# COMPARISON OF $^{18}F$ AND $^{99m}Tc$-POLYPHOSPHATE IN ORTHOPEDIC BONE SCINTIGRAPHY

Jan Heerfordt, Lise Vistisen, and Hans Bohr

*Rigshospitalet and The Niels Bohr Institute, Copenhagen, Denmark*

***To compare $^{99m}Tc$-polyphosphate and $^{18}F$ for use in orthopedics, 79 patients were examined with both. Fifty cases were suitable for analysis. While the extraskeletal uptake of $^{18}F$ was found to be negligible, $^{99m}Tc$-polyphosphate may accumulate considerably in pathologic soft tissue, e.g., in soft-tissue tumors and in inflamed synovial tissue. This soft-tissue Tc accumulation may obscure the osseous uptake, notably in the examination of joint regions, commonly the regions of interest in orthopedics. After simultaneous administration of both agents, quantitative measurements were performed on specimens of bone and synovial tissue from diseased joints in human patients and in rabbits. The uptake of $^{99m}Tc$-polyphosphate in synovial tissue was shown to be about seven times that of $^{18}F$, while their uptakes in bone were equal. In short, $^{99m}Tc$-polyphosphate, a valuable tracer in general, is hardly the agent of choice in orthopedics.***

This paper is based on experience with bone scintigraphy in orthopedic diagnostics, mainly in degenerative joint disease and in primary bone tumors. Initially, only $^{18}F$ was used, but $^{99m}Tc$-polyphosphate (Tc-PP) was introduced due to its easier access. Since differences of importance in orthopedic diagnostics were observed, a comparative study of the uptakes of Tc-PP and $^{18}F$ was made.

## METHODS AND MATERIALS

The scintigraphic measurements were carried out with a 5-in. dual-probe whole-body rectilinear scanner (Elscint, Palisades Park, N.J.) with photorecorder and videodisplay processor. The ratio between right and left sides was determined from the number of counts in chosen regions of interest, including the whole of the abnormal field. For $^{18}F$, collimators suitable for energies greater than 140 keV were used, although these collimators are not optimal for the 511-keV emission of $^{18}F$ (FWHM = 14 mm). For Tc-PP, collimators suitable for energies below 140 keV were used (FWHM = 10 mm for 140 keV). The collimators mentioned have a nearly depth-independent response over the range of 3–5 in. This geometry is preferable to one with a variable depth response, since the latter invites errors when two sites not strictly comparable in depth are compared. In a few cases a similar scanner, the Scintimat 2 (Siemens, Iselin, N.J.), was used

Fluorine-18 was produced by cyclotron bombardment of neon with 11-MeV deuterons. The $^{99m}Tc$ generator was delivered from Amersham/Searle (Arlington Heights, Ill.) and the polyphosphate kits came from Diagnostic Isotopes (Upper Saddle River, N.J.). The directions of the manufacturer were followed for the preparation and use of Tc-PP. Almost all doses were administered less than 1 hr after preparation, and in no case later than 3 hr. Scintigraphy was performed 1 hr after administration of about 5 mCi of $^{18}F$ and 2.5–3 hr after administration of 12 mCi of Tc-PP. The patients were asked to void immediately before the scintiscans.

Altogether, 79 patients were examined with both agents. Twenty-nine sets of scintigrams were ruled out. These represented eight patients in whom scintigrams were for technical reasons not suitable for ratio calculations, nine patients with suggestive complaints, but in whom scintigrams and radiograms were normal, six patients examined on account of non-neoplastic spinal disease, and six patients with bilateral involvement of the same joint. The remaining 50 sets of scintigrams were suitable for analysis; this included calculating the ratio between the two sides. The quantitative measurements on tissue speci-

Received May 20, 1975; revision accepted Sept. 20, 1975.

For reprints contact: Hans Bohr, Lab. of Osteopathology, Dept. of Orthopaedics 2161, Rigshospitalet, 2100 Copenhagen Ø.

mens were performed simultaneously for both nuclides with a Ge(Li) detector equipped with a pulse-height analyzer.

