial diagnostic parameter**

BMD allows early diagnosis of osteoporosis. Bone densitometry transformed the diagnostic and therapeutic approach of bone metabolism diseases. Several technical progresses were achieved since

Cameron and Sorensen initially described monophotonic absorptiometry in 1963.<sup>8</sup>

BMD is the most objective, reliable and quantifiable parameter for diagnosis of osteoporosis and to monitor therapy. It is useful to clarify some terms. We talk about bone density measurement, but in reality the “real” bone density is never measured (Faulkner – 2001).<sup>9</sup> The precise definition of bone density is the ratio between bone mass and volume unit, excluding bone marrow and other tissues. In bone densitometry the “BMD” is related to bone tissue mass including both bone compound and marrow compartment.

BMD provides the following information:

- detects osteopenia and/or osteoporosis before occurrence of fracture;
- predicts risk for later development of osteoporosis;
- indicates the rate of bone loss – progression – in sequential measurements;
- documents the efficacy or failure of therapy;
- increases compliance of doctor and patient.

The relation between BMD and fracture risk is well established. The association between bone density (measured at hip and lumbar spine) and hip fracture is three time stronger than that between cholesterol levels and heart disease. The main techniques for measuring bone mineral density (BMD) are summarized in Table 3:<sup>6</sup>

- Dual-energy X-ray Absorptiometry (DXA);
- Single-energy X-ray Absorptiometry (SXA);
- Quantitative Computed Tomography (QCT);
- Radiographic Absorptiometry (RA);
- Quantitative Ultrasound (QUS).

**Table 3.** Techniques for measuring bone mineral density (BMD)(Ref. 6, modified)

Method	Precision (%)	Accuracy (%)	Scan time (min)	Radiation dose (mrems)
Dual-energy X-ray Absorptiometry (DXA) Lumbar spin- AP Lumbar spine lateral Proximal radius Distal radius Proximal Femur Total body	1-2	3-5	2-8	1-3
Simple-energy X-ray Absorptiometry (SXA)				
Quantitative Computed Tomography (QCT) Lumbar spine Radius	2-10	5-20	10-15	100-1,000
Radiographic Absorptiometry (RA)				
Quantitative Ultrasound (QUS) Calcaneus Phalanges Patella		2-8	5-10	0

The bone mineral content (BMC) is measured in grams and the bone mineral density (BMD) in  $\text{g}/\text{cm}^2$  (area) or  $\text{g}/\text{cm}^3$  (volumetric). The precision and accuracy of a measurement depend on: type of instrument, regular check and setting of the instrument, cooperation of the patient, exact adjustment of the instrument by the investigator, degree of osteoporosis (the less the bone mass the more inaccurate the measurement). Among the methods we will describe further, DXA is the most used instrument. It is the most completely developed, the “gold standard” of BMD measurement techniques.

## **METHODS**

### **1. Single energy X-ray absorptiometry (SXA)**

Absorption depends on emission energy, the nature and the thickness of traversed tissue.

Single Photon Absorptiometry (SPA) is the oldest method. SPA used a mono-energy gamma fascicle provided from a  $^{125}\text{I}$  or  $^{246}\text{m}$  source. Later on the radioactive source was replaced by a X-ray tube. The fascicle belays the studied segment. A detector connected to the source measures the transmitted energy. The measurement of scanned segment area allows the use of  $\text{g}/\text{cm}^2$  unit. The principle of DXA is identical to that of SPA. In extension it allows the measurement of deeper bones (spine, proximal femur) and the whole skeleton. Initially a  $^{153}\text{Gadolinium}$  source was used. Single energy X-ray absorptiometry is still used today to measure the bones of the ankle because of the paucity of surrounding soft tissue.<sup>10</sup>

### **2. Dual-energy X-ray Absorptiometry (DEXA, DXA, QDR, DPX, DER)**

In 1987 the radioactive source was replaced with an X-ray tube (life time 4-5 years). There are two types of machines using this principle:

1. Simulation of two energy peaks, using a filter with rare grounds (cerium for Lunar, samarium for Norland).

2. Variation of X-ray tension in order to get two continuous specters. On Hologic machines this system is associated with an intern calibration using a calibration wheel containing a known quantity of bone and soft tissue equivalents, placed in energy fascicle trajectory.<sup>8</sup>

DXA is the gold standard of BMD. The skeletal site is exposed to two X-ray beams of different intensity and the mineral content of the bone is calculated by means of computer programs from the amount of radiation. DXA can measure central (hip and spine) and peripheral (forearm sites), and can even perform a total body scan (“full body DXA scanner”).

The lumbar spine and the hip joint are routinely

measured anteroposteriorly or from lateral. The combined evaluation of these two measurements improves the assessment of a patient’s bone mineral status and the fracture prediction. The International Society of Clinical Densitometry (ISCD) suggests measurements of at least two sites if possible and recommends that diagnosis is based on the lowest T-score.

The rachis is measured at L1-L4 or L2-L4 level in AP or lateral incidence. The patient is placed in supine position, calves are elevated, thighs in  $45^\circ$  flexion in order to eliminate lumbar lordosis. The patient will not move. Metallic objects have to be removed. Contra-indications: pregnant women, recent GI interventions (2-3 days), recent bone scintigraphy (24-48 hours). Measurement has to be discussed in case of intervertebral arthrosis, laminectomy and rachis orthopedic material. The thickness of abdominal fat tissue over 25 cm represents a cause of error. On the image it has be checked: rachis rectitude, central position, the presence of iliac bone and the last pair of costal bone. Vertebrae with fractures have to be excluded from analysis. Lateral measurement of lumbar spine is possible only on machines with a powerful energy beam and a rotative arm (Hologic QDR 2000, QDR 4500, Delphi A, Lunar Expert etc). Due to bone superposition (last costal bone over L2, iliac bone over L4) often only L3 can be measured in this incidence. A volumetric BMD can be calculated by combining both AP and lateral measurements.

The proximal femur is scanned with the patient in supine position. The leg is fixed in extension and  $30^\circ$  internal rotation. Ward’s triangle corresponds to a reduced resistance anatomic region delimited by three bone traveae of the principal axes of proximal femur. There is a correlation between the BMD of two femurs and no equality.

BMD can be also measured at the distal forearm level (ulnae or radius bone or both). There are two regions of interest: distal forearm – 75% cortical bone, ultradistal forearm – 65-70% trabecular bone. Fracture region Pouteau-Colles contains 61% (weight) and 71% (volume) trabecular bone (autopsy studies). The position of forearm is extremely important.

Other measurements can be performed: density of whole skeleton, long bones daphysis, (humerus, femur) and hand.

The important advantages of DXA are:<sup>1,6</sup>

- it is not invasive, the patient remains clothed and it is therefore not a burden to the patient.
- It is very quickly carried out (5-10 min)
- It is cost-effective
- It has a very low radiation dose (1-3 mRem)

equivalent to 1/10 – 1/100 of a normal X-ray film)

- It measures those skeletal areas most vulnerable to osteoporosis and to fractures – the lumbar spine and the hips.

- The measurements are accurate and therefore ideal for follow-up and control investigations (accuracy error 1%-10%, precision 1%)

- It is recognized by the WHO as the standard method for definition of diagnosis.<sup>11</sup>

The only real disadvantage of DEXA is that everything in the selected area is included. Sometimes it may be difficult to decide what an ossification is due to (for example aorta, calcified lymph nodes or muscles, spondylophytes, etc). Other X-ray dense substances such as metal-fasteners on clothes, X-ray dense contrast media, or calcium tablets may also be included in the overall measurements. A prior X-ray is sometimes useful.

In order to report BMD results, relative scores depending on sex, age and race are employed. Z-score is the number of SDs below or above mean BMD value for people of the same age (age-and sex matched controls). T-score number of SDs below or above mean BMD value for young (20-30 year old) adults (“peak bone density”).

$Z\text{-score} = (\text{BMD} - \text{AMN}) / \text{SD}$ ;  $T\text{-score} = (\text{BMD} / \text{YN}) / \text{SD}$ . SD (standard deviation) represents the normal variability in a measurement in a population: the difference between the 5<sup>th</sup> and the 95<sup>th</sup> percentile of a group covers about 4 SDs. One SD of the hip or spine BMD corresponds to about 10%-15% of the mean value.

