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Conf-731036--(Edit)

INTERNATIONAL CONFERENCE ON BONE MINERAL MEASUREMENT

OCTOBER 12-13, 1973

Chicago, Illinois, USA

U.W. Bone Mineral Laboratory

Chairmen: Richard B. Mazess and John R. Cameron

DISCLAIMER

INTERNATIONAL CONFERENCE ON BONE MINERAL MEASUREMENT

Chicago, Illinois
October 12-13, 1973

SCHEDULE OUTLINE

Friday, October 12, 1973 - PHYSICAL SESSIONS

9:00 - 10:30	INTRODUCTION AND ERRORS
10:30 - 11:00	Coffee Break
11:00 - 12:00	INTERPRETATION AND CORRELATIONS
12:00 - 2:00	Lunch
2:00 - 3:45	DUAL PHOTON TECHNIQUE
3:45 - 4:00	Break
4:00 - 4:55	DATA HANDLING AND EXCHANGE
5:00 - 6:00	Cocktail Party
8:00 - 9:00	OTHER METHODS RUMP SESSION

Saturday, October 13, 1973 - BIOMEDICAL SESSIONS

8:30 - 9:30	BONE DISEASE
9:30 - 9:40	Break
9:40 - 10:30	OSTEOPOROSIS
10:30 - 11:00	Coffee Break
11:00 - 12:05	NORMATIVE DATA
12:05 - 1:35	Lunch
1:35 - 2:35	NON-DISEASE INFLUENCES
2:35 - 2:45	Break
2:45 - 3:45	RENAL
3:45 - 4:10	Coffee Break
4:10 - 5:45	ACTIVITY AND INACTIVITY

INTERNATIONAL CONFERENCE ON BONE MINERAL MEASUREMENT - CHICAGO, ILLINOIS, U.S.A.

PHYSICAL SESSIONS - FRIDAY, October 12, 1973

INTRODUCTION AND ERRORS (Chairman: M. Greenfield)

9:00 - 9:15 HISTORY OF PHOTON ABSORPTIOMETRY
J. R. Cameron

9:15 - 9:40 PHYSICAL ASPECTS OF BONE MINERAL ABSORPTIOMETRY
P. F. Judy

9:40 - 9:55 UNIVERSITY OF ALBERTA BONE MINERAL ANALYSIS SYSTEM - CALIBRATION, PERFORMANCE AND CLINICAL APPLICATION
T. R. Overton

9:55 - 10:15 A METHOD FOR THE DETERMINATION OF THE COMPACTA AREA AND THE MEAN ABSORPTION DENSITY OF HUMAN BONES
P. Rüegsegger, P. Neiderer and M.Anliker

10:15 - 10:30 TWO-DIMENSIONAL SCANNING PHOTON ABSORPTIOMETRY
C. Christiansen

INTERPRETATION AND CORRELATIONS (Chairman: T. R. Overton)

11:00 - 11:15 CORRELATION OF TOTAL-BODY CALCIUM (BONE MASS) AND REGIONAL BONE MASS IN OSTEOPOROSIS
C. H. Chestnut III, E. Manske, D. Baylink and W. B. Nelp

11:15 - 11:30 CORRELATION OF RADIAL BONE MINERAL CONTENT WITH TOTAL-BODY CALCIUM IN VARIOUS METABOLIC DISORDERS
S. H. Cohn, K. J. Ellis, I. Zanzi and J. Aloia

11:30 - 11:40 INTERRELATIONSHIPS AMONG SITES AND WITH BONE STRENGTH
C. R. Wilson

11:40 - 12:00 BONE MINERAL ASSAY - CHOICE OF MEASURING SITES
N. Dalen

DUAL PHOTON TECHNIQUES (Chairman: L. Zeitz)

2:00 - 2:15 DUAL PHOTON DIRECT READOUT SYSTEM
W. Kan, R. B. Mazess and C. R. Wilson

2:15 - 2:30 ANALYSIS OF ^{153}Gd AND OF ^{125}I-^{241}Am SOURCES
J. Hanson

2:30 - 2:50 THE ASSESSMENT OF BONE MINERAL CONTENT BY MEANS OF ALTERNATING TUBE VOLTAGE
K. H. Reiss, K. Killig and W. Schuster

2:50 - 3:05 DUAL ENERGY ABSORPTIOMETRY TECHNIQUE FOR BONE MINERAL CONTENT MEASUREMENT
J. M. McDonald and L. Zeitz

3:05 - 3:25 BONE MINERAL MEASUREMENTS USING A DICHROMATIC ATTENUATION TECHNIQUE WITH SIMULTANEOUS REGISTRATION OF TWO ENERGIES
E. Dissing and P. Schmeling

3:25 - 3:45 A NEW APPARATUS FOR BONE MINERAL MEASUREMENT IN VIVO
M. Gebhardt and H. Zwicker

DATA HANDLING AND EXCHANGE (Chairman: P. Schmeling)

4:00 - 4:10 STANDARDS AND INTERCOMPARISONS
R. Witt

4:10 - 4:25 ORGANIZATION AND PROCESSING OF BONE MINERAL DATA USING A GENERAL PURPOSE STORAGE AND RETRIEVAL PROGRAM AND A MINICOMPUTER
R. E. Zimmerman, T. Daily and H. J. Griffiths

DATA HANDLING AND EXCHANGE (continued)

4:25 - 4:40 BONE MINERAL COMPUTATION WITH A RECTILINEAR SCANNER
S. Brown, A. Silverstein, J. Ullman, J. Vogel

4:40 - 4:55 A COMPUTERIZED METHOD OF DETERMINATION OF BONE MINERAL CONTENT BY A TRANSMISSION-SCANNER. METHODOLOGY.
U. Schneider and D. Banzer

OTHER METHODS RUMP SESSION (Chairman: K. H. Reiss)

8:00 - 8:15 IN VIVO CALCIUM DETERMINATION BY PROTON ACTIVATION ANALYSIS
R. Eilbert

8:15 - 8:30 A THEORETICAL EVALUATION OF SEVERAL NUCLIDES FOR BONE DENSITY DETERMINATIONS BY COMPTON SCATTERING
D. G. Piper, L. E. Preuss and F. P. Bolin

8:30 - 8:45 RESULTS OF CORRELATION RESEARCH ON MINERAL CONTENT OF OS CALCIS AND SPINE USING SEVERAL RESEARCH METHODS
R. Luther

8:45 - 9:00 PROGRESS IN RADIOGRAPHIC PHOTODENSITOMETRY
C. Colbert

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BIOMEDICAL SESSIONS - SATURDAY, October 13, 1973

BONE DISEASE (Chairman: H. Griffiths)

8:30 - 8:45 SKELETAL MINERALIZATION IN PRIMARY HYPERPARATHYROIDISM
H. K. Genant, J. Vander Horst and L. H. Lanzl

8:45 - 9:00 ARTHRITIC PATIENTS AND CORTICOSTEROIDS
M. Mueller

9:00 - 9:15 OSTEOMALACIA IN EPILEPTIC PATIENTS TREATED WITH ANTI-CONVULSANTS. A CONTROLLED THERAPEUTIC TRIAL
C. Christiansen and P. Rødbro

9:15 - 9:30 A COMPUTERIZED METHOD OF DETERMINATION OF BONE MINERAL CONTENT BY A TRANSMISSION-SCANNER. CLINICAL STUDIES.
D. Banzer and U. Schneider

OSTEOPOROSIS (Chairman: C. Johnston)

9:40 - 10:00 DYNAMICS OF BONE MINERAL LOSS IN THE MENOPAUSE
K. Heer, J. Guncaga, Th. Lauffenburger, A. Rösli, M. A. Dambacher and H. G. Haas

10:00 - 10:15 DISCRIMINATION OF OSTEOPOROSIS AND BONE DISEASE
J. Shapiro, W. T. Moore and G. D. Whedon

10:15 - 10:30 PHOTON ABSORPTION METHOD AND SINGH INDEX IN THE DETECTION OF OSTEOPOROSIS. A COMPARATIVE STUDY
H. W. Wahner, B. L. Riggs and J. W. Beabout

NORMATIVE DATA (Chairman: P. J. Atkinson)

11:00 - 11:15 WISCONSIN NORMATIVE OUTLINE
R. B. Mazess and J. R. Cameron

11:15 - 11:30 NORMATIVE DATA FROM THE OSTEOPOROSIS PREVALENCE SURVEY, OAKLAND, CALIFORNIA, 1969-1970
N. F. Goldsmith

11:30 - 11:50 INFLUENCE OF THE NATURAL Ca AND F SUPPLY AND OF A Ca SUPPLEMENTATION ON BMC OF HEALTHY POPULATION IN SWITZERLAND
A. Donath, P. Indermühle and R. Baud

11:50 - 12:05 MINERAL LOSS WITH AGING MEASURED PROSPECTIVELY BY THE PHOTON ABSORPTION TECHNIQUE
D. M. Smith and C. Conrad Johnston, Jr.

