VISUALIZATION OF BONE TUMORS WITH ^{99m}Tc-GP: A COMPARATIVE STUDY

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SUMMARY: The potential of ^{99m}Tc-GP as a lung tumor scanning agent was reported. In this study, we adressed the question of whether ^{99m}Tc-GP can accumulate in various bone disease. 22 patients with various bone disease were studied by ^{99m}Tc-GP as well as by ^{99m}Tc-MDP. We report the results of the visualization and quantitation of ^{99m}Tc-GP uptake and a comparison with ^{99m}Tc-MDP. All bone pathologies demonstrated by ^{99m}Tc-MDP were also visualized with ^{99m}Tc-GP. Althoungh the target/nontarget ratios obtained by ^{99m}Tc-GP were inferior to those obtained by ^{99m}Tc-MDP, the differences were not significant for all kinds of bone pathologies ($p>0.05$). It was concluded that although ^{99m}Tc-GP can demostrate the bone pathologies; it is not as sensitive and specific as ^{99m}TcMDP. The mechanism of ^{99m}Tc-GP uptake in bone pathologies is not clearly understood.

Key Words: ^{99m}Tc-GP, ^{99m}Tc-MDP, bone tumors.

INTRODUCTION

The labelling of α-D-glucose-1-phospate (GP) with ^{99m}Tc-GP with a high efficiency and its accumulation in primary lung cancer was previously reported by our group (1). ^{99m}Tc-GP was further compared to ^{67}Ga in another group of subjects (2) and found to be useful in the scintigraphic visualization of lung carcinoma. The uptake mechamism was attributed to its being a glucose anologue; so an active transport by metabolically active tumor tissue. ^{99m}Tc-GP was also successfully used in gated cardiac blood pool imaging (3) and in labelling RBC's for spleen imaging (4). All these studies proved ^{99m}Tc-GP to be an ideal radiopharmaceutical prepared in-house by a simple and rapid procedure, being stable both *in vitro* and *in vivo*.

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Many phospate compounds have been labelled with ^{99m}Tc and tested for bone imaging since the introduction of the first radiopharmaceutical by subramanian *et al.* in 1971 (5). ^{99m}Tc-methylene diphosphonate (MDP) proved to be the ideal bone imaging agent and is currently in routine use (6). The normal bone accumulates these radiopharmaceuticals and as a result the skeleton is visualized. In bone pathology there is increased uptake. However, ^{99m}Tc-GP is not accumulated by normal bone (1,2), although GP is a phosphate compound. This promted the idea that it might accumulate in primary bone tumor with higher uptake and target-to-nontarget concentration ratios. THe present study was undertaken to test the sensitivity and specificity of ^{99m}Tc-GP as a radiopharmaceutical in primary bone tumor imaging in comparison to ^{99m}Tc-MDP.

