JUN 18 1968

B.R.

MASTER

hadm
4/4-6) 68
in pens

CONF-680435--1

CLINICAL APPLICATION

I-125 BONE DENSITOMETRY

Nels M. Strandjord, M.D., Department of
Radiology, The University of Chicago
Marvin Forland, M.D., Department of Medicine,
The University of Chicago
Lawrence Lanzl, Ph. D., Department of Radiology
and Argonne Cancer Research Hospital, The
University of Chicago
Ann Cox, B.S., Argonne Cancer Research Hospital,
The University of Chicago

LEGAL NOTICE

This report was prepared as an account of Government sponsored work. Neither the United States, nor the Commission, nor any person acting on behalf of the Commission:

A. Makes any warranty or representation, expressed or implied, with respect to the accuracy, completeness, or usefulness of the information contained in this report, or that the use of any information, apparatus, method, or process disclosed in this report may not infringe privately owned rights; or

B. Assumes any liabilities with respect to the use of, or for damages resulting from the use of any information, apparatus, method, or process disclosed in this report.

As used in the above, "person acting on behalf of the Commission" includes any employee or contractor of the Commission, or employee of such contractor, to the extent that such employee or contractor of the Commission, or employee of such contractor prepares, disseminates, or provides access to, any information pursuant to his employment or contract with the Commission, or his employment with such contractor.

fly

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency Thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

METHODS OF BONE DENSITOMETRY

By the time a patient has become osteoporotic enough to lose several inches in height the diagnosis is obvious. Assessment of bone mineralization, by viewing conventional radiographs, is not sensitive as one must lose at least 25% of the bone for osteoporosis to become apparent. Consequently, numerous methods have been developed to quantitatively determine bone mineral content.

Omnell (12) presents an excellent summary of the work done prior to 1957 using a standard X-ray tube as the radiation source and photographic film as the detector. Numerous investigators have used sophisticated methods of film densitometry; however, inherent problems in this technique leave much to be desired.

The determination of loss of bone by measurements of cortical thickness of metacarpal and femur and the biconcavity index of the vertebrae have been shown by Barnett and Nordin⁽¹⁾ to be applicable to population studies. By the time biconcavity is present the disease is far advanced. Garn (5) and Virtima (16,17) have also used cortical thickness in association with radiographic densitometry in measuring bone density.

Direct measurements of transmission of X-rays were used by Mayer (10) and Vose (18). Gershon Cohen (6) used a gamma source with direct counting of the transmitted beam by a scintillation counter. Cameron (2) has done extensive work with this method and summarizes the requirements for accurate bone densitometry as:

1. The transmission of photon beam is measured directly by counting techniques employing a scintillation counter;
2. the photon beam used is essentially monochromatic;
3. the photon beam and detector are well collimated; and
4. the effects of the tissue around the bone are taken into account.

We have utilized this method using the phalanx as the skeletal sample. Overlying soft tissue is at a minimum and immobilization during measurement is easily attained. The choice of a phalanx has been influenced by the work of many, Virtima, (16,17) Jackson, (7) Garn, (5) Barnett and Nordin (1). Our instrumentation and techniques have been reported in detail. (9,14)

The ideal energy for discrimination of differences between bone and muscle is between 20 and 30 KV. I^{125} decays by electron capture to a 0.354 meV excited state of Te^{125} , which in turn decays by means of a gamma-ray which is internally converted in the K-shell, giving in turn two X-ray photons, $K_{\alpha} = 27$ keV (75%) and $K_{\beta} = 31$ keV (20%). The K_{α} of 27 keV is ideally suited for bone densitometry unless the part to be measured is thick.

We have expressed our results as the linear coefficient of absorption. The thickness of the bone is measured from radiographs which also localize the position for the transmission studies. The unit is programmed to make transmission measurements at 1 mm. intervals across the entire width of the finger automatically, the finger being held immobile at the position determined from the radiographs.

As no uniform method of expressing bone density has evolved, we express our results as a linear coefficient of absorption of overall bone (μ_B $^{-cm}$). The thickness of the phalanx is determined from the radiograph. A bone of equal diameter, but a thinner cortex will give a lower linear coefficient of absorption. Osteomalacia would also give a lower linear coefficient of absorption. A distinction, therefore, cannot be made between osteoporosis and osteomalacia.

The phalanx is a good example of cortical bone. It is also desirable to measure trabecular bone. The calcaneus represents trabecular bone and is the most accessible of all cancellous bone for direct measurements. We

have recently used an apparatus for assessment of bone density of the os calcis using americium 241 as the source of photons. While the energy of 59.4 keV is above the ideal energy for discrimination, its increased energy will penetrate the increased thickness and its long half life is a great advantage. Spring (13) has used americium in a similar manner. To eliminate the effects of soft tissue a H₂O bath is used (Figure 1). The os calcis, while an irregular bone, has a broad flat area just anterior to the Achilles tendon. Radiographs (Figure 2) are exposed with a jig in the lateral position to permit localization of the site for transmission measurements. A 30° angle film (Figure 3) is made to measure the transverse diameter of the os calcis at its narrowest point. Again we have expressed our results as a linear coefficient of absorption (μ_B -cm).