NON-DISEASE INFLUENCES (Chairman: L. Riggs)

1:35 - 1:50 TIBIAL BONE MINERAL DISTRIBUTION AS INFLUENCED BY CALCIUM, PHOSPHORUS, AND VITAMIN D
F. A. Spurrell, J. Brenes and P. Waibel

1:50 - 2:05 EFFECT OF DIETARY CALCIUM ON JAW BONE DENSITY
L. Lutwak

2:05 - 2:20 TRANS - IMAGING OF BONE ALLOGRAFTS - A RAPID METHOD FOR EVALUATING OSSEOUS INCORPORATION
R. W. Bright, V. L. McManaman and A. M. Strash

2:20 - 2:35 EFFECTS OF SKELETAL RADIUM DEPOSITS ON BONE MINERALIZATION
R. A. Schlenker and R. G. Oltman

RENAL (Chairman: A. Donath)

2:45 - 3:05 FOLLOW-UP EXAMINATIONS OF THE MINERAL SALT CONTENT IN THE SKELETON WITH VARIOUS VITAMIN D RESISTANT FORMS OF RICKETS OF RENAL ORIGIN
W. Schuster

3:05 - 3:25 CHANGES IN SKELETAL MINERAL IN PATIENTS WITH RENAL FAILURE
P. J. Atkinson, F. M. Parsons, G. W. Reed and D. A. Hancock

3:25 - 3:45 PHOTON ABSORPTIOMETRY IN RENAL FAILURE
H. J. Griffiths, R. E. Zimmerman and G. Bailey

ACTIVITY AND INACTIVITY (Chairman: B. Nilsson)

4:10 - 4:25 BONE MINERAL CHANGES IN THE APOLLO ASTRONAUTS
J. M. Vogel

4:25 - 4:45 OSTEOPOROSIS BEFORE AND AFTER FRACTURE OF THE FOREARM
B. E. Nilsson and N. E. Westlin

4:45 - 5:00 CHANGES IN BONE MINERALIZATION IN HEMIPLEGIA
C. H. Marshall, A. T. Viau, L. Berkovits, W. S. Davis, D. S. Chu and N. E. Naftchi

5:00 - 5:15 BONE MINERALIZATION AND PHYSICAL ACTIVITY
R. C. Watson

5:15 - 5:30 THE EFFECT OF DIPHOSPHONATE (EDHP) THERAPY ON IMMOBILIZATION OSTEOPOROSIS
A. R. Arnstein, F. S. Blumenthal and D. S. McCann

5:30 - 5:45 THE EFFECTS OF PHYSICAL ACTIVITY ON BONE IN THE AGED
E. L. Smith

INTERNATIONAL CONFERENCE ON BONE MINERAL MEASUREMENT - Chicago, Illinois
October 12 - 13, 1973

Speaking Schedule

ARNSTEIN, A. Robert, Frank S. Blumenthal and Daisy S. McCann	Saturday	5:15 - 5:30
ATKINSON, P. J., F. M. Parsons, G. W. Reed, and D. A. Hancock	Saturday	3:05 - 3:25
BANZER, D. and U. Schneider	Saturday	9:15 - 9:30
BRIGHT, Robert W., Vince L. McManaman and Alfred M. Strash	Saturday	2:05 - 2:20
BROWN, S, A. Silverstein, J. Ullman and J. Vogel	Friday	4:25 - 4:40
CAMERON, J. R.	Friday	9:00 - 9:15
CHESTNUT, C. H., E. Manske, D. Baylink and W. B. Nelp	Friday	11:00 - 11:15
CHRISTIANSEN, Claus	Friday	10:15 - 10:30
CHRISTIANSEN, Claus and Paul Rødbro	Saturday	9:00 - 9:15
COHN, S. H., K. J. Ellis, I. Zanzi and J. Aloia	Friday	11:15 - 11:30
COLBERT, C. and Richard S. Bachtell	Friday	8:45 - 9:00 p.m.
DALEN, Nils	Friday	11:40 - 12:00
DISSING, Erik and Per Schmeling	Friday	3:05 - 3:25
DONATH, A, P. Indermühle and R. Baud	Saturday	11:30 - 11:50
EILBERT, Richard	Friday	8:00 - 8:15 p.m.
GEBHARDT, M. and H. Zwicker	Friday	3:25 - 3:45
GENANT, Harry K, Jean Vander Horst and Lawrence H. Lanzl	Saturday	8:30 - 8:45
GOLDSMITH, N. F.	Saturday	11:15 - 11:30
GRIFFITHS, Harry J., Robert E. Zimmerman and George Bailey	Saturday	3:25 - 3:45
HANSON, J.	Friday	2:15 - 2:30
HEER, K, J. Guncaga, Th. Lauffenburger, A. Rösli, M. A. Dambacher and H. G. Haas	Saturday	9:40 - 10:00
JUDY, Philip F.	Friday	9:15 - 9:40
KAN, W. C., R. B. Mazess and C. R. Wilson	Friday	2:00 - 2:15
LUTHER, Robert	Friday	8:30 - 8:45 p.m.
LUTWAK, L.	Saturday	1:50 - 2:05
MARSHALL, C. H., A. T. Viau, L. Berkovits, W. S. Davis, D. S. Chu and N. E. Naftchi	Saturday	4:45 - 5:00
MAZESS, R. B. and John R. Cameron	Saturday	11:00 - 11:15
McDONALD, Joseph M., Louis Zeitz	Friday	2:50 - 3:05
MUELLER, Mark N., Richard B. Mazess and John R. Cameron	Saturday	8:45 - 9:00
NILSSON, Bo E. and Nils E. Westlin	Saturday	4:25 - 4:45
OVERTON, T. R.	Friday	9:40 - 9:55
PIPER, Dennis G., Luther E. Preuss, and Frank P. Bolin	Friday	8:15 - 8:30 p.m.
REISS, K. H., K. Killig and W. Schuster	Friday	2:30 - 2:50
RUEGSEGGER, P., P. Niederer and M. Anliker	Friday	9:55 - 10:15
SCHLENKER, Robert A. and Billie G. Oltman	Saturday	2:20 - 2:35
SCHNEIDER, U. and D. Banzer	Friday	4:40 - 4:55
SCHUSTER, W.	Saturday	2:45 - 3:05
SHAPIRO, J., W. T. Moore and G. D. Whedon	Saturday	10:00 - 10:15
SMITH, David M., and C. Conrad Johnston	Saturday	11:50 - 12:05
SMITH, Everett L.	Saturday	5:30 - 5:45

SPURRELL, Francis A., Juan Brenes and Paul Waibel	Saturday	1:35 - 1:50
VOGEL, John M.,	Saturday	4:10 - 4:25
WAHNER, H. W., B. L. Riggs and J. W. Beabout	Saturday	10:15 - 10:30
WATSON, Ronald C.	Saturday	5:00 - 5:15
WILSON, Charles R., Richard B. Mazess and John R. Cameron	Friday	11:30 - 11:40
WITT, R. M.	Friday	4:00 - 4:10
ZIMMERMAN, Robert E., Tim Daily and Harry J. Griffiths	Friday	4:10 - 4:25

HISTORY OF PHOTON ABSORPTIOMETRY

J. R. Cameron

Medical Physics and Engineering Center, University of Wisconsin, Madison, Wisconsin

Quantitative bone absorptiometry began early this century with efforts to standardize radiographs. During the thirties there was a large effort on radiographic photodensitometry using aluminum and ivory calibration wedges. That radiographic approach culminated in the systems of the late fifties and early sixties, but even today there are large inherent errors due to scattered radiation from the broad beam, to spectral hardening of the polychromatic beam, and to variations in exposure, development and processing.

During the fifties attempts were made to use scintillation detectors with x-ray beams and even with radionuclide sources. During the past decade direct photon absorptiometry using monoenergetic sources has evolved from an experimental technique to an accepted research method, and in the present decade with the advent of direct readout units, it has become important to normative and clinical biological applications.

During the remainder of this decade we may expect an expansion of dual-photon absorptiometry so that it will supplant the single-photon technique and elaboration of that dual-photon approach for determination of soft-tissue composition as well as bone mineral. We may also expect growth of video-densitometry for measurement of bone mineral content.

PHYSICAL ASPECTS OF BONE MINERAL ABSORPTIOMETRY

Philip F. Judy

Department of Radiology, Harvard Medical School, Boston, Massachusetts

The magnitude of the errors in the absorptiometric measurement of bone mineral mass has estimated from a detailed physical description of the measurement and an analysis of the validity of the assumptions made in the derivation of the formula used to calculate the bone mineral mass from the transmission of the body. The derivation assumes exponential attenuation and a division of the human body into two components, each having a unique mass attenuation coefficient and density.

The accuracy of bone mineral absorptiometry using the radionuclide, ^{125}I, as the photon source was found to be determined by hardening the photon beam and variation in the distribution of adipose tissue in the body. The hardening of the photon beam was caused by the polyenergetic character of ^{125}I emissions and was altered by tin filtration. This error was estimated to be ±2% when the system was calibrated over the biological range of bone mineral mass. The variations of adipose tissue thickness inside the bone and subcutaneously have been shown to each cause an error of 5% for the measurement of the radius, but tend to cancel out. This error depended critically on the method of determining the baseline. The errors caused by the detection of scattered radiation and the finite size of the photon beam have been shown to be less than 1% for a system calibrated by an ash study.

