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The value of lateral chest radiographs in the assessment of bone density and detection of osteopenia

Monica Anna Medynski
Yale University

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ABSTRACT

THE VALUE OF LATERAL CHEST RADIOGRAPHS IN THE ASSESSMENT OF BONE DENSITY AND THE DETECTION OF OSTEOPENIA. Monica A. Medynski. Department of Diagnostic Radiology, Yale University, School of Medicine, New Haven, CT

The reading of "osteopenia" on a lateral chest radiograph, using a high KvP technique, does not correlate with the presence of osteoporosis as demonstrated on bone biopsy. 35 lateral chest films of patients with identified osteoporosis through a bone biopsy and 26 lateral chest films of patients with no evidence of osteoporosis on bone biopsy were coded. All the radiographs were reviewed by three radiologists, two chest and one bone specialist, who were asked to use specified criteria for the detection of osteopenia. The data was analyzed for interobserver and intraobserver variability using weighted kappa. Odds ratios were calculated to see if any of the criteria we used in evaluating lateral films could correctly predict the presence of osteoporosis. The radiologists seemed relatively consistent in their evaluation of osteopenia. Weighted kappa comparing viewing one and viewing two were equal to 0.60, 0.58, and 0.60 for the three readers, representing "moderate/acceptable" agreement. As is usual, there was less agreement between the readers: the interobserver variability fell into the range of "fair/moderate" with weighted

kappa for general assessment of osteopenia equal to 0.40, 0.45, and 0.53. None of the criteria seemed to reliably predict the presence of osteopenia based on the calculation of odds ratios with a 95% confidence interval. In conclusion, our results prove osteopenia in the thoracic spine may not be consistently detected on lateral chest radiographs, at least with this physician sample. The fact that one radiologist was capable of detecting osteopenia suggests that there may be as yet an inarticulated template that corresponds to osteopenia of the spine. This has major implications for radiology education. Further efforts to either articulate the template or provide multiple shared experiences of film interpretation to transmit the template are warranted.

PROPER TERMINOLOGY

Prior to beginning any discussion about osteoporosis, it is necessary to understand the proper terminology. In 1885 Pommer made the first distinction between osteoporosis, decreased skeletal mass associated with increased porosity, and osteomalacia, decreased mineralization associated with nonmineralized osteoid seams due to vitamin D deficiency. Osteoporosis consists of qualitatively normal but quantitatively deficient bone. Another important term to comprehend is osteopenia. Osteopenia simply means poverty of bone and on an x-ray presents as increased radiolucency.[1] Osteopenia is "a nonspecific term used to describe a pathologically decreased quantity of bone without implying the cause."[2] The appearance of osteopenia on an x-ray is not automatically equivalent to osteoporosis. Major causes of diffuse osteopenia include osteoporosis, osteomalacia, hyperparathyroidism, and neoplasms. Characteristic radiographic findings can distinguish the various causes of osteopenia. Osteomalacia presents with linear radiolucent areas termed Looser's zones; hyperparathyroidism displays aggressive subperiosteal and subchondral resorption of the bone; and neoplasms, such as plasma cell myeloma, have focal skeletal radiolucent lesions. In order to diagnose osteoporosis roentgenographically osteopenia of the bones must be combined with the appropriate clinical and histological picture.[1] When a radiologist evaluates a film without

proper history he/she can only comment on the presence or absence of osteopenia not osteoporosis.

GENERAL BACKGROUND

Osteoporosis is the most common adult metabolic bone disease and an important cause of morbidity in the elderly.[1] Osteoporosis is defined as a generalized decrease in bone mass with increased fragility but no chemical abnormalities in the remaining bone. The term describes a heterogeneous group of disorders of bone remodeling (Table I) with a common final outcome - decreased density (mass/unit volume) of normally mineralized bone.[3] Increased rate of bone resorption rather than reduction in the rate of bone formation leads to osteoporosis.[4] Osteoporosis is a serious disease which affects approximately 25 million Americans, results in 1.5 million skeletal fractures per year, and incurs a direct and indirect cost of $18 billion annually.[5] It usually presents with low back pain, shortening of trunk height, brittle bones, and recurrent fractures at quite irregular intervals.[6] Skeletal fractures constitute the gravest consequence of osteoporosis; hip fractures are fatal in 12-20% of the patients and more than 50% of the survivors require long term nursing home care.[7] Life time risk of hip fractures for women in United States at the age of 50 is between 11-18%.[8] No real cure exists for osteoporosis. Osteoporosis can be prevented through education and proper nutrition early in life.

Table I: Classification of generalized osteoporosis

Primary	Secondary
Idiopathic juvenile osteoporosis	Hypercortisolism
Idiopathic osteoporosis in young adults	Hypogonadism
Involution osteoporosis	Hyperthyroidism
type I (postmenopausal)	Diabetes Mellitus
type II (senile)	Hyperparathyroidism
type III (associated with increased parathyroid function)	Seizure disorders (anticonvulsants)
	Gastrectomy
	Malabsorption syndrome
	Rheumatoid arthritis
	Connective tissue disease
	Chronic obstructive lung disease
	Chronic neurologic disease
	Malignancy

EPIDEMIOLOGY OF OSTEOPOROSIS

Overall, the majority of victims of osteoporosis are postmenopausal females. Osteoporosis can be subdivided into three categories: generalized - involving major portions of the skeleton, usually the axial component; regional - involving one segment of the skeleton; and localized - involving single or multiple focal areas.[1] As Table I demonstrates osteoporosis can be primary or secondary. Secondary osteoporosis can present at any age, in males and females of any racial background. It can be "treated" by correcting the specific underlying condition; the affected bone may never revert to normal, but future bone loss can be prevented. In primary osteoporosis prevention of further bone loss is much harder. Primary involution osteoporosis describes the condition of gradual, progressive bone loss often accompanied by fractures. It is separated into three types: type I - postmenopausal, type II - senile, and type III - associated with increased parathyroid function. Type I osteoporosis arises from estrogen deficiency in postmenopausal women age 50 to 65. It is dominated by accelerated and disproportionate trabecular bone resorption leading to vertebral and Colles' fractures.[3] About 50% of women have osteoporosis by the age of 65 and almost 100% by age 80.[9] In one study of ambulatory women age 45 to 79, the incidence of radiographically demonstrable osteoporosis (wedge-shaped vertebrae or compression fractures) was 29%.[10] Type II osteoporosis affects both sexes equally after the age of 75, has

proportionate loss of both trabecular and cortical bones, and leads predominantly to fractures of the hip, proximal humerus, tibia, and pelvis.[3] The prevalence of osteoporosis with increasing age becomes exponential after the age of 50.[8] Type III osteoporosis is a consequence of hyperparathyroidism which leads to increase in both bone formation and resorption.[1]

According to G. Alan Rose everyone begins to display progressive loss of bone starting at the age of 25, regardless of sex or race.[4] His age estimate is on the early side and most authors believe that true age-related bone loss begins around the age of 40 in both men and women.[5] Up to the age of 80 women appear to develop osteoporosis four times as frequently as their male counterparts.[1] Accelerated bone loss in postmenopausal women is superimposed on the age-related bone loss, which is believed to be of a greater degree in women. Women lose about 35%-40% of their cortical bone and 55%-60% of trabecular bone, while men lose approximately two-thirds of the above amounts.[5] The cumulative losses of bone mass range from 20% to 30% in men and 40% to 50% for some women.[11] By the age of 75 skeletal mass maybe reduced to one half of what it was at the age of 30.[5]

Certain risk factors for osteoporosis are genetic and can not be altered by the individual. However, other risk factors can be eliminated by changes in life style or medication regimens (Table II). The amount of bone at the peak bone mass in the young adult is genetically

predetermined as is the number of mast cells in the bone marrow capable of producing heparin and other substances that modulate bone cell function.[11] Kaplan believes the peak bone density is reached around the age of 35 and is ultimately determined by heredity, race, nutrition, and exercise.[5] The mass of the skeleton varies with sex and race. White females have the lightest skeleton, white males and black females have an intermediate mass, while black males have the heaviest skeletons.[12] Women who are small, white, sedentary, nulliparous, and postmenopausal, with lifetime history of dietary calcium deficiency, are prime candidates for developing osteoporosis.[5]

Table II Risk factors for osteoporosis

smoking	chronic vitamin C deficiency
excessive alcohol use	anorexia nervosa
immobilization	vitamin D deficiency
lack of weight-bearing activity	long-term heparin use
low calcium intake	methotrexate
steroid use	phenytoin
oophorectomy	barbiturates
thinness	heavy metals
inactivity	excessive acid intake

In order to understand the mechanism of osteoporosis, a general idea of bone formation and resorption must be grasped. Although people think of bones as formed solid supports for the body, the human skeleton is a dynamic organ - it is in a constant state of remodeling. As much as 15% of total bone mass turns over each year. Two types of bone comprise the human skeleton: cortical bone and trabecular bone. Approximately 80% of bone mass comes from cortical bone and 20% from trabecular bone, but trabecular bone has a much larger surface area and is metabolically more active.[13] "Vertebral trabecular bone appears to be the most active trabecular bone of the human body in terms of mineral turnover rate."[15] Cortical (compact) bone makes up the dense outer layers of the appendicular skeleton and the thinner outer layer of flat bones. Trabecular (cancellous) bone is composed of bridges of bone spicules chiefly in the inner parts of the axial skeleton and smaller interior of shafts of long bones.[13]

