OSPEDALE GENERALE PROVINCIALE, CASTELFRANCO VENETO

MEDICINA NUCLEARE
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QUANTITATIVE BONE SCANNING

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INTRODUCTION

The recent availability of ^{99m}Tc-labelled phosphorus compounds (polyphosphate, diphosphonate, pyrophosphate) has certainly improved bone imaging results which had become a difficult task in bone metastases research and in estimating the behaviour during radiant or pharmacological therapy [1, 2, 4-9].

In fact, the high counting efficiency produced by these tracers allows excellent images to be projected, with a negligible irradiation of the patient, so that it is possible to examine rapidly the whole skeletal system using the gamma-camera. Examinations with the Anger-camera still have limitations: small lesions with low uptake can be overlooked because the discrimination of suspected areas is purely qualitative and is entrusted to the experience of the clinician and to his ability in distinguishing a different contrast in the images; on the other hand, this is directly correlated with the number of impulses accumulated during the exposure time of the film and with the intensity of the luminous dots on the oscilloscope.

The possibility of utilizing a computer coupled with the scintillation camera has induced us to estimate if the re-examination of the skeletal scintiphotos by means of the processing system will allow us to overcome such limitations.

MATERIALS AND METHODS

The tests were carried out 2 or 3 hrs after administering intravenously 4-5 mCi of ^{99m}Tc-pyrophosphate, using a Pho-gamma IV fitted with a low energy diverging collimator (Divcon): in the presence of small or doubtful lesions, a high-resolution collimator was used. All the scintiphotos were taken with an exposure time of 2 min, and the information was simultaneously registered on a 64 x 64 magnetic memory of a Clincom computer (Nuclear-Chicago) coupled on-line with the gamma-camera. Processing of the data then began, using the following operations, for which the computer had already been programmed:

1) presentation of the scintiphotos in digital form which, although less definite, are analogous to those obtained directly from the gamma-camera, that is the spatial distribution of the radioactivity is expressed as a linear variation of the intensity.

Using a variable scale, which selected the number of impulses accumulated at each point, images with different luminosity were obtained; varying the gray scale, from the faintest intensity, which

Key-words: Bone lesions; Bone scanning; Neoplasms; Scintigraphy; ^{99m}Tc-pyrophosphate.

Received, June 13, 1975.

La Ricerca Clin. Lab. *5*, 263, 1975.

corresponded with zero impulses, to the brightest, which represented the value of the background scale selected, the contrast was modified opportunely, obtaining successive and gradual 'cuts' which allow the isolation of areas of different activity;

2) selection of the different count zones by means of a threshold with a variable window, so that it is possible to identify the levels of activity over and above the minimal value of the threshold in the dark areas, and the counts contained in the window width in the light areas. Relating these values to the value of the background scale it is possible to know the activity of the identified areas;

3) smoothing, which performs a considered average of the counts on 9 points, and allows a homogeneity of the image;

4) projection of 3-dimensional images, in which the spatial distribution of the radioactivity is represented as a vertical linear disposition from the base of each point, the lines of the base being divided horizontally into quarters;

5) choice of a vertical or horizontal profile and calculation of the activity ratio between single points selected by means of areas of interest defined with a light-pen.

RESULTS

In 55 patients the scintigraphic examination gave no evidence of areas of hyperfixation circumscribed by the radioindicator, and the successive processing of the scintiphotos confirmed the normality of the test, furnishing in 164 estimates an uptake ratio of 1.07 ± 0.06 between symmetrical or adjacent regions.

Fig. 1 shows the analysis procedure applied, in a normal case, to a segment of the lumbar spine. The original scintiphoto (A) is presented in the digital form (B) on the computer oscilloscope, and successively (C) the areas are marked by different activities; the dark areas are those over and above the minimal value of the fixed threshold and the light areas are those comprised in the window. Varying the level of the scale, therefore, the contrast (D, E, F) is modified progressively to isolate the areas of major uptake; the relative vertical outline (G) is chosen, in which the positive peaks corresponding to the vertebral body and the negative peaks or *plateau* of the discs are recognized. Also represented in fig. 1 is the vertical profile (H) relative to the sacro-lumbar spine of the image (I); note the first *apex* corresponding to the bladder; the horizontal profile (L), placed across the *ilium* and the *sacrum*, shows a prevalence of activity of the right *ilium*, which presented an uptake ratio of 1.10 in respect of the contralateral. The last images represent the two vertical profiles of the right (M) and left (O) hemithorax which show greater peak heights in relation to the clavicles, with a slightly tendency to an increased uptake of the right clavicle also imaged in the scintiphoto (N); the fixation ratio was 1.22.