The instrumental reproducibility of the ^{125}I measurement of bone mineral mass has been limited by the number of photons detected. The activity of ^{125}I, the detector geometry, and scan rate in the clinical instruments have been such that the precision of measurement of bone mineral mass of the radius is 1% - 2%. The NaI (Tl) scintillation detector was operated near its upper rate limit. The practical consequences of this limit have indicated a parallel detection system would be required to improve the reproducibility *in vivo*.

UNIVERSITY OF ALBERTA BONE MINERAL ANALYSIS SYSTEM - CALIBRATION, PERFORMANCE AND CLINICAL APPLICATION

T. R. Overton

Division of Biomedical Engineering, University of Alberta, Canada

A bone mineral analysis system using Am^{241} is described. Features of this system include:

- mechanical adaptability for possible studies at a number of bone sites. Provision for two source mounting (eg. I^{125} and Am^{241}) is made,
- precision mechanical drive system,
- fully automatic scan sequencing following a single "initiate scan" command,
- no system "dead-time" in data acquisition.

Digital data is recorded via teletype on printed roll and punched tape. A chart record is also available for immediate evaluation. Data analysis, carried out on a laboratory computer system, provides values for BMC and bone width as well as a variety of derived parameters.

Measurements of "small" phantoms (eg. Wisconsin #2016) demonstrate that good reproducibility can be obtained using Am^{241} as photon source (Am^{241}(cv = 3.5%), I^{125}(cv = 1.2%) for smallest chamber, and Am^{241}(cv = 1.2%). I^{125}(cv = 0.92%) for the largest chamber).

However, this system was developed for investigation of BMC in large bones (eg. femur) and measurements of appropriately sized phantoms and bone samples give very good reproducibility (Am^{241}, cv = 1.0%, N = 108 for K_2HPO_4 phantom and Am^{241}, cv = 1.0%, N = 50 for in vitro femur samples - all measurements made in 10 cm water).

The accuracy of this bone mineral analysis system has been investigated by measuring known amounts of mineral (K_2HPO_4) in phantoms and also bone samples which were subsequently ashed. The correlations between measured and calculated values for K_2HPO_4 and between measured value and ash weight per cm were high ($r = 0.99$).

About 500 clinical measurements have been made, including normals and various disease groups. These measurements of the distal femur were found to be greatly influenced by variations in tissue composition. However, techniques for measurement and analysis have been developed which minimize these difficulties and good reproducibility in clinical measurements is routinely obtained (cv = 2.0% for 15 measurements of "normal" femur during 5 weeks).

A METHOD FOR THE DETERMINATION OF THE COMPACTA AREA AND THE MEAN ABSORPTION DENSITY OF HUMAN BONES

P. Rüegsegger, P. Niederer and M. Anliker

Institut für Biomedizinische Technik, Rämistrasse 100, CH-8006 Zürich, Switzerland

Cameron's concept of bone mineral measurement using soft γ-rays has been extended to determine the area of the compacta cross-section (A_B) and the corresponding mean absorption density (β). By repeating the scanning process at the same section for different directions a polygon is defined which circumscribes the outer contour of the bone section. With the aid of a PDP11-20 computer and an iterative technique the compacta area and the mean absorption density are evaluated. In addition to A_B and β the computer produces an image of the actual compacta cross-section. Thanks to the redundancy of the absorption data the values for A_B and β can be determined as many times as the scanning process has been carried out. The fluctuations in A_B and β are small and appear to be measures for the regional variation of the bone mineral density. To validate the method and assess the accuracy and statistical fluctuations of the measurements an aluminium tube with circular cross-section has been used and the data indicate that A_B and β can be determined with an error on the order of 1%. Data from measurements on excised human femurs have been obtained and will be presented. The scanning apparatus can readily be adapted for use on patients.

TWO-DIMENSIONAL SCANNING PHOTON ABSORPTIOMETRY

Claus Christiansen

Department of Clinical Physiology, Clinical Chemistry and Neurology, Glostrup Hospital, 2600 Glostrup, Denmark

CORRELATION OF TOTAL-BODY CALCIUM (BONE MASS) AND REGIONAL BONE MASS IN OSTEOPOROSIS

C. H. Chestnut, III, E. Manske, D. Baylink and W. B. Nelp

University of Washington Hospital and VA Hospital, Seattle, Washington

Total-body calcium determined by in vivo neutron activation analysis (NAA) is a unique and accurate measurement; however, it requires special facilities for neutron exposure and total-body counting. On the other hand, measurement of regional bone mass (RBM) by photon absorption is relatively simple and utilizes readily available equipment. There is, however, uncertainty if the mass of a small segment of one bone reflects total skeletal mass. The purpose of this study was to measure RBM at six sites along the radius, ulna, and humerus, and to compare the multiple RBM measurements to TBC and to each other. Fourteen patients with osteoporosis, ages 56-76, (two males, twelve females) were studied.

TBC was measured in grams by NAA with an accuracy of $\pm$ 5% using methods established at the University of Washington. RBM was measured by ^{125}I photon absorption with a precision of $\pm$ 5%.

TBC ranged from 482 to 1,076 gm. RBM of the distal radius (predominantly trabecular bone) ranged from 0.5679 to 1.3949 gm/cm and was highly correlated with TBC to give the expression RBM = 0.133 $\pm$ 0.001 (TBC). The r value was 0.94 and $p < 0.001$. Good correlations bewween TBC and RBM were also found at other sites in the radius, ulna, and humerus ($r = 0.93$ to 0.84). In general, the correlation with TBC was somewhat higher for RBM in trabecular rather than in cortical bone. The strength factor, derived from the mass and geometry of the distal radius, was also highly correlated with TBC ($r = 0.93$). In contrast, no relationship between combined cortical thickness, internal diameter, or cortical index to TBC was apparent. The intercomparison of RBM at the various sites was also good with r values ranging from 0.89 to 0.94.

It is concluded that in osteoporosis RBM in selected sites of radius, ulna, and humerus correlate well with total-bone mineral mass; therefore, it may be possible to predict TBC in grams from a single RBM measurement and to predict calcium balance from sequential RBM measurements.

CORRELATION OF RADIAL BONE MINERAL CONTENT WITH TOTAL-BODY CALCIUM IN VARIOUS METABOLIC DISORDERS

S. H. Cohn, K. J. Ellis, I. Zanzi and J. Aloia

Medical Research Center, Brookhaven National Laboratory, Upton, N.Y.

It has been shown that the loss of bone mineral content of the skeleton in osteoporosis and in other metabolic disorders can be measured directly by total-body neutron activation analysis (TBNAA). It has also been shown that the densitometric technique (using monochromatic photons from ^{125}I) applied to the appendicular skeleton (radius) reflects the loss of bone mineral in osteoporosis.

In the present study the results of these two techniques are compared in 80 patients with various metabolic disorders. It is apparent that there is good correlation between total-body calcium and bone mineral content (BMC) in all groups studied. The correlation was highest in a normal contrast group (0.97) and lowest in osteoporotic patients (0.826) and in renal patients on dialysis (0.835).

In order to measure the relative deficit in total-body Ca in individual patients from the absolute Ca measurement, it is necessary to normalize the data for sex, age and skeletal size. For this purpose an algorithm was developed to predict the normal skeletal Ca in each subject based on weight, height, sex and age. In similar manner, to facilitate intercomparison of bone mineral content measured by densitometry, an index of size and age is required. Dividing the BMC by the width of the radius does tend to reduce the variability in the group but is not satisfactory as a normalizing factor.

The diagnostic value of these data, both separately, and when used together will be discussed.

THE DETERMINATION OF SKELETAL STATUS BY BONE MINERAL CONTENT

Charles R. Wilson, Richard B. Mazess and John R. Cameron

Medical Physics and Engineering Center, University of Wisconsin, Madison, Wisconsin

The bone mineral content (BMC) is being extensively utilized to provide physiological data about the skeleton. Changes in BMC are employed to evaluate the skeletal effect of various drugs, both beneficial and detrimental, disease states, weightlessness, exercise, renal dialysis, etc. These studies are based on the hypothesis that the BMC provides information concerning the status of the entire skeleton. Evidence from our laboratory and others of the validity of this hypothesis will be discussed. Also, the relation between BMC and maximum strength of bone and the apparent strength of the femoral neck will be presented.

BONE MINERAL ASSAY - CHOICE OF MEASURING SITES

Nils Dalén

Department of Medical Engineering, Karolinska Institutet, Stockholm, Sweden

In most earlier clinical studies only one site was studied by each investigator. The object of the present study was to collect data by the x-ray spectrophotometric method on the bone mineral content at various sites during different clinical conditions, such as alcoholics, patients with primary hyperparathyroidism, patients with chronic renal failure, non-patients and athletes. The sites were radius and ulna distal and shaft, head of humerus, third lumbar vertebra, femur neck and shaft, and calcaneus.