Frost introduced the concept of intermediary organization of the skeleton with discrete functional systems where bone cells do not work as individuals, but in groups. The cell types in different functional systems are the same, but the final outcome of their work is very different - for instance growth vs. remodeling.[14] Until about the age of 20 bone formation exceeds bone resorption and results in linear growth. Peak bone mass is reached between the ages of 20 and 30. Bone resorption

equals bone formation until age 35 to 40 and thereafter bone resorption exceeds bone formation.[13]

Three basic cell types exist in human bone: osteoblasts, osteoclasts, and osteocytes. Bone formation belongs to the osteoblasts which deposit the bone matrix and are responsible for its mineralization. These cells arise from osteoprogenitor cells which are related to fibroblast precursors. Osteoblasts secrete soluble collagen which aggregates into fibrils where nucleating points become established in association with phosphate binding. Mineralization proceeds spontaneously if normal plasma levels of calcium and phosphorus exist. Osteoblasts secrete the matrix at 1*um*/day; this osteoid matures and becomes mineralized in 5 to 10 days. Osteoclasts have the job of bone resorption. They secrete enzymes which dissolve the mineral and lyse the matrix. Osteoclasts are multinuclear giant cells which need a free surface, not one covered with osteoid, to resorb. The osteoclast's life span of a few days allows resorption of eight times the amount of bone that can be formed by an osteoblast during its life of several weeks. An osteocyte is simply an osteoblast which decreased its synthetic activity during mineralization process. It is contained in a lacuna and has the capacity to resorb perilacunar bone.[13]

A well-regulated coupling process of bone formation and bone resorption occurs within osteons and results in bone remodeling. When bone formation lags behind bone resorption, the two processes uncouple, and osteoporosis develops.[14]

CLINICAL PRESENTATION OF OSTEOPOROSIS

The majority of the patients suffering from osteoporosis, especially early in the course of the disease, have no symptoms. Some postmenopausal women might notice a slight decrease in height and encounter nonspecific lower back pain. Height loss (kyphosis) is most rapid between the ninth and twelfth postmenopausal years and then slows down; loss of height may even cease spontaneously.[4] Osteoporosis becomes a clinical problem when patients begin to experience pathologic fractures accompanied by excruciating pain, usually localized to the fracture site. Acute episodes of pain may be accompanied by abdominal distention and an ileus due to retroperitoneal hemorrhage associated with compression fractures. Patients can also experience loss of appetite as well as muscular weakness.[11]

Fractures occur because decreased bone mass leads to increased skeletal fragility. Bone mineral mass is not the only determinant of fracture incidence[16]; bone structure is also important to the mechanical strength of bone and its tendency to fracture.[17] A surprisingly high number of fractures occur in bed without any exertion or strain, while others tend to be temporally related to standing up, walking, light lifting, bending or jumping. The three most common site of fractures in descending order are: vertebral body, hip, and distal radius (Colles').[8] In the vertebral column a predilection for fractures of T8, T12, L1, and L3 exists.[18] Cervical and upper thoracic vertebra are never involved in

osteoporosis.[19] Any fracture above T5 can not be dismissed as osteoporosis and needs further work-up, especially to rule out cancer. When vertebral fractures occur, they are usually anteriorly located leading to a wedge shaped deformity (figure 1) and contributing to height loss. Complications of vertebral fractures include loss of axial height, loss of exercise tolerance, early satiety, loss of self esteem, and positive body image, fear of additional compression fractures, and chronic back pain while standing. Appendicular fractures especially those of proximal femur are among the most dreaded complications of osteoporosis.[5] Many patients either die from complications of femoral fractures or are quite debilitated and never return to their pre-fracture level of functioning.

DIAGNOSIS OF OSTEOPOROSIS

Three methods can be implemented to diagnose osteoporosis: histologic, radiographic, and volumetric.[20] Osteoporosis is usually diagnosed radiographically since no good noninvasive laboratory tests exist. In asymptomatic postmenopausal osteoporosis, results of routine laboratory tests are all normal. Plasma levels of alkaline phosphatase may rise transiently following a fracture for several weeks. Urinary calcium is high during the active phase of demineralization, but later in the "burnt-out" phase urinary calcium becomes normal or even low. Only raised fecal calcium is a feature of osteoporosis of almost any etiology. It results from impaired absorption of dietary calcium not

increased calcium secretion.[4] Fecal calcium measurements are not routinely performed for screening purposes.

Roentgenographic procedures are not good at early detection of osteoporosis. Actually some authors go as far as to say osteoporosis can only be diagnosed on plain films in the presence of spontaneous fractures.[21] Controversy surrounds the actual amount of skeletal calcium loss needed before characteristic patterns (Table III) can be observed on x-rays, but most authors agree it lies between 30-60%.[4,2] Landoff believes detection is possible at a mineral loss of only 10-15%.[22]

Table III. Characteristic Radiographic Appearance of Osteoporosis

increased transradiancy (reduced bone density of vertebral bodies)
loss of horizontal trabeculae
sharper than normal definition of superior and inferior plates
reduction of the thickness of the cortex
Schmorl's nodes
increased biconcavity
presence of fractures
21,23,24,25

HISTOLOGIC DIAGNOSIS OF OSTEOPOROSIS

Multiple noninvasive techniques have been designed for diagnosis of osteoporosis, but the gold standard continues to be an invasive bone biopsy. Bone histomorphometry remains the only method which gives access to a direct and precise analysis of both static and dynamic cellular and tissue abnormalities and in particular to the measurements

made at the intermediary level of organization of bone - the osteon.[3] Bone biopsy, usually of the iliac crest represents an invasive procedure. The majority of the patients seeking medical advise for osteoporosis do not need bone biopsies. When the differential diagnosis includes multiple myeloma, bone metastases, osteomalacia, or chronic major organ system disease bone biopsies are generally performed.[14] Bone biopsies are also performed for research purposes to help understand the pathophysiology of complex processes.[3]

Since bone biopsy is an invasive procedure and not all patients will consent to it, non-invasive diagnostic and screening techniques were developed. Chest, lumbar spine, and femoral neck radiographs, as well as single photon absorptiometry, dual photon absorptiometry, dual x-ray absorptiometry, quantitative computed tomography, and magnetic resonance imaging have all been used. Various centers rely on some or all of the above techniques.

RADIOGRAPHIC DIAGNOSIS OF OSTEOPOROSIS

One of the most commonly used and simplest radiologic examinations is the chest radiograph. Whole body dose equivalents of radiation from a chest radiograph equal 8 mrems for males and 11 mrems for females.[26] Assessment based upon the image of the lateral spine provided by chest radiograph has a low level of sensitivity and large interobserver variability problem compounded by poor contrast present on high KvP films.[2] Multiple authors have criticized the use of

plain chest radiographs as a diagnostic tool for osteoporosis, yet radiologists continue to comment on the presence or absence of osteoporosis on lateral chest films.

In 1967 Doyle evaluated six criteria used to study spinal osteoporosis on chest films and concluded none of them were reliable indicators of osteoporosis:

1) Reduced bone density and increased translucency. Detection relied on contrast difference to adjacent tissue. Radiographs taken at inspiration or those with a slight tilt in the sagittal axis appeared more osteoporotic

2) Loss of horizontal trabeculae. It was impossible to identify individual trabeculae and to asess them reliably on a lateral chest radiograph. Besides, not every person with osteoporosis demonstrated accentuation of the vertical trabeculae due to the loss of horizontal trabeculae

3) Reduction of cortex to at least half of those without osteoporosis. Cortical thickness was too small to measure with the degree of precision required and no standard thicknesses had been identified.

4) Sharper than normal definition of the superior and inferior plates. A model using aluminum sheets of similar thickness clearly had variations in the apparent thickness that resulted from differences in x-ray tube centering and x-ray beam divergence (figure 2).

5) Increased biconcavity of the vertebral body evaluated by looking at L3. Large apparently random fluctuations were due to projectional differences in the radiographs.

6) Presence of fractures.

Doyle concluded that only a "limited amount of reliable information can be derived from routine lateral radiographs of the thoracic and lumbar spine in the diagnosis and follow-up of patients with osteoporosis."[23]

Schnitzler et al., concentrated on the vertebral trabecular pattern. They felt the trabecular pattern could be clearly visualized in the spine on a lateral chest film since the aerated lungs provide a uniform background. They invented the vertebral trabecular pattern indices - VTPI (figure 3)

4 - normal, trabecular texture glandular, individual trabeculae cannot be distinguished
3 - moderate bone loss, vertical trabeculae accentuated, closely spaced and thick
2 - marked bone loss, vertical trabeculae widely spaced and thin
1 - severe bone loss, "empty box" appearance

Fractures were found only below VTPI of 3, hence defining a fracture threshold.[21] Currently, the general consensus states that osteoporosis, especially when mild, can not be diagnosed by lateral chest radiographs and there are no objective diagnostic criteria for evaluating those films.

An increase in the number of Schmorl's nodes has also been described in osteoporotic patients. A Schmorl's node is an "intrusion of intervertebral disk material into the vertebral body centrum through

defects (probably vascular) in the end plates."[24] The most common location is at the thoracolumbar junction. Visualization on a radiograph is dependent on the development of sclerotic margins around intruding elements. However many authors state that Schmorl's nodes are not indicative of osteoporosis.[24,25]

The measurement of clavicular cortical thickness on antero-posterior chest radiographs has been advocated as a way to assess osteoporosis and fracture risk.[27,28] Cortical thickness has been previously used as an index of bone aging.[29] Although the actual measurement of clavicular cortical thickness is not difficult, obtaining a consistent projection of the clavicle on various chest films is rather difficult. In positioning of the clavicle, for example a slight tilt, will change the apparent clavicular thickness on the radiograph. The clavicle is also not a weight bearing bone and does not have a high trabecular content. Thus it is not a very reliable method for assessing osteoporosis.

Lumbar radiographs have been reported to be of little value when less than 40% of bone mineral has been lost or in the absence of compression fractures.[28] The whole body dose equivalents of radiation for lumbar spine films are 175 mrems for males and 91 mrems for females.[26] Researchers have tried to devise objective criteria for the use of lumbar films in the study of osteoporosis.

Since spontaneous compression fracture of the vertebral bodies is the main problem of osteoporosis, measurements of vertebral body

height have been proposed to monitor progress of osteoporosis. Jensen and Tougaard devised a formula for measuring the height of vertebral bodies from T6 to L5 to follow the course of the osteoporotic process. On gross inspection of spine films a greater than 25% reduction in the vertebral body height becomes obvious. Yet vertebral bodies in osteoporotic patients can undergo milder degrees of compression before and after fractures. The ability of this method to "register changes in vertebral body heights even when no fracture has occurred makes it valuable for monitoring the progress of osteoporosis.[30] Raymaker et al. devised a mathematical model for assessment of severity and progression of osteoporosis. The method can be applied to one set of radiographs, is objective, not dependent on projection errors, and adaptable to the shape of the individual spine.[16] Barnett and Nordin devised a spine score for L3: the vertical height in the middle of the vertebral body divided by the vertical height anteriorly. This method demonstrated unequivocal osteoporosis without biconcavity. And the x-ray scores bore a reasonable relationship to the histology of the iliac crest in the few cases that were studied. The actual measurements, however, are time consuming and should be performed by the same radiologist each time to guarantee accurate results. More research needs to be done in order to prove the usefulness of this system.[31] To confound this method, O'Neill et al. reported that the distribution of vertebral heights varies in different population centers and between men and women. This

obviously creates problems when using reference values derived from different ethnic populations.[32]

Most authors agree that the diffuse nature of osteoporosis in the spine tends to be fairly uniform.[33] Bhambhani found heterogeneous distribution in eleven patients who had normal lumbar spines yet osteoporotic dorsal spines.[34] He therefore advocated examination of both dorsal and lumbar spine.

Singh stressed analyzing the trabecular pattern of the upper end of the femur as an index of osteoporosis on plain films.[35] Singh's index has been proven to have good correlation to the amount of trabecular bone in the vertebrae and to the incidence of compression fractures.[36] The general idea behind the index is that in the femoral neck there are five anatomic groups of trabeculae and as certain trabeculae are lost with increasing osteoporosis, other groups of trabeculae become accentuated (figure 4).[35]

VOLUMETRIC DIAGNOSIS OF OSTEOPOROSIS

Following the unsatisfactory results from plain radiographs, Cameron and Sorensen introduced the single photon absorptiometry (SPA) in 1963. The original instruments used either Iodine^{125} or Americium^{241} as their energy sources. SPA requires a constant soft-tissue thickness. SPA assesses the status of peripheral long bones, primarily cortical bones.[37]

Since most pathologic fractures occur in the spine, it would be necessary to somehow correlate bone density of the peripheral bones with the bone density of the spine. "Unfortunately, little correlation exists between the density of peripheral bones and spinal osteoporosis."[38] Wilson also concluded that "the relationship between the bone-mineral content of the radius and that of the hip or spine is not sufficient for accurate prediction of the bone-mineral content of the femoral neck or the spine, but one can, on the basis of that relationship, assign any individual to one of two broad classes - that is, osteopenic or non-osteopenic."[39] Since vertebral fractures are such a grave consequence of osteoporosis and SPA can not provide measurements of vertebral bodies, several other methods have been developed to assess the mineral content of the spine with precision and accuracy. They include dual photon absorptiometry (DPA), dual x-ray absorptiometry (DXA) and quantitative computed tomography (QCT).

Constant soft-tissue thickness was no longer required with the use of two distinct photon energy sources in dual photon absorptiometry (DPA). The chosen source was gadolinium which has photons of predominantly 44 keV and 100 keV. The bone mineral content is reported in g/cm^2, an areal rather than a density measurement. Because DPA measures both compact and cancellous bone, its sensitivity is less than that of QCT.[37]

In 1987 the first commercial DXA was introduced. Numerous acronyms such as DER (dual energy radiography), QDR (quantitative digital radiography), DEXA (dual energy x-ray absorptiometry) and DXA (dual x-ray absorptiometry) all stand for the same procedure. Generally the spine from L1 to L4 and the hips are evaluated in the anteroposterior projection. The total body measurement requires 10 to 20 minutes at a radiation dose of approximately 2-3 mrem. DXA is widely available for clinical use today.[37]

Bone densitometry measures the mineral component of the bone but can not distinguish between osteoporosis, too little bone, and osteomalacia, too little mineral in the bone.[9] Criteria for analyzing the results of bone densitometry state:

- Normal bone < 1 standard deviation (SD) below young adult mean value
- Low bone mass (osteopenia) between 1-2.5 SD below young adult mean value
- Osteoporosis >2.5 SD below young adult mean value
- Severe osteoporosis or established osteoporosis >2.5 SD below young adult mean value with one or more fragility fracture[7]

Bone density is not a sensitive predictor of fracture risk. Too many patients with fractures had bone densities identical to their control counterparts without fractures. Osteoporosis is no longer considered a fracture-nonfracture dichotomy, but rather part of a continuum, with greatest fracture risk among those with lowest absolute bone density values. Although controversy exists about the appropriate

use of bone densitometry, Lang et al. consider the following clinical applications valid. Evaluation of patients with metabolic diseases that affect the skeleton, evaluation of perimenopausal women for initiation of estrogen therapy, detection of osteoporosis and assessment of its severity, and monitoring of treatment and evaluation of disease course. The current recommendations for the use of bone density in detection of osteoporosis state that quantitative evaluation of the skeleton should be performed in individuals with suspected osteoporosis based on radiographic findings. The goal is to assess fracture risk and propose appropriate treatment (conservative vs. aggressive).[37]

Quantitative computed tomography (QCT) provides precise three-dimensional anatomic localization and can distinguish cancellous bone from cortical bone and exclude extraosseous minerals like aortic calcifications from the measurement. Vertebral bodies are most commonly measured; the utility of hip QCT is currently under investigation.[31] QCT evaluates the density of both vertebral spongious and compact bone from 10 mm-thick section from the middle of the vertebra. Single sections are performed from T12 to L3 for a total radiation dose of 1.75-2.0 mGy (1/5 of the dose of a lateral lumbar radiograph).[37]

Magnetic resonance imaging shows potential for assessing bone mineral density and perhaps even bone structure without ionizing radiation. The vertebral body is composed of bone tissue, hematopoetic

marrow and fatty marrow. With age, there is loss of vertebral mineral content, decrease in the hematopoetic marrow, and increase in fatty marrow. T1 and T2 relaxation times of vertebral marrow decrease with age.[37]

Various centers throughout the country use all or some of the above techniques to diagnose osteoporosis. Nordin argues for bone densitometry as the single most useful tool in diagnosis, prevention, and management of osteoporosis.[9] Others disagree with him. To date no consensus exists as to the best way to diagnose osteoporosis or even when screening should be implemented. After all, once the damage from osteoporosis is incurred it is too late; at that time only further damage can be prevented. Even when bone mineral density increases during treatment it does not necessarily mean that the bone strength has improved and fracture risk decreased.[30]

TREATMENT OF OSTEOPOROSIS

Only secondary osteoporosis can be effectively treated by simple correction of the underlying cause, such as removal of steroid use, correction of hyperthyroidism, etc.. Once the source is identified and removed, if possible, further bone loss can be prevented and symptoms alleviated.

For a large number of patients treatment of osteoporosis starts only after symptoms presents, usually fractures or pain. Besides the

pharmacological therapies, supportive care for sufferers of osteoporosis is very important. The issue of pain control must be addressed. Bed rest immediately following a fracture and an exercise program afterwards must be discussed. Instruction in proper back care is essential for rehabilitation. Certain patients might benefit from orthotic devices. Family member must be made aware of what osteoporosis is and what kind of limitation will their loved ones experience. Education is key.

Multiple pharmacological approaches to osteoporosis treatment have been tried, are being currently tried, or have been found ineffective. Further discussion will include: estrogen replacement therapy, calcium supplementation, calcitonin, fluorides, calcitriol, bisphosphates, and vitamin D therapies.

