INTRODUCTION AND AIM OF THE WORK

Osteoporosis is a chronic bone disease that affects mainly females (80%), usually after the onset of menopause. It is characterized by decrease bone mass and deterioration of bone at the microscopic level, the structural integrity of trabecular bone is impaired. Cortical becomes more porous and thinner, resulting in increased fragility and high risk fracture ***(Rosen et al., 2003) (Milotti et al., 2003)***

Bone is a living tissue that remodels itself throughout life. However peak bone maturation is reached at about age 30 years and begins to decline there after. Menopause the rate of bone mass loss ***(Milotti et al., 2003).***

In the years following menopause, women will naturally experience bone loss because of a disease in estrogen, most will have no symptoms, ever while the disease progresses. Age thin or small built, alcohol abuse, low sun exposure, family history, early menopause, certain medications, inadequate calcium intake, previous fracture, are all risk factors for osteoporosis ***(Vogt et al., 1996; Milotti et al., 2001 and Van Schoor et al., 2003).***

To accurately diagnose osteoporosis a physician must be able to exclude other causes of low bone mass. A

complete medical history, physical examination and a laboratory test is to check for secondary causes of osteoporosis such as cases of renal or hepatic failure, anemia, hypercalciuria, and abnormalities of calcium and phosphors ***(Hodgson et al., 2001 and Milotti et al., 2003).***

For bone mass measurement, several technique are available including:

- Quantitative computed tomography for measurement of both central and peripheral sites.
- Quantitative ultrasonometry.
- Radiographic absorptiometry.
- Single –energy X-ray absorptiometry.

(Wasnich and Miller, et al., 2000).

Dual energy X-ray absorptiometry (DEXA) on the other hand is the most accurate and advanced test available for measuring bone mass with excellent resolution and reproducible precision. Mineral radiation (less than 1/120 of a chest X-ray) is used to determine the bone density of the spine, hip or wrist. A DEXA test is more sensitive than ordinary X-ray, more accurate than radiograms (radiographic absorptiometry) and can diagnose bone loss at an earlier stage. safer and painless, the average 10 - 15 min DEXA scan is most reliable test to determine even the

earliest stages of bone loss associated with osteoporosis. Most institutions consider it the preferred diagnostic method to determine your actual bone density and fracture, to reveal signs of bone loss with the fewest false positive or false negative results, to diagnose low bone mass that may signal the need for treatment ***(Vogt et al., 1996 and Milotti et al., 2003).***

AIM OF THE WORK

The aim of this work is to study the role of DEXA in quantifying bone mineral mass loss at risk areas in non-influenced post menopausal females in relation to age.

PATHOGENESIS OF OSTEOPOROSIS

Definition of osteoporosis:

Old definition: a reduced amount of bone that is qualitatively normal ***(Albright, 1947).***

(1) Modern definition: a systemic skeletal disease characterized by low bone mass and micro architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture ***(Anonymous, 1993).***

(2) Newest definition: osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture, bone strength reflects the integration of two main features; bone density and bon ***(Lindsay et al., 2001).***

The composition of bone :

(1) Bone matrix is 90% collagen (type 1 collagen crosslinks of N-telopeptides, C-telopeptides and deoxypyridinolines) and 10% other proteins (osteocalcin, osteonectin, osteopontin) they are the basis for the commercial assays for bone turnover markers.
(2) Bone mineral is hydroxyapatite (calcium and phosphorus)

(3) Bone cells are osteoclasts, osteoblasts, osteocytes, and lining cells.

(Jachna et al., 2003)

Bone modeling and remodeling :

(1) Bone growth occurs as a result of modeling: renewal of bone substance and alteration in the size and shape of bone.

(2) Bone health is maintained by remodeling: replacement of old bone with new bone. The bone remodeling cycle is a coordinated sequence of activation, resorption, and formation.

(3) Bone remodeling is done by osteoclasts (cells derived from bone marrow precursors) that remove old bone (resorption) and osteoblasts (cells derived from mesenchymal precursors) that produce new bone matrix which then becomes mineralized mature bone (formation).

(4) Bone loss occurs when resorption exceeds formation.

(Jachna et al., 2003)

Peak bone mass:

(1) Peak bone mass is the maximum bone mass or density achieved during a lifetime. it is reached when the growth in the size of bones and accumulation of bone mineral has stabilized (consolidation).

(2) Different skeletal sites reach maturity at different times: trochanter, mid-teens; femoral neck, late teens, spine early 20s.

(3) Determinations of peak bone mass include heredity (70-80%) (sex and race) and life style factors (20-30%) (calcium, vitamin D exercise, smoking, alcohol intake …etc).

(Liel et al., 2003)

Changes in bone density with age :

(1) There is a dramatic increase in BMD during adolescence.

(2) Peak bone mass is achieved in the teens or early 20s.

(3) A plateau is maintained for a time.