MATERIALS AND METHODS

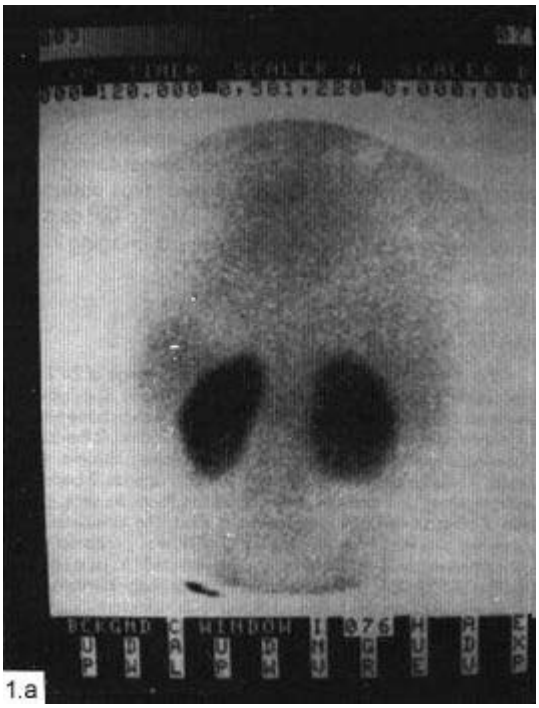
22 patiens (11 female, 11 male) with an age range of 2-72 underwent both ^{99m}Tc-MDP bone scan and ^{99m}Tc-GP study. They gave their informed consent to be included in this study. 6 malign bone tumors (2 osteosarchoma, 1 giant cell tumour, 1 chondrosarcoma, 2 metastases), 7 benign bone tumors (2 chondroma, 1 ossifying fibroma, 4 bone cysts), 5 inflammatory bone diseases (2 septic arthritis, 2 bone Tbc, 1 osteomyelitis), 2 metabolic bone disease (both Paget's disease) and 2 other bone pathologies were studied. The time interval between the two tests was 2-7 days. ^{99m}Tc-GP was prepared as described previously (1-3). The patients were injected I. V. as a bolus with 15-20mCi ^{99m}Tc-GP; dynamic and blood pool images were recorded in order to evaluate the lesion in respect to its vascularity, using a parallel hole all purpose low energy collimator and a gamma camera (Toshiba GCA-601 E and Siemens ZLC 75). At 3 h post-injection static images were recorded. Target/nontarget ratios were calculated by the use of ROI drawn over the diseased areas (if any) and corresponding nondiseased areas at the opposite side. The ratios of target/nonvascular structure were also calculated. The same procedure was performed for routine ^{99m}Tc-MDP bone scanning. 20 mCi ^{99m}Tc-MDP was injected to each patient. Whole body scintigrams were obtained at 3 h post-injection.

Table 1: Summary of information on patients.

No. of Patients	sex		Pathology			
	M	F	Tumor	Inflammatory	Metabolic	Others
22	11	11	13	5	2	2

RESULTS

Summary of information on patients who underwent both ^{99m}Tc-GP and ^{99m}Tc-MDP is outlined in Table 1. The normal bone was not visualized in ^{99m}Tc-GP scintigrams (Figure 1a). There was some soft tissue activity due to blood background. The radiopharmaceutical was mainly excreted by the kidneys. The kidneys were more prominent than the liver. Epyphisis lines could be visualized very clearly in case the patient was still in the growing period. All bone pathologies demonstrated by ^{99m}Tc-MDP, even nonvascular were also visualized by ^{99m}Tc-GP. In some pathologies, bone uptake was increased. Figure 1b is a posterior ^{99m}Tc-GP image of a patient with widespread vertebral column metastases. Note the vertebral column uptake not visualized in the normal case (Figure 1a) Figure 2 shows a comparison of ^{99m}Tc-GP and ^{99m}Tc-MDP images of a 22-year-old girl with painful left knee for 1 mo. Lesion is extremely vascular as demonstrated by blood pool study. Both ^{99m}Tc-GP and ^{99m}Tc-MDP scans



