RADIOGRAPHIC ALUMINUM EQUIVALENT VALUE OF BONE.

The development of a registration method and some clinical applications.

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PROEFSCHRIFT

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To Jeany, Maurits and Jan.

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CHAPTER 1

INTRODUCTION AND AIMS

1.1. Introduction.

Already during his early experiments, 6 weeks after the discovery of X-rays, Wilhelm Conrad Röntgen succeeded in producing an image of the bone structure in his wife's hand.

Medical use of the new technique, which made it possible to produce images of patients' skeletons, spread rapidly all over the world and is now an accepted practice.

The skeleton is defined as an anatomical structure comprising bone, skeletal cartilage, certain periarticular tissues adhering to the joints and the red and yellow marrow. Unless otherwise specified, the term "skeleton" applies to the totality of these tissues, as present in the human body, i.e. including the blood and body fluids which normally form part of them. When cartilage, periarticular tissue and the red and yellow marrow are removed, the remainder of the skeleton can be classified simply as "bone". Bone can be divided into two, general categories: cortical (compact or dense) and trabecular (cancellous or spongy). Bone, as distinct from marrow, cartilage and periarticular tissue, can be further subdivided into bone cells, fluids, mineralized substance and organic matrix. Bone hardness is the result of bone mineral deposit within a supporting lattice consisting of the organic matrix. This bone mineral consists mainly of hydroxyapatite. The bone matrix contains collageneous fibers and a cement, or basic substance, consisting of mucopolysaccharides and mucoproteins. In adults, the bony structures constitute approximately 6% of the total body weight. The bone mineral contains Ca and P which represent respectively 2 and 1% of the total body weight.

The gross shape of the respective bones or bony structures can be studied on an X-ray image. Evaluation of the morphology can be extended to the thickness of the cortical bone and the trabecular bone pattern. Differences between the image which the interpreter expects, on the basis of his knowledge and experience and the image on the radiograph lead to the "discovery" of pathologic conditions.

The images originate through the differences in attenuation of the X-ray beam. This attenuation is determined by the atomic structure of the tissues, the concentration of the different types of atoms present and the length of travel through these structures of different composition. Since bone consists mainly of hydroxyapatite, which has a relatively high average atomic number, bone images are principally produced by the concentration of this mineral present in the bones.

It can be stated that the amount of hydroxyapatite present per unit area determines the attenuation of the beam in that, specific, area. Consequently, the X-ray image not only provides information on the amount of mineral present, but can be considered as determined by the projection of the mineral distribution in the object on the image recording plane.

This quantitative information can be used to evaluate the average mineral content of a certain bone. It can further be used for qualitative study of the trabecular bone pattern.
Provided that this information can be obtained with sufficient precision, it can be useful for the purpose of studying changes in bone mineral content over relatively short intervals. This could be of importance for diagnostic procedures and therapy evaluation. Individual, momentaneous measurements are also possible, but their usefulness depends upon the existence of standard norm-value tables which are not available at the moment.
This promising, quantitative evaluation of the images does, however, meet with certain difficulties which can be classified as follows:

1. Exact orientation, in relation to the bones, is made difficult by the presence of the soft tissues which surround them. Consequently, it is also difficult to standardise the direction of the X-ray beam in relation to the object.
2. The technical factors vary in many instances, i.e. the composition of the X-ray beam, the type of recording-medium used, the dark room or other technique applied for production of the visual image and the average blackening of the image.
3. Anatomical conditions also vary, e.g. the amount of soft tissue present.
4. The subjectivity of the observer makes quantitative evaluation difficult. It is, therefore, also difficult to standardise individual interpretations. Furthermore, the influence of light from areas adjacent to the X-ray film must be taken into consideration, as well as the degree of fatigue, a factor which might limit the reliability of subjective evaluation.

Any attempt to eliminate or, at least, reduce these difficulties calls for standardisation of the procedures involved.

1. A standardised and, therefore, reproducible direction of the beam in relation to the object and the film is required. This is the reason why the investigation described in this thesis is based on a technique whereby the patients' teeth were used as an extention of the bone through the soft tissues, for the purpose of orientating the X-ray beam.
   The teeth were used to position a beam-guiding instrument and a film in relation to the lower jaw.
2. Standardisation of the technical factors is a further requirement. The effect of variation in these factors can also be reduced by simultaneous exposure of a standard absorber for comparative purposes. In most instances, this was an aluminum alloy machined into a wedge profile.
3. It was necessary to devise a suitable technique for eliminating the effect produced by the soft tissues.
4. Subjectivity can be eliminated by measuring the blackening of the film. Measuring is carried out with the aid of a small scanning spot. A microdensitometer tracing is thus obtained which can be used for evaluation purposes.

This thesis deals with the development of a technique along these lines. The characteristics of the system were studied and its limitations determined.

1.2. Aims.

The aim of this thesis is to establish and develop a method suitable for obtaining an objective analysis of bone as registered on a radiographic image. This analysis concerns determination of the quantity of bone mineral present. The system has been tested in-vitro and in a clinical study on patients.
Finally, the complete system of microdensitometric analysis must be potentially suitable as a basis for the development of equipment which can be used for routine clinical measurements.

CHAPTER 2

REVIEW OF LITERATURE

2.1. Technical literature.

Many publications concerning investigations in the basic principles of radiology and microdensitometric bone analysis are available. A short summary of the most relevant findings follows.

Origin of registration of the architectural pattern, the lamina dura and the alveolar crest in the dental radiograph.
Goldman, Millsap, Brenman, 1957.
Removal of buccal and lingual alveolar plates had no effect on the architectural trabecular pattern around the teeth in a radiograph, only a loss of radiodensity. The difference in density could not be determined by observation.

An investigation of the normal variations in alveolar bone trabeculation.
Parfitt, 1962.
Normal variations in the trabecular pattern have been classified as fine, medium and coarse.
Serial radiographs to determine changes in bone volume are more indicative than trabecular pattern changes with time. The pattern can change according to the angulation of the film and tube. Changes in bone pattern suggest local or general disease.
The use of a digital computer in the measurement of roentgenographic bonedensity.
Vogt, Meharg, Mack, 1969.
Changes in mineralization must be in the order of 25 - 30% for visual detection on radiographs. Radiographs of the os calcis were investigated with an optical scanning system. The light transmission data from the object and an added Al. wedge were analysed with a computer; no standardised radiographs were used.

Radiographic interpretation of experimentally produced bony lesions.
Shoha, Dowson, Richards, 1974.
Artificial bony lesions were created on a phantom, the radiographic image of the lesion was compared with the size and appearance of the actual lesion.
The lesions were always larger than the radiographic image.

Interpretation and densitometric quantification of periapical structures in dental radiographs.
Duinkerke, 1976.
Reproducible dental radiographs were made of bone phantoms and of one patient.

Densitometric analysis to quantify changes in the bone structures is superior to visual interpretation but time consuming and complex.

A radiographic technique for measuring the powder packing density in the cavities of trabecular bone.
King, 1977.
A technique is developed to determine the difference in density of an empty bone specimen and one filled with lithium fluoride powder, on radiograhps using a microdensitometer. It shows a decrease in packing density with an increase in the percentage of bone, i.e. a decrease in cavity size.

Zur Röntgendichte von Kunststoffen.
Diller, 1978.
The relative densities of available plastic materials were studied (nylon).

Radiopacity of impression materials.
Eliasson, Haasken, 1979.
Radiographic densities were measured and the values expressed in Al. eq value. None of the examiners were able to detect an Al. eq value of 0.71 mm or less, an Al. eq value of 1.3 mm or more was required for diagnosis.

Conclusions:
From the literature, it appears that densitometric quantification of bone is more sensitive than a subjective evaluation. A combination of radiologic techniques and densitometric analysis can be useful for analysis of bone structure. Investigation of the possibility to create optimum circumstances for the procedure is required to gain an insight in the various components and to study them in detail.

2.2. Clinical Literature.

The diagnostic limitations of radiographic procedure is a well-known problem and many supplementary investigations in the field of microscopy and specialized radiology (CT scan, γ absorption) have been carried out to check the reliability of the radiographs. A short review of the most relevant findings follows:

Quantitative roentgenologic studies on changes in mineral content of bone in vivo.
Omnell, 1957.
Omnell studied the Al. eq values of bone and read the values on the calibration curve from the 9 step Al. wedge.

Modern radiological methods of bone densitometry- a survey.
Bentley, 1967.
Densitometric analysis for accurate assessment of osteoporosis was carried out and compared with the subjective radiologic interpretation. An Al. stepwedge (8 steps) was used.

Spongy bone architecture of edentulous mandibles: A television radiographic evaluation.
De Aquiar, Klein, Beck, 1968.
The remodelling process of bone undergoes changes when teeth are removed. This was related to atrophy and aging of the patient. This investigation counts bone trabecular and medullary spaces and measures maximum cross-sectional diameters of medullary spaces within a standardised sample area (5 mm) with a television subtraction read-out unit.
When comparing the non-denture wearing group and the denture-wearing group, an increase of 17 - 27% was noted for the first group in the average width of the medullary spaces.

Microdensitometric analysis of human autogenous alveolar bone implant.
Matsue, Collings, Zimmermann, Vail, 1970.
Reproducible radiographs were taken with a Rinn Paralleling Instrument and an Al. stepwedge. Figures for the serial radiographs illustrate the reproducibility of the technique.

Study of in vivo radiographic densitometry.
Plotnick, Beresin, Simkins, 1970.
An intensive study of densitometry to determine the reliability as a biologic measuring method. Two duplicate Al. penetrometers were used (steps 1 - 7 mm) one extra-oral and one intra-oral.

A technique for standardised serial dental radiographs.
Plotnick, Beresin, Simkins, 1971.
The description of an accurate technique for achieving standardised serial dental radiographs with the aid of a biteblock. Two stepwedges were used for densitometric studies.

Quantitative longitudinal study of alveolar bone tissue in man.
Bergström, Henrikson, 1970.
This investigation deals with the reaction of alveolar tissue on surgery, observed from radiopacity changes determined with the aid of an intra-oral Iodine^{125} radiation source. A reference Al. stepwedge was used and the density of the 5 steps was determined.
Reproducibility of the positioning was obtained with an individual capsplint, covering the crowns of the teeth and a part of the palate.

Iodine - 125 apparatus for measuring changes in X-ray transmission and the thickness of alveolar process.
Henrikson, Julin, 1971.
This article describes measurement of the transmission of radiation from an Iodine^{125} source through the alveolar process with simultaneous measurement of the thickness of the same region. There was a very high reproducibility and it was possible to determine the amount of hydroxyapatite in the region studied.

Microdensitometric analysis of human autogenous bone implants II. Two dimensional density and pattern analysis of interproximal alveolar bone.
Matsue, Zimmermann, Collings, Best, 1971.
Quantitative and qualitative assessment of alveolar bone was determined with a microdensitometer and also visually. An Al. stepwedge was used with a range in thickness from 1 - 8 mm. Densities above Al. scale 5 indicate normal or higher degrees of mineralization.

Reproducible radiographs and photographs in periodontal diagnosis.
Renggli, Steiner, Curilović, 1971.
The purpose was to determine the reproducibility of radiographs made with a precision X-ray instrument. Differences in horizontal and vertical measurements were analysed.

A new method of gamma-ray osteodensitometry of the mandible.
Wowern, 1974.
Frontal scans were made of phantoms and patients, the results obtained were reproducible and the method can be used for longitudinal studies of mineral content changes.

The interrelationship between bone mineral at different skeletal sites in male and female cadavera.
Aitken, 1974.
Unfortunately the techniques used for radiographic and photonabsorption measurements do not provide much information on the relationship between the particular site selected and other parts of skeleton, on the assumption that the site selected is representative of the remainder of the skeleton. The third metacarpal, the radius, the femur and the third lumbar vertebra were investigated. In females a significant and in males a much less significant correlation was found.

Measurements of fine structures in roentgenograms. A microdensitometric method.
Hedin, Lundberg, Wing, 1974.
The methodological error and the precision of the densitometric equipment was described and judged adequate for the measurement of small differences in the dentine substance.

A method for obtaining periodic, identical bitewing radiographs.
Kirkegaard, Zeuner, 1974.
For obtaining periodical, identical bitewing radiographs, impressions of the occlusal surface of molars and premolars were used. Changes in the distance between measuring points were determined by means of a stereoautograph.

A comparative histological and radiographic study of extraction socket healing in the rat.
Smith, 1974.
The densitometric values were limited, due to difficulties in the standardisation of the radiographs. Bone accretion in the bone socket can be detected after about 5 days.

Herstellung von reproducierbaren und deckungsgleichen Röntgenbildern bei Knochenstructuruntersuchungen.
Adolph, Lichtenau, Epple, 1975.
Reproducible radiographs are a prerequisite for diagnosis. The radiographs are photometrically scanned and entered into a computer to check the reproducible radiographs at different moments.

Herstellung von Röntgenaufnahmen des menschlichen Unterkiefers Methode und Nachweis der Genauigkeit der Reproducierbarkeit des Ortes.
Lichtenau, Bollinger, 1975.
Reproducible radiographs taken at different moments were analysed by means of data processing. Identification of the same spot was possible.

Bone scan in chronic dialysis patients with evidence of secondary hyperparathyroidism and renal osteodystrophy.
Sy, Mittal, 1975.
Radiopharmaceuticals used for radionuclide scanning made it possible to determine bone activity in patients with renal osteodystrophy, especially in the mandible. The manifestations appeared earlier than visible changes in the radiograph.

Röntgendensitometrische Knochenstructuruntersuchungen nach Zahnextractionen.
Lichtenau, Bollinger, Böhringer, 1976.
Reproducible radiographs were examined with a densitometer and computer-aided techniques with regard to bone structure changes during wound healing. The findings were quantitatively presented.

Television radiographic evaluation of periapical osseous radiolucencies.
Kasle, Klein, 1976.
Periapical lesions were experimentally induced in dogs. Radiographs were evaluated visually and with television subtraction. A histologic examination was carried out. The subtracted image indicated an improved radiographic interpretation.

Erfassung des Desmodontalspalts und dessen Veränderung aus dem Röntgenbild des menschlichen Unterkiefers mit Hilfe einer Datenverarbeitungsanlage.
Lichtenau, Faust, 1978.
Reproducible radiographs were examined with regard to measurements of the periodontal space and visual interpretation.

Periodic identical intra-oral radiographs.
Refshauge, Tolderlund, 1978.
A modified long-cone technique with a modified Eggen film positioner was described. The short term and long term error was determined.

Reproduction of the lamina dura in dental radiographs.
Kilpinen, Hakala, 1978.

Visual interpretation of radiographs was compared with recorded curves. The mineral content of the alveolar wall had a higher mineral content in comparison with the rest of the alveolar bone.

Bone mineral measurements using an EMI scanner and standard methods: a comparative study.
Pullan, Roberts, 1978.
Three techniques for the analysis of bone mineral content are compared: scanning photodensitometry, radiographic microdensitometry and a modified EMI scanner. The EMI scanner has the added advantage of visualising and measuring the density of trabecular bone.

A roentgenologic study of cortical bone resorption in chronic renal failure.
Meema, Oreopoulos, Meema, 1978.
Bone changes, both in the hands and the radius, were evaluated by microradioscopy, radiographic morphometry and photodensitometry. Densitometry of the handbones generally conformed with the findings obtained by the 2 other methods.

Radiological determination of changes in bone mineral content.
Lindsay, 1978.
Densitometric and morphometric measurements of the 3rd metacarpal midshaft were compared annually, over 3 - 4 years, with the photonabsorption technique. An 11 step Al. wedge was used. For this investigation, morphometry is the most accurate method.

Periapical bone lesions.
Van der Stelt, 1979.
Color conversion makes an improvement in the perceptibility of periapical anomalies possible in comparison with the observation of the black and white image.

Therapy of osteogenesis imperfecta with synthetic salmon calcitonin.
Castells, Colbert, 1979.
Bone density of the phalanx was analysed with the densitometer and an Al. reference wedge with the computer.

Strukturanalyse des Knochens aus Röntgenbildern.
Heuck, Bloss, Saackel, Reinhardt, 1980.
Two different procedures were used for the evaluation of bone structure, namely: digital image processing and coherent optical image processing. Frequency spectra for analysis of the two-dimensional bone structures were determined with the F.F.T. (Fast Fourier Transform) in the computer.

2.3. Conclusions.

A survey of the clinical and radiodiagnostic aspects is presented. Advancement of the research is based on experimental studies with the use of bone phantoms on animals and by means of radiological studies on patients. Microdensitometry has a distinct advantage over the more traditional visual method as a basis for the investi-

gation of bone mineral. Computer processing makes it possible to store the data and to study the changes which take place in certain areas with time. This type of technique could be of special interest if used for routine longitudinal clinical investigations. In their assessment of longitudinal radiological studies, many investigators did not realize the limitations of their method. Literature concerning the precision of the method can be classified as follows:

1. The positioning of the beam in relation to the object.

   The radiographs were more or less identical, dependent on the precision of the technique used. In order to test the reproducibility of the technique, measurements were carried out by using clearly definable landmarks. It proved possible to determine the precision of the method by means of measurements.

2. The technical factors.

   Even the identical radiographs showed differences in blackening which influenced interpretation of the trajects of interest. The effects of variation of these factors were reduced by the use of reference material.
   An objective interpretation is only possible when a calibrating gauge with exact known values is radiographed simultaneously with the object. Aluminum and calcium solutions were used for calibrating purposes.

3. The analysis method.

   An objective estimation was achieved by measuring the blackening of the film. Microdensitometry was used to produce scans for evaluation of changes in the tissues. Different conversions were used to provide real Al. eq values of bone. Computer help is sometimes used for a fast evaluation of Al. eq values of bone.
   It provides digital values of bone and scans which show recognizable structures.

4. The investigation method.

   The literature contains descriptions of a number of investigations carried out in the form of laboratory experiments and experiments on patients in order to evaluate a method which reflected bone mineral values. No conclusive answer was obtained to the question of how long the observation period should be or how many registrations need to be made in order to permit observation of changes in bone mineralization.

General conclusion.

The limitation in a subjective radiographic diagnosis concerning bony structures is the limitation of visibility of the changes in mineralization. A radiograph, however, not only provides a picture of the bone morphology, but also permits a microdensitometric, quantitative analysis.
These features may prove important for the purpose of improving diagnostic procedures. The need for a refined clinical diagnostic method for the registration of bone mineral content and distribution is under discussion.

CHAPTER 3

THE MEASURING AND RECORDING SYSTEM, INCLUDING THE INFORMATION PROCESSING.

3.1. Introduction.

The blackening of a radiograph is caused by the number of silver grains/cm^2 in the exposed and processed film and it depends on the exposure, the quality of the X-ray beam and the processing to which the film has been exposed.

The visual blackening of the radiograph, as experienced by the observer, depends on the light absorbing and scattering properties of the silver grains as well as on the fraction of light that is transmitted.
The density quantitatively defines the degree of blackening of the emulsion.
Hurter-Driffield (1890) defined density as follows:

$$D = \log. \frac{\text{incident light radiant flux}}{\text{transmitted light radiant flux}}$$

The density range useful for practical radiological diagnosis, depends on the physiological and psychological processes involved. In clinical practice, density values (D) from 0.25 to 2 above fog in the field of interest are acceptable. A more objective visual interpretation of the bone mineral can be made when an object of a known composition and thickness is radiographed simultaneously with the object. This permits a comparison between the known standard and the specimen. In 1937 Stein radiographed an object in combination with an ivory wedge. Hodge (1935 - 1938) used aluminum, Björn, Henrikson and Omnell in 1951 and Richards in 1953 used various Ca. concentrations with exact known values. We endeavoured to develop a method which makes it possible for us to give objective information on the radiograph in the relatively low density as well as in the high density levels.

In this study, aluminum was chosen as reference material because the absorption and the scatter properties are simular to those of bone. In addition to this, aluminum is a material which is homogeneous and easily machined. If an Al. wedge is exposed simultaneously with the object, a comparison can be made on the radiograph between the density (blackening) as produced by the wedge and the points of interest of the object.

It is possible to read the Al. values of the wedge which produce the same optical density in an area of interest on the radiograph. The technique, using the physical properties of aluminum, represents an advancement in the evaluation of the radiograph.

The technique can be described as follows:

On the radiograph, the microdensitometer scans the images of the Al. wedge and the object, which results in density curves. The curves permit us to find the Al. thickness which for each spot along the bone scan, shows the same absorption, resulting in the same blackening on the film. This Al. thickness is called the Al. eq value of bone.

This procedure is time-consuming. Computer processing is convenient, because it provides fast data manipulation. This method automatically transforms the measurements into mm Al. eq by comparison of the density in the image with the density of the calibrating wedge. The combination of microdensitometer and computer data processing is favourable and enables us to assess the radiographic bone density and several indications of bone mineralization. This computerized microdensitometrical procedure will be tested in a pilot study and in clinical practice.

3.2. Conversion methods.

Registration with a photomultiplier of the light transmitted by the image of an Al. calibrating wedge results in a curve with irregularities. These irregularities are produced by irregularities in the photographic image, dust, scratches etc. The measured fluctuation is called noise. Precision in determination of the Al. thickness of the wedge from the output of the photomultiplier is influenced by the irregularities which reduce precision.
The measured values of the object in the radiograph are compared with the values of the image of the calibrating wedge, resulting in Al. eq values.
In order to eliminate the effects of the irregularities of the registered mV. photomultiplier output versus mm Al. thickness on the precision, it was decided to use a mathematical defined curve with a minimum deviation from the registered curve. The formular for this curve was determined and used for the "translation program" of the computer.
First, the fit of a linear, a quadratic and a logarithmic curve were compared to select the most suitable mathematical formula. The fit of these three curves in relation to the real data-points is shown in fig. 1.

The deviations of the three curves from the correct value are shown in fig. 2.

The quadratic curve-fit shows the least deviation from the correct data and was therefore used for the transformation of the readings into Al. eq values in the computer calculations (fig. 3.).

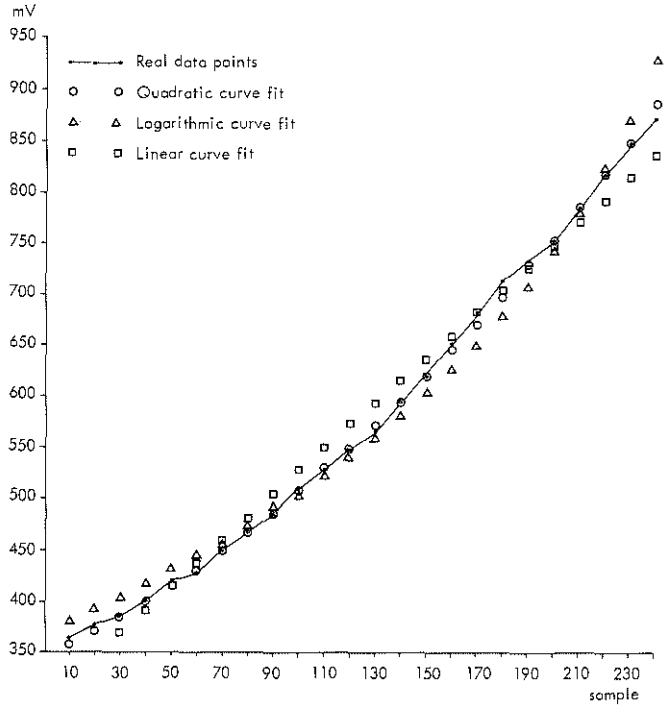


Fig. 1. Graph showing the output of the photomultiplier against the thickness of the wedge, the samples 10 to 230 were taken along the wedge (respectively from 11 - 2 mm Al.). The three mathematical curves are shown with three different symbols.

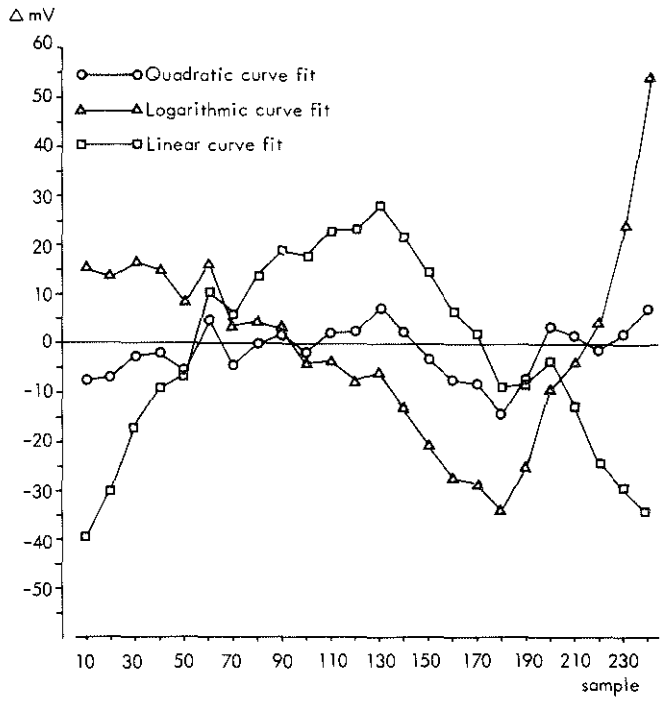


Fig. 2. Graphs showing the deviation of the mV values from the three conversions against the real datapoints.

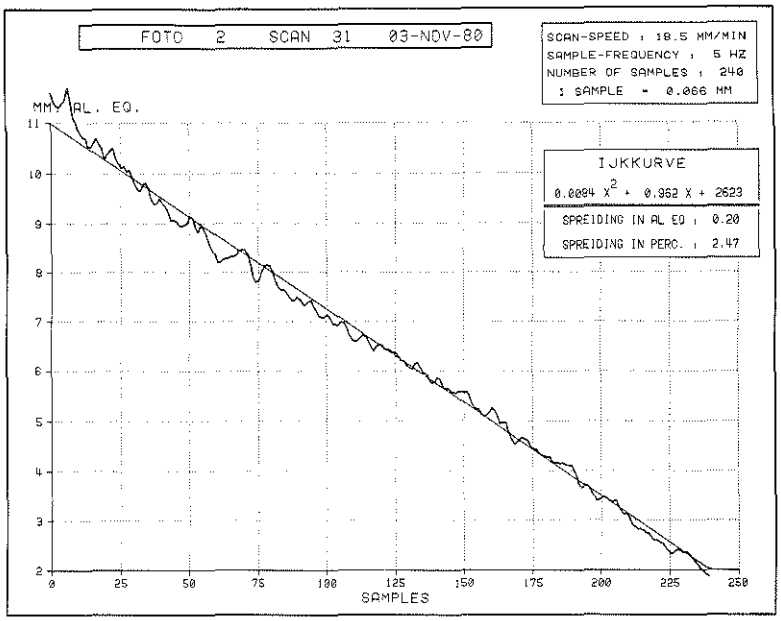


Fig. 3. The quadratic curve-fit shows the Al. eq values (11 - 2 mm Al.) the straight line indicates the real Al. eq values, the curved line shows the Al. eq values of the wedge as computed according to the quadratic formula from the registered data.

3.3. Aids to improve repositioning.

Various methods have been used and described in chapter 2.2. It was concluded that development of a positioning instrument was necessary for the purpose of precise repositioning. A constant target to film distances and correct beam angulations will be more easily attained by means of the extension-tube paralleling technique. This improves the reproducibility of the measurements and makes serial images possible.

The Positioning Instrument (P.I.)

