International Research Journal of Engineering and Technology (IRJET) e-ISSN: 2395-0056
Volume: 07 Issue: 10 | Oct 2020 www.irjet.net p-ISSN: 2395-0072

A Comprehensive Survey on Bone Densitometry Methods

Nazia Fathima S M[1], Tamilselvi R[2], Parisa Beham M[3]

[1,2,3]*Department of Electronics and Communication Engineering, Sethu Institute of Technology, Tamil Nadu, India*

Abstract - *In early days, morphometric methods were used to evaluate bone density. Initially, only by the visual interpretation of radiographs the bone density was assessed qualitatively. Quantitative analysis of bone density was given by Radiographic Absorptiometry(RA). Scientists are interested in BMD measurement using absorption technique. Photon absorptiometric techniques (SPA and DPA) used radionuclides to generate photon energy. Then, to overcome the limitations of photon absorptiometry techniques such as high cost and radiation safety considerations, X-ray tube was introduced as the radiation source as it has high photon output. It led to the development of SEXA (Single Energy X-ray Absorptiometry) and DEXA (Dual Energy X-ray Absorptiometry). A brief review of these techniques augments the appreciation of the capabilities of modern testing and provides a background for the understanding of modern technologies. Latest improvement in bone mineral densitometry techniques result in precise and accurate methods of estimating bone mineral density. Yet, with a focus on the limitations of the current gold standard method DEXA, paves way for future research for better methodology for estimation of bone density more precisely, easily and accurately.*

Key Words: Bone densitometry, Conventional radiographs, RA, SPA, DPA, SEXA, DEXA

1. INTRODUCTION

Bone mineral loss in early stage is estimated by the densitometry methods in bone which provides accurate quantitative measurement of BMD. Measurements in bone density is separated into two types: assessments of fracture risk or quantification of bone mineral content or density (BMC or BMD). Assessments of fracture risk can be further divided into global fracture risk assessments or site specific fracture risk assessments. [1]

Researchers have developed densitometers to detect bone loss that determines bone density by measuring changes in the absorption of energy passing through bone. This enabled physicians to detect osteoporosis in its early stages, well before fractures occur. The bone mineral content (mass per centimetre) as measured by SPA method and areal density (mass per square centimetre) as measured by DPA. Bone densitometry comprises the art and science of measuring the bone mineral content (BMC) and bone mineral density (BMD) of particular skeletal sites or the whole body. The bone measurement values are used to measure bone strength, helps to diagnose diseases associated with low bone density particularly osteoporosis, monitor the effects of treatment for such diseases, and predict risk of future fractures. BMD denotes the amount of mineral matter (mostly calcium and phosphorous) per square centimetre of bones. To balance for differences in bone size, the measurements of bone mineral were divided by the bone width to give a ratio (g/cm ^{2}). Bone density is used as an indirect predictor of osteoporosis and fracture risk. The relation between BMD and fracture risk is well established. In particular, hip fractures are strongly associated with BMD. [2] To treat, prior to the incidence of first fracture, it is necessary to evaluate absolute fracture risk by BMD measurements and inclusion of other risk factors. BMD value alone can be used for a fine distinct assessment when desired. Literature review shows that bone mineral density values are affected by many factors, such as age, sex. Also, there is much argument on which site BMD should optimally be measured. The principle of bone densitometry is detailed below:

The interaction of electromagnetic radiation with tissue is considered as small packets of energy called photons. In both cases, energy is absorbed by tissue through the electron as it loses kinetic energy in ionising atoms of the tissue. If all the photons initially have monoenergetic or monochromatic, the attenuation of a radiation beam by a thickness 'x' of a single tissue is given by an expontential law:

$$I_r = I_i e^{(-\upsilon x)} \qquad (1)$$

where I_i , I_r are the incident and transmitted intensities and υ is the linear attenuation coefficient which is a property of the tissue. If a monoenergetic radiation beam is passed through part of the body that has bone surrounded by soft tissue, the transmitted intensity is given by:

$$I_r = I_i \, e^{(-\upsilon_b x_b - \upsilon_s x_s)} \qquad (2)$$

where b,s represent bone mineral and soft tissue respectively, x_b is equivalent thickness of bone mineral and x_s is the equivalent thickness of some average soft tissue. This equation is the basis for bone densitometry by experimental

measurement of the incident and transmitted intensities and assumed values are used for the attenuation coefficients. The tissue thickness x is replaced by its area density (in g cm-2).

$$x = \frac{1}{\rho}.\frac{m}{A} \qquad (3)$$

x= 1/ ρ. m/A where m is the mass of tissue in the beam and A is the area of the beam. Thus in eqns 1 and 2, the product v_x can be replaced by μM, where μ is the mass attenuation coefficient (in cm^2g^{-1}) and M is the area density (m/A). X-ray tube produces radiation with a continuous spectrum of photon energies from low values up to a well defined high value. [3]

Thus, in bone mineral density (BMD) scan by SXA and DXA, the energy of *X*- ray beams are used. Some energy that is passed through bones is absorbed, and the non-absorbed energy is detected on the other side of the body. For denser bones more energy is absorbed, and the less energy detected at the other side of the body. Fig-1: depicts the basic principle of bone densitometry. The radiation energy per pixel is detected and converted into an "areal density" measured in g/cm. The number of pixels in the area is added up, and then the amount of bone in each pixel is calculated. Thus the bone density is calculated based on the amount of X-ray energy absorbed by the bone.

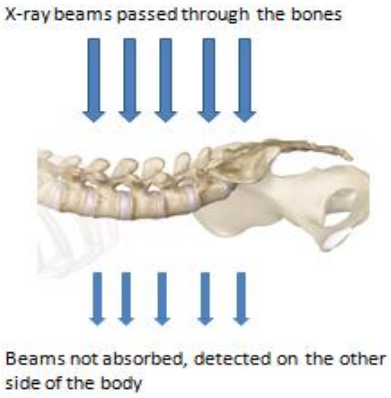


Fig-1: Basic Principle of bone densitometry

There is a correlation between BMD measured by different techniques for a same person. It is variously correlated around r=0.2-0.9. The reason for such variable correlations is the techniques measure in various skeletal sites and different types of bone such as cortical, trabecular and integral of bones. On contrary, due to the dispersion around regression line of correlations between techniques, BMD results obtained by one method cannot be used to predict the result that was got by using method in the same or a different anatomical site. The ideal time interval between BMD measurements in a patient would be associated to the method used, the site of measurement such as axial or appendicular skeleton, the type of bone measured such as cortical, trabecular or integral, its precision, and the expected rate of change in bone density.[4] To assess a technique, it must be both accurate and precise, so that medical opinion can be based on single test values and measured changes over time can be significant. Thus, to diagnose and monitor the treatment of osteoporosis needs accurate and precise BMD measurements.

This article discusses the various techniques for BMD assessment and along with the procedure aspects as well as the advantages and limitations of each technique. The overall presentation of the survey is made on the radiologic methods for evaluation of osteoporosis such as morphometric or photon absorptiometric techniques. These methods give either qualitative or quantitative measurements. Fig-2: depicts the various types of bone densitometry methods. Bone densitometry is a non-invasive test that measures the density of bone quickly and accurately. There are various techniques developed to estimate the bone mineral density and thereby evaluate the condition of osteoporosis. There are morphometric methods and photon absorptiometric methods. Each method is discussed elaborately in the following sections. Nevertheless, a brief review of these techniques should both enhance the appreciation of the capabilities of modern testing and provide a background for the understanding of modern technologies.

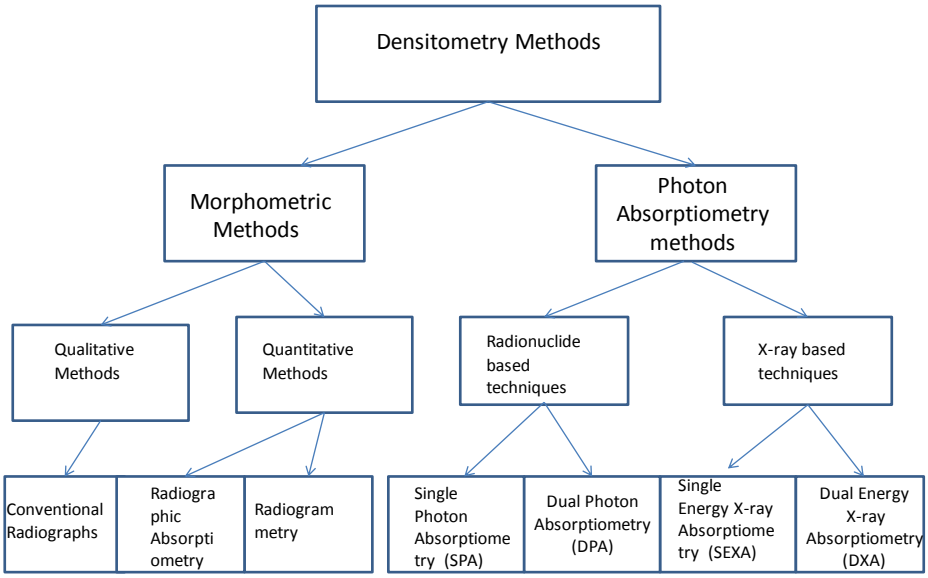


Fig.2: Various techniques for Bone Density measurement

The paper is organized as Section 1, Introduction – gives brief outline on osteoporosis and its impact, along with a summary on principles of how BMD will be calculated and its significance, Section 2, discusses the morphometric techniques of bone densitometry, Section 3, discusses Photon Absorptiometry methods, Section 4 describes the comparison of various Absorptiometry methods, Section 5 gives the summary and conclusion of the advantages and disadvantages of Absorptiometry methods.

2. MORPHOMETRIC TECHNIQUES

Morphometric techniques have been used to assess the bone density in early days. It gives either qualitative or quantitative analysis of skeletal structure from the plain radiographs. [5,6]

2.1 Qualitative methods

Qualitative analysis is given as gradings based on the visual interpretation radiographs by the radiologist.

2.1.1 Conventional Radiographs

As early as in the 1930s and 1940s, conventional radiographs were used to determine bone mineral density. It used ivory edges for calibration. Radiography is a cheap and widely available modality that gives a simple clear-cut way to assess the bone health. Conventional Radiograph is commonly used in evaluation of back pain. Osteoporosis is one of the common causes of back pain in post menopausal women and elderly patients. Thus conventional radiographs aids in subjectively assess the bone density and detect fractures and changes in morphology. The basic principle behind X-rays is, the amount of X-ray energy absorbed increases with the third power of atomic number therefore the absorption is directly proportional to the amount of calcium. If the bone mass is reduced less energy is absorbed that increases lucency of the bones.[5,6] Thus as the bone mass is lost, changes in bone structure occurs and that can be observed radiographically. Radiography image results are very poor in early days. With maximum destruction in bone only, osteopenia is noticed. Early methods didn't give much more good results due to the deformation in the image features. Being a generalized disease, osteopenia may be seen all over, but spine and femur may show special characteristics of osteopenia. Several grading and scoring systems have been established for defining osteoporosis. Some of them are Singh's Index for femur neck and Saville's Index for femur spine.

