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CONTINUOUS METHOD OF BONE MINERAL DENSITY MEASUREMENT "IN VIVO"

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1. INTRODUCTION

In recent years, methods of bone mineral component control in human "in vivo" have been quickly developing. An opportunity to determine the density of bones ($g \cdot cm^{-3}$) or surface mass ($g \cdot cm^{2}$) is a very important factor in diagnosis and treatment of bone-wasting diseases /1-4,6/. Changes of bone mineral content are observed in:

- osteoporoses:
  - drugs (steroids, hormons and others)
  - past monopause
  - normal aging
- condition of hipokinezia
- vitamin D-deficiency
- renal osteodystrophy
- intestinal malabsorption
- vascular diseases and others.

Bone mineral component is practically hydroxy-apatite - $Ca_{10}(PO_4)_6(OH)_2$, it is valid to establish especially the total value of Ca and P. Some methods permit determining the level of bone mineral content "in vivo":

- radiography (especially for spine)
- densitometric gamma measurement
- particle radiation interaction on the human body or parts of the body (X-ray emission and nuclear reactions).

By this time, osteoporosis has been classified by means of radiography. According to Colbert /3/, the routine radiologic skeleton survey techniques for assessment of bone changes do not always permit satisfactory and statistically valid correlative studies. At least 30% of a bone are lost before changes in the concellous bone of the spine can be recognised radiologically in the relation to the densitometric bone mineral methods of component /3,5,6/. Basing on Horsman and Mazess /8,9/ it was assumed for adult that changes of mineral component in radius and ulna reflect changes in the whole skeleton. It was shown that the densitometric measurement of mineral component of forearm bones can be referred to a skeleton weight index (total mass divided by total volume) and can be used as an indicator for the mean values of density. The method of bone mineral

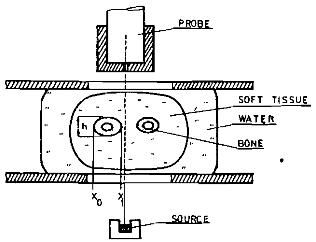


Fig. 1. Scheme of measurement

content (BMC) "in vivo" was introduced in scientific and clinical practice by Comeron and Sorenson /7/.

This method allows measuring bone mineral content (BMC) of radius and ulna ($g \cdot cm^{-1}$), and the width (W) of a bone (cm) and the value of BMC/W ($g \cdot cm^{-2}$) can be determined.

At some international conferences, papers with the methods elaborated in other laboratories, were presented as well /2,8,15/.

Methods based on particle radiation interaction on the human body are also interesting, as they give an opportunity to determine the level of Ca and P and their ratio (Ca/P) in the bones. Unfortunately, now the minimum absorbe dose for a patient is approximate 10 mGy and the radiation source is a large stable arrangement.

Muon-rentgen-technique developed in the Laboratory of Nuclear Problems in JINR gives considerably lower absorbed dose against others (order 0.1) /17,18/. Combining this method with the densitometric measurement of bone mineral density (BMD) "in vivo" and "in vitro" is of great interest.

In this paper, the continuous method of BMD measurement "in vivo" for radius and ulna is presented. This technique allows determining the density and width of the investigated bones.

2. METHOD OF MEASUREMENT

Geometry of measurement the bones of radius and ulna is presented in Fig. 1. The patients hand is fixed perpendicular to a gamma radiation beam (6 cm from distal). Thickness of soft tissue is compensated to the determined constant size using a water cuff. The source with the detector is moving with a constant speed. The counting rate is recorded (scanning). When the probe with the detector reaches the end position, the automatic control system changes the direction and measurement can be continued. The number of photons in the detector area will be determined:

$$N = N_0 \int_{x_0}^{x_1} e^{-\mu_{mw} \rho_w [H - h(x)] - \mu_{mk} \rho_k h(x)} dx , \qquad (1)$$

where μ_m - mass absorption coefficient, ρ - density, H - thickness of total shielding, h - thickness of bone, w - water, k - bone, v - speed of the detector movement, t - time of measurement, N - number of photons with the phantom, N_0 - number of photons without the phantom, x - width of bone, f - calibration sample.

Taking into consideration: $x = v \cdot t ; \quad \bar{h} = \int_0^t h(t) dt ; \quad B = \frac{N}{t}$

and distribution of exponential value on the row, the solution will be:

$$\rho_k = \frac{\mu_{mw} \cdot \rho_w}{\mu_{mw}} \quad \frac{B/B_0 - 1}{\mu_{mk} \bar{h}} , \qquad (2)$$

where B/B_0 - measurement values.

On the basis of Mazess and Cameron measurements /21/ it is possible to assume for adult:

$$\bar{h} \approx const$$

and under calibration conditions the simple algorithm can be obtained:

$$\rho_k = A - C \frac{N}{t} , \qquad (3)$$

where A, C - constant values.