The P.I. was designed and produced by the "Centrale Research Werkplaats" Department (Erasmus University, Rotterdam) (fig. 4.). It is made of nylon (Diller 1978) because this material has suitable properties: a low specific gravity, a smooth surface, is easily obtainable and also has a low X-radiation absorption.
The P.I. consists of:

A. a biteblock with a sleeve to accept the interchangeable acrylic resin impression of patients. It contains a stepless Al. calibrating wedge to provide a continuous aluminum thickness scale. The wedge dimensions are: length 26 mm, width 4 mm, height varying from 0 to 12 mm.
   The biteblock also has eight measuring points, constituted by injection needle segments with a length of 1 mm and a diameter of 0.4 mm.
B. a filmholder 3 x 4 cm for radiographs. Two wires were mounted perpendicular to each other in the filmholder. The image of these lines on the radiograph serve to start the computer program.
C. a direction indicator rod with protective shield and diaphragm.

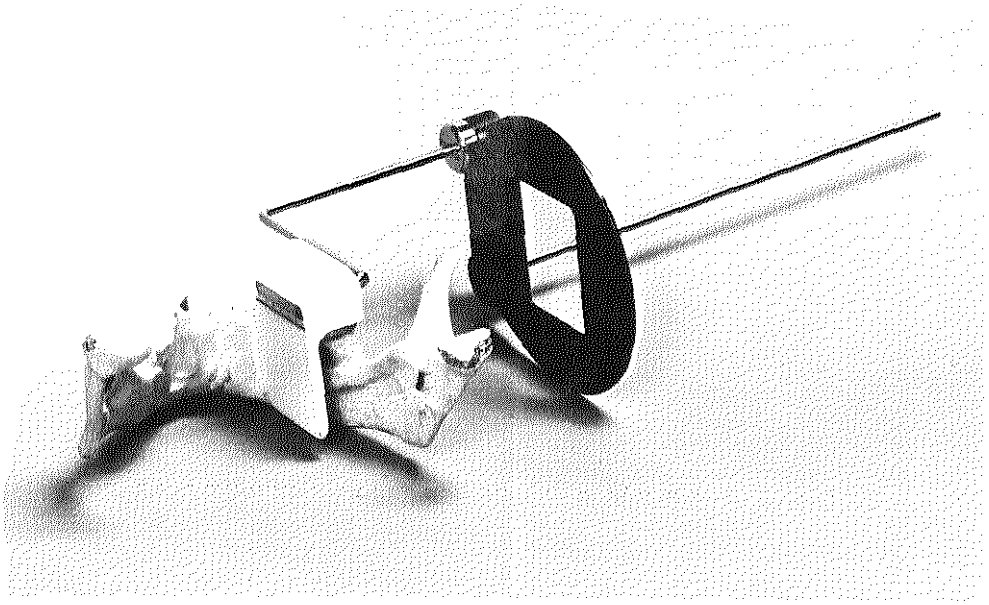


Fig. 4. Positioning Instrument P.I. Positioned on the mandible.

3.4. X-ray apparatus, X-ray beam.

The X-ray beam contains a mixture of radiation with different wavelengths. Fluctuations in line voltage affect the composition of the beam. From the heterogeneous radiation, the radiation with a longer wave length will be absorbed more than the radiation which has a shorter wave length. The choice of a suitable quality of radiation is important for a quantitative radiological investigation.

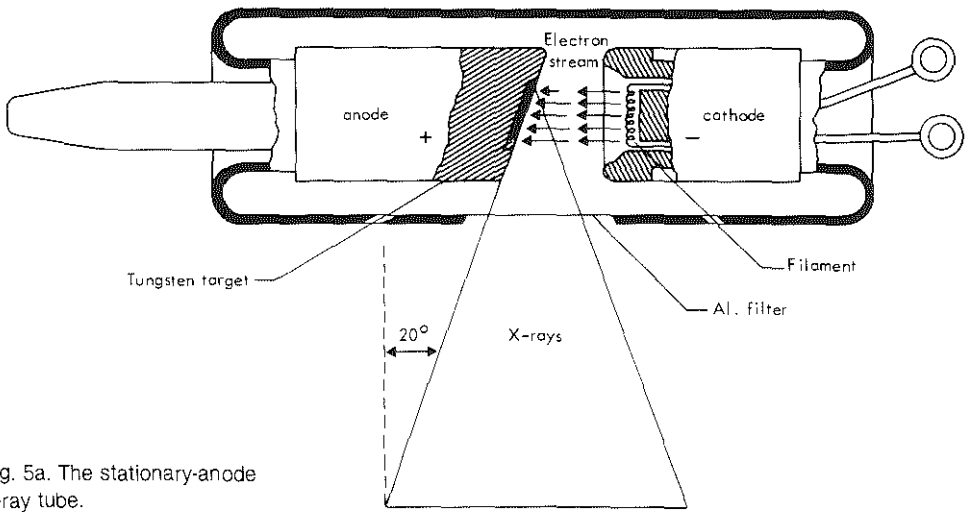


Fig. 5a. The stationary-anode X-ray tube.

The inclination of the target gives a significant decrease in the intensity of the X-rays from the cathode towards the anode (heel-effect) (fig. 5a., 5b.).
The uniform emission of X-rays is often disturbed, due to roughening of the target.
The radiation source used for our investigations was a Ritter Explorer Dental X-ray unit type III, with a long-cone and a total aluminum equivalence filtration of 3 mm. The film and specimen were exposed (15 mA and various kV) to a target at a film distance of 40 cm. Various exposure conditions were used for each specimen.

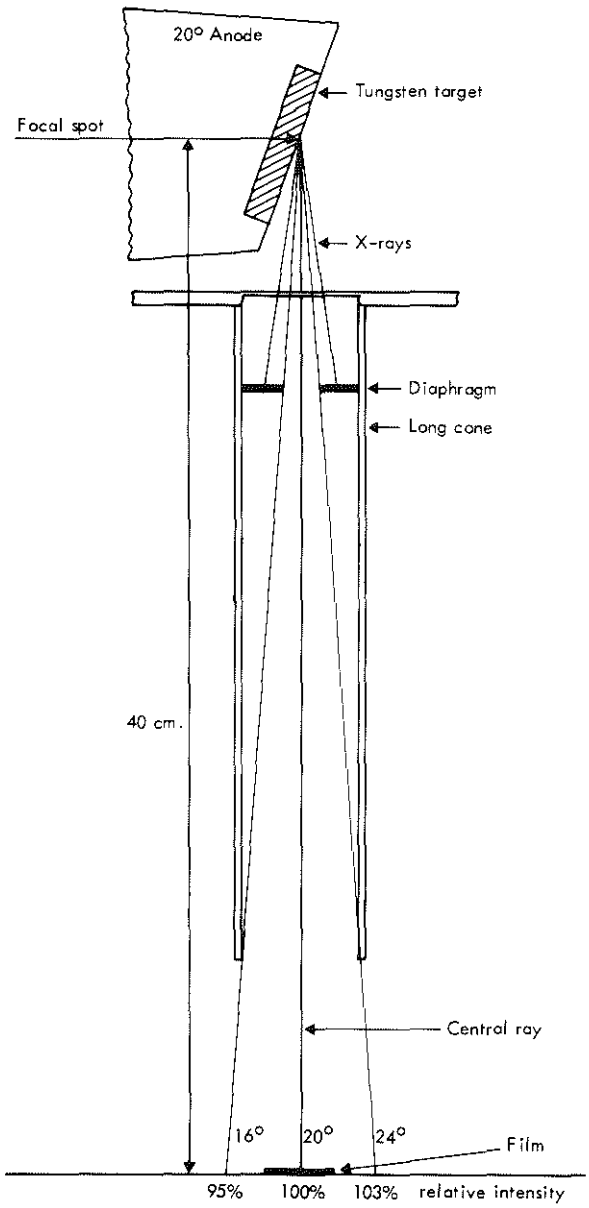


Fig. 5b. The heel-effect as given in the literature adapted to the long-cone technique (ref. The Fundamentals of Radiography).

3.5. Image recording by the microdensitometer.

A light beam of high intensity is used to measure the density of a radiograph. This beam passes the film perpendicularly. The transmitted (and part of the scattered) light, was measured by an extremely sensitive photomultiplier. The instrument used to measure optical densities is called a microdensitometer (fig. 6.). A microdensitometer Gamma Scientific (2900 HR) was used.

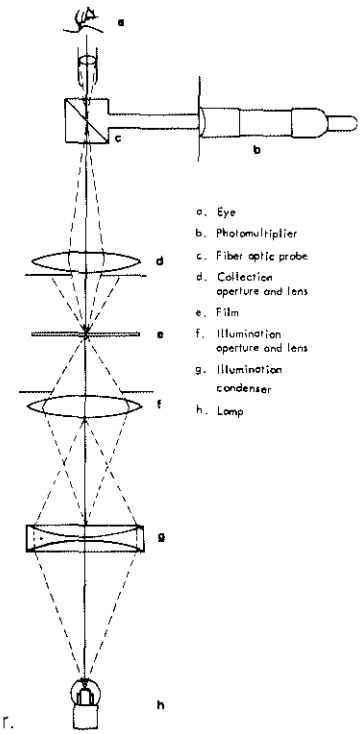


Fig. 6. Schematic drawing of a microdensitometer.

All recording microdensitometers consist of a light source (h) an optical arrangement (f, g) for illuminating the sample (e) an optical arrangement for collecting the light transmitted by the sample (d) a receiver to sense the collected energy (c) a device to measure the energy (b) and a read-out device (fig. 8.). The illuminator and the collector are microscope components with varying apertures, the light detector is a photomultiplier. The view attachment (a) permits focusing of the microscope upon the desired area.

The film is mounted on a motor-driven stage and its movement is synchronized with a chart-recorder on which the photomultiplier output is plotted against the distance. Unsuccessful experiments and incorrect film orientation can be eliminated by a visual inspection of the plot on the chart-recorder. The unit automatically reads and records photomultiplier outputs of each of the desired areas of the film. The chart-recording shows the mV output of the photomultiplier as it passes the image of the

mineral distribution of the bone section (fig. 7.). It can be noted that soft tissues also contribute to the mV values. If an exact replica of the positioning of the scanned track can be obtained, it is possible to compare the signals obtained from radiographs made at different moments.

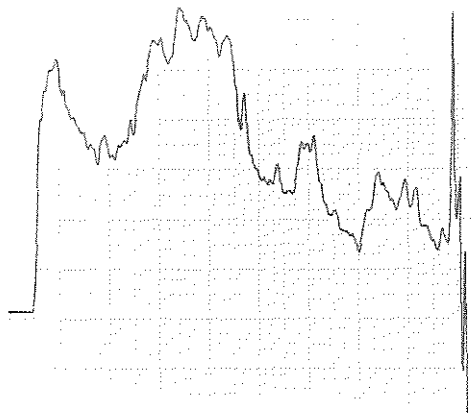


Fig. 7. Bone scan on the chart-recorder.

The instruments comprising the scanning and recording system are shown in fig. 8.

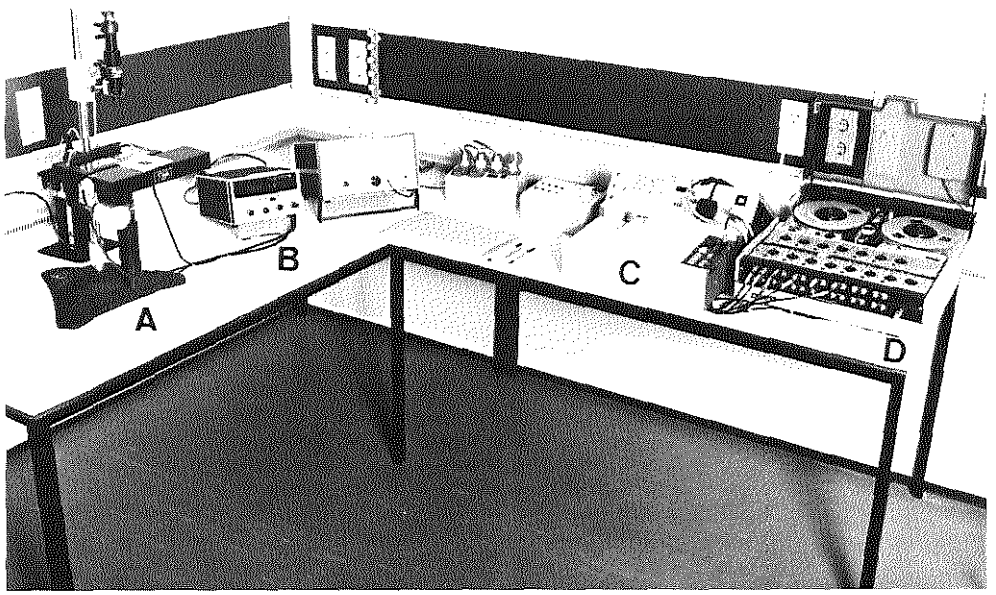


Fig. 8.
A. Gamma Scientific densitometer B. Read-out device C. Chart-recorder D. Instrumentation-recorder. The values, obtained from the densitometer, are stored on an instrumentation-recorder (Racal Store 14).

3.6. Computer Processing.

Variations in optical density occur in the image of the bone. Recording of these variations with a densitometer and computer processing can be useful for the development of a fast system for the evaluation of optical bone density and bone pattern. A computer program was developed for processing bone density measurements. The complete system is shown in block design (fig. 9.).

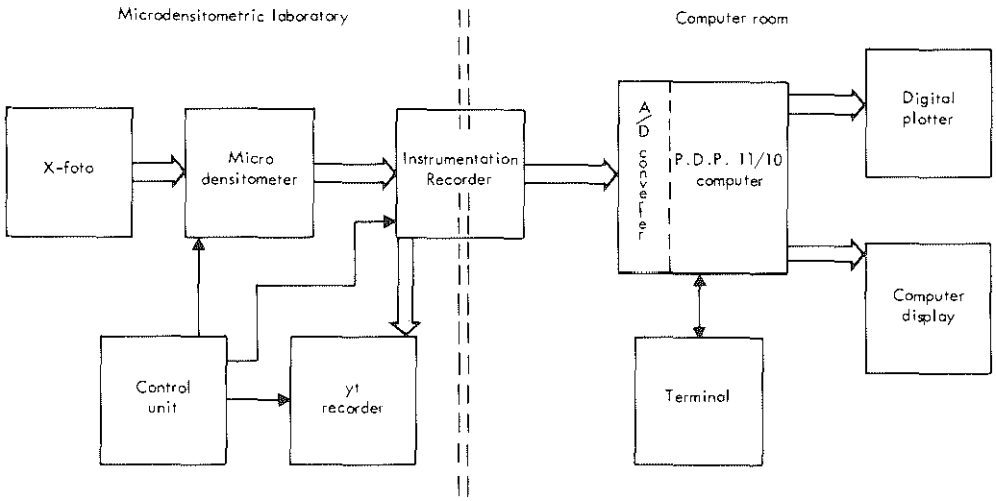


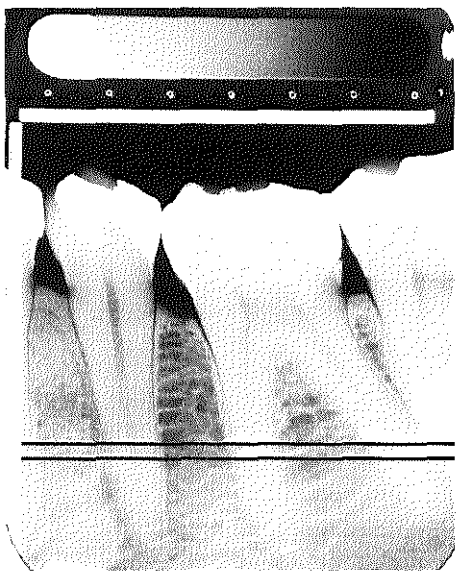
Fig. 9. Diagram of computing facility and microdensitometric laboratory.

During replaying for digitization, the Analog Digital Converter of the computer (Digital P.D.P. 11/10) converts the measured values of the densitometric scan of the X-ray image into a digital signal. These values are recorded on a disk for subsequent calculations.

The wedge-image is scanned and the resulting transmission data stored in terms of wedge-thickness. The bone image is scanned and the resulting transmission-data stored. After the wedge and bone scans have been completed, the computer calibrates the stored bone data in terms of Al. eq wedge thickness, using the stored wedge data.

The system provides a storage capacity for 240 samples along the wedge and 400 samples for the bone scan. The distance between the samples is 0.066 mm. The sample rate of 5 Hz, as indicated on the graphs, is equivalent to this inter-sample distance. The data relating to each scan is stored in the computer for future evaluation. Computer input and commands can be performed manually or in automatic batch mode. The computer terminal monitor shows the Al. eq values. A crosshair cursor is used to enable the operator to designate a specific section of the curve. The computer program can make calculations with the data from selected areas and the resulting values are recorded. For example: the average of the values of a scantraject was calculated; this was repeated for five adjacent scans (the distance between two successive scans was 0.2 mm). The average value of five adjacent scans, a track of 1 mm, was calculated and gave the mean Al. eq values of 1 mm^2;

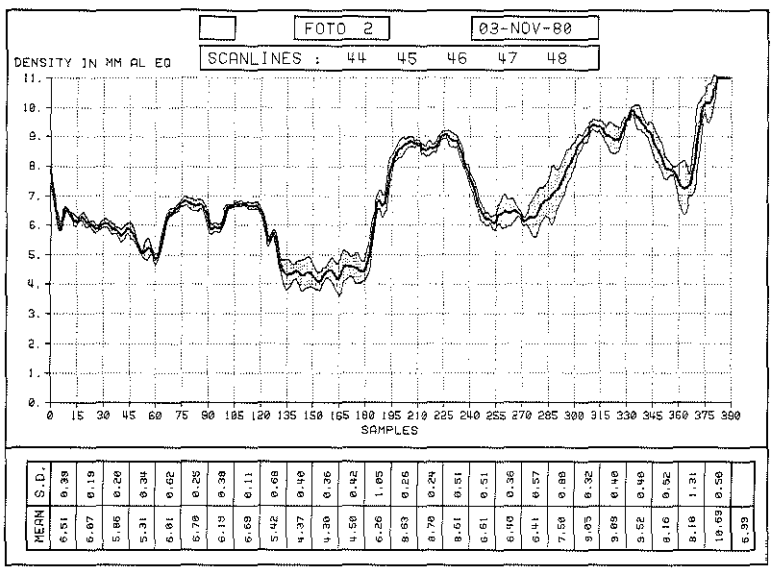
the standard deviation can also be produced. The value (fig. 10a., 10b.) can be used to study changes in the Al. eq values of bone which take place with time. If the location of the measurement can be reproduced exactly, we can subtract the primary values to compare the density values. Instead of adjacent scans, scans of different radiographs of the same subject can be evaluated. If a horizontal alignement is not correct, the computer can correct the scan position until a maximum correlation between the scans is obtained.



◀ Calibrating wedge

◀ Reference line (measuring points)
◀ Startline computer

◀ Area covered by five scans in alveolar ridge.



S.D.	0.39	0.19	0.20	0.34	0.62	0.25	0.38	0.11	0.68	0.40	0.36	0.42	1.65	0.26	0.24	0.51	0.51	0.36	0.57	0.80	0.32	0.40	0.40	0.52	1.31	0.58	
MEAN	6.51	6.07	5.86	5.31	6.01	6.79	6.19	6.69	5.42	4.37	4.30	4.58	6.26	8.63	8.79	8.61	8.61	8.40	8.41	7.58	9.05	9.69	9.52	8.16	8.16	10.69	6.99

Fig. 10a, 10b. Radiograph and computer-generated scan showing the average Al. eq values/mm² and the standard deviation.

CHAPTER 4

THE SYSTEM PRECISION (REPRODUCIBILITY).

THE PILOT STUDY.

The precision denotes the reproducibility of repeated measurements irrespective of their absolute accuracy.
The microdensitometric technique depends on equipment which, nowadays, has probably attained a sufficient degree of technical perfection.
In this chapter, the technical and mathematical aspects of the procedure will be studied.

The following aspects were tested for precision:
4.1. The precision along the calibrating wedge.
4.2. The precision of the positioning instrument.
4.3. The precision of the X-ray timer.
4.4. The homogeneity of the X-ray beam.
4.5. The precision of the X-ray film and the developing procedure.
4.6. The influence of the exposure time on the Al. eq value determination of:
   a. an Al. phantom
   b. a mandible phantom.
4.7. The influence of a soft tissue substitute on the precision.
4.8. The precision of the microdensitometer and recording system
   a. positioning of the film
   b. fluctuations in the intensity of the light beam
   c. direction and speed of the motor-driven assembly
   d. the response of the photomultiplier to density variations.

4.1. The precision along the calibrating wedge.

Relatively small irregularities are visible in the curve of the image of the Al. calibrating wedge. Investigation is necessary to ascertain whether these irregularities could be caused by the Al. wedge.
The calibrating wedge was machined in one piece from an aluminum block and tapered from 0 - 12 mm Al. Aluminum 51 ST = 98.4% Al, 0.6 Mg, 1% Si. Variations in the image of the calibrating wedge give an indication of the homogeneity of the material.
The following method was used: five adjacent scans were made, parallel with the long axis and in the centre, in order to ascertain whether the location of the scantraject is important (table I.).

Table I: Al. eq values of the five scans in the centre of the wedge.

Scan no.	Selected areas of one mm wedge, in mm Al. eq															
1	10.95	9.91	9.31	8.62	8.20	7.85	7.24	6.75	6.29	5.70	5.25	4.62	4.03	3.37	2.81	2.18
2	11.41	10.25	9.49	8.91	8.47	7.89	7.47	6.89	6.36	5.76	5.14	4.61	4.04	3.44	2.84	2.14
3	11.09	10.07	9.49	8.95	8.41	7.95	7.40	6.74	6.25	5.84	5.07	4.59	4.02	3.40	2.75	2.13
4	11.21	10.26	9.60	9.01	8.51	8.00	7.32	6.91	6.42	5.82	5.24	4.71	4.01	3.39	2.83	2.11
5	11.36	10.30	9.67	8.98	8.38	8.07	7.46	6.89	6.46	5.91	5.28	4.65	4.07	3.33	2.82	2.17
Mean	11.20	10.16	9.51	8.89	8.39	7.95	7.38	6.84	6.36	5.81	5.20	4.64	4.03	3.39	2.81	2.15
SD	0.19	0.16	0.14	0.16	0.12	0.09	0.10	0.08	0.09	0.08	0.09	0.05	0.02	0.04	0.04	0.03
Coefficient of variation	1.7	1.6	1.4	1.8	1.4	1.1	1.3	1.2	1.4	1.4	1.7	1.0	0.6	1.2	1.3	1.3

In the five adjacent scans, small variations in the measurements were found between scans at 0.2 mm distance along the axis; the variation coefficients ranged from 1.8 to 0.6%. It can be concluded that the selection of a scan traject of the calibrating wedge within a path of one mm shows only small differences.

4.2. The precision of the positioning instrument (P.I.)

For testing of the developed P.I. (3.3.) and long-cone technique, a dried mandible was used to test the precision of the method. An autopolymerizing acrylic block was made on the molars and premolars of the mandible. A connection was made with the P.I. by means of a slot, in such manner that the film was parallel to the axis of the teeth.

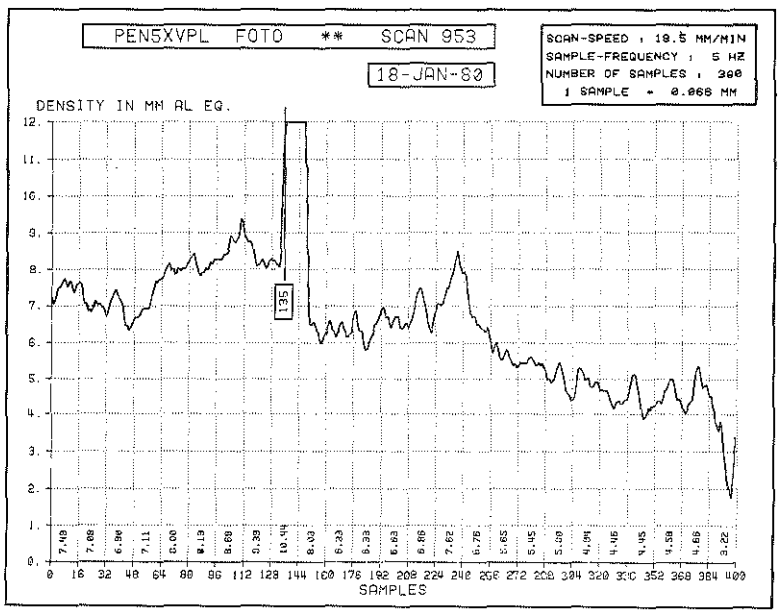


Fig. 11. Scan of traject d. (fig. 12.) showing the border of the landmark indicated by the cursorline (sample 135).

The biteblock can be reseated for each examination. A metal wire (landmark) was incorporated in the mandible to simulate soft tissues (cheek) and a 2 cm thick layer of perspex® was used. Five radiographs were made of the molar region, since differences in the positioning of the X-film influence the reproducibility of the measurements. To test the reproducibility (precision) of serial radiographs, distances were measured according to the following criteria (landmarks): the position of the startlines of the computer in the P.I. both in relation to the image of the wire in the mandible.
The reproducibility of consecutive measurements (a horizontal distance on the graph of fig. 11.) depends, among other factors, on the error made in identifying the border of the wire. This error will be small when the vertical parts in the curves are used and the error will be larger for less steep sections in the curve. In general, well defined landmarks with vertical borders in the graphs were used.

Horizontal and vertical scans were made to test the reproducibility of the five different radiographs.

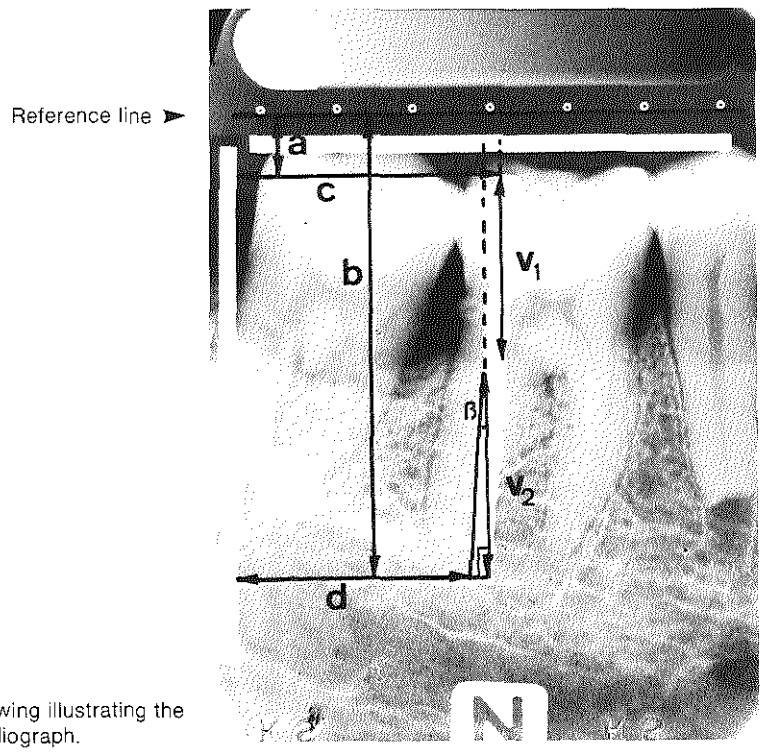


Fig. 12. Schematic drawing illustrating the scantrajects on the radiograph.

The following scantrajects were used: in order to measure horizontal distances c. and d. (fig. 11, 12.) scans were made passing the vertical startline and passing respectively, the top and the bottom of the wire. The length of the scantrajects was also determined in order to measure the vertical distances v_1 and v_2 between the horizontal startline and the top and the bottom of the wire.

Table II: The number of samples along the four scanlines c, d, v_1 and v_2.

Radiograph	Horizontal scan in samples		Vertical scan in samples	
	c.	d.	v_1	v_1
1	169	142	79	91
2	169	143	80	85
3	170	143	80	74
4	170	143	71	83
5	169	140	80	88
Mean	169	142	78	84
SD	0.55	1.30	3.94	6.46

Results.

The horizontal scans show small differences (1 sample). As expected, the vertical scans showed larger differences for the vertical traject v_1, a mean of 78 samples SD 3,94 coefficient of variation 5% and for the vertical traject v_2, a mean of 84 samples SD 6,46 coefficient of variation 8%.

The investigated vertical scan trajects form a more unfavourable, small angle with the border of the object. This might explain why the coefficient of variation is higher in comparison with the horizontal distances.

The precision of the repositioning was also tested by the mean Al. eq value of a scan-traject in a radiograph of the mandible. The same 5 radiographs, used for investigation of the distance measurements, were evaluated.

Table III: The mean Al. eq values of five radiographs.

Radiograph	Mean Al. eq (mm) bone traject.
1	7.32
2	7.30
3	7.28
4	7.30
5	7.27
Mean	7.29
SD	0.02

We found small differences in Al. eq values between the 5 measurements, the SD of the Al. eq value was found to be 0.02.

It can be concluded that reproducible "high precision" radiographs can be made of a dried, human mandible. A small coefficient of variation was found, namely 0.3%.

In chapter 5 the additional influence of the clinical circumstances will be studied.

4.3. The precision of the X-ray timer.

Serial exposure with the same kV and mA demands negligible exposure time errors in

order to eliminate variations in blackening. For this reason, the reliability of the X-ray timer was tested. The method is based on the fact that the unit produces radiation during only half the duration of each line voltage cycle. If the input current has 50 cycles per second, the tube produces 50 radiation emissions per second.
We used a fluoroscopic screen in combination with photosensitive transistors for the production of an image on a storage oscilloscope. It is possible to count the number of pulses that occur during the exposure. If the frequency of the line voltage is stable, the measuring system can be considered as reliable. There is a reduced output in the initial stage of each exposure (fig. 13.).

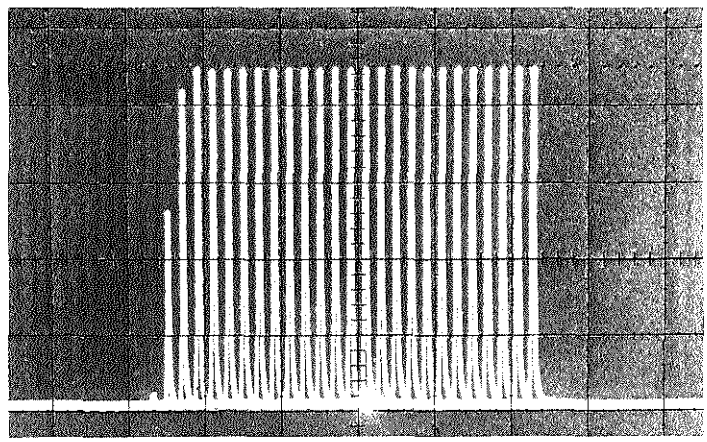


Fig. 13. Photograph of the monitor screen of the storage oscilloscope showing differences in output per each period of 1/50 sec. The oscillogram represents a set of radiation pulses. Especially during the initial stage, there is a reduction in the height of the pulses.

The relation between the time of exposure and the exposure setting is shown in fig. 14.

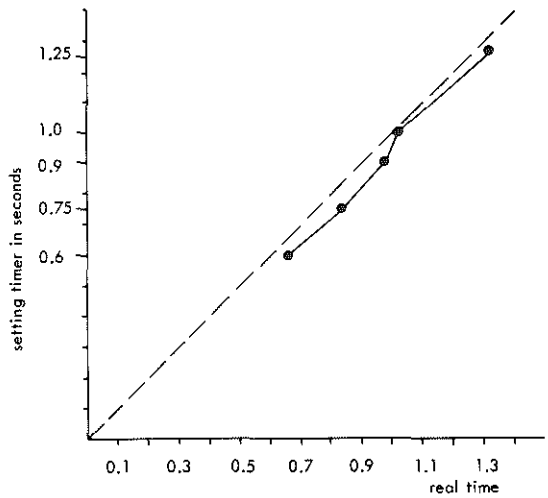


Fig. 14. Graph showing the relation between the exposure time and the exposure setting.

Results.
The time error is less than 10%. Only the time of 1s. is accurate. Later on, it will be

shown that even exposure time variations of 100% do not influence the Al. eq value determination of an aluminum testobject or bone phantom. The timer error can, therefore, be considered as having no significance.

4.4. The homogeneity of the X-ray beam.

In a longitudinal investigation, it is reasonable to expect that the calibrating wedge, the location of the scan traject of the object and the X-ray beam will have the same position in relation to each other. It is, therefore, useful to investigate the non-uniformity effects of the X-ray beam. The heel-effect can exercise a negative influence on the Al. eq values in an object (fig. 5b.).
Homogeneity was investigated with the aid of an aluminum sheet with a thickness of five mm. Differences in the shape and properties of the object were thus eliminated.
The object was radiographed simultaneously with the P.I. aluminum calibrating wedge. In order to investigate the heel-effect, two radiographs with identical exposures were made with 0 and 90 degree rotations of the X-ray tube (80 kV, 15 mA and 1 s).

Table IV: Distribution of the Al. eq values in the two radiographs made with a rotation of 0 and 90 degrees of the X-ray tube.

0° Rotation of the X-ray tube. (values in mm Al. eq)									
80 kV 1.0 s	15 mA	0-4 mm	4-8 mm	8-12 mm	12-16 mm	16-20 mm	Mean	SD	Coefficient of variation
↓	0 mm	5.22	5.12	5.08	5.08	5.16	5.13	0.06	1.2
	5 mm	5.34	5.20	5.20	5.23	5.26	5.25	0.06	1.1
	10 mm	5.38	5.30	5.24	5.30	5.37	5.32	0.06	1.1
	15 mm	5.50	5.41	5.44	5.46	5.48	5.46	0.03	0.6
	20 mm	5.59	5.58	5.54	5.56	5.51	5.56	0.03	0.6
	Mean	5.41	5.32	5.30	5.33	5.36	5.34		0.9
	SD	0.14	0.18	0.19	0.19	0.15			
Coefficient of variation		2.7	3.4	3.5	3.6	2.6	3.2		

90° Rotation of the X-ray tube. (values in mm Al. eq)									
80 kV 1.0 s	15 mA	0-4 mm	4-8 mm	8-12 mm	12-16 mm	16-20 mm	Mean	SD	Coefficient of variation
↓	0 mm	5.15	5.15	5.17	5.09	5.20	5.15	0.04	0.8
	5 mm	5.16	5.21	5.21	5.23	5.21	5.20	0.03	0.5
	10 mm	5.23	5.32	5.26	5.32	5.35	5.30	0.05	0.9
	15 mm	5.42	5.46	5.44	5.44	5.42	5.44	0.02	0.3
	20 mm	5.61	5.65	5.64	5.49	5.51	5.58	0.07	1.3
	Mean	5.31	5.36	5.34	5.31	5.34	5.33		0.8
	SD	0.20	0.20	0.20	0.16	0.13			
Coefficient of variation		3.7	3.8	3.7	3.0	2.5	3.3		

Microdensitometric scans of the Al. object were made of five different tracks parallel with the short film axis. The track was divided into sections of four mm. Average mean Al. eq values were determined for each section and these values were compared (table IV.).

The non-uniformity effects of the X-ray beam on the radiograph can be divided into a horizontal, respectively vertical non-uniformity aspect. The horizontal non-uniformity for both radiographs was relatively small: coefficient of variation 0.9 respectively 0.8%, vertical non-uniformity 3.2 and 3.3%.
It may be concluded that rotation of the X-ray tube has no influence on the distribution of the blackening. It can, therefore be concluded that the heel-effect has a relatively insignificant effect.

4.5. The precision of the X-ray film and the developing procedure.

All the films used during the investigation period came from the same batch number in order to avoid the use of films of different makes with possible differences in the photographic emulsion.
As an additional precaution, the radiographs were stored in the dark, in a refrigerator. Single filmpacks were used.

Sensitometric characteristic of the radiographs.
The characteristic curve of Kodak U. Speed represents the relationship between photographic density against the logarithm of the exposure times. Successive exposures were made with the available exposure setting on the X-ray timer. The curve obtained represents the reaction of the particular emulsion on the exposure and the processing conditions to which it is subjected. The base density plus fog density can be determined by processing and measuring an unexposed film from the same batch. Part of the curve is a nearly straight line; it shows a linear relation between density and log exposure. All the exposed films were developed in an automatic developing machine (Siemens Pantomat) under standardised conditions, with fresh developer and fixative, at a temperature of 28.0°C.
The short axis of the film was brought first into the developing machine, to avoid inconsistencies in the development direction. Film sensitometry was carried out to assess the properties of the Kodak X-ray films used during the year of investigation and the resulting characteristic curves for the respective periods Sept. 1980 and June 1981 were thus obtained.
The slope of the curve indicates the contrast of the film. The estimated slopes for the two periods are shown in fig. 15. The decrease in the slope of the curve could be the result of:
a. a change in the properties of the X-ray film;
b. a change in the developing procedure.
Density variations on radiographs are caused by background irradiation during storage and/or emulsion and processing inconsistencies.
Technical discrepancies and processing techniques limit the scope of radiographic interpretation. If an Al. calibrating wedge is radiographed simultaneously with the object, it can be assumed that both have the same exposure and developing factors.

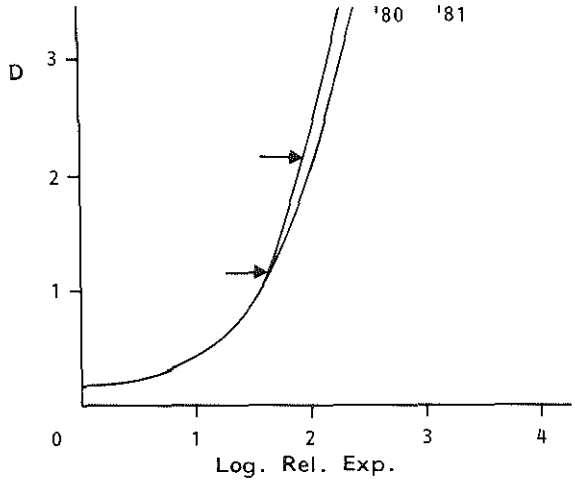


Fig. 15. Characteristic Curve Kodak Morelight U. Speed DF. 57. Standardised Processing. Investigation 1980 - 1981.

Differences in blackening of the radiograph are thus eliminated by comparing the density values of the structures with the values of the calibrating wedge.

Differences on the X-ray films.

Differences on X-ray films can be divided into two categories: differences between individual X-ray films and differences within the X-ray films themselves.

In order to study the influence of film differences and developing procedures between and within films, five films were exposed simultaneously with a sheet of aluminum, radiographed five times (80 kV, 15 mA 1 s) and developed. The Al. eq values were then determined.

Five tracks, covering the whole film, were used at a distance of 5 mm (table V.). This shows the local values of these five films. Table VI gives the mean values of these five tracks for each film and table VIIa., b. give the selected local values of each film.

Table V: Distribution of the Al. eq values in five radiographs of an object of five mm thickness with a 1 s exposure. Complete information used to study the precision between and within films.

Radiograph I. (values in mm Al. eq)									
80 kV 1.0 s 15 mA		0-4 mm	4-8 mm	8-12 mm	12-16 mm	16-20 mm	Mean	SD	Coefficient of variation
↓	0 mm	5.33	5.21	5.19	5.15	5.17	5.21	0.07	1.4
	5 mm	5.43	5.30	5.29	5.28	5.31	5.32	0.06	1.2
	10 mm	5.53	5.40	5.35	5.38	5.38	5.41	0.07	1.3
	15 mm	5.76	5.66	5.62	5.57	5.62	5.65	0.07	1.3
	20 mm	5.89	5.82	5.80	5.77	5.72	5.80	0.06	1.1
	Mean	5.59	5.48	5.45	5.43	5.44	5.48		1.3
	SD	0.23	0.25	0.25	0.24	0.23			
	Coefficient of variation	4.2	4.7	4.6	4.5	4.2	4.4		

Radiograph II. (values in mm Al. eq)									
80 kV 1.0 s	15 mA	0-4 mm	4-8 mm	8-12 mm	12-16 mm	16-20 mm	Mean	SD	Coefficient of variation
	0 mm	5.42	5.25	5.25	5.24	5.26	5.28	0.08	1.5
	5 mm	5.44	5.33	5.33	5.36	5.40	5.37	0.05	0.9
	10 mm	5.57	5.43	5.42	5.40	5.46	5.40	0.07	1.2
	15 mm	5.79	5.70	5.63	5.69	5.68	5.70	0.06	1.0
	20 mm	5.89	5.79	5.81	5.78	5.75	5.80	0.05	0.9
	Mean	5.62	5.50	5.49	5.49	5.52	5.52		1.1
	SD	0.21	0.23	0.23	0.23	0.20			
Coefficient of variation		3.7	4.3	4.2	4.2	3.7	4.0		

Radiograph III. (values in mm Al. eq)									
80 kV 1.0 s	15 mA	0-4 mm	4-8 mm	8-12 mm	12-16 mm	16-20 mm	Mean	SD	Coefficient of variation
	0 mm	5.50	5.44	5.42	5.38	5.42	5.43	0.04	0.8
	5 mm	5.59	5.54	5.53	5.53	5.59	5.56	0.03	0.6
	10 mm	5.68	5.58	5.52	5.50	5.58	5.57	0.07	1.3
	15 mm	5.78	5.70	5.81	5.74	5.79	5.76	0.04	0.8
	20 mm	6.10	6.10	6.04	6.06	6.08	6.08	0.03	0.4
	Mean	5.73	5.67	5.66	5.64	5.69	5.68		0.8
	SD	0.23	0.26	0.26	0.27	0.25			
Coefficient of variation		4.0	4.5	4.5	4.7	4.5	4.4		

Radiograph IV. (values in mm Al. eq)									
80 kV 1.0 s	15 mA	0-4 mm	4-8 mm	8-12 mm	12-16 mm	16-20 mm	Mean	SD	Coefficient of variation
	0 mm	5.36	5.23	5.17	5.19	5.20	5.23	0.08	1.5
	5 mm	5.35	5.22	5.12	5.12	5.13	5.19	0.10	1.9
	10 mm	5.41	5.26	5.24	5.21	5.25	5.27	0.08	1.5
	15 mm	5.74	5.59	5.62	5.54	5.57	5.61	0.08	1.4
	20 mm	5.84	5.76	5.67	5.66	5.65	5.72	0.08	1.4
	Mean	5.54	5.41	5.36	5.34	5.36	5.40		1.5
	SD	0.23	0.25	0.26	0.24	0.23			
Coefficient of variation		4.2	4.6	4.9	4.5	4.4	4.5		

Radiograph V. (values in mm Al. eq)									
80 kV 1.0 s	15 mA	0-4 mm	4-8 mm	8-12 mm	12-16 mm	16-20 mm	Mean	SD	Coefficient of variation
	0 mm	5.28	5.24	5.14	5.20	5.28	5.23	0.06	1.1
	5 mm	5.32	5.26	5.19	5.23	5.37	5.27	0.07	1.4
	10 mm	5.27	5.19	5.26	5.25	5.31	5.26	0.04	0.8
	15 mm	5.53	5.48	5.44	5.52	5.57	5.51	0.05	0.9
	20 mm	5.77	5.74	5.76	5.73	5.77	5.75	0.02	0.3
Mean		5.43	5.38	5.36	5.39	5.46	5.40		0.9
SD		0.22	0.23	0.25	0.23	0.21			
Coefficient of variation		4.0	4.3	4.7	4.3	3.8	4.2		

The differences between the mean Al. eq values in the five films (table VI.).

Table VI: Mean Al. eq values of five radiographs of a 5 mm Aluminum object.

Radiograph	Exp. time	Object 5 mm Al.	
		Mean	SD
1	1 s	5.48	0.07
2	1 s	5.52	0.05
3	1 s	5.68	0.03
4	1 s	5.40	0.08
5	1 s	5.40	0.04
Mean		5.50	0.12 (2%)

From table VI it can be concluded that five radiographs produce an average mean Al. eq value of 5.5 SD 0.12 and a coefficient of variation of approximately 2%.

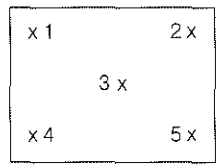
The differences between the 5 selected areas in the same series of 5 radiographs (table VIIa.) were investigated.

Differences were analysed by comparing the coefficients of variation of the five radiographs. From table VIIa. it can be concluded that the maximum for the coefficient of variation was 2.9% and the minimum for the coefficient of variation was 1.6%. The coefficient of variation has a tendency to be slightly larger than the coefficient of variation of the mean for the whole film.

Differences within the X-ray film.

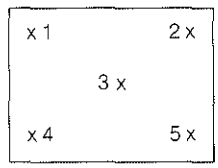
In the 5 radiographs (table V.) the difference between the coefficients of variation for the horizontal trajects was approximately 1% and the difference between the coefficients of variation for the vertical trajects was approximately 4%.
A summary of the values of selected sections (x) of four mm in the five tracks choosen in five radiographs and given in table VIIb.

Table VIIa: Al. eq values of five selected areas in the same series of five radiographs as in table VI.



Radiograph	Section				
	1	2	3	4	5
1	5.33	5.17	5.35	5.89	5.72
2	5.42	5.26	5.42	5.89	5.75
3	5.50	5.42	5.52	6.10	6.08
4	5.36	5.20	5.24	5.84	5.65
5	5.28	5.28	5.26	5.77	5.77
Mean	5.38	5.27	5.36	5.90	5.79
SD	0.08	0.10	0.12	0.12	0.17
Coefficient of variation	1.6	1.8	2.2	2.1	2.9

Table VIIb: Al. eq values of five selected areas in the same series of five radiographs as in table VIIa.



Radiograph	Section				
	1	2	3	4	5
1	5.33	5.17	5.35	5.89	5.72
2	5.42	5.26	5.42	5.89	5.75
3	5.50	5.42	5.52	6.10	6.08
4	5.36	5.20	5.24	5.84	5.65
5	5.28	5.28	5.26	5.77	5.77
Mean	5.38	5.27	5.36	5.90	5.79

From table VIIb. it can be concluded that the local vertical differences in the mean Al. eq values in each film between the top (section 1 - 2) and the bottom (section 4 - 5) were approximately 10%.
The local horizontal differences were approximately 1%.

4.6. The influence of the exposure time on the Al. eq value determination.

The experiments on the influence of the exposure time in the precision of the Al. eq values involved an investigation of aluminum and a bone phantom. Specimens of aluminum (5 mm) and bone (mandible) were radiographed with use of the P.I.

a. The influence of the exposure time tested with an aluminum phantom.

The 5 mm Al. object was exposed (80 kV, 15 mA) with increasing exposure times. Mean Al. eq values were calculated (table VIII).

Table VIII: The Al. eq values of the 5 mm Al. phantom with different exposure times.

Radiograph	Exp. times	Mean Al. value
1	0.75	5.39
2	0.90	5.40
3	1.00	5.41
4	1.25	5.15
5	1.50	5.39
Mean		5.35
SD		0.11
Coefficient of variation		2.1

A series of increasing exposure times gives a mean Al. eq value of 5.35 SD 0.11 and a coefficient of variation 2.1%. It may be concluded that the developed conversion method can eliminate changes in the exposure times with an increase of 100% in the 0.75 - 1.50 s range.

b. The influence of the exposure time tested with a bone phantom.

A series of three radiographs of the mandible were made with different exposure times (0.5, 1 and 1.50 s, 90 kV and 15 mA). The relation object-film was fixed. The microdensitometric analyse of each radiograph is shown (fig. 16.), five scans, covering the same area, were made at a distance of 0.2 mm.

Table IX: Mean Al. eq values of bone phantoms with exposure times of 0.5, 1 and 1.50 s.

Exp. time	Visual interpretation.	Mean Al. eq value	Mean Al. eq value, 1mm track.
0.5 s.	light	7.11	4.93
1.0 s.	good	6.88	4.80
1.5 s.	too dark	6.83	4.57
	Mean	6.94	4.77
	SD	0.15	0.18
Coefficient of variation		2.2	3.8

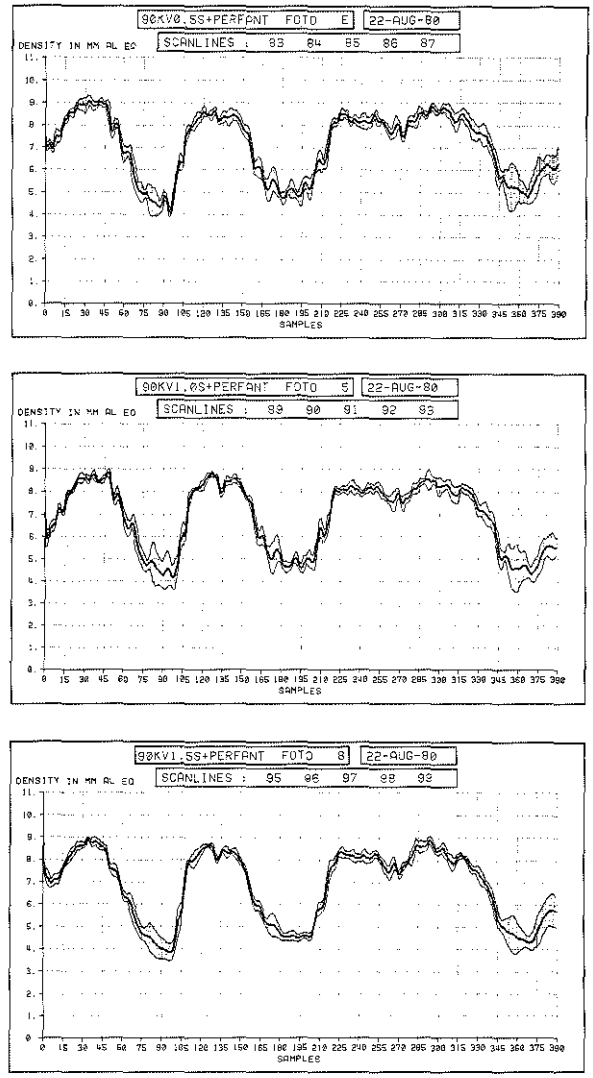


Fig. 16. Mean Al. eq value of the five scans and the standard deviation are shown. A one mm section of the curve track (sample 180 to 195) is evaluated in table IX.

From the graph (fig. 16.) it can be seen that the resolution of details in the image decreases in dark radiographs.
The effect of the exposure time (table IX.) on the mean Al. eq value of the bone scan is small, the average mean Al. eq value is 6.94 SD 0.15, the coefficient of variation 2% and for the track sample respectively 180 - 195, mean 4.77 SD 0.18, coefficient of variation 4%.

4.7. The influence of a soft tissue substitute on the precision.

In order to investigate the influence of a soft tissue substitute on precision, a layer of 25 mm Perspex® was used. It simulates the cheek and covers the complete area of

investigation, as well as the aluminum sheet with a thickness of 5 mm, including the calibrating wedge. Two radiographs were made: one with the 25 mm Perspex® layer and one without the Perspex® (80 kV 15 mA 1 s - table X.).

Table X: Mean Al. eq values in two radiographs of an aluminium object (one covered by Perspex®).

Without 25 mm Perspex® (values in mm Al. eq)									
80 kV 1.0 s	15 mA	0-4 mm	4-8 mm	8-12 mm	12-16 mm	16-20 mm	Mean	SD	Coefficient of variation
↓	0 mm	5.36	5.23	5.17	5.22	5.20	5.24	0.07	1.4
	5 mm	5.35	5.22	5.12	5.15	5.13	5.19	0.10	1.8
	10 mm	5.41	5.26	5.24	5.24	5.25	5.28	0.07	1.4
	15 mm	5.74	5.59	5.62	5.57	5.57	5.62	0.07	1.3
	20 mm	5.84	5.76	5.67	5.69	5.65	5.72	0.08	1.4
	Mean	5.54	5.41	5.36	5.37	5.36	5.41		1.5
	SD	0.23	0.25	0.26	0.24	0.23			
Coefficient of variation		4.2	4.6	4.9	4.5	4.4	4.5		

With 25 mm Perspex® (values in mm Al. eq)									
80 kV 1.0 s	15 mA	0-4 mm	4-8 mm	8-12 mm	12-16 mm	16-20 mm	Mean	SD	Coefficient of variation
↓	0 mm	5.47	5.26	5.19	5.05	5.16	5.23	0.16	3.0
	5 mm	5.31	5.21	5.07	5.04	5.16	5.16	0.11	2.1
	10 mm	5.49	5.26	5.16	5.12	5.22	5.25	0.14	2.8
	15 mm	5.62	5.36	5.20	5.26	5.32	5.35	0.16	3.0
	20 mm	5.68	5.53	5.47	5.40	5.41	5.50	0.11	2.1
	Mean	5.51	5.32	5.22	5.17	5.25	5.29		2.6
	SD	0.14	0.13	0.15	0.15	0.11			
Coefficient of variation		2.6	2.4	2.9	3.0	2.1	2.6		

The mean Al. eq values of the object radiographed, respectively without and with the Perspex® layer, were 5.41 and 5.29 mm Al. It appeared that the influence of the Perspex® on the Al. eq values is relatively small. There was a greater similarity between the coefficients of variation for the horizontal and vertical values in the radiographs made with the Perspex® layer. This material probably influences the distribution of secondary radiation reaching the film.

4.8. The precision of the microdensitometer and recording system.

The reproducibility also depends on the mechanical construction of the densitometer. Differences can be expected between readings made at different moments on

the same instrument. In order to understand the causes of such discrepancies, it is necessary to analyse the factors influencing the readings. The following factors were investigated:

a. the precision of repositioning of the film in the densitometric system.
b. the fluctuation in the intensity of the light source.
c. the direction and speed of the motor-driven assembly.
d. the photomultiplier response to density variations.

ad. a. In order to test the precision of the repositioning in the densitometric system, one dental radiograph was repositioned five times in the densitometer. The area of investigation was determined in the following way: we chose a traject parallel to the reference line. The identified area of interest has a fixed vertical distance from the reference line (fig. 17.).

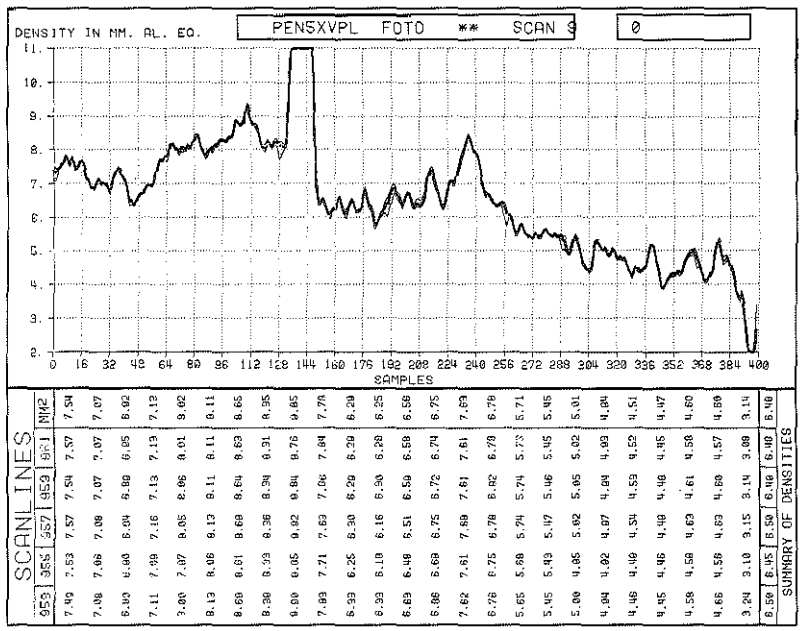


Fig. 17. The spread of five identical trajects of 0.2 mm and the mean Al. eq values.

The mean Al. eq values of the five scans were calculated as 6.48 mm Al. eq SD 0.02 and a coefficient of variation of 0.3. In conclusion: it is possible to reposition a film in the microddensitometric system with an extremely small coefficient of variation.

ad. b. The fluctuation in the intensity of the light source.
The influence of the warming-up time of the densitometer can be avoided by starting the measurement after 30 minutes warming-up. Time instability of the light source was determined by a repeated density recording of a 6 mm Al. image on a non-moving film for 30 minutes (fig. 18.).

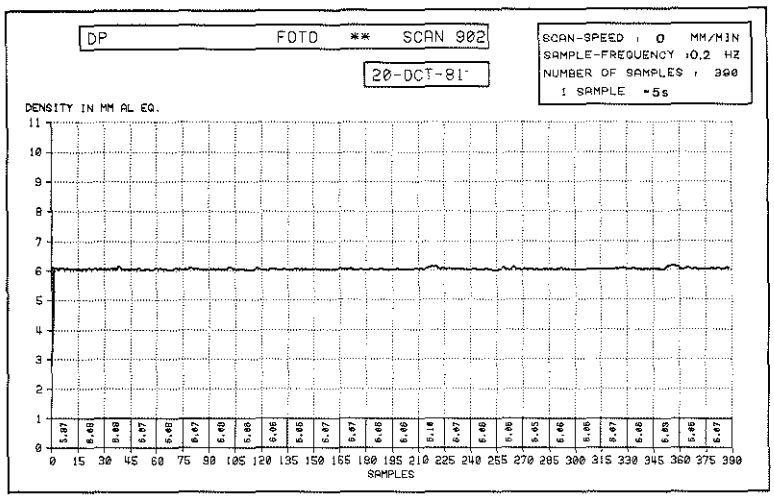


Fig. 18. Scan indicating variations in half an hour.

Results.

During the 30 min. test there is a maximum deviation of 0.05 mm Al. which is negligible. Since stabilization of the electronics of the densitometer is very expensive, the variation was accepted and classified as an "error of the method".

ad. c. The direction and speed of the motor-driven assembly.
Precision depends upon constancy of the scanning speed. It was, therefore, necessary to determine whether there is any difference between the L - R and R - L speeds. The densitometer has a motor-driven assembly which passes through the film via the light beam. It is possible that the scan-speed may not be constant. In order to check the motor-driven assembly, two plots of a sample were made in opposite directions. The scans should be identical, irrespective of the direction Left to Right or Right to Left. The signal was transmitted to the chart-recorder.

Fig. 19. Bone scans made in two opposite directions.

It can be seen from the figure that the scan-speeds are not identical. The difference is approximately 1 %. To overcome the influence of fluctuations in directional scanning speeds, only one direction will be used in future. The chosen direction is Left to Right. The absolute values, registered in both directions are, however, identical.

ad. d. The photomultiplier response to density variations.
The densitometer is used to analyse density patterns. It is probable that the photomultiplier response can influence density measurement. The density, scanned at any

moment, should be the same, but there is a possibility of deviation from the exact values as a result of rapid density changes.

Experiments were carried out to test:
1. The step-response. The image of a step in the object between 11 mm Al. and 2 mm Al. was investigated.
2. The time-response. A pattern was scanned at various scan-speeds.

ad 1. The step between 11 and 2 mm Al. eq values was used to test the photomultiplier response. Such extreme values occur in dental radiographs between enamel and bone. The results are shown in fig. 20. It can be seen that the step-up response 0.18 s (black to white) is immediate whereas the step-down response 0.71 s (white to black) is more delayed.

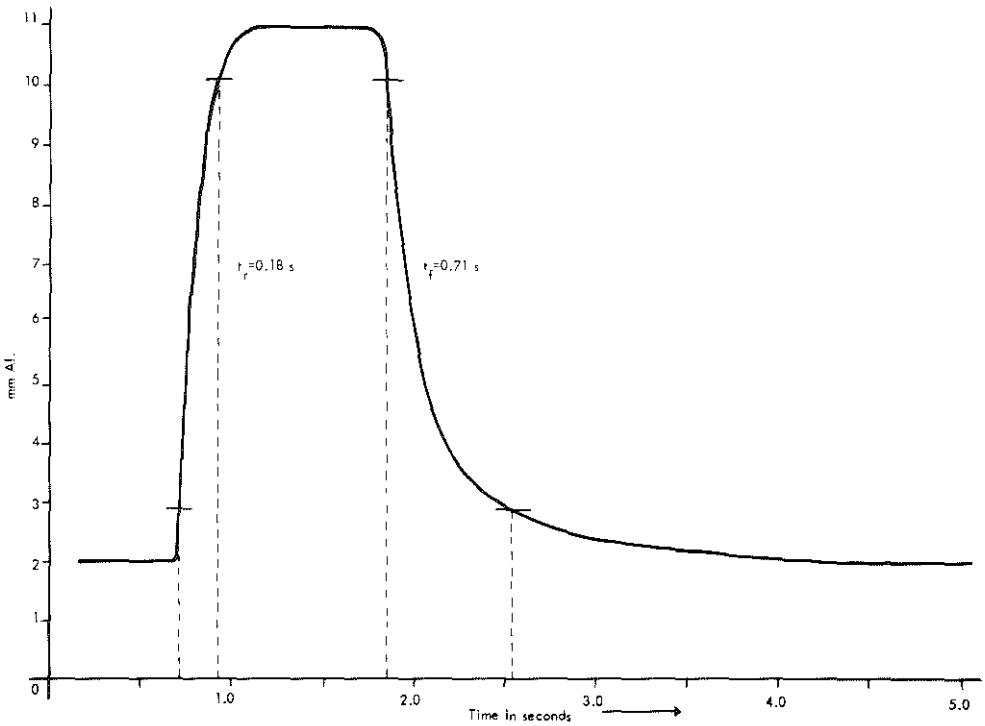


Fig. 20. Step-up and step-down response. The values indicated correspond to 10% and 90% of the total step height.

ad 2. The scan-speed is very important. If the scan-speed is such as to prevent the microdensitometer from attaining true equilibrium, there can be no correct response to variations in density. The quantitative performance of the densitometer can be studied by scanning a spatial black and white step-function pattern. This scanning pattern shows steps from white to black and from black to white. We can expect a symmetric response. The response was tested at two speeds: 2½ mm/min. and 18½ mm/min.

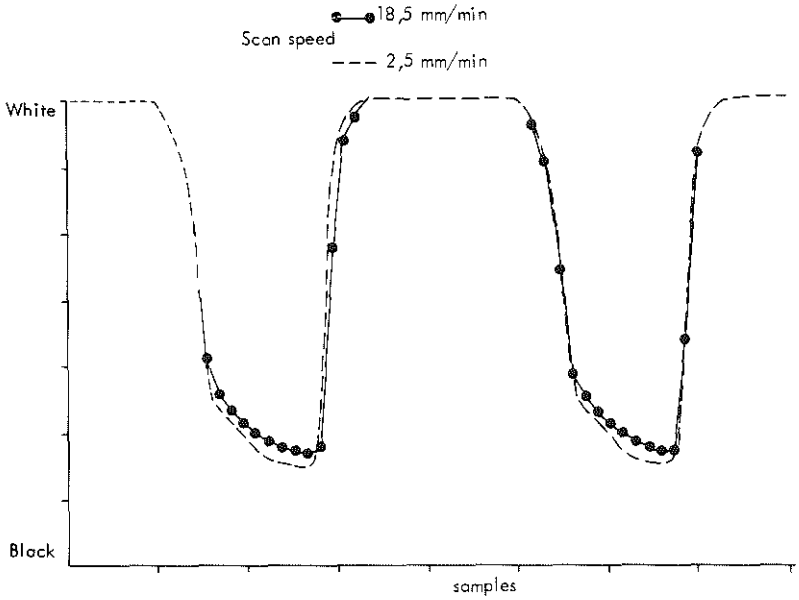


Fig. 21. Combination of 2 scans of a white and black test pattern at 2 speeds: 2½ and 18½ mm/min.

The recording (fig. 21.) was made from left to right.

From the results shown in fig. 21, it can be concluded that:

1. There is no symmetric response from this white and black test pattern and no super-imposing of the curves (small variations). Although the scan-speed does influence the recording, the differences are small.
2. It is advisable to scan from high to low density (step-up response).
3. If steps are to be recorded, difficulties may be anticipated when exceeding a difference of several mm Al.
   It should be noted, however, that the variations used in this experiment will never occur in the images of bone density. Consequently, the effects will be far less pronounced than was the case for this experiment. For practical reasons, a scan-speed of 18½ mm/min. was selected for microdensitometric analysis.

4.9. Conclusions and discussion of the precision of the system.

To test the developed method which transfers density values of an object into mm Al. eq values, the value of a simultaneously radiographed calibrating wedge was used for conversion. Various conversion methods were analysed and a second degree function was selected for the computer calculation.
In this chapter, our interest was centered on the precision of the microdensitometric method to quantify the bone in mm Al. eq values.
The results of the study have been arranged in figures and tables, in which the standard deviation is given as a percentage of the mean "coefficient of variation".
This percentage gives an indication of the precision of the different steps in the newly developed method. Information concerning the errors in the method provides a measure of overall precision for the developed technique.

4.1. The precision along the Al. calibrating wedge.

We found a coefficient of variation of approximately 1.3% between areas along five adjacent scans at 0.2 mm distance. The location of the scantraject used for conversion is not critical within a 1 mm band in the centre of the calibrating wedge.

4.2. The precision of the positioning instrument (P.I.).

The precision of the method was tested by means of measuring distances in a radiograph of a bone phantom, using sharply defined landmarks. In a series of five radiographs, measurements were taken in two directions, as well as in horizontal as in vertical direction. As expected, we found a large coefficient of variation for small angles between the scan line and the border of the landmark 5% and 8%.
The horizontal trajects which formed an angle of approximately 90° with the landmark gave a coefficient of variation of ± 1%. When using the mean Al. eq value of a scantraject, we found a coefficient of variation of 0.3% between the five radiographs.

4.3. The precision of the X-ray timer.

The error margin is less than 10% and can be considered as insignificant, especially because radiographs with exposure variations of 100% have only a slight influence on the conversion in Al. eq values (see 4.6.).

4.4. The homogeneity of the X-ray beam.

The non-uniformity effect of the X-ray beam was investigated (heel-effect). Exposures of an aluminum testobject were made with a 0 and 90 degrees rotation of the X-ray tube. It was found that the X-ray tube rotation had no measurable influence on radiation distribution.

4.5. The precision of the X-ray film and the developing procedure.

The properties of X-ray films and the developing procedures influence the blackening of a radiograph.
A long term investigation of the X-ray film indicated a decrease in the slope of the characteristic curve of the Kodak U. Speed film. The use of the calibrating wedge will practically eliminate this effect.

The difference between films.

This effect was investigated in a series of 5 radiographs, all with the same exposure of the aluminum testobject. The mean of the Al. eq values in a series consisting of the same 5 radiographs were calculated. This resulted in a coefficient of variation of 2%. Local differences between the films were found to vary between 1.6% and 2.9%.

The differences within the film.

The values for the horizontal, non-uniformity effects were respectively 1% and 4%. This effect was also investigated by comparing the horizontal Al. eq values at top and bottom of the object. The coefficient of variation was about 10%. For the vertical Al. eq values the coefficient of variation was about 1%.
The effect of the differences between top and bottom of the radiograph can be avoided in practice by giving the area of investigation and the calibrating wedge the same location on the X-ray film.

4.6. The influence of the exposure time on the Al. eq value determination.
An aluminum and a bone phantom were exposed with an increase of 100% in the exposure time (from 0.75 to 1.5 s).
For the Al. object, a coefficient of variation of 2.1% was found. In the mandible, the coefficient of variation between the mean Al. eq values of 3 films was 2.2% and 3.8% for 1 mm of the tracks. It should be noted that the radiograph of the bone phantom with an exposure time of 1.5. s was too dark for visual interpretation.

4.7. The influence of a soft substitute on the precision.
Changes in the volume of the soft tissues of patients may influence the reproducible measurements. It was found that these soft tissues probably influence the distribution of the secondary radiation reaching the film.

4.8. The precision of the microdensitometer and the recording system.
The following factors were investigated:
— the precision of repositioning of the film in the densitometric system. It appeared that a radiograph can be repositioned in the system with a high degree of precision (0.3%).
— the fluctuation in the intensity of the light source can be estimated at approximately 0.4%.
— the direction and speed of the motor-driven assembly was chosen from left to right because the L - R and R - L speeds are not identical.
— the photomultiplier response to density variations was tested. The bone scans do not contain sharp steps so that most of the response errors can be excluded. Response errors will occur during investigations which also include sharp step errors.

Discussion.
The differences within the film (discussed in chapter 4.5.) could not be explained. It would be of practical significance if they could be eliminated. Further investigation of this aspect is, therefore, needed. The same holds for the effects of the soft tissues as shown in chapter 4.7.
In order to improve the precision of the method, it could be useful to pay more attention to the factors showing the largest coefficients of variation during further investigation. From the information obtained with regard to the precision aspects of the method, it could be erroneously concluded that the total of all the coefficients of variation will indicate the precision of the method as a whole.
It must be realised, however, that the factors could not be completely separated and that the coefficients of variation are not additioned. To give an example: the precision of the developed technique influences the coefficients of variation of all the other factors. Because of these overlaps, the total coefficient of variation is much smaller than the sum of the coefficients for the different steps of the procedure which are not distinctly separated.
In chapter 5, an estimation of the precision in a clinical experiment will be determined and it will be used to estimate the minimum difference in Al. eq values which can be registered by comparing duplicate measurements.

CHAPTER 5

CLINICAL INVESTIGATIONS

When viewing a two-dimensional radiograph, the third dimension (depth) is absent. The interpretation of a radiograph is very complex, due to the superimposing of the structures. Knowledge of anatomy and particularly knowledge of cross-sectional anatomy is the basis for radiological interpretation. The axial cross-section is of interest because the spatial relationship of the structures can be seen. If two radiographs of one object are made in different directions, both views can be used to reconstruct a cross-sectional image which permits separation of the superimposed structures.
An investigation of bone and the changes in bone preferably requires a method which consents measurement of an object in three dimensions. It depends on the technique whether a two-dimensional or a three-dimensional view can be obtained. Different techniques for the measurement of bone mineral content have been used. These include the γ absorption technique, dual energy computer tomography and radiographic densitometric methods. In the case of γ absorptiometry and dual energy computer tomography, the bone mineral is measured in vivo. Both methods are based on measurement of radiation transmission through a medium consisting of two different materials: the bones and the soft tissues surrounding them.
Dual energy computer tomography is based on measurement of the radiation transmission of two energies through the object. The beam passes through the layer to be visualised in all directions. Beam-hardening effects and the diameter of the X-ray beam influence the measurements. The computer performs a point-to-point determination of bone mineral density in the field under investigation. In the reconstructed image, density determination of soft tissue, compact bone and spongy bone is possible.
The photonabsorption method is applied with a Norland Cameron Bone Mineral Analyser which has been amply described in the literature. The method utilizes a monochromatic beam from a 125 J. source. The forearm is wrapped in a tissue-equivalent material to give an uniform, standardised thickness and is transversally scanned. The amount of bone mineral is inversely related to the integrated transmission-count rate across the bone.

The bone width and Bone Mineral Content (BMC) per unit length of bone (gram bone mineral/cm bone) are measured.
Repeat scans of the same persons have a coefficient of variation of 2% and repeat scans made of the same persons at different moments have a coefficient of variation of 3 - 4% for the distal radius. They provide a simple, accurate and reproducible mineral estimation in a segment of the radius with a thickness of 3 mm. A more useful index is, however, necessary when comparing radiographs which concern groups of individuals with varying bone dimensions.

Bone Mineral Mass (BMM) was, therefore, introduced. It represents the Bone Mineral Content (BMC) value divided by the bone width of the investigated bone sample: gram bone mineral/cm² of bone.

Radiographs of the mandible offer a two-dimensional image of the object and the bone mineral content equivalent values (3.6.) can be measured. Many experiments have been carried out with a densitometer in order to register the Bone Mineral Content eq in the mandible: Omnell 1957, Bergström, Matsue and Plotnic 1970 and 1972, Adolph, Lichtenau 1975, Duinkerke, Lichtenau 1976 and Lichtenau 1978.

They demonstrated that the Al. eq values of bone in the mandible can be measured, but the method proved to be time-consuming in practice. Microdensitometry was also used for BMC eq measurements in the skeleton: Balz 1956 - thumb; Bentley 1967 - femur, hand and lumbar spine; Vose 1969 - bone phantom; Nagel 1974 - calcaneum; Melsen 1975 - iliac crest; Wing 1976 - maxilla and phalanx Dig. III; King 1977 - bone phantoms; Pullan 1978 - animal experiments; Lindsay 3rd metacarpal midshaft; Castells 1979 - phalanx; Paice - hands, phalanx and metacarpal and Parker - animal bone experiments.

The departments dealing with metabolism and internal medicine, pathology, radiology, surgery and dentistry are all interested in bone or bone mineral from different points of view. This explains the variety in the bones chosen from the skeleton. The fact that diagnosis is only possible in cases of substantial bone loss and that clinical, radiographic criteria are not precise, explains the need to measure routine-made radiographs. The procedure for determination of the Al. eq values was analysed in an in-vitro study and the precision of the method was determined.

In this chapter, the developed radiographic method was tested in-vivo, first to analyse the Al. eq values in a longitudinal study of the mandible in volunteers and secondly to analyse the Al. eq values of the phalanx in volunteers and patients. The results were compared with the BMC values of the radius, measured at 1/3 of the length from the distal end.

CHAPTER 6

A STUDY OF THE AL. EQ VALUES OF THE MANDIBLE

6.1. Introduction and aims.

The changes in bone mineral which take place with time were studied on volunteers.
The bone mineral content equivalent is the mineral content expressed in mm^2 Al. eq under the bone scan.
The study comprised 4 investigations over a period of one year. In longitudinal studies, the reproducibility of radiographs and identification of the same area for measurement may pose a problem. The technique submitted here is relatively simple and does not require great skill or complicated equipment, nor does it cause inconvenience to the patient. In each investigation, a pair of radiographs was made with the positioning instrument described in chapter 3.3., including the aluminum calibrating wedge which excludes variations in the radiographic exposure, in the energy spectrum and in the developing procedure.

The method relies on measurement of the Al. eq values of a reproducible image of the mandible. The radiographs were studied by densitometric analysis, in order to compare the Al. eq values at regular intervals. The scans were examined to determine their reproducibility, together with possible changes in the Al. eq values with time.

The regions were located in the duplicate radiographs and identified. Microdensitometry is more reliable for measuring the changes in bone mineral content provided that the soft tissue component does not change to a significant extent.
The effect on precision caused by variations in the scans with time must be quite small to permit a reliable, quantitative analysis of bone biology.

The aim of this investigation was:
— to test the microdensitometric method for reproducibility in a clinical study;
— to analyse changes in mineralization (a) at 3 month intervals and (b) in a longitudinal study using in-duplo determination of the Al. eq values;
— to compare visual and microdensitometric interpretation.

6.2. Volunteers and methods.

Twenty individuals were investigated:
Men: average age 43,7 years old SD 11 - range: 28 - 61 years old.
Women: average age 39,3 years old SD 13.6 - range: 21 - 60 years old.
As far as known, none of these volunteers suffered from specific diseases of the skeleton. The mandible was studied at 3 month intervals over a period of 9 months.

The investigation-areas consisted mainly of cortical bone, but the overlying and underlying soft tissue contributed to the density. The analysis of the results obtained from reproducible radiographs, taken at different moments, is important for evaluation of changes which take place with time. We considered two interrelated items.

— the findings concerning the reproducibility of radiographs taken during one session and

— the implications of these findings for evaluation of possible changes with time.

Radiographs may be considered as identical when they can be perfectly superimposed. To test the reproducibility of the technique, two radiographs of the same subject were taken during each session. Both under normal and pathologic conditions, a standardised paralleling technique is required when identical radiographs need to be compared in a longitudinal examination of bone changes. We used individual biteblocks to obtain identical radiographs of the volunteers. An autopolymerizing, acrylic biteblock was made on a plaster model of each mandible, avoiding impressions of undercuts and then pressed into a slot prepared in the positioning instrument. These plastic biteblocks are interchangeable (fig. 22.).

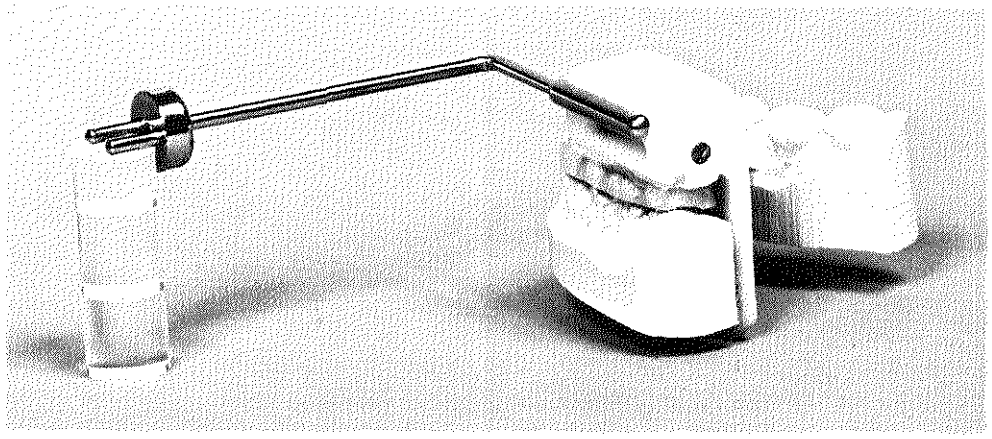


Fig. 22. Fixation of the film is secured by the acrylic biteblock.

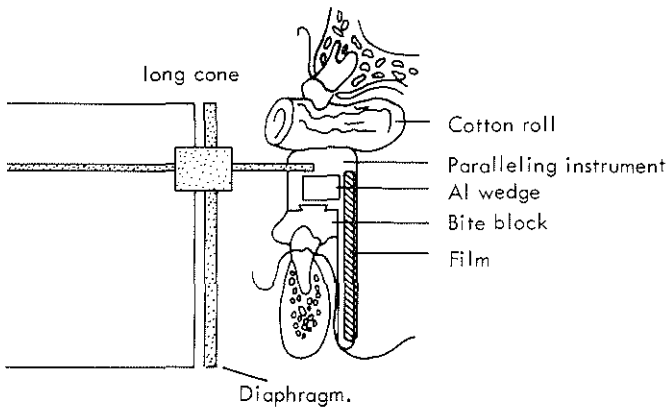


Fig. 23. Schematic representation of the radiographic method for the estimation of bone density in the mandible.

The film was placed parallel to the axis of the teeth and the patient was asked to hold the biteblock in place with a finger. A cotton roll was sometimes used to secure the relationship object-film (fig. 23.).
The biteblock was adapted for the first radiograph and then removed for insertion of the second film for the same area. Any differences in the measurements on duplicate radiographs made in this manner will mainly be due to faulty repositioning of the biteblocks.
Most of the volunteers tolerated the radiographic investigation with minimum inconvenience. A few experienced slight nausea, but the symptoms disappeared after a few moments.
The films (fig. 24.) were immediately developed in freshly prepared developer, using a Siemens Pantomat automatic processor, according to a standard procedure (4.5.).

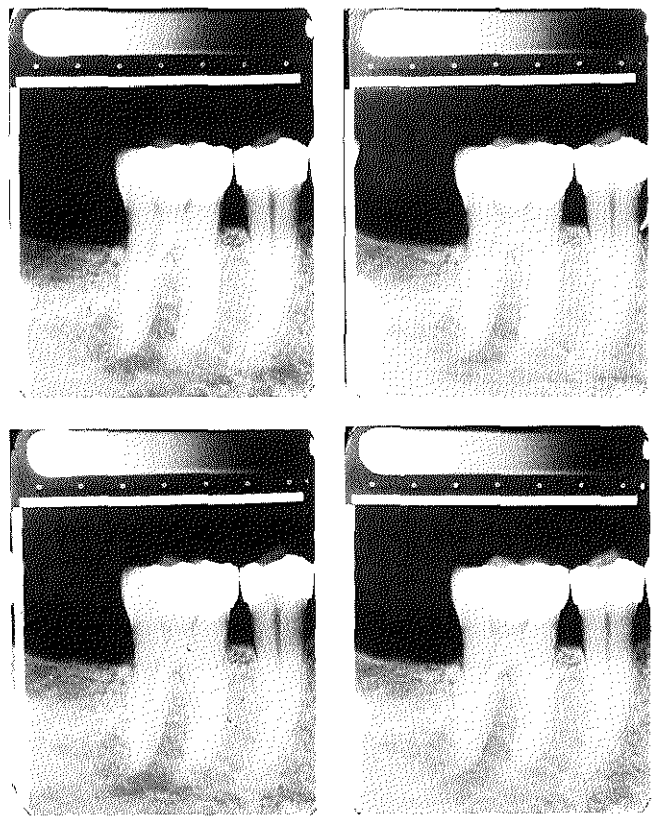


Fig. 24. Four radiographs taken at intervals of 3 months.

The areas studied on the radiographs were determined as follows: we chose a traject parallel to the reference line (fig. 10a.). We were thus able to identify the area under investigation. Sharply defined reference points such as the roots of molars were used for identification of the bone trajects.
A series of five scans in the field of interest were made at a distance of 0.2 mm. The mean value and the standard deviation were determined (fig. 25.).

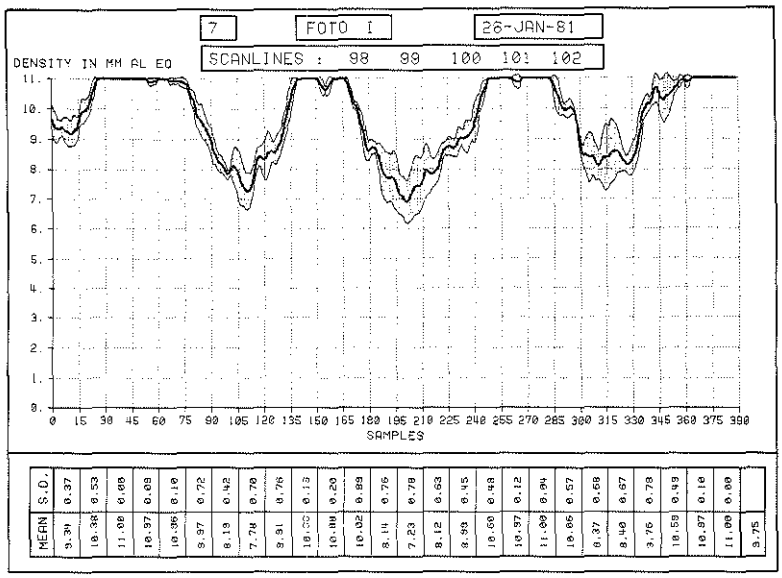


Fig. 25. Example of the spread of five horizontal trajects of 0.2 mm and the average value (mean) in one radiograph. The mean Al. eq value over a scan length of one mm (15 samples) and the standard deviation of the five scans is given.

Measurements of the same traject were taken to evaluate the reproducibility in duplicate radiographs. The spread provides information on the differences which can be detected. The reproducibility error (precision of the method) was determined by evaluating the differences between the two radiographs taken during one session. The difference between two bone scans was also calculated and is shown in the upper curve (fig. 26.).

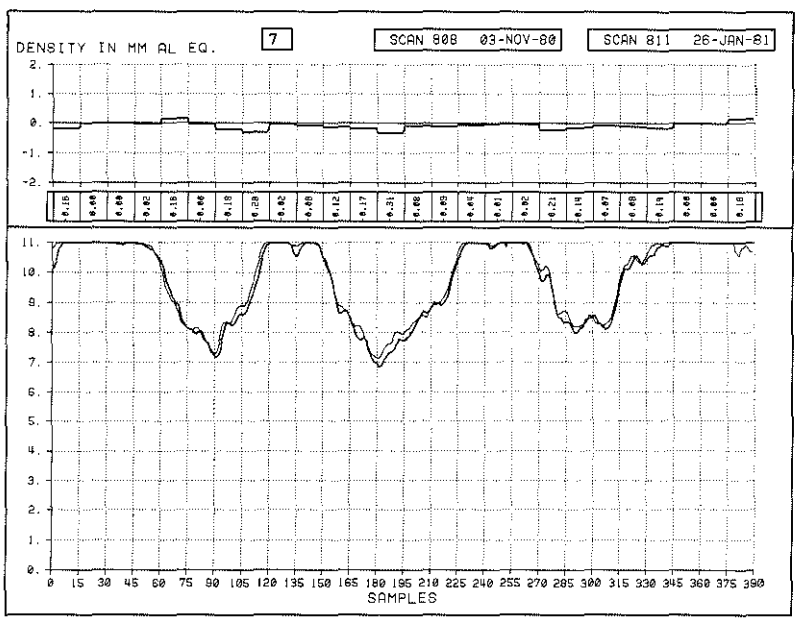


Fig. 26. The mean values, each representing the mean of 5 scans on 2 radiographs used to analyse the precision between exposures taken during one session.

In order to make a comparison between measurements over a period of time, the mean values of two radiographs made during one session were used and expressed in mm Al. eq (fig. 27.).

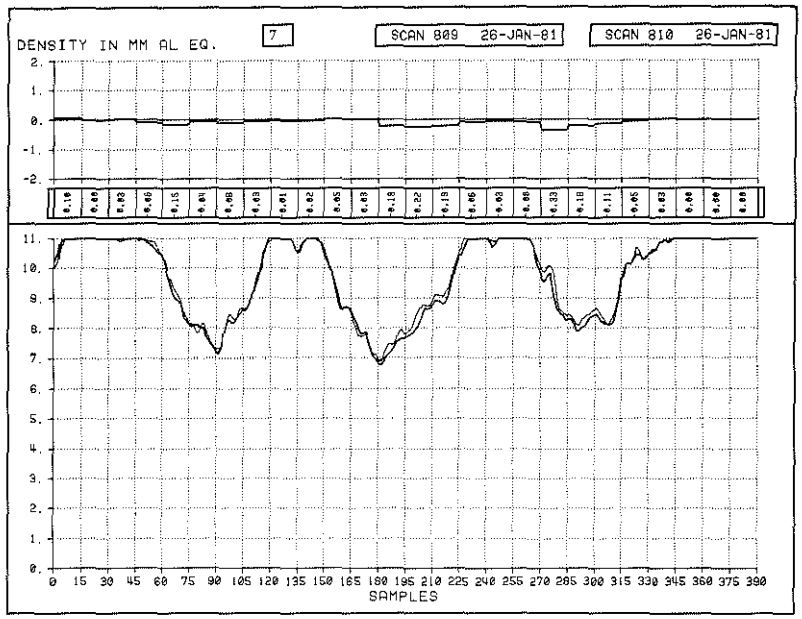


Fig. 27. Example of two scans illustrating the mean Al. eq values of two radiographs made during different sessions (interval of three months).

6.3. Results.

The total number of radiographs of the 20 volunteers which were suitable for the radiographic investigation was 160 (4 x 2 per person). The results of the densitometric measurements during the period are presented in table XI. The Al. eq values for individual volunteers were calculated. Separate linear regressions and correlation coefficients were calculated for the in-duplo Al. eq values.

The duplicate of a measurement has been omitted in the cases where one scan did not cover the second one. (no. 4, 6, 10 and 22 in session II, IV, IV and III).

The precision of the average of duplicate measurements (for comparison see Addendum page 90) S_2 is the estimated standard deviation of the random error in the mean of two values obtained in one session.

As shown in table XI, the S_2 values were determined for each session and varied between 0.09 - 0.22. The mean S_2 value was determined for the whole group $S_2 = 0.16$, so it may be said that S_2 approximately equals 0.2 mm Al. eq.

The difference between two sessions contains a random error with a standard deviation of approximately $\sqrt{2} \times 0.2 = 0.3$ mm Al. eq. Consequently, such a difference may be considered a significant difference if it is greater than twice $0.3 = 0.6$ mm Al. eq. When patients show no change with time, about five percent of the differences are erroneously considered as real differences ($\alpha = 0.05$).

Table XI: Duplicate Al. eq values over the time of investigation.

♂	Age	Session I			Session II			Session III			Session IV			Period I-IV	Corr. coeff.	
		Photo		Δ	Photo		Δ	Photo		Δ	Photo		Δ	Linear regression		
		I	II		I	II		I	II		I	II				
1	28	7.50	7.65	0.15	7.89	7.64	0.25	7.16	6.76	0.60	7.19	7.25	0.06	$y = -0.062\ x + 7.66$	−0.623	NS
2	43	7.52	7.37	0.15	7.70	8.16	0.46	7.19	6.88	0.31	7.26	6.95	0.31	$y = -0.064\ x + 7.67$	−0.549	NS
3	34	6.09	6.31	0.22	5.69	6.16	0.47	5.75	5.78	0.03	6.09	5.87	0.22	$y = -0.027\ x + 6.09$	−0.436	NS
4	40	7.04	7.25	0.21	7.44	—	—	7.14	6.86	0.28	7.21	7.28	0.07	$y = 0.000\ x + 7.18$	−0.005	NS
5	33	6.91	7.18	0.27	6.76	6.84	0.08	6.64	7.21	0.57	6.78	7.33	0.55	$y = 0.005\ x + 6.93$	0.074	NS
6	61	9.06	9.16	0.10	9.34	9.40	0.06	8.53	8.39	0.14	8.30	—	—	$y = -0.111\ x + 9.31$	−0.796	S
7	54	9.93	9.81	0.12	9.83	9.77	0.06	9.49	9.90	0.41	9.81	9.85	0.04	$y = -0.008\ x + 9.83$	−0.199	NS
8	55	9.05	9.14	0.09	8.90	8.63	0.27	8.40	9.14	0.74	8.38	9.10	0.72	$y = -0.035\ x + 9.00$	−0.388	NS
9	51	7.51	7.52	0.01	6.32	7.30	0.98	6.43	6.58	0.15	6.30	6.67	0.37	$y = -0.113\ x + 7.34$	−0.769	S
10	38	9.22	8.91	0.31	8.79	9.26	0.47	9.03	8.68	0.35	8.68	—	—	$y = -0.042\ x + 9.10$	−0.583	NS
			S_2	0.09		S_2	0.22		S_2	0.21		S_2	0.19			
♀																
21	34	6.51	6.55	0.04	6.15	6.33	0.18	5.79	5.60	0.19	5.70	7.62	0.08	$y = -0.105\ x + 6.50$	−0.941	S
22	21	7.60	7.92	0.32	7.62	7.74	0.12	—	7.52	—	6.89	7.16	0.27	$y = -0.082\ x + 7.84$	−0.883	S
23	28	7.24	7.13	0.11	6.76	7.26	0.50	6.99	6.64	0.35	5.93	6.09	0.16	$y = -0.124\ x + 7.31$	−0.871	S
24	60	8.40	8.58	0.18	8.41	8.04	0.37	8.41	8.13	0.28	8.50	7.92	0.58	$y = -0.026\ x + 8.42$	−0.401	NS
25	52	5.50	5.09	0.41	4.69	4.76	0.07	5.04	4.80	0.24	4.73	4.56	0.17	$y = -0.029\ x + 5.21$	−0.597	NS
26	50	7.46	7.16	0.30	6.98	7.06	0.08	7.21	7.02	0.19	6.90	6.97	0.07	$y = -0.034\ x + 7.25$	−0.688	NS
27	47	5.95	6.42	0.47	6.09	6.44	0.35	5.95	6.04	0.09	6.23	6.08	0.15	$y = -0.012\ x + 6.20$	−0.222	NS
28	25	6.94	7.05	0.11	7.28	7.24	0.04	7.17	7.50	0.33	7.30	7.52	0.22	$y = 0.044\ x + 7.05$	0.787	S
29	28	9.31	9.20	0.11	8.96	8.47	0.49	8.68	9.09	0.41	9.12	9.02	0.10	$y = -0.013\ x + 9.04$	−0.166	NS
30	48	8.12	8.16	0.04	7.59	7.26	0.33	7.53	7.97	0.44	7.48	7.43	0.05	$y = -0.058\ x + 7.95$	−0.605	NS
			S_2	0.13		S_2	0.15		S_2	0.15		S_2	0.12			

The analysis of the mean Al. eq values of the mandible, calculated for four sessions at intervals of 3 months.

In the foregoing paragraph the standard deviation of the mean Al. eq values of the two duplicate radiographs from one session were calculated.

Table XII: Mean Al. eq values of the duplicate radiographs over four sessions.

♂	Session I	△ 1-2	Session II	△ 2-3	Session III	△ 3-4	Session IV
1	7.58	+0.19	7.77	−0.20	6.96	+0.24	7.22
2	7.45	+0.48	7.93	−0.89•	7.04	+0.08	7.11
3	6.20	−0.27	5.93	−0.15	5.77	+0.19	5.98
4	7.15	+0.29	7.44	−0.44	7.00	+0.25	7.25
5	7.05	−0.25	6.80	+0.13	6.93	+0.13	7.06
6	9.11	+0.26	9.37	−0.91•	8.46	−0.16	8.30
7	9.87	−0.07	9.80	−0.10	9.70	+0.13	9.83
8	9.10	−0.33	8.77	0	8.77	−0.03	8.74
9	7.52	−0.71•	6.81	−0.30	6.51	−0.02	6.49
10	9.07	−0.04	9.03	−0.16	8.86	−0.18	8.68
♀							
21	6.53	−0.29	6.24	−0.56	5.70	−0.03	5.66
22	7.76	−0.08	7.68	−0.16	7.52	−0.49	7.03
23	7.19	−0.18	7.01	−0.19	6.82	−0.81•	6.01
24	8.49	−0.26	8.23	+0.05	8.27	−0.06	8.21
25	5.30	−0.57	4.73	+0.20	4.92	−0.27	4.65
26	7.31	−0.29	7.02	+0.10	7.12	−0.18	6.94
27	6.19	+0.08	7.27	−0.26	6.00	+0.16	6.16
28	7.00	+0.26	7.26	+0.08	7.34	+0.07	7.41
29	9.26	−0.54	8.72	+0.17	8.89	+0.18	9.07
30	8.14	−0.71•	7.43	+0.33	7.75	−0.29	7.46

A difference between two sessions may be considered significant if this difference is greater than 0.6 mm Al. eq. This was the case for the male volunteers (indicated with a dot in table XII). for no. 2 session II - III
no. 6 session II - III
no. 9 session I - II
for the female volunteers: no. 23 session II - III
no. 30 session I - II

In another approach to analyse the effect of changes noted in individual volunteers over a period of time, the correlation coefficients and the linear regressions were determined from the values obtained in the course of the four sessions. A significant loss of bone mineral content with time was found in five volunteers and a significant increase of bone mineral content was found in one volunteer (nos. 6, 9, 21, 22, 23 and 28).

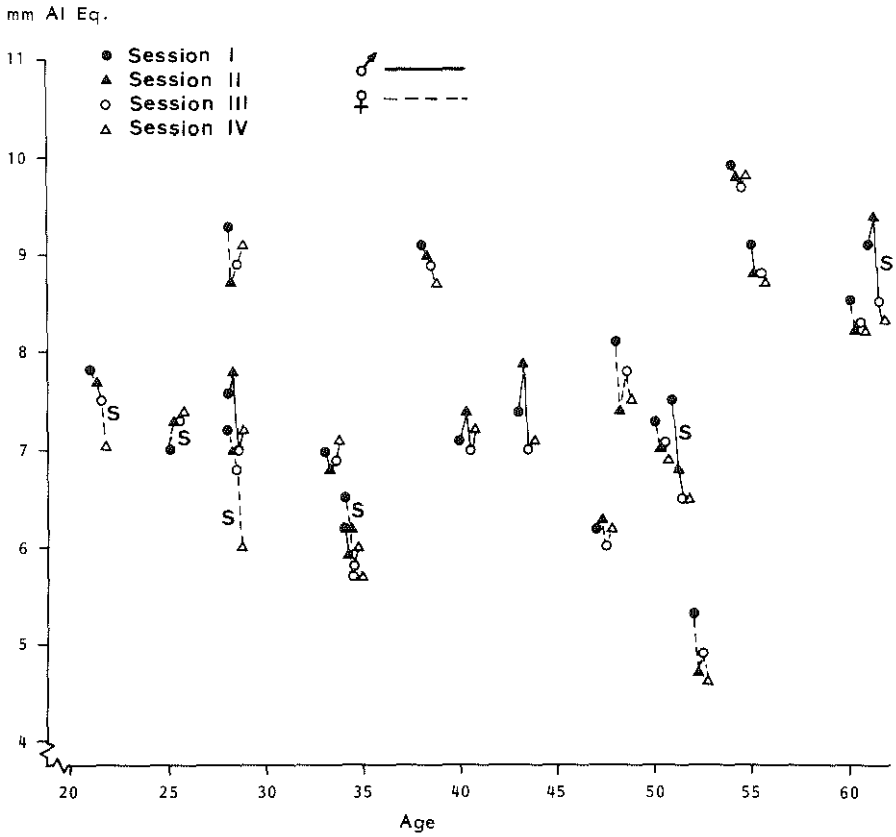


Fig. 27. Graphical representation of the changes in mean Al. eq values found during the whole observation period (four sessions with intervals of three months). Significance is indicated with an S.

In one patient there was a local change of the bone mineral in the alveolar ridge. The degree of resorption of the bone was determined (fig. 28.). The difference between the two bone scans reflects the loss of bone mineral in Al. eq values.
During the experiment, the same areas were compared. The two scans were shifted horizontally to give a maximum fit between the scans. The decline of the bone mineral in the first three months is evident. It can also be observed in the second period of three months but to a lesser degree. The comparison of the values from the bone scans indicates that there is a difference in the activity of the bone for the scan traject, sample 90 - 210.

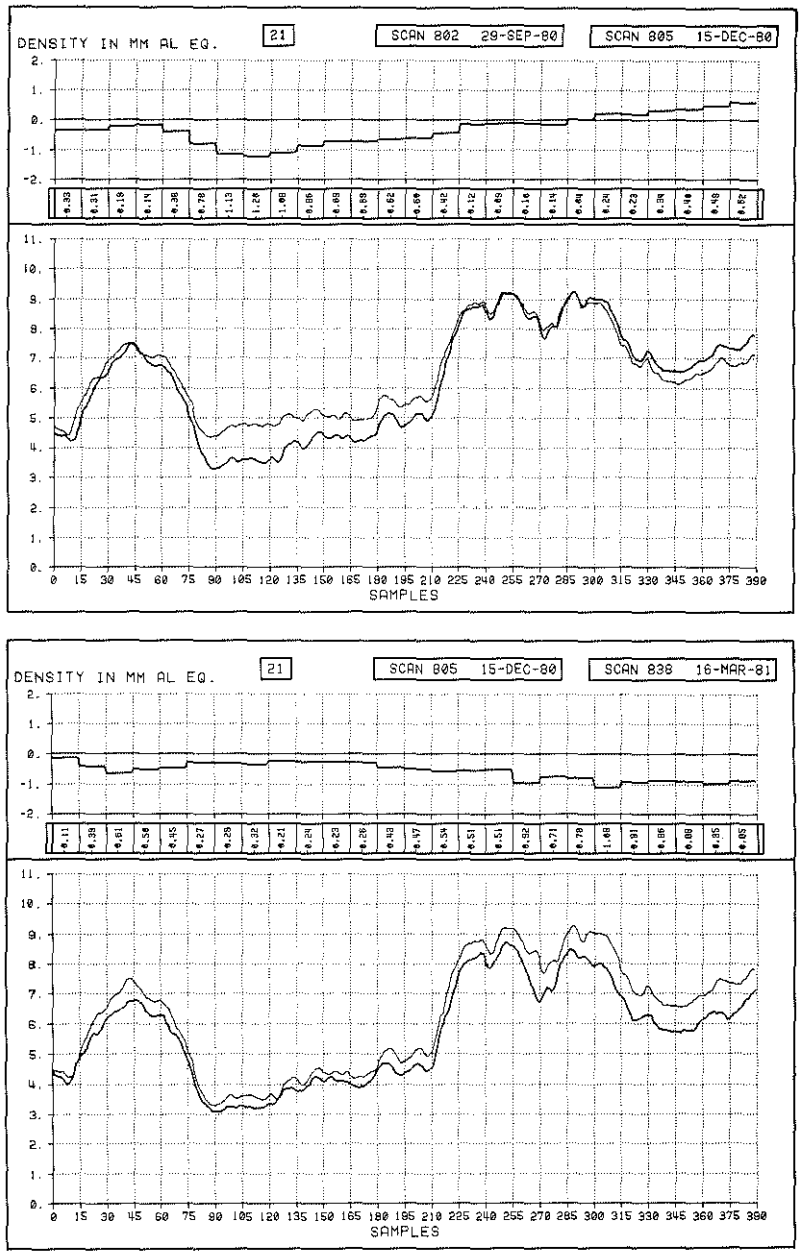


Fig. 28.
Decreased Al. eq values of scan traject over two periods of three months.

A comparison between visual and microdensitometric interpretation.
This study was carried out to determine whether subjective, optical density estimations agreed with objective bone mineral Al. eq values. Microdensitometry uses values which can be obtained with instruments; the radiologist assesses optical density visually. Individual and age-dependent differences in the anatomy of the mandible impede comparison between individuals.

Method.
The bone mineral content of the basal region of the mandible was measured. The scan traject was positioned for the male volunteers at ± 18 mm from the occlusal surface and for females at ± 16 mm from the occlusal surface (fig. 29.). The Al. eq values from the scans were used for comparison purposes.

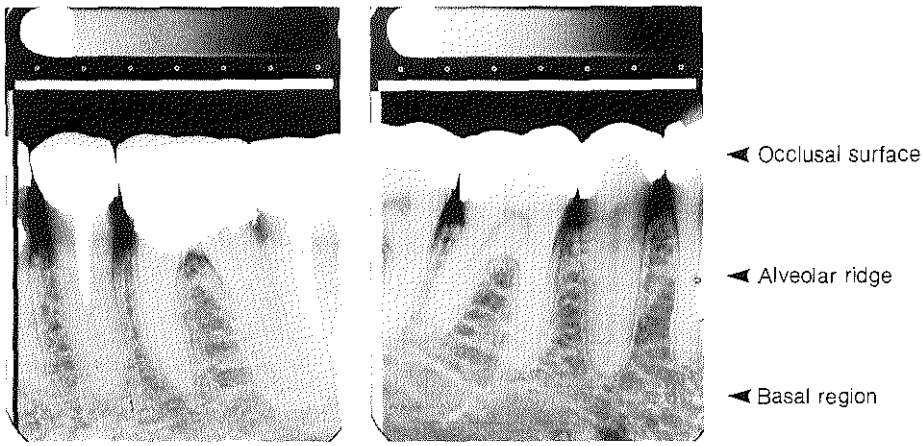


Fig. 29. Two radiographs with different optical densities.

For males, the bone mineral Al. eq values ranged between 5.08 and 7.86 mm Al. eq and for females, the bone mineral Al. eq values ranged between 4.69 and 6.46 mm Al. eq (table XIII.).

Visual interpretation.
The optical bone density is constituted by the sum of the cortical bone and of the trabecular bone which is a spongy network of boneplates creating a maze of interconnecting cavities of various dimensions. The radiographs of the 20 volunteers showed considerable variation in optical density and in spongy bone pattern. In order to distinguish deviations from normal, it is essential to define the normal range of variations in bone density. Eight observers ranked the 20 radiographs of the mandible in order of bone density.
The observers had no knowledge of the results obtained by densitometric analysis. The objective was to obtain an answer to the following question.
What is the correlation between subjective ranking of density values and that of the objective Al. eq values of the basal region of the mandible?

Instruction.
Each observer was asked to put the radiographs in an order ranging from low to high optical density in the indicated region.
The ranking numbers (1 - 10) were so designated that a low optical density corresponded to a low ranking number and a high optical density corresponded to a high ranking number. The radiographs were presented in a darkened room and observed on a viewbox with adjustable light intensity. The radiographs of the individuals (code 1 -10

and 20 - 30) were examined, classified and arranged in rank from low to high density.

Results.

The relationship between the quantitative radiographic density determinations and the subjective findings are summarized in table XIII.

Table XIII: Ranking of bone density in the periapical region by visual interpretation of radiographs as compared to the corresponding quantitative microdensitometrical data.

Code ♂	Al. eq value	Visual density Observer							
		1	2	3	4	5	6	7	8
9	5.08•	3	3	4	3	4	2	2	8
3	5.52	1	1	1	1	1	1	1	1
5	5.64	7	7	7	9	10	5	6	9
4	5.90	5	5	6	4	3	4	5	4
1	6.22•	2	2	2	2	7	3	3	2
2	6.32	8	10	10	7	8	8	4	3
8	6.91•	4	6	8	10	9	7	8	7
6	7.54	10	9	9	8	6	9	7	10
10	7.55	9	8	3	6	2	6	10	5
7	7.86•	6	4	5	5	5	10	9	6

Code ♀	Al. eq value	Visual density Observer							
		1	2	3	4	5	6	7	8
27	4.69•	6	3	3	2	4	2	6	8
21	5.21	1	1	1	1	3	1	1	1
24	5.54	9	9	7	9	9	9	9	4
25	5.61•	7	6	8	8	7	5	5	5
26	5.91	8	7	5	5	1	3	4	6
30	6.03	2	2	2	3	2	4	8	7
23	6.06	4	4	6	4	5	6	2	2
29	6.39	5	5	4	7	8	8	7	9
22	6.46•	3	8	9	6	6	7	3	3
28	—	—	—	—	—	—	—	—	—

The variation in optical bone density between the radiographs is small. This partly explains the variations in ranking by the observers. We therefore divided our material into two groups according to the mean densitometric characteristics indicated by a dot in table XIII:

For the men (group I) four levels with a difference of ± 1 mm Al. eq values ranging between 5.08 - 7.86 mm.

For the women (group II) three levels of ± 1 mm Al. eq values, ranging between 4.69 - 6.96 mm.

Table XIV: The ranking given by the observers.

♂	Al. eq value	Observer 1	2	3	4	5	6	7	8
	5.08	1	1	1	1	2	1	1	4
	6.22	3	3	3	2	1	2	2	1
	6.91	2	4	4	4	4	3	3	3
	7.86	4	2	2	3	3	4	4	2
♀	Al. eq value	Observer 1	2	3	4	5	6	7	8
	4.69	2	1	1	1	1	1	3	3
	5.61	3	2	2	3	3	2	2	2
	6.46	1	3	3	2	2	3	1	1

These findings demonstrate the unreliability of the clinical judgement. Two observers in group I and three observers in group II were able to detect the order of density according to the Al. eq values correctly. On the other hand, two observers gave a reverse ranking. Comparison of the microdensitometric determination of mineral content and the visual, radiographic interpretation indicates that the predictive potential of the latter is limited. It is difficult for the observer to exclude the surrounding optical densities and structures during interpretation. Furthermore, radiographic density criteria are not precise and this could well explain the discrepancies between the visual interpretations and the microdensitometric analysis.

6.4. Conclusions and discussion.

The results of this longitudinal study have been presented in a number of figures and tables in which reproducibility, bone mineral content changes with time and a comparison between visual interpretation and the Al. eq values were analysed.

A. Inter and intra-individual differences are significant when the differences between the average of duplicate measurements exceeds 0.6 mm Al. eq.
   In the follow-up observations, differences of > 0.6 were found in 3 male and in 2 female volunteers. Statistically, approximately 3 cases must be attributed to chance in the 60 comparisons made.
   A persistent tendency to bone mineral loss was observed in five individuals and bone mineral gain was observed in one individual by means of regression analysis. These results cover twenty cases so that only one case is likely to have ocurred by chance. In the course of follow-up observations, a local change was found in the alveolar bone of one person.
B. Comparison between visual estimation of bone density and the measured Al. eq values of bone showed considerable discrepancies. For group I, 2 observers out of 8, for group II 3 observers out of 8 were able to detect the order of bone density correctly.

Discussion.

The experiments described in this chapter were carried out with two aims:
— to test the developed method in a longitudinal study of healthy control groups and
— to investigate the accuracy of visual interpretation of bone mineral on radiographs.

As a result of in-vitro studies of the mandible, the difficulty of observing changes in the structure of spongy bone has been recognized, together with the fact that cortical bone must be affected in order to make it possible to detect changes (ref: chapter 2.1.). Some data is available in literature (ref: chapter 2.2.) concerning the quantity of bone mineral in the mandible, but no estimates of the physiological loss of bone mineral in healthy volunteers.

In this investigation, mean Al. eq values of a 1 mm track were calculated and these values were used to determine the precision of the method by measuring two radiographs made during one investigation session. The reproducibility must be taken into account in order to be able to detect the real bone mineral changes which take place

intra and interindividually with time. The average Al. eq value of the investigated tracks in the alveolar process was 8 mm Al. eq. Differences between the average of duplicate measurements which exceed 0.6 mm Al. are significant. This implies that discrimination of differences < 0.6 is not possible. In other words, small bone mineral changes cannot be detected. Intra and interindividual differences were found between the volunteers, but it should be noted that about five percent of the differences compared will show significant differences purely by chance and these will be erroneously interpreted as real differences (false positives). The series of radiographs did not show any changes related to dental illness and bone lesions were not noticed during the investigation period.

The observers' evaluation of the radiographs according to increasing density steps showed considerable, individual differences in their ranking of the films. It is possible that observation conditions for location of the comparable trajects were not optimal and this may be one of the reasons for the differences in the opinions of the observers.

CHAPTER 7

A STUDY OF THE AL. EQ VALUES OF THE PHALANX.

7.1. Introduction and aims.

For estimation of the amount of mineral present in bone, it is preferable to use a recording method capable of measuring in three dimensions. For this reason, the analysis was based on radiographs of the mid-phalanx (Dig. II) made with beam directions of 0 and 90 degrees in relation to the object. From these 2 two-dimensional radiographs, it is possible to obtain mean bone mineral concentration values.
In order to determine values which can be compared to BMC determinations, the surface under the bone scan was included in the calculations. To exclude the effect of a rotation of the phalanx on the results, the separate data obtained from two radiographs taken perpendicularly to each other was combined. The data corresponding respectively to the soft tissue and to the cortical and trabecular bone was separated and the value corresponding to the soft tissue was subtracted to determine the real bone values.
Measurements on specific areas of one bone do not necessarily reflect the changes in mineral content of this entire bone and still less that of the entire skeleton.
The microdensitometry of the phalanx and γ -ray photonabsorptiometry of the radius have been compared in this study.

7.2. Method.

Phalanx radiography.

The volunteer's right finger is placed flat against the paralleling instrument with the axis parallel to the short axis of the X-ray film. Two perpendicular views of the object, are obtained. The X-ray exposure factors are 80 kV, 15 mA 0.9 s, focal distance 40 cm.

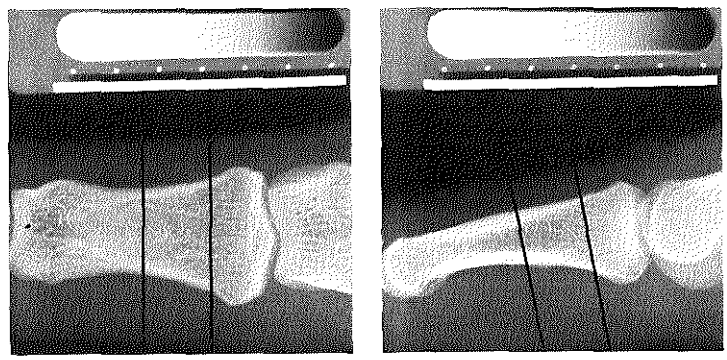


Fig. 30. Postero-anterior and lateral radiograph of the phalanx Dig. II.

Marking off.

The interpreter records the location of the midshaft by tracing the field of interest, using a fine point marking pen. The middle of each phalanx is marked by a line in the center of the object, perpendicular to the long axis (fig. 30.). The dimensions of the various components, soft tissue and cortical bone of the phalanx were measured with a magnifying-glass equipped with a micrometer. The quality of the radiographs makes it possible to distinguish compact from spongious bone. A distinction can furthermore be made between bone and the covering soft tissues.

A scan, perpendicular to the axis, is passed through the mid position of each phalanx. A section with a thickness of 0.2 mm is obtained with the densitometer (fig. 31.).

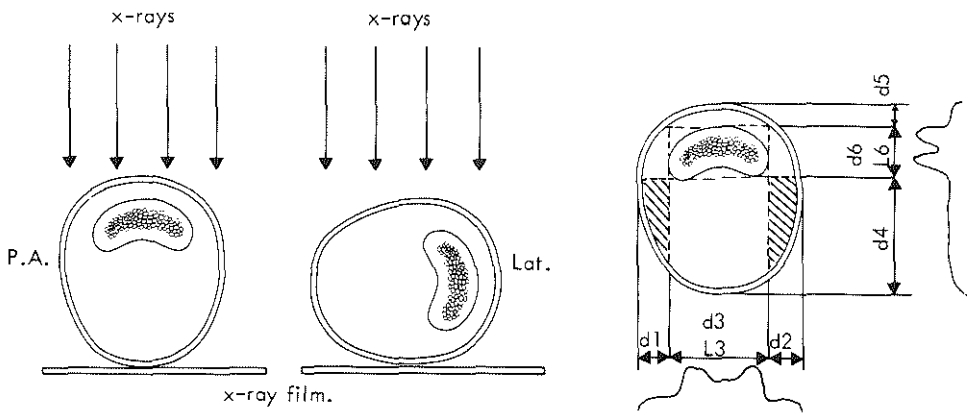


Fig. 31. Diagrammatic representation of two exposures of axial sections of the middle phalanx at right angles to each other.

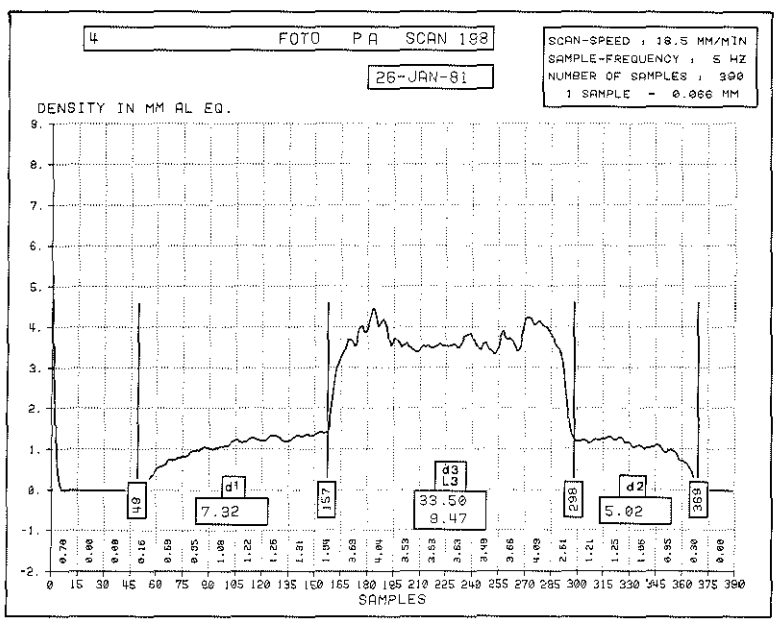


Fig. 31a. Illustrative scan in the centre of the middle phalanx Dig. II. of a postero-anterior radiograph with soft tissue density values. d_1 and d_2.

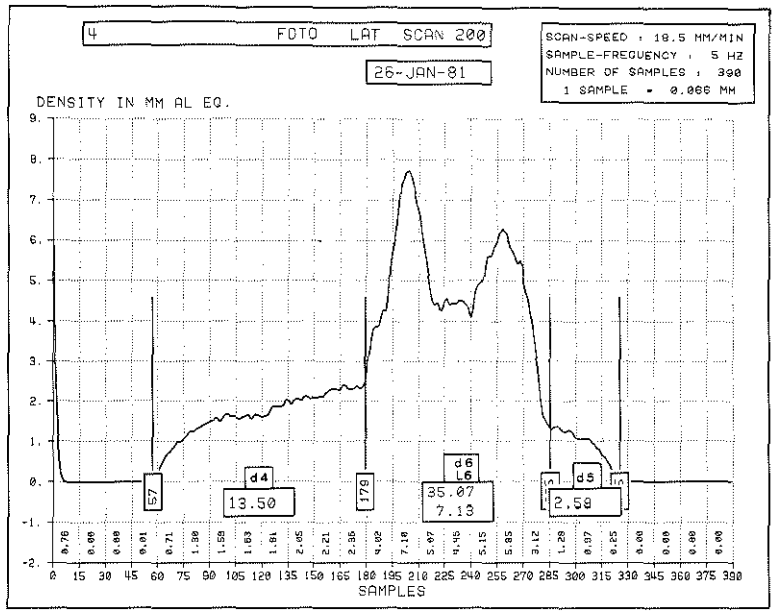


Fig. 31b. Illustrative scan in the centre of the middle phalanx Dig. II. of a lateral radiograph with soft tissue density values. d_4 and d_5.

The cross-section of the phalanx in the midshaft suggests an ellipse and that of the metaphyseal region a circle. These cross-sections can be divided into a bone (d_3 and d_6) and the soft tissue component (d_1 d_2 d_4 and d_5). As can be seen in fig. 31., the blank sections in the drawing (soft tissue) do not contribute to the Al. eq value of the bone. In the following text, an attempt is made to exclude the contribution made by the soft tissues to the Al. eq values obtained. The surface of the bone cross-section can be determined from the values L_3 and L_6 (fig. 31a., fig. 31b.). The surface of the bone section is indicated by:

$$A_{surface} = L_3 . L_6 . \frac{\pi}{4} \qquad \left[mm^2 \text{ skeleton}\right]$$

The Al. eq value of the surface of the cross-section under the bone scan in the postero-anterior direction (D_1) and in the lateral direction (D_2) is expressed in mm² Al. eq by the formulas:

$$D_1 = d_3 - (d_4 + d_5) \qquad \left[mm^2 \text{ Al. eq}\right]$$

$$D_2 = d_6 - (d_1 + d_2) \qquad \left[mm^2 \text{ Al. eq}\right]$$

It should be noted that a more accurate value will be obtained if the shaded sections in fig. 31. are subtracted. In other cases, there may be four instead of two shaded

sections to be subtracted. In this preliminary approach, no correction of these imperfections in the calculations was made. Both the values D_1 and D_2 were used for calculation of the Bone Mineral Content Equivalent (BMCE) according to the formula:

$$BMCE = D_{mean} = \frac{D_1 + D_2}{2} \qquad \left[mm^2 \text{ Al eq} \right]$$

Since the BMCE values represent the Bone Mineral Content of phalanges which may have different dimensions, it is advisable to determine the average bone mineral content per mm^2 surface area of the cross-section of the phalanx. This is accomplished by dividing the BMCE value by the surface of the cross-section. The figures obtained will be referred to as the Bone Mean Mineral Equivalent (BMME).

$$BMME = \frac{D_{mean\ (mm^2\ Al.eq)}}{A_{surface\ (mm^2\ skeleton)}}$$

To obtain an impression of the precision of the radiographic technique and the developed measuring method, the phalanges of 10 volunteers were radiographed in triplo, in postero-anterior and in lateral directions (experiment I).
To estimate the variation of the measurements along adjacent scanlines in the centre of the midphalanx, one radiograph was scanned five times in adjacent zones in an area of one mm (experiment II).
The same volunteers mentioned in chapter 6.2., (10 males and 10 females) were investigated 4 times at three month intervals. Two radiographs were taken during each session, resulting in a total of 160 radiographs. Measurements of the midsection of the phalanx Dig.II. were taken, BMCE and BMME values, linear regressions and correlation coefficients were calculated (experiment III).

Results.
Measurements in the midsection of the phalanx were taken and the BMCE and BMME values were calculated (experiment I). The calculated values are shown in Table XV.

Triplicate radiographs, made on the same persons had a coefficient of variation for BMCE values of 4% and a coefficient of variation for BMME values of 3%.

The values of the densitometric measurements of the five adjacent scans were determined (table XVI) (experiment II).
The five adjacent scans show small variations in the measured values, coefficient of variation 1% (fig. 32.).

In order to permit analysis of changes during the investigation period, the coefficients of variation, the linear regression and correlation coefficient were determined for the BMCE and BMME values of the group (experiment III, table XVIIa, XVIIb).

Table XV: Mean BMCE and BMME values of the phalanx, calculated from three postero-anterior and three lateral radiographs with standard deviation and coefficient of variation.

	BMCE			BMME		
Nr.	Mean	SD	%	Mean	SD	%
1	21.94	0.10	0.5	0.42	0.01	2
2	10.57	0.96	9	0.34	0.01	3
3	20.28	0.90	4	0.42	0.02	5
4	10.25	0.41	4	0.32	0.02	6
5	14.26	0.36	3	0.47	0.01	2
6	12.86	1.19	9	0.45	0.01	2
7	18.97	0.38	2	0.39	0.01	3
8	19.60	0.70	4	0.41	0.02	5
9	15.72	0.24	2	0.38	0.01	3
10	14.76	0.31	2	0.37	0.00	0
	Coefficient of variation 4%			Coefficient of variation 3%		

Table XVI: Al. eq values of five adjacent scans with mean standard deviation and coefficient of variation.

Scan	Al. eq value
1	3.17
2	3.22
3	3.25
4	3.20
5	3.15
Mean	3.20
SD	0.04
Coefficient of variation 1%	

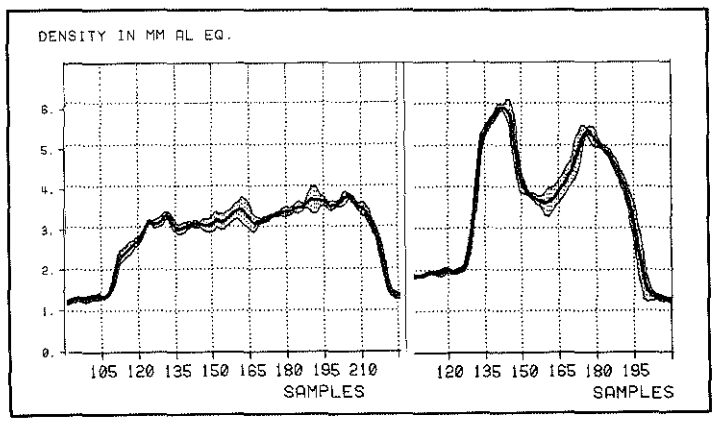


Fig. 32. The five adjacent scans.

Table XVIIa: BMCE values of the midphalanx Dig. II. in four sessions (two radiographs per session and one measurement on each radiograph).

♂	Session I	Session II	Session III	Session IV	Mean	SD	Var. coeff. %	Period I-IV Linear regression	Corr. coefficient
1	18.54	20.47	21.27	17.05	19.33	1.90	10%	y = −0.122 x + 19.88	−0.249
2	18.96	20.98	15.39	16.81	18.04	2.45	14%	y = −0.401 x + 19.84	−0.634
3	23.47	24.56	22.89	17.93	22.21	2.94	13%	y = −0.610 x + 24.96	−0.804
4	20.07	20.07	22.07	18.19	20.10	1.58	8%	y = −0.121 x + 20.65	−0.297
5	15.22	15.59	18.97	15.49	16.32	1.78	11%	y = 0.140 x + 15.69	0.305
6	18.89	18.86	19.64	18.78	19.04	0.40	2%	y = 0.015 x + 18.98	0.145
7	17.37	18.67	17.19	17.33	17.64	0.69	4%	y = −0.053 x + 17.88	−0.299
8	22.63	20.09	19.40	16.28	19.60	2.61	13%	y = −0.326 x + 21.90	−0.845
9	22.85	22.94	21.51	21.13	22.11	0.92	4%	y = −0.122 x + 22.90	−0.700
10	21.10	21.85	19.78	19.30	20.51	1.17	6%	y = −0.128 x + 21.39	−0.564
♀									
21	13.45	17.11	15.09	14.30	14.99	1.57	10%	y = 0.018 x + 14.91	0.044
22	16.14	16.31	14.70	14.10	15.31	1.08	7%	y = −0.258 x + 16.47	−0.921
23	15.52	15.35	14.32	14.24	14.86	0.67	5%	y = −0.162 x + 15.59	−0.937
24	11.45	9.50	12.05	9.83	10.71	1.24	12%	y = −0.077 x + 11.05	−0.241
25	10.36	11.10	11.82	11.42	11.18	0.62	6%	y = 0.130 x + 10.59	0.815
26	17.39	15.29	15.99	16.68	16.34	0.90	6%	y = −0.048 x + 16.55	−0.205
27	17.66	16.93	17.03	16.63	17.06	0.43	3%	y = −0.100 x + 17.51	−0.891
28	13.07	13.45	12.94	14.73	13.55	0.82	6%	y = 0.149 x + 12.88	0.706
29	16.77	16.84	17.76	17.89	17.32	0.59	3%	y = 0.143 x + 16.67	0.933
30	12.46	16.87	14.24	14.65	14.56	1.81	12%	y = 0.131 x + 13.96	0.281
Mean coefficient of variation 8%									

Table XVIIb: BMME values of midphalanx Dig. II.in four sessions.

♂	Session I	Session II	Session III	Session IV	Mean	SD	Var. coeff. %	Period I-IV Linear regression	Corr. coefficient
1	0.42	0.40	0.36	0.37	0.39	0.03	8%	$y = -0.006\ x + 0.42$	−0.891
2	0.49	0.48	0.37	0.40	0.44	0.06	14%	$y = -0.013\ x + 0.49$	−0.829
3	0.47	0.48	0.47	0.49	0.46	0.04	9%	$y = 0.002\ x + 0.47$	−0.674
4	0.42	0.38	0.41	0.34	0.39	0.04	10%	$y = -0.007\ x + 0.42$	−0.754
5	0.39	0.39	0.42	0.38	0.40	0.02	5%	$y = 0.000\ x + 0.39$	0
6	0.39	0.41	0.37	0.37	0.39	0.02	5%	$y = -0.003\ x + 0.40$	−0.674
7	0.32	0.31	0.31	0.33	0.32	0.01	3%	$y = 0.001\ x + 0.31$	0.405
8	0.36	0.38	0.38	0.35	0.37	0.02	5%	$y = -0.001\ x + 0.32$	−0.258
9	0.42	0.42	0.38	0.38	0.40	0.02	5%	$y = -0.005\ x + 0.42$	−0.894
10	0.43	0.45	0.41	0.42	0.43	0.02	5%	$y = -0.002\ x + 0.44$	−0.529
♀									
21	0.37	0.47	0.39	0.43	0.42	0.04	10%	$y = 0.003\ x + 0.40$	0.291
22	0.56	0.53	0.49	0.50	0.52	0.03	6%	$y = -0.007\ x + 0.55$	−0.898
23	0.50	0.40	0.45	0.43	0.45	0.04	9%	$y = -0.005\ x + 0.47$	−0.491
24	0.34	0.35	0.37	0.34	0.35	0.01	3%	$y = 0.001\ x + 0.35$	0.183
25	0.38	0.43	0.42	0.43	0.42	0.02	5%	$y = 0.005\ x + 0.39$	0.759
26	0.55	0.46	0.49	0.47	0.49	0.04	8%	$y = -0.007\ x + 0.52$	−0.673
27	0.49	0.49	0.46	0.49	0.48	0.02	4%	$y = -0.001\ x + 0.49$	−0.258
28	0.35	0.38	0.41	0.43	0.39	0.04	10%	$y = 0.009\ x + 0.35$	0.996
29	0.41	0.46	0.45	0.41	0.43	0.03	7%	$y = 0.000\ x + 0.43$	−0.049
30	0.35	0.47	0.41	0.44	0.42	0.05	12%	$y = 0.007\ x + 0.39$	0.529
Mean coefficient of variation 7%									

The BMCE values had a coefficient of variation of 8% and BMME values one of 7% for the group.
These values are greater in comparison with the previous reproducibility determination of 4% and 3% and may be the result of changes in the bone mineral over the duration of the investigation. For the second individual approach, separate correlation coefficients were taken for the BMCE and BMME values.
For the assessment of the changes with time, the correlation coefficients were evaluated for significance. One significant bone change was found: an increase of the BMME value in volunteer no. 28.

7.3. Clinical investigations.

In order to evaluate the usefulness of BMCE and BMME Al. eq values, we examined a group of healthy volunteers and a group of patients suffering from Chronic Renal Failure CRF (a selected group of patients under treatment at the Department of Internal Medicine III). Twenty persons in the age group 30 - 47 and free from skeletal disease were examined. This control group consisted of 10 men, 37.0 SD 3.89 years of age and 10 women 36.2 SD 4.24 years of age. The patient group was made up as follows: 12 men and 8 women in the age group 21 - 61 with the distribution: male 43.83 SD 11.34 and female 51.13 SD 7.97 years of age.
Immediately after photonabsorptiometry of the right radius at 1/3 of its length from the distal end, radiographs of the midphalanx of the Dig. II. were obtained, for visual interpretation and for microdensitometry.
The diaphyseal portion of the phalanx is a relatively uniform shaft of compact bone: ½ the distance point was selected. The metaphyseal region contains more trabecular bone, a cross-section at ¼ point of the length of the bone from proximal was selected. The ¼ and ½ points of the length from the proximal of the phalanx Dig. II. were located on the postero-anterior and lateral radiograph and the widths were measured. A

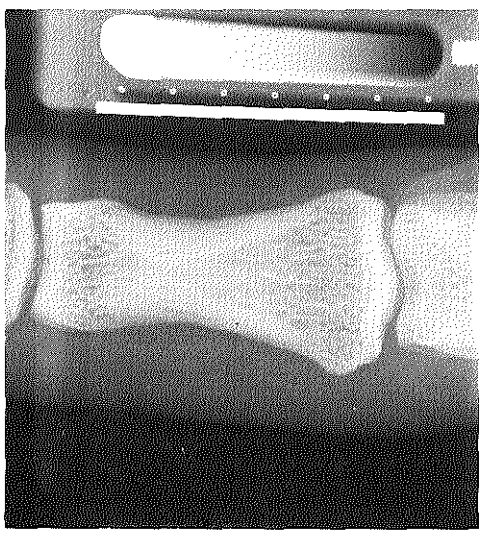


Fig. 38a. Radiograph of phalanx of a volunteer.

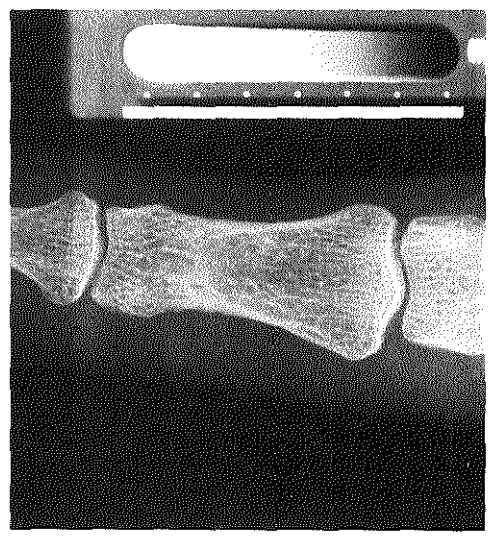


Fig. 38b. Radiograph of phalanx of a CRF patient.

densitometric scan was made across the phalanx at these points. The reproducibility of the method has been described previously and the calculation has been outlined. Microdensitometric measurements of the diaphyseal and the metaphyseal part of the midphalanx Dig. II. were correlated with the results of the γ photonabsorption analysis of the radius.
The correlation between the measurements of the bone mineral of the phalanx and the measurements of the bone mineral of the radius was investigated and also the correlation between the measurements at the ½ and ¼ point of the phalanx.

7.4. Results.

The data obtained from microdensitometry and from photonabsorptiometry are shown in Table XVIII.

Table XVIII: Findings on controls (A).

Control group ♂	BMC	BMCE		BMME	
		½	¼	½	¼
1 ge	1.124	19.24	23.50	0.43	0.32
2 gd	1.142	17.11	24.20	0.36	0.32
3 gc	1.292	18.59	27.65	0.42	0.35
4 gb	1.122	14.23	17.57	0.36	0.29
5 ga	0.952	13.33	15.24	0.32	0.23
6 gn	1.235	15.42	18.32	0.36	0.30
7 gm	1.358	23.78	28.34	0.45	0.34
8 gi	1.172	21.12	25.81	0.42	0.33
9 gj	1.100	17.70	24.48	0.46	0.38
10 gk	1.160	19.05	23.31	0.41	0.32
Mean	1.166	17.96	22.84	0.40	0.32
SD	0.11	3.15	4.39	0.05	0.04

Control group ♀	BMC	BMCE		BMME	
		½	¼	½	¼
1 go	0.912	13.13	17.57	0.36	0.31
2 gp	0.842	12.77	19.60	0.35	0.31
3 gf	1.010	20.50	22.76	0.44	0.34
4 gg	0.966	19.75	25.72	0.41	0.32
5 gi	0.950	21.12	25.81	0.42	0.31
6 gr	1.212	24.56	24.34	0.52	0.38
7 gt	0.875	16.25	18.19	0.52	0.36
8 gh	0.912	12.91	16.12	0.35	0.28
9 gq	0.996	16.16	20.07	0.40	0.30
10 gs	1.064	14.24	17.93	0.47	0.33
Mean	0.974	17.14	20.81	0.42	0.32
SD	0.11	4.11	3.58	0.06	0.03

Table XVIII: Findings on CRF patients (B).

Patient ♂	BMC	BMCE		BMME	
		½	¼	½	¼
1 a	1.075	20.57	23.86	0.35	0.23
2 c	1.284	16.32	18.75	0.38	0.24
3 g	1.384	20.57	34.78	0.44	0.36
4 i	0.988	17.32	22.20	0.36	0.32
5 h	1.290	33.46	40.22	0.47	0.37
6 f	1.254	15.85	26.19	0.35	0.32
7 j	1.240	19.82	23.24	0.36	0.29
8 k	0.966	15.59	18.26	0.41	0.32
9 o	1.128	17.24	18.59	0.34	0.24
10 t	1.193	16.62	17.93	0.35	0.27
11 p	0.910	13.06	20.59	0.37	0.31
12 q	1.008	20.58	22.59	0.40	0.26
Mean	1.143	18.92	23.93	0.38	0.29
SD	0.153	5.16	6.93	0.04	0.05

Patient ♀	BMC	BMCE		BMME	
		½	¼	½	¼
1 b	0.772	12.20	15.03	0.36	0.28
2 d	0.738	13.53	16.26	0.39	0.25
3 e	0.854	7.43	11.11	0.18	0.24
4 l	0.658	10.47	16.64	0.29	0.25
5 m	0.760	8.76	15.61	0.29	0.24
6 n	0.793	11.71	13.69	0.37	0.28
7 r	0.694	16.55	19.69	0.44	0.32
8 s	0.860	16.53	21.50	0.45	0.37
Mean	0.766	12.15	16.19	0.34	0.28
SD	0.071	3.32	3.26	0.09	0.05

Correlation was attempted for the following groups:
A. between BMC and BMCE ½ and BMCE ¼ respectively in the whole group and:
B. between BMME ½ and BMME ¼ for the control and patient groups.

A. there is a significant correlation between BMC of the radius and BMCE ½ and ¼ values of the phalanx $P < 0.001$ $r = 0.657$ and $r = 0.642$. (fig. 39a., 39b.).

B. significant correlations between BMME ½ and BMME ¼ respectively ($P < 0.001$) were obtained in controls and patients (fig. 40.) (for males and females).

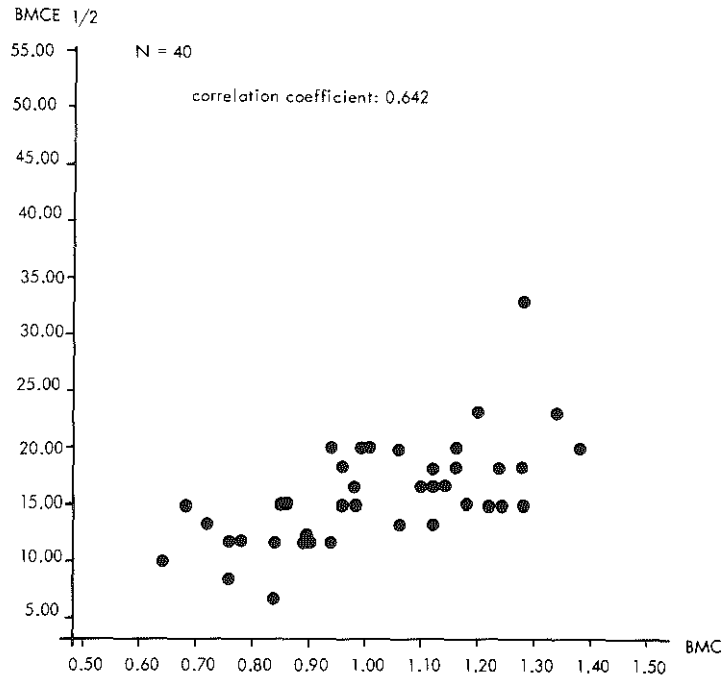


Fig. 39a. Scatter diagram showing the relation between BMCE ½ and BMC.

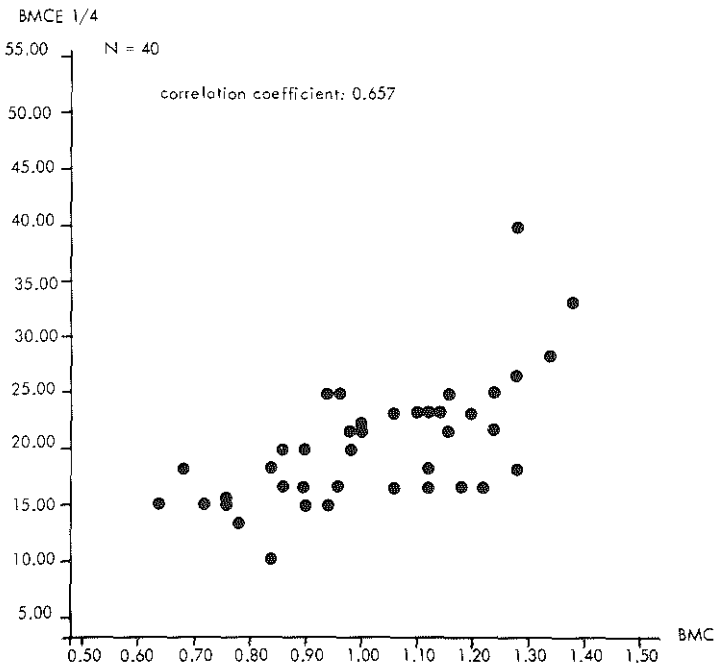


Fig. 39b. Scatter diagram showing the relation between BMCE ¼ and BMC.

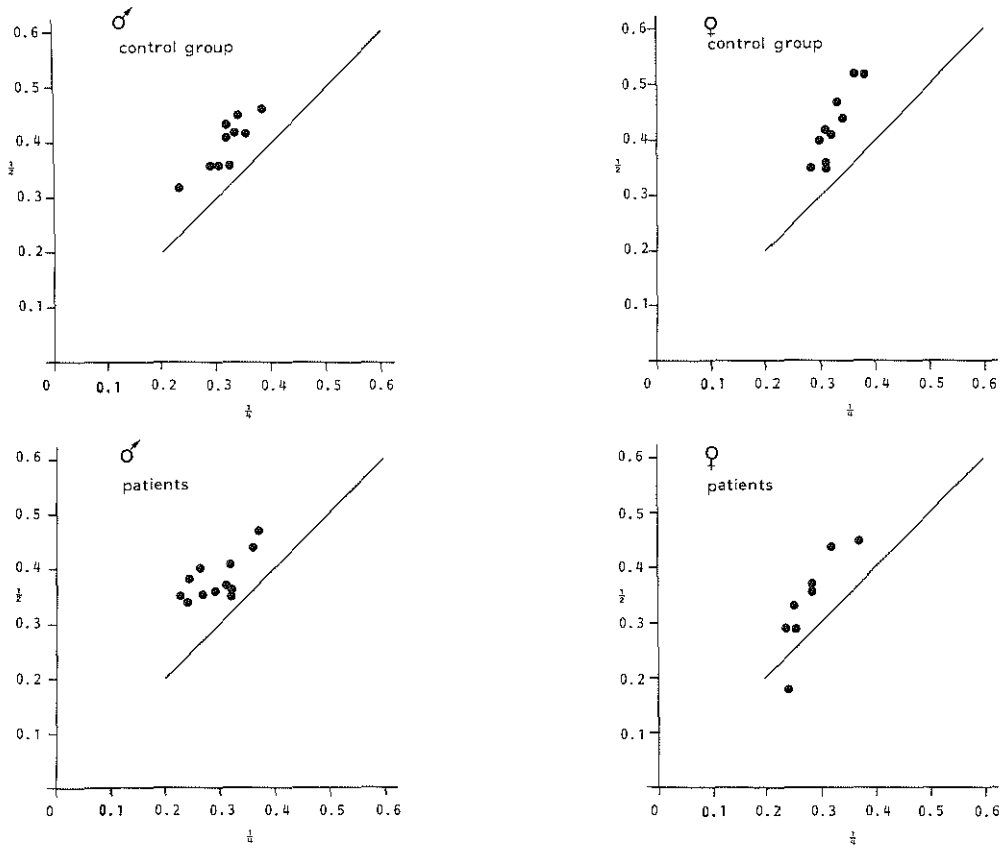


Fig. 40. Scatter diagram showing the relation between BMME of ¼ point and BMME of ½ point for control group and CRF patients. Lower BMME values can be seen in the female patients.

An additional scatter diagram shows that there is no relation between BMME of ¼ point of the phalanx and age (fig. 41a., 41b.).

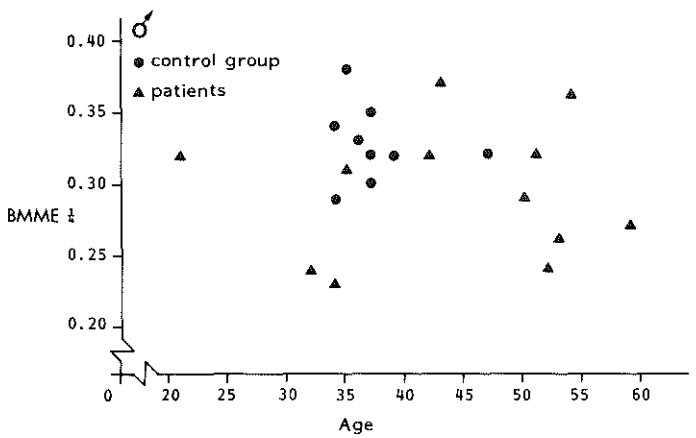


Fig. 41a. Scatter diagram, showing the comparison between BMME ¼ point from proximal and age for male controls and patients.

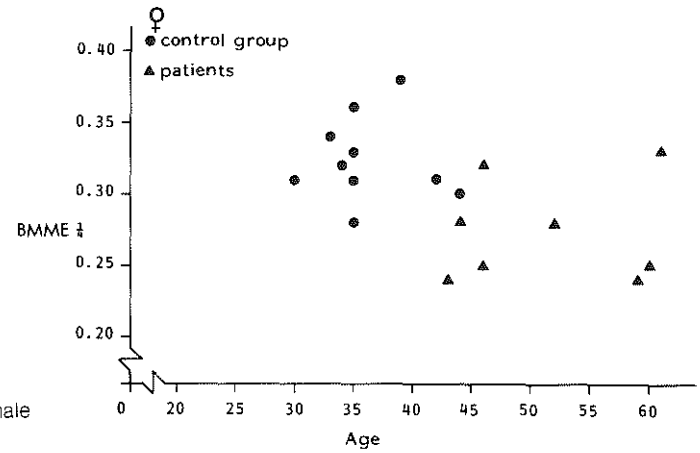


Fig. 41b. Scatter diagram, showing the comparison between BMME ¼ point from proximal and age for female controls and patients.

7.5. Conclusions and discussion.

The following conclusions concerning Al. eq values of the phalanx were reached:
Precision of the developed technique was determined for the phalanx Dig. II., the coefficient of variation was found for BMCE 4% and for BMME 3%.
The coefficient of variation of five scans covering a band of one mm was 1%, as found on one radiograph.
In the following observations, we found over a period of nine months, a coefficient of variation for BMCE and BMME for the whole period of respectively 8% and 7%. It indicates a change during the investigation period. The BMME values were lower in the patients than in the volunteers, but the groups were small and such variables as age and sex account for variations.
Correlations were obtained between BMC and BMCE ½, and BMCE ¼ respectively:

A. a significant correlation, between BMC of the radius and both BMCE ½ and ¼ of the phalanx in the whole group.
B. a significant correlation, between BMME ½ and BMME ¼ in controls and patients; no significant correlation between BMME ¼ and age.

Discussion.

In order to test the method, the bone mineral was quantified for determination of the Al. eq values of the phalanx. When the precision of the method was measured, it appeared that the BMCE values and the BMME values have approximately the same precision. When the BMCE and BMME values of the same traject were compared, it appeared that the coefficient of variation of the BMCE values is comparable with the coefficient of variation of the BMME values. BMCE and BMME values were investigated in a follow-up examination of volunteers during a period of one year. The coefficient of variation of the group and the linear regressions and the correlation coefficient of each volunteer were determined. The coefficient of variation of the BMCE values and of the BMME values were also comparable. The coefficient of variation shows, however, greater values in comparison with the triplicate determination in one session.

For determination of significant, individual bone mineral content changes, the calculated correlation coefficient was analysed. A significant increase in bone mineral content was found in one volunteer.
The clinical application of the recording method was tested on the volunteers and on the CRF patients and compared with the photonabsorption method. These methods do not show significant differences, they measure g.bone mineral/cm BMC values and mm^2 Al. eq/mm BMCE values but no definite conclusion concerning the usefulness of the BMCE and BMME values can be drawn at the moment. Further investigation is necessary on that subject.
Both methods resulted in similar findings. However, microdensitometry also provides a detailed, qualitative assessment of bone characteristics and spatial distribution of bone mineral changes (see appendix).

CHAPTER 8

GENERAL DISCUSSION.

Radiology is based on visual interpretation of radiographs and is directly connected with important decisions in the diagnosis sector. Radiologic interpretation is important in diagnosis, despite the fact that its reliability has frequently been questioned. A consequence of the imperfection of the qualitative, visual evaluation method is that its application produces results which are not suitable for comparison purposes.
Moreover, analysis of an object during a case history, requires reproducible radiographs which can be considered part of the standard radiographic technique. Radiographs with standardised projections may, however, still differ considerably in blackening, due to technical factors. The bony structures also vary considerably between individuals. These two factors complicate the estimation of bone densities. One of the fundamental problems in the visual determination of bone densities on individual images is the absence of useful criteria. Moreover, visual estimation of bone density is not optimal and this leads us to the conclusion that the results are not reliable.
It leads also to the conclusion that a more wide-spread use of measuring instruments should be encouraged, in order to make use of more of the information contained in the radiograph. The question arises whether visual radiologic interpretation without quantitative evaluation is justified.
Microdensitometry may increase the reliability of some diagnostic decisions and open a new field of information.
The precision of the method was determined and this could be useful for future experiments, e.g. when planning the length of observation periods, the number of films to be taken in each session and the number of patients in test and control groups.

Volunteers and patients were investigated for the purpose of testing the developed method clinically and determining its precision.
During a longitudinal study of bone changes in the mandible, the in-duplo method was tested and used at three month intervals. The degree of precision between the radiographs taken at two different sessions was calculated and it was noted that significant bone changes had taken place during the intervening three months. The in-duplo values obtained over the investigation period made it possible to analyse the effects which take place with time. Significant bone changes were observed in six volunteers. Three of them also showed bone changes in the short term analysis.
The information was limited to a relatively small series in which sex, age and case history were not given sufficient consideration. In one case, for instance, use of contraception pills was probably the cause of bone diminuation in one female volunteer.
Up till now, there is insufficient information available on calcium mobility at different

skeletal sites and it is difficult to explain the changes noted in radiographic density within a single bone.
Physiological bone (mineral) loss in the peripheral skeleton (e.g. in metacarpal cortical bone) increases progressively, from the age of about 45, to 1 percent per annum in women and 0.3 percent per annum in men (ref. Garn 1967). CT-scanning has shown that the loss of bone (mineral) in the axial skeleton which consists largely of trabecular bone (the first and second lumbar vertebrae) is five times greater in women during 1 - 2 years after oöphorectomy than in the radial diaphysis as measured by photonabsorptiometry (ref. Cann 1980). It must be stressed that measuring carried out by the same method has shown that even the yearly peripherical (cortical) bone loss can take place at a rate of 2 - 3 percent per annum during the 4 - 6 years following oöphorectomy. This loss can be prevented by treatment with oestrogens (ref. Lindsay 1980).
It is not known whether the ratio of axial to peripheral loss in normal individuals is in the same order of magnitude nor how the normal mandible behaves in this respect. It is possible that the relative content of trabecular bone in the mandible and changes in mechanical stress are factors which contribute to a considerable loss of bone (mineral) in this part of the skeleton, even in middle-aged people.
In order to obtain more information about the Al. eq values of the phalanx, we compared microdensitometry with γ absorptiometry. The radiological method of investigating CRF patients relies on visual interpretation of radiographs of the hand and other skeletal sites and on γ absorptiometry of the radius. In this investigation, we radiographed the phalanx Dig. II. Our immediate aim was to see whether or not there is any correlation between absorptiometry of the radius and microdensitometry of the phalanx. The significant correlation noted demonstrates the usefulness of the method. It not only determines bone mineral values, but also provides detailed knowledge of the mineral distribution over a bone cross-section.
The experiments described in this thesis evoke many, further questions. Knowledge in the field of bone biology has increased, but additional research is necessary to provide standard tables of norm values, as reference on individual patients and to gain more insight into bone morphology in order to learn more about the changes caused by bone healing and the basic mechanism of morphological bone changes.

Summary

Chapter 1 contains a general **Introduction** to the problems involved in the method for quantitative bone analysis. This is followed by a definition of the **Aims** of this study, namely to establish and develop the densitometric analysis method, to permit quantification and qualification of the various components of the image which is normally assessed visually by the radiologist.

Chapter 2 contains a **Review of Literature** which elaborates the problems inherent to the basic aspects of radiographic technique and microdensitometry. This is followed by **Conclusions.**

Chapter 3 describes the **Measuring and Recording System,** including the **Data Processing System.** It explains the importance of the various components selected for the investigation and contains a description of the criteria, conversion methods, techniques and instruments used.

Chapter 4 deals with **System Precision.** It is obvious that experiments carried out in a phantom set-up study provide more definite information and greater, detailed knowledge of the influence of the different aspects of the system on precision. A selection of compatible combinations was made by means of experiments. The purpose of the experiments described was to obtain better insight into the clinical situation.

Chapter 5 describes the **Clinical Investigation** with a survey of methods and techniques suitable for measuring bone mineral content in-vivo. A clinical study was added to test the radiographic microdensitometric method in practice.

Chapter 6 contains a **Study of the Al. eq values of the Mandible.** It starts with an **Introduction,** followed by an analysis of the procedures and their consequences for the X-ray department. Reproducible radiographs of the mandible were measured in a longitudinal study and the methods used for analysis of the density values are described.
The aim was to test the method in practice and no attention was paid to the case history or age distribution of the volunteers.

Chapter 7 contains a **Study of the Al. eq values of the Phalanx.** Standardised radiographs of the phalanx in postero-anterior and lateral directions were analysed in various ways, to determine the bone mineral eq values.

Chapter 8, contains a **General Discussion** in which the significance of the method and its practical application are handled.

Samenvatting.

Het onderzoek, dat in dit proefschrift wordt beschreven, is gericht op het verkrijgen van meer kennis over densitometrische waarden van het bot en botstrukturen.
In hoofdstuk 1 worden het probleem en de doelstelling van het onderzoek uiteengezet en een densitometrische methode voor een kwantitatieve en kwalitatieve analyse van het röntgenbeeld beschreven. Het literatuuronderzoek in hoofdstuk 2 betreft basale radiologische en microdensitometrische technieken met de konklusies.
In hoofdstuk 3 wordt het belang van de verschillende komponenten, die gebruikt zijn bij het onderzoek, aangegeven. Bovendien worden de verrekeningsmethoden, kriteria, technieken en instrumenten toegelicht.
In hoofdstuk 4 worden achtereenvolgens de faktoren, die de precisie van het systeem bepalen, onderzocht.
Hoofdstuk 5, omvat de introduktie van een klinisch onderzoek om de ontwikkelde techniek in de praktijk te toetsen en een bespreking van de gebruikte methoden ter bepaling van bot mineraal gehalte.
In hoofdstuk 6 worden reproduceerbare röntgenopnamen van de mandibula in een longitudinaal onderzoek geanalyseerd. Een beschrijving wordt gegeven van de analysemethode. De meetmethode in de kliniek te testen was de primaire opzet van dit onderzoek. Er wordt geen aandacht besteed aan faktoren zoals anamnese en samenstelling van de proefpersonengroep.
In hoofdstuk 7 worden gestandaardiseerde röntgenopnamen gemaakt van de phalangs Dig. II. Twee opnamen onder een hoek van 0 en 90 graden worden gemaakt. Een beschrijving wordt gegeven hoe men de verkregen densitometrische waarden uit de posterior-anterior en uit de laterale röntgenopnamen kan analyseren en kombineren.
Voor een juist inzicht in de botstofwisseling zou bij een statistisch verantwoorde opzet een onderzoek gedaan moeten worden, waarbij tevens de anamnese van belang is.
In hoofdstuk 8 wordt ingegaan op de vraag welke praktische betekenis aan deze methode toegekend kan worden in de radiodiagnostiek.

Appendix.

In radiographs, not only the amount, but also the structure of the spongy bone is of importance for bone evaluation. These factors are usually assessed according to the subjective judgement of the observer.
The specific trabecular patterns are based on the patterns formed by trabecular and medullary spaces. Different classifications of trabecular patterns are possible. The number and size of trabeculae and medullary spaces are measurable factors. Rectilinear scans permit visualization of the structures. The visual interpretation should be replaced by an estimate of the bone quality through pattern classification.
Radiological diagnosis is based on the recognition of patterns. However, the recognition is subjective and not sufficient to qualify the various bone patterns.
It is possible to obtain objective information by using a **F**ast **F**ourier **T**ransform, F.F.T., of the scan which results in a frequency spectrum. It may be possible to classify bone patterns by using these frequency spectra. This technique could be a new supplement to the existing routine procedures and could provide quantitative and qualitative information.
To demonstrate the relation between a signal and the frequency spectra, three simulated mathematical models were analysed (fig. 42.). A possible scheme for interpretation of the frequency spectra of bone patterns is presented, showing scan lines and related frequency spectra for a fine and a coarse bone pattern.

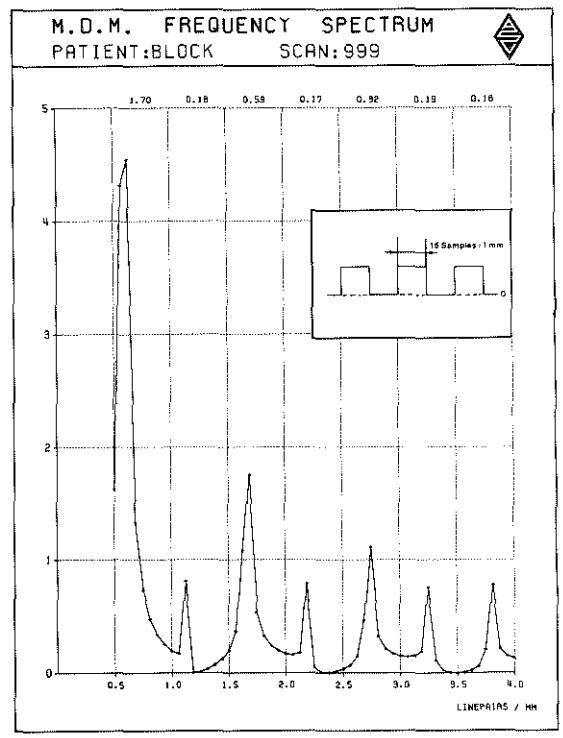


Fig. 42a. Spectrum of block model.

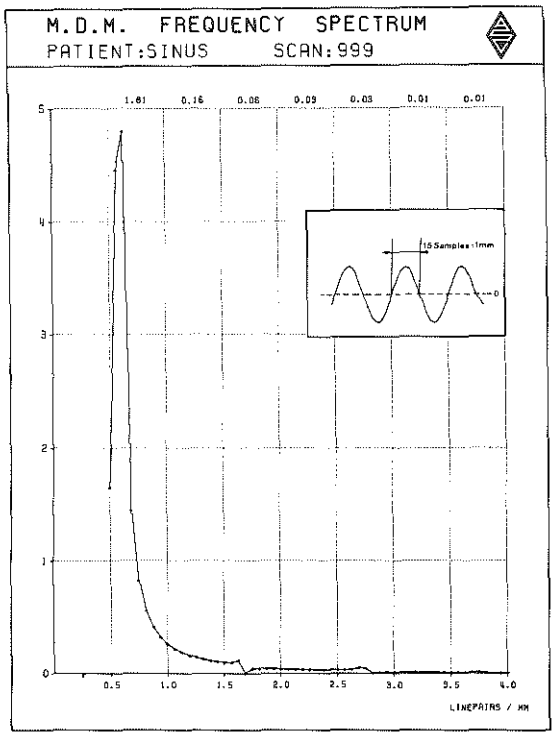


Fig. 42b. Spectrum of sinus model.

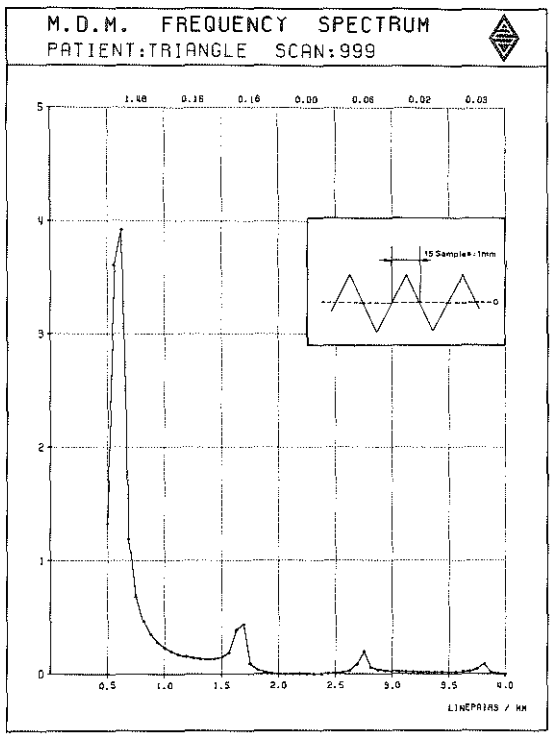


Fig. 42c. Spectrum of triangle model.

Computer simulated models.
A block, sinus and triangle with horizontal distances of 15 samples (1 mm) 30 samples per period were simulated, we chose a traject of 128 samples.
The characteristic frequency spectra were determined to grade the pattern into a classification. There are considerable frequency components of 0.7 lp/mm and few low frequency components after 1 lp/mm.

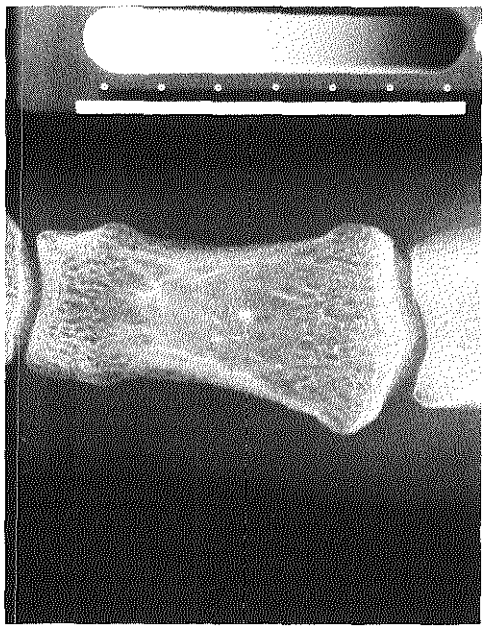


Fig. 43a. Radiograph of phalanx with a coarse bone pattern.

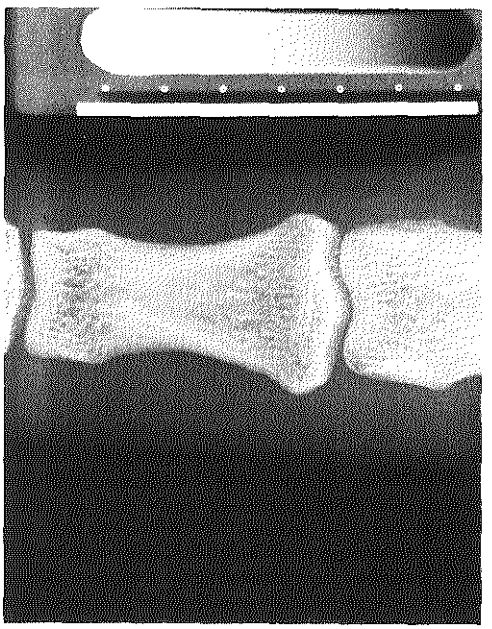
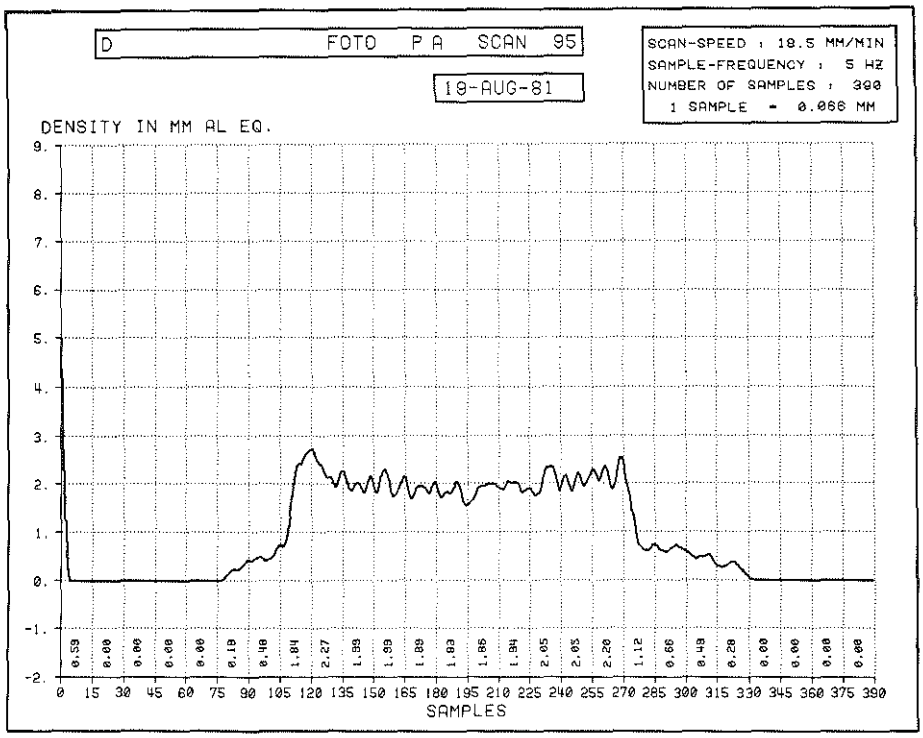


Fig. 43b. Radiograph of phalanx with a fine bone pattern.

To recognize the differences in bone patterns, a coarse and a fine bone pattern was analysed (fig. 43a., 43b.).
Frequency spectra were produced and the values were determined in order to grade the patterns into a classification.
The X-ray pattern shows details of different sizes, the properties of the pattern can be analysed to determine the frequency content or the spectrum of the scan.
The characteristic scan traject was 128 samples long, frequency components were determined and contain linepairs/mm. varying between 0.5 - 1 - 1,5 - 2 - 2,5 lp/mm., indicating distances of 1, 0.5, 0.33, 0.25 and 0.2 mm.
The objective values can be used for a statistical analysis and it must be possible to determine the significantly representative class values.
The comparison of the spectrum of two objects, a phalanx with coarse and one with fine bone pattern shown together (fig. 44a., 44b.) reveals the presence of low spatial frequencies for fine bone pattern and considerably higher frequency components of 0.5 to 1.5 lp/mm. for coarse bone pattern.



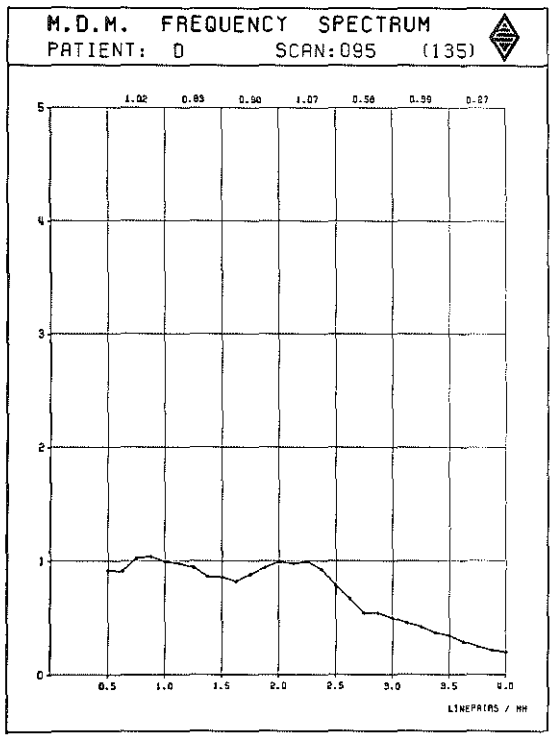
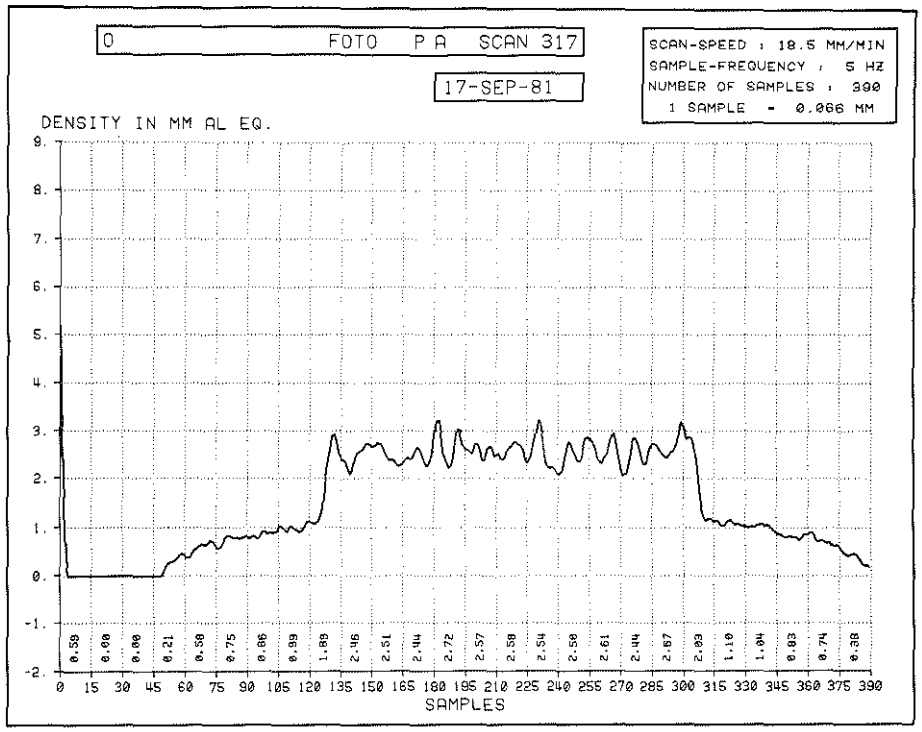


Fig. 44a. Bone scan of phalanx of ¼ point from proximal and frequency spectrum of fine pattern.



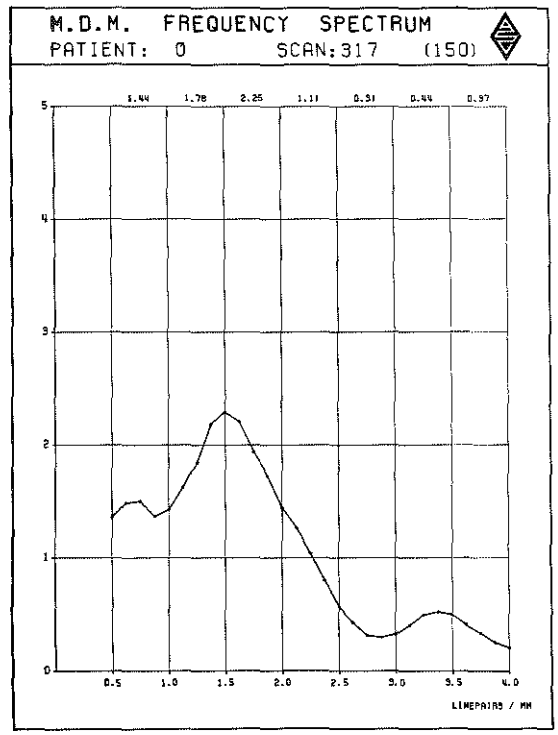


Fig. 44b. Bone scan of phalanx of ¼ point from proximal and frequency spectrum of coarse pattern.

Addendum. (Drs. H.J.A. Schouten).*

Measurement Errors Mandible.

The measured value from a radiograph may be written as:

$$\text{measured value} = \text{true value} + \text{random error}$$

Since measured values are to be compared with one another, it is not necessary to take a possible bias into account.
The true value may be considered as the mean of a great many measured values, if these could be obtained.
An estimate of the standard deviation of the random error is:

$$s_1 = \sqrt{\frac{\sum \triangle^2}{2n}}$$

Where the sum is taken over n patients and $\triangle$ is the difference between the values of two radiographs in one session.
This means that the difference between measured value and true value is about s_1, and this difference is less than $2 \times s_1$ in about 95% of the cases.
An estimate of the standard deviation of the random error in the mean of two measured values from two radiographs is:

$$s_2 = \sqrt{\frac{\sum \triangle^2}{4n}}$$

The difference between this mean measured value and the true value is about s_2 and this difference is less than $2 \times s_2$ in about 95% of the cases.
Thus s_1 and s_2 indicate the order of magnitude of the random error.

* Wetenschappelijk Hoofdmedewerker Biostatistica.

References

W. ADOLPH., L. LICHTENAU., E. EPPLE.
Herstellung von reproduzierbaren und deckungsgleichen Röntgenbildern bei Knochenstructuruntersuchungen. Dtsch. zahnärtztl. Z. 30, 765 - 770, 1975.

A.E. DE AGUIAR., A.I. KLEIN., J.O. BECK.
Spongy bone architecture of edentulous mandibles. A television radiographic evaluation. J. Prosth. Dent. 19, 12 - 21, 1968.

J.M. AITKEN., C.B. SMITH., P.W. HORTON., D.L. CLARK., J.F. BOYD., D.A. SMITH.
The interrelationships between bone mineral at different skeletal sites in male and female cadavera. J. Bone Jt. Surg. 56B, 370 - 375, 1974.

American Standards Association.
American National Standard method for the sensitometry of medical X-ray films, ANSI PH2-9, 1974.

G. BALZ., R. BIRKNER.
Die Bestimmung des Aluminiumschwächungsgleichwertes von Knochengewebe beim Lebenden. Strahlentherapie 99, 221 - 226, 1956.

B. BENTLEY.
Modern radiological methods of bone densitometry - a survey. Radiography 33, 155 - 162, 1967.

J. BERGSTRÖM., C.O. HENRIKSON.
Quantitative longitudinal study of alveolar bone tissue in man. J. Periodont. Res. 5, 237 - 247, 1970.

H.M. BERRY.
The Lore and the Lure O' the Lamina Dura. Radiology 109, 525 - 528, 1973.

U. BINSWANGER., J. FISCHER., R. SCHENK., W. MERZ.
Osteopathie bei chronischer Niereninsuffizienz. Dtsch. med. Wschr. 96, 1914 - 1919, 1971.

K.L. BOON.
Computer, Informatie en Geneeskunde. Spruyt, Van Mantgem en De Does b.v., Leiden, 1973.

H. BRABAND., W.P. COCKSHOTT., K.T. EVANS.
Die röntgendiagnostische Bedeutung der Lamina Dura des Zahnes. Fortschr. Röntgenstr. 102, 447 -453, 1965.

J.R. CAMERON., J.A. SØRENSEN.
Measurement of bone mineral in vivo: An improved method. Science 142, 230 - 232, 1963.

J.R. CAMERON., R.B. MAZESS., J.A. SØRENSEN.
Precision and accuracy of bone mineral determination by direct photonabsorptiometry. Invest. Radiol. 3, 141 - 150, 1968.

C.E. CANN., H.K. GENANT., B. ETTINGER., G.S. GORDAN.
Spinal mineral loss in oophorectomized women. J. Amer. Med. Ass. 244, 2056 - 2059, 1980.

G. CAPPELLINI., P. PAVLICA., G. STASI., R. TONTI., G. VIGLIETTA.
Temporo-Mandibular Joint Changes in Renal Osteodystrophy. Radiol. clin. biol. 47, 330 - 333, 1978.

S. CASTELLS., C. COLBERT., C. CHAKRABARTI., R.S. BACHTELL., E.G. KASSNER., S. YASUMURA.
Therapy of osteogenesis imperfecta with synthetic salmon calcitonin. J. Pediat. 95, 807 - 811, 1979.

S. CLERGEAU - GUERITHAULT.
Vergleichende rasterelektronenmikroskopische Untersuchungen über die Lamina Dura Interna. Dtsch. zahnärtztl. Z. 28, 333 - 336, 1973.

W.W. DANIEL.
Biostatistics: A foundation for analysis in the health sciences.
John Wiley and Sons Inc., New York, London, Sydney, Toronto, 1974.

K. DIEM., C. LENTNER.
Wissenschaftliche Tabellen. Documenta Geigy, 7. auflage,
J.R. Geigy A.G. Pharma, Basel, 1968.

W.F. DILLER.
Zur Röntgendichte von Kunststoffen. Fortschr. Röntgenstr. 128, 758 - 762, 1978.

A.S.H. DUINKERKE.
Interpretation and densitometric quantification of periapical structures in dental radiographs. Thesis. Nijmegen, 1976.

Densitometrie in der Radiologie.
Symposium der: "Gesellschaft für Biomedizinische Technik" gemeinsam mit der "Deutschen Röntgen Gesellschaft". Stuttgart 1971.
Georg Thieme Verlag, Stuttgart, 1973.

S.T. ELIASSON., B. HAASKEN.
Radiopacity of impression materials. Oral Surg. 47, 485 - 491, 1979.

E. EPPLE., H. BAUER., D. DECKER., M. NAGEL.
Recognition of changes in the structure of bones by dataprocessing. Digis of the 10th International conference on medical and biological engineering. Dresden, 1973.

P.D. FLETCHER., I.W. SCOPP., R.A. HERSH.
Oral manifestations of secondary hyperparathyroidism related to long-term hemodialysis therapy. Oral Surg. 43, 218 - 226, 1977.

The fundamentals of radiography. Publication: Eastman Kodak Company, Rochester N.Y., 1966.

S.M. GARN., C.G. ROHMANN., B. WAGNER.
Bone loss as a general phenomenon in man. Fed. Proc. 26, 1729 - 1736, 1967.

H.K. GENANT., K. DOT., J.C. MALL.
Optical versus Radiographic Magnification for Fine-detail Skeletal Radiography. Invest. Radiol. 10, 160 - 172, 1975.

H.M. GOLDMAN., A.H. PEARSON., N. DARZENTA.
Reliability of radiographic interpretations. Oral Surg. 38, 287 - 293, 1974.

H.M. GOLDMAN., J.S. MILLSAP., H.S. BRENMAN.
Origin of registration of the architectual pattern, the lamina dura, and the alveolar crest in the dental radiograph. Oral Surg. 10, 749 - 758, 1957.

H. GRIFFITHS.
The Radiology of renal bone disease revisited. Dial. Transplant. 8, 579 -583, 1979.

P. DE GRAAF.
Renal bone diseases and extraskeletal calcification during dialysis and after transplantation. Thesis, Leiden, 1980.

V.A. DE GROOTE.
Een introductie tot computer in geneeskunde. Dr. G.J. Mulder Stichting M.F.R., Rotterdam, 1972.

I. GROSSMANN., U.J. SCHMIDT., G. BRÜSCHKE., I. TÖPELMANN.
Röntgenologische Möglichkeiten zur Bestimmung der Knochendichte. Dtsch. Ges. Wesen. 25, 1984 - 1990, 1970.

S. HAMILTON., W.J. KNICKERBOCKER.
Peri-articular erosions in the hands and wrists in haemodialysis patients. Clin. Radiol. 33, 19 - 24, 1982.

M. HEDIN., M. LUNDBERG., K. WING.
Measurement of fine structures in roentgenograms. Acta Odont. Scand. 32, 357 - 364, 1974.

T. HELELÄ., P. VIRTAMA.
Bone density of the Ulna. Invest. Radiol. 3, 103 - 107, 1968.

C.O. HENRIKSON., P. JULIN.
Iodine - 125 apparatus for measuring changes in X-ray transmission and the thickness of alveolar process. J. Periodont. Res. 6, 152 - 158, 1971.

F. HEUCK., W.H. BLOSS., L.R. SAACKEL., E.R. REINHARDT.
Strukturanalyse des Knochens aus Röntgenbildern. Biomed. Techn. 25, 35 - 42, 1980.

G. ISENBERG., H.M. GOLDMAN., J. SPIRA., F.G. PARSONS., P.N. STREET.
Radiograph analysis by two-dimensional microdensitometry. J. Amer. dent. Ass. 77, 1069 - 1073, 1968.

International Commission in Radiological Protection. (I.C.R.P.)
no. 23, Report of the task group on reference man.
Pergamon Press, Oxford - New York - Toronto - Sydney - Braunschweig, 1975.

International Commission in Radiological Protection. (I.C.R.P.)
no. 26, Recommendations of the I.C.R.P.
Pergamon Press, Oxford - New York - Frankfurt, 1977.

International Workshop on Bone and Soft Tissue densitometry using computed tomography.
Clinical Evaluation of Periapical Bone by CT Densitometry.
San Francisco California June 7 - 9, 1979. J. Comput. Assist. Tomogr. 3, 847 - 862, 1979.

H. JAEGER.
Physikalisch-technische Grundlagen zur Röntgenphotographischen Abbildung von Weichteilen.
Röntgen. Bl. 22, 323 - 333, 1969.

J.R. JUTTMANN., J.C.W. HAGENOUW-TAAL., L.D.F. LAMEYER., A.M. RUIS., J.C. BIRKENHÄGER.
A Longitudinal Study of Bone-Mineral Content and Intestinal Calcium Absorption in Patients with Chronic Renal Failure. Metabolism 28, 1114 - 1121, 1979.

J.R. JUTTMANN.
Renale Osteodystrofie. Thesis. Rotterdam, 1980.

M.J. KASLE., A.I. KLEIN.
Television radiographic evaluation of periapical osseous radiolucencies. Oral Surg. 41, 789 - 796, 1976.

S. KENNETT., H. POLLICK.
Jaw Lesions in familial hyperparathyroidism. Oral Surg. 31, 502 - 510, 1971.

S.D. KING.
A Radiographic Technique for Measuring the Powder Packing. Density in the Cavities of Trabecular Bone. Phys. in Med. Biol. 22, 681 - 692, 1977.

E. KILPINEN., P.E. HAKALA.
Reproduction of the lamina dura in dental radiographs. Dentomaxillofac. Radiol. 7, 51 - 54, 1978.

E. KIRKEGAARD., P. ZEUNER.
A method for obtaining Periodic Identical Bitewing Radiographs. Scand. J. dent. Res. 82, 632 - 635, 1974.

I.E. KLEIN.
The effect of thyrocalcitonin and growth hormones on bone metabolism. J. Prosth. Dent. 33, 365 - 379, 1975.

F.J.H. KLEVANT.
Results of endodontic treatment of filled, partly filled and unfilled root canals. Thesis. Utrecht, 1981.

M. LEFKE., H.G. SIEBERTH., G. FRIEDMAN.
Röntgenologische Veränderungen bei Calciumstoffwechselstörungen im Terminalstadium der Niereninsuffizienz. Dtsch. med. Wschr. 96, 283 - 290, 1971.

L. LICHTENAU., K. BOLLINGER., H. BÖHRINGER.
Röntgendensitometrische Knochenstrukturuntersuchungen nach Zahnextraktionen. Dtsch. zahnärztl. Z. 31, 585 - 590, 1976.

L. LICHTENAU., K. BOLLINGER.
Herstellung von Röntgenaufnahmen des menschlichen Unterkiefersmethode und Nachweis der Genauigkeit der Reproduzierbarkeit des Ortes. Dtsch. zahnärztl. Z. 30, 392 - 395, 1975.

L. LICHTENAU., U. FAUST.
Erfassung des Desmodontalspalts und dessen Veränderung aus dem Röntgenbild des menschlichen Unterkiefers mit Hilfe einer Datenverarbeitungsanlage. Electromedica 46, 118 - 121, 1978.

R. LINDSAY., J.B. ANDERSON.
Radiological determination of changes in bone mineral content. Radiography 44, 21 - 26, 1978.

R. LINDSAY., D.M. HART., C. FORREST., C. BAIRD.
Prevention of spinal osteoporosis in oophorectomised woman. Lancet II. 1151 - 1153, 1980.

B.S. LIPKIN., A. ROSENFELD.
Picture processing and psychopictorics. Academic Press, New York-London, 1970.

E. MACHTENS., H. GIRGENSOHN., H. OPPERMANN.
Klinische röntgenologische und histologische Untersuchungen im Kieferbereich bei osteolytischen Prozessen nach Dauerdialyse. Dtsch. zahnärztl. Z. 29, 721 - 724, 1974.

J.D. MASON.
The Lamina Dura. Oral Surg. 16, 432 - 438, 1963.

I. MATSUE., C.K. COLLINGS., E.R. ZIMMERMANN., W.C. VAIL.
Microdensitometric Analysis of Human Autogenous Alveolar Bone Implants. J. Periodont. 41, 489 - 495, 1970.

I. MATSUE., E.R. ZIMMERMANN., C.K. COLLINGS., J.T. BEST.
Microdensitometric Analysis of Human Autogenous Bone Implants II. Two-dimensional Density and Pattern Analysis of Interproximal Alveolar Bone. J. Periodont. 42, 435 - 438, 1971.

H.E. MEEMA., S. MEEMA.
Cortical bone mineral density versus cortical thickness in the diagnosis of osteoporosis. A roentgenologic-densitometric study. J. Amer. Geriat. Soc. 17, 120 - 141, 1969.

H.E. MEEMA., D.G. OREOPOULOS., S. MEEMA.
A Roentgenologic Study of Cortical Bone Resorption in Chronic Renal Failure. Radiology 126, 67 - 74, 1978.

F. MELSEN., B. MELSEN.
The relation between densitometric and quantitative histological analysis of bone specimens from the iliac crest. Clin. Orthop. 117, 321 - 326, 1976.

R.D. MOSELEY., J.H. RUST.
Television in diagnostic radiology. Aesculapius Publishing Company, Birmingham-Alabama U.S.A., 1969.

M. NAGEL., F. HUECK., E. EPPLE., D. DECKER.
Bestimmung des Knochenmineralgehaltes aus den Röntgenbild mit Hilfe der digitalen Datenverarbeitung. Fortschr. Röntgenstr. 121, 604 - 612, 1974.

M. O'CONNOR., F.B. WOODFORD.
Writing scientific papers in English. Elsevier-Excerpta-Medica, North-Holland, Amsterdam Oxford New York, 1976.

K.A. OMNELL.
Quantitative Roentgenologic Studies on changes in mineral content of bone in-vivo. Thesis, Stockholm, 1957.

F. PAICE.
Measuring radiographic bone density and irregularity in normal hands. Brit. J. Radiol. 52, 925 - 935, 1979.

G.J. PARFITT.
An investigation of the normal variations in alveolar bone trabeculation. Oral Surg. 15, 1453 - 1463, 1962.

C.M. PARKER., R.P. SHARMA., J.L. SHUPE.
The Interaction of Dietary Vitamin C, Protein and Calcium with Fluoride: Effects in Guinea Pigs in Relation to Breaking Strength and Radiodensity in Bone. Clin. Toxicol. 15, 301 - 311, 1979.

K. PFEIFLE., H. KOCH., B. GRABENSEE., H.I. KNIERIEM.
Montröse tumorartige Veränderungen des Gesichtsschädels bei sekundärum Hyperparathyreoidismus. Dtsch. med. Wschr. 99, 389 - 391, 1974.

K.U. PHILIPP.
Die Lamina Dura alveoli dentis bei renaler Osteopathie. ZWR Zahnärtztl. Welt Rdsch. Ref. 81, 704 - 709, 1972.

G.J. v.d. PLAATS.
Medische Röntgentechniek. De Tijdstroom, Lochum, 1972.

I.J. PLOTNICK., V.E. BERESIN., A.B. SIMKINS.
Study of in-vivo Radiographic Densitometry. J. Dent. Res. 49, 1034 - 1041, 1970.

I.J. PLOTNICK., V.E. BERESIN., A.B. SIMKINS.
A Technique for Standardized Serial Dental Radiographs. J. Periodont, 42, 297 - 299, 1971.

Practical densitometry. Publication no. E59, Eastman Kodak Company, Rochester N.Y., 1972.

P. PRAGER., R. SINGER., E. RITZ., B. KREMPIEN.
Diagnostischer Stellenwert der Lamina dura dentium beim sekundären Hyperparathyreoidismus. Fortschr. Röntgenstr. 129, 237 - 240, 1978.

B.R. PULLAN., T.E. ROBERTS.
Bone mineral measurement using an EMI scanner and standard methods: a comparative study. Brit. J. Radiol. 51, 24 - 28, 1978.

N. REFSHAUGE., J. TOLDERLUND.
Periodic identical intraoral radiographs. Oral Surg. 45, 311 - 316, 1978.

E.R. REINHARDT., W. GREINER., F. HEUCK., J. PIRSCHEL.
Structure analysis of X-ray images obtained form bones. J. Comput. Assist. Tomogr. 6, 210 - 211, 1982.

U. REISER., F. HEUCK., L. LICHTENAU.
Untersuchungen der Mineraltopographie am menschlichen Wirbelkorper mit der Röntgen-Computer-Tomographie. Radiologe 20, 554 - 557, 1980.

H. RENGGLI., E. STEINER., Z. CURILOVIĆ.
Reproducible Radiographs and Photographs in Periodontal Diagnosis. Parodontologie 25, 66 - 74, 1971.

E. RITZ., P. PRAGER., B. KREMPIEN., J. BOMMER., H.H. MALLUCHE., H. SCHMIDT-GAYK.
Skeletal X-ray findings and bone histology in patients on hemodialysis. Kidney int. 13, 316 - 323, 1978.

D.M. ROBERTSON., D.C. SMITH., S.K. DAS., A. KUMAR.
Microdensitometry as a clinical tool for diagnosing the progress of fracture healing. J. Oral Surg. 38, 740 - 743, 1980.

P.J.A. ROBINSON., G.S. WALKER., M. PEACOCK., M.S.F. McLACHLAN., A.M. DAVISON.
l-alpha-hydroxy vitamin D in dialysis bone disease: Radiological changes after 6 and 12 months of treatment. Clin. Radiol. 33, 9 - 17, 1982.

P. RUEGSEGGER., U. ELSASSER., M. ANLIKER., H. GNEHM., H. KIND., A. PRADER.
Quantification of Bone Mineralisation Using Computed Tomography. Radiology 121, 93 - 97, 1976.

H. RUNGE., F. FENGLER., J. FRANKE., W. KOALL.
Ermittlung des peripheren Knochenmineralgehaltes bei Normalpersonen und Patienten mit verschiedenen Knochenerkrankungen, bestimmt mit Hilfe der Photonenabsorptionstechnik am Radius. Radiologe 20, 505 - 514, 1980.

A. SAMIZADEH., H. LOEW., G. BUSCH., H. MÜLLER., H. LOSSE.
Bestimmung des Knochenmineralgehaltes mit Hilfe der Photonenabsorptionstechnik bei renaler Osteopathie. Klin. Wschr. 55, 1005 - 1011, 1977.

R.R. SHOHA., J. DOWSON., A.G. RICHARDS.
Radiographic interpretation of experimentally produced bony lesions. Oral Surg. 38, 294 - 303, 1974.

S. SILVERMAN., G. GORDAN., T. GRANT., H. STEINBACH., E. EISENBERG., R. MANSON.
The dental structures primary hyperparathyroidism. Oral Surg. 15, 426 - 436, 1962.

S. SILVERMAN., W.H. WARE., C. GILLOOLY.
Dental aspects of hyperparathyroidism. Oral Surg. 26, 184 - 189, 1968.

N. SMITH.
A comparative histological and radiographic study of extraction socket healing in the rat. Aust. dent. J. 19, 250 - 254, 1974.

G. SÖDERHOLM., L. LYSELL., A. SVENSSON.
Changes in the jaws in chronic renal insufficiency and haemodialysis Report of a case. J. Clin. Periodont. 1, 36 - 42, 1974.

Society of Photographic Scientists and Engineers, Handbook of Photographic science and engineering. Edited by T. Woodlief. J. Wiley and Sons, New York - London - Sydney - Toronto, 1973.

P.F. VAN DER STELT.
Periapical bone lesions. Thesis. Amsterdam, 1979.

W.M. SY., A.K. MITTAL.
Bone scan in chronic dialysis patients with evidence of secondary hyperparathyroidism and renal osteodystrophy. Brit. J. Radiol. 48, 878 - 884, 1975.

T. VILLAFANA.
Temporal response of microdensitometers. Med. Phys. 5, 34 - 36, 1978.

F.B. VOGT., L.S. MEHARG., P. BEERY MACK.
Use of a digital computer in the measurement of roentgenographic bone density. Amer. J. Roentgenol. 105, 870 - 876, 1969.

G.P. VOSE.
Estimation of Changes in Bone Calcium Content by Radiographic Densitometry. Radiology 93, 841 - 844, 1969.

TH. WEISS., S. LANGE., G. GAHL.
Ossäre Veränderungen bei Patienten in Langzeitdialyse. Med. Klin. 74, 1357 - 1362, 1979.

K.R. WING., E. BIRRING.
An Electronic Device for Direct Read out of Bone. Mineral Content for Roentgenograms scanned with a Microdensitometer. Conference on Bone Mineral Measurement. Amer. J. Roentgenol. 126, 1269 - 1270, 1976.

N. VON WOWERN.
A new method of gamma-ray osteodensitometry of the mandible. Int. J. Oral Surg. 3, 353 - 357, 1974.

X-rays in dentistry. Publication: Eastman Kodak Company, Rochester N.Y., 1977.

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