Initial studies with calcaneus specimens and patients indicate that the density of the os calcis can be measured accurately (reproducible) and that the density expressed as μ_B -cm changes with age and in various disease states. An americium 241 instrument for densitometry studies will be available from Packard Instrument Company.*

CLINICAL APPLICATIONS OF BONE DENSITOMETRY

Normal Males - The effect of aging on bone density has been studied in normal males. Only males who were active and without known systemic disease were utilized. The results are given in Table I and Figure 4, and the group is divided into ten-year intervals.

There is a decrease in bone density with advancing age, most marked between the 40-49 and 50-59 age groups. The linear coefficient of absorption for males is higher than for females of a corresponding age.

As is anticipated, there is a range of values for normals in each age group. This may be dependent upon activity, but this is difficult to substantiate. .

* 2200 Warrenville Road, Downers Grove, Illinois 60515

POSTMENOPAUSAL OSTEOPOROSIS

Dr. Davis, Department of Obstetrics and Gynecology, The University of Chicago, has used estrogen therapy for the past 25 years in the majority of his patients postmenopause. Bone density studies were attempted initially by obtaining radiographs. It was soon obvious that no meaningful data was obtained by the routine radiographs.

Since the previous reports (3,15) we have examined 29 additional patients who have since been on supplemental estrogen therapy. The results are given in Table II and Figure 5. Normal females show a progressive decrease in bone density with advancing age, with the sharpest drop at the five-year to ten-year interval and a slower decline with subsequent years postmenopause.

Females who have been on estrogen supplementation have a definitely higher bone density than females who have not had estrogens. The estrogen treated patients, for the most part, were not allowed to develop symptoms of estrogen lack. Johnston (8) and Meema (11) have also demonstrated a greater bone mass in postmenopause females on estrogen therapy than those not treated.

HYPERPARATHYROID DISEASE

We have studied 20 patients with hyperparathyroidism all surgically confirmed. These are being reported elsewhere in detail. (4) The results of bone density studies are shown in Figures 6,7. All but three had low bone density. Two had the lowest coefficients of absorption measured in any patients. (μ_B^{cm} 1.25 and 0.94).

Four patients with hyperparathyroidism have been followed serially. Table III, Patient R.T. initially refused surgery and demonstrated a further decrease in bone density over 9 months. Three patients showed an increase in bone density, 12 to 22 months post surgery respectively. The increase in Patient J.G. is not statistically significant. The majority

of these patients did not demonstrate the classical radiographic changes of hyperparathyroidism. The decrease in bone density is, however, evident when measured by a more sensitive means than viewing of radiographs.

SUMMARY

Bone densitometry using I^{125} has been used clinically. It has been demonstrated that bone density, after reaching a peak, decreased with age in males and females. Females given supplemental estrogens postmenopausal have a higher bone density than untreated females of a corresponding interval postmenopausal.

Seventeen of twenty patients with hyperparathyroidism had significantly decreased bone density as compared to normals of the same age. This method of densitometry in several patients has been used to measure the degree of improvement under therapy.

BIBLIOGRAPHY

1. Barnett, E. and Nordin, B. E. C.: The Clinical and Radiological Problem of Thin Bones. *Brit. J. Radiol.*, vol. 34, Nov. 1961, pp. 683-692.
2. Cameron, J. R. and Sorenson, J.: Measurement of Bone Mineral in Vivo: An Improved Method. *Science*, vol. 142, no. 3589, Oct. 1963, p. 230.
3. Davis, M. C., Strandjord, N. M. and Lanzl, L. H.: Estrogens and the Aging Process. *JAMA*, vol. 196, no. 3, Apr. 1966, pp. 219-224.
4. Forland, M., Strandjord, N. M., Paloyan, E. and Cox, A.: Bone Density Studies in Hyperparathyroidism. Submitted for publication.
5. Garn, S. M., Rohmann, C. G. and Nolan, P. Jr.: Studies on the Development of Compact Bone, in Normal Individuals and in Endocrine and Nutritional Abnormalities. Final Progress Report Part 1, Department of Growth and Genetics, Fels Research Institute, Yellow Springs, Ohio, Dec. 31, 1963.
6. Gershon-Cohen, J., Cherry, N. H. and Boehnke, M.: Bone Density Studies With a Gamma Gage. *Radiation Res.*, vol. 8, June 1958, pp. 509-515.
7. Jackson, H.: Problems in the Measurement of Bone Density. *Brit. J. Radiol.*, vol. 24, Nov. 1951, pp. 613-616.
8. Johnston, C. C. Jr.: Measurement of Bone Mass in the Radius. Conference on Progress in Methods of Bone Mineral Measurement, National Institutes of Health, Bethesda, Maryland, Feb. 15-17, 1968, p. 29.
9. Lanzl, L. H. and Strandjord, N. M.: Radioisotopic Device for Measuring Bone Mineral. AEC Report ORNL-IIC-5, pp. 257-276. Proceedings of Symposium on Low-Energy X-Gamma Sources and Applications Held at Illinois Institute of Technology Research Institute, Chicago, Illinois, October 20-21, 1964.
10. Mayer, E. H., Trostle, H. G., Ackerman, E., Schraer, H. and Sittler, O.D.: A Scintillation Counter Technique for the X-ray Determination of Bone Mineral Content. *Radiation Res.*, vol. 13, July 1960, pp. 156-167.
11. Meema, H. E. and Meema, S.: The Interrelationships Between Cortical Bone Thickness, Mineral Mass, and Mineral Density in Human Radius: A Roentgenologic-Densitometric Study. Conference on Progress in Methods of Bone Mineral Measurement, National Institutes of Health, Bethesda, Maryland, Feb. 15-17, 1968, p. 13.
12. Omnell, Karl-Ake: Quantitative Roentgenologic Studies on Changes in Mineral Content of Bone in Vivo. *Acta Radiol. Suppl.* 148, 1957, pp. 7-86.
13. Spring, E.: A Simplified Method for Bone Mineral Measurements in Vivo. *Internat. J. Applied Radiation and Isotopes*, vol. 18, 1967, pp. 709-711.
14. Strandjord, N. M. and Lanzl, L. H.: Iodine-125 Bone Densitometry. Progress in Development of Methods in Bone Densitometry, NASA SP-64, 1966, pp. 115-126.