According to the constant relation between thickness and width of radius and ulna in the determined cross section, it can be assumed in general case:

$$\bar{h} = \alpha \cdot t .$$

And taking into account (eq. 2), one can obtain bone mineral density (BMD) of radius and ulna:

$$\rho_k = A_1 + \frac{C_1}{t} + D_1 \frac{N}{t^2} ,$$

where

A_1, C_1, D_1 - constant values.

This algorithm can also be used for those, whose anatomic structure considerably differs from the standard man /13/, e.g. children. According to Mechanik /22/, Table 1 presents some results of measurements "in vitro" of percentage ratio the volume of individual bones to the total volume of skeleton, against age. A constant value of this ratio for the forearm bones, during growth of children is an important factor. This allows a conclusion, that the mass of forearm bones is proportional to the total skeleton mass of children, too.

3. INSTRUMENTATIONS

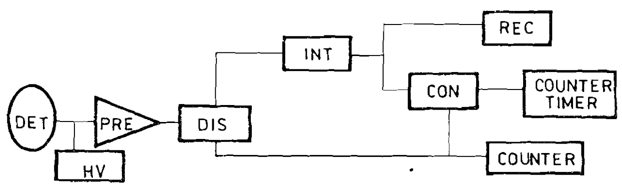
3.1. Measuring facility

The facility is schematically drawn in Fig. 2. It is divided into two parts:

A. Table for investigation
- mechanical arrangement
- control system

Table 1

Body region	Bones in body region	Volume at various ages (years)					
		0	1	5	10	15	20
Head	Cranium, mandible	28	25.2	15.7	10.5	7.7	7.2
Trunk	Vertebrae, sternium ribs, scapulae, clavicles, os coxae	49.5	50.6	52.3	51.0	53.0	52.7
Upper legs	Femora	6.3	7.0	12.2	16.2	16.4	16.9
Lower legs	Tibiae, fibulae, patellae	4.8	5.6	7.8	8.8	9.4	9.4
Feet	Ankle and foot bones	2.4	2.6	3.0	3.5	2.9	2.9
Upper arms	Humeri	4.70	4.69	4.66	4.70	6.17	6.37
Forearms	Ulnae and radii	2.85	2.90	2.94	2.95	3.12	3.32
Hands	Wrist and hand bones	1.45	1.41	1.40	1.84	1.30	1.20



Where: DET - detector
PRE - preamplifier
HV - high voltage supply
DIS - discriminator
CON - control unit
REC - recorder
INT - integrator and amplifier

Fig. 2. Scheme of facility.

- radiation source
- collimators.

B. Apparatus
- counter system
- registration system
- scintillation probe
- supplier.

3.2. Technical characteristics

Radiation source $_{95}Am^{241}$

$A = 1.1$ GBq $\quad T_{1/2} = 458$ yr.

$E_\gamma = 59.54 \pm 0.015$ keV $\quad \eta = 36\%$

Speed $u = 8.5 \cdot 10^{-4}\ m \cdot s^{-1}$

Time of measurement:

hand ~ 40 s

finger ~ 11 s

total period ~120 s

Absorbed dose $D = 6 \cdot 10^{-6}$ Gy

Distance source-detector $10^{-2} \div 2 \cdot 10^{-1}$ m

NaJ(Tl) detector efficiency $\varepsilon \sim 98\%$

Detector resolution $R \div 6$ keV

Integration constant $\tau - 2$ s

Detection limit* $Q - 40$ ppm

Instrumental constant** $C = 1.25\ keV^{1/2} . mGy^{-1/2} imp \cdot min^{-1}$.

* $Q = 2\sqrt{N_6}$

N_6 - counting rate for background

** According to /14/ for this type arrangement the following dependence exists:

$$Q = C(R/\varepsilon D)^{1/2} \quad .$$

4. CALIBRATION AND DISCUSSION

Experimentators present the results of measurement of the bone mineral component, in different units:
- linear mass $(g \cdot cm^{-1})$
- surface mass $(g \cdot cm^{-2})$
- density $(g \cdot cm^{-3})$.

These units can be recounted. However, comparison of these results will depend on the conditions of the apparatus calibration and the method of measurement. Different standards are used in laboratories for calibration e.q. natural parts of bones, pressed bone ash, phantom with Ca compound or Al. From that point of view comparison of