Specimens were obtained from five patients with severe osteoarthritis of the hip who underwent total hip prosthetic operations. Approximately 10 mCi of $^{18}F$ and 10 mCi of Tc-PP were injected simultaneously 1.5–2 hr before surgical removal of specimen tissue. These specimens included synovial tissue, subchondral bone from the femoral head, cancellous bone from the central part of the femoral head, and cancellous bone from the femoral neck as far distal as possible.

For the animal specimens we operated upon the right knees of five adult rabbits, using the method of Hulth et al (*1*) for the induction of degenerative joint changes. These changes could be shown macroscopically, histologically, and scintigraphically ($^{18}F$). One to six months after operation the rabbits were given 10 mCi of $^{18}F$ and 5 mCi of Tc-PP simultaneously and were killed 1.5–2 hr later. Specimens were taken from both knee joints, including bone tissue from the subchondral part of a tibial condyle, the tibial shaft, and the patella, as well as tissue samples from the synovial membrane, the joint capsule, and the quadriceps muscle. Activity measurements were performed 1–2 hr after death. The specimens were then dried at 45°C for 2 days. In human specimens drying reduced the bone weight to about 50% and the soft-tissue weight to 30%; the corresponding figures for rabbit samples were 80% and 40%. The activity of the human specimens was measured before and after 0.5 hr of flushing in water; this reduced the activities of both agents to about 70%.

**TABLE 1. SCINTIGRAPHIC MEASUREMENTS ON THE UPTAKE OF $^{18}F$ AND Tc-PP***

| Lesion | No. of cases | Ratio of diseased side to normal side | | Relative $^{18}F$ uptake† |
|---|---|---|---|---|
| | | $^{18}F$ | Tc-PP | |
| Fracture | 6 | 10 | 4 | 2.4 |
| | | (5) | (1) | (0.9) |
| Sarcoma of bone | 4 | 9 | 4 | 2.0 |
| | | (6) | (1) | (0.9) |
| Soft-tissue sarcoma invading bone‡ | 3 | 3 | 3 | 1.1 |
| | | (1) | (1) | (0.4) |
| Osteoarthritis | 7 | 2.1 | 1.7 | 1.2 |
| | | (0.5) | (0.4) | (0.2) |
| Osteonecrosis | 4 | 2.5 | 2.2 | 1.2 |
| | | (0.7) | (0.2) | (0.4) |
| Osteitis\|\| | 3 | 3 | 3 | 1.1 |
| | | (1) | (1) | (0.1) |
| Cartilaginous sarcoma of bone | 4 | 1.4 | 1.4 | 1.0 |
| | | (0.5) | (0.5) | (0.1) |
| Synovitis | 7 | 3 | 5 | 0.8 |
| | | (2) | (6) | (0.3) |
| Subclinical synovitis | 5 | 1.1 | 1.9 | 0.7 |
| | | (0.2) | (0.9) | (0.3) |
| Soft-tissue tumor accumulation§ | 7 | — | — | — |

* Figures are given as mean values. (Standard deviations are given in parentheses.)
† Defined as ($^{18}F$ ratio) ÷ (Tc-PP ratio).
‡ Region of interest limited to the osseous lesion.
|| Weakly virulent infections.
§ Quantitative evaluations could not be obtained.
*Note:* The collimators used for $^{18}F$ were designed for a much lower γ-energy than the 511 keV from $^{18}F$. The resulting high penetration background is responsible for most of the uncertainty in the evaluation of the $^{18}F$ uptake in any one patient.

## RESULTS

**Scintigraphic series.** Table 1 summarizes the uptakes of $^{18}F$ and Tc-PP, each compared with the normal side and grouped according to the final diagnoses. Within each group there was great variation in clinical and hence in scintigraphic behavior. Nevertheless, $^{18}F$ uptake clearly predominates in mainly osseous lesions, whereas Tc-PP predominates in mainly synovial lesions. Bone fractures and sarcomas showed good tracer concentration, and the uptake of $^{18}F$ was superior to that of Tc-PP to a degree beyond statistical uncertainty.