BIBLIOGRAPHY

(continued)

15. Strandjord, N. M. and Lanzl, L. H.: Estrogens and Postmenopausal Osteoporosis. Progress in Development of Methods in Bone Densitometry, NASA SP-64, 1966, pp. 163-167.
16. Virtama, P., Kajanoja, P., Hopsu, V. K. and Telkka, A.: Density of Human Carpal, Metacarpal and Digital Bones, Ann. Med. Exptl. Biol. Fenniae (Helsinki), vol. 38, 1960, pp. 467-471.
17. Virtama, P. and Mahonen H.: Thickness of the Cortical Layer as an Estimate of Mineral Content of Human Finger Bones. Brit. J. Radiol., vol. 33, Jan. 1960, pp. 60-62.
18. Vose, G. P.: X-ray Transmission Factor in Estimating Bone Density. Radiology, vol. 71, July 1958, pp. 96-101.

LINEAR ABSORPTION COEFFICIENT OF OVERALL BONE, μ_B , vs CHRONOLOGICAL AGE

Data Summary From January 1964 Through January 1968

FEMALES

Group	No. of Patients	$\mu_B(\text{cm}^{-1})$	$\sigma(\text{cm}^{-1})$	$\sigma\mu_B(\text{cm}^{-1})$
Pre-menopause Ages 18-50	39	2.20	± 0.22	± 0.04
Post-menopause Without Estrogens				
0 - 4 years	27	1.96	± 0.33	± 0.06
5 - 9 years	23	1.72	± 0.32	± 0.08
10 - 14 years	24	1.77	± 0.31	± 0.06
15 - 19 years	6	1.65	± 0.16	± 0.06
20 - 24 years	<u>10</u>	1.58	± 0.28	± 0.09
TOTAL	90			
Post-menopause With Estrogens				
0 - 4 years	27	1.99	± 0.26	± 0.05
5 - 9 years	44	2.00	± 0.29	± 0.04
10 - 14 years	35	1.97	± 0.33	± 0.06
15 - 20 years	<u>10</u>	1.86	± 0.32	± 0.10
TOTAL	116			

LINEAR ABSORPTION COEFFICIENT OF OVERALL BONE, μ_B , vs CHRONOLOGICAL AGE

Data Summary From January 1964 Through January 1968

MALES

Group	No. of Patients	$\mu_B(\text{cm}^{-1})$	$\sigma(\text{cm}^{-1})$	$\sigma_{\mu_B}(\text{cm}^{-1})$
Ages 20 - 50	38	2.26	± 0.24	± 0.04
Ages 20 - 29	21	2.25	± 0.21	± 0.05
Ages 30 - 39	9	2.34	± 0.30	± 0.10
Ages 40 - 49	8	2.21	± 0.22	± 0.08
Ages 50 - 59	8	1.91	± 0.17	± 0.06
Ages 60 - 69	7	1.84	± 0.18	± 0.07
Ages 70 - 79	<u>5</u>	1.89	± 0.26	± 0.11
TOTAL	58

Schematic Am-241
Densitometry Calcaneus

$\hat{\mu}$ TOTAL BONE VS AGE (NORMAL MALES
IN TEN-YEAR AGE GROUPS FROM 20-80)

$\hat{\mu}$ TOTAL BONE VS NUMBER OF YEARS
POST MENOPAUSE (NORMAL FEMALES)