
Technetium-99m-Methylene Diphosphonate Uptake in the Fetal Skeleton at 30 Weeks Gestation

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Retention of ^{99m}Tc -MDP in the fetal skeleton and placenta at 30 and 32 wk gestation was observed during bone scan examination of the maternal skeleton for staging of malignant tumors. The implications and significance of these observations are discussed.

Key Words: pregnancy; bone scintigraphy; radiation; technetium-99m-methylene diphosphonate

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Information regarding the biologic distribution of bone-seeking and other radiopharmaceuticals at different stages of gestation is limited. Previous reports relating to fetal absorbed dose between 8 and 18 wk gestation have suggested there is no uptake in the fetus and little or no residual activity in the uterine wall or placenta (1,2).

This report of two patients demonstrates that ^{99m}Tc -MDP (methylene diphosphonate) concentrates in the placenta and fetal skeleton by 30 wk gestation and suggests, therefore, that estimation of the fetal absorbed dose should consider these sources in the later stages of gestation.

PATIENT ONE

A 28-yr-old woman was investigated for a giant-cell tumor of the right proximal tibial metaphysis by whole-body bone scanning using 740 MBq of ^{99m}Tc -MDP. At the time, she was pregnant with a fetus of 32 wk gestational age (Fig. 1). The maternal bladder was not catheterized, but the patient was encouraged to void at frequent intervals.

A male child was born at 37 wk gestation by normal vaginal delivery. His birth weight was 3.32 kg. He developed normally but had maldescent of one testis which was surgically corrected at age three. The child was last examined at age four and was found to be normal.

PATIENT TWO

A 29-yr-old gravida three, para one woman presented with a 7.5 × 5.0 cm left breast mass with angiolymphatic invasion. She underwent modified radical mastectomy when her fetus was of 28 wk gestation. Histologic examination revealed that 33 of 33 resected axillary nodes were positive for metastatic tumor.

At 30 wk gestation, a bone scan was performed as a staging procedure using 540 MBq of ^{99m}Tc -MDP (Fig. 2). The patient was not catheterized but was encouraged to void frequently and was given liberal amounts of oral fluids during the examination. The scan demonstrated no evidence of metastatic disease but fetal uptake was noted. Based on the absence of metastatic bone disease, chemotherapy was delayed to decrease the risks of toxicity to and premature delivery of the fetus.

An elective Cesarean Section was subsequently performed at gestational age 33 wk and a normal child was delivered. The patient was well and clinically free of disease at 1 yr but has since been lost to follow-up. Her child was also well at 1 yr.

DISCUSSION

Previous studies have indicated that a fetus of between 8 and 18 wk gestation does not concentrate radionuclide activity above maternal background levels when ^{99m}Tc -MDP was administered to the mother (1,2). However, the bone scans of our cases clearly show fetal and placental uptake of radionuclide by 30 wk gestation. Therefore, when estimating absorbed radiation dose to the fetus from maternal injection of ^{99m}Tc -MDP in such cases one must consider the absorbed radiation dose from direct fetal uptake in addition to irradiation from maternal tissues.

The uptake and retention of activity in the fetal skeleton are likely to reflect both new bone formation in the fetus and the permeability of the placenta to ^{99m}Tc -MDP. Ossification of the fetal skeleton begins with endochondral calcification during 8 wk gestation, and bone remodeling continues throughout life (3). There have been various estimations of placental permeability during different stages of pregnancy. While no specific human data are available for placental permeability to ^{99m}Tc -MDP, placental permeability to many substances increases gradually throughout pregnancy, reaching approximately 75% of maximum permeability at around 26 wk and maximum

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FIGURE 1. Anterior projection of a whole-body bone scan obtained 3 hr postinjection of 740 MBq of ^{99m}Tc -MDP in a 32-wk pregnant female demonstrates uptake in fetal skeleton (arrow), persistent activity in placenta (arrowhead) and marked uptake in giant-cell tumor in right proximal tibia metaphysis.

permeability at around 32 wk with little change in later stages of pregnancy (4). For the purposes of dosimetry estimation in our cases, it was assumed that ^{99m}Tc -MDP was freely diffusible across the placenta by 30 wk gestation.