2.1.1.1 Singh's Index

Singh's index is a qualitative morphometric technique. It is an index for femur proposed to diagnose osteoporosis. It is based on the assumption that the trabeculae in the proximal femur disappear in a predictable sequence that is, as trabecular bone loss occurs, those trabeculae that are subject to less mechanical stress are lost first. X-rays are graded 1 through 6 according to the disappearance of the normal trabecular pattern. The classification was given as:

Grade VI: All the bones are visualized;
Grade V: Predominant ward feature.
Grade IV: Traced from the lateral cortex to the upper part of the femoral neck.
Grade III: Continuity of the principal tensile trabeculae is broken opposite the greater trochanter.
Grade II: Predominant trabeculae stand out clearly; others are nearly absorbed.
Grade I: This grade indicates severe osteoporosis. [7,8]
Later Grade VII was added to the scale for individuals with dense bone that is the Ward's triangle.[8]
Studies were made to compare spinal radiography with DPA. Test was carried in 132 women; films of lumbar spine were graded for osteopenia, spondylosos and calcification of the abdominal aorta based on morphologic criteria. Results show that there were highly significant inverse correlation between radiographic grade of osteopenia and BMC of the 2nd, 3rd and 4th lumbar vertebrae. Also, the mineral content at each radiographic grade of osteopenia differed considerably. Thus spinal radiography and dual photon absorptiometry (DPA) can be regarded as complementary rather as alternate diagnostic procedures.Quantitative digital radiography is faster and cheaper than DPA and involves less radiation exposure. Also quantitative digital radiography has greater image resolution and better short and long term reproducibility [9]. Thus, measurement of the SI in radiographs correlates with histological findings in osteoporosis.[10]
The advantages of SI are it is simple, inexpensive, and the availability. These gradings are made based on the visual interpretation of the radiologists thus SI cannot replace bone densitometry measurements for individual bone assessment. Also it lacks in the consistent interpretation, as there is a wide deviation in the reproducibility and the overlapping of the parameters. SI might be used as an alternative technique for a rough estimation of the mechanical quality of the femur if densitometry is not available. But, recent studies suggest that Singh's index doesn't correlates well with hip fractures and DXA measurements.[11-13]

2.1.1.2 Saville's Index

Osteopenia score for vertebrae was given by Saville. The classification is as follows:
Grade 0 as Normal bone density
Grade 1 as minimal loss of density that is endplates begin to stand out giving a stencilled effect
Grade 2 as vertical striation is more obvious and endplates are thinner
Grade 3 as more severe loss of bone density than grade 2 and endplates is becoming less visible
Grade 4 as density is no greater than soft tissue and no Trabecular pattern is visible.[14]

Several studies were made on plain radiographs of spine to diagnosis osteopenia and osteoporosis. It was also compared with the results from DXA. Also, relationship between vertebral deformity and BMD was examined. In an analysis 200 subjects of which 107 are men and 93 are women of averaged between 52 and 82, radiographs of14 vertebrae ie, between T4 and L5 were analysed. The osteopenia score was given based on Saville's Index. BMD was measured in AP lumbar spine and femoral neck (left hip) using DEXA. Both the results were compared. Results show that lateral spine scans show stronger correspondence with radiologic osteopenia. There was overlap between gradings, but the BMD was in fact significantly related to visually estimated osteopenia. Also, the BMD measured at the hip and spine was related to vertebral deformity in women but not in men. Yet, radiographic results of bone density can only used to provide a broad guide to BMD even under optimal conditions. Though it has also been utilized in other investigations, the Saville index has not been widely implemented because the radiographs are uncalibrated and interpretation is affected by interobserver variability.[15]

Studies were made to show radiographic evidence of osteopenia as a strong predictor of osteoporosis. The patients were compared to a group of one or more age and sex matched patients with one or more low impact vertebral fractures. However, plain film estimation could not differentiate specifically between osteopenia and osteoporosis. In a work, 3530 referrals of women were reviewed for bone density measurements of the spine and femur to determine the relationship between BMD measurements and the initial reason to recommend performing a BMD screening service.[16]

However, some researchers have provided contradictory results. It was suggested that there was little ability to accurately diagnose osteopenia by chest film and proposed that it was unjustified to comment on the presence or absence of osteopenia on the basis of chest films. In [17], the estimated degree of bone density on 45 lateral chest films was read by nine radiologists, was compared with DXA of only the lumbar spine taken within the same 6 month period. One likely limiting factor of this study was that the radiologists reported an overall impression of bone density rather than referring to specific criteria which would have justified their impression. Furthermore, the bone density values were not reported as T and Z-scores but were as grams of hydroxyapatite/square centimetre. At last in another work, it was recommended that this study was underpowered.
In [18], routine radiographs and PA DXA of the lumbar spine were compared in the diagnosis of osteopenia using a T-score of -2SD as the threshold for the diagnosis of osteopenia. They found a poor correlation between BMD, as measured by DXA, and a lumbar spine index (LSI). Also, in this study, radiographs of the lumbar spine obtained in both the anterioposterio and lateral

planes were evaluated by nine observers in order to verify observer variation. The readers were not given specific training or criteria. Results show that osteopenia can reliably be detected from lumbar spine radiographs by all readers only after a substantial amount of BMD is lost i.e., more than 60%. Also, it was noted that the most inconsistency between DXA and observers occurred in cases where the reduction in BMD was between 10% and 20%.

2.2 Quantitative Methods

Quantitative methods compute the bone density in almost every region of the skeleton.

2.2.1 RADIOGRAPHIC ABSORPTIOMETRY (RA)

The above discussed indexes are given based on the visual interpretation of radiologist which may results in interpretation errors thus may lead to wrong diagnosis of diseases. Photo densitometry or radiographic absorptiometry, is one of the first quantitative techniques developed.

2.2.1.1 Procedure

The basic principle for quantitative method for measurement of integral that is, cortical and trabecular bone, Bone mineral density is, the photographic density of a bone on a plain radiograph is approximately proportional to the mass of bone located in the beam of X-ray. It measures the X-ray absorption on radiographs.

Standardized radiographs of various bones of the peripheral skeleton are obtained together with an aluminium or calcium hydroxyapatite reference wedge for calibration. RA measures bone mass in the peripheral skeleton sites, usually metacarpals,phalanges,radius,ulna,femur and tibia. RA can also be applied to measure bone density in calcaneus. This method requires standard, film x-ray device to capture radiographs of the hand, together with an aluminium wedge, by direct exposure at two different exposure settings using a single x-ray film. The film is then transferred to a central reading facility where the image is digitized using a high resolution video camera. The result is then compared to that of the aluminium wedge to compute the equivalent aluminium thickness of each bone which gives the bone density.[19,20]Fig-3. X-ray of hand along with the aluminium wedge.[19]

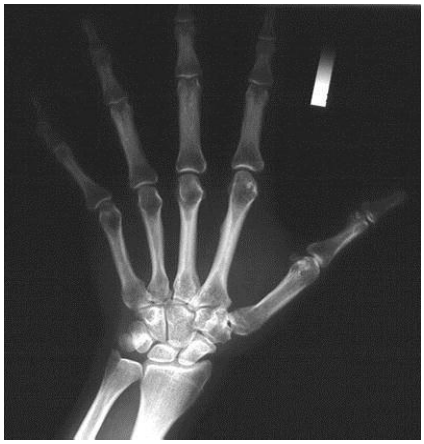


Fig-3: X-ray of hand and the aluminium wedge[19]

2.2.1.2 Correlation of RA with other methods

Though the correlation between different sites as measured by other methods are statistically significant, the correlations are too weak to allow prediction of bone mass or density at one site from measurement at another. To predict hip fracture risk, data of NHANES I was analysed, which had 1559 hand radiographs of Caucasian women taken using photodensitiometry. [21] Some studies have shown that Radiographic Absorptiometry (RA) is useful in population screening of postmenopausal women for osteoporosis. A small, low cost RA scanner were introduced in Denmark to measure bone density in the phalangeal bone of the hand.178 patients were studied with fracture of wrist, hip or vertebra out of which 136 had low energy fractures and in 76 patients both RA and DXA was performed. Results of BMD from RA and T-score of Spine from DXA were compared. Some studies show, RA has high precision and a significant correlation to data obtained by DXA scan.[22]

2.2.1.3 RA- Precision and Accuracy

Correlation with BMD of spine is in order of r=0.6 to 0.8. A good precision was obtained with original techniques with short term coefficient of variation of 1-2%. The site at which RA is performed also affects the precision. Finger bones measurement instead of forearm reduces scatter and beam-hardening effect. Thus RA has been used as a screening technique for primary-care physicians as they need to access only to conventional radiographic equipment and a small aluminium wedge. Yet, the use

of computed RA is limited to appendicular bones as it is sensitive to changes in overlying tissue. Studies show that RA seems to be suitable for BMD measurement to be with excellent precision and accuracy in the phalanx.[23]

2.2.2 RADIOGRAMMETRY

Radiogrammetry is a quantitative morphometric technique that measures dimensions of bones using skeletal radiographs . In Metacarpal Radiogrammetry the dimensions of the metacarpals were measured using a plain radiograph of the hand and rulers or fine callipers was also used. It used cortical width as the measure of bone strength.Calculations such as metacarpal index(MI) and the hand score(HS), percent cortical area(%CA), the cortical are(CA) and cortical area to surface area ratio(CA/SA) was done. The MI is calculated as cortical width divided by the total width. HS is the percent cortical thickness which is nothing but MI expressed as percentage. Thus to calculate bone density, these measurements along with the knowledge of the gravimetric density of bone was used. There were good correlation between such measurements and weight of ashed bone. Metacarpal Radiogrammetry also showed a reasonable good correlation with photon absorptiometric techniques to bone density at other skeletal sites. Radiogrammetry can also be performed at other sites such as femur, phalanx and distal radius. Radiogrammetry measurement of combined cortical widths of second metacarpal and distal radius showed high correlation with bone density in the spine measured by dual photon absorptiometry. Cortical measurement in Radiogrammetry is metabolically less active than trabecular bone.[24]

Analysis in digitized image is done by Digital Radiogrammetry(DXR). The image is digitized. The metacarpals are identified using algorithm of active shape models(ASMs).ASM algorithm identifies points on the boundaries of the metacarpals. There is no operator activity involved in placing the regions. Cortical thickness plays a main role.[25]

Several studies were done to evaluate the correlation between BMD measured by DXR and other techniques. DXR-BMD of the metacarpal was strongly correlated with the distal and proximal radial BMD measured by single-photon absorptiometry. The correlation values are 0.68 and 0.75 respectively. There was a more unassuming correlation with femoral neck and lumbar spine BMD measured by DXA. The values of correlation are 0.50 and 0.44 respectively. Metacarpal DXR-BMD predicted fracture risk at spine and wrist.[26]

3. PHOTON ABSORPTIOMETRIC TECHNIQUES

Photon absorptiometric techniques are based on the quantification of the degree of attenuation of the X-ray photon energy. It enables to quantitatively assess the tissue density also. The earliest photon absorptiometric techniques used radio nuclides to generate photon energy, which later used X-ray sources. Yet, the basic principles on which they operate are same.

3.1 RADIONUCLIDE BASED TECHNIQUES

Initially radio nuclides isotopes such as Iodine 125, Americium 241, Gadolinium 153 were used to generate energy.

3.1.1 SINGLE PHOTON ABSORPTIOMETRY (SPA)

Single photon absorptiometry (SPA) was acknowledged by Cameron and Sorenson in 1963.SPA is the first method employed after the conventional X-ray, to overcome the drawbacks in the use of photo densitometry, such as non-uniformity of sensitivity of the film and development, by using single energy gamma ray source.[27,28]

3.1.1.1 Principles

In this method, a radionuclide source (^{125}I) generates a monoenergetic photon beam of 27.5 keV is used. A scintillation detector is positioned on opposite sides of the structure to be evaluated and the detector is passed over the tissue to be evaluated. Attenuation can be measured as it passes through a region of the skeleton. The amount of attenuation of the photon beam is evaluated with the attenuation caused by standards produced from ashed bone. In this way, the bone mineral content can be quantified for the region of interest. For regions of large and irregular soft tissue masses, water or tissue equivalent material is used to maintain constant thickness across the measuring path.[32,33] Fig-4, shows the working principle of SPA. Here the thickness 'x' is given by Equation Eqn.4

$$x = \frac{(\rho \ln(I_0/I))}{(\mu_b - \mu_s)} \quad (4)$$

where ρ is the density of bone mineral, μ_b , μ_s, are the linear attenuation coefficients of bone mineral and soft tissue for the primary beam energy, I_0 is the transmitted count rate for the soft tissue next to the bone, and I is the transmitted count rate for the path containing bone and soft tissue. I is measured over the regions containing both bone and soft tissue in which the total tissue thickness is the same fixed thickness. Thus area density of bone mineral at a point is given by the equation eqn.5

$$M_b = \frac{\ln(I_s/I_b)}{(\mu_b - (\rho_s/\rho_b)\mu_s)} \quad (5)$$

M_b is the bone mineral density at a measurement point that corresponds to a particular path of the radiation beam through the body. I_b is the measured transmitted intensity at a point through bone surrounded by water and soft tissue and I_s is the measured transmitted intensity through a point adjacent to bone comprising only soft tissue and water. The values are assumed for the physical density and mass attenuation coefficients of bone mineral and soft tissue. If the thickness of soft issue is constant throughout the scanned region, then single gamma-ray energy is sufficient for the calculation.[27,30]

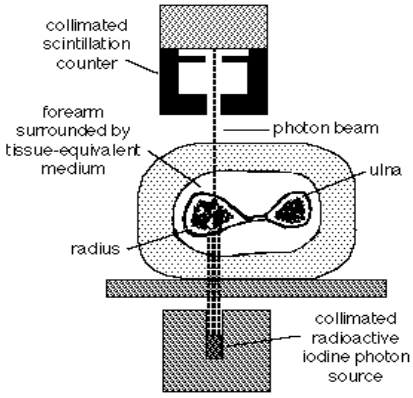


Fig-4: Working Principle of SPA[27]

3.1.1.2 BMD Measurement

The signal was graphically displayed on a cathode-ray tube or X-Y plotter. This display was a logarithm of the count rate observed by the detector. A collection of points is obtained representing a plot of transmission versus position. The intensity is noted at each position for a preselected time interval which was usually one second. The count rate which is counts per minute was determined over regions of soft tissue and bone.[27,29] Fig.5, sample SPA printout of cortical bone site.The printout contains the information on the scan site and values of bone width, bone density ,BMC and the constant values used for calculation[34].