Because BMD decline with the age at all sites, after age 30 the T score are lower than the Z cores, and the differences increase with the age. By definition, diagnosis of osteoporosis is based on a T-score of  $\hat{1} - 2,5$  SD (normal BMD  $> -1$ , osteopenia  $[-1, -2,5]$ ).

**3. Quantitative computed tomography (QCT)** has two particularities: is the only technique that allows the measurement of a true volumetric mineral density in  $\text{g}/\text{cm}^2$ ; cross sectional images provide separate measurements of trabecular and cortical bone. Furthermore CT is used to quantify the trabecular bone architecture.

In clinical studies, QCT has been used for assessment of vertebral fracture risk. The measurements take about 20 min and have a relatively high radiation exposure of about 100-1000 mSv. QCT can be performed in single-energy (SEQCT) or dual-energy (DEQCT). Special, small instruments are used to measure bone density in the fingers and the wrist (pQCT). The values obtained, however, cannot be considered as representative to the skeleton as a whole. The future of computed tomography lies in the field

of direct visualization of trabecular bone architecture by high-resolution and 3 dimensional (volumetric) imaging – 3D-CT. However, this development does entail a greater amount of radiation.

#### **4. Radiographic absorptiometry (RA)**

This is an established technique to measure BMD by a computerized analysis of a hand X-ray. Advantages: quickly to carry out, not expensive.

Two postero-anterior radiographs of the hand are taken, one at 50kVp and the other at 60 kVp using nonscreen film. The film is sent to a central laboratory where they are digitized by a high-resolution imaging system.

BMD is calculated in arbitrary units using the aluminum reference wedge as a calibration material.

RA measures both trabecular and cortical bone.

RA has a high precision and accuracy

The radiation exposure of about 100 mRems is lower than that of QCT but higher than that of DEXA.

RA has a high sensitivity in predicting low bone mass of lumbar spine and femoral neck (90% and 82% respectively).

RA plays an important role in pediatric osteology as radiographs of the hand are taken routinely in pediatric individuals for the purpose of determining skeletal age.

#### **5. Quantitative ultrasound (QUS)**

The use of ultrasound techniques in BMD determination started in 1984. Two major parameters are used in measuring bone by QUS: speed of sound through bone (transit velocity, SOS); attenuation of sound as it passes through bone (broad-band ultrasound attenuation, BUA dB/MHz). These measurements are possible for easily accessible bones (calcaneus, radius, tibia and phalanges). Some instruments combine SOS and BUA to formulate a clinical index (quantitative ultrasound index, QUI). Calcaneus QUS is a predictor for hip fracture risk, independent of femoral BMD. Thus QUS proved its ability to discriminate between normal and osteoporotic subjects. For every SD decrease in BUA of the calcaneus, the risk of hip fracture increases twofold, comparable with the results of DEXA. QUS is used as a screening method though it cannot yet replace DEXA measurements of the spine and hips. Normal values for the fingers using QUS do not rule out the possibility of a severe osteoporosis of the spine or hips.<sup>12</sup> Conversely if the phalanges show osteoporotic values then this should be regarded as a manifestation of generalized osteoporosis and DEXA should be carried out for the clarification and WHO classification. QUS is not recommended for monitoring of treatment.

### Which bones to measure?

Measuring BMD at the hip and/or lumbar spine is the best way of predicting fractures. Identical sites must be measured to monitor therapy and/or progression of disease.

A fundamental rule states that “the result of a bone density measurement applies only to the particular site measured”. Osteoporosis does not affect all the bones of the skeleton to the same degree. Bones with a high proportion of trabecular bone, such as vertebrae and hip bones, are the first victims of the destructive process. The more sites measured, the higher the likelihood that a diagnosis of osteoporosis will be made. In the elderly female population, measuring only the hip to make a diagnosis of osteoporosis will detect slightly less than 50% of the affected people, whereas measuring multiple skeletal sites in this population will detect nearly 80% of the affected people. Aspects regarding the principal areas for DXA measurements have been previously described.<sup>6,7,13</sup> When the bone density is checked for monitoring therapy or progression of disease, it is crucial to measure the same areas, with the same machine at one-year interval. Annual BMD measurements increase the patient’s compliance. Other intervals can be chosen. Clinical trials have documented significant increases in bone density under therapy with bisphosphonates after 3 months in the vertebrae and after 1 year in the hips. Biannual measurements should be carried out in the high-risk patients, for the example, those on corticoid therapy or patients with rapid bone loss (as indicated by biochemical markers).