Estrogen replacement therapy

Estrogen replacement therapy (ERT) starting at menopause is the single most effective way of preventing Type I osteoporosis. Estrogen regulates osteoclastic bone resorption by modulating differentiation and activation of osteoclasts via inhibition of osteoblast and monocyte derived cytokines and stimulation factors (IL-1, IL-6, GM-CSF). Various studies have demonstrated that estrogen can prevent bone loss and actually increase bone density in the spine.[40,41] Prior to the start of therapy, the risks of endometrial and breast cancer as well as the benefit of reduction of cardiovascular disease must be considered. The risk of endometrial cancer with unopposed ERT increases by 1% per year;

however, this risk can be eliminated with addition of progestin. The regimen of estrogen and progestin is called hormone replacement therapy (HRT). Progestins may also prevent bone loss, and possibly lower the incidence of breast cancer, but may also reduce the beneficial effects of estrogen on plasma lipids. Progestins increase low density lipoprotein and decrease high density lipoprotein in the plasma. Estrogen can be administered orally or transdermally with a patch. The beneficial effect of HRT extends up to 10-15 years. The optimal duration of treatment is currently unkown.[42] ERT may prevent osteoporosis and effectively treats established osteoporosis in women who already have fractures. The risk/benefit ratio must be carefully considered and current recommendations state that only women at high risk should be treated with HRT. Women whose bone mineral density is below 33rd percentile for age-matched controls should be considered at risk for osteoporosis and treated with hormone replacement therapy.[43]

Calcium

Estrogens are more effective than calcium in decreasing the rate of bone loss, yet calcium supplementation has been proven to be more effective than placebo. Because estrogen replacement therapy poses side effects, some women decide to only take calcium supplements, which for the general population have no side effects. Patients with primary hyperparathyroidism can acquire hypercalcemia, hypercalciuria, and nephrolithiasis from calcium supplements.[44] Some studies have shown

that calcium supplementation decreases fracture risk and reduces the rate of bone loss but does not prevent bone loss.[45] Other studies have demonstrated no effect on spinal bone density. Long term benefits of high calcium intake have been inferred from a Yugoslavian population with high calcium intake and documented decrease in hip fracture rate as compared to those with low calcium intake. The National Osteoporosis Foundation recommends an intake of 1200 mg of calcium per day up to the age of 24, 1000 mg per day for adults, and 1500 mg per day for postmenopausal women. Calcium can be obtained in many forms. It often is difficult to obtain enough calcium by eating alone and antacids with calcium carbonate and calcium carbonate pills maybe added.[42] The only known side effects of calcium supplements are dyspepsia and constipation. Calcium is not a substitute for HRT.

Calcitonin

Calcitonin, a 32 amino acid peptide, binds to osteoclasts and prevents bone loss by inhibiting bone resorption. Salmon calcitonin is most widely used because of its potency (40 times that of human calcitonin).[46] Synthetic human clacitonin and salmon calcitonin are approved by the Food and Drug Administration to be administered only by intramuscular injection, are expensive, and may cause side effects of nausea and flushing. A nasal spray version exists in Europe and is presently being tested in the United States. The spray appears to prevent bone loss in early and late postmenopausal women for at least

two years,[42] yet the bioavailability is only 25% that of intramuscular calcitonin.[47] Support for the use of calcitonin comes from a study demonstrating that bone histology was normal in osteoporotic subjects treated with calcitonin for two years.[48] Also postmenopausal women treated for two years with salmon calcitonin had an increase in mean spinal bone mineral density of 2.5% as compared with a 5.7% decrease in the control group.[49] Calcitonin is the only medication used in the treatment of osteoporosis which has the ability to relieve pain; it is an attractive medication for back pain from sustained vertebral fractures. The reasons that pain relief occurs are not well understood; one possibility is the a rise in endorphin levels induced by calcitonin.[47] Conflicting data exists as to the effectiveness of calcitonin on bones other than the spine. Long term safety and efficacy of calcitonin in prevention of osteoporosis remains unproven.

Fluorides

In high doses fluorides stimulate osteoblasts to form new osteoid. Unfortunately, the newly synthesized bone is radiographically denser, structurally and minerally abnormal and has decreased elasticity and decreased tensile strength. Fluoride therapy has a multitude of adverse effects: osteomalacia-like condition, gastrointestinal irritation and ulceration, peripheral edema, periarticular tenderness, and stress microfractures.[5] Despite the increase in spinal bone mass, a long term study by Riggs et al did not demonstrate a reduction in fractures.[3]

Currently, fluoride therapy remains investigational and quite controversial.[42]

Bisphosphates

Bisphosphates have a potential of becoming important agents in the treatment of osteoporosis. Bisphosphates are synthetic compounds which bind to bone mineral and inhibit bone mineralization and resorption. Cyclic administration of etidronate increased spinal bone mineral density by 2-3% per year, and significantly decreased the rate of spinal fractures. Clinical trials are presently underway.[42]

Vitamin D

It is a well known fact that Vitamin D stores decline with age.[50] This is most prominent in the winter called "vitamin D winter."[51] The net effect is that many elderly patients experience hypocalcemia and elevated levels of PTH in the winter months due to mild vitamin D deficiency. This secondary hypoparathyroidism can be alleviated with vitamin D.[52] Many elderly individuals experience hypovitaminosis D; some have age-related defect in renal hydroxylation of 25-(OH)-vitamin D to active vitamin D (calcitriol) leading to osteomalacia.[42] Occult osteomalacia has been shown to account for 5% to 10% of hip and spine fractures in England.[44] Studies demonstrate conflicting results as to the benefit of calcitriol therapy. At this time no definitive conclusions can be reached and calcitriol needs further examination. Vitamin D

supplementation is recommended in all patients with dietary intake of less than 400 IU/day (equivalent to four cups of milk).

The best treatment of osteoporosis is prevention. There is no effective method of restoring lost bone tissue and normalizing bone architecture. Research into new therapies is ongoing.

PREVENTION OF OSTEOPOROSIS

The best way to avoid the complications of osteoporosis is to prevent the onset of the disease in the first place. The primary goal remains the achievement of as high a peak bone mass as genetically possible. This can be accomplished through education, proper nutrition, exercise, and elimination of risk factors (Table II). Once osteoporosis develops only further deterioration can be prevented; complete restoration of lost bone is currently impossible. To evade the enormous financial, physical and emotional costs of osteoporosis, we must teach the young about osteoporosis.

STATEMENT OF PURPOSE

The reason for this study was the finding that patients were being referred to metabolism clinics for bone density measurements based only on the appearance of the spine on chest radiographs. Interpretation of the lateral film of the thoracic spine is highly subjective since the perception of density is influenced by surrounding background

structures. Large interobserver and intraobserver variability have been documented.[9] Williamson et al noted "there is little ability to reliably diagnose osteoporosis in the absence of vertebral compression fractures" on lateral chest films.[54] Epstein et al concluded that identification of osteopenia from lateral views of thoracic spine was highly subjective and variable not only from film to film but also from observer to observer as well as within the readings of one observer.[54] Currently, radiologists rely on their own pattern recognition "looks like osteoporosis to me," rather than objective or codified systems to make the diagnosis. Since both chest radiography and comments about presumed "osteopenia" are nearly ubiquitous in patient care, such observations and evaluations about how to solve such problems have great clinical importance.

We set out to answer the following questions:

1) Are criteria currently used by radiologists useful in detection of osteopenia on chest films?

2) Is the lateral chest radiograph useful in the assessment of bone density and detection of osteopenia?

3) How reliable is the radiologist's reading of osteopenia on chest films?

4) How consistent are the readings of osteopenia on lateral chest films among various radiologists?

Our hypothesis is that the reading of "osteopenia" on a lateral chest radiograph, using a high KvP technique, does not correlate with the presence of osteopenia as demonstrated on bone biopsy.

METHODS

This study employed a very arbitrarily assembled sample of both cases and controls. All the bone biopsy data were obtained from the department of pathology database at Yale New Haven Hospital (YNHH). The subjects were not a random sample from the biopsy records of YNHH, but rather a sample that happened to have also undergone the desired radiographic examinations.

Study population:

Patient population: 160 bone biopsies diagnostic of osteoporosis were performed at Yale New Haven Hospital from 1988 to 1995. Out of that population 35 female patients were chosen based on the availability of their lateral chest roentgenographs. 22/35 patients (63%) had lateral chest films taken in the same year as their bone biopsy. The remaining 12 patients had lateral chest films within three years of their bone biopsy [within one year 5/12 (42%), within two years 4/12 (33%), and within three years 3/12 (25%)]. The locations of the bone biopsies were: 29 femur/hip (83%), 3 knee (9%), 1 trapezium (3%), and 1 tibia (3%). Among the reported reasons for bone biopsy were hip or femoral neck fracture, osteomyelitis, and hip pain. Ages of the patients at the time

the lateral chest film was taken ranged from 40 to 100 years old with the mean of 77 years old. We had no information about the menopausal status of our patients. This did not affect our study since we were simply comparing certain radiographic findings with bone biopsies. The mean age of menopause is 51 years old with 95% of women being menopausal between 45 and 55 years of age.[55] According to the above standard our study had 34/35 (97%) postmenopausal women and only 1/35 (3%) premenopausal.