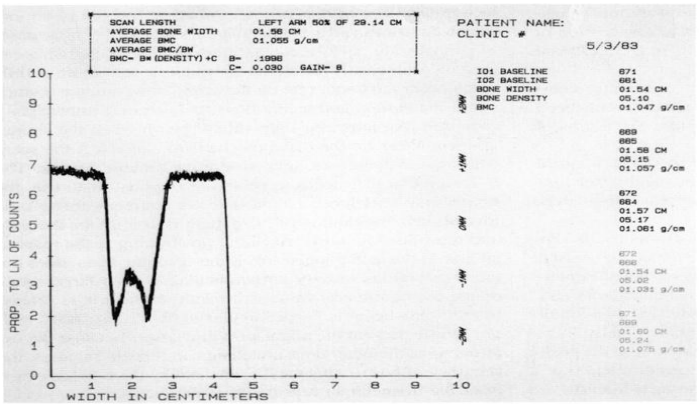


Fig-5: Sample SPA printout[34]

3.1.1.3 Region of Interest

The method is only relevant to appendicular bones such as forearm, specially the radius and legs. The SPA method has been considered the gold standard method for the determination of the BMD of the forearm due to its relatively high precision.[37]. SPA method was used for differential estimate of rate of loss in trabecular and cortical bones. Since female bone contains about 900mg of calcium, the changes in bone mass is very small. Since there was a need for methods, that has high reproducibility in order to access differential rates of bone loss, SPA was more suitable.[31].In post menopausal women, on a group basis, bone loss at forearm site by SPA closely corresponded to that at spinal site by DPA. Measuring set-ups suitable for repeated measurements would have to be quick and convenient. Thus single photon absorptiometry scan procedure in the most distal part of the forearm was more appropriate. Positioning of the patient is crucial for accuracy and reproducibility. The precision depends on the calibration procedure, if calibration is not done, reproducibility error increases two or threefold[30]. Single-photon absorptiometry was employed to make precise measurements of hand BMC and therefore to study local bone loss. It is

relatively insensitive to variations in placing and replacing the marker band, the effect of which is included in the estimation of precision. Fat deposits around the hand or wrist will result in a small inaccuracy in some patients. The early apparatus used a horizontal scan with the hand in a pronated position. Later, vertical scans with the hand gripping a rod in a water bath resulted in enhanced precision.[32]

3.1.1.4 SPA for neonates and children

SPA was widely used to determine bone mineral content in neonates and children.SPA was considered as a valuable tool in the study of the prenatal bone mineralization. SPA was used to determine bone mineral content in human fetus where scanning is performed in five sites along the length of the specimens. Results show that midshaft site produced minimum positioning error for BMC measurements. The radius was preferred as a suitable bone to measure BMC in infants and very low radiation dose was used. Single photon absorptiometry was used to monitor and treat children with disorders of bone growth and mineralization.[34,35,36,37].

3.1.1.5 SPA for Prediction of Fracture Risk

SPA was used to assess future fracture risks too. SPA was a widely used and recognized bone density method, the results of which were able to predict fracture risk in the appendicular skeleton, hip and spine. Studies show the risk of all non-spine fracture can be estimated from the single measurement of radius and also it is independent of age. The calcaneus measurements and femoral neck measurements predicted intertrochanteric fractures. Thus the measurement by SPA at radius and calcaneus can predict risk of future fractures. Using fracture risk values as the criteria for normal and osteopenia, the midradial site is less sensitive than the distal radial site up to the age of 60 years.[39,40,41]

3.1.1.6 Precision and Accuracy

SPA had a very low radiation dose, effective dose equivalent EDE approximately 0.6 mSv. Precision or coefficient of variation CV% for BMC in the mid shaft and distal metaphysic was 1%.The precision of SPA depends on the site either ultradistal or proximal and the type of measurement such as BMC or BMD.The scanning time was 10–15 min. The SPA method has been considered the gold standard method for the determination of the BMD of the forearm due to its relatively high precision.[28]

3.1.2 DUAL PHOTON ABSORPTIOMETRY(DPA)

Cameron and Somersen suggested that two or more different photon energies can be used at transmission measurements to determine the relative amount of elements in tissue. [DPA1]DPA was developed to overcome the limitations of SPA. Also, to determine bone content of bones such as spine. [42]

3.1.2.1 Principles

DPA scanners employed photon energies higher than I-125 or Am-241. A number of radionuclide sources were used for DPA such as Ba-133, Gd-153.Thus using DPA, Trabecular bone sites and major fracture sites are evaluated, that overcome the limitations of SPA. A high-intensity source of 153 Gadolinium is mounted below the scanning table and a scintillation detector on the yoke above the subject. The detector has a slit collimator. The intensity of the attenuated beam was measured by a collimated scintillation counter, and the bone mineral was quantified. Fig-6, depicts the working principle of DPA.

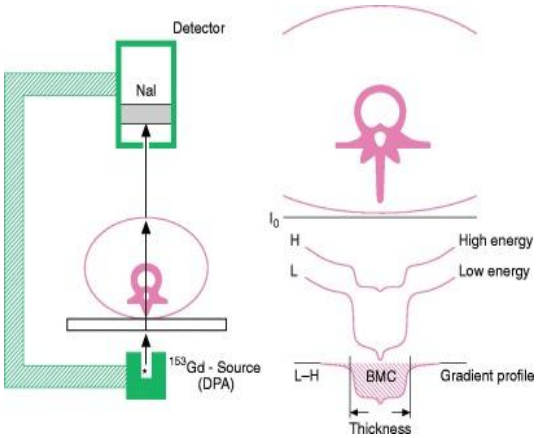


Fig-6: Working Principle of DPA[43]

Two absorption curves are obtained from which bone mineral density is calculated. The principle of dual photon transmission can be stated as follows: if the transmission measurements made at two different energies, then at each point are given by the equations 6 and 7.

$$I^1 = I_0^2 \, e^{\left((-\mu_t^1 M_t) - (-\mu_b^1 M_b)\right)} \quad (6)$$

$$I^2 = I_0^2 \, e^{\left((-\mu_t^2 M_t) - (-\mu_b^2 M_b)\right)} \quad (7)$$

Where μ's are the mass attenuation coefficients for tissue and bone at two different given energies, M_t and M_b is the mass of tissue and bone in the beam in g/cm^2 and I_0 is the unattentuated beam. Thus measuring I, I_0, and taking the known values of μ's, yields two equation with two unknowns M_t and M_b, which solves for M_b.

$$M_b = \frac{ln\left(\frac{I_i^L}{I_r^L}\right) - R_s \cdot ln\left(\frac{I_i^H}{I_r^H}\right)}{\left(\mu_b^L - R_s \cdot \mu_b^H\right)} \quad (8)$$

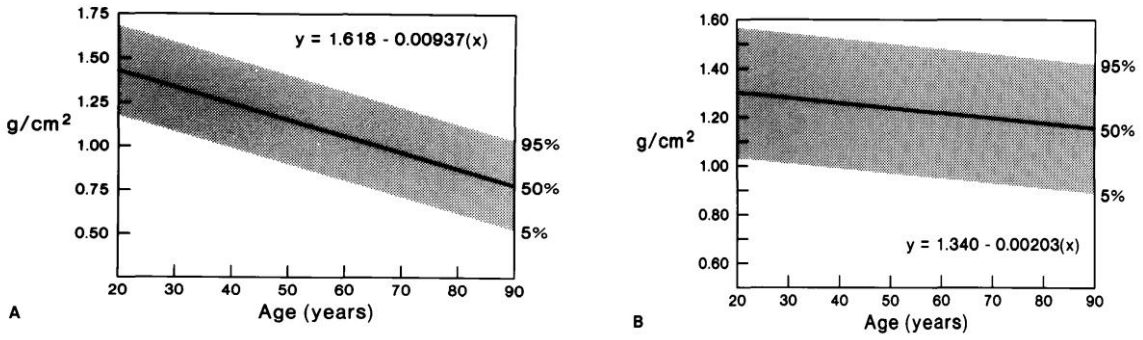
The value of R_s is calculated as equation 9.

$$R_s = \frac{\mu_S^L}{\mu_S^H} \quad (9)$$

In Equation eqn.9 H and L represent high and low photon energies respectively. Ratio R_s measured for individual subjects. M_b is the mineral mass in the beam at each point of the scan, when expressed as amount of mineral per square centimetre scanned, is called bone mineral density (BMD) in g/cm^2. DPA doesn't not require the soft tissue that was used to maintain uniform thickness as in SPA. In simple words, fundamental principle on which DPA is based involves the differential attenuation by bone and soft tissue, of transmitted photons at two energy levels.[43]

3.1.2.2 BMC Measurement and ROI

DPA was used for precise and accurate measurement of bone mineral content in spine and total body . The scan on the spine is usually performed from L1 to L5. Region of Interest (ROI) is selected from L2 to L4. Calculations for BMC are done by the computer. If previous studies were done on a patient, the ROIs must be the same to assess good precision and test accuracy. The final BMC is compared with a normal range that is adjusted for age and sex. The normal range for females and males (Fig- 7(a) and Fig-7(b)) must be obtained for a scan area routinely used, and race must be considered in scan interpretation. A normal range for white persons cannot be applied to black or Asian persons. Fig-8. Shows a sample printout of DPA.[44]



(a) (b)

Fig-7: Normal BMC in L-2-L-4 region in 105 women (a) and 82 men (b) of various ages from a study performed. Data are expressed as g/cm^2[44]

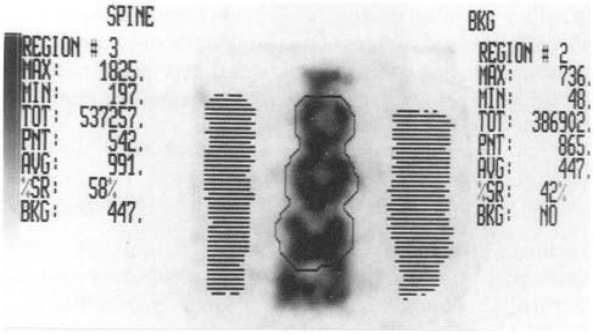


Fig-8: Sample Printout of DPA[44]

This is not the actual bone density, but represents the total mineral in a column 1cm in cross-sectional area. Thus large bone would yield large value of bone density than the small bone would for the same average density. Hence wide range of normal values was available for DPA methods. Measurements were made on radius, ulna and vertebrae for same subjects. Results show that there were only moderate correlations of 0.6-0.7 between bone content of radius and ulna. In lumbar vertebrae the standard error of estimate was about 15 – 17%. The rate of bone loss with age was greater in peripheral sties than spine. By scanning the total body it was possible to specify the distribution of bone mineral in specific areas such as limbs or trunk. Lumbar spine is an great interest for bone metabolic disease as fractures occurs the most in post menopausal women. DPA was used to analysis the Total Body Bone Mineral which was a good indicator as of spine.[45]

Total body bone mineral (TBBM) can be measured using DPA. A computer program was developed that provided an estimate of the fat-lean ratio, which was necessary for calculation of TBBM. The errors appeared quite small.[46]

3.1.2.3 DPA Scanners

Many investigators developed instruments to measure bone mineral content by DPA. The first apparatus built for patient measurement was in 1965 by G.W.Reeds using Am-241 and Cesium-137 to measure calcium content in various bones. In late 1975, a modified scanner with source of Gd-153 was used to measure in vivo bone mineral of the spine. Later scanners were specially designed for lumbar vertebrae measurements. [6]Then scanners were modified to make calibrated measurements on three areas of the femur. Fig-9. Lunar DPA scanner.

