

# Guidelines for paediatric bone scanning with $^{99m}\text{Tc}$ -labelled radiopharmaceuticals and $^{18}\text{F}$ -fluoride

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**Abstract** The purpose of these guidelines is to offer nuclear medicine teams a framework that could prove helpful in daily practice. The guidelines include information related to the indications, acquisition, processing and interpretation of bone scans in children, focusing primarily on  $^{99m}\text{Tc}$ -labelled diphosphonate scintigraphy, and also recommendations with regard to the emerging use of PET with  $^{18}\text{F}$ -fluoride.

**Keywords** Paediatrics · Bone scan · Guidelines

**Disclaimer** These guidelines summarize the views of the Paediatric Committee of the European Association of Nuclear Medicine and reflect recommendations for which the EANM cannot be held responsible. These recommendations should be taken in the context of “good practice” of nuclear medicine and do not substitute for national and international legal or regulatory provisions. The guidelines have been reviewed by the EANM Dosimetry Committee, the EANM Physics Committee and the EANM Radiopharmacy Committee.

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## Purpose

The purpose of these guidelines is to offer nuclear medicine teams a framework that could prove helpful in daily practice. The guidelines include information related to the indications, acquisition, processing and interpretation of bone scans in children, focusing primarily on  $^{99m}\text{Tc}$  labelled diphosphonate scintigraphy, and also recommendations with regard to the emerging use of PET with  $^{18}\text{F}$ -fluoride. The corresponding adult bone scanning guidelines from the European Association of Nuclear Medicine [1] and the Society of Nuclear Medicine [2], together with the previous EANM Paediatric bone scan guidelines [3], have been taken into consideration, reviewed and partially integrated into this text.

## Background

Since the introduction of  $^{99m}\text{Tc}$  labelled diphosphonates, bone scintigraphy has become a widely accepted method for the evaluation of paediatric bone metabolism. Its strengths are high sensitivity and the ability to investigate the entire skeleton in a single examination. Although whole-body MRI has been on the horizon for many years, it is expected that nuclear medicine bone scanning will remain an important diagnostic tool in the foreseeable future due to its scientific validation, availability and, most importantly, in contrast to MRI, bone scintigraphy can routinely be performed without sedation, even in very young children. Bone scintigraphy shows high sensitivity in the early detection of pathological bone metabolism, complementing conventional x-ray techniques, which are in general less sensitive, but often add important specificity, e.g. for characterization of primary bone tumours.

High-quality images are crucial and require correct positioning and often immobilization of the child as well as optimal equipment. Due to the age-dependent differences in bone metabolism in the developing skeleton, the interpretation of bone scanning in children is challenging and requires knowledge of the appearances of the maturing skeleton. Excellent atlases are available for reference [4, 5].

### Common indications

Common clinical indications for bone scanning are:

- A. Infection or inflammation [6–12]
  - acute osteomyelitis versus soft-tissue inflammation
  - subacute and chronic osteomyelitis
  - septic arthritis complicating osteomyelitis
  - aseptic arthritis
- B. Bone tumours [7, 10, 13–18]
  - benign bone tumours, e.g. osteoid osteoma
  - malignant bone tumours
  - tumour-like lesions such as Langerhans histiocytosis
  - bone metastases
- C. Aseptic necrosis [11, 19–23]
  - aseptic necrosis, e.g. Legg-Calvé-Perthes disease [24]
  - sickle cell disease
- D. Traumatic bone disease [11, 14, 25–29]
  - equivocal radiographic findings after trauma
  - stress fractures
  - child abuse (battered child syndrome) [30]
  - polytrauma
  - complications of fractures and therapy
- E. Sudeck's atrophy [11]
  - reflex sympathetic dystrophy
- F. Bone scintigraphy-guided surgery [11, 31]
  - e.g. osteoid osteoma
- G. Bone dysplasia and other metabolic diseases [11, 32]
  - Camurati-Engelmann disease
  - evaluating skeletal involvement (brown tumours) in children with hyperparathyroidism [33]
- H. Other clinical situations in paediatrics [8, 11, 34–36]
  - pain possibly due to bone pathology
  - limp or backache
  - fever of unknown origin
  - evaluating apophyseal activity in the mandibular condyles in children with mandibular asymmetry

### Contraindications

Although uncommon in the paediatric age group, the possibility of pregnancy in female patients of child-bearing age should be ruled out. As in any diagnostic procedure in a patient who is known or suspected to be pregnant, a clinical decision is necessary to consider the benefits against the possible harm of carrying out the scan.

### Bone scintigraphy

#### Patient preparation

The scan should be thoroughly explained to the patient and his/her parents by the technologist or physician. The explanation should include the need for hydration, time/duration of the scan, and details of the procedure itself, including the waiting time between injection and image acquisition. Ideally, parents should receive written information together with the appointment letter, and in addition should be contacted in advance by phone to provide information, answer questions, and to identify possible problems.

#### *Information pertinent to the procedure*

All previous bone scans should be available for review to ensure that sufficient time has elapsed since the previous study (depending on the disease). Also current radiographs and CT or MRI scans, if relevant, should be available for comparison.

Pertinent information should be gathered from the child or carer prior to the procedure, including:

- Current symptoms
- