In vivo bone-mineral measurement

How and why—a review

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We often wish to estimate bone stock in our patients, because decreased quantity and impaired quality of bone are signs of aging and disease and the cause of most fractures. In recent years, an impressive increase in the risk of fractures in the elderly has been observed (Obrant et al. 1989), which has intensified the search for causes of osteoporosis and bone fragility, and has initiated attempts at prevention.

The occurrence of fractures—particularly fractures belonging to the bone-fragility group—is, rightly, considered to be the best sign of bone quality impairment. Estimation of osteoporosis from roentgen films has the disadvantage that only severe bone loss (30% or more) is noticeable. Therefore, for more than 80 years, attempts have been made to quantify bone mass from roentgen films or by other radiometric methods. For more than 20 years, devices for in vivo bone-mineral measurement have been commercially available; and today, a variety of products are available, certainly enough variety and number to confuse most presumptive users.

Older methods have been summarized by Garn (1962) whereas more recent developments have been reviewed by Mazess and Wahner (1988).

We will attempt to describe the principles of the most commonly used bone-mineral measuring techniques.

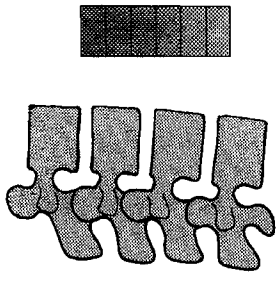

Figure 1. A tracing of the light transmission through vertebral bodies compared with a standard, an aluminum step wedge exposed on the same film.

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Methods

Roentgen methods (Figures 1 and 2)

As early as the turn of the century an American dentist, Price (1901), attempted to quantify bone on dental radiographs. Later on, with more advanced light-meters, more reliable, but still difficult, methods were developed (Mack et al. 1939, Omnell 1957, Vose et al. 1964); but the variability of roentgen sources and film development and the nonlinear and irregular relationship between film blackening and bone mineral were so discouraging that these methods were abandoned.

More useful were the semiquantitative evaluations of cortical thicknesses; favorite measuring sites have been the metacarpals (Barnett and Nordin 1960), the proximal end of the radius (Meema and Meema 1963), and the shaft of the femur (Garn et al. 1963). A more difficult, but still useful, measuring site is the femoral-neck cortex at the level of the calcar femorale (Fredensborg and Nilsson 1977). Vertebral deformation, compression of vertebral bodies,

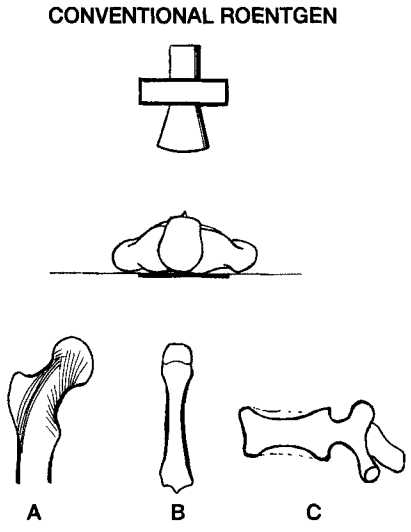

Figure 2. Semiquantitative measurements in roentgen films, e.g., hip trabecular pattern (Singh index; A), second metacarpal cortex (B), and vertebral end-plate compression (C).

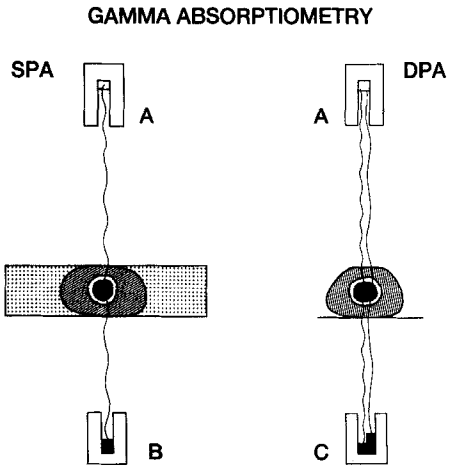

Figure 3. Principles of gamma absorptiometry. Single-photon absorptiometry (SPA) and dual photon absorptiometry (DPA) with soft tissue equivalent enclosure and dual photon energies. Gamma-radiation detectors (A), single-photon radiation source (B), and dual-photon radiation source (C).

and bulging of end plates can be measured. The method of Singh et al. (1972) uses the change of the trabecular pattern of the upper end of the femur with increasing age and decreasing bone mass.