### BMD assessment indications

Two crucial facts determine the indications for BMD measurement:

- Its ability to accurately determine fracture risk;
- The availability of therapies that increase BMD.

With the introduction of quantitative techniques of bone densitometry, the diagnosis of osteoporosis can now be established in the early asymptomatic phase of the disease.

The indications for BMD measurement have been already mentioned.<sup>7</sup>

### Bone densitometry in children

Reduced dimensions of bones and soft tissue thickness determine technical difficulties of BMD measurement in children. It is recommended to use special software for children under 12 years. There are standard values curves that show that bone mass acquisition ends by 17 years in boys and 16 years in girls (11).

In pediatrics four current techniques are currently employed:

- the most widely used: DXA
- the most versatile: QCT
- the newest: QUS
- under investigation: MRI

The preferred sites for scanning include the lumbar spine, the hip and the whole body but also peripheral sites such as the forearm and the hand.

### Bone densitometry in men

WHO criteria for osteoporosis are not totally applicable in men. Over the age of 65 years a T-score  $\leq -2.5$  sustains the diagnosis of osteoporosis. Between 50 and 65 years, a T-score inferior to  $-2.5$  in association with risk factors sustains the diagnosis of osteoporosis. Independently of age, men with secondary causes of bone mass loss (corticoids, hypogonadism, hyperparathyroidism etc) can be diagnosed with osteoporosis when BMD is decreased. The diagnosis of osteoporosis in men under 50 years cannot lie only on densitometry criteria (11).

### The risks of BMD assessment

Bone density tests (DXA) present no danger for the technician and for the patient. The “natural” exposure to radiation is about 2-8 microSv, 100 microSv during a transatlantic flight, and 10 microSv for a DXA. (Table 4)<sup>1,14</sup> DXA irradiation is so low that the technician can stay in the room during the scan.

**Table 4.** Effective radiation dose (Ref. 1, 14 modified)

Radiation source	Effective dose ( $\mu$ Sv)
SXA	1
DXA	1-10
QCT	60
Lateral spine film	700
Natural background (per day)	2-8
8-10 Hour airplane flight	60-100

### Instruments capabilities. Precision. Reproducibility.

**The precision** of a measurement is the error we get while estimating the real value. The precision can be calculated by regression between measured value and the real one or by using SD of the two values difference.

Precision error has to be interpreted in relation with the biologic variation to measure.

Precise bone densitometry measurements are acquired by comparing the results with ashes weight from cadavers. There is a strong correlation between ashes weight and the vertebrae mineral content measured by DXA. A less accurate approach is noticed in current practice: the measurement of anthropomorphic phantom or step-by-step stairs phantom.

**The reproducibility** is the error achieved on the same sample when repeating the measurement. Reproducibility is quantified by using intra-class correlation coefficient, reported in literature as the coefficient of variation (CV). To calculate the reproducibility of a instrument, 3-4 measurements has to be performed with repositioning, in at least 15 subjects. SD and then CV are calculated:

$$CV=100*SD/x \text{ (x-mean results value).}$$

Reproducibility on long term is difficult to evaluate because of permanent variation of bone density. The difference between two measurements of the same subjects is analyzed using the reproducibility of the measure. Thus the variation is significant (95% confidence interval) if superior to **2"2CV – "least significant change"**. For example if reproducibility is 1%, the difference is significant when  $\hat{a}$  2.8%. When reproducibility is 3% (ex. aged subjects) the difference has be > 8.3% to reach the significance level. This element allowed estimating the optimal period before repeating a BMD measure in one subject. This entire math seems to be difficult to understand and arid but it is very important for the clinician. Fortunately modern machines display these elements automatically.

### Quality control

It is mandatory for DXA specialist to daily calibrate and verify the functionality of the instrument. In practice it is recommended to perform quality control following manufactory's instructions. On Lunar machines calibration is performed using a block containing bone equivalents. On Hologic machines an anthropomorphic phantom is daily measured. Norland and Sophos have their own quality control.