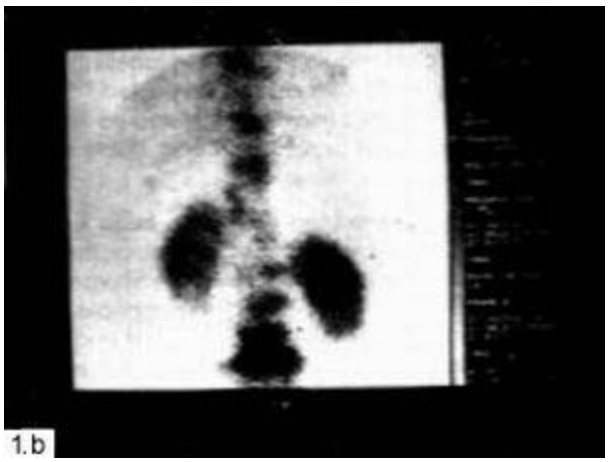
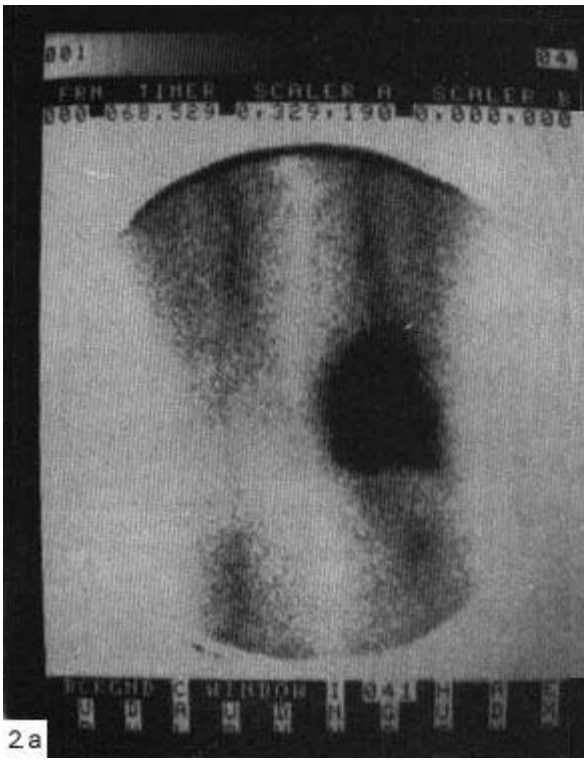
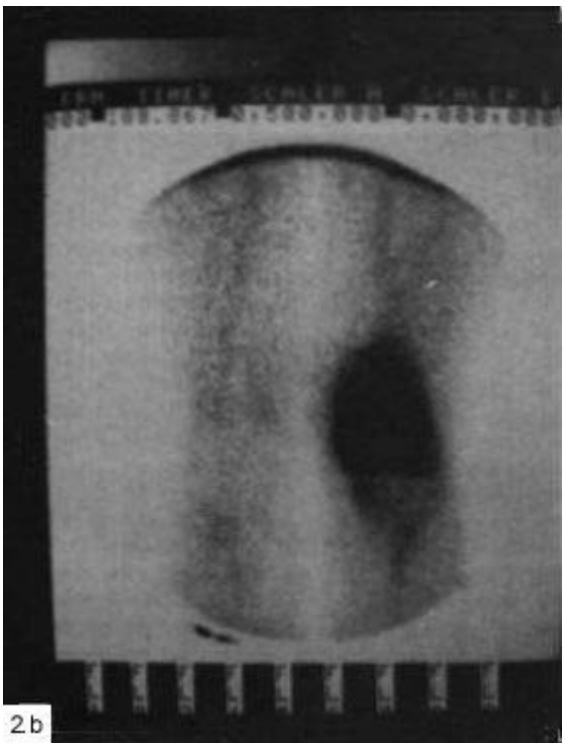


Figure 1: A normal scintigram obtained with ^{99m}Tc-GP(a) and a patient with multiple vertebral metastases (b) showing diffusely increased uptake of the vertebrae. Adenocarcinoma metas tosis to vertebral column was confirmed by biopsy.





illustrate increased uptake around the left knee. Selected benign bone tumors and a case with septic arthritis showing increased abnormal accumulation in involved areas