Fig-9:Lunar Dual-Photon Absorptiometer. Photo courtesy of GE Medical Systems, Madison, WI.

3.1.2.4 Accuracy and Precision

DPA in body composition studies showed relatively high precision, but it takes long scanning time and the counting efficiency reduces for obese persons. The accuracy of DPA in vertebrae and femur is adequate to assess the true bone mineral mass and hence to access the fracture risk. Hence for a better analysis of vertebrae, a gamma camera was fitted with the collimator assembly, to diverge the beam. This produces a magnified image. But the region of interest is uncertain that prevents accurate calculation of BMC and use of fixed ROIs in follow-up measurements. Hence, the precision of DPA with a gamma camera is insufficient compared to DEXA, so this method cannot be suggested for follow-up of individual patients. [47]

3.2 X-RAY BASED TECHNIQUES

Due to high cost and radiation safety considerations led to the USE of X-ray tube as the radiation source as it has high photon output.

3.2.1SINGLE ENERGY ABSORPTIOMETRY (SEXA)

3.2.1.1 Principles

The method of SEXA is similar to that of SPA [52].The equipment photon source is the X-ray system which emits X-rays at an energy level of 40kVp and 0.2mA with k-edge filtration and solid state detectors .SEXA measures bone density in the regions of distal radius, ulna, and calcaneus, with the region of interest Forearm. As a single energy x ray beam is used, the arm has to be placed in a water bath or tissue-equivalent gel for correction for the soft tissue overlying the bone being measured. [44] Fig- 10. Sample scan printout of BMD measurement of distal radius with BMD plotted in reference range.[6]

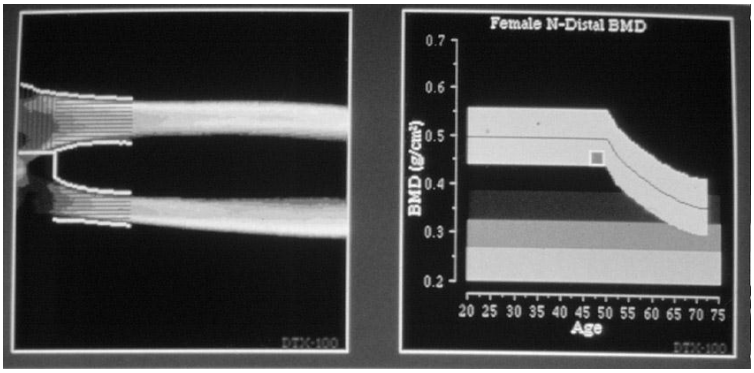


Fig-10: Sample scan output of SEXA scanner[6]

3.2.1.2 SEXA- Comparison with other methods

Studies were made to compare the performance characteristics of SEXA with other measurement techniques. In a work, Evaluation was made on the distal forearm of 377 subjects. Results showed that SXA device has a precision error somewhat lower than that of the SPA, also in ultradistal site there were only minor differences between SPA and SXA measurements. Thus based on the performance characteristics of SEXA, it was suggested that SEXA can be used for diagnostic purposes and the follow-up of treatment.

In another work the spine measurement by DEXA, was compared with forearm measurement using SEXA. Study was made on three groups of women such as normal premenopausal women, elderly women with fracture and elderly women without fracture. Here, the Forearm measurement with SEXA gave diagnostic values comparable to that of measurement of the spine by DEXA.[53]

Studies were made to establish reference ranges of calcaneus in various ethnics. In a work, 7428 people from Chinese population were taken for study. BMD in the calcaneus was correlated with the BMD in the spine and hip. Data such as age, sex, date of birth, height and weight were also considered. The linear regression equations were used derived to measure BMD. The equations of BMD for women and men were given as equations 10 (a) and 10 (b) [48].

$$BMD = 353.8 - 3.852 * age + 3.304 * weight \text{ (women)} \qquad 10(a)$$

$$BMD = 275.3 - 1.419 * age + 3.434 * weight \text{ (men)} \qquad 10(b)[54]$$

Similarly, in another work, 605 Japanese women were taken for study to establish the reference range. The calcaneus BMD measured by SXA showed a high correlation with the spine BMD by DXA thus the measurement of calcaneus BMD using SXA has almost the same value in diagnosing osteoporosis as that of spine BMD using DXA. The BMD value after menopause is indicated as equation 11.

$$\text{calcaneus BMD} = -6.489 \times YSM + 371.56 \qquad (11)$$

where YSM is years since menopause.

There was a high correlation between calcaneus BMD measured by SXA and spine BMD measured by DXA in the 420 cases. The relation between Spine BMD and Calcaneus BMD was given as equation eqn 12[49].

$$\text{Spine BMD} = 1.839E\text{-}3 \times \text{Calcaneus BMD} + 0.356. \qquad (12)$$

SXA reference data were generated by measuring non-dominant forearm of 151 healthy causcasian American women with age range of 23-85 years. A relationship between SXA BMC and DXA BMC was given as SXA_BMC = 0.9169±0.031 X DXA_BMC + 0.1100±0.109 (r=0.972) and the relationship between SXA BMD and DXA BMD was given as SXA_BMD = 0.9639±0.038 X DXA_BMD + 0.0090±0.109 (r=0.961).[55]

Studies were made, to compare methods such as cross sectional BUA (Broadband Ultrasound Attenuation), DEXA and Single Energy X-ray Absorptiometry measurements of BMD at the calcaneus in 259 healthy postmenopausal women. Measurements were made on the heel. A coefficient of variation (CV) was calculated for each individual for each methods.BUA and BMD of the heel were also compared to BMD of the lumbar spine and femoral neck measured using DEXA. Results show that BUA was significantly correlated with BMD at the calcaneus. Heel BUA was also correlated with lumbar spine BMD and femoral neck BMD, but the correlations were lower than those between heel BMD and spine or femoral neck BMD.[50]

From the above literature, it is suggested that the calcaneus can be an efficient skeletal site for screening and diagnosing osteoporosis and also for long term follow ups.

3.2.1.3 Accuracy and Precision

The accuracy and precision of SXA were equivalent with SPA. Scanning of the forearm takes about 5 minutes in the standardised position.Accuracy is 3% and precision is better than 1% in distal site. Radiation dose, effective dose equivalent (EDE) is less than 0.1uSv. There are SXA scanners to measure BMD in os calcis with scanning time of two minutes and precision is better than 1%.[55]

3.2.2 DUAL ENERGY X-RAY ABSORPTIOMETRY(DXA)

Dual Energy X-ray Absorptiometry(DEXA), is based on x-ray spectrophotometry, that uses a dual-energy X-ray source to eliminated problems associated with decaying isotopes, that were used in previous methods. It has been considered as the 'gold standard' technique to measure Bone Mineral Density(BMD).[57]

3.2.2.1 Principles of DXA

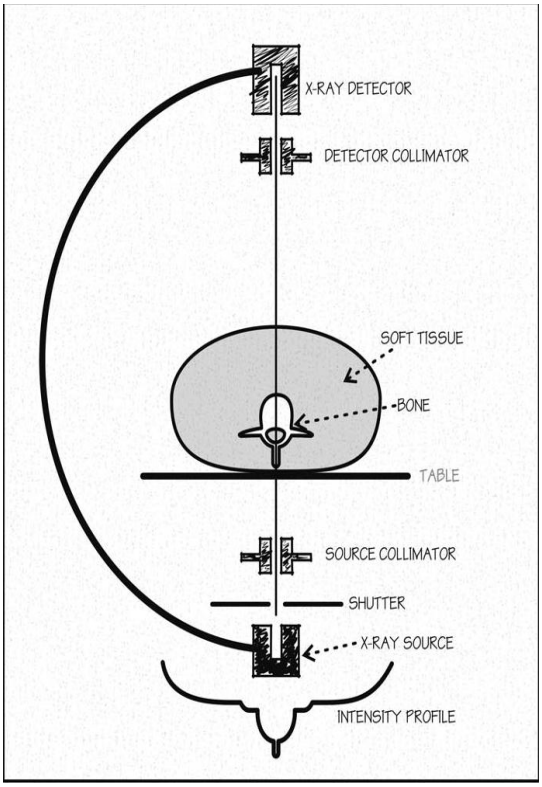
DEXA uses two energies to find the bone density. Individual image pixels of the human body can be described with two components i.e. soft tissue and bone mineral. The equations can be derived for two X -ray beams with a high and low energy. The attenuation equation for each beam is given by equations: Eqn 14 (a) and Eqn 14(b).

$$I^L = I_0\, e^{-\left[\left(\frac{\mu}{\rho}\right)_s^L \sigma_s + \left(\frac{\mu}{\rho}\right)_b^L \sigma_b\right]} \qquad 14\ (a)$$

$$I^H = I_0\, e^{-\left[\left(\frac{\mu}{\rho}\right)_s^H \sigma_s + \left(\frac{\mu}{\rho}\right)_b^H \sigma_b\right]} \qquad 14(b)$$

where the H and L superscripts represent the high and low energy X ray beams, respectively, I_0 is the initial intensity of the x-ray beam; μ, mass attenuation coefficient (cm^2g^{-1}) and σ is the areal density in units of g/cm^2 .where s denotes for soft tissue and b for bone.[60]

DXA systems are similar to X-ray imaging systems, with many of the common components. DXA system includes the X ray tube, filtration, pre-patient aperture, examination table or surface, pre-detector aperture and detector. Schematic diagram of a DXA system is shown in Fig-11. The various tissue densities are separated based on the higher and lower attenuation levels. These are shown in Fig-12.