### Results standardization

When measurements are performed on the same model of the same manufacturer, variations are minimal and they depend only of subject positioning and not of calibration. Results acquired with instruments from different manufacturers are different. Between Lunar and Hologic the differences are about 16% for rachis and 10-17% for proximal femur (in vivo). In vitro these differences are: 17.4% for BMD, 8.4% for BMC and 9.8% for bone surface. Differences are caused by different calibration, different soft tissue correction, etc. The highest values are displayed on Lunar, the smallest on Hologic and intermediary with Norland. Cross calibration equations have been proposed. Furthermore there are formulas to standardize lumbar mineral density (SBMD):

$$SBMD=1.0755 \text{ Hologic} = 0.9522 \text{ Lunar} = 1.0761 \text{ Norland (units – mg/cm}^2\text{)}$$

Using these equivalences the difference between

Lunar and Hologic is 2.2%, Lunar vs. Norland – 2.8%, Hologic vs. Norland – 2.7%.<sup>8</sup> These differences are important in multicentric studies.

### DXA vs. QUS densitometry

As it was mentioned before BMD assessment by DXA is considered the gold standard in osteoporosis diagnosis and treatment follow-up. QUS techniques are recommended as screening tests.

In order to confirm literature data, we performed a clinical study where risk fracture predictive values of DXA and QUS were compared. 150 women (mean age 51.6 years old) were assessed for their bone mass density (BMD) by both methods – QUS and DXA. 109 women were in postmenopausal period (mean age for the last menstruation 44.7 years) and 41 were in their perimenopausal years. WHO definition was used to define osteoporosis, osteopenia and normal status of bone mineralization.

Results of DXA and QUS are presented in Tables 5 and 6.

**Tables 5, 6.** DXA vs. QUS BMD assessment

T-QUS intervals	T-QUS	T-DEXA	Paired T test
<b>-1</b> (n=26)	<b>-0.27 ± 0.64</b>	<b>-1.09 ± 1.12</b>	<b>p &lt; 0.001, S</b>
<b>-1 -- -2.5</b> (n=59)	<b>-1.6 ± 0.41</b>	<b>-2.1 ± 1.1</b>	<b>p = 0.088, NS</b>
<b>&lt; -2.5</b> (n=15)	<b>-2.9 ± 0.23</b>	<b>-2.64 ± 1.2</b>	<b>p = 0.39, NS</b>

T Score DXA \ QUS T Score	> -1 <b>Normal</b> (n=36)	(-2.5; -1] <b>Osteopenia</b> (n=71)	≤ -2.5 <b>Osteoporosis</b> (n=43)
> -1 <b>Low Risk</b>	<b>61.5%</b>	<b>26.7%</b>	<b>13.95%</b>
(-2.5; -1] <b>Moderate Risk</b>	<b>33%</b>	<b>43.12%</b>	<b>65%</b>
≤ -2.5 <b>High Risk</b>	<b>5.5%</b>	<b>30.18%</b>	<b>20.9%</b>

↓                      ↓                      ↓  
 100%                  100%                  100%

The conclusions of our study confirm literature data:

1. When compared with DXA (lumbar spine) method for the BMD assessment and prediction of

the risk for osteoporosis, QUS (heel) examination displayed 14.3% false negative and 14.7% false positive results.

2. As screening method QUS BMD measurement preserves its value. In order to start up a treatment or to survey osteoporosis evolution, DXA assessment is required.

## **CONCLUSIONS**

1. Osteoporosis is a frequent disease with social impact and economic cost extremely high.

2. Chronic pain, deformities, reduced mobility and disability due to osteoporosis will alter the quality of life.

3. Endocrine factors have a major etiologic contribution in primary osteoporosis as well as in most of secondary osteoporosis.

4. The essential element in osteoporosis diagnosis is represented by BMD assessment.

5. There are several methods to determinate BMD.

6. DXA is the gold standard of BMD assessment.

7. Quantitative ultrasound (QUS), a widely used method in Romania, represents a screening instrument and is not recommended in treatment monitoring.

8. DXA has to be used in therapy monitoring at the bone site, preferable with the same machine, at one-year intervals.

9. Biannual measurements are necessary in patients with high risk of osteoporosis (e.g. patients on chronic corticosteroid therapy) or when bone markers indicate a rapid bone loss.

10. At the beginning of the 21<sup>st</sup> century, endocrinologists have to be familiarized with the modern techniques of osteoporosis diagnosis.

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