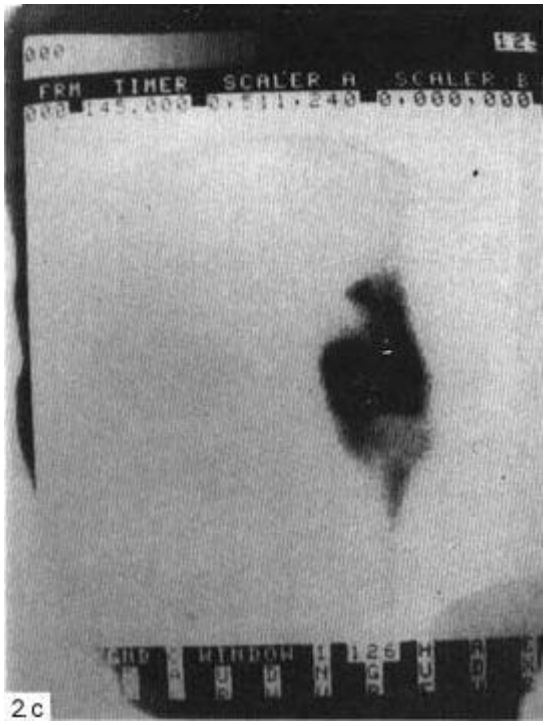
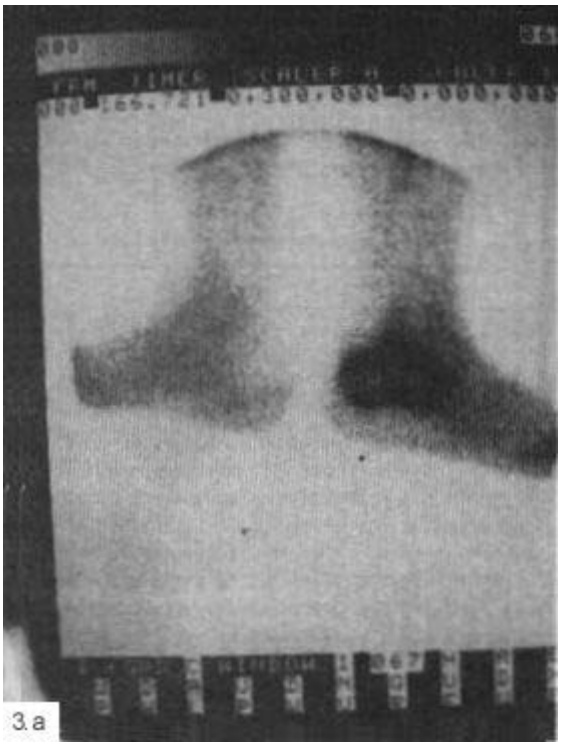


Figure 2: Anterior lower limb ^{99m}Tc-GP (a-blood pool, b-static) and ^{99m}Tc-MDP images (c) of a patients with left femur osteosarcoma.

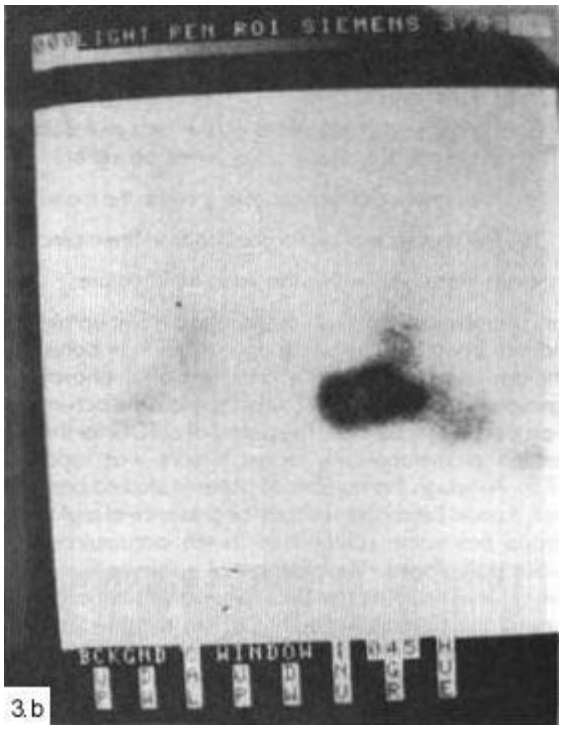
are illustrated in Figures 3, 4 and 5. Marked uptake in the left hip, left femoral and vertebral column due to Paget's disease is seen in Figure 6a. In Table 2 the target/nontarget ratios for ^{99m}Tc-GP and ^{99m}Tc-MDP are summarized. The mean target/nontarget ratios for ^{99m}Tc-GP and ^{99m}Tc-MDP were 2.58 ± 1.01 and 3.69 ± 1.70 for benign ($p>0.05$) and 3.59 ± 1.87 and 6.65 ± 3.91 for malign bone tumors ($p>0.05$), respectively.

DISCUSSION

Since the introduction of ^{99m}Tc-GP as a lung tumor agent by Ercan *et al.* (1), in order to test the value of ^{99m}Tc-GP in bone pathologies a prospective study has been performed, including patients with various bone pathologies. The results were compared to those obtained by ^{99m}Tc-MDP bone scan, both qualitatively and quantitatively. Following the administration of ^{99m}Tc-GP, its distribution in total body is a reflection of vascular structures. Faint visualization of bony structure was noticed. Increased uptake of bones was considered as pathological.