In 21 patients affected with bone metastases, and in which the gamma-camera tests revealed single and multiple 'hot' areas, the re-examination confirmed the evidence demonstrating, in 44 conclusions, an activity ratio of 1.80 ± 0.32 in comparison with the normal uptake of the bone.

In two cases it was possible, both on the processing basis and on the activity quantification, to demonstrate areas of increased uptake which in the original scintiphoto appeared doubtful. Fig. 2 demonstrates one of these: it concerns a patient who had already undergone a mastoidectomy for cancer, and in which the scintiphotos (A-D) showed a 'hot' area corresponding to the right transverse apophysis of C4, with an evident peak of activity (C) and a ratio of 2.37 compared to the adjacent regions. The scintiphoto of the sacro-lumbar (G) region originated a doubt of a slight hyperfixation in L4, which only a re-examination (H, I, M) enabled to interpret as a 'hot' area, which corresponded to a peak in the vertical profile (L) with a ratio of 1.77, well visible even in the 3-dimensional image (N).

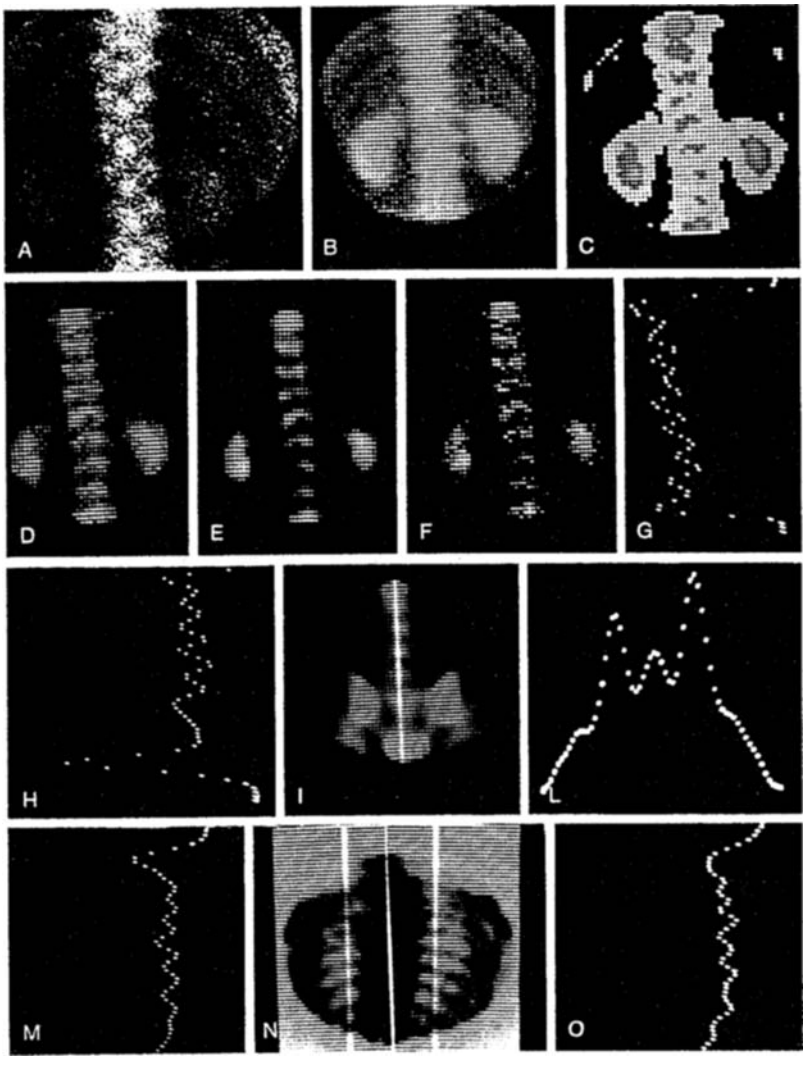


Fig. 1 - Processing procedure with the computer of the scintiphotographic images in a normal case (see text).