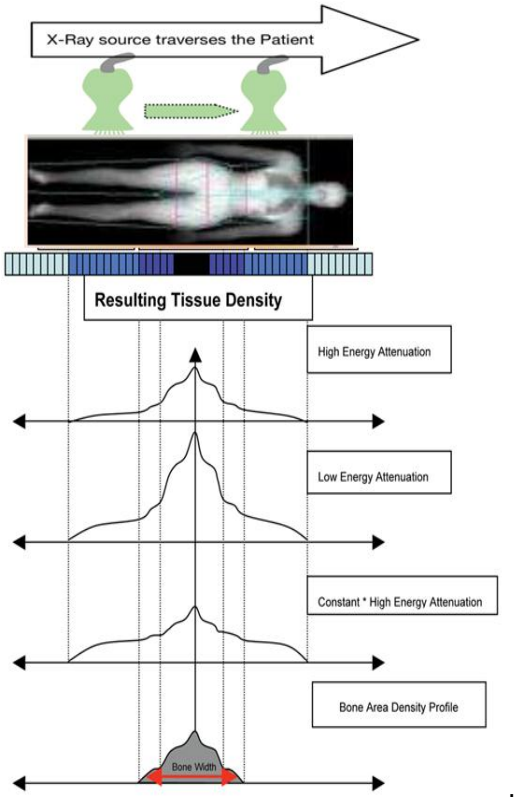


Fig-11: Schematic diagram showing the components **Fig-12:** Tissue Density based on the attenuation of a DXA System

Various techniques is used to produce X-ray beams of two peak energies which differs with manufacturers. The energies are selected to optimize separation of mineralized and soft tissue components of the scanned regions which allow an estimate to be made for soft tissue absorption separately from that of the bones. Top manufacturers of DEXA scanners are Hologic, Lunar Corporation and Norland Medical Systems. In some scanners energy switching system is used in which the X-ray tube potential is switched rapidly with an internal rotating disc of calibration materials, while some other manufacturers' uses a constant potential X-ray source combined with a rare earth filter with energy specific absorption characteristics. Filters separate the X-ray beam into two components of high energy of 70-80 keV and low energy of which is 40-50keV.[61,62,63]

3.2.2.2 DEXA Regions of Interest

To determine the bone density, regions with higher contents of cancellous bone is considered as they are more sensitive to osteoporotic changes. Studies suggest that regions such as spine, femur, radius and calcaneus are useful for predicting general fracture risk. DEXA helps to determine BMD,BMC and AREA. OF these, BMD is the best for assessment of risk of osteoporosis. Also, the whole body scan mode can measure fat, lean and bone mass. The regions analyzed in DEXA are lumbar spine(L1-L4) and in the proximal femur(femoral neck, trochanter,Ward's area and total hip). DXA also helps in the evaluation of bone quality such as for analysis of hip structure and trabecular bone score. Also, for vertebral fracture assessment, Detection of a typical femur fracture.[64,65]

Spine:

Spine is the most common Region of Interest for diagnosis of osteoporosis. The scan includes the inferior portion of T12 and the superior portion of L5. But, the aBMD measure of interest is usually the total of L1 – L4 in the posterioanterior projection. This region may be considered as the source of error for older patients due to extraneous calcifications in the walls of the aorta or any deformations. This may result the aBMD to be falsely high.But by combining the lateral scan with the vertebral width from the PA scan, the true volumetric density of the vertebral bone can be determined. But, due to the overlap of the iliac crest and L4 and the ribs with L1,ROI of L2-L3 is used.[53] Fig.13: The figure includes labels showing numbering of the vertebrae. For accurate numbering, a lumbar spine radiograph can be used. Hence correct numbering of the vertebrae is important for accurate interpretation. Especially, when a scan is being repeated, numbering of the vertebrae should be consistent. The BMD is determined in the area that includes the outlines of the four lumbar vertebrae.[66]

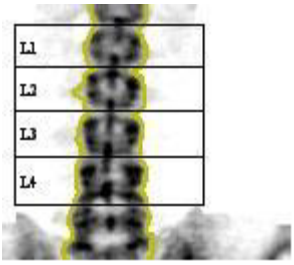
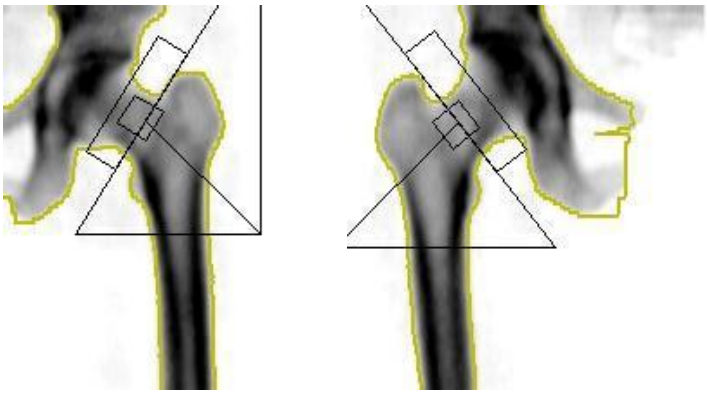


Fig-13: DXA scan image of spine with vertebrae numbering

Proximal Femur

The proximal femur is another scan site because most fractures occur at this site and it may cause mortality.The scanning of the proximal femur, involves slightly abducting the leg and rotating internally using a positioning device so that the projection of the femoral neck is maximised. Each DXA manufacturer has a different and unique positioned to carry out this. If the femur is not rotated effectively, the femoral neck is foreshortened and this will falsely increases the BMD. Positioning of the femoral neck is vital for accurate results. The regions included for analysis are the total and femoral neck.. There should be no artefacts within the measured regions of interest. Fig.14(a) and Fig.14(b) DXA scan images of left and right femur.[67]



(a) (b)

Fig-14:DXA scan image: (a)right femur (b) left femur

Forearm

The regions in forearm includes the ultradistal, distal (mid-radius) and shaft (one-third radius) regions. The ultradistal site and shaft are useful as it contains the highest percentage of trabecular bone and cortical bone respectively. Mostly forearm is considered only when spine and hip cannot be measured and also during conditions such as hyperparathyroidism and very obese. Fig.15. DXA scan image of a forearm.[69]

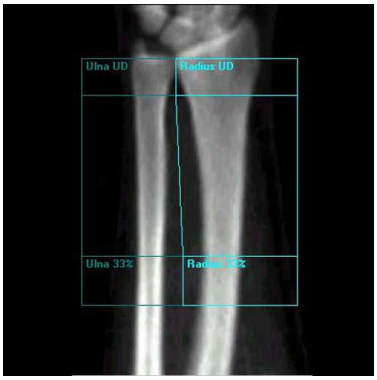


Fig-15: DXA scan image of a forearm

Total Body

Total body DXA for bone mineral is of interest because it offers a broad view of total body mineral. This can be useful for calcium balance studies and paediatric studies interested in developmental bone mass. DXA measures integral (trabecular and cortical) bone mass with cortical/trabecular ratios of 50/50 in the lumbar spine, 10/90 in the lateral spine projection, 60/40 in the proximal femur and 80/20 in the whole body. Fig.16. DXA scan of a whole body.[70,75]

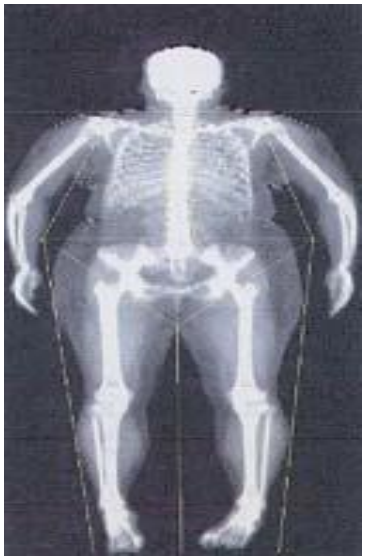


Fig-16: DXA scan of a whole body

3.2.2.3 Accuracy and Precision

The accuracy of DEXA is 3-8%. Precision which is expressed as CV%, of spine (PA) is better than 1%, of proximal femur is between 1-5% which depends on the site analysed, in the neck and trochanter is 1-2% and Ward's area is 2.5-5%.[56] The scan time is approximately 10-15 minutes per site scanned. Radiation dose, for pencil beam DXA it is around 1 uSv upto 6 uSv depending on the site scanned and for fan beam it may be upto 62uSv.[71,72]

3.2.2.4 DXA Printout Analysis and Interpretation

The printout of DEXA scan report, contains the patients details, region of interest the area analysed for each region of interest(expressed in cm^2), the Bone Mineral Content(expressed in grams) and Bone Mineral Density(expressed in g/cm^2). A table with the BMD in gm/cm , the T-score and the Z-score is also given. BMD results states the mass of bone mineral per unit projected area averaged over the ROI take in the analysis box. BMD is also expressed as the value of T-score and Z-score. The BMD results are compared with appropriate race or sex matched reference ranges generally given by the manufacturers. Comparisons can be made with either age match reference data or peak bone mass which is the BMD of young normals. It also contains a graph of where the patient fits within the reference population.[71,72] For diagnostic classification, the region with the lowest T-score is identified from among the lumbar spine, hip, or radius. For the spine, the L1–L4 region is used but a single vertebra should not be used. For the hip, the lower T-score between the femoral neck and total hip is used. For the forearm, the mid third radius (also called 33 % or 1/3) is used. It is also suggested that BMC and BMD of the femoral neck and lumbar spine must be normalized to avoid under diagnosis in tall ones and over diagnosis of osteoporosis in persons of short body structure. [76]

The bone mineral content (BMC) is expressed as grams. This value is divided by the area of bone scanned to provide BMD in g/cm^2.Values for bone density are converted into values related to the average female (or male) peak bone mass or to the bone mass related to the patient's age. These are T scores and Z scores, and involve the following calculations:

$$\text{T score} = (BMD_{patient} - \text{Mean-BMD}_{\text{young normal population}}) \,/\, \text{SD-BMD}_{\text{young normal population}}$$

$$\text{Z score} = (BMD_{patient} - \text{Mean-BMD}_{\text{age-matched group}}) / \text{SD-BMD}_{\text{age-matched group}}$$

The concept of T-score simplifies the interpretation of BMD measurement results and allows comparability among different DXA devices. T score is calculated by taking the difference between patient's measured BMD and the mean BMD of the young normal population that is matched for ethnicity and gender. T-score along with the patient's age helps to estimate the number of fractures expected in a patient's remaining lifetime. The T-score enables classification of patients into one of three diagnoses: normal, low bone mineral density, or osteoporosis. Assuming a normally distributed population, if 0 is the mean, then a T-score

of -1 is one standard deviation below the mean, a T-score of -2 is two standard deviations below the mean, etc. According to World Health Organisation (WHO),T-scores, with a BMD T-score >=1 SD being normal, between -2.5 and -1.0 SD being osteopenic (or low bone mass), and <= -2.5 SD being osteoporotic. To have a T-score of -2.5, a patient must fall within the lowest two percent of the reference population. Fig.17. Shows a pictorial representation of values of T score and the catergory.

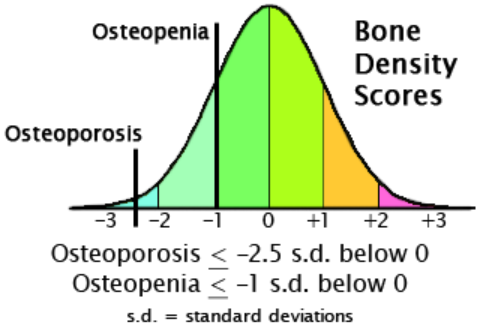


Fig-17: T score and corresponding categories

Z score describes the number of SDs by which the BMD in an individual differs from the mean value expected for age matched group. Z score is used for clinical decision-making and estimation of fracture risk. Z scores may be used to monitor long term follow up of treatment. Z score helps to investigate the cause of osteoporosis unrelated to age. For children, young adults, premenopausal women and men younger than 50 years, the WHO criteria should not be used. For these groups diagnosis is based on the Z-score. Patients with Z-scores below -2 are categorized a ''low bone density for age''.[58,59,73]

3.2.2.5 Standardization of manufacturers

BMD measurements for the same patients made on different DXA scanners of same or different manufacturers are different. The differences are caused by different edge detection algorithms, scanner design and calibration. Results with Lunar DPX scanner are approximately 12% higher than those with Hologic QDR or Norland XR26. Thus, the IDSC (International DXA Standardization Commitee) was set up to counsel appropriate cross-calibration procedures. Conversion equations were obtained to standardize posteroanterior spine(L2-L4) BMD results. The standardization is denoted as sBMD. The equations are:

For Hologic DXA scanners:

$sBMD=1000[BMD_{Hologic} \times 1.0755]$

For Lunar DXA scanners:

$sBMD=1000[BMD_{Lunar} \times 0.9522]$

For Norland DXA scanners:

$sBMD=1000[BMD_{Norland} \times 1.0761]$

Scanners with specialized software provide the physician with the sBMD results. There are differences in normative data between manufacturers as they have their own reference database. Thus it is recommended to perform serial measurements using same DXA scanner.[77]

Values differ with different manufacturer, that is with Lunar instruments there was reduction in total body mineral density with loss of weight, whereas with the Hologic scanners it appears to increase. For the diagnosis of osteoporosis, BMD of the spine and hip are more commonly used than the total-body BMD, thus possible errors due to anomalies during weight change need to be considered for those regions also.[78]