3.a



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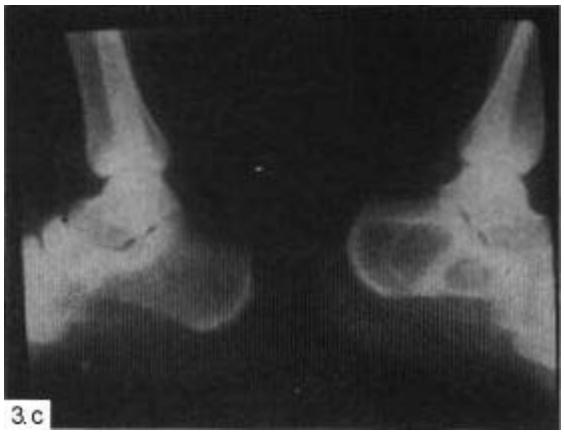

3.c

Figure 3: a) Posterior ^{99m}Tc-GP scan from a patient with bone cyst located in right calcenous, b) ^{99m}Tc-MDP bone scan and c) X-ray study of the same patient.

The underlying mechanism of the accumulation of ^{99m}Tc-GP in any bone pathology might be either:

a. The presence of a phosphate group in the molecule,

b. The presence of a glucose group in the molecule,

c. Its remaining within the vascular structures

or a combination of these mechanisms. Faint uptake by normal bone but prominent accumulation in bone pathology suggests that the presence of a phosphate group within the molecule can not explain the accumulation mechanism by itself. The potential of FDG for the detection of metabolically active tumors was reported (7,8). Although the number of patients studied are limited; it could be concluded that the presence of a glucose group has some contribution to the accumulation in bone pathologies. Visualization of epiphyseal regions which are known as metabolically active sites might be one of the supportive findings of this hypothesis. With ^{99m}Tc-GP only the pathologic bone is visualized. Although the target-to-nontarget ratios are lower (but not significant, $p>0.05$) the images are more prominent (Figures 1,2). This is a clear advantage of ^{99m}Tc-GP compared to ^{99m}Tc-MDP which is accumulated by normal bone.

Its remaining within the vascular structures may contribute to the visualization of the pathologies. But its ability to demonstrate not only vascular but also nonvascular pathologies suggested that, it alone can not explain the uptake mechanism.

Finally, having a phosphate molecule has been considered a more likely explanation for the accumulation mechanism. ^{99m}Tc-GP is a nonspecific agent because it can accumulate in almost all kinds of bone pathologies including inflammatory and metabolic diseases. Image quality in the visualization of the bone pathologies was

Table 2: Target/nontarget ratios obtained with ^{99m}Tc-GP and ^{99m}Tc-MDP.

	Tumor		Inflammation (n=5)	Metabolic (n=2)	Others (n=2)
	Benign (n=7)	Malign (n=6)			
^{99m}Tc-GP; Target/Nontarget Target/Nonvascular	2.58 ± 1.01* 11.47 ± 2.98	3.59 ± 1.87* 22.4 ± 7.29	1.51 ± 0.38* 10.3 ± 6.13	3.3 ± 0.97* 20.2 ± 0.85	1.41 ± 0.34* 4.7 ± 1.84
^{99m}Tc-MDP; Target/Nontarget Target/Nonosseos	3.69 ± 1.70 52.7 ± 40.5	6.65 ± 3.91 59.2 ± 44.8	1.98 ± 0.40 50.3 ± 34.9	9.19 ± 5.75 71.3 ± 0.85	3.49 ± 0.80 14.2 ± 8.20

* p value > 0.05 vs ^{99m}Tc-MDP.