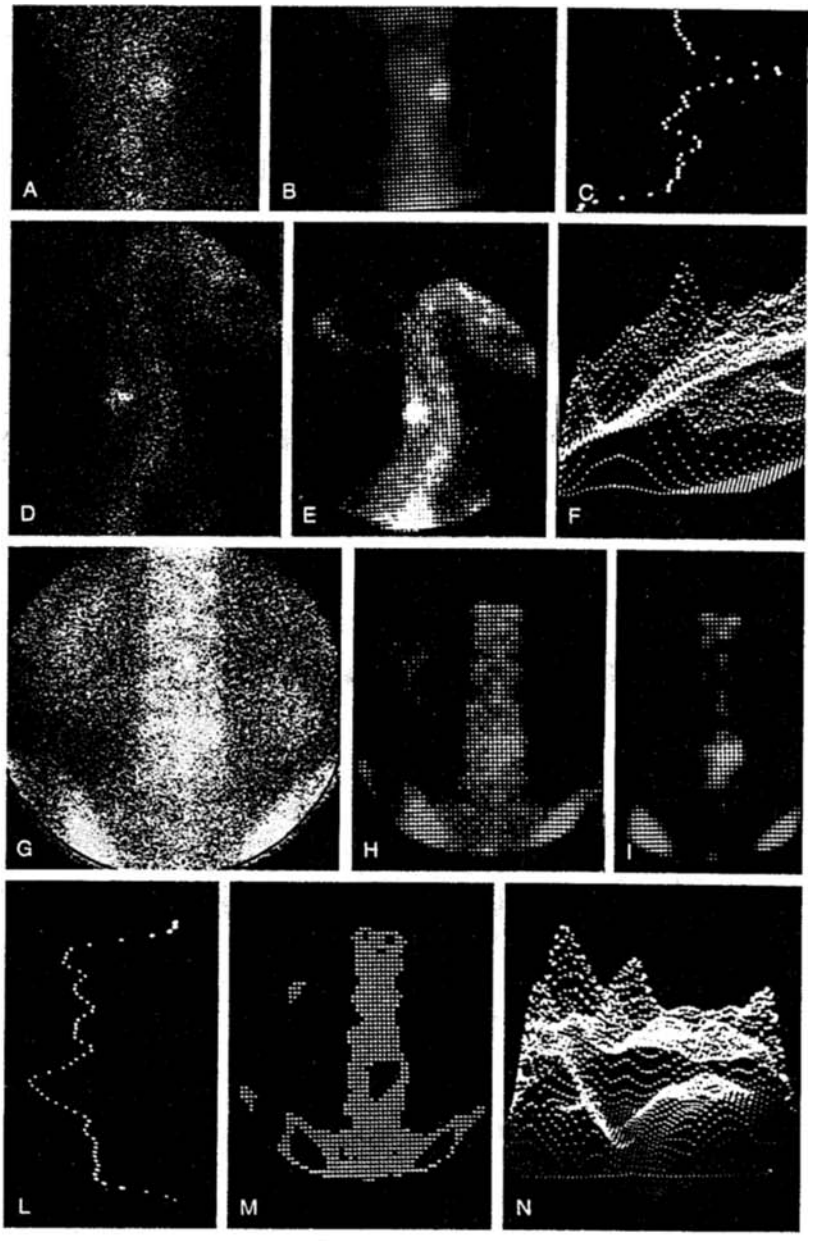


Fig. 2 - Evidence of 'hot' area corresponding to the right transversal apophysis of C4, posterior view (A, B) and right lateral (D, E) which corresponds with an evident activity peak in the vertical profile (C) well visible also in the 3-dimensional image (F). The scintiphoto of the sacro-lumbar (G) region gives rise to the suspicion of a relative increased uptake also in L4, which the processing (H, I, M) and the 3-dimensional presentation (N) allow to demonstrate and which corresponds to the peak in the vertical profile (L).