Differences in interpretation of lumbar spine BMD Z-score results from different scanners of the manufacturer Hologic, were found as it has used non-sex specific reference data. Whereas no changes were found when sex-specific datasets were compared. Even with same manufacturer comparison between sex and age specific hologic DXA databases for the most frequently scanned regions such as Lumbar Spine(LS) and total body(TB) are largely scarce. This may complicate DXA interpretation and may results in misdiagnosis and unnecessary treatments when BMD in children is falsely calculated too or too high for their age and size.[79]

3.2.2.6 BMD Measurements in Pediatrics

Pediatric BMD measurements present several technical problems. One such is certain algorithms designed for adults may not be suitable for pediatric studies. Hologic provided alternative algorithms for low bone density studies. Several studies were made to study the BMD measurements in pediatric cases. In a work, Study was made with 450 normal children. A subgroup of

103 children was selected and the group was distributed evenly between males and females and in age group of 5-17 years. Scan was taken for whole body and lumbar spine. Both scans were analysed with the standard adult protocol. Using adult protocol only two of the selected vertebrae were analysed. In pediatric protocol all four selected vertebrae were analysed. Results show BMD increases with age and thus, for spine,pediatric algorithm is used and for whole body, adult algorithm shows no major failures. A low density spine(LDS) software was developed to assess bone mineral density in children as the standard software failed to identify the bon edges of low density vertebrae. One hundred children were studied their height and weight were also noted. BMD of lumbar spine is measured by DXA and each scan was reviewed and analysed for both softwares for identical region of Interest. Results show that the LDS software increases the detection of low density bone in children. But reference data to analyze children with osteopenia needed to be developed. Studies were made to provide reference values for bone mineral density and body composition measured with DXA for white children and young adults. The mean and standard deviation are given for boys and girls from age of 4 to 23 years, which enables calculation of age and sex matched standard deviation scores. Studies were made to examine comparability of BMD Z-scores generated by the largest currently available pediatric DXA reference data on different hologic scanners. Six reference database were included in the study. Also, Z-score for interdatabase differences among age groups are assessed. Also how well Z-scores correlate among databases are tested. BMD Z-scores computed from the six age- and sex-specific databases were highly correlated but differed considerably in both scan regions and sexes among almost every database pairing. In addition, Z-score differences between databases vary largely depending on the child's age. Hence, these six pediatric databases are not interchangeable with each other. The main prediction parameter was height, followed by age. But with adjustments needed for gender and ethnicity. Studies with 982 healthy children showed the prediction accuracy of the model for an individual child within that population. There are limited reference data available for children of all ethnic groups. As DEXA is not a true volumetric, density is very much dependent on size, thus limits the application in children. But, the extremely low doses and the high spatial resolution involved in DXA make it a suitable tool in the investigation of skeletal development in children.[68,74,83,84]

3.2.2.7 Inconsistency with database

There are various factors influences the effective diagnosis of osteoporosis by DXA. Of which the type of normal reference range is very important. As it vary in accordance with the genetic makeup, the environmental set up, personal habits, life style, etc. of that particular geographical area/race/sex. In DEXA, most of the reference data are Caucasian races; there is a lack of suitable reference data for other ethnic groups.[93] Even small differences between ranges might have a large effect on the number of individuals with BMD below a diagnostic threshold. Calibrations for average bone densities are often based on a database of the upper femur called the NHANES database. Currently, National Health and Nutrition Examination Survey (NHANES) III reference database in women aged 20–29 years as the reference range is recommended by International Osteoporosis Foundation and the World Health Organization. These data collected from the Caucasian race ofUS population. [84]

The Lunar scanners use this Caucasian-based BMD normative data for the calculation of the *T*-score. Caucasian female reference database is used for *T*-score calculation in men also. As, at the same areal BMD (g/cm2), men and women have an approximately similar fracture risk even though having the difference in *T*-score.[65]

The DXA output gives the areal BMD which gives the actual bone strength. Hence, the classification of osteoporosis is based on the T-score, which is derived from areal BMD using normative data. Hence, T-score is dependent on both areal BMD and reference data. Many studies showed that there is a discrepancy in T-score when different normative data were used.[73]

Studies by Indian Council of Medical Research(ICMR) show that Indians have lower bone mineral density than North Americans. Therefore, ICMR has published a reference data for BMD in the Indian population derived from the population-based study conducted in healthy 808 Indian individuals aged 20– 29 yr in different parts of the country. Studies were made to compare the Indian Council of Medical Research database (ICMRD) and the Lunar ethnic reference database of DXA scans in the diagnosis of osteoporosis in male patients. Study was made with 238 male patients. Results show that there is discrepancy in the results. That is, out of the 250 sites of the DXA scan, 28.8% and 60% of the cases classified as osteoporosis by Lunar database whereas, as normal and osteopenia by ICMRD respectively. Thus the decision on the treatment of osteoporosis should be based on the multiple fracture risk factors and less dependable on the BMD T-score.[81]

Studies were made to determine the normal reference values for Indian women aged 20-80. In this study, 50 women from each decade were included. Scan of lumbar spine and left hip neck were considered for each women. The mean and standard deviation were calculated for the BMD in each group. The values were compared with the reference values for European and US populations. The study indicates mean spinal BMD in Indian Females in the 20-60 years age group is about 30% less than that in the European/American references, which means the mean Indian BMD is about 2SD lower than the Western BMD. Also, mean hip BMD in Indian Females in the 20-60 years age group is about 27% less than that in the European/American references, which means the mean Indian BMD is about 2SD lower than the Western BMD, which means This means that the mean hip neck BMD is about 1.5SD lower than the Western BMD.[80]

A normal reference of BMD for Southeast Asian children was also proposed. Studies also show that BMD values of Chinese and Japanese individuals are lower than that of Caucasians. Also, African American men have higher BMD than Caucasian men. Though Normative BMD data for children are available for Caucasians from different parts of the world including US, Spanish,

Dutch and Swedish children, BMD references for Asian children are limited.Only little attention has been paid to the comparability of reference databases.[82]

4. COMPARISONS OF DENSITOMETRY METHODS

RA provides advantages of low cost, rapidity and easiness in use in wide variety of clinical settings. Thus RA has been used as a screening technique for primary-care physicians as they need to access only to conventional radiographic equipment and a small aluminium wedge. Numerous physical factors influence the radiographic images such as inconsistencies in beam quality, instability of the X-ray source, film response, processing conditions, radiation scattering conditions and beam hardening effects also have an adverse effect on precision and accuracy of the method. When X-ray beam is passed through the tissue, there is loss of low energy spectrum which causes hardening of the beam. These errors may cause miscalculations of the BMD. Yet, newer computer aided calibration and analysis methods enhanced the suitability of the method. RA was labor intensive and highly operator dependent, thus it was unsuitable for routine diagnostic use. With the introduction of nonradiographic absorptiometric methods, RA became obsolete. But, recent advances in the ability to capture and digitize high resolution radiographic images and computerized methods for analysis of images that can correct for differences in factors such as soft tissue thickness, degree of radiographic exposure, have resulted in better enhanced precision yet less sophisticated forms of RA. SPA was considered as a suitable method for bone mineral quantization for it was simple, less radiation and uniformity of radiation field intensity. Also, SPA helps in early determination of trabeculae osteopenia and hence for osteoporosis screening.[38] But, the radionuclide source needs to be replaced two or three times a year, which increased the maintenance cost. Also, SPA has limited ability to discriminate between normal and osteoporotic and cannot be applied on spine and proximal femur.DPA had greater accuracy in measuring the BMD of central skeletal bones. With regard to distinction between normal and abnormal subjects, data from Dual Photon Absorptiometry of lumbar spine was superior to that from Single Photon Absorptiometry of radius and ulna. DPA did have several limitations also. Machine maintenance was expensive. The 153Gd source had to be replaced yearly at a high cost. The decay of radioactive source affects the values obtained with DPA. Although mathematical formulas were developed to compensate for the effect of source decay, it remained a cause for concern, as it affects both accuracy and precision. The forms of errors in DPA may be technical, operational and during interpretation. Technical problems such as wear and tear on the disk drive, terminal, and mechanical parts of the device. Operator errors include incorrect positioning of the patient, failure to remove all metal objects from the abdominal area, incorrect entry of patient data. Interpretation errors may occur from vertebral fractures, severe degenerative disease and spinal fusion in the lumbar spine area, such physiological problems may lead to false BMC values. Later, photon source is replaced by X-ray energy source. With regard to SEXA, equipment is relatively compact and portable. Though SEXA was considered to be superior than SPA, in measuring bone density in sites such as wrist, heel and calcaneus, but with the advance of portable DXA devices for the measurement of forearm and heel bone density that do not require a water bath or tissue-equivalent gel, SXA is largely outdated. DXA is simple, precise and safe as it uses less radiation, hence can be used for children, elderly and weak persons. Scanning time is less when compared with other methods. It is the only diagnostic method to detect osteoporosis before a fracture occurs. Precision of all DXA measurements is excellent but varies with the region under investigation. Precision is best for young healthy subjects (coefficient of variation is about 1% for the spine and whole body bone measurements) but is less good for osteoporotic and obese subjects.[64] Though DXA is considered as a gold standard method it has its own limitations too. The accuracy of DXA measurements, still, can be problematic. Marked systematic differences in bone and soft tissue values are found between the three commercial systems due to differences in calibration, bone edge detection, and other factors. In addition, differences in reference data provided by each manufacturer can lead to an individual appearing normal on one machine but at risk of osteoporosis on another. It is sometimes difficult to interpret results of a DXA scan. For instance, it may be difficult to interpret the result of a scan of a spine with condition such as osteoarthritis. Thus, abnormalities or previous spine fractures may give false result. DXA scan doesn't indicate the cause for low Bone density.[63]

Irjet Template sample paragraph .Define abbreviations and acronyms the first time they are used in the text, even after they have been defined in the abstract. Abbreviations such as IEEE, SI, MKS, CGS, sc, dc, and rms do not have to be defined. Do not use abbreviations in the title or heads unless they are unavoidable.

Table -1: Comparision of Densitometric methods

Method	Source of Energy	Principles	Amount of Radiation/ Scan Time	Area of Scan
RA (Radiographic Absorptiometry)		Measurement of BMD is based on the aluminium or ivory phantom		Hand

SPA (Single Photon Absorptiometry)	Gamma ray energy.	Measurement of BMD is based on the gamma rays. Bone density is calculated by means of subtraction of the photons attenuated by the soft tissue from the photons attenuated by bone and soft tissue.	Radiation dose: 2-5 mrems Scan time:10-15 min	Wrist
DPA (Dual Photon Absorptiometry)	Gamma ray energy	Based on the Concurrent transmission of gamma rays with photon energies of 44 keV and 100 keV from Gd-153.		spine, hip or total body
SXA (single Energy X-ray Absorptiometry)	X-ray energy	Based on the photon source as a X-Ray system with solid state detectors	radiation dose EDE is 0.1 m5v scan time: about 5 min	wrist or heel
DEXA (Dual Energy X-ray Absorptiometry)	X-ray energy	Based on the measurement of the transmission of x-rays, produced from a stable x-ray source, at high and low energies	Less; Radiation dose:1-3 mrems Scan time: 2-3 mins	spine, hip or total body

5. SUMMARY AND CONCLUSION

This survey elaborates the various techniques that have been used for the measurement of bone mineral density. Bone densitometry was first described more than 100 years ago in the field of dental radiology where the bone density was determined in mandible. With today's techniques, bone density can be quantified in almost every region of the skeleton. The earlier attempts to quantify bone mineral density(BMD) used plain skeletal radiography. But, only after 40% or more bone density has been lost, it was visually apparent in radiographs. Qualitative morphometric techniques for the measurement of bone mineral density used the grading systems for the spine. It relied on the appearance of the trabecular patterns within vertebral body and appearance and thickness of the cortical shell. Singh Index was based on the patterns on proximal femur. Both of these qualitative morphometric techniques are highly subjective. Radiogrammetry is the quantitative morphometric technique that measures the dimensions of the bones using skeletal radiographs. Metacarpal Radiogrammetry measures the dimensions of the metacarpals using a plain radiograph of the hand. It demonstrates a reasonably good correlation to bone density at other skeletal sites measured with photon absorptiometric methods. Digital Radiogrammetry system performs the computerized analysis of the digitized images. DXR-BMD of the metacarpals was strongly correlated with distal and proximal radial BMD measured by SPA. Later, SPA and DPA were the techniques that were used for bone mineral analysis which allowed proper selection of the measuring site on the basis of bone composition, high accuracy and precision. SPA method was applied only to appendicular bones. To overcome the limitations of DPA, SEXA was introduced which differs with radiation source. SEXA was considered advanced than SPA that measures bone density in sites such as wrist, heel and calcaneus. After the introduction of DXA, this doesn't use water bath or tissue-equivalent gel, SEXA become obsolete. The best evaluation method for osteoporosis continues to be densitometry.

