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STUDIES OF OSTEOPOROSIS IN RUSSIA USING ISOTOPE-RELATED TECHNIQUES

(Part of Coordinated Programme: COMPARATIVE INTERNATIONAL STUDIES OF OSTEOPOROSIS USING ISOTOPE TECHNIQUES)

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Presented is the programme to study bone characteristics of healthy men and women aged 20-54 comprising the urban population of Moscow and near-by cities to define those of normal population. The study will also include patients with characteristics for early osteoporosis symptoms. The latter includes subjects who took part in the Chernobyl clean-up operation. DEXA (spine, femoral neck, whole body) and ultrasound (heel) will be used to examine those of the normal population group. To study osteoporosis patients the iliac crest biopsy samples will be taken for subsequent neutron activation analysis. Contents of major and trace elements in bone specimens (rib, iliac crest) and teeth (molar, premolar) will be estimated by neutron activation and X-ray fluorescent analysis in autopsy material of healthy accident victims depending on the age and sex.

1. SCIENTIFIC BACKGROUND AND SCOPE OF THE PROJECT

Osteoporosis is a widespread bone disease of the elderly (particularly, post-menopausal women). This disease greatly limits the life quality of the elderly and is placing an incresing burden on the health-care system in some developed countries.

There are additional reasons for the ever-increasing interest in osteoporosis diagnostics and treatment in Russia due to the Chernobyl disaster. 6–8 years after this disaster symptoms of osteoporosis are being found more and more often in 40–50 year old men who took part in the clean-up operation.

Bone changes (increase in number of fractures, lingering period of knitting, etc.) are marked in citizens (including children and adolescents) of regions exposed to the heavy radionuclide contamination.

In Russia much experience has been gained in diagnostics, prevention and treatment of osteoporosis induced by prolonged antiorthostatic hypokinesia in healthy volunteers. Studies were undertaken by the Institute of Medical and Biological Problems in coordination with scientists of some other research centres of Moscow and Obninsk according to the space programme.

2. METHODS

For bone analysis of healthy male volunteers prior to and within different periods after antiorthostatic hypokinesia the following methods were used [1]:

1. QUANTITATIVE COMPUTED TOMOGRAPHY. Bone density in the lumbar spine region, femoral and tibia diaphysis was measured using the X-ray computed tomograph of the fourth generation, KBAD-1 (USA).
2. DUAL PHOTON ABSORPTIOMETRY. Bone density in spine, femoral neck and the central part of the diaphysis was measured using the densitometer, DBD-2600 (USA).
3. SINGLE PHOTON ABSORPTIOMETRY. Bone density in the tibia and forearm diaphysis was measured using Bone Mineral Detector (Gambro, Sweden) while Bone Skanner 7102 (Sweden) was used to measure bone density in the right heel.
4. IN VIVO NEUTRON ACTIVATION ANALYSIS. The total calcium content was measured in the lumbar and pectoral spine regions, foot, and wrist using a complex of equipment developed by the Medical Radiological Research Centre [2].
5. ULTRASOUND MEASUREMENT. The rate of ultrasonic tibia surface distribution was measured using the standard, Russian, ultrasound equipment.

6. IN VITRO MEASUREMENTS OF THE ILIAC CREST BIOPSY. Contents of the major bone minerals (Ca, P, Mg, Na, Cl, K, Sr) was measured using the instrumental neutron activation analysis

3. RESULTS

In addition to the results of choosing the optimum measures for the prevention and treatment of osteoporosis induced during pilot studies, we drew several conclusions based on our prepositions and data:

1. The greatest bone losses occur in the lower limbs (foot, heel, femoral neck).
2. Significant seasonal changes in mineral saturation can exist in the lower limbs [3].
3. Data acquired from the same skeleton part using different methods is poorly comparable.

The third conclusion points out the necessity for carefully interpreting the results of bone analysis by whatever methods are available.

4. PLANS FOR FUTURE WORK

The main purpose of our proposed study is to develop methods for early diagnostics of radiation-induced osteoporosis. Examined are people who took an active part in the Chernobyl clean-up operation and those who live in the regions exposed to the heaviest radionuclide contamination. It is impossible to gain this subject without a detailed study of bone mineral characteristics for the relatively healthy people of different age and sex. Studies of normal population are planned for the urban population of Central European Russia including Moscow, Obninsk and other near-by cities. The modern in vivo and in vitro methods will be used to analyze bone mineral characteristics.

1. IN VIVO METHODS. Among them, DEXA (LUNAR-DPX-L, Serial 6469) and ultrasound (LUNAR-ACHILLES) will be used. Bone density will be measured in the lumbar spine region (anterior and posterior) and at the femoral neck using DEXA. Whole body measurements will be included if possible. The results will be estimated both automatically and manually for DEXA studies of lateral spine.

The results of DEXA femoral neck scanning will be extended, if possible, to capture the iliac crest region. Thus, supplementary information about the iliac crest density can be manually obtained along with the standard data treatment of femoral neck analysis.

The heel density of both feet will be measured by DEXA in addition to the standard data manual treatment.

