

## BONE SCANNING WITH $^{99}\text{Tc}^{\text{m}}$ COMPOUNDS IN METASTASIZING MAMMARY CARCINOMA

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Since the introduction of short-lived isotopes ( $^{18}\text{F}$ ,  $^{87}\text{Sr}^{\text{m}}$ ) for bone scanning, this method has been generally accepted and its value recognized for the detection of bone metastases as it seems to be more sensitive than radiography (GREENBERG et coll. 1966, GALASKO & DOYLE 1972). Other lesions of the skeleton may also cause an increased uptake of the bone-seeking isotope, however, and it is thus important that the results of scanning and of radiography be compared (GALASKO & DOYLE).

The use of this method in the routine clinical work has further increased after application of the  $^{99}\text{Tc}^{\text{m}}$  polyphosphate compounds (SUBRAMANIAN et coll. 1972), which have an energy more suitable for the gamma camera.  $^{99}\text{Tc}^{\text{m}}$  also gives a lower radiation dose to the patient than do  $^{18}\text{F}$  and  $^{87}\text{Sr}^{\text{m}}$  (PENDERGRASS et coll. 1973, QUINN et coll. 1973).

$^{99}\text{Tc}^{\text{m}}$  polyphosphate has been used routinely at our department since 1972 for the detection of bone metastases, mainly in patients with mammary and prostatic carcinoma. However, more stable compounds, with a higher and more regular uptake in the metastatic lesions and with as low an uptake as possible in the soft tissues would seem desirable.  $^{99}\text{Tc}^{\text{m}}$ -labelled diphosphonate, polyphosphate and pyrophosphate were compared by DUNSON et coll. (1973) for bone scanning in animal experi-

ments. They reached the conclusion that the diphosphonate compound was to be preferred.

HOSAIN et coll. (1973) compared the same three  $^{99}\text{Tc}^{\text{m}}$  compounds, and  $^{18}\text{F}$  and  $^{87}\text{Sr}^{\text{m}}$ , in animal experiments as well as in a number of patients. They concluded that  $^{18}\text{F}$  was the best agent for the rectilinear scanner, but that pyrophosphate appeared to be better from the aspect of ease of preparation, reproducibility and quality of scan.

Bone scanning with the gamma camera, using  $^{99}\text{Tc}^{\text{m}}$  polyphosphate, diphosphonate and pyrophosphate, was performed in patients with metastasizing mammary carcinoma, and the results are presented in the present report.

*Material and Methods.* The material consisted of 9 patients with mammary carcinoma and with several roentgenologically demonstrated and cytologically verified metastases in the skeleton. All had been subjected to either pre- or postoperative radiation therapy to the mammary region and to the axillary glands, in some cases also to local radiation therapy of some of the metastases. All patients were treated with cortisone or anabolic steroids. Cytostatic or radiation therapy was however not delivered during the period of or immediately before the bone scanning procedures.

Seven patients had a low-differentiated and two a moderately well-differentiated mammary carcinoma. In each patient all three types of bone-imaging compounds were tested with an interval of at least two days between each examination in order to exclude any remaining activity from the previous compound. The order of the different compounds was chosen at random.  $^{99}\text{Tc}^{\text{m}}$  polyphosphate and  $^{99}\text{Tc}^{\text{m}}$  diphosphonate were obtained from Diagnostic Isotopes Inc. (New Jersey, USA) and  $^{99}\text{Tc}^{\text{m}}$  pyrophosphate from Nyegaard & Co. (Oslo, Norway) and were prepared in strict accordance with the instructions supplied from the manufacturers.

Each  $^{99}\text{Tc}^{\text{m}}$  kit used was checked with respect to chemical purity through the use of descending paper chromatography with methanol 85 % as solvent. Polyphosphate, diphosphonate and pyrophosphate remained at the application point while the  $R_f$  value of free pertechnetate was 0.40 to 0.60. The amount of unbound pertechnetate present in the different preparations was in all cases below 5 per cent. The chromatograms of pyrophosphate showed 0 to 20 per cent of the activity in the  $R_f$  0.70 to 0.85 region. This part we have not been able to identify chemically.