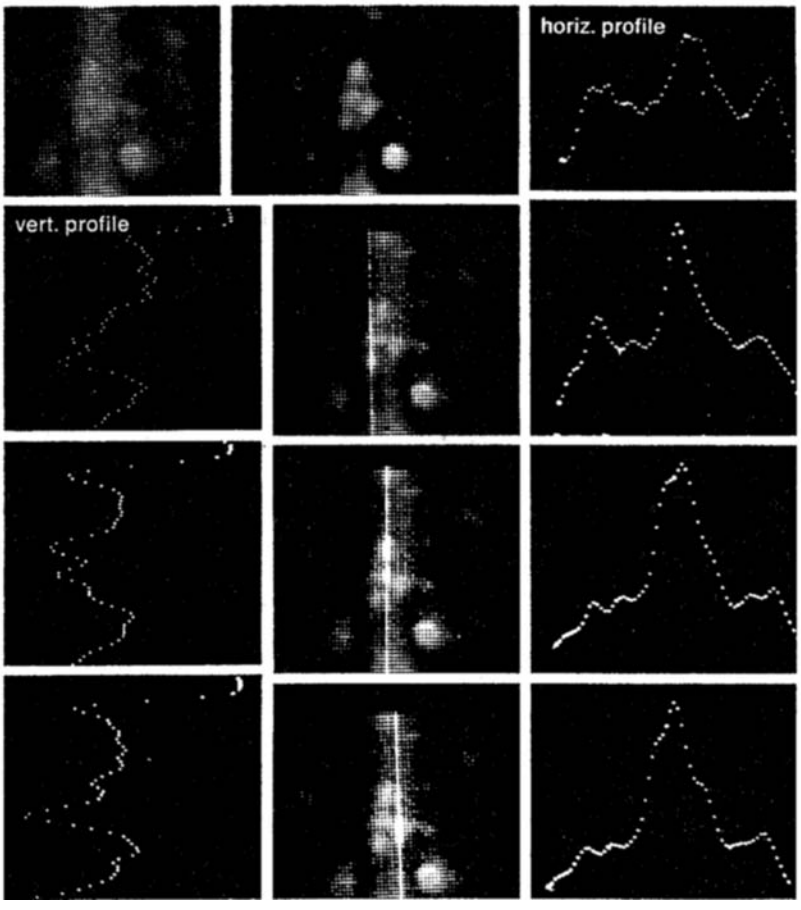


Fig. 3 - Multiple 'hot' areas corresponding to the lumbar spine; on the left the vertical profiles relative to the left transversal apophysis, the vertebral body and the right transversal apophysis; on the right the horizontal profiles at the level of single *vertebrae*.

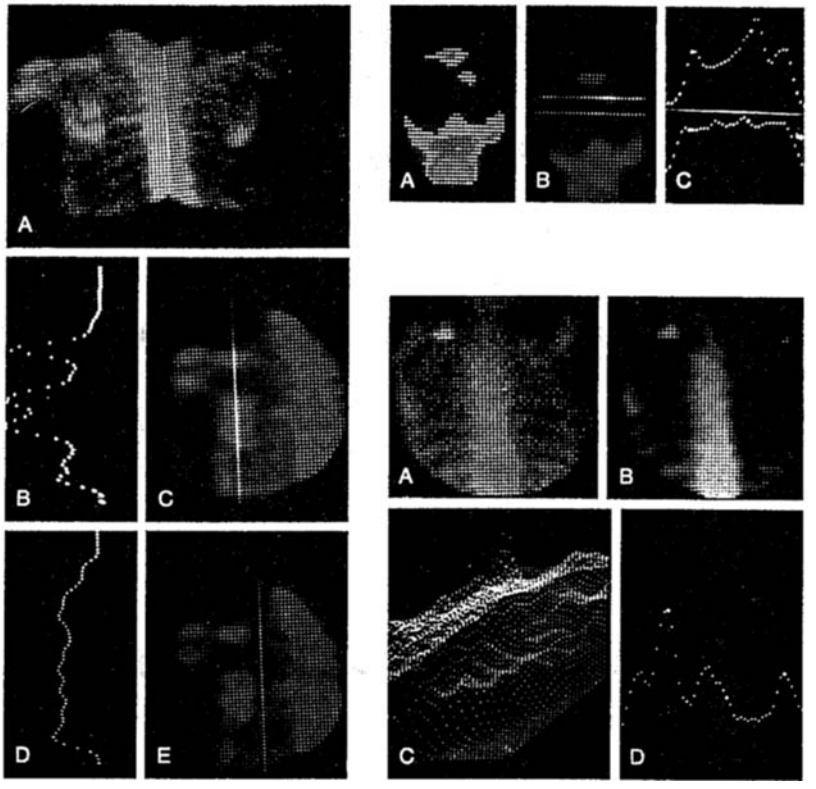


Fig. 4 - On the left: processed image, anterior view (A) which shows the 'hot' areas at the level of the shoulder, the clavicle and the two right costal tracts. The vertical outline (B) placed in correspondence with the lesions (C) shows activity peaks not recognized in that (D) placed outside (E). On the right: above, a case of skull metastases with relative horizontal profile on the lesion and that below (B, C). Below: small metastases of the left clavicle (A, B) which correspond to a clear activity peak both in the 3-dimensional image (C), and in the horizontal profile (D).