These methods are still being used and have two advantages: they require no equipment other than a conventional roentgen machine, and they can be applied retrospectively in existing roentgen films.

SPA—single-photon absorptiometry (Figure 3)

As early as 1901, Price, without much success, attempted to use radionuclides rather than a roentgen radiation source for bone-mass measurements. With the technical development more radionuclides became available, several with radiation properties suitable for measurement of bone. Also, radiation detection techniques improved. A radionuclide has the advantage over a roentgen source because it usually emits radiation of distinct energies rather than a continuous spectrum of radiation. This, at least in the early stage of this development, was necessary for the mathematical calculation of the output. The radioisotopes used were usually iodine-125 and americium-241 (Cameron and Sorensson 1963, Nilsson 1966). The usual approach is to move the detector and the source across the limb to be measured, the forearm being the most popular measuring site. The only permissible geometry—flat parallel surfaces—is provided by enclosing the limb in water or some other agent with soft-tissue equivalent absorption.

The SPA-method has proved its value and is the method that so far has produced the most data. Several devices are commercially available. (Figure 3).

DPA—dual-photon absorptiometry (Figure 3)

A more complicated method includes two distinct radiation qualities either by using two radionuclides, such as americium-241 and cesium-137 or one nuclide with two distinct energies, such as gadolinium-153 (Roos et al. 1970, Mazess et al. 1972, 1989). The advantage of DPA is that surrounding soft tissue can be accounted for, not by enclosing the specimen in water but by calculating the thickness of the surrounding tissue and the bone mineral separately from the attenuation of the two energies.

With this method, it became possible to measure deeper structures, such as the lumbar spine and the hip. The method is not without flaws; measuring-site localization, the importance of variation in fat content in the measurement area, and various technical difficulties tend to make measurements less reliable in those patients that are the most interesting: namely, those with very little bone. Presently, DPA appears to be losing its market.

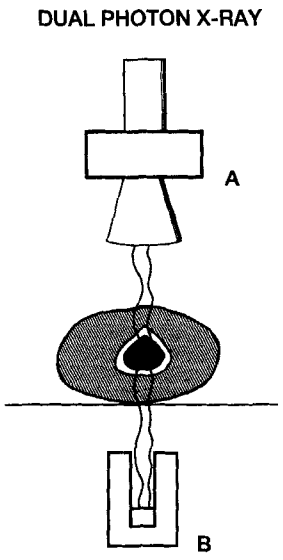

Figure 4. Double-photon absorptiometry, but with a roentgen source (DPX) with a roentgen source (A) and detector (B).

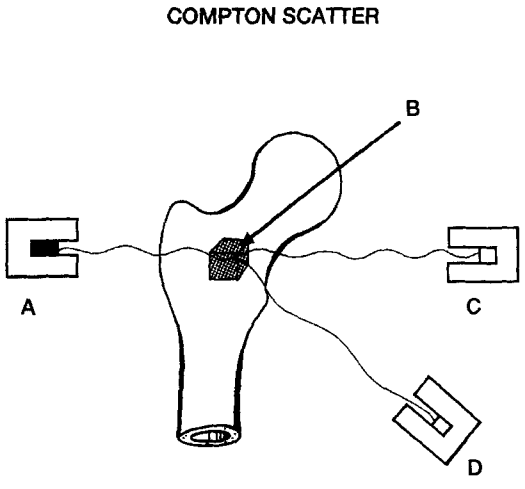

Figure 5. Compton scatter measurement—geometric principle with single-photon radiation source (A), volume of interest (B), detectors for transmitted radiation (C), and scattered radiation (D).

DPX—dual photon x-ray (Figure 4)

Jacobsson (1964) was the first to design a bone-mineral measuring device based on a roentgen source with filtered radiation and a detector—the equipment permitted measurements of appendicular bones but also hip and spine. Perhaps because it was too advanced for its time, the method was never developed commercially, and 10 years passed before the principle was used again. Filtered radiation, modern detectors, and software capable of handling beam hardening and scatter effects are the basic requirements for the DPX approach. With the DPX machines, also a scout view—an image of the spine—can be produced that is sufficiently clear to permit proper localization and relocalization of the measuring sites. An optimum photon flux reduces the measuring time. For vertebral BMC measurements, a precision of 2 per cent or even better can be expected. Also, it is possible to measure total body calcium with a DPX machine. There are three commercially available products today, and there is good reason to expect further developments along this and similar lines in the near future.