The 3-hr images from the whole-body bone scans show persistent activity in the placenta in addition to retention of activity in the fetal skeleton. This indicates that the extremely rapid clearance rate from the placenta demonstrated in earlier gestations does not apply at later gesta-

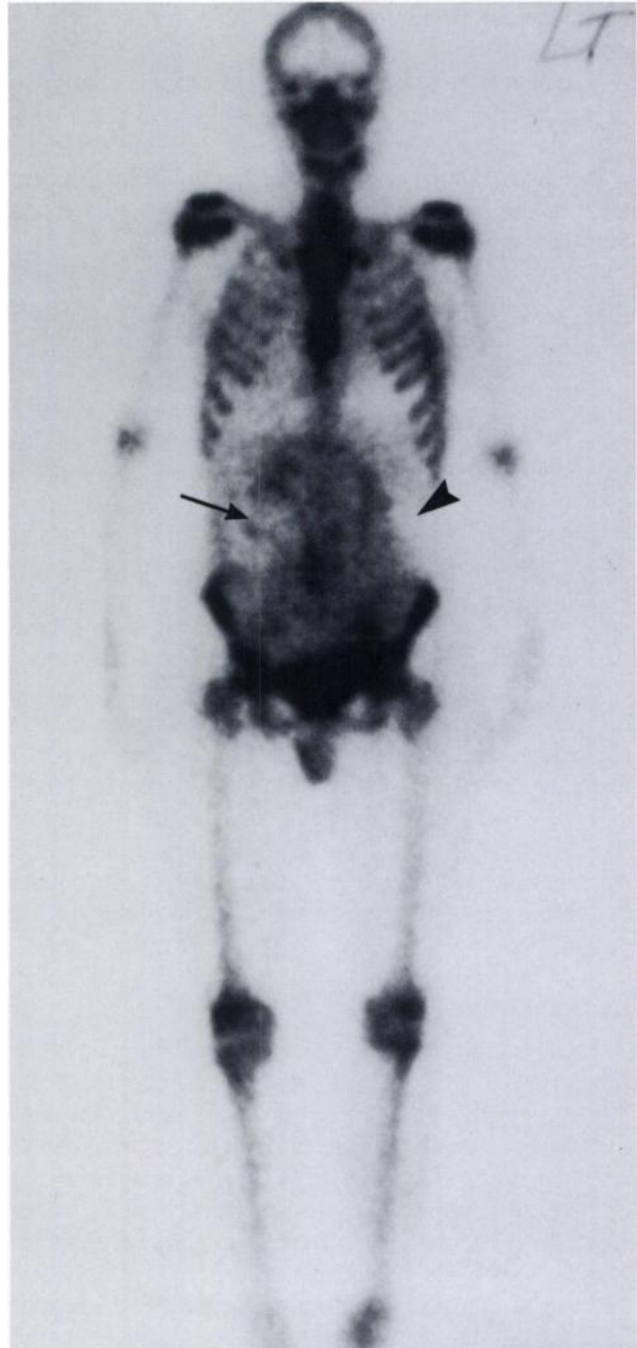


FIGURE 2. Anterior projection of a whole-body bone scan obtained 3 hr after injection of 540 MBq of ^{99m}Tc -MDP in a 30-wk pregnant female demonstrates uptake in fetal skeleton (arrow), persistent activity in placenta (arrowhead) and uptake in the left ankle consistent with a known site of prior trauma.

tions. Therefore, contribution from this source to total absorbed fetal dose may also become significant.

Unfortunately, no quantification of radionuclide uptake and elimination in maternal or fetal tissues were performed in either of these cases limiting the accuracy of fetal dose estimates from various potential sources. With these limitations in mind and using previously described dosimetry models and physiological parameters (5-7), the fetal dose

from maternal tissues, the maternal bladder, direct uptake in the fetal skeleton and persisting activity in the placenta were estimated to be of relatively low magnitude (2.9 mGy in Patient One and 2.1 mGy in Patient Two, Table 1). These dose estimates are similar to those previously reported (1,2) at earlier stages of gestation and to estimates of radiation to the uterus from soft tissues following bone scanning in nonpregnant females (6).

The radiation exposure occurred outside the critical period when the brain stem is formed (8–15 wk after conception) and so potential for mental retardation is also considered negligible (6,8). Exposure also occurred well after the critical period of organogenesis and limb budding. Consequently, there was no risk for major fetal malformations. The risk of cancer induction in these fetuses would appear to be insufficient to justify intensive screening for lymphatic leukemia, lymphoma, thyroid carcinoma, bladder carcinoma or bone sarcoma (1,8). However, follow-up of the children should include regular medical review with specific attention to central nervous system, thyroid gland, reticulo-endothelial system and musculoskeletal system.