(4) Age-related bone loss occurs at a rate of 0.5%-1.0% per year.

(5) Bone loss accelerates with menopause (1.0%-2.0% per year) this acceleration phase lasts 5-10 years.

(6) Age-related bone loss continues, with bone loss eventually going back down to pre-adolescent levels.

(Feldstein et al., 2004).

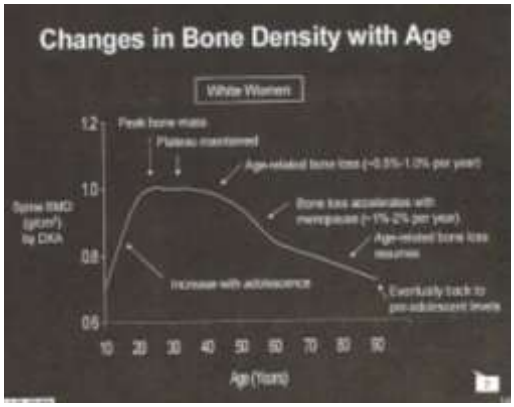

Fig. (1): Quoted from ISCD version, 2009

Different skeletal regions have different types of bone: (Types of bones according to skeletal site)

(1) Cortical or compact bone makes up the shaft of long bones and the outer envelope of all bones. Cortical bone makes up about 80% of the skeleton, but is only about 20% of the surface area. 3% of cortical bone is renewed each year.

(2) Cancellous or trabecular bone makes up the inner part of the bones of the central skeleton, Cancellous bone accounts for about 20% of the skeleton but 80% of the surface area. about 25% of cancellous bone is renewed each year.

(3) About 10% of the skeleton is being remodeled at any one time.

(Kamel et al., 2000).

Bone loss occurs at different times and rate (cancellous and cortical):

(1) Cancellous bone loss is rapid in the early menopause, wrist fracture increase in the frequency as cancellous bone loss begins. As cancellous bone loss continues the risk of the vertebral fracture increases.

(2) Cortical bone loss is more gradual, but also more persistent .the risk of hip fracture increases as a result of the loss of both cancellous and cortical bone.

(Panneman et al., 2004).

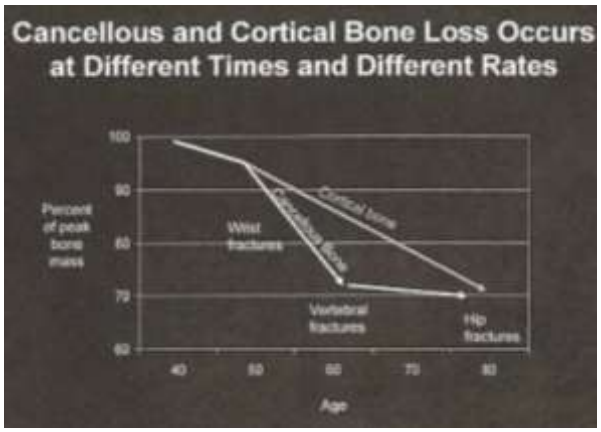

Fig. (2): Quoted from ISCD version, 2009

Osteoporosis may result from low peak bone mass or bone loss or both, women have low bone peak mass than men, whites have lower peak bone mass than blacks, bone loss occurs with advancing age, because resorption is greater than formation, as bone loss occurs, there is loss of quality as well as quantity, there are no symptoms from low bone mass or from bone loss ***(Seeman, 2002).***

WHO classification for postmenopausal osteoporosis:

(1) The T-score compares an individual BMD with the mean value for young normal, and expresses the difference as a standard deviation score.

(2) Normal, T-score -1.0 and above.

(3) Low bone mass (osteopenia (low bone density) between -1.0 and -2.5.

(4) Osteoporosis, -2.5 and below.

(WHO, 1994)

Types of fracture, epidemiology and incidence of osteoporotic fracture:

(1) Traumatic fracture.

(2) Pathological fracture –a fracture that occurs in an area of bone previously weakened by another process .(tumor, infection, inherited bone disorder)

(3) Stress fracture –a hairline fracture of bone resulting from repeated stress.

(4) Osteoporotic fracture ((fragility fracture or low – trauma occurring with minimal trauma, such as force equal to or less than falling from standing height.

(Port et al., 2003).

Fracture incidence is bimodal, with peaks in youth (15-25) and again over age 45, in young people, fracture of long bones predominate, often occur following substantial trauma, and the incidence is greater in men than women, above the age of 45, fracture incidence in women increases so that the rate in women becomes twice that of men, and fractures are of the fragility type ***(Harrington et al., 2002)***.