In the cases of soft-tissue sarcomas invading bone, of osteitis, of osteoarthritis, and of osteonecrosis, only a small preference for $^{18}F$ was seen. In the cartilaginous sarcoma group the uptake of both agents was only modest, with no measurable difference between them.

The cases of synovitis and subclinical synovitis showed a suggestive tendency towards $^{18}F$/Tc-PP ratios below unity, although these were not statistically significant. The synovitis group was rather diverse—these cases ranged from those with only slight synovial symptoms and signs, in whom no specific rheumatologic diagnosis could be obtained, to a patient with a severe septic arthritis. Great variation in uptake was found, although the uptake of Tc-PP was consistently higher than that of $^{18}F$. The patient with septic arthritis showed the highest ratio for both agents (17 for Tc-PP and 5 for $^{18}F$), as well as a 3:1 advantage for Tc-PP.

In the subclinical synovitis group we collected cases where an unexpected Tc-PP accumulation was seen in an otherwise normal joint. This Tc-PP uptake turned up in scans made for nonarthritic reasons, and the joint in question showed neither symptoms nor signs, including normal x-ray examination and a normal $^{18}F$ scintigram. In these cases a limp or a similar unconnected dysfunction seems to have produced a subclinical synovitis which we think accounts for the increased synovial uptake of Tc-PP. An example is shown in Fig. 1.

In cases of mesenchymal soft-tissue tumors Tc-PP

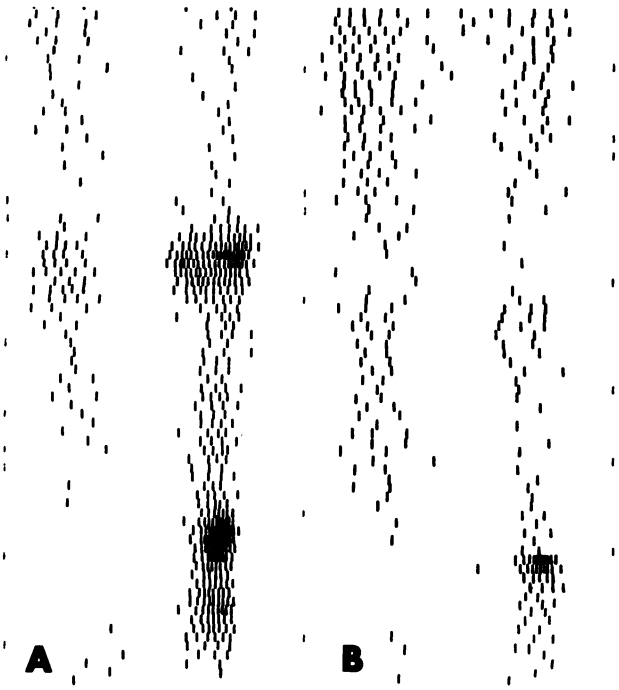


**FIG. 1.** Man aged 52 with pseudoarthrosis distally in left tibia, weightbearing in below-knee cast. Knee was clinically and radiologically normal. Increased uptake of both Tc-PP and $^{18}F$ was seen in pseudoarthrosis. Uptake of Tc-PP (A) in left knee was increased, despite normal uptake of $^{18}F$ (B), indicating subclinical synovitis.

accumulation in the tumor tissue was sometimes seen, in spite of a normal or only slightly accentuated uptake in the $^{18}F$ scintigrams. This group includes three cases of soft-tissue sarcomas, three cases of benign soft-tissue tumors, and one case of a sarcoma-like fibrotic process. An example is shown in Fig. 2.

**Specimen series.** The measurements on the animal specimens are given in Table 2, where the uptakes of $^{18}F$ and Tc-PP are expressed as fractions of the uptake in the proximal part of the tibial diaphysis on the normal side. Table 2 shows that in both knee joints the $^{18}F$/Tc-PP ratio is near unity in all specimens from bone, and about $\frac{1}{7}$ in all specimens from synovial and capsular tissue. The ratio of the uptakes of Tc-PP in synovial tissue and bone per unit dry weight is about 1:2 for the normal (left) knee and only 1:10 for $^{18}F$. In the diseased (right) knee joint the uptakes of both Tc-PP and $^{18}F$ in the subchondral part of the tibial condyle are increased about four times, and in the synovial tissue about ten times, as compared with the intact knee. In muscle tissue no difference was found between the two sides, and the uptake was about equal to the uptake in the synovial tissue of the normal side.