It is planning to regularly measure the LUNAR spine phantom.

Heel will be ultrasonically analyzed in subjects examined previously by DEXA. The heel of both feet will be studied.

The in vivo methods will be used to study 105 women and 105 men aged 20-54. The age range includes the following seven groups: 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54. Thus, at least 15 women and 15 men will be included in each study group. In 1995 measurements will be preferably carried out on subjects aged 40-54. A selection of this age period can be explained by the most possible early osteoporosis symptoms. So the normal population group just of this age period is of the most interest.

The subjects' height (cm), weight (kg), and age will be recorded.

The following subjects will be excluded from studies of normal population:

1. Subjects with a history of renal disease, hyper- or hypoparathyroidism, thyroid disease, adrenal disorders, malignancy, chronic gastrointestinal disease, liver disease, diabetes, Paget's disease, early oophorectomy, hypogonadism, osteomalacia, vitamin-D defficiency, rheumatoid arthritis, renal lithiasis, and chronic disorders of menstrual cycle

2. Subjects who regularly use or have used any of the following medications: glucocorticoids, estrogen (replacement therapy), anticonvulsives, sodium fluoride, heparin, thyroxin, vitamin-D metabolites, sedatives, and soporifics.

3. Subjects with a history of fracture of the lower limbs, spine, or wrist or evidence of vertebral compression fracture on thoraco-lumbar spine X-ray, and those with prosthetic appliances.

4. Subjects with a current history of alcohol or drug abuse.

5. Subjects with prolonged hospitalization or other extended immobilization including those of "sedentary" occupation (seamstresses, collectors of electronic equipment, etc.).

6. Subjects who occupationally deal or have dealt with toxic metals (Pb, Cd, Hg), and those who work or have worked at factories that use or produce hazardous chemicals.

7. Subjects who have occupational contact with ionizing irradiation (group A), or those exposed to an accident irradiation or participated in the Chernobyl clean-up operation, and who were residing within the rediocontaminated regions for a long time.

Winter and spring have been chosen the best time to study the normal population. A minimum of the lower limb mineral saturation is supposed to appear just at these periods of the year. Usually at this time, the population of Central Russia suffers from UV-, vitamin-D and Hypodynamy defficiency connected with climatic, social and economic conditions.

Osteoporosis patients will be examined by DEXA and ultrasound the same way as the relatively healthy people of the normal population.

2. IN VITRO METHODS. Among them, instrumental neutron activation analysis (INAA) and X-ray fluorescent analysis (XRF) will be used to study bone minerals. Contents of major and trace elements in

bone specimens (rib, iliac crest) and teeth (molar, premolar) will be estimated. Autopsy samples from healthy accident victims will be used. Autopsy data will be divided into several groups according to age ang sex the same way as for the in vivo bone density study of the normal population. However, for the great deal of work, a number of sibjects in each age group will be smaller than this for the in vivo study. At least 8 subjects of either sex will be included in each study group.

Besides the autopsy material, contents of major and trace elements in the iliac crest biopsies of osteoporosis patients will be estimated by INAA and XRF. Bone density of the same patients will be measured prior to biopsy by the in vivo DEXA and ultrasound the same way as for the normal population studies.

A special instrument made of titanium will be used to collect the autopsy and biopsy bone specimens and teeth. Then bone and tooth specimens will be placed into the polyethylene ampules, lyophilized there (dried at the temperature below 0°), and kept until the moment of INAA and XRF.

Estimation of the data obtained will make it possible:

1. To determine the age peak of mineral density in the lumbar spine region, at the femoral neck, iliac crest, heel, and bone skeletal mass using the DEXA data of normal population.
2. To quantify differences in bone density and bone mass as functions of the age and sex of persons in the study group using the DEXA data of population norms.
3. To determine the age peaks for concentrations of major minerals (Ca, P, Mg, K, Na, Cl, Sr) and trace elements in bone and tooth specimens using the INAA and XRF data for the normal population.
4. To quantify differences in contents of major and trace elements in bone and tooth specimens as functions of the age and sex using the INAA and XRF data for the normal population.
5. To estimate the interdependence between mineral densities of different bone regions (lumbar spine, femoral neck, iliac

crest, heel) while comparing the DEXA data for the same person of the normal population.

6. To assess the DEXA informativity comparing the age dynamics of bone mineral density in ribs and iliac crest with that of the major element contents in the appropriate bone samples.
7. To estimate the DEXA informativity comparing the data about heel mineral density with that of the heel ultrasound analysis for the same person of the population norms and osteoporosis patients.
8. To evaluate the DEXA informativity comparing the results of the iliac crest mineral analysis for osteoporosis patients with those of the major element analysis in the iliac crest biopsies of the same patients.
9. To determine differences in contents of major and trace elements in bone specimens for the norms and osteoporosis.
10. To determine correlations between bone and tooth contents of major and trace elements thus evaluating the possibility of applying teeth as indicators of the skeletal minerals and trace elements.
11. To choose the most informative method (or complex of methods) for the early osteoporosis diagnostics.

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