Compton scatter (Figure 5)

When a gamma quantum interacts with matter, various events may take place: the radiation is photoelectrically absorbed, it passes through matter without interaction, or it changes direction with or without changing its wave length or energy or both. The Compton scatter refers to radiation that changes direction and energy as it "bounces off" an electron. The relation between transmitted and scattered radiation at specific angles is a measure of electron density and, indirectly, physical density and therefore it is also an approximation of bone-mineral content in a given volume of bone. This concept has been developed to measure bone mineral—so far only in the appendicular skeleton (Garnett et al. 1973, Reiss and Steinle 1973, Olkkonen and Karjalainen 1975). One difficulty is to find a specific volume inside the body and to identify the same volume over and over again. For some reason, this method has not been developed into a commercial product.

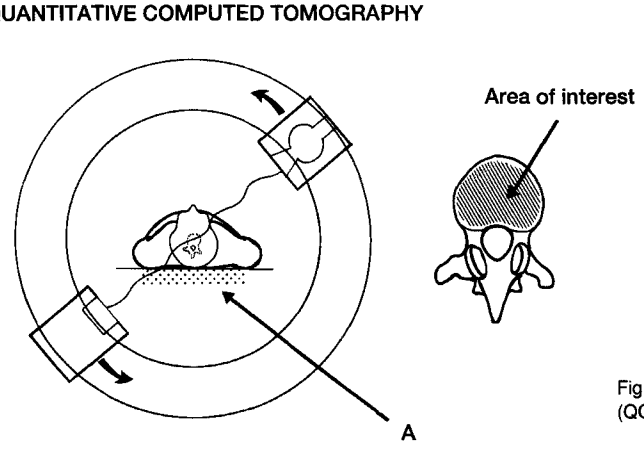

Figure 6. Quantitative computed tomography (QCT) with phantom body (A).

QCT—quantitative computed tomography (Figure 6)

The CT scanner was not really designed to quantitate tissue density, but rather to produce clear and attractive pictures. Therefore, even the last generations of scanners do not easily provide physical quantities. The Hounsfield units presented with the picture are relative and very much related to the calibration of the machine. Photon or gamma or both sources with distinct energies, not suitable for conventional CT diagnostics, may provide much better quantitative data. This extensive field was recently reviewed by Genant et al. (1988). It is possible, by careful calibration of late generation CT scanners, to produce quantitative data that rather well correspond with the bone-mineral content measured by vertebral excision or by other absorptiometric methods (Nilsson et al. 1988). Again, owing to the scout view, it is possible to localize a predetermined measuring site and to find the site again and again. The radiation dose is modest today although not as low as when using radionuclide sources or even DPX. A real difficulty is unavailability, because most CT scanners are being constantly used in clinical diagnostic work and most researchers cannot afford a CT scanner exclusively for the purpose of bone-mineral measurements.

Activation analysis (Figure 7)

Calcium in nature and also in the human skeleton is a constant mixture of isotopes, Calcium-40 being the predominant one. One of the isotopes, the nonradioactive calcium-48, is present in small amounts; but calcium-48 is able to capture neutrons and becomes calcium 49, which decays with a half-life of a few minutes emitting high-energy gamma radiation, which is convenient to measure. A limb or the whole body is being irradiated by fast neutrons. The neutron source may be a reactor, a neutron accelerator, or a radionuclide neutron source (Cohn and Dombronski 1971, Cohn et al. 1972, Nelp et al. 1972, Smith and Tothhill 1979). Immediately after or even during the activation of Calcium-48, the Calcium-49 is being measured and the amount of calcium is determined. The measurement can readily be repeated, and the radiation dose is, which may be surprising, not a problem. This method is best suited for whole-body calcium measurements.

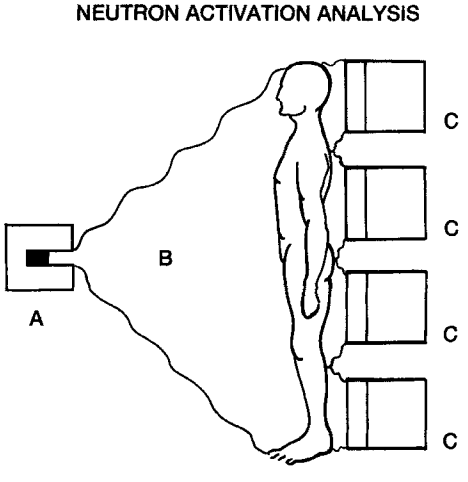

Figure 7. Neutron activation (Calcium-48 → Calcium-49) analysis with neutron source (A), neutron flux, and detectors for calcium 49 gamma radiation (C).