The deviation in bone mineral content in cross-sectional studies, the change in bone mineral content with time in longitudinal studies and the correlation to morphological signs of osteoporosis in skeletal radiographs, were more pronounced at sites containing trabecular bone than at sites containing cortical bone. The sites containing trabecular bone are therefore usually to be preferred, in spite of the great biological variation and the comparatively low attainable precision at these sites.

The correlation between different sites in the same individual is weak, and the bone mineral content at the different sites deviates relative to controls in a varying way. Therefore, several sites should be measured to avoid erroneous conclusions.

DIRECT READOUT OF BONE MINERAL CONTENT WITH DICHROMATIC ABSORPTIOMETRY

W. C. Kan, R. B. Mazess, and C. R. Wilson

Medical Physics and Engineering Center, University of Wisconsin, Madison, Wisconsin

An analog device has been constructed which provides immediate readout of bone mineral content and bone width from absorptiometric scans with two photon beams with different energies such as ^{153}Gd (43 keV and 100 keV) or $^{125}I/^{241}Am$ (28 keV and 60 keV). The system and preliminary results will be presented.

ANALYSIS OF ^{153}Gd AND OF ^{125}I-^{241}Am SOURCES

J. Hanson

Medical Physics and Engineering Center, University of Wisconsin, Madison, Wisconsin

The precision of the dual photon bone mineral technique was modeled mathematically as an expression based on counting statistics. For a given amount of bone and soft tissue there is an optimal photon energy pair. When the initial intensities of the photon beams are equal, the optimal lower photon energy increases with increasing mass of bone and soft tissue for a given higher photon energy. Dual sources of interest are $^{125}I/^{241}Am$ (28 and 60 kev) and ^{153}Gd (43 and 100 kev). The bone mineral measured in thin anatomical locations (i.e. hand and forearm) with $^{125}I/^{241}Am$ is more precise than with ^{153}Cd. For thick locations (i.e. upper arm and calf) ^{153}Gd is more precise than $^{125}I/^{241}Am$.

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J. Hanson

Medical Physics and Engineering Center, University of Wisconsin, Madison, Wisconsin

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THE ASSESSMENT OF BONE MINERAL CONTENT BY MEANS OF ALTERNATING TUBE VOLTAGE

K. H. Reiß, K. Killig and W. Schuster

Siemens Aktiengesellschaft, Erlangen, Germany

The present situation on the field of bone mineral content determination is characterized by a multiplicity of methods, each of them applied by a group of authors and restricted to particular purposes.

The technical problem for bone mineral determination is to combine a convenient localization and a simple measuring system, which has a sufficient beam intensity for all parts of the skeleton.

The technical solution, we want to offer, is an X-ray "beam of different quality" coming out of the same tube in the same location, which is monitored by a television set. The tube voltage is alternating between a lower adjustable value (60 to 90 kV) and a constant higher value (150 kV). To compensate for the different intensities behind the patient, an oscillating copper filter easily adjustable from 1.5 to 4.5 mm of copper is in the beam when the higher tube voltage is switched on. The frequency of the alternation of the tube voltage is about 5 cycles per sec.

To avoid scatter we use a rather narrow beam (0.5 to 2 cm diameter) during the measurement. The location is acheived by the normal viewing field of an X-ray 7" image intensifier.

A digital quotient measuring system compares the intensities and gives a figure of the relation "intensity at higher tube voltage divided by intensity at lower tube voltage".

The intensities of both beams give sufficient quanta, to perform a single measurement in about ten sec., even behind a body of 40 cm water equivalent thickness.

DUAL ENERGY ABSORPTIOMETRY TECHNIQUE FOR BONE MINERAL CONTENT MEASUREMENT*

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A dichromatic, or dual energy photon, technique has been developed for direct photon absorptiometry scan measurements of bone mineral content. This technique is an extension of the constant sample thickness, monochromatic method of Cameron (J.R. Cameron, et al, Invest. Rad. 3, 1968, 141) for the in vivo determination of the mineral content of human bones, in particular the radius and ulna.

While the monochromatic method has been shown in general to be a fast, safe, and accurate technique for evaluating bone mineralization, it has been demonstrated that it is subject to errors due to the presence of adipose tissue (L. Zeitz, Acta. Rad. 11, 1972, 401; W. Wooten, et al, Invest. Rad. 8, 1973, 84). Using our dichromatic system, with artificial bone standards and paraffin (simulating fat) in plexiglass, we have been able to correct for the presence of the fat component, which would have otherwise produced errors of from zero to approximately thirty percent in the mineral content using the monochromatic technique. Corrected integral values had standard deviations from the true (no paraffin) values of up to a few percent, while the precision of the technique was approximately two percent for these measurements. The next step in this study will be to extend these measurements to actual human bones, soft tissue or equivalent, and fat.

*This work was supported in part by A.E.C. Contract AT (11-1) - 3521 by N.C.I. C.A. 08748.

BONE MINERAL MEASUREMENTS USING A DICHROMATIC ATTENUATION TECHNIQUE WITH SIMULTANEOUS REGISTRATION OF TWO ENERGIES

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In vivo measurements of bone minerals using a single gamma energy require the use of water or other tissue equivalent substances. The dichromatic technique makes measurements in air possible, and by using the gamma rays from ^{241}Am and ^{125}I the influence of soft tissue can be easily eliminated when measuring the arm.

Simultaneous registration of two energies together with an automatic and continuous elimination of soft tissue was demonstrated. The primary results could be obtained directly on a recorder. It was easily possible to measure radius, ulna, humerus, femur, tibia, fibula, and patella. Even the cranium and the spine could be registered. With the used equipment the detector and electronic module were not good enough to permit an ideal resolution of the two energies, and the standard deviation could therefore not be brought below the 3% limit. It is expected that improvement of the electronics will lower this limit.

A NEW APPARATUS FOR BONE MINERAL MEASUREMENT IN VIVO

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A grant of the "Deutsche Forschungsgemeinschft" permitted the development of an apparatus which enables an accurate determination of the mineral content of the finger-bone with the application of monochromatic x-rays of two wavelengths.

A finger-holder keeps the middle phalanx of the finger in an exact fixable position, whereby the soft tissue parts are slightly pressed between two parallel plexiglass-windows. The total width of the finger can be measured with the help of a gauge having a calibration of 1/100 mm. The bone thickness is determined by a film photograph, whereby the measuring space is kept fixed.

The absorption measurement is carried out by:

1) A transmission of a monochromatic x-ray beam only through the soft tissue parts and by central passage, thereby enabling a calculation of the mean absorption coefficient of the bone together with the bone thickness obtained by the film photograph.

2) Consecutive transmisstion of two different energetic x-ray beams through the central passage and the soft tissue parts; this allows the use of the double isotope method developed by Rassow et al.

3) Through the scanning of the entire cross-section of the finger, with one or two of the radiation types; this enables among other things, the application of the one isotope method developed by Börner et al. for the separated determination of Compakta and spongiosa.

In all, the advantage of this equipment vis-à-vis others permits the application of many measurement methods on the same object, also achieving high precision by the use of highly stabilized x-ray tubes with high primary impulse rates instead of the radioactive sources normally used. The disadvantage of this equipment lies on the confinement on measurements of finger-bone only.

BONE STANDARDS FOR THE INTERCOMPARISON AND CALIBRATION OF PHOTON ABSORPTIOMETRIC BONE MINERAL MEASURING SYSTEMS

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In order for different laboratories to compare and collate results there must be uniform calibration and standardization.

Bone standards have been constructed to provide for the intercomparison and calibration of photon absorptiometric bone measuring systems. The standards are composed of polymethyl methacrylate blocks with three annular cavities which are filled with a saturated solution of dipotassium hydrogen phosphaté, KHP. The saturated KHP solution has linear attenuation properties similar to those of compact bone and the dimensions of the inner and outer diameters of the annular cavities are similar to those for the midshafts of radii and metacarpals. The bone mineral content, BMC, of these standards was calibrated by ashed bone sections in units of g/cm of bone ash.

Six of these standards, all identical, were scanned in six different laboratories with bone mineral measuring systems with digital output of the transmission counts. The coefficient of variation of the BMC for each chamber for all laboratories was the same as the coefficient of variation of the same chamber measured by a single laboratory. For comparison our clinical laboratory has measured a standard over a 33 month period with a direct readout device. The coefficients of variation for the BMC's were 2.3% for the small chamber, 1.5% for the medium chamber, and 1.2% for the large chamber.

The bone standards can be used to linearly calibrate absorptiometric bone measuring systems in terms of the ashed bone sections. A calibration equation for a system can be determined from a linear regression analysis of the assigned calibration values and the output units of the system for the three chambers of the standard. This linear calibration has been shown to be valid for various radionuclide photon sources useful in the absorptiometric method. For the case of ^{125}I sources, the linear calibration only would be valid for bones ranging in size from metacarpals to radii because of spectrum hardening.