In women, the incidence of forearm fracture begins to rise about age 45 or 50 and levels off around age 65. The incidence of clinical vertebral fracture begins to increase around the age 55 or 60 and rises linearly thereafter; the incidence of hip fracture begins to rise about 65 and increases exponentially ***(Khan et al., 2001).***

Patients with prior fracture are at high risk for future fragility fractures, patients with wrist or vertebral fracture are at increased risk of wrist, spine and hip fracture, patients with hip fracture are at increased risk of spine and hip fracture ***(Siris et al., 2003).***

BASIC PRINCIPLES OF DEXA

Technique for bone mass measurement:

Wide range of commercially bone densitometry devices, classified according to their capability to measure specific skeletal sites:

(i) Central devices are capable of measuring spine and hip. these devices can also measure the forearm and total body .

(ii) Peripheral devices are capable of measuring wrist, heel, fingers, etc.

Instruments may be classified by their technology platform(x-ray based or ultrasound based)

Classification according to skeletal sites into:

(i) Central sites are the vertebral column, ribs and sternum, pelvis and femur .

(ii) Peripheral sites include the upper and lower extremities (but not the proximal femur)

Principles of DEXA operation

(1) Principles behind absorptiometry (X-ray attenuation):

Attenuation refers to a reduction in the number and energy of photons in an X-ray beam (its intensity) attenuation is determined largely by tissue density and thickness, the more the tissue, the more electrons it contains, the number of electrons in the tissue determines the ability of tissue to attenuate photons in the X-ray beam.

If the degree of attenuation can be quantified, then it would be possible to quantitatively asses the tissue density as well, when using a single energy X-ray beam the incident beam (I0) is attenuated proportionally to the total amount of mass through which it passes and the beam that is transmitted (I) is detected. (We can not separate how much of that mass is due to bone or soft tissue or both) ***(Blake et al., 1997).***

(2) Dual energy why ?

The proportion of radiation transmitted through the patient depends on the energy of X-ray photons, physical density of the body, and body thickness, using two different X-ray energies allows a DEXA device to record attenuation profiles at two different photons energies, at low energy (30-50Kev) bone attenuation is greater than soft tissue attenuation, whereas at high energy (greater than 70 Kev) bone attenuation is similar to soft tissue attenuation. Thus,

two types of tissue are distinguished: bone (hydroxyapatite) and soft tissue (everything else).

Solving the two unknowns (bone and soft tissue mass) two equations are needed. The equations for attenuation for two different X-ray energies results in two unique equation, as such one can solve for both bone and soft tissue mass.

Integral bone mass in the path of an X-ray beam (BMC in grams) divided by projection area of bone (all pixel recognized as bone by edge-detection algorithm, cm2) results in BMD (reported in g/cm2) ***(Formica et al., 1998).***

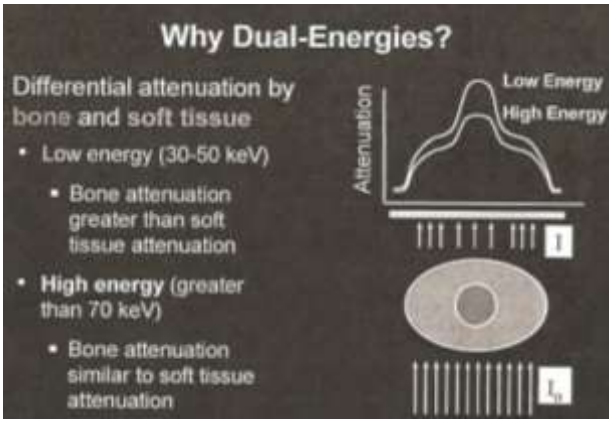

Fig. (3): Quoted from ISCD version, 2009

(3) DEXA system requirements (X-ray tube, collimator and X-ray detector)

X-ray photons are produced by an X-ray tube. An X-ray tube consists of a cathode (negative charged) and an anode (positive charged) encased in a vacuum tube. It uses

a high-voltage source. Approximately 99% of X-ray tube energy is lost to heat. Less than1% appears as X-rays. Before it reaches the patient the X-ray beam is collimated (shaped) into a narrow pencil-beam (using a pinhole collimator) or fan-beam (using a collimator), collimation is used to keep the scattered electrons from reaching the detector, beam passes through the patient and is selectively attenuated by the patients bone and soft tissue.

After the X-ray beam leaves the patient, it passes to the x-ray detector where the intensity of transmitted radiation is recorded, the type of the detector depends on the type of system (K-edge filter VS voltage switching, pencil-beam VS fan-beam) X-ray tube, collimator, and detector are aligned and mechanically linked using a scanner arm ***(Yu et al., 1995).***

(4) <u>Different approaches of producing dual-energies</u>:

(i) K-edge filtering, use a constant –potential generator and a K-edge filter to split the polyenergetic X-ray beam into high and low energy component, either by using a cerium filter that results in energy peaks of 40 and 70 Kev or a samarium filter that results in energy peaks of 45 and 80 Kev. Because either a low or high energy photon can hit the detector at any given moment, the detector needs to determine if the photon was high or low energy, this is done with an energy