In human specimens no comparison could be made with the normal side; the results are normalized to the uptake in cancellous bone from the distal part of the femoral neck (Table 3). As in the animal specimens the ratio between $^{18}F$ and Tc-PP is almost unity in all bone specimens, whereas in the synovial tissue it averages $\frac{1}{3}$, although with rather large variation (0.7–0.05). A very low value was found in a patient with severe hypertrophic synovitis.

## DISCUSSION

Fluorine-18 is considered a reliable agent for bone scintigraphy (*2,3*) and in our opinion it has considerable potential in orthopedic applications (*4*). The biologic properties of $^{18}F$ are considered superior to those of Tc-PP and $^{18}F$ is used as the standard agent with which newer agents are compared (*3,5,6*). For scintigraphy, however, the physical properties of $^{18}F$ are inferior to those of Tc-PP, the half-life of $^{18}F$ being 110 min and its photon energy 511 keV.

Technetium-99m-polyphosphate (*7*) has been increasingly used in recent years. It avoids the economic and technical problems associated with $^{18}F$ and high-quality bone scintigrams can be obtained. For detection of skeletal metastases Tc-PP has proved to be an excellent tool, presumably superior to $^{18}F$ (*5,8*).

In comparative series of rectilinear scintigrams some investigators favor Tc-PP (*5,6,8*) and others $^{18}F$ (*3,9,10*). Quinn et al (*11*) concluded that neither of the agents is ideal, and this agrees with our experience.

On the whole, we find no major differences between Tc-PP and $^{18}F$ in the osseous uptake patterns (Fig. 3). A somewhat higher soft-tissue background is almost the rule in the Tc-PP scintigrams, though this is immaterial from a practical point of view. Our Tc-PP scintiscans are usually better resolved than their $^{18}F$ counterparts, since we have no collimators optimized for 511-keV radiation.

On the other hand, Tc-PP concentrates well in abnormal mesenchymal soft tissues—whether inflamed (Fig. 1) or neoplastic (Fig. 2)—and may be

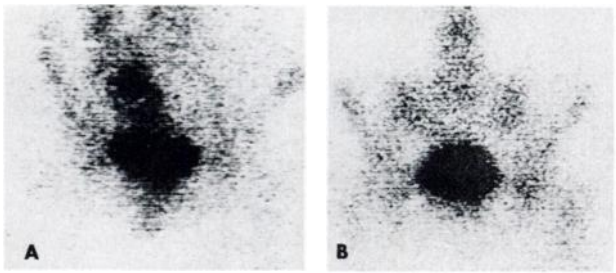


**FIG. 2.** Woman aged 56 with synovial sarcoma in left tibia. Pelvic x-ray showed uncharacteristic increased density in right side of pelvis where poorly defined tumor could be palpated. Scintigram using Tc-PP (A) showed pronounced extensive uptake corresponding to tumor; $^{18}F$ scintigram (B) showed only slightly increased uptake to right above bladder. Metastases to pelvis were suspected, but biopsy from pelvic tumor showed lymphangioma. Femoral amputation was carried out.