ORGANIZATION AND PROCESSING OF BONE MINERAL DATA USING A GENERAL PURPOSE STORAGE AND RETRIEVAL PROGRAM AND A MINICOMPUTER

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The measurement of bone mineral content utilizing the photon absorption method has become routine at major medical centers. Organization and correlation of this data with disease states and various epidemiological factors is a formidible problem. An information storage and retrieval program operating on a minicomputer has been used to aid in processing data from over 3000 scans on 1890 patients. The program will be described along with the human factors including source documents, accuracy, reliability and method of interrogation of the data. A normal population has been studied along with renal disease, spinal cord injury, and endocrine disorders. The computer has proven to be an indispensable tool in correlating the bone mineral content with the radiological, biochemical and physical parameters of the individual patients and patient populations.

BONE MINERAL COMPUTATION WITH A RECTILINEAR SCANNER

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A portable rectilinear transmission scanner and associated computerized data reduction techniques for estimating bone mineral content are described. This unit can be easily disassembled for transport to various measurement sites and has been used to estimate the bone mineral content of the os calcis, radius, and ulna in the Apollo and Skylab Astronauts. The scanner is used to obtain multiple rows of data from which a bone profile is derived. Bone edges are determined with the aid of a digital computer program which employs an algorithm that determines the greatest rate of change of the counting rate. This program is particularly useful for determining the edges of bones surrounded by varying tissue distributions.

A COMPUTERIZED METHOD OF DETERMINATION OF BONE MINERAL CONTENT BY A TRANSMISSION-SCANNER. METHODOLOGY.

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Based on the method of Cameron and Sorenson a transmission-scanner has been developed including a movable x-ray tube. Additional information about geometry and structure of the bone which has been examined are obtained by several radiographs in the plane of measurement. The data is evaluated by a computer and is stored on magnetic tape, together with clinical information. Automatic reports for the physician are printed and scientific evaluation is possible by several programs. With a special piece of equipment the bones of small animals are measured. Most of the human measurements were done on the calcaneus. Normal ranges for this bone were evaluated.

IN VIVO CALCIUM DETERMINATION BY PROTON ACTIVATION ANALYSIS

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A method for in vivo calcium measurement is being developed at Harvard University's 160 Mev proton cyclotron. Advantages of the technique include direct measurement of calcium in the lumbar vertebrae and restriction of dose to the immediate vertebral region. Activation of ^{40}Ca produces the radionuclide ^{38}K, which subsequently beta decays with 7.7 minute half-life and emits a 2.2 Mev gamma ray. A large NaI (Tl) detector adjacent to the spine is used to count gamma rays in the photopeak. Preliminary results indicate 750cts/rad are feasible from one lumbar vertebra. The technique may be of particular use in plotting serial changes of a patient's calcium level in response to treatment.

A THEORETICAL EVALUATION OF SEVERAL NUCLIDES FOR BONE DENSITY DETERMINATIONS BY COMPTON SCATTERING

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The table of radioactive isotopes was surveyed for nuclide applicability in Compton scattering determinations of bone density. This two photon technique corrects for soft tissue attenuation and thus allows a direct measurement of density. Assuming a possible experimental design, we imposed the following parameters: 5 mm (diam) photon beam, scattering from a 3 cm (diam) compact bone cylinder surrounded by 2 cm of soft tissue, source-detector distance of 10 cm, scattered beam intensity of 50 counts per min, a 20 minute exposure, primary beam energy of 80 - 200 kev, and half-life longer than 100 days. Prediction of merit of the nuclides was based on dosage, scattering efficiency, radiation purity, photon output efficiency, self-absorption, availability, and cost. Twelve isotopes were selected for scrutiny and, of these, seven nuclides in sundry combinations were considered to exhibit usable potential. The two primary-secondary combinations judged to have greatest general promise are ^{153}Gd (100 kev) - ^{170}Tm (84 kev) and ^{144}Ce (134 kev) - ^{57}Co (122 kev).

RESULTS OF CORRELATION RESEARCH ON MINERAL CONTENT OF OS CALCIS AND SPINE USING SEVERAL RESEARCH METHODS

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With a newly developed measuring device, using the Compton scattering method, we have measured the mineral content of 50 os calcis and 50 spines and checked the results by ashing. All results have been statistically analyzed. It was demonstrated that the mineral is so inhomogeneously distributed in the os calcis, that a single measurement is insufficient to accurately characterize the average HA-percentage of this bone.

The investigations of the HA-percentage of the spine showed a statistically significant negative correlation with age, but this was not evident for the os calcis.

Although both the os calcis and spine were spongy, there was neither a significant nor a statistically significant correlation in the HA-percentage of the two bones.

The publications of several authors indicate prediction is possible from the periphery to femur or spine and this was contradicted by our results.

An unequivocal HA-reduction of os calcis in more than 300 individuals measured could only be proved in the case of local or general rarefaction diseases.

PROGRESS IN RADIOGRAPHIC PHOTODENSITOMETRY

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Hospital X-ray equipment cannot be relied on to maintain uniform exposure so it becomes necessary for radiographic photodensitometry to make corrections when analyzing the film. Recent progress not only uses a ramp wedge calibration, but correction is made for film background and exposure kilovoltage. This process is automated under computer control.

SKELETAL MINERALIZATION IN PRIMARY HYPERPARATHYROIDISM

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Skeletal mineralization has been assessed in 84 patients with primary hyperparathyroidism. Qualitative studies included a review of conventional radiographs of the spine and hands by two radiologists. Fifteen patients were studied, in addition, by fine-detail radiography using industrial film and optical magnification to 10X. Quantitative assessment included radiographic morphometry using the cortical thickness (C) of the second metacarpal, and photon absorptiometry using the middle phalanx of the third digit (Lanzl and Strandjord). This technique utilizes an ^{125}I source and a NaI crystal detector; the result is expressed as the linear absorption coefficient of overall bone (μ_B in cm^{-1}).

Radiographic osteopenia was detected on 20% of spine and 36% of hand radiographs, and was usually considered consistent with patient age. The agreement between two radiologists in judging the severity of demineralization was 68% for spine and 53% for hand radiographs. Osteitis fibrosa was detected in 8% of patients on conventional radiographs. However, 10 of the 15 patients studied by fine-detail radiography had evidence of increased bone resorption - i.e., subtle subperiosteal resorption or excessive cortical tunnelling. Metacarpal C and phalangeal μ_B were decreased by more than 1 standard deviation in 50% and 48% of patients respectively. μ_B and C were closely correlated ($r = .64$). There was no correlation between μ_B and tumor weight, serum calcium, or alkaline phosphatase.

Conclusions regarding skeletal disease in primary hyperparathyroidism:

1. Radiographic osteopenia is uncommon and difficult to assess.
2. Fine-detail radiography reveals excessive bone resorption undetected on conventional radiographs.
3. Metacarpal cortex (C) and bone mineral content (μ_B) correlate well and are reduced in approximately 50% of patients.

CORTICOSTEROID THERAPY ACCELERATED OSTEOPOROSIS IN RHEUMATOID ARTHRITIS

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Bone mineral content (BMC) at two sites of the radius was assessed in 236 Caucasian women with rheumatoid arthritis (RA), using monoenergetic absorptiometric scanning. To evaluate the effects of disease on bone separately from superimposed effects of corticosteroid therapy, examination at distal (D) and midhsaft (M) sites of the radius were made on 127 rheumatoid women with no exposure to steroids (non CS) and 109 who had been treated with corticosteroids (CS). Individuals were matched for age, duration and severity of disease.

BMC, % change from normal

			RA, non CS			RA, CS	
Severity	Stage@	N	D %	M %	N	D %	M %
Mild	I/II	47					
Definite	II/III	33	+1.3	-1.3	20	-12.5+	-8+
Classic	II	15	-6.3	-5.0	19	-17.5+	-18+
Classic	III	32	-13.8+	-15.0+	56	-30.0+	-25+
Classic	IV				14	-40.0+	-41.3+

+P is less than .05; @ function impairment (Steinbrocker); N = number of patients.

Decline in BMC was clearly related to duration of RA, and was significant after 3 years in the CS group, but only after 15 years in the non CS group. Loss of BMC was similar at both sites of measurement, and was equally severe in premenopausal and postmenopausal patients.

The data suggest that corticosteroid therapy has early and marked detrimental effects on the skeleton of women with RA which are superimposed on the disease effects. The premenopausal group were not spared such bone mineral loss.

Similar observations of bone mineral were made in a population of 77 male and female patients with a diagnosis of asthma. Preliminary analysis indicates that:

1. Asthma untreated with corticosteroids has no discernible detrimental effect on bone mineral content.
2. Superimposition of corticosteroid therapy on the disease asthma is associated with no discernible effect on bone mineral content.

Thus, asthma patients treated with corticosteroids, even for prolonged periods with equivalent daily dosages, appear to be at less risk than patients with rheumatoid arthritis in terms of their bone mineral content.