Fig. 5 - Above: neoplasm of the right maxillary *sinus*, anterior view (A) and right lateral (B) with the relative horizontal profile (C); vertical profile corresponding to the right (D) and left (F) maxillary sinuses (E). Centre and below: vertebral metastases (B) with relative vertical profiles (A). ▶

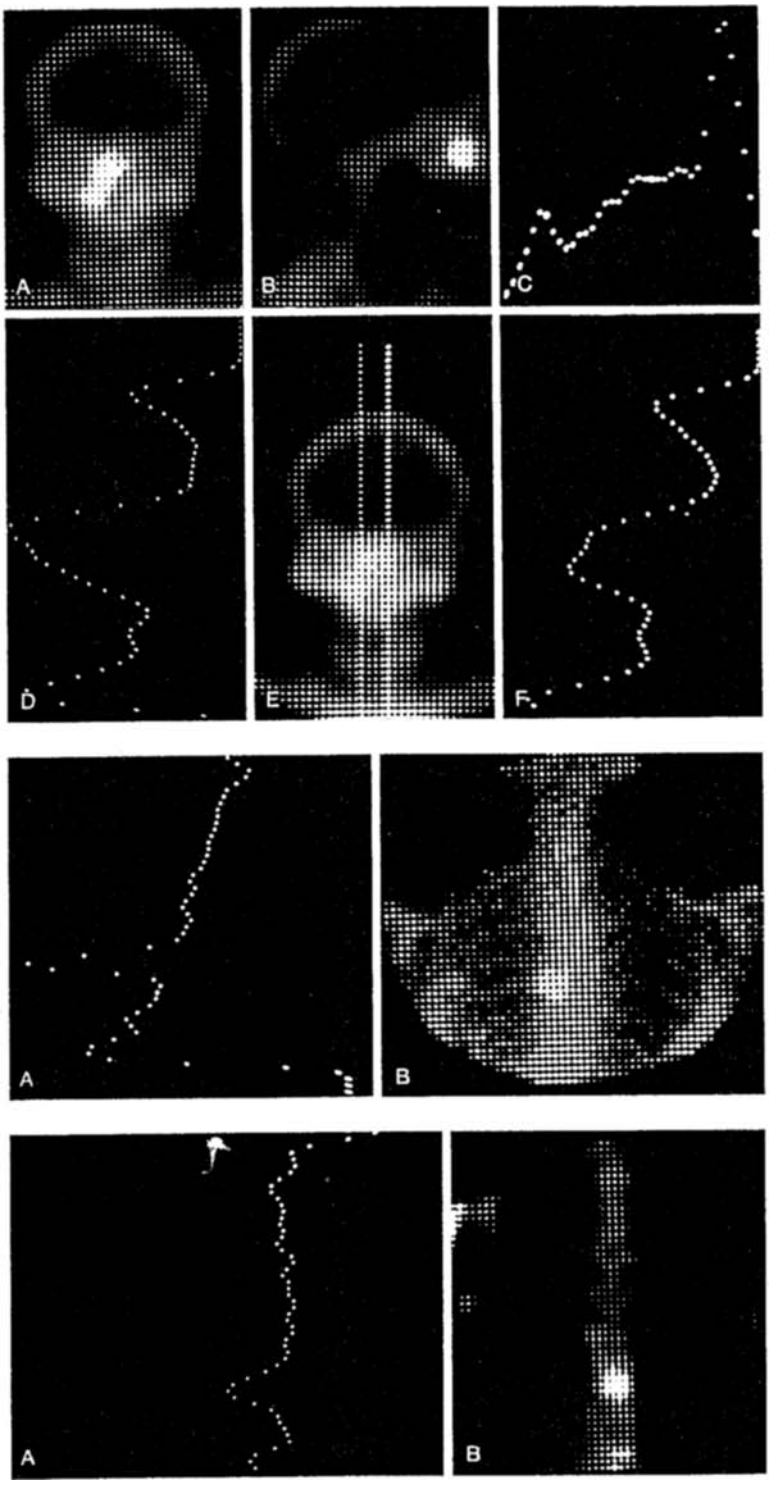
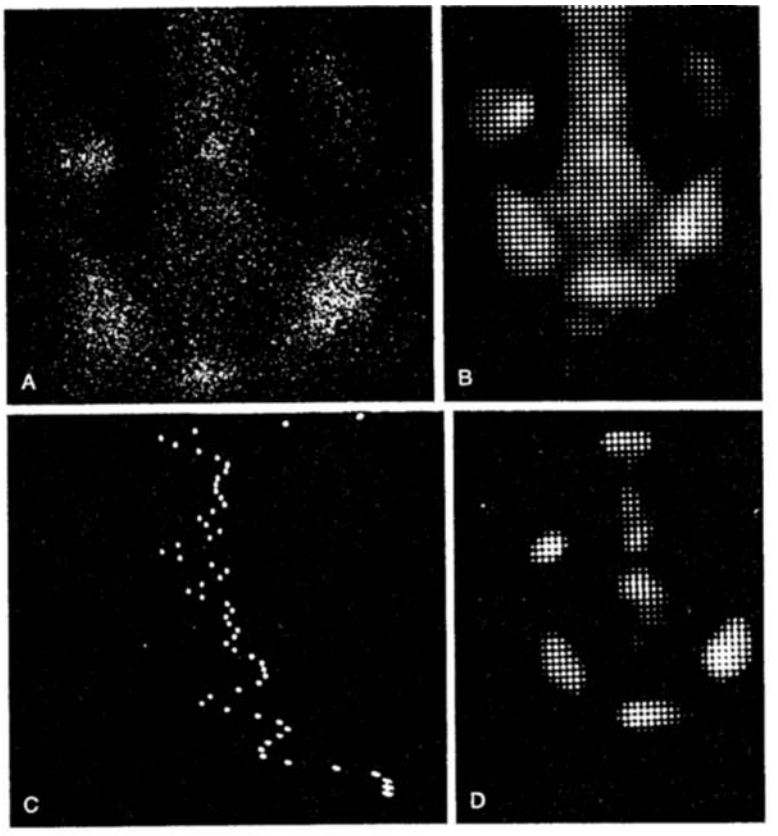