**TABLE 2. UPTAKES OF Tc-PP AND $^{18}F$ IN SPECIMENS FROM FIVE RABBITS WITH DEGENERATIVE JOINT DISEASE***

| Specimen | $^{18}F$/Tc-PP uptake ratio | | Tc-PP uptake per unit dry weight | | $^{18}F$ uptake per unit dry weight | |
|---|---|---|---|---|---|---|
| | Normal | Diseased | Normal | Diseased | Normal | Diseased |
| Tibial shaft | 1 | 0.9 (0.1) | 1 | 1.2 (0.1) | 1 | 1.1 (0.1) |
| Tibial condyle | 0.9 (0.1) | 0.9 (0.1) | 2.3 (0.4) | 9 (2) | 2.1 (0.4) | 8 (1) |
| Patella | 1.0 (0.1) | 1.0 (0.1) | 1.2 (0.3) | 3 (1) | 1.2 (0.2) | 3 (1) |
| Synovial membrane | 0.15 (0.05) | 0.14 (0.09) | 0.5 (0.2) | 5 (5) | 0.08 (0.06) | 0.8 (0.7) |
| Capsule | 0.14 (0.04) | 0.19 (0.09) | 1.2 (0.7) | 4 (2) | 0.2 (0.1) | 0.7 (0.4) |
| Quadriceps muscle | 0.3 (0.1) | 0.3 (0.1) | 0.3 (0.1) | 0.4 (0.3) | 0.09 (0.03) | 0.09 (0.06) |

* Figures are given as mean values in relation to normal tibial shaft. (Standard deviations are given in parentheses.)

used in the early detection of synovitis (*12–14*). While making use of this property, we must stress the point that soft-tissue uptake can be a disadvantage in orthopedic diagnosis since it may simulate or obscure a bone reaction in situations where the skeletal component is the matter of primary concern. Thus, in osteonecrotic and osteoarthritic lesions it is essential to distinguish the osseous component in a joint region from the synovial component. An increased uptake in the subchondral bone will precede radiographic changes, and the uptake pattern will give information about the extent and etiology of the lesion. Such information is of diagnostic and therapeutic importance (*4,15*).

The evaluation of an osseous uptake, without interference from a superimposed soft-tissue accumulation, may be of special importance in primary bone tumors in the proximity of joints. The following example illustrates this point. In planning the treatment of a sarcoma of the pelvic bone, particular attention is paid to the question whether or not the sarcoma involves the sacroiliac joint. If the joint is involved, a hemipelvectomy will not be a radical procedure. Scintigraphy often gives a hint here, but in Tc-PP scintigrams this important information may be obscured by a synovial uptake in the sacroiliac joint of the diseased side. In our experience this synovial uptake does not indicate invasion of the joint by tumor tissue. Based on supplementary $^{18}F$ scintigraphy we find that $^{18}F$ uptake will not be increased in the sacroiliac joint unless the subchondral bone is affected (*16*).

In several cases our scans showed an uptake of Tc-PP in pathologic soft tissue where no visible accumulation of $^{18}F$ took place. This increased ratio of Tc-PP to $^{18}F$ in cases of synovitis and subclinical synovitis can be explained from the specimen results. These show that while the uptake of Tc-PP and $^{18}F$ in bone tissue are of the same magnitude, the uptake of Tc-PP in inflamed synovial tissue is much greater than that of $^{18}F$. In addition, any primarily subchondral osseous lesion will lead to a secondary synovial inflammation and a more or less pronounced synovial hypertrophy. The result is an increase not only in the synovial Tc-PP uptake per unit of weight, but in the total amount of synovial tissue as well.

The Tc-PP accumulation in diseased soft tissue has been discussed previously (*10,12,17–20*), as has the question of the chemical stability and the uniformity of biologic behavior of this agent (*7,10,11,17,21*).

**TABLE 3. UPTAKES OF Tc-PP AND $^{18}F$ IN SPECIMENS FROM FIVE PATIENTS WITH OSTEOARTHRITIS OF THE HIP JOINT***

| Specimen | $^{18}F$/Tc-PP uptake ratio | Tc-PP uptake per unit dry weight | $^{18}F$ uptake per unit dry weight |
|---|---|---|---|
| Femoral neck, distal | 1 | 1 | 1 |
| Femoral neck, proximal | 0.9 (0.1) | 0.8 (0.4) | 0.7 (0.4) |
| Femoral head, subchondral bone | 1.1 (0.0) | 1.5 (1.3) | 1.6 (1.4) |
| Synovial membrane | 0.3 (0.2) | 2.1 (1.5) | 0.9 (1.3) |

* Figures are given as mean values normalized to the cancellous bone from the distal part of the femoral neck. (Standard deviations are given in parentheses.)