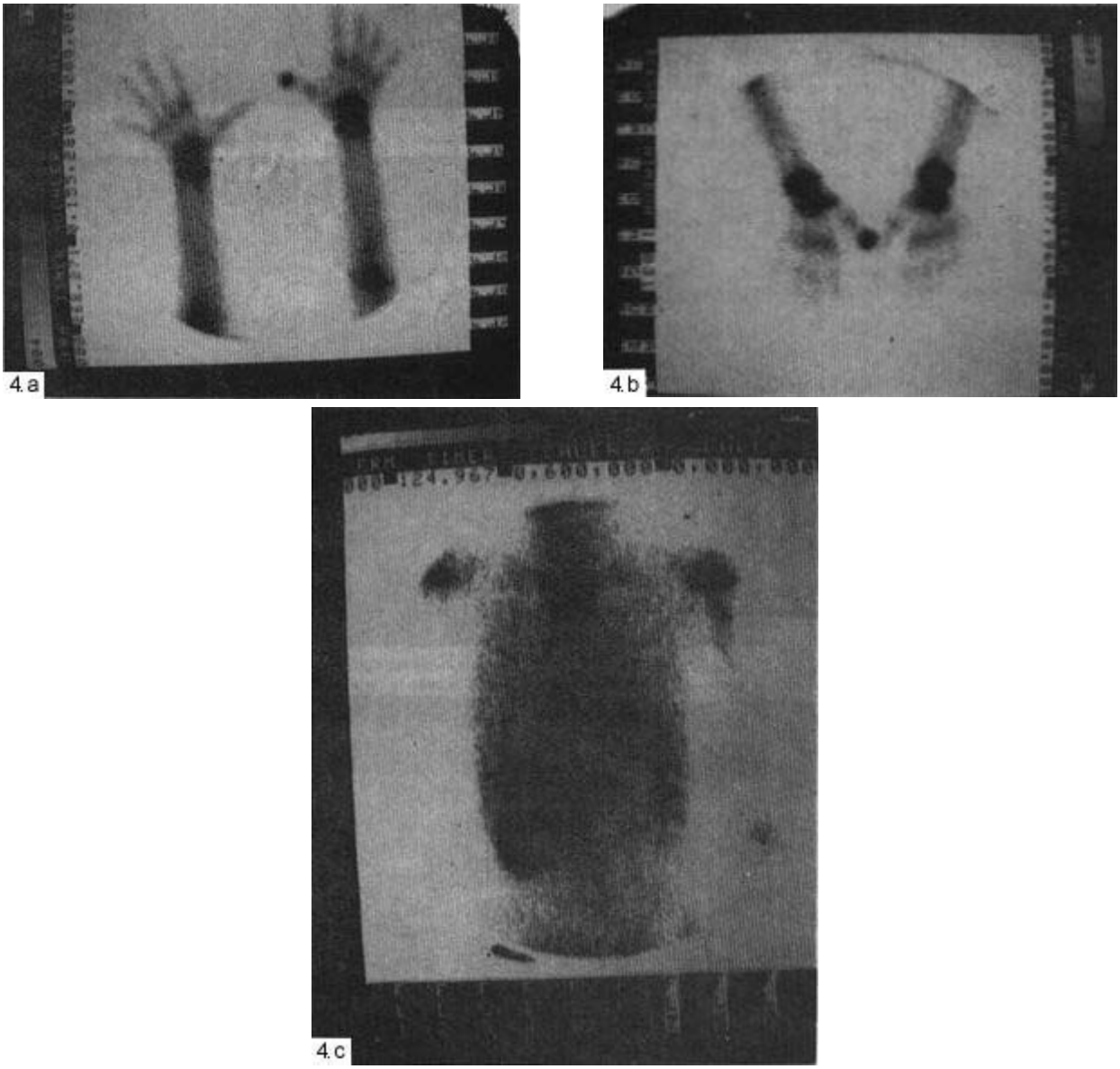

Figure 4: a) ^{99m}Tc-GP scan in a 4 year old-girl showing increased uptake in the right 1. phalanx, b) ^{99m}Tc-MDP image of the same patient and c) anterior ^{99m}Tc-GP image of thorax and abdomen. Note nonvisualization of left kidney. The diagnoses of left kidney aplasia was confirmed by ultrasonography.