Table 2. Weight and volume of the parts of cartial bones

Symbol of bone	Sex	Fresh bone			Dried bone *		
		Weight g	Volume mm^3	Density $g \cdot cm^3$	Weight g	Volume mm^3	Density $g \cdot cm^3$
1	F_1	7.5114	4975	1.51	5.440	4800	1.13
2	F_1	7.4047	4800	1.54	4.923	4800	1.03
3	F_2	6.8023	4125	1.60	5.606	3950	1.42
4	F_2	6.7023	3950	1.69	5.542	3875	1.43
5	F_3	7.5402	5060	1.49	6.181	4800	1.29
6	F_3	7.7886	5120	1.52	6.394	5023	1.27
7	F_4	7.3750	4800	1.53	5.367	4750	1.12
8	F_4	7.3650	4725	1.56	5.556	4600	1.21
9	F_5	5.2650	3580	1.48	3.971	3850	1.03
10	F_5	5.2690	3525	1.49	4.166	3400	1.22
11	F_6	5.3710	3350	1.60	3.905	3850	1.01
12	F_6	5.3640	3200	1.67	3.741	3050	1.23
13	F_7	7.412	5120	1.44	6.248	5150	1.21
14	F_7	7.295	5190	1.41	5.810	5150	1.13

* Drying: time 1 month and temperature 40°C .

Table 3

Kind of bone	Weight g	Volume cm^3	Mean density $g \cdot cm^{-3}$	%
radius	9.150	4.5	2.03	3
ulna	10.450	4.6	2.25	3

the absolute values obtained in other laboratories ought to be taken into consideration together with the calibration conditions. Using the same natural parts of bones, in the longer time for calibration can be source of an error. Table 2 shows as an example, the weight and volume of the parts of cardial bones as a function of the time of drying /11/.

Calibration of our arrangement was conducted using the middle parts of radius and ulna bones in water area (man - ap. 30 yr.). Earlier bones were dried at the temperature 30°C for 60 days. The

Table 4. Densitometric measurements on the distal third of the radius and ulna shaft in adult males and females by half decades

Age group	N	Mean density	Standard deviation	Coeff. of variat. CV(%)	Stand. deviat.of mean value ( )
MALES					
20 ÷ 24	10	2.09	0.122	5.8	0.040
25 ÷ 29	9	2.09	0.130	6.2	0.043
30 ÷ 34	9	2.13	0.156	7.3	0.052
35 ÷ 39	9	2.14	0.150	7.0	0.050
40 ÷ 44	9	2.12	0.156	7.3	0.052
45 ÷ 49	9	2.09	0.112	5.3	0.037
50 ÷ 54	9	1.98	0.104	5.2	0.035
55 ÷ 59	9	2.00	0.116	5.7	0.038
60 ÷ 64	5	1.92	0.166	8.6	0.075
65 ÷ 69	3	1.87	0.156	8.3	0.091
FEMALES					
19 ÷ 24	9	1.91	0.118	6.1	0.039
25 ÷ 29	8	1.90	0.146	7.6	0.052
30 ÷ 34	9	1.94	0.098	5.1	0.033
35 ÷ 39	9	1.91	0.119	6.2	0.040
40 ÷ 44	9	1.91	0.109	5.7	0.036
45 ÷ 49	9	1.88	0.120	6.4	0.040
50 ÷ 54	9	1.81	0.087	4.8	0.029
55 ÷ 59	9	1.76	0.080	4.6	0.026
60 ÷ 70	8	1.66	0.096	5.8	0.034
70 ÷ 74	3	1.60	0.051	3.2	0.029

density of the bones was determined by measuring the weight and volume of each part. The results are presented in Table 3.

In Table 5 some measurements, which determine precision of our method, are shown. Repeated measurements of the bone mineral density (BMD) of radius and ulna, for a certain patient give an opportunity to investigate kinetics of the changes in the bones.

During two years BMD for the forearm bones of approximately 200 normal adult Polish persons has been measured. The maximum and minimum values of each group were neglected. The results of this measurements and counted errors for each group of age and sex of

Table 5. Characteristic of precision

Subjects	Number of measur. N	Density (r.u.)	Standard deviation	Coeff. of variat. CV(%)	Stand. deviat. of mean value ( )
Standard Fe	41	1.148	0.0105	0.91%	0.0016
Standard bone	8	3080	33.8	1.09%	11.9
I.S.	8	2336	27.4	1.2%	9.7
R.M.	9	2351	34.3	1.5%	11.4
B.F.*	10	2.04	0.0896	4.4%	0.029

* From JINR, Dubna.

persons, are presented, in Table 4. The standard curve for males and females (SAD) - the mean density for the forearm bones against the age of persons on the basis of these data (Fig. 3) was derived. In this figure the data from other laboratories are presented too. These data were normalized to our curve in the point of 25 year old man. SAD can be used for diagnostic purposes assuming as an edge criterion of normal subject the bone density deviations from the mean value of BMD by more than 2SD. However it is necessary to notice the following circumstances:

- if the anatomic structure at the subject is very different from a standard man /13/, the calculation based on algorithm (2) can give results with the error greater than ±10%;