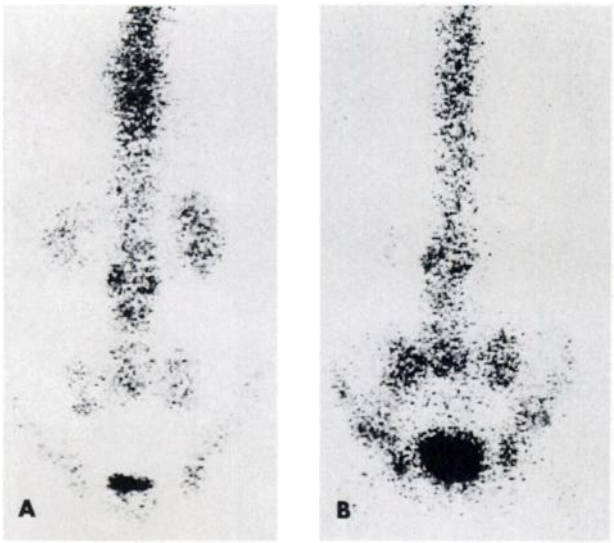


**FIG. 3.** Scintigrams in 29-year-old man. Osseous uptake pattern is identical for Tc-PP (A) and $^{18}F$ (B). Recurrence of excised fibrosarcoma is located posterior to left kidney, in paravertebral muscles. Invasion of third lumbar vertebra is seen on both scintigrams.

The differences noted between $^{18}F$ and Tc-PP may only be quantitative in nature; however, in some cases the Tc-PP uptake in pathologic soft tissue is so pronounced that it becomes a qualitative one in practice. In our experience the $^{18}F$ uptake in pathologic soft tissue is hardly ever marked enough to cause interpretative errors, whereas such uptake of Tc-PP is often pronounced and therefore more likely to mislead. While it would be too sweeping to say that this extraskeletal uptake will lead to mistaken diagnoses or incorrect therapy in other disciplines, we find this to be the case in the examination of joint regions in orthopedics.

## CONCLUSION

As compared to $^{18}F$, Tc-PP is cheaper, more readily available, and somewhat superior in skeletal delineation. However, $^{18}F$ shows only minimal extraskeletal uptake. Technetium-99m-polyphosphate may accumulate considerably in abnormal mesenchymal soft tissue (e.g., in inflamed synovial tissue), whether the synovial affection is detectable clinically or not.

In the examination of joint regions the authors consider $^{18}F$ more reliable, and in doubtful cases we do not hesitate to add an examination with $^{18}F$.

## ACKNOWLEDGMENTS

The authors wish to express their gratitude to Carl C. Arnoldi for valuable support and to the Cyclotron Department of the Niels Bohr Institute for technical assistance. This study was supported in part by the National Danish Association against Rheumatic Diseases.

## REFERENCES

1. HULTH A, LINDBERG L, TELHAG H: Experimental osteoarthritis in rabbits. *Acta Orthop Scand* 41: 522–530, 1970

2. BLAU M, GANATRA R, BENDER MA: $^{18}F$-fluoride for bone imaging. *Semin Nucl Med* 2: 31–37, 1972

3. ACKERHALT RE, BLAU M, BAKSHI S, et al: A comparative study of three $^{99m}Tc$-labeled phosphorus compounds and $^{18}F$-fluoride for skeletal imaging. *J Nucl Med* 15: 1153–1157, 1974

4. MCGRAIL JW, VULPETTI AT, SHIFRIN LZ: $^{18}F$ scintigraphy of non-neoplastic skeletal lesions. A preliminary report. *Clin Orthop* 101: 292–298, 1974

5. KRISHNAMURTHY GT, WALSH CF, SHOOP LE, et al: Comparison of $^{99m}Tc$-polyphosphate and $^{18}F$. II. Imaging. *J Nucl Med* 15: 837–843, 1974