The equipment used for the recordings was either the HP Gamma Camera or the Pho/Gamma III from Nuclear Chicago. In both cases, the 140 keV diverging collimator was used. For every patient, the same type of gamma camera was used throughout and the time between the injection of the active compound and the beginning of the scanning was three hours. In each examination 5 recordings were made; posterior scans were obtained of the head and neck region, the thoracic region, the lower thoracic and lumbar region, and finally the pelvic region. For the pelvic region, an anterior scan was also regularly obtained. Each recording was evaluated independently by the two physicians in the team without knowledge of the type of

**Table**

*Comparison of gamma camera images using  $^{99}\text{Tc}^m$  polyphosphate,  $^{99}\text{Tc}^m$  diphosphonate and  $^{99}\text{Tc}^m$  pyrophosphate. Mean numbers from 9 patients. The uptake was estimated blindly by two independent examiners and scored 1-3, where 1 is low and 3 is high*

	Pyrophosphate	p	Diphosphonate	p	Polyphosphate
Number of separate lesions observed $\pm$ SE	11.0 $\pm$ 2.2	—	18.1 $\pm$ 3.1	—	13.4 $\pm$ 3.1
Gradient skeleton/background $\pm$ SE	2.0 $\pm$ 0.1	<0.05	2.6 $\pm$ 0.2	—	2.1 $\pm$ 0.2
Gradient separate lesions/skeleton $\pm$ SE	2.1 $\pm$ 0.1	<0.01	2.7 $\pm$ 0.1	<0.05	2.1 $\pm$ 0.2

compound used for the recordings. The gradient of uptake in normal skeleton to background activity, the gradient of uptake in metastatic lesions to the normal skeleton and the number of lesions observed were evaluated from the Polaroid views.

In the last three patients examined, the number of counts within a specified area was recorded for soft tissue activity, uptake in normal vertebrae and a vertebra with a metastatic deposit using the image data processing system Med II from Nuclear Data.

### Results

In all patients the best results for each of the criteria evaluated were obtained with  $^{99}\text{Tc}^m$  diphosphonate (Table). For  $^{99}\text{Tc}^m$  polyphosphate and  $^{99}\text{Tc}^m$  pyrophosphate the results varied. The diphosphonate was significantly better than the pyrophosphate ( $p < 0.01$ ) and polyphosphate ( $p < 0.05$ ) in regard to the gradient separate lesions/skeleton. The diphosphonate was also significantly ( $p < 0.05$ ) better than the pyrophosphate in regard to the gradient skeleton/background. More metastatic lesions were identified by the gamma camera than by radiology in all cases, and the lesions were more evident and better outlined using diphosphonate. When reviewing the computer data from the three patients, it was also found that diphosphonate exhibited the best results for the gradient skeleton/background and for the gradient separate lesions/skeleton.

One patient with a metastasizing follicular thyroid carcinoma was also examined in the same way as the patients with mammary carcinoma. This patient is not included in the table but also in this type of tumour the same results were obtained.

*Discussion.* In patients with mammary carcinoma the most suitable of the three tested compounds was the  $^{99}\text{Tc}^m$  diphosphonate, as in the animal experiments of DUNSON et coll.

All patients were undergoing therapy with cortisone or anabolic steroids. The uptake of  $^{18}\text{F}$  in metastatic lesions of the skeleton during the first four months after beginning of chemotherapy or hormonal therapy remains unchanged (KAMPFFMEYER et coll. 1967). Thus, it is probable that the anti-tumour therapy in the present material did not influence the results obtained.

## SUMMARY

A comparison of three compounds for bone scanning has been carried out in 9 patients with metastatic mammary carcinoma for evaluating their effectiveness. The best results were obtained with  $^{99}\text{Tc}^m$  diphosphonate. For the other two compounds tested,  $^{99}\text{Tc}^m$  polyphosphate and  $^{99}\text{Tc}^m$  pyrophosphate, no difference could be demonstrated.

## ZUSAMMENFASSUNG

Für einen Vergleich von drei Substanzen wurden Knochenszintigraphie bei 9 Patienten mit metastatischen Mammakarzinom vorgenommen, um deren Effektivität festzustellen. Die besten Ergebnisse wurden mit  $^{99}\text{Tc}^m$  Diphosphat erhalten. Für die anderen beiden untersuchten Substanzen,  $^{99}\text{Tc}^m$  Polyphosphat und  $^{99}\text{Tc}^m$  Pyrophosphat, konnte kein Unterschied nachgewiesen werden.

## RÉSUMÉ

Pour apprécier l'efficacité de trois composés destinés à la scintigraphie osseuse les auteurs ont effectué une étude comparative sur 9 malades atteintes de métastase de cancer du sein. Les meilleurs résultats ont été obtenus avec le diphosphate de  $^{99}\text{Tc}^m$ . Ils n'ont pas constaté de différence entre les deux autres composés expérimentés, le polyphosphate de  $^{99}\text{Tc}^m$  et le pyrophosphate de  $^{99}\text{Tc}^m$ .

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