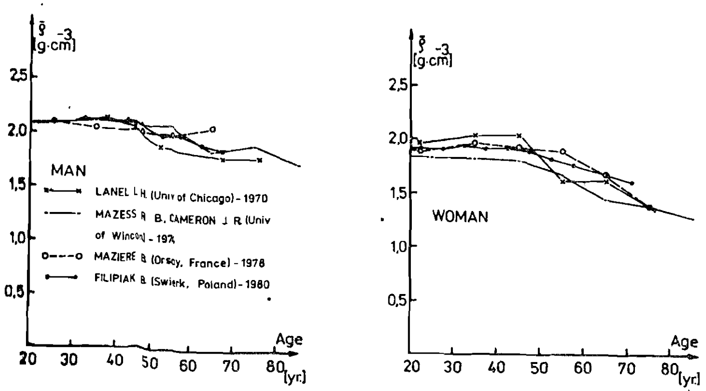


Fig. 3. Standard curve of BMD.

- for the people of 60÷80 years old, it is very difficult to determine the criterion of "good health".

Between forearm bone mineral density and results of the total body calcium measurement there is good correlation /19,20/. The results of the investigation /21/ of the total body calcium content in normal people (9 males and 5 females) and our curve SAD taking to consideration, the following algorithm was obtained:

$$MCa = A \cdot H \cdot \sqrt{W} \cdot \rho ,$$

where MCa - predicted total body Ca (g), H - the height (m), W - the weight (kg), ρ - density of forearm bones.

It was determined:

for males	$\bar{A} = 34$	SD = 1.99	CV = 5.8%	n = 9
for females	$\bar{A} = 35$	SD = 2.01	CV = 5.9%	n = 5

In Table 6 the total body calcium (TBCa) measured in osteoporotic subjects /20/ is compared with that calculated on the basis of our algorithm. Cohn's results were obtained using the total body neutron activation analysis (TBNAA). Density of bones was determined from the surface mass (BMC/W) using the normalization of Cohn's data to our SAG (0.847 $g \cdot cm^{-2}$ + 2.09 $g \cdot cm^{-3}$).

It can be concluded from this comparison, that this algorithm allows one to establish approximately TBCa for all cases.

5. CONCLUSIONS

The densitometric continuous method of BMD presents some advantages over other elaborated methods:

- opportunity to repear many times measurements for each person (very low absorbed dose)
- opportunity to carry out measurements under any conditions, e.g., in hospital.

Aknowledgements: I would like to aknowledge the help of P.Molenda and J.Szczechura. Patients studies were carried out with the help of Prof. Tolloczko. I wish to thank Director of Reactor Centre and Isotope Production, Swierk, Poland and Director of the Laboratory of Nuclear Problems, Joint Institute of Nuclear Research, Dubna, USSR.

Table 6. Total-body calcium and radial bone mineral content of osteoporotic subjects measured and calculated

Number	Age (yr)	Weight (kg)	Height (cm)	Surface mass BMC/W ($g\cdot cm^{-2}$)	Total body Ca measur. (g)	Total body Ca calcul. (g)	Density ($g\cdot cm^{-3}$)
OSTEOPOROTIC MALES							
1.	76	64	166	0.583	832	650	1.44
2.	65	62	162	0.506	658	541	1.24
3.	46	67	169	0.653	788	757	1.61
4.	58	94	178	0.757	904	1091	1.86
OSTEOPOROTIC FEMALES							
1.	81	57	148	0.600	636	581	1.48
2.	50	43	154	0.526	606	461	1.30
3.	63	70	152	0.622	524	683	1.53
4.	78	63	152	0.317	590	331	0.782
5.	53	48	153	0.486	564	447	1.20
6.	70	70	154	0.588	632	656	1.45
7.	73	75	156	0.484	691	562	1.19
8.	55	61	156	0.653	674	686	1.61

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Филипяк Б. E19-86-405
Непрерывный метод измерения минерального компонента кости человека "in vivo"

Рассматривается метод измерения плотности минерального компонента кости (BMD) человека "in vivo". Описано устройство для измерения BMD локтевой и лучевой кости и его технические параметры. Обсуждаются условия калибровки и стандартизации. Приведены первые результаты измерений. Плотность кости предплечия у мужчин и женщин представлена как функция возраста. В работе выведена также формула для определения содержания кальция во всем скелете человека.

Работа выполнена в Лаборатории ядерных проблем ОИЯИ.

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Filipiak B. E19-86-405
Continuous Method of Bone Mineral Density Measurement "in vivo"

The method of densitometric continuous measurement of bone mineral density (BMD) "in vivo" is presented. A facility for BMD in radius and ulna is described. The technical characteristics are discussed. Special consideration is given to calibration and standardization. Preliminary measurements involving patients and volunteers are presented as well. BMD of forearm bones for normal males and females are plotted against age. The report also discusses an algorithm, which allows establishing the total body calcium (TBCa).

The investigation has been performed at the Laboratory of Nuclear Problems, JINR.

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