6. WEBER DA, KEYES JW, LANDMAN S, et al: Comparison of $Tc^{99m}$Polyphosphate and $F^{18}$ for bone imaging. *Am J Roentgenol Radium Ther Nucl Med* 121: 184–190, 1974

7. SUBRAMANIAN G, MCAFEE JG, BELL EG, et al: $^{99m}Tc$-labeled polyphosphate as a skeletal imaging agent. *Radiology* 102: 701–704, 1972

8. BARRETT JJ, SMITH PHS: Bone imaging with $^{99}Tc^{m}$-polyphosphate: A comparison with $^{18}F$ and skeletal radiography. *Br J Radiol* 47: 387–392, 1974

9. RAYUDU GVS, TROUTT ED, FORDHAM EW: A comparison of $^{99m}Tc$-tin(II)-polyphosphates, $^{87m}Sr$, and $^{18}F$ in bone imaging. *J Nucl Med* 13: 462–463, 1972

10. HOSAIN F, HOSAIN P, WAGNER HN, et al: Comparison of $^{18}F$, $^{87m}Sr$, and $^{99m}Tc$-labeled polyphosphate, diphosphonate, and pyrophosphate for bone scanning. *J Nucl Med* 14: 410, 1973

11. QUINN JL, CREWS MC, WESTERMAN BR: $^{99m}Tc$ versus $^{18}F$ bone-scanning agents: Advantages and disadvantages. In *Proceedings of the IAEA Symposium "Radiopharmaceuticals and Labelled Compounds," Copenhagen, March 1973*, SM-171 STI/PUB/344, Vienna, IAEA, 1973, pp 119–126

12. HENNE W, PFANNENSTIEL P, PIXBERG HU: Knochen- und Gelenkszintigraphie mit $^{99m}Tc$-markiertem Pyrophosphat bzw. Polyphosphat. Ein vorläufiger Erfahrungsbericht. *Fortschr Geb Roentgenstr Nuklearmed* 119: 187–193, 1973

13. DESAULNIERS M, FUKS A, HAWKINS D, et al: Radiotechnetium polyphosphate joint imaging. *J Nucl Med* 15: 417–423, 1974

14. LACOURCIÈRE Y: La scintigraphie avec polyphosphate marqué au technétium dans la détection des maladies articulaires inflammatoires. *Union Med Can* 103: 662–667, 1974

15. BAUER G: Progress in the use of radionuclides in orthopaedics. *Acta Orthop Scand* 46: 315–322, 1975

16. HEERFORDT J, VISTISEN L, VOETMAN V: Bone scintigraphy as an aid in assessing the indication for hemipelvectomy in sarcomas of the pelvis. *Acta Orthop Scand*: to be published

17. BÜLL U, FREY KW: Untersuchungen zur Knochenanreicherung von $^{99m}Tc$-Pyrophosphat, $^{99m}Tc$-Polyphosphat und Radiostrontium. *Fortschr Geb Roentgenstr Nuklearmed* 119: 569–577, 1973

18. WELLMAN HN, BROWNE A, KAVULA M, et al: Optimization of a new kit-prepared skeletal-imaging agent, $^{99m}Tc$-Sn-EHDP, compared with $^{18}F$. In *Proceedings of the*

*IAEA Symposium "Radiopharmaceuticals and Labelled Compounds," Copenhagen, March, 1973*, SM-171 STI/PUB/344, Vienna, IAEA, 1973, pp 93–108

*19.* CHAUDHURI TK, CHAUDHURI TK, GULESSERIAN HP, et al: Extraosseous noncalcified soft-tissue uptake of $^{99m}$Tc-polyphosphate. *J Nucl Med* 15: 1054–1056, 1974

*20.* GENOE GA, MOELLER JA: Normal shoulder variations in the technetium 99m polyphosphate bone scan. *South Med J* 67: 659–662, 1974

*21.* BOWEN BM, GARNETT ES: Analysis of the relationship between $^{99m}$Tc-Sn-polyphosphate and $^{99m}$Tc-Sn-pyrophosphate. *J Nucl Med* 15: 652–655, 1974