OSTEOMALACIA IN EPILEPTIC PATIENTS TREATED WITH ANTICONVULSANTS. A CONTROLLED THERAPEUTIC TRIAL

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The bone mineral content was estimated by photon absorptiometry in 226 epileptic patients on long term treatment with phenytoin, phenobarbitone or primidone, and in 20 normal subjects before and during treatment with vitamin D or placebo.

Initially subnormal values of bone mineral content were found in the epileptic patients. The group of epileptic patients showed on treatment with vitamin D (2000 IU daily) a significant increase in bone mineral content. The group of epileptic patients treated with placebo and the normal subjects treated with vitamin D or placebo showed no change in bone mineral content.

A COMPUTERIZED METHOD OF DETERMINATION OF BONE MINERAL CONTENT BY A TRANSMISSION-SCANNER. CLINICAL STUDIES.

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The value of clinical applications of our method has been studied in 1500 measurements on patients with different diseases involving the skeletal system. Measurements on patients with chronic renal disease, including those on hemodialysis or post renal transplant were performed. A bone mineral loss up to 50% was observed. The mineral content of the calcaneus depends on the duration of the disease and the given therapy as seen in follow-up studies over two years. About 50 measurements were done on patients with disturbance of the ovarial function. These patients showed a significant demineralization. Follow-up studies showed characteristic changes of bone density in patients under therapy with estrogens. Follow-up studies of hyperparathyroidism and osteoporosis of different origin demonstrate the prognostic value of the method. Systematic experiments with femurs and tibias of rats were performed, in order to see the influence of different therapy on renal osteopathy.

DYNAMICS OF BONE MINERAL LOSS IN THE MENOPAUSE

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1. A group of premenopausal women aged 50 was compared to 40 women who are ten years younger. All subjects have normal menstruation, are healthy and working. Bone mineral values obtained by the Sorenson-Cameron method were compared and correlated with standard X-rays of the lumbar spine, serum alkaline phosphatase and urinary hydroxyproline. These biochemical indices are thought to reflect bone turnover. A discriminant bone mineral value of .65 g/cm^2 at the standard site of the right radius was used to separate normal subjects from those with less bone mineral who are termed "osteoporosis-prone".

2. 16% of all subjects were found to be "osteoporosis-prone". The cortical bone density was the same for both age groups, but the trabecular density of the older "osteoporosis-prone" women was significantly lower than that of the younger group. Alkaline phosphatase and urinary hydroxyproline appeared to be higher in the "osteoporosis-prone" subjects.

3. It is concluded that bone mineral loss is accelerated with advancing age in women with a low cortical bone density. This loss of bone appears to be a dynamic process due to an increased bone turnover.

DISCRIMINATION OF OSTEOPOROSIS AND BONE DISEASE

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The Norland bone mineral analyzer has been used for the diagnosis of osteoporosis and to evaluate long-term therapy in a group of 22 osteoporotic females. The diagnosis of osteoporosis was based on the presence of unequivocal radiographic demineralization of the spine or on vertebral fracture.

Initial measurements on the mid and distal radius disclosed normal values of mineral content for age in 9 of 22 osteoporotic females. Values were lower than expected for age in 5 of 5 osteoporotic males but patient selection was important in this group. No age related trend in bone mineral content was observed in osteoporotic patients. The mid-distal ratio in osteoporotics did not differ significantly from that in age-matched normals. Mean mid-distal ratios were 1.033 in normals, 1.071 in osteoporotics and 1.105 in a group of patients with hyperparathyroidism.

Ten female osteoporotics have been treated for two years on the following sequential regimens: (a) first year - usual diet and placebo, (b) second year - diet supplemented to contain 2400 mg Ca, 1300 mg P, and (c) thereafter - diet (b) plus 50,000 units vitamin D three times weekly. No significant change in mineral content was seen during placebo or treatment regimen. Serum Ca remained unchanged as did urinary Ca. Urinary P increased; serum P was unchanged. Variable effects on serum PTH were seen: elevations in some patients on high Ca-high P intake. Three weeks of vitamin D therapy failed to surpress elevated PTH in some patients.

We conclude: (1) as many a large percentage of patients with significant osteoporosis may have normal bone mineral content in the mid and distal bone of the radius, (2) no significant change in mineral content was produced by one year of therapy on high Ca-high P intake. Elevated PTH was seen in phosphate treated patients in spite of 2400 mg Ca intake.

PHOTON ABSORPTION METHOD AND SINGH INDEX IN THE DETECTION OF OSTEOPOROSIS. A COMPARATIVE STUDY.

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A number of techniques for the estimation of bone mineral are under study by different laboratories but none is accepted unconditionally for routine clinical use. One intercomparison of different methods from different laboratories has been published. Our report describes a comparative study of two methods, namely the photon absorption method of Cameron and Sorenson and the skeletal grading method of Singh, in their abilities to separate normal females over 45 years of age from females of the same age but with compression fractures of the spine.

1. Cameron Method. Absorption scans were made using the technique described by Cameron and Sorenson. The commercially available ^{125}I source and a direct readout were employed. Scanning sites were distal radius and mid-radius. Normal values were obtained by scanning 153 normal female subjects. Ninety-two women with spinal osteoporosis (spinal crush fractures) underwent an identical procedure.

2. Singh Method. The same population with osteoporosis had x-rays of the hips with slight internal rotation for determination of the Singh index. X-rays were read by experienced observers. Normal values were obtained from a review of 187 x-rays as described previously.

Results: There was no difference between the normal and the osteoporosis population by bone mineral determination with the Cameron method at the mid-radius. However a significant separation between the two populations was seen with the distal scanning site. A significant overlap between the two populations however limits the usefulness of the procedure for routine clinical diagnosis. A better separation was achieved with the Singh index. Eighty-two % of all normal subjects over 45 years had index values 5 or above. Ninety-five % of all women with crush fractures had index values 4 or below. It is concluded that the evaluation of the trabecular structure of the femur better and perhaps earlier reflects spinal changes in osteoporosis.

BONE MINERAL CONTENT IN NORMAL U.S. WHITES

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Photon absorptiometry with ^{125}I was used to measure bone mineral content and bone width on 763 children between the ages of 5 and 19, on 538 adults between the ages of 20 and 49, and 550 adults over age 50. Measurements were made on the middle-shaft area, and also the distal 2 cm, of the radius and ulna, and on the middle of the humerus shaft. Tables of yearly bone growth in children, and decade bone changes in adults are presented.

Male and female children grew at about the same rate (8% per year) until adolescence. After adolescence growth spurt the girls virtually stopped (2%/year) but boys continued growing at 4% per year.

Males were relatively constant between the second and fifth decade of life, and declined slowly (4% per decade) thereafter. Females were constant until the fourth decade of life but between age 45 and 75 they declined by about 10% per decade; the decline was only about 4% per decade after age 75.

Age is an important consideration in examination of bone changes and disease only in children and in females between 45 and 75; bone and body size is far more critical for the age-sex groupings.

NORMATIVE DATA FROM THE OSTEOPOROSIS PREVALENCE SURVEY, OAKLAND, CALIFORNIA, 1969-1970. BONE MINERAL AT THE DISTAL RADIUS: VARIATION WITH AGE, SEX, SKIN COLOR, AND EXPOSURE TO ORAL CONTRACEPTIVES AND EXOGENOUS HORMONES; RELATION TO AORTIC CALCIFICATION, OSTEOPOROSIS, AND HEARING LOSS

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The prevalence of osteoporosis was evaluated in 8,434 persons, a population of insured workers and their families, of three ethnicities, who came for annual screening examination to Kaiser-Permanente Medical Center, Oakland, California, between April 1969 and November 1970. A total of 5,355 persons was examined by miniature roentgenography; 3,515 were examined by photon absorption applied at the distal radius; 939 were studied by both methods; 4,535 examined by either method were tested for auditory acuity. Subjects were questioned about fractures, usage of oral contraceptives and other exogenous hormones, age at menopause, number of children, and duration of lactation if any.

A low degree of mineralization was found in lactators, women undergoing early menopause, and nonusers of hormones, and in association with fracture, aortic calcification, and vertebral osteoporosis. A high degree of mineralization was associated with bilateral hearing impairment in older men and was found in younger women after childbearing or the use of high-mestranol contraceptives, in older women after treatment with sulfated estrogens, and in all women after treatment with all steroid hormones and thyroid.

Mineralization, in both sexes, was maximal at approximately 35 years, with precipitate declines after 45 years in women and after 65 years in men. Thus, in terms of absolute differences, the major determinants of bone mineral at the distal radius were age > sex > parity > early menopause > skin color > exogenous hormone usage > lactation.

INFLUENCE OF THE NATURAL CALCIUM AND FLUORIDE SUPPLY AND OF A CALCIUM SUPPLEMENTATION ON BONE MINERAL CONTENT OF HEALTHY POPULATION IN SWITZERLAND

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Measuring the bone mineral content of 3000 inhabitants of the city of Geneva aged between 6 and 99 years, of 800 people living in a Swiss mountain village and of 400 inhabitants of the closest village, where water is naturally fluoridated and contains about 10 mg F/liter, does not show any significant difference in bone mineralometry, although the alimentation contains 1100 mg/day of calcium for the male population of Geneva and 2150 for the one of the mountains, and for the women respectively 870 and 1270 mg calcium/day.

