METHODS FOR MEASURING THE MINERAL STATUS OF BONE TISSUE

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A number of new methods for evaluating the mineral status of bone tissue have been developed over the last 20 years. Both noninvasive radiological approaches and radionuclides are employed in many of such methods for measuring bone tissue mass, density, and mineral exchange. The methods have been used in diagnosis and treatment of metabolic diseases of bones for assessing the efficacy of prescribed therapy.

Numerous clinical trials have revealed a close relationship between the degree of skeleton mineralization and the risk of bone fracture. The axial human skeleton consists mainly of trabecular (spongy) bone tissue, while peripheral bones of limbs consist mainly of cortical (compact) tissue. Since the rate of metabolism in trabecular tissue is higher than that in cortical bones, the former is more susceptible to various metabolic bone diseases. Therefore, evaluation of the mineral content in trabecular bone tissue is seemingly a more sensitive indicator of early metabolic diseases than similar monitoring in cortical bone tissue. Some authors have reported significant correlation between mineral status of axial skeleton and of the parts of peripheral skeleton which have a high share of trabecular bones [8].

Osteoporosis (loss of bone mass and subsequent mechanical injury of the skeleton) is the most frequent metabolic disease of bones. Osteoporosis can be induced by drugs, postmenopausal processes, or senescence. Injury of vertebrae, femoral cervix fracture, and fracture of distal forearm are quite often found in patients with osteoporosis, even under low loads, and osteoporosis is usually diagnosed only when a fracture has occurred. Measuring the mineral content of bone tissue can distinguish patients with a tendency to osteoporosis from patients whose bone mineral content is decreased as a result of age, sex, or racial difference without inclination to bone fracture.

Radiogrammetry and radiographic densitometry (photodensitometry) antedate contemporary methods for quantitative monitoring of mineral content of bone tissue. Radiogrammetry measures the thickness of compact bone tissue on standard X-ray photographs of the arm. The "cortical thickness" is suggested to be a measure of the bone mass, and the ratio of cortical to total width to be a measure of the "density". The discrepancy between radiographic and physical width was shown to require systematic reevaluation of thickness. Radiogrammetry can measure neither absolute mineral content in bones nor intracortical porosity [5]. It provides only information about changes in bone volume. The distance between the radiographic film and the studied bone is a critical parameter, since a 1 cm change in the distance can cause an error of 2-3%. As a result of such inaccuracy, the area of the compact bone correlates poorly with the actual mass of the bone (error of 10-20%).

Photodensitometry uses a bone image on a standard radiographic film as an indicator of photon absorption by the bone; therefore, it indirectly measures the mineral content of bone tissue. Visual assessment of photographs allows only considerable changes in bone mineralization (20-40%) to be detected. Significant efforts have been made in the past 50 years to improve the ability of photodensitometry to quantitatively evaluate bone mass using the measured optical density of X-ray photographs (decrease in X-ray scattering, scanning of special standard wedges, and improvement of optical photodensitometers and their computerization). The efforts, however, reached their limits because physical restrictions inherent in X-ray tubes as radiation sources and in X-ray film as detectors became limiting factors. These restrictions are: significant scattering of radiation; nonuniformity of irradiation field intensity; variable, polychromatic spectrum of radiation; irreproducibility of radiation spectrum, and, therefore, irreproducibility of resulting photographs. These factors cause the measuring error of the method. The reproducibility of routine photodensitometry is 5-10%. The accuracy of the method is high for individual samples of test-bones (3-5%); however,

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in bones with a small amount of soft tissues it is lower (5-10%), and measuring error may reach 10-30% in bones with significant masses of soft tissue. In addition, the projection of the bone on an X-ray film does not exactly correspond to the bone cross-section geometry, and it does not disclose intracortical porosity and injury of endosteal edges of long bones.