Control population: 26 female controls who had femur/hip bone biopsies without evidence of osteoporosis were selected from 467 bone biopsies without evidence of osteoporosis performed at Yale New Haven Hospital from 1988 to 1995. 15/26 (58%) had lateral chest films in the same year as the bone biopsy and the remaining 11 had their lateral chest x-rays performed within two years of the bone biopsy [within one year 6/11 (55%) and within two years 5/11 (45%)]. All 26 biopsies were taken from the femur/hip area. Among the reported reasons for bone biopsy were hip/femoral neck fracture and femoral head for allograft. Ages of the patients at the time the lateral chest film was taken ranged from 34 to 93 years old with the mean of 68 years old. Using Mishell's criteria,[55] in this group 22/26 (85%) were postmenopausal women and 4/26 (15%) were most likely premenopausal.

Study design and film evaluation techniques

35 lateral chest films of patients with osteoporosis identified through a bone biopsy and 26 lateral chest films of patients with no evidence of osteoporosis on bone biopsy were coded using a random numbers table. All 61 films were assigned random numbers and patient data was masked prior to film interpretation in order to eliminate observer bias. The radiologists were also unaware of any clinical information. Three experienced radiologists, two chest and one bone specialist, were asked to view all the films on two separate occasions and fill out the following form:

FILM # _____Please circle the correct description of the lateral chest film
INITIALS OF RADIOLOGIST: _____

	1st viewing	2nd viewing
1. definition of superior and inferior plates	normal	prominent
2. biconcavity	normal	severe
3. fractures	none	present
4. herniation of disk material into the vertebral body - Schmorl's node	none	present

5. Trabeculations

a) normal, trabecular texture glandular, individual trabeculae cannot be distinguished
b) moderate bone loss, vertical trabeculae accentuated, closely spaced and thick
c) marked bone loss, vertical trabeculae widely spaced and thin
d) severe bone loss, "empty box" appearance

6. overall assessment of osteopenia in the thoracic spine	absent	present

The above form was intentionally designed without measurements. The belief being that in general a radiologist would not measure vertebral heights on daily basis. The radiologists at Yale New Haven Hospital whom we asked about their standard for evaluating osteoporosis on plain films were unable to articulate clear standards. None had a set routine that they followed. Most felt that only experience allowed them to know which spines appeared osteoporotic. Our intent was to use some simple criteria which might be useful in routine film reading.

A few assumptions were made in the study design:

1. The finding of "osteopenia" on the lateral chest film was equivalent to the presence of osteoporosis. The presence or absence of osteoporosis was established by bone biopsy, still the gold standard.

2. Osteoporosis in the hip/femur as established by bone biopsy correlates with the presence of osteoporosis in the thoracic spine. Weaver and Chalmers who studied generalized metabolic bone diseases concluded that the decrease in bone mineral and bone strength develops earlier in the vertebrae than the calcaneus.[56] Barnett and Nordin felt that peripheral osteoporosis was simply a late manifestation of the disease primarily involving the cancellous bone of the spine.[31] If this assumption is correct than our patients who had femoral neck and hip biopsies positive for osteoporosis should certainly have involvement of the spine.

Biases to consider:

1. The fundamental problem in selecting the sample for a retrospective study involves avoidance of biased selection. Since our interpretations were limited to a discussion of observer variability, biased selection was not a problem because the radiologists saw the same radiographs during each session.

2. It is always possible that some of the observed agreement could be attributed to reader/observer bias. If a reader has a tendency to draw consistently erroneous conclusions concerning certain radiographic findings, he/she will continue to do so when viewing the films for the second time and therefore, will agree with the previous reading leading to good intraobserver agreement. Lack of any interobserver agreement should identify this bias. Only the presence or absence of osteoporosis was confirmed by bone biopsy; there was no way to know whether the other variables were truly present or not.

Statistical Analysis:

Data were entered on PowerBook 520 computer using the Microsoft Excel Version 5.0[57] Dr. Robert Lange performed the statistical analyses. Kappa and weighted kappa values were calculated to measure the concordance between readers for each of the chest x-ray characteristics, using a program based on the paper by Kramer and Feinstein.[58] Statistical associations between chest x-ray characteristics and

osteoporosis were sought using univariate logistic-regression analysis. For the chest x-ray characteristics, odds ratios and 95 percent confidence intervals were calculated using SYSTAT Version 5.2 (Systat, Inc., Evanston, IL) statistical package.

To evaluate the interobserver and the intraobserver variability in the detection of osteopenia on lateral chest films, the data was analyzed using weighted kappa statistics (k_w). Weighted kappa is an index of concordance which also takes into account agreement possible by chance alone.[59]

Weighted kappa values range from -1 to +1. K_w of 0 indicates expected agreement from chance alone, k_w less than 0 indicates that observed agreement is less than expected by chance alone, and k_w of +1 implies perfect agreement between observers. Landis and Koch suggest the following interpretation of weighted kappa values:[60]

Value of k_w	Strength of agreement
<0	Poor
0-0.20	Slight
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Substantial
0.81-1.00	Almost perfect

Kramer and Feinstein feel that "given reasonably competent observers k_w should probably approach +0.5 or +0.6 to be considered an acceptable degree of agreement.[58]

We also attempted to see if any of the criteria we used in evaluating the lateral films could correctly predict osteoporosis. The analysis involved calculating the odds ratio. The odds ratio is an estimate of the relative risk calculated in case-control studies. It is the odds that a patient was exposed to a given risk factor (in our study it was the presence of a certain radiographic finding on the lateral chest film) divided by the odds that a control was exposed to the risk factor (had the same radiographic finding).[61] Our goal was to see if a specific radiographic findings such as increased definition of superior and inferior plates, prominent biconcavity, presence of fractures, presence of Schmorl's nodes, or the specific appearance of trabeculae could correctly predict the presence of osteoporosis. An obvious bias is that of a preselected study population. Our calculations of the odds ratios are still statistically valid since we are only trying to correlate specific radiographic findings with the presence of osteoporosis on bone biopsy.

RESULTS

INTRAOBSERVER AGREEMENT

The k_w values calculated to determine the degree of agreement between the two viewings for each reader are listed by radiological findings in Table IV.

Table IV. Intraobserver agreement

READER #1

Parameters	Kappa Value	Standard Deviation
Plate definition	0.49	0.09
Biconcavity	0.64	0.10
Fractures	0.50	0.10
Schmorl's nodes	0.50	0.10
Trabeculation	0.40	0.13
Osteopenia	0.60	0.10

READER #2

Parameters	Kappa Value	Standard Deviation
Plate definition	0.19	0.10
Biconcavity	0.00	0.10
Fractures	0.78	0.10
Schmorl's nodes	0.00	0.10
Trabeculation	0.43	0.12
Osteopenia	0.58	0.09

READER #3

Parameters	Kappa Value	Standard Deviation
Plate definition	-0.02	0.10
Biconcavity	0.19	0.10
Fractures	0.68	0.09

Schmorl's nodes	0.10	0.09
Trabeculation	0.24	0.14
Osteopenia	0.60	0.09

READER # 1

Presence or absence of biconcavity was the variable producing the heighest k_w value of 0.64. This score falls into the range of "substantial" agreement. No other radiographic findings fell into this range. "Moderate" agreement was demonstrated with the radiologic findings of: increased plate definition (k_w = 0.49), presence of fractures (k_w = 0.50), and presence of Schmorl's nodes (k_w = 0.50). Only "fair" agreement appeared for the type of trabeculations seen (k_w = 0.40).

READER # 2

The highest k_w value, demonstrating "substantial" intraobserver agreement, was the finding of fractures (k_w = 0.78). "Moderate" agreement existed between the viewings for overall assessment of osteopenia (k_w = 0.58) and for trabecular pattern (k_w = 0.43). Plate definition yielded a k_w = 0.19 while both biconcavity and Schmorl's nodes had k_w equal to 0.00. The above three k_w values represent only "slight" agreement.

READER # 3

Fractures once again were the variable which gave the highest k_w value (k_w = 0.68) - "substantial" agreement. Overall assessment of

osteopenia had k_w = 0.60, "moderate" agreement. "Fair" agreement existed for trabecular patterns (k_w = 0.24). Only "slight" agreement was demonstrated for biconcavity (k_w = 0.19) and presence of Schmorl's nodes (k_w = 0.10). Less than the agreement expected from chance alone was seen in the plate definition variable (k_w = -0.02).

INTEROBSERVER AGREEMENT

The k_w values calculated for determination of agreement between the three observers during the first viewing of lateral chest radiographs are listed by radiologic findings in Table V.

Table V. Viewing # 1 - Interobserver agreement

READER # 1 vs. READER # 2

Parameters	Kappa Value	Standard Deviation
Plate definition	0.08	0.09
Biconcavity	-0.12	0.10
Fractures	0.46	0.12
Schmorl's nodes	0.06	0.06
Trabeculation	0.32	0.14
Osteopenia	0.53	0.10

READER # 1 vs. READER # 3

Parameters	Kappa Value	Standard Deviation
Plate definition	0.16	0.10
Biconcavity	0.09	0.09
Fractures	0.48	0.11
Schmorl's nodes	0.26	0.10

Trabeculation	-0.30	0.31
Osteopenia	0.40	0.09

READER # 2 vs. READER # 3

Parameters	Kappa Value	Standard Deviation
Plate definition	0.15	0.09
Biconcavity	0.00	0.10
Fractures	0.30	0.10
Schmorl's nodes	-0.15	0.04
Trabeculation	0.08	0.33
Osteopenia	0.45	0.09

READER # 1 vs. READER # 2

The highest k_w obtained, $k_w = 0.53$, was that associated with the overall assessment of osteopenia in the thoracic spine. The next $k_w = 0.46$ was associated with the presence of fractures. For the above two radiographic findings, the reader agreement was "moderate". Only "fair" agreement was associated with the evaluation of the trabeculations ($k_w = 0.32$). The evaluation of plate definition and presence of Schmorl's nodes revealed "slight" agreement ($k_w = 0.08$ and $k_w = 0.06$). K_w equivalent to - 0.12 was associated with biconcavity; the interobserver agreement was less than expected from chance alone.