The children are grouped per year of age, the adults in groups of 5 years, and the standard deviation in each group is usually about 2% of the average mean for the group. All the values lie about 5 to 10% below the values published by Cameron et al.

Two hundred persons showed a mineralometry value lying more than 2 standard deviations below the ones published by Cameron and received a calcium supplementation for a period of 6 months: 2g/day Ca for adults, 1g/day for children. Controls after 3 and 6 months show practically no improvement in elderly people, a partial success in younger people and a remarkable correction in most children. The implications will be discussed.

MINERAL LOSS WITH AGING MEASURED PROSPECTIVELY BY THE PHOTON ABSORPTION TECHNIQUE

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The rate of mineral loss measured by the photon absorption technique in postmenopausal Caucasion females prospectively was compared to the rate predicted from a matched population survey.

Thirty women, ages 50 to 65 (mean 57.4), had bone mass measurements of the right radius at midshaft and distal sites made every three months. They were followed for periods ranging from 0.8 to 2.4 years (mean 1.9). The rate of loss was computed as the regression coefficient of bone mass versus time.

These results were compared to a group of 214 women ages 50 to 69 (mean 57.7) who had measurements on one visit only.

The rate of loss for distal mass observed prospectively (-.0303 gm/cm/yr $\pm$ S.E. .0028) was significantly greater than that predicted from the population survey (-.0117 $\pm$ .0021 gm/cm/yr). The source of this difference requires further evaluation. The rate of loss observed prospectively for midshaft mass (-.0135 $\pm$ S.E. .0023) approximated that predicted from the population survey (-.0090 $\pm$ .0018) demonstrating its usefulness in following age related loss of bone mineral prospectively in a group of subjects.

TIBIAL BONE MINERAL DISTRIBUTION AS INFLUENCED BY CALCIUM, PHOSPHORUS, AND VITAMIN D FEEDING LEVELS IN THE GROWING TURKEY

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Roentgen signs, subperiosteal, endosteal, and trabecular bone growth are evaluated in turkeys fed phosphorus at the 0.5, 0.56, 0.68, 0.90, and 2.70 percent levels. Control rations contained 1.2 percent calcium, 0.9 percent phosphorus, and 900 I.U. of vitamin D. These studies were conducted at 10, 24, 70, and 168 days of age.

Calcium levels of 0.30, 0.40, 0.60, 1.2, and 3.60 percent were also tested. Vitamin D levels of 0, 100, 300, 900, and 27,000 I.U. per day were likewise evaluated.

Roentgen signs, bone mineral as measured by ^{125}I gamma ray absorption, and bone mineral growth patterns as shown by radiograph area projection are correlated with calcium, phosphorus, and vitamin D feeding levels.

These reported observations were able to detect differences in bone growth at the various feeding levels which were not reflected by differences in other studied parameters. They also provided greater insights into the acceptable ranges of feeding levels of these nutrients than did other parameters studied.

EFFECT OF DIETARY CALCIUM ON JAW BONE DENSITY

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Previous work with animals demonstrated that periodontal disease with associated demineralization of the jaw was a precursor of generalized systemic osteoporosis. A pilot study in human subjects with periodontal disease confirmed an animal project which had demonstrated reversal of the clinical signs of this disorder by supplementation of the diet with calcium. In the present study 90 adult subjects with periodontal disease received either placebo or 1 gm calcium per day for 12 months. Monthly measurements of blood and urine chemistries demonstrated no significant changes. Photon densitometric measurements of the radius at 6 cm from the ulnar styloid process showed no significant differences between placebo and calcium groups. Measurements of the ulna at the same position demonstrated a borderline significant decrease of density in the group receiving placebo for 12 months. Densitometry of the os mentis showed a highly significant increase in bone density in the patients receiving calcium supplementation for 12 months.

TRANS-IMAGING OF BONE ALLOGRAFTS - A RAPID METHOD FOR EVALUATING OSSEOUS INCORPORATION

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In order to reconstruct patients who have sustained massive bone losses, either traumatic or post-surgical, large osseous bone grafts have been implanted. These allografts must become incorporated, however, before structural and functional integrity is regained. A non-invasive technique for quantitative evaluation of graft incorporation is required in order to assess and direct the post-operative care of such a patient. Rectilinear scanning with Americium-241 seemed to provide a method for such evaluations, and a number of 2 cm bone grafts in dog ulnas were scanned sequentially. Bone resorption was followed proximally, distally and through the body of the graft by multiple passes with the probe. Since this technique proved to be so time-consuming, the high performance gamma camera was selected to image the entire extremity area. Maximum utilization of the grid was accomplished by focusing the source and bone specimen some distance from the camera so as to project an enlarged image. A computer was then repeatedly directed to bisect the image and to plot the multiple scans from the single image. Bone mineral content throughout the graft and surrounding host bone was then determined, and this data was stored for comparison with sequential scans. This latter method was not only much faster, but the sensitivity of the technique was maintained. It is felt that this method can play an important clinical role in patient care as well as provide the researcher with a better tool for evaluating and selecting the best possible grafting material.

EFFECTS OF SKELETAL RADIUM DEPOSITS ON BONE MINERALIZATION

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A population of persons who acquired abnormal body burdens of radium and mesothorium through occupational exposure, for therapeutic purposes or through the consumption of patent medicines is being studied at Argonne National Laboratory. X-ray examination of these radium cases has revealed abnormal patterns of bone mineralization, among which are coarsening of trabeculation, large areas of bone resorption and areas of unusually high density. Similar changes, but to a much smaller degree, have been observed in controls.

The radiological abnormalities suggest that radium and mesothorium have an effect on bone mass. In order to quantify bone mass radium cases have been scanned using the Cameron-Sorenson technique. The midshafts of the radius and ulna, the distal end of the radius and the distal end of the third proximal phalanx have been used as scan locations. To date, more than 300 cases have been scanned.

Preliminary analyses of the data show that the bone mass diminishes more rapidly as a function of age among radium cases with residual body burdens greater than 0.1 μCi Ra-226 than among cases with residual burdens less than 0.1 μCi Ra-226.

Results of the data analyses will be presented and discussed.

*Work performed under the auspices of the U.S. Atomic Energy Commission.

FOLLOW-UP EXAMINATIONS OF THE MINERAL SALT CONTENT IN THE SKELETON WITH VARIOUS VITAMIN D RESISTANT FORMS OF RICKETS OF RENAL ORIGIN

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With the aid of experimental facilities specially developed for pediatric requirements, 10 patients affected by chronic phosphatic diabetes, 2 patients with the Debré-de Toni-Fanconi syndrome, 2 children with distal tubular acidosis of the Albright type and 8 children with uremic osteodystrophy were examined during the last four years to determine the mineral salt content in peripheral parts of the skeleton and, in some, also in the spine. The results of the long-term follow-up reveal the different response to the therapeutic measures so far possible, in the case of the various vitamin D resistant forms of rickets of renal origin.

In chronic phosphatic diabetes, even long-term treatment fails to replenish the calcium depots in bones to any noticeable extent. With the Debré-de Toni-Falconi syndrome and Albright's disease, therapy brings about a rapid increase of the mineral salt concentration in the skeleton. Also with uremic osteodystrophy the treatment usually leads to a marked increase of the mineral salt content and occasionally even to raised values.

CHANGES IN SKELETAL MINERAL IN PATIENTS WITH RENAL FAILURE

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Bone measurements have been made at regular intervals over several years on 15 patients with renal failure, using a technique that employs the 60 KeV emission of ^{241}Am scanned across the femoral shaft. Some bone loss is usual in the normal adult population with time but is often more marked in renal failure. Individual patients, however, show different degrees of bone mineral change. Although measures can be taken to reduce avoidable calcium loss during treatment by dialysis, this does not correct the underlying abnormalities of mineral metabolism. In some cases, vitamin D therapy not only prevented bone loss but also enhanced bone mineralization. Patients having had bilateral nephrectomy showed a tendency to lose bone and this may perhaps have reflected a deficiency of 1-25 d.h.c.+ Two transplanted patients, on the other hand, also showed a tendency to lose bone rapidly. In the light of such changes occurring during the treatment of renal failure, the need to measure bone changes at regular intervals cannot be too strongly recommended.

+ 1-25 dihydrocholecalciferol

PHOTON ABSORPTIOMETRY IN RENAL FAILURE

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Using a Packard Photon absorptiometer to measure bone mineral in the lower radius and ulna, over 2,000 scans on 500 patients representing all stages of renal failure have been performed. The age range is from 14 to 75 and covers most of the diseases which cause renal failure. Although there is inexorable loss of bone mineral before and during dialysis, prolonged azotemia leads to rapid decrease in bone mineral detectable only by photon absorptiometry. Once the bone mineral has been lost it appears that neither renal transplantation nor parathyroidectomy will cause any obvious replacement of the lost mineral.