A
B
C
D
E
F
A
B
A
B

Fig. 6 - Slightly increased uptake of the tracer corresponding to L2-L3 (A), more visible in the ▶ processed images (B, D) corresponding to two activity peaks in the vertical profile (C). Below: same findings at the level of right transversal processes of D10-D11 (A) well shown in the digital image (B) with activity peaks in the vertical profile (D), absent in that placed on the left transversal apophysis (C).


A
B
C
D

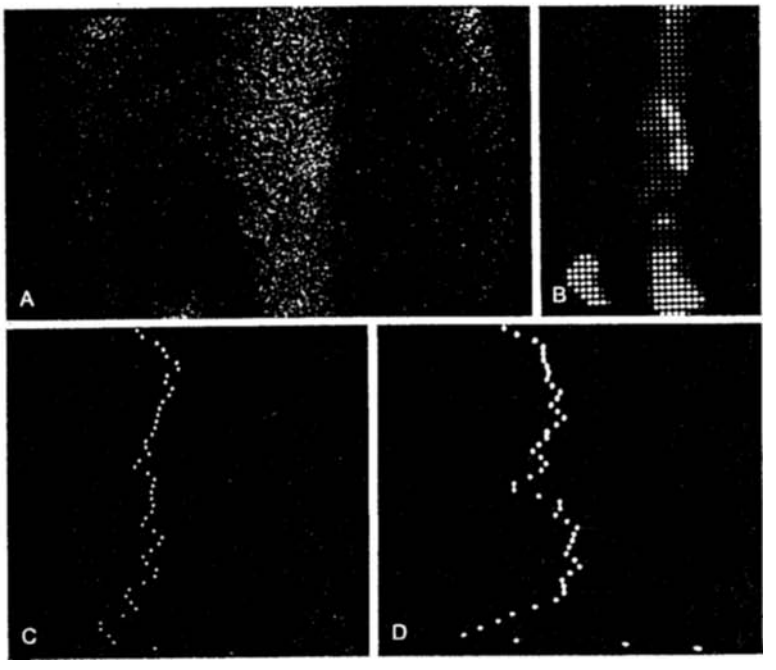

A
B
C
D

Fig. 3, which refers to another case of vertebral metastases, shows not only the best definition of the small areas of uptake circumscribed by the tracer, available with the digital treatment of the information but, above all, by gradually moving the profile, the possibility of estimating the uptake entity of single skeletal regions of slight dimensions.