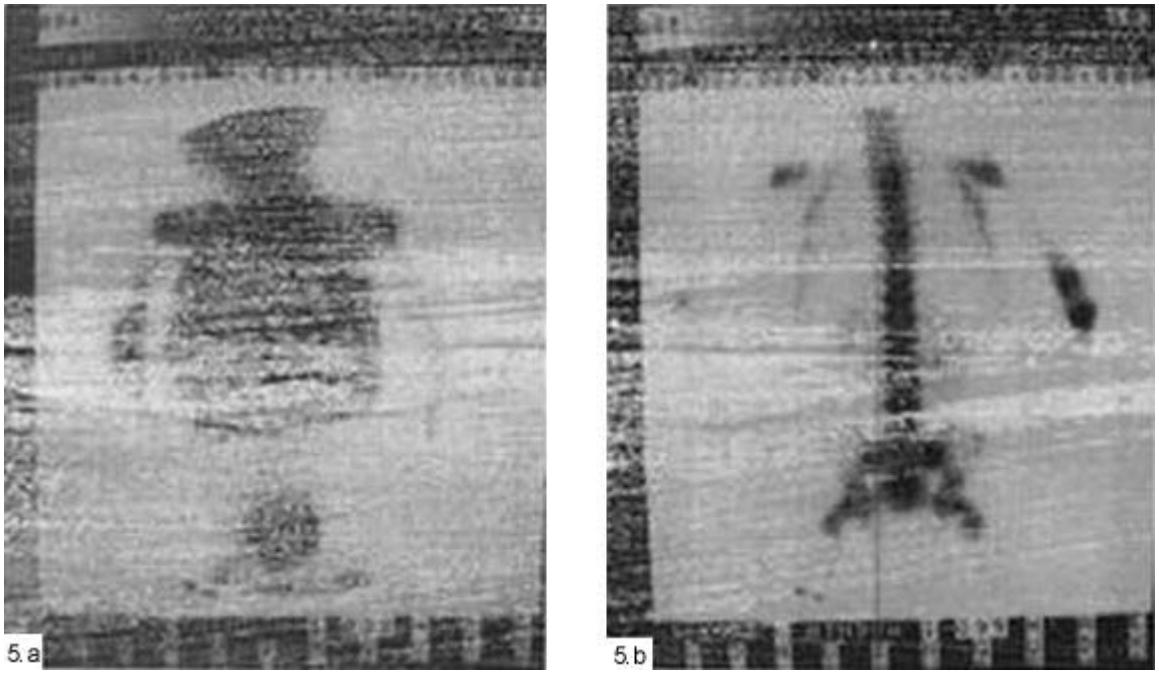

Figure 5: Images of a patient with septic arthritis involving right elbow. Left: anterior ^{99m}Tc-GP image, Right: posterior ^{99m}Tc-MDP bone scan. In both images increased accumulation is seen in in rignt elbow.