Though there are various other methods such as Computed Tomography(CT), Quantitative ultrasound(QUS), Currently, Dual energy X-ray Absorptiometry (DXA) has become the most common method for measuring bone mineral density (BMD). Dual-energy X-ray absorptiometry (DXA) was the first imaging tool developed to assess fracture risk, especially in postmenopausal women. DEXA is based on differential attenuation by tissues of two levels of X-rays. DXA is able to differentiate body weight into components of lean soft tissue, fat soft tissue and bone. This method is considered to be precise, accurate and reliable. It uses a very small dose of ionizing radiation to produce pictures of the inside of the body. The method is simple, quick and non-invasive. DXA is also effective in tracking the effects of treatment for osteoporosis and other conditions that cause bone loss.

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. Although osteoporosis in adults is diagnosed based on a T-score equal to or below – 2.5 SD, most individuals who sustain fragility fractures are above this arbitrary cutoff. DXA scanners generate 2 dimensional images of complex 3 dimensional structures, and report bone density as the quotient of the bone mineral content divided by the bone area. An obvious pitfall of this method is that a larger bone will convey superior strength, but may in fact have the same bone density as a smaller bone. The reference data used in DXA scan is based on Caucasian race. Racial differences

in bone mineral density values have been well recognized. Africans-Americans have a higher bone density than Caucasians. It is thus important to compare women to the appropriate ethnic normative reference data. The relationship between bone mineral density and fracture risk is not well defined in the non-Caucasian population. Although Asians have a lower bone density than Caucasians, data from the National Health and Nutrition Examination Survey (NHANES) study in fact have demonstrated that Asian women actually have a lower risk of hip fractures. This may be explained on the basis of differences in skeletal size between Asians and Caucasians. It is important for the technologist to ensure that the appropriate race is identified when scanning a non-Caucasian patient as misidentification will affect the results of the study. Also, the equipment is expensive, hence not widely available in developing countries like India. Often requires trained personnel to perform the scan.

Thus a new methodology that measures BMD without the influence of other factors such as race, height, weight and gender, need to developed. Even better, having as a device that is affordable and appropriately sized allowing clinicians to assess fracture risk in the clinic is the future of osteoporosis care. Also, Bone mineral density (BMD) should be considered in conjunction with independent clinical risk factors for fracture, including: low body weight, history of postmenopausal fracture, family history of fracture, and other data such as age.race and gender The World Health Organization (WHO) diagnostic criteria for osteoporosis and osteopenia are appropriate for postmenopausal Caucasian women and are applicable to DEXA assessments at the hip, spine, or forearm. But, a standardized method can be developed and assessments at various other sites such as neck, clavicle can also be considered.

Digital Xrays are one of the common imaging techniques for diagnoses of several diseases. Digital Xrays can be used to measure the bone mineral density and thereby determine the condition of risk of osteoporosis. Image processing algorithms and deep learning algorithms can be used for effective measurement of bone density. Mathematical model can be developed for the determination of bone density and T-score, based on the features of the image and independent of the factors such as age, gender, height, weight and race. Thus, a low cost, handheld device can be proposed for the diagnose of the condition of risk of osteoporosis.

Although bone density is currently the best method for assessing and quantifying fracture risk, it is important to interpret bone density assessments with caution, being aware of the limitations of current densitometry technology. As the correct diagnosis is fundamental for the identification of persons who need treatment and are at risk for complications. Advanced and complementary technologies are being developed in an attempt to help diagnose osteoporosis in its early stages, thereby reducing social and economic costs and preventing patient suffering. Osteoporosis can be prevented with an early diagnosis of this disease before fractures occur and by assessing the bone mineral density and with early treatment. Therefore, increasing awareness among doctors and the normal population, will be effective in preventing this epidemic.

REFERENCES

1. Ostlere, Simon J., and Richard H. Gold. "Osteoporosis and bone density measurement methods." *Clinical orthopaedics and related research* 271 (1991): 149-163.
2. Nelson B Watts., et al. “FRAX Facts”. Journal of Bone and Mineral Research, 2009, 24(6), 975-979.
3. (2006). Physical Principles and Measurement Accuracy of Bone Densitometry, semantic scholar.
4. Adams, J. E. (1998). Single-and dual-energy: X-ray absorptiometry. In *Bone densitometry and osteoporosis* (pp. 305-334). Springer, Berlin, Heidelberg.
5. Barnett, E., & Nordin, B. E. C. (1960). The radiological diagnosis of osteoporosis: a new approach. Clinical radiology, 11(3), 166-174.
6. Scane, A. C., Masud, T., Johnson, F. J., & Francis, R. M. (1994). The reliability of diagnosing osteoporosis from spinal radiographs. Age and ageing, 23(4), 283-286.
7. C. M. Koot, S. M. M. J. Kesselaer, G. J. Clevers,P. De Hooge, T. Weits, Chr. Van Der Werken , “Evaluation Of The Singh Index For Measuring Osteoporosis”, The Journal Of Bone And Joint Surgery, 1996.
8. Manmohan Singh, B. Lawrence Riggs, John W. Beabout, Jenifer Jowsey, ‘Femoral Trabecular-Pattern Index for Evaluation of Spinal Osteoporosis’ Annals of Internal Medicine,1972.
9. Krølner, B., Berthelsen, B., & Nielsen, S. P. (1982). Assessment of vertebral osteopenia: comparison of spinal radiography and dual-photon absorptiometry. Acta Radiologica. Diagnosis, 23(5), 517-521.
10. Doyle, F. H., Gutteridge, D. H., Joplin, G. F., & Fraser, R. (1967). An assessment of radiological criteria used in the study of spinal osteoporosis. The British journal of radiology, 40(472), 241-250.
11. N Shankar, A Vijay, Aroba Sahaya Ligesh, Ashok Kumar, M Anburajan, ‘Comparison of Singh’s Index with Dual energy x-ray Absorptiometry (DXA) in Evaluating Post-menopausal Osteoporosis’ IEEE, 2011.
12. Ovidiu Alexa, Bogdan Puha, Ioana Dana Alexa, Teodor Stefan Gheorghevici, Alexandru Filip,Bogdan Veliceasa, , ‘Is the Singh Index Useful for Evaluating Osteoporosis?’, IEEE, 2017.
13. Hauschild, O., Ghanem, N., Oberst, M., Baumann, T., Kreuz, P. C., Langer, M., ... & Niemeyer, P. (2009). Evaluation of Singh index for assessment of osteoporosis using digital radiography. European journal of radiology, 71(1), 152-158.

14. Kelly, T. L., Slovik, D. M., Schoenfeld, D. A., & Neer, R. M. (1988). Quantitative digital radiography versus dual photon absorptiometry of the lumbar spine. The Journal of Clinical Endocrinology & Metabolism, 67(4), 839-844.
15. Saville, P. D. (1967). A quantitative approach to simple radiographic diagnosis of osteoporosis: its application to the osteoporosis of rheumatoid arthritis. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *10*(5), 416-422.
16. M.J.Garton, E.M.Robertson, F.J. Gilbert,L.Gomersall and D.M.Reid, 'Can Radiologists detect osteopenia on Plain radiographs?' Clinical Radiology, 1994.
17. Masud, T., Mootoosamy, I., McCloskey, E. V., O'Sullivan, M. P., Whitby, E. P., King, D., ... & Spector, T. D. (1996). Assessment of osteopenia from spine radiographs using two different methods: the Chingford Study. The British journal of radiology, 69(821), 451-456.
18. Ahmed, A. I., Ilic, D., Blake, G. M., Rymer, J. M., & Fogelman, I. (1998). Review of 3,530 referrals for bone density measurements of spine and femur: evidence that radiographic osteopenia predicts low bone mass. Radiology, 207(3), 619-624.
19. Cosman, F., Herrington, B., Himmelstein, S., & Lindsay, R. (1991). Radiographic absorptiometry: A simple method for determination of bone mass. Osteoporosis International, 2(1), 34–38.
20. Yates, A. J., Ross, P. D., Lydick, E., & Epstein, R. S. (1995). Radiographic absorptiometry in the diagnosis of osteoporosis. The American Journal of Medicine, 98(2), 41S–47S
21. Mussolino ME, Looker AC, Madans JH, et al. Phalangeal bone density and hip fracture risk. Arch Intern Med. 1997;157:433–8.
22. Buch, I., Oturai, P. S., & Jensen, L. T. (2010). Radiographic absorptiometry for pre-screening of osteoporosis in patients with low energy fractures. Scandinavian Journal of Clinical and Laboratory Investigation, 70(4), 269–274.
23. Yang, S. O., Hagiwara, S., Engelke, K., Dhillon, M. S., Guglielmi, G., Bendavid, E. J., ... Genant, H. K. (1994). Radiographic absorptiometry for bone mineral measurement of the phalanges: Precision and accuracy study. Radiology, 192(3), 857-859.
24. Rosholm, A., Hyldstrup, L., Bæksgaard, L., Grunkin, M., & Thodberg, H. H. (2001). Estimation of Bone Mineral Density by Digital X-ray Radiogrammetry: Theoretical Background and Clinical Testing. Osteoporosis International, 12(11), 961–969.
25. Forsblad-d'Elia, H., & Carlsten, H. (2011). Bone mineral density by digital X-ray radiogrammetry is strongly decreased and associated with joint destruction in long-standing Rheumatoid Arthritis: a cross-sectional study. BMC Musculoskeletal Disorders, 12(1).
26. Bouxsein ML, Palermo L, Yeung C, Black DM. Digital X-ray radiogrammetry predicts hip, wrist and vertebral fracture risk in elderly women: a prospective analysis from the Study of Osteoporotic Fractures. Osteoporos Int. 2002;12:358–65.
27. Cameron JR, Sorenson J (1963) Measurement of bone mineral in vivo: an improved method. Science 142: 230–232
28. Whitehouse, R. W. (1991). Methods for measuring bone mass. *Curr Imaging*, *3*, 213-220.
29. Cameron JR, Mazess RB, Sorenson JA (1968) Precision and accuracy of bone mineral determination by direct photo absorptiometry. Invest Radiol 3: 141–150
30. Faulkner KG, Gluer CC, Majumdar S, Lang P, Engelke K,Genant HK (1991) Non invasive measurements of bone mass, structure and strength: current methods and experimental techniques. Am J Radiol 157: 1229–1237
31. Nilas L, Borg J, Gotfredsen A, Christiansen C (1985) Comparison of single and dual-photon absorptiometry in post menopausal bone mineral loss. J Nucl Med 26: 1257–1262
32. Single- and Dual-Photon Absorptiometry Techniques for Bone Mineral Analysis, Linda M. Thorson and Heinz W. Wahner, Journal of nuclear medicine technology,1986.
33. Nicoll, J. J., Smith, M. A., Reid, D., Law, E., Brown, N., Tothill, P., & Nuki, G. (1987). Measurement of hand bone mineral content using single-photon absorptiometry. *Physics in Medicine & Biology*, *32*(6), 697.
34. J . Z . Ilich, L . C. Hsieh, M . A. Tzagournis, J. K. Wright,M. Saracoglu,H . S. Barden And V. Matkovic, A Comparison of Single Photon and Dual X-Ray Absorptiometry of the Forearm in Children and Adults', The Bone Journal, 1994.
35. NJ Bishop, JA dePriester, TJ Cole and A Lucas, 'Reference values for radial bone width and mineral content using single photon absorptiometry in healthy children aged 4 to 10 years', Acta Paediatr. 1992 Jun-Jul; 81(6-7):463-8.
36. J.R. James a, J. Truscott b, P.J. Congdon a and A. Horsman b, 'Measurement of bone mineral content in the human fetus by photon absorptiometry', Early Hum Dev. 1986 Apr;13(2):169-81.
37. Jean J. Steichen, Paule A. Steichen, Reginald C. Tsang, 'Bone mineral content measurement in small infants by single-photon absorptiometry: current methodologic issues', The Journal of Pediatrics,1988.
38. Gordon L Bilbrey, Jeff WEix, Gordon D Kaplan , 'Value of Single photon absorptiometry in osteoporosis screening' , Journal of clinical nuclear medicine, 1988.
39. Dennis M. Black,Steven R. Cummings,Harry K. Genant, Michael C. Nevitt, Lisa Palermo and Warren Browner, 'Axial and Appendicular Bone Density Predict Fractures in Older Women' ,Journal Of Bone Mineral And Research, 1992.