Clinical requirements for the measurement of bone mineral content can be defined as follows [7]. First, for periodic repetitive measurements over long intervals of time, high accuracy and reproducibility is required. Systematic error caused by inaccurate positioning should be reduced to the minimum. Second, to record osteopenia (loss of bone mass), it is very important to know the true content of bone minerals. For comparison, the normal population should be studied. Third, the method should be sensitive enough to distinguish clinically significant losses of bone mineral. These losses amount to about 0.8% per year in healthy women and up to 15% during the post menopause period in women suffering from osteoporosis. For long-term studies which are required to monitor medical treatment, the reproducibility should be about 2% (coefficient of variation). This allows statistically significant changes of the bone mineral content (5%) to be detected. The method should allow separate measurements of regional domains which mainly contain either cortical or trabecular bone tissue. These requirements are met by modern methods of measurement of bone mineral content based on radionuclides and X-ray absorption.

The drawbacks of radiographic densitometry stimulated development of radionuclide absorption methods. In 1963 Cameron and Sorenson introduced the method of single photon absorption for examination of peripheral skeletal bones [2]. A typical single photon absorption bone densitometer consists of a scintillation detector and a 125I-source of radiation with an activity of ~7.7 GBq. These are arranged in opposition to each other on an axis which moves perpendicularly to the longitudinal axis of the radial bone of the forearm. Detailed description of the method is given in [1].

The accuracy (deviation of the measured value from true mineral content) and reproducibility of the method depend on various factors, and first of all, on the fat content in the soft tissue surrounding the bone. The varying thickness of the soft tissue results in nonuniformity of the baseline, and therefore, in higher measuring error. In practice, the measuring error related to this factor is reduced by optimal positioning of the baseline and by reducing inhomogeneity of the fat layer by compressing soft tissues. The measuring error depends also on the accuracy in positioning of the examined area of scanning and on the operator’s experience.

Low resolving power of the single photon absorption method and its limited applicability (only peripheral bones can be examined) raised the problem of indirect evaluation of mineral content in various parts of the skeleton by correlation estimation. Using this approach it is possible, for example, to extrapolate the mineral content of radial bone to other bones which cannot be directly examined by the single photon absorption method. Sufficiently high correlation was found between the mineral contents of radial bone and of the head of the femur. The mineral content of radial bone also correlates with the mineral content of the heel bone, although the mineral content of radial and heel bones poorly correlates with the mineral content of spine. High correlation between the mineral content of radial bone and total calcium content was found in patients with osteoporosis [8].

Although it is rather informative, the correlation method cannot replace direct measurements of the mineral content in parts of the skeleton which are not accessible to the single photon absorption method.

The abilities of two photon absorption instruments significantly exceed those of single photon absorption. In two photon absorption, either two radioactive sources (e.g., 241Am and 57Co, or 241Am and 133Ba) or one source with two gamma lines (e.g., 153Gd, 44 and 100 keV) are used. In contrast to single photon absorption, two photon absorption allows the mineral content in spine and in any other parts of the skeleton where large masses of soft tissues are present to be measured.

The method of two photon absorption was developed in [9, 10] and adapted to measurements of calcium content in the whole body, lumbar spine [11], and femur [4]. It is based on measurements of transmittance of two photons of different energy in a medium that mainly consists of two materials, bone and soft tissue. The energy spectrum of 153Gd with the NaI (Tl) detector contains peaks at 44 and 100 keV (X-ray K-lines of Eu at 42 and 48 keV and gamma-lines at 97 and 103 keV). Detailed description of the two photon absorption method is given in [1].

The method of two photon absorption is used for examination of vertebrae (most frequently in the L2-L4 area), proximal segments of femoral and upper arm bones, and of the whole skeleton. It can also measure the mineral content of individual vertebrae and the whole spine. The two photon absorption method can measure surface mineral density (g/cm²), mineral content (g), and bone surface area in the zone of interest (cm²).

The drawbacks of the two photon absorption method are: long scanning time (from 20 min for 4 vertebrae to 40-70 min for the whole body), drift of results caused by radiation source decay, necessity for periodic replacement of radiation sources (153Gd should be replaced every 1.5 years).

In the X-ray bone densitometers developed abroad in recent years, the radionuclide point source of radiation was replaced by an X-ray tube. The Hologic (USA) X-ray bone densitometer is described in [3]. An original method for taking X-ray