READER # 1 vs. READER # 3

The radiologic variable of fractures was associated with the highest k_w in this set (k_w =0.48, "moderate" agreement). Overall assessment of osteopenia in the thoracic spine (k_w = 0.40) and presence of Schmorl's nodes (k_w = 0.26) yielded " fair" interobserver agreement. "Slight" interobserver agreement was seen with both end plate definition (kw = 0.15) and biconcavity (k_w = 0.09). The assessment of the trabecular pattern within the vertebral bodies conveyed interobserver agreement of less than expected by chance alone (k_w = -0.30).

READER # 2 vs. READER # 3

The overall assessment of osteopenia in the thoracic spine yielded the highest kappa (k_w = 0.45), signifying "moderate" interobserver agreement. The variable of fractures had a k_w = 0.30, a "fair" interobserver agreement. Only "slight" interobserver agreement was demonstrated with end plate definition (k_w = 0.15), trabeculations (k_w = 0.08), and biconcavity (k_w = 0.00). Interobserver agreement of less than expected by chance alone was seen with the variable of Schmorl's nodes (k_w = -0.15).

Since the interobserver agreements were not very good for the first viewing, we decided not to analyze the interobserver agreements for the second film viewing.

In order to determine if any of the criteria used in the evaluation of the lateral chest films could reliably predict osteoporosis, odds ratios were calculated (Table VI, VII). We were able to calculate the odds ratios because we knew from bone biopsies which patients had proven osteoporosis and which did not.

Table VI. Odds ratios for the first viewing of all three readers

READER # 1

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	1.27	0.75	2.16	NS#
biconcavity	1.21	0.41	3.63	NS
fracture	0.81	0.24	2.73	NS
Schmorl's nodes	0.80	0.31	4.01	NS
trabeculations	0.94	0.46	1.99	NS
osteopenia	1.14	0.40	3.27	NS

READER # 2

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.95	0.50	1.84	NS
biconcavity	1.26	0.37	4.28	NS
fracture	0.37	0.09	1.42	NS
Schmorl's nodes	1.25	0.32	4.86	NS
trabeculations	1.40	0.78	2.52	NS
osteopenia	1.60	0.58	4.47	NS

READER # 3

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	1.38	0.69	2.63	NS
biconcavity	1.58	0.63	3.96	NS
fracture	1.18	0.41	3.39	NS
Schmorl's nodes	0.73	0.19	2.85	NS
trabeculations	1.62	0.76	3.41	NS
osteopenia	23.10	5.59	95.60	<0.001

* Relative risk of osteoporosis when a given radiographic characteristic is present

Non significant

Table VII. Odds ratios for the second viewing of all three readers

READER # 1

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.98	0.57	1.68	NS
biconcavity	0.94	0.28	3.13	NS
fracture	0.95	0.24	3.82	NS
Schmorl's nodes	1.57	0.50	4.90	NS
trabeculations	1.68	0.80	3.55	NS
osteopenia	4.53	1.45	14.21	NS

READER # 2

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.73	0.36	1.49	NS
biconcavity	0.87	0.21	3.55	NS
fracture	0.46	0.13	1.67	NS
Schmorl's nodes	1.10	0.10	10.00	NS
trabeculations	1.20	0.67	2.15	NS
osteopenia	1.80	0.63	5.16	NS

READER # 3

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	1.50	0.58	3.89	NS
biconcavity	1.43	0.47	4.31	NS
fracture	0.34	0.06	2.00	NS
Schmorl's nodes	1.41	0.39	5.12	NS
trabeculations	1.18	0.49	2.82	NS
osteopenia	1081.00	42.12	27694.00	<0.001

* Relative risk of osteoporosis when a given radiographic characteristic is present

The results reveal that none of the criteria we designed for radiologists to use while evaluating lateral chest radiographs can reliably predict the presence of osteopenia. Only one of the senior chest radiologists was able to call osteopenia correctly on films of patients' who had proven osteoporosis by bone biopsy.

We also removed all the data which came from patients who did not have lateral chest x-rays within the same year as the bone biopsy. We wanted to see if this would make a difference in our odds ratios since there always is the possibility that osteoporosis might not have been present at the time of the chest x-ray, but appeared by the time the bone biopsy was performed. The odds ratios calculated without the films not performed within the same year as the bone biopsy appear in Tables VIII and IX.

Table VIII. Odds ratios for the first viewing of x-rays performed within the same year as the bone biopsy by all three readers

READER # 1

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.94	0.51	1.76	NS
biconcavity	1.26	0.35	4.57	NS
fracture	0.80	0.20	3.22	NS
Schmorl's nodes	0.76	0.20	2.85	NS
trabeculations	1.13	0.47	2.71	NS
osteopenia	1.05	0.30	3.65	NS

READER # 2

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	1.02	0.49	2.14	NS
biconcavity	0.91	0.02	47.94	NS
fracture	0.42	0.09	2.05	NS
Schmorl's nodes	1.18	0.24	5.77	NS
trabeculations	1.33	0.67	2.64	NS
osteopenia	1.99	0.50	7.05	NS

READER # 3

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	1.76	0.79	3.94	NS
biconcavity	1.34	0.34	5.36	NS
fracture	1.10	0.32	3.86	NS
Schmorl's nodes	0.51	0.08	3.41	NS
trabeculations	1.90	0.74	4.87	NS
osteopenia	30.60	5.22	179.50	<0.001

* Relative risk of osteoporosis when a given radiographic characteristic is present

Table IX. Odds ratios for the second viewing of films taken within the same year as the bone biopsy by all three readers

READER # 1

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.73	0.38	1.43	NS
biconcavity	0.86	0.19	3.80	NS
fracture	0.93	0.18	4.83	NS
Schmorl's nodes	1.80	0.50	5.94	NS
trabeculations	1.45	0.62	5.62	NS
osteopenia	4.28	1.13	16.31	<0.001

READER # 2

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.84	0.36	1.99	NS
biconcavity	0.81	0.02	43.16	NS
fracture	0.38	0.08	1.88	NS
Schmorl's nodes				
trabeculations	1.13	0.58	2.19	NS
osteopenia	1.35	0.38	4.80	NS

READER # 3

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.84	0.36	1.99	NS
biconcavity	0.81	0.02	43.16	NS
fracture	1.68	0.45	6.25	NS
Schmorl's nodes	0.34	0.06	2.10	NS
trabeculations	2.02	0.59	6.93	NS
osteopenia	495.22	18.95	12938.98	<0.001

We also decided to analyze the data for odds ratios without the few films of the women we assumed were premenopausal to see if any differences will emerge. These results are in Tables X and XI.

Table X. Odds ratios for the first viewing of all three readers of only "postmenopausal" films taken within the same year as the bone biopsy

READER # 1

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.67	0.33	1.36	NS
biconcavity	0.98	0.25	3.48	NS
fracture	0.53	0.12	2.27	NS
Schmorl's nodes	0.21	0.12	1.95	NS
trabeculations	0.76	0.30	1.96	NS
osteopenia	0.52	0.13	2.19	NS

READER # 2

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.87	0.41	1.86	NS
biconcavity	0.72	0.01	38.36	NS
fracture	0.30	0.06	1.52	NS
Schmorl's nodes	0.98	0.20	4.81	NS
trabeculations	1.08	0.54	2.19	NS
osteopenia	1.37	0.37	5.13	NS

READER # 3

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	1.42	0.62	3.22	NS
biconcavity	1.14	0.28	4.55	NS
fracture	0.74	0.20	2.74	NS
Schmorl's nodes	0.38	0.06	2.61	NS
trabeculations	1.51	0.60	3.81	NS
osteopenia	23.38	3.91	139.90	<0.001

* Relative risk of osteoporosis when a given radiographic characteristic is present

Table XI. Odds ratios for the second viewing of all three readers of only "postmenopausal" films taken within the same year as the bone biopsy

READER # 1

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.53	0.24	1.16	NS
biconcavity	0.59	0.13	2.75	NS
fracture	0.67	0.12	3.57	NS
Schmorl's nodes	1.41	0.39	5.12	NS
trabeculations	0.99	0.40	2.43	NS
osteopenia	2.57	0.62	10.74	NS

READER # 2

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.77	0.32	1.83	NS
biconcavity	0.72	0.01	38.36	NS
fracture	0.32	0.06	1.60	NS
Schmorl's nodes	1.19	0.10	10.00	NS
trabeculations	0.96	0.47	1.92	NS
osteopenia	1.05	0.28	3.92	NS

READER # 3

Characteristic	Relative risk*	-95% conf int	+95% conf int	p value
plate definition	0.47	0.01	25.17	NS
biconcavity	0.70	0.24	2.07	NS
fracture	1.20	0.31	4.65	NS
Schmorl's nodes	0.36	0.05	2.49	NS
trabeculations	1.35	0.37	4.92	NS
osteopenia	375.03	14.20	9907.03	<0.001

* Relative risk of osteoporosis when a given radiographic characteristic is present

None of the exclusions seemed to make a difference in the odds ratios. The criteria we used in our study can not be reliably implemented to diagnose osteoporosis on lateral chest films.