In our group of patients, osteomalacia (as diagnosed radiologically) was present in 40%, evidence of secondary hyperparathyroidism is seen in 22%, osteosclerosis occurred in 10% and "pure" osteoporosis in 2%.

Renal osteodystrophy is a term representing four very different disease entities which involve the skeleton in patients with renal failure - namely osteomalacia, secondary hyperparathyroidism, osteosclerosis and osteoporosis. Of these conditions the first two are the most important clinically, whilest pure osteoporosis is probably rare and the etiology of osteosclerosis is only poorly understood. In classical osteomalacia, there is a marked increase in bone mineral however in some dialysis centers with the addition of calcium and one of the metabolically active metabolites of vitamin D to the patient's diet, a form of "normocalcemic" osteomalacia is being seen - with normal bone mineral but widened osteoid seams and remodelling. In secondary hyperparathyroidism, there is resorption of all types of bone and thus the bones change in size as well as in bone mineral content. In osteosclerosis the bone architecture remains normal with a normal osteoid width but with actual increase in the size of the trabeculae. These conditions usually occur in combination and hence to measure bone mineral alone may produce fallacious results.

Thus to further our understanding of renal bone disease it behooves us to use methods of bone mineral analysis in conjunction with routine radiographs of the skeleton - and to follow the individual patient rather than to perform population studies.

BONE MINERAL CHANGES IN THE APOLLO ASTRONAUTS

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Loss of mineral from bone during periods of immobilization, recumbency or weightlessness have been observed. These losses are more apparent in the lower extremity than the upper and have been observed to exceed 30% in the case of the central os calcis during 36 weeks of bedrest. No mineral losses were seen in the upper extremity during this same period of time.

In early Gemini studies using x-ray densitometry, large losses of bone mineral were observed in the radius and ulna. This observation was not validated in the Apollo 14, 15 and 16 crewmen when a more precise technique, gamma ray absorptiometry, was used. The mineral losses from the central os calcis previously reported have been variable. The large losses reported for the early Gemini missions were not seen when this newer measuring technique was employed. Indeed, 7 of the 9 crewmen studied lost no mineral during the 10 and 12 day missions. Since two crewmen did lose mineral from the os calcis, it is clear that losses can occur even in these short periods of time, even though losses are not seen in 14 days of bedrest. If these losses were allowed to continue unabated for a prolonged period of time, the consequences might be severe, since the losses observed are probably not confined to the os calcis.

OSTEOPOROSIS BEFORE AND AFTER FRACTURE OF THE FOREARM

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The mineral content in the forearm was compared between women with fracture of the distal end of the radius, Colle's fracture and age matched control women without fracture. The measurements were undertaken in the distal end at the fracture site and more proximally on the shafts of the radius and the ulna by gamma absorptiometry. Also, the width of the marrow cavities of the shafts were evaluated from the absorptiometry scan. In the fracture cases there was a significant reduction of the mineral content in the shafts and a corresponding increase of the marrow cavity. In the distal end of the forearm, on the fracture site, there was no significant difference between the groups. This indicates a change of quality causing fracture before a significant reduction in the mass can be detected.

Following fracture a series of women were measured prospectively. There was an 18 per cent reduction of the mineral content in the shafts and the reduction continued even after the plaster cast had been removed. When the function, measured by the force of the hand, increased during the first year there was no corresponding restoration of the bone mineral. The post-traumatic mass reduction was due to porosity rather than thinning of the cortex.

CHANGES IN BONE MINERALIZATION IN HEMIPLEGIA

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Hemiplegia is characterized by paralysis on one side of the body. In order to relate bone mineral changes to the effect of paralysis, the non-paralyzed side was used as a control for the paralyzed side. The bone mineral content was measured in 45 hemiplegic subjects matched for age and sex, using a modified Packard device (Cameron type) with ^{125}I as the source. There was also an approximately equal number of right-dominant, right-paralyzed and left-dominant, left-paralyzed subjects. The bone density was compared bilaterally at two sites on radius and ulna, two and four centimeters from the wrist. The results at equivalent sites were expressed as the ratio between the absorption on the paralyzed and non-paralyzed sides. There was a decrease of $6.8 \pm 8.8\%$ in the average ratio of relative bone density at the site four centimeters from the wrist, and $7.3 \pm 10.8\%$ at the site two centimeters from the wrist. The results will be further discussed in terms of the time after the onset of injury, male versus female, and subjects paralyzed on the dominant versus non-dominant side.

(Supported by The Edmond A. Guggenheim Clinical Research Endowment and in part by S.R.S., Dept. of H.E.W.)

BONE MINERALIZATION AND PHYSICAL ACTIVITY

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Photon absorptiometry (^{125}I) was utilized to probe the relationship between bone mineral content and the physical activity of amateur baseball players ranging in age from 8 to 19 years (N = 203). The study focused principally upon the dominant non-dominant differences in mineral content within age groups and the changes in this variable over age. Two small groups of non-competitive individuals (N = 10), and baseball players over 19 years (N = 9) were also measured. Upper and lower arm limb girths as well as grip strength were measured to validate physical stress dominance.

The most consistent finding throughout the investigation was that the dominant humerus was significantly ($p < 0.001$) more mineralized for all age groups and the degree of dominance increased significantly ($p < 0.001$) with age. This characteristic held when the influence of bone size was accounted for by testing the mineral/width ratio. The patterns for mineral dominance of the radius and ulna were inconsistent. Inspection of the data for the three groups gave the impression that bone mineral differences between arms increased from the non-competitive group to the main baseball sample to the older baseball group. However, analysis of the relationship between mineral dominance and the stress factors revealed insignificant relationships. While humeral mineral dominance was real, its relationship to physical stress remained in doubt.

THE EFFECT OF DIPHOSPHONATE (EHDP) THERAPY ON IMMOBILIZATION OSTEOPOROSIS

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The effectiveness of EHDP in the inhibition of acute osteoporosis was studied in men with paralysis due to spinal cord trauma. Patients with quadriplegia (motor level, C1 - T1) and high paraplegia (T2 - T5) were assigned on a random double-blind basis to EHDP therapy (EHDP, 9 patients) or placebo therapy (PLBO, 10 patients) for 12 weeks. Mineral mass of distal right radial metaphysis and distal right tibial and fibular diaphysis were measured by ^{125}I photon absorptiometry before and weekly during treatment; plain radiographs were taken of the right forearm and right leg before and in the final week of treatment. Serum immunoreactive parathyroid hormone (IPTH) and other chemistries were measured serially. Results of absorptiometry: (1) Final tibial mineral mass (TMM) as % pre-treatment TMM: EHDP = 101.0 ± 1.19 SE, PLBO = 95.7 ± 1.12 SE ($p < .01$); (2) final radial mineral mass did not differ significantly between EHDP and PLBO or from pre-treatment value. Results of qualitative radiography read by 4 radiologists showed trabecular bone loss in the tibial metaphyses and/or foot in 15 patients (6 EHDP, 9 PLBO) and in the distal radius and/or hand in 10 patients (6 EHDP, 4 PLBO). Pre-treatment IPTH levels were above the normal range (0 - 150 pg/ml) in 11 of 20 patients whose median level was 170 pg/ml, compared to a median level of 10 pg/ml for 13 normals, a statistically significant difference ($p<.05$ by rank sum test). Final median IPTH (week 12): EHDP = 340 pg/ml, PLBO = 430 pg/ml (p = N.S.). IPTH levels correlated poorly with serum and urine chemistries; log IPTH correlated with urinary calcium ($r = +.63$, $p < .01$). Conclusions: In these patients with paralysis due to spinal cord trauma, (1) EHDP inhibited loss of tibial diaphyseal bone mass as measured by ^{125}I photon absorptiometry; (2) EHDP did not prevent loss of metaphyseal trabecular bone radiographically; (3) high IPTH levels are unexplained but are not increased by EHDP as compared to PLBO.

THE EFFECTS OF PHYSICAL ACTIVITY ON BONE IN THE AGED

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Physical activity has been used as a preventive and rehabilitative therapy for osteoporosis. Few studies have accumulated data to support the concept that physical activity will prevent bone loss or increase bone accretion in an aged population. The purpose of this investigation was to study physical activity in slowing bone mineral loss and increasing bone accretion in the aged. Thirty-nine subjects were involved and included both sexes with an age range of 55 to 94 years. The subjects were studied for eight months with 21 in a control group, twelve in a physical activity group, and six in a physical therapy group.

The physical activity group demonstrated a significant, ($P < .05$) bone mineral increase of 2.6 percent during the 8-month study while the control group demonstrated no bone mineral change. The bone mineral value of the physical therapy group increased 7.8 percent ($P < .05$). The bone mineral change from the first to the last measurement (T_4-T_1) between the control group and physical activity group was not significant of the .05 level. The bone mineral change (T_4-T_1) between the control group and the physical therapy group was significant ($P < .05$).

A progress report will be given on the first year of a three year physical activity program, which seems to support the above results.