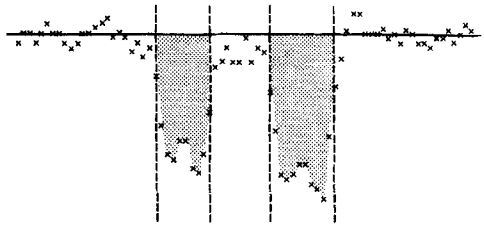

Figure 8. Printout of measuring points (SPA) across the radius and the ulna.

Ultrasound

In the past and more recently, attempts have been made to measure bone with ultrasound. Only superficial bony structures, such as the os calcis or the patella, can be measured (Langton et al. 1984, Avioli et al. 1987). The conductivity and velocity of ultrasonic waves are, however, not really a measure of the mass of the conductive matter, but rather a parameter of its elasticity. Again, this variable may be useful for assessing bone quality: In a recent study (Heaney et al. 1989), patellar ultrasonic velocity was, in women, closely related to fracture.

BMC and BMD

Scanning across a limb produces a profile where the base is the width of the bone and the ordinate the thickness of bone mineral at various points across the bone (Figure 8). The bone mineral content, BMC, is usually presented as grams of mineral in a piece of bone 1 cm long (g/cm). It is possible to correct for the dimensions of the bone by dividing by the width, and to calculate the thickness of mineral/surface of bone facing the detector ("areal density", g/cm^2). We have now corrected, to some extent, for the size of the bone or the person we are measuring, but instead would really like to obtain bonemineral density (g/cm^3). The only way to achieve this, whether we use SPA, DPA, or DPX, is to make assumptions about the shape of the bone and divide by a constant. This manipulation should then give us a parameter of bone-mineral density BMD. We can calculate true BMD only if we know the volume of bone involved in our measurement. Only the Compton and the QCT methods actually present, as their basic output, a variable that can be approximated to BMD, mass per volume. BMC is wholly sufficient and useful for monitoring a single patient or population; the difficulty begins when we want to compare distinctly different groups—men and women, Americans and Japanese, etc.—that is, when we have to find methods for correcting for size and shape of bones.

Applications

What are the uses of bone-mineral measurements?

Bone-mineral measurements have added a great deal to our knowledge of bone metabolism and pathology as regards to normal aging, including the effects of menopause. Life-style factors such as physical activity, alcohol, smoking, and other habits have been examined in relation to bone mass. Effects of disease have been estimated and side effects of drugs on bone, hemodialysis, and surgical procedures. Bone mineral measurements and fracture epidemiologic studies together, have provided a list of risk factors for fracture that is the basis of future preventive strategies.

We will not attempt to even summarize the thousands of studies in which bone-mineral measurements have been used; but instead, we will endeavor to examine the usefulness of such measuring methods in orthopedic practice today.

Individual patient care

If a roentgen examination is confusing, for instance, shows osteoporosis in a young individual, we will get a better estimate of bone mass and also, perhaps, fracture risk with a quantitative measurement. Also, if on an individual basis we are trying to prevent or treat osteoporosis, repeated measurements monitoring bone mineral will be useful. Today, bone-mineral measurements have little application in the handling of individual patients, but this may well change.

Collecting risk groups

There is ample evidence that bone mineral content measurements of young and middle-aged persons have a good predictive value for future fragility fractures (Gärdsell et al. 1989). Because we are now in the progress of studying preventive regimens, such methods of selecting study groups are already in full use. The opposite is also possible; we can with a single bone-mineral measurement exclude those perimenopausal women who are unlikely to develop osteoporosis and sustain a fracture.

Monitoring

The final proof of fracture-preventing treatment is that fractures are being prevented! However, so far, only one preventive measure, namely estrogen supplementation, has been demonstrated to have that effect, whereas other studies—briefer and involving smaller populations—have demonstrated that the bone mineral content may improve from treatment with fluoride, calcitonin, anabolic steroids, diphosphonates, exercise, and so on. It is generally accepted that a quantitative bone-mineral measurement is, besides side-effect control, a necessary requirement for an acceptable study of fracture prevention, even if, again, fracture is the natural end point!

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