40. R. Cummings et.al, 'Appendicular Bone Density and Age Predict Hip Fracture in Women', Steven JAMA, 1990.
41. M. Kleerekoper, E. Peterson, D. Nelson', B. Tilley, E. Phillips, M.A. Schork and J. Kuder, 'Identification of women at risk for developing postmenopausal osteoporosis with vertebral fractures: role of history and single photon absorptiometry', Journal of Boner and Mineral,1989
42. WahnerHW, Dunn WL, Mazess RB (1985) Dual photon (Gd- 153) absorptiometry of bone. Radiology 156: 203–206\
43. Krblner B. & Pors Nielsen S. Measurement of bone mineral content (BMC) of the lumbar spine. 1. Theory and application of a new two-dimensional dual-photon attenuation method. Scand. J. Clin. Lab. Invest. 40 (1980). 653.
44. Valkema, R., Prpic, H., Blokland, J. A. K., Camps, J. A. J., Papapoulos, S. E., Bijvoet, O. L. M., & Pauwels, E. K. J. (1994). Dual Photon Absorptiometry for Bone Mineral Measurements Using a Gamma Camera. Acta Radiologica, 35(1), 45–52.
45. Cullum, I. D., Ell, P. J., & Ryder, J. P. (1989). X-ray dual-photon absorptiometry: a new method for the measurement of bone density. The British Journal of Radiology, 62(739), 587–592.
46. Dunn, W. L., Wahner, H. W., & Riggs, B. L. (1980). Measurement of bone mineral content in human vertebrae and hip by dual photon absorptiometry. Radiology, 136(2), 485–487.
47. Thorson, L. M., & Wahner, H. W. (1986). Single-and dual-photon absorptiometry techniques for bone mineral analysis. Journal of nuclear medicine technology, 14(3), 163-171.
48. Xu, S. Z., Zhou, W., Mao, X. D., Xu, J., Xu, L. P., & Ren, J. Y. (2001). Reference data and predictive diagnostic models for calcaneus bone mineral density measured with single-energy X-ray absorptiometry in 7428 Chinese. Osteoporosis international, 12(9), 755-762.
49. Sekioka, Y., Kushida, K., Yamazaki, K., & Inoue, T. (1999). Calcaneus bone mineral density using single X-ray absorptiometry in Japanese women. Calcified tissue international, 65(2), 106-111.
50. Salamone, L. M., Krall, E. A., Harris, S., & Dawson-Hughes, B. (1994). Comparison of broadband ultrasound attenuation to single X-ray absorptiometry measurements at the calcaneus in postmenopausal women. Calcified tissue international, 54(2), 87-90.
51. Jimenez-Mendoza, D., Espinosa-Arbelaez, D. G., Giraldo-Betancur, A. L., Hernandez-Urbiola, M. I., Vargas-Vazquez, D., & Rodriguez-Garcia, M. E. (2011). Single x-ray transmission system for bone mineral density determination. Review of Scientific Instruments, 82(12), 125105.
52. Borg, J., Møllgaard, A., & Riis, B. J. (1995). Single X-ray absorptiometry: performance characteristics and comparison with single photon absorptiometry. Osteoporosis international, 5(5), 377-381.
53. Bjarnason, K., Nilas, L., Hassager, C., & Christiansen, C. (1995). Dual energy X-ray absorptiometry of the spine—decubitus lateral versus anteroposterior projection in osteoporotic women: Comparison to single energy X-ray absorptiometry of the forearm. Bone, 16(2), 255-260.
54. Sone, T., Imai, Y., Tomomitsu, T., & Fukunaga, M. (1998). Calcaneus as a site for the assessment of bone mass. Bone, 22(5), 155S-157S.
55. Kelly, T. L., Crane, G., & Baran, D. T. (1994).Single X-ray absorptiometry of the forearm: precision, correlation, and reference data. Calcified tissue international, 54(3), 212-218.
56. Greenspan, S. L., Bouxsein, M. L., Melton, M. E., Kolodny, A. H., Clair, J. H., Delucca, P. T., ... & Orwoll, E. S. (1997). Precision and discriminatory ability of calcaneal bone assessment technologies. Journal of Bone and Mineral Research, 12(8), 1303-1313.
57. Bennett, H. S., Dienstfrey, A., Hudson, L. T., Oreskovic, T., Fuerst, T., & Shepherd, J. (2006). Standards and measurements for assessing bone health—workshop report co-sponsored by the International Society for Clinical Densitometry (ISCD) and the National Institute of Standards and Technology (NIST). Journal of Clinical Densitometry, 9(4), 399-405.
58. John J. Carey • Miriam F. Delaney, 'T-Scores and Z-Scores', Clinic Rev Bone Miner Metab (2010) 8:113–121
59. Binkley, N., Kiebzak, G. M., Lewiecki, E. M., Krueger, D., Gangnon, R. E., Miller, P. D, Drezner, M. K. (2004). Recalculation of the NHANES Database SD Improves T-Score Agreement and Reduces Osteoporosis Prevalence. Journal of Bone and Mineral Research, 20(2), 195–201.
60. Lorente Ramos, R. M., Azpeitia Armán, J., Arévalo Galeano, N., Muñoz Hernández, A., García Gómez, J. M., & Gredilla Molinero, J. (2012). Dual energy X-ray absorptimetry: Fundamentals, methodology, and clinical applications. Radiología (English Edition), 54(5), 410–423
61. Sturtridge, W., Lentle, B., & Hanley, D. (1996). The Use Of Bone Density Measurement in the Diagnosis and Management of Osteoporosis. Cmaj. Canadian Medical Association journal, 155(7), 924-929.
62. Knapp, K. (2015). Dual Energy X-Ray Absorptiometry: Beyond Bone Mineral Density. Imaging & Therapy Practice, 5.
63. Garg, M. K., & Kharb, S. (2013). Dual energy X-ray absorptiometry: pitfalls in measurement and interpretation of bone mineral density. Indian journal of endocrinology and metabolism, 17(2), 203.
64. Choplin, R. H., Lenchik, L., & Wuertzer, S. (2014). A Practical Approach to Interpretation of Dual-Energy X-ray Absorptiometry (DXA) for Assessment of Bone Density. Current Radiology Reports, 2(6), 48.

65. Van der Sluis, I. M., De Ridder, M. A. J., Boot, A. M., Krenning, E. P., & de Muinck Keizer-Schrama, Sp----. M. P. F. (2002). Reference data for bone density and body composition measured with dual energy x ray absorptiometry in white children and young adults. Archives of disease in childhood, 87(4), 341-347.
66. Dhainaut, A., Hoff, M., Syversen, U., & Haugeberg, G. (2016). Technologies for assessment of bone reflecting bone strength and bone mineral density in elderly women: an update. Women's Health, 12(2), 209-216.
67. Crabtree, N. J., Leonard, M. B., & Zemel, B. S. (2007). Dual-energy X-ray absorptiometry. In Bone Densitometry in Growing Patients (pp. 41-57). Humana Press.
68. Binkovitz, L. A., & Henwood, M. J. (2007). Pediatric DXA: technique and interpretation. Pediatric radiology, 37(1), 21-31.
69. Lorente-Ramos, R., Azpeitia-Armán, J., Muñoz-Hernández, A., García-Gómez, J. M., Díez-Martínez, P., & Grande-Bárez, M. (2011). Dual-energy x-ray absorptiometry in the diagnosis of osteoporosis: a practical guide. American Journal of Roentgenology, 196(4), 897-904.
70. Lewiecki, E. M., Binkley, N., Morgan, S. L., Shuhart, C. R., Camargos, B. M., Carey, J. J., ... & Leslie, W. D. (2016). Best practices for dual-energy X-ray absorptiometry measurement and reporting: International Society for Clinical Densitometry Guidance. Journal of Clinical Densitometry, 19(2), 127-140.
71. Blake, G. M., & Fogelman, I. (1997, July). Technical principles of dual energy x-ray absorptiometry. In Seminars in nuclear medicine (Vol. 27, No. 3, pp. 210-228). Elsevier.
72. DeVita, M. V., & Stall, S. H. (1999). Dual-energy X-ray absorptiometry: a review. Journal of Renal Nutrition, 9(4), 178-181.
73. Dimai, H. P. (2017). Use of dual-energy X-ray absorptiometry (DXA) for diagnosis and fracture risk assessment; WHO-criteria, T-and Z-score, and reference databases. Bone, 104, 39-43.
74. , K. J., Shypailo, R. J., Hardin, D. S., Perez, M. D., Motil, K. J., Wong, W. W., & Abrams, S. A. (2001). Z score prediction model for assessment of bone mineral content in pediatric diseases. Journal of Bone and Mineral Research, 16(9), 1658-1664.
75. Tothill, P. (2005). Dual-energy x-ray absorptiometry measurements of total-body bone mineral during weight change. Journal of Clinical Densitometry, 8(1), 31-38.
76. Theodorou, D. J., Theodorou, S. J., & Sartoris, D. J. (2002). Dual-energy X-ray absorptiometry in diagnosis of osteoporosis: basic principles, indications, and scan interpretation. Comprehensive therapy, 28(3), 190-200.
77. Singh, S. K., Patel, V. H., & Gupta, B. (2017). Comparison of Indian Council for Medical Research and Lunar Databases for Categorization of Male Bone Mineral Density. Journal of Clinical Densitometry.
78. Simpson, D. E., Dontu, V. S., Stephens, S. E., Archbold, L. J., Lowe, V., O'doherty, M. J., ... & Coakley, A. J. (2005). Large variations occur in bone density measurements of children when using different software. Nuclear medicine communications, 26(6), 483-487.
79. International Atomic Energy Agency. (2011). Dual Energy X Ray Absorptiometry for Bone Mineral Density and Body Composition Assessment: IAEA Human Health Series. International Atomic Energy Agency.
80. Patni, R. (2010). Normal BMD values for Indian females aged 20–80 years. Journal of mid-life health, 1(2), 70.
81. Diagne-Gueye, N. M., Soko, T. O., Ndiaye, B., Diedhiou, I., & Ndiaye, A. R. (2016). DEXA Contribution in Bone Densitometry Evaluation on Osteoporosis in Senegal: Results of a Study Realized in African Black Populations. Open Journal of Rheumatology and Autoimmune Diseases, 6(04), 85.
82. Nakavachara, P., Pooliam, J., Weerakulwattana, L., Kiattisakthavee, P., Chaichanwattanakul, K., Manorompatarasarn, R., ... & Viprakasit, V. (2014). A normal reference of bone mineral density (BMD) measured by dual energy X-ray absorptiometry in healthy thai children and adolescents aged 5–18 years: a new reference for Southeast Asian Populations. PLoS One, 9(5), e97218.
83. Leonard, M. B., Feldman, H. I., Zemel, B. S., Berlin, J. A., Barden, E. M., & Stallings, V. A. (1998). Evaluation of low density spine software for the assessment of bone mineral density in children. Journal of Bone and Mineral Research, 13(11), 1687-1690.
84. Kocks, J., Ward, K., Mughal, Z., Moncayo, R., Adams, J., & Hogler, W. (2010). Z-score comparability of bone mineral density reference databases for children. The Journal of Clinical Endocrinology & Metabolism, 95(10), 4652-4659.