DISCUSSION

Results generally confirmed our hypothesis that lateral chest films cannot be used reliably to diagnose osteopenia and therefore infer the presence of osteoporosis in the thoracic spine. The readers seemed to be relatively consistent in their evaluation of osteopenia on the chest radiographs. Weighted kappas comparing viewing one and viewing two

were equal to 0.60 for reader 1, 0.58 for reader 2, and 0.60 for reader 3; therefore, intraobserver agreement was "moderate" according to Landis and Koch[60], and "acceptable" according to Kramer and Feinstein[58] who set a $k_w = 0.50$ as a cutoff indicative of adequate reader consistency. Fractures for reader 2 and reader 3 had even higher kappas ($k_w = 0.78$ and $k_w = 0.68$). This might be attributed to the fact that out of all the criteria evaluated in the study, fractures seem to be the most "objective". Vertebral body fractures are a rather common finding on chest films and experienced readers should be able to notice them. There appears to be a set template for fractures which the radiologists may learn during their training. If a reader noticed a fracture during the first viewing, using his/her way of evaluating the film, then it is more likely that he/she would also notice the same fracture the second time around. This assumes that he/she is still using the same mental criteria for identifying a fracture. This points to possible observer bias as a source of agreement. The other variables evaluated had kappas ranging from -0.02 to 0.64.

As is usual, there was less agreement between the readers: the interobserver variability fell into the range of "fair/moderate" with weighted kappas for general assessment of osteopenia equal to 0.40, 0.45, and 0.53. These values represent an unacceptable level of agreement.[59] The other variables evaluated in the study (definition of end plates, biconcavity, fractures, Schmorl's nodes, and trabeculations) yielded even

lower kappas representing even poorer agreement between the three readers - range of k_w from -0.30 to 0.48.

Epstein et al. looked at observer variation in the detection of osteopenia by having two radiologists and one orthopedic specialist evaluate 30 lateral chest radiographs (15 pairs). The inclusion criteria were 1) two lateral films taken no more than two weeks apart, 2) absence of compression fractures or disease overlying the thoracic spine, and 3) film considered technically adequate. The readers were asked to simply comment on the presence or absence of osteopenia using their own methods of analyzing the films. In their study the true presence of osteopenia was not established by bone biopsy or other methods. They found the intraobserver average kappa to be "0.54 (0.49 to 0.64) indicating only fair agreement of each reader with himself," while the interobserver agreement was even worse; average kappa of 0.38.[54] Our results for intraobserver agreements showed kappas between 0.58 and 0.60 with average kappa of 0.59. Our values closely agree with the findings by Epstein and are only slightly better. We consider them to represent "moderate" agreement as well as "acceptable" agreement indicating adequate reader consistency. Our interobserver agreements for general assessment of osteopenia had kappa values ranging from 0.40 to 0.53 with the average kappa of 0.46. Therefore, our readers had a better interobserver agreement than in the Epstein study.

The fact that our readers managed to agree with themselves and with each other above the level of chance alone in a significant number of cases, demonstrates that it might be possible to consistently extract some signs from a standard lateral chest radiograph that are pertinent to the evaluation of osteopenia or the templates of osteopenia was not articulated. Yet, when our criteria were put to the test, none was able to predict reliably the presence of osteoporosis. Perhaps the readers were using some other clues to detect the presence of osteopenia. For instance, one reader was noted to have marked all the categories as normal on the film evaluation form except for the general assessment of osteopenia which was marked as "present".

Interestingly the interobserver agreement on the overall assessment of the thoracic spine was much higher than for the other variable (except fractures - discussed previously). Individual variables usually associated with osteoporosis such as increased definition of the inferior and superior end plates, level of biconcavity, herniation of disk material into the vertebral body, and the appearance of the trabecular pattern, were more difficult to identify consistently than was the final conclusion regarding the presence of osteopenia.

Kovarik et al. evaluated anteroposterior and lateral views of the spine as well as anteroposterior radiographs of both hips for presence of osteoporosis and correlated the results with bone density measurements. They found that "the estimation of bone mineral content by routine

evaluation of radiographs is greatly influenced by subjective grading of the radiologists," but the diagnostic value of routine x-rays of the spine can be improved considerably by joint readings of more than one radiologist.[62] Perhaps the diagnostic value of lateral chest radiographs in the detection of osteopenia could also be improved by joint readings, but that is the subject for yet another study. The need for at least two radiologists to evaluate each film together would increase the cost of this routine examination and the reason to use chest radiographs in the first place for screening of osteoporosis is that they are so inexpensive and common.

Michel et al. discovered that the "overall assessment of L1" on a lateral roentgenogram of the lumbar spine was the most accurate method to correctly classifying a subject above or below a bone density of 110 mg/cm^3 (vertebral fracture threshold which reflects a bone loss of about 40% from the normal young adult value of 175 mg/cm^3).[33] Based on their results we decided to ask our readers to make an overall assessment of osteopenia in the thoracic spine. We did not specify which vertebral body should be looked at closely since the quality of the radiograph, the positioning of the patient, as well as the degree of kyphosis might effect the way a specific vertebral body appears.

Williamson et al. studied how the diagnosis of osteoporosis by plain chest film correlates with the lumbar spine bone density readings performed by dual photon densitometry. Nine experienced chest

radiologists evaluated 45 left lateral films and were asked to estimate bone density: 1 - severe osteoporosis, 2 - mild osteoporosis, 3 - normal, and 4 - increased bone density. The radiologists were allowed to use any clues on the films. The results were analyzed using receiver operating characteristic (ROC) curves. A density level of 0.96 g HA/cm^2 was chosen as the fracture threshold and the dividing value between normal and abnormal; at this level the mean ROC curve for the entire group was 0.638+/-0.05 SD (0.5 represents a reading no better than obtained by chance alone). They concluded that "there is little ability to diagnose osteoporosis in absence of vertebral compression fractures."[53]

Our results reveal the following: each reader was able to correctly read the film as either osteoporotic or not (based on the results of bone biopsies) in the following number of cases (the number of films read varies since some of the readers forgot to answer all the questions for each film). Reader # 1 made the correct diagnoses in 41/59 cases (69%) during the first viewing and 31/58 cases (53%) during the second viewing. Reader # 2 correctly diagnosed the presence or absence of osteopenia in 32/60 cases (53%) during the first viewing and 34/59 cases (58%) in the second viewing. Reader # 3 was correct for the first viewing in 30/59 cases (51%) and for the second viewing 34/61 (56%).

Although Williamson et al. addressed issues of interest to us, they did not describe any criteria for assessing osteopenia on plain films. We do not know how the various radiologists reached their conclusions

about the presence and the degree of osteoporosis. In our study we compared the radiologists' reading of osteopenia with bone biopsy results - the gold standard in diagnosis of osteoporosis. With our project we forced the radiologists to use certain criteria during evaluation of the lateral chest films for osteoporosis. However, they were not required to assess "osteopenia" as consistent with the individual criteria.

Unfortunately, none of the criteria seemed to reliably predict the presence of osteopenia based on the calculation of odds ratios with a 95% confidence interval. The radiographic findings of increased definition of the superior and inferior plates, the presence of biconcavity, the presence of fractures, the presence of Schmorl's nodes, various kinds of trabeculations, and overall assessment of osteopenia did not provide us with significant odds ratios.

Surprisingly, one of the senior chest radiologists was very good at calling the spine osteopenic when the bone biopsy was indeed positive for osteoporosis. The 95% confidence intervals for true relative risk did not include 1; therefore, we can be 95% confident that the relative risk is not 1,[62] ie that there is an elevated risk of osteoporosis when this radiologist reads generalized osteopenia of the thoracic spine on a lateral chest film. Both viewings had $p < 0.001$. When asked what findings were useful, the radiologist told us there were no specific findings. That radiologist simply looks at the film and identifies it as either osteopenic or not based on prior experience.

Unlike Schnitzler et al, who felt the evaluation of the trabecular pattern is easy against the constant background of aerated lung,[21] both of our chest radiologists felt it was very difficult to assess the trabecular pattern on standard lateral chest films. They noted the lung markings seemed to be "covering up" the trabecular pattern. One of our experienced radiologists did not answer most of the questions about trabecular pattern claiming inability to see trabeculae at all.

Also it must be taken into consideration that multireader evaluation of lateral chest radiographs for presence of osteoporosis may be fraught with problems. Variables and biases which can not be accounted for include: level of experience, use of subtle clues not related to the area being evaluated, training during the study,[53] everyday familiarity with this type of radiograph, and others.