Despite the evidence of placental and fetal skeletal uptake of ^{99m}Tc -MDP, maternal bone scanning is not, in our opinion, absolutely contraindicated during pregnancy. The need for and timing of bone scanning in pregnant females should be influenced by the implications of positive and negative bone scan results on further management of the primary maternal disease and her pregnancy. The potential benefits and risks must be balanced and discussed with the patient (10).

CONCLUSION

These cases demonstrate several pertinent points. First, direct skeletal uptake of radionuclide can occur in a fetus of 30–32 wk gestation. Second, persistent uterine wall activity suggests slow clearance of ^{99m}Tc -MDP from the placenta beyond 30 wk gestation so that this source should be considered in estimating absorbed fetal dose of ionizing radiation from maternal bone scans. Third, the maternal bladder is probably still the main source of exposure for the older fetus, and the insertion of a urinary catheter in the maternal bladder should be considered to reduce the fetal absorbed dose of ionizing radiation in cases where there is known pregnancy and clinical justification for the examination. At least, good oral hydration and frequent voiding should be encouraged. The dose used for bone scanning should be the lowest practical to obtain an adequate diagnostic study.

APPENDIX: ESTIMATION OF ABSORBED DOSE TO FETUS ASSOCIATED WITH MATERNAL SKELETAL SCINTIGRAPHY

Patient One

Data and assumptions upon which calculations were performed:

1. 740 MBq of ^{99m}Tc -MDP were administered to the mother.

TABLE 1
Comparison with Other Reports

Author	Age (wk)	Activity (MBq)	$\mu\text{Gy}/\text{MBq}$	Dose (mGy)
Hedrick et al. (1)	8	851	4.6	3.9
	18	888	2.6	2.3
Palestro et al. (2)	16	740	4.4	3.3
	Dose to uterus in nonpregnant female	740	6.1	4.5
Patient One	32	740	3.9	2.9
Patient Two	30	540	3.9	2.1

2. The fetal age was approximately 32 wk.
3. The patient emptied her bladder at approximately 2-hr intervals.
4. The mother was of average weight at around 58 kg.
5. The total fetal radiation dose will arise from maternal bladder, maternal soft tissues, maternal skeleton and direct fetal uptake.

Dose from Maternal Bladder

$$\text{Using } D = 1.33 \times 10^8 f A_0 T D (6)$$

$f = 0.9$ (number of photons of 140 keV per disintegration, i.e., abundance)

$T =$ residence time in hours

$T = 0.7$ hr assuming voiding every 2 hr

$A_0 =$ administered activity (740 MBq = 20,000 μCi)

$D =$ average dose per photon (D for 140 keV photon in a 32-wk-old fetus was estimated using linear interpolation of data previously reported by Cloutier et al. (5) and was calculated to be 3.4×10^{-14} rad.

$D = 0.057$ rad (0.57 mGy)

Dose from Maternal Skeleton, Soft Tissues and Kidneys

$$\text{Using } D = A_0 T S (6)$$

$S =$ cumulated activity in source organ rad/ $\mu\text{Ci-hr}$

From S factors for a 58-kg female and representative T values as quoted by Hedrick et al. (1);

Dose from maternal skeleton = 0.059 rad (0.59 mGy)
 Dose from maternal soft tissues = 0.016 rad (0.16 mGy)
 Dose from maternal kidneys = 0.005 rad (0.05 mGy)

Dose from Direct Fetal Uptake

ICRP Publication 53 documents radiation dose from a wide variety of radionuclides and quotes total dose per unit activity for an adult and children of ages 15, 10, 5 and 1 yr.

Extrapolating these data back to zero years for ^{99m}Tc -MDP gives a value of

$$7 \times 10^{-2} \text{ mGy}/\text{MBq}.$$

Assuming a maternal blood volume of 4.5 liters and a fetal blood volume of 150 ml i.e. 50% of full term blood volume assuming that the percentage of total mass contributed by blood does not alter between 32 and 40 wk of gestation (4), the fetal blood volume is approximately 3% of total maternal and fetal combined blood volume. Also assuming 100% permeability of the placenta to ^{99m}Tc -MDP at this stage of gestation;

$$D = 7 \times 10^{-2} \times 740 \times 3/100$$

$$= 0.155 \text{ rad (1.55 mGy)}$$

Total Dose Estimate

$$D_{\text{Total}} = 0.57 + 0.59 + 0.16 + 0.005 + 1.55$$

$$= 2.9 \text{ mGy}$$

Patient Two

All assumptions and calculation as per Case One but using lower administered activity of 540 MBq.

$$D_{\text{Total}} = 0.41 + 0.43 + 0.16 + 0.004 + 1.13$$

$$= 2.1 \text{ mGy}$$

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