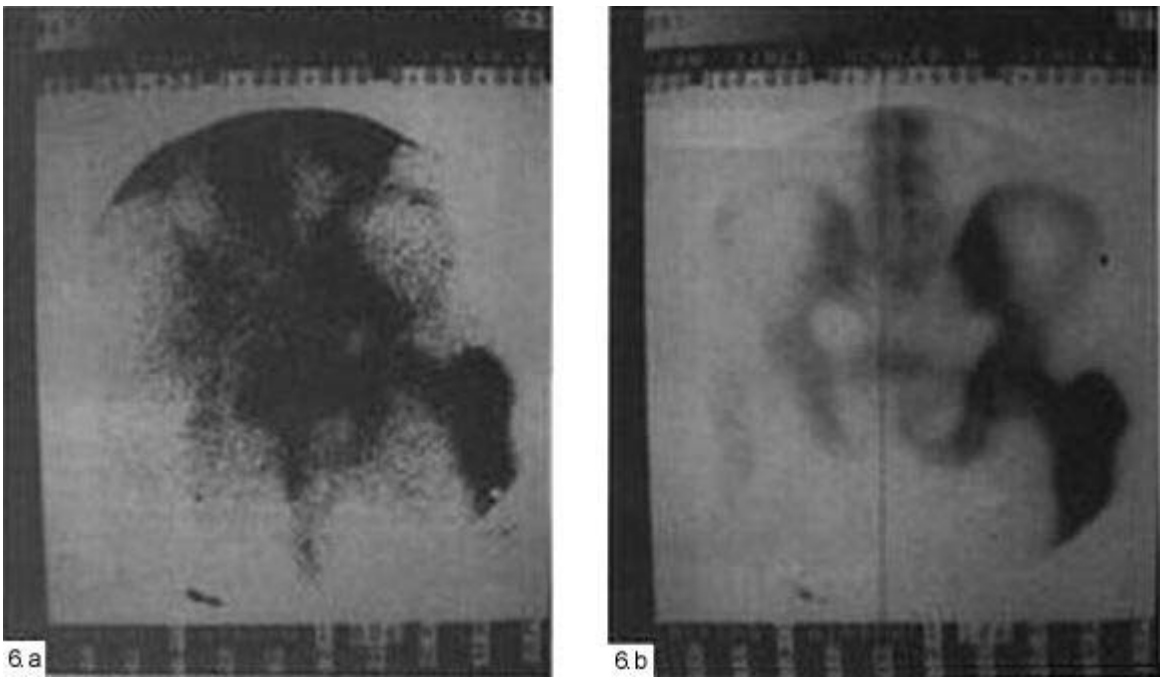

Figure 6: a) Anterior ^{99m}Tc-GP scan in a 45 year-old-man showing diffusely increased uptake in left pelvic bony structures as well as left femur and lumbar vertebrae. Note almost nonvisualization of the right hemiportion of pelvis b) ^{99m}Tc-MDP bone scan in the same patient shows abnormal accumulation in the same areas demonstrating increased uptake in ^{99m}Tc-GP image. He was diagnosed as having paget's disease.

inferior to that of ^{99m}Tc-MDP; but adequate hydration may improve it. Although the images were sufficient to clearly visualize bone pathologies; the target-to-nontarget ratios for ^{99m}Tc-GP were always less than those for ^{99m}Tc-MDP, suggesting that ^{99m}Tc-GP as a bone scanning agent is not as good as ^{99m}Tc-MDP. Visualization of lesions adjacent to the great vascular structures may be difficult with ^{99m}Tc-GP; because of the prolonged retention of this agent in these structures. As a side benefit, ^{99m}Tc-GP may also aid in the evaluation of kidneys (Figure 4), since it is mainly excreted through the kidneys. This radiopharmaucetical will be evaluated in this respect in a future communication. In short, it appeared from this study that ^{99m}Tc-GP behaves a similar manner to a bone scanning agent. The glucose group might increase its tumor affinity. Further investigation is necessary in order to evaluate its uptake mechanism properly.

REFERENCES

1. Ercan MT, Caner BE, Bekdik CF, Durak HS, Erbengi GF : ^{99m}Tc-α-D-Glucose 1-Phosphate imaging in lung cancer. Proceedings of European Nuclear Medicine Congress 1987, Nucl Med, 27:735-739, 1988.

2. Bekdik CF, Ercan MT, Caner BE, Baris I, Bernay I, Duman Y : ^{99m}Tc-GP for Lung Carcinoma Imaging: A Comparative study with ^{67}Ga. The Soc of Nucl Med 36th Annual Meeting, Sanit Louis, Mo USA, 13-16 June, 1989. Abst in J Nucl Med, 30:913, 1989.

3. Ercan MT, Aksut S, Aras T : Labelling and evaluation of ^{99m}Tc-α-D-Glucose 1-Phosphate for radionuclide angiocardiography. Hacettepe Med J, 20:1-9, 1987.

4. Ercan MT, Bernay I : A simple and efficient method of labelling RBC'S with ^{99m}Tc for spleen imaging. Nucl Med Biol (accepted).

5. Subramanian G, Mc Affee JG : A new complex of ^{99m}Tc for skeletal Imaging. Radiology, 99:192, 1971.

6. Bell EG, Subraminian G : The skeleton. In Textbook of Nuclear Medicine: Clinical Applications. Rocha AFG, Harbert JC, Lea and Febiger, p 109-128, 1979.

7. Wahl RL, Kaminski MS, Hutchins GD : The potential of F-18-deoxyglucose for the detection tumor involvement in lymph nodes. Abst in J Nucl Med, 29:904, 1988.

8. Okada J, Yoshikawa K, Uno K, et al : Evaluation of Flourine-18 2 Deoxy-2-Fluoro-D-glucose as an imaging agent in malignant lymphoma. Abst in J Nucl Med, 30:738, 1989.

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