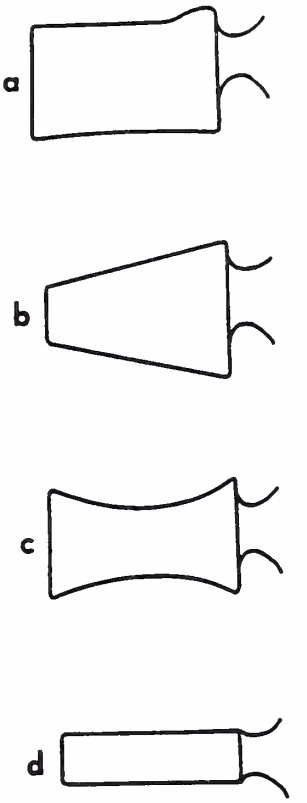
In conclusion, our results prove osteopenia may not be consistently reported on chest radiographs, at least with this physician sample. Lateral chest radiographs cannot be used to reliably detect osteopenia of the thoracic spine. One of our radiologists was capable of correctly determining osteopenia. Overall this study suggests that the lateral radiograph is not particularly useful in detecting osteopenia. The fact that one radiologist was capable of detecting osteopenia suggests that there may be as yet an inarticulated template that corresponds to osteopenia of the spine. This has major implications for radiology

education. Further efforts to either articulate the template or provide multiple shared experiences of film interpretation to transmit the template are warranted. Validation of shared experiences is easily done using interactive electronic media. Our film set could be formatted in this fashion and multiple studies done with both attendings and residents looking at past learning curves.

The take-home message from this study is that radiologists should probably stop commenting on the presence of osteoporosis in the thoracic spine on lateral chest films, or at least be aware of the variability associated with the observations.

Figure 1

Osteoporotic changes in the vertebral shape



a) Normal. The superior and inferior vertebral outlines are relatively parallel, although a slight elevation or protuberance can be seen at posterosuperior aspect of the vertebral bodies

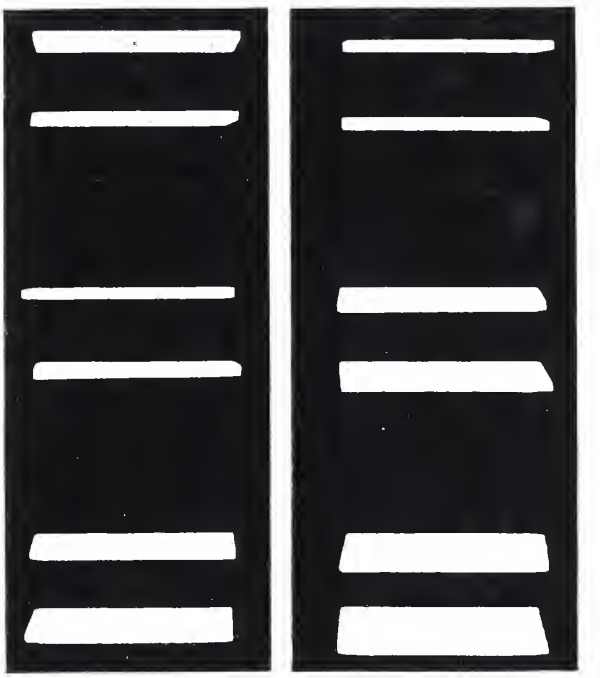
b) Wedge-shaped vertebrae relate to the collapse of the anterior aspect of the vertebral body

c) Biconcave or "fish vertebrae" are characterized by biconcave deformity of the superior and inferior surfaces of the vertebral body

d) Flattened or "pancake" vertebrae are associated with compression of the entire vertebral surface[1]

Figure 2

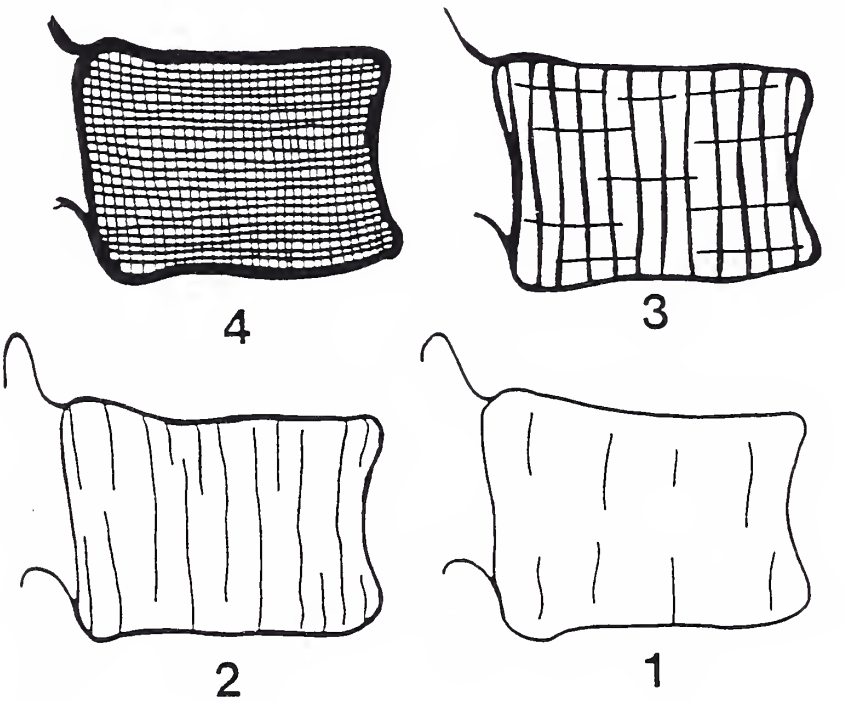
Radiograph of model end-plates of the same thickness, corresponding to the view of the end-plates seen on a lateral radiograph of a lumbar spine



The film on the left was taken with the x-ray beam centered on the middle end-plates, the film on the right centered on the upper end-plates, the difference in centering being only about 1 inch. Note the remarkable variation in the apparent thickness of the end-plates on each film and between the two films.[23]

Figure 3

Vertebral trabecular pattern index (VTPI) on lateral radiographs of vertebral bodies



VTPI 4 - normal, trabecular texture glandular, individual trabeculae cannot be distinguished

VTPI 3 - moderate bone loss, vertical trabeculae accentuated, closely spaced and thick

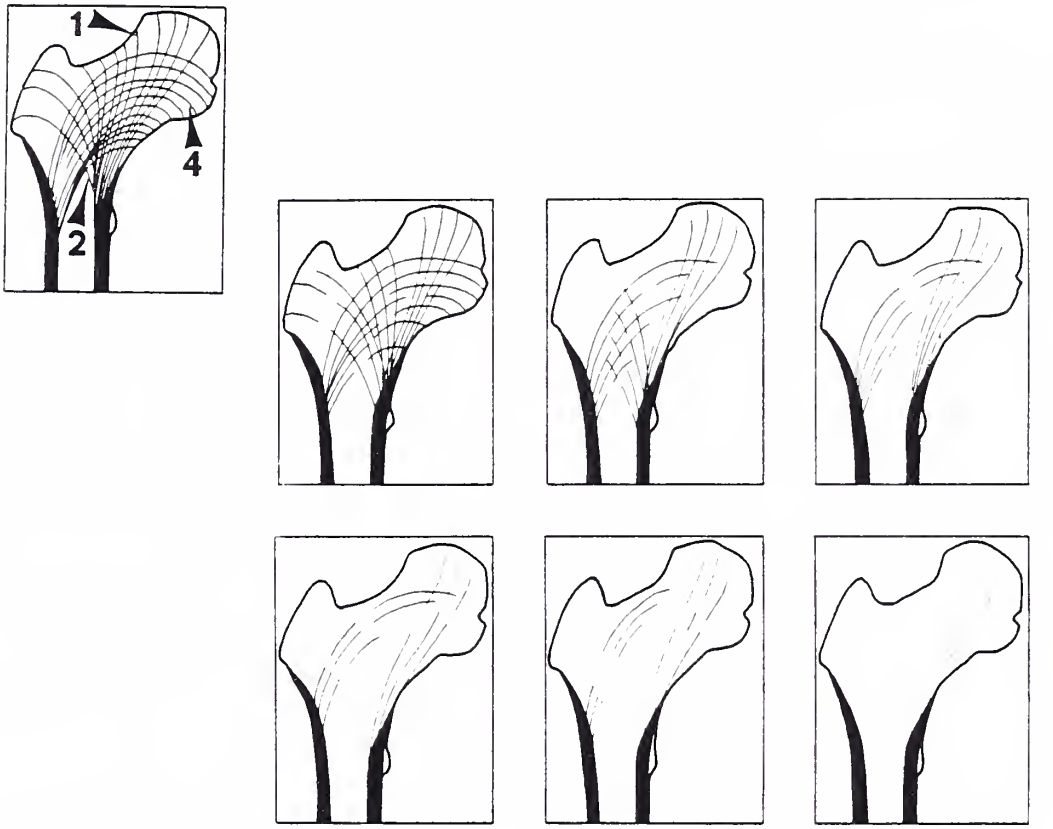
VTPI 2 - marked bone loss, vertical trabeculae widely spaced and thin

VTPI 1 - severe bone loss, "empty box" appearance

VTPI 1 and 2 are associated with fractures[21]

Figure 4

Proximal femur Singh index for osteoporosis



In the proximal femur there are five groups of osseous trabeculae. In the normal situation, it is frequently difficult to identify all of these groups, but with increasing osteoporosis, they initially may be identifiable and subsequently may be resorbed. In the top drawing the, three groups can be well seen: the principal compressive group (1); the secondary compressive group (2); and the principal tensile group (4). In the subsequent drawings, increasing degrees of osteoporosis lead to trabecular resorption. The principal compressive group is the last to be obliterated.[1]

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