Fig. 4 shows other examples of quantification of the findings; on the left, a case of shoulder, ribs and right clavicle localization in which only the processing permits the discrimination of the single 'hot' areas which correspond to a profile (B) clearly different from that (D) placed outside it. On the right, other examples of the definition of small lesions to the skull and clavicle. Fig. 5 shows a finding in three patients: above, a case of neoplasm of the right maxillary *sinus* in which the vertical and horizontal profiles confirm the scintiphotographic evidence; at centre and below, two cases of vertebral metastases.

In 4 patients suffering from metastatic bone neoplasms, the scintigraphic examination showed zones of slight increase of uptake of the tracer which, although resulting well-defined after processing, presented a gradient of 1.24 ± 0.09 in 14 determinations. Two of these cases are illustrated in fig. 6: above, note the increased uptake of L2-L3, which corresponds to two slight peaks in the vertical profile with a ratio of 1.39 and 1.22; the other images demonstrate an increased uptake of the tracer to the transversal apophysis of D10 and D11, with points characterized by a gradient of 1.33 and 1.24. The profile relative to the left transversal processes seems regular, with a ratio between the *vertebrae* of 1.02-1.04. In all these cases the radiographic examination was negative for 'hot'-bed lesions showing, in some, development of osteoarthrosis.

DISCUSSION

The coupling of a computer with the gamma-camera offers unquestionable advantages in interpreting skeletal scintigraphy, firstly the best definition of scintiphotos, with the possibility of isolating the smallest areas of increased uptake circumscribed by the tracer. As shown by some of the cases presented, it is possible to identify lesions seen with difficulty in the original scintiphoto, or even to bring out zones of hyperfixation which otherwise could go unnoticed.

But the main advantage is consequent to the quantification of the pyrophosphate uptake in single bone areas, which allows the comparison between regions of interest, and therefore suspected areas, with normal zones, and to estimate the regional distribution of the radioactivity.

Using a standard method for the dosage of radiopharmaceuticals and for the execution and projection times of the scintiphotos, it was possible in this way to establish that the gradient of activity in the altered areas is clearly higher in respect of that in the normal bone.

The finding of a lowest uptake ratio by small zones of uptake to which radiologically corresponded *foci* of arthrosis gives us the hope, from the examination of wider case reports, of a differential diagnosis of metastases. Dealing with patients operated for breast carcinoma, however, as in the cases observed by us, it is not to be excluded that such finding can, with regular controls, assume importance concerning initial metastatic lesions; this would contribute to the further estimation of the already noted precocity of scintigraphy in revealing skeletal alterations before the bone erosion becomes radiologically visible.

The control of the fixation entity should, moreover, assume particular importance in estimating the response to treatment of the metastases, because every significant variation would represent a different biological activity of the lesions [3].

On the basis of our first experiences we can conclude that the use of a computer coupled with the gamma-camera improves the representation of skeletal lesions and, above all, furnishes more objective information in bone scintigraphy.

SUMMARY

The use of a computer coupled on-line with the scintillation camera allows an improvement of the finding of skeletal scintigraphy realized with ^{99m}Tc-pyrophosphate, making possible the identification of the smallest bone lesions. It also makes possible the quantification of the uptake degree of the radioindicator demonstrating, in normal subjects, an uptake ratio between the various skeletal segments of 1.07 ± 0.06. In 44 metastatic lesions the ratio was 1.80 ± 0.32, whilst in 14 areas of slight hyperfixation of the tracer a value of 1.24 ± 0.09 was found. Since we were dealing with patients suffering from metastatic bone neoplasms, the authors outline the possibility that the quantification of data will allow the demonstration of the bone metastases even more precociously than with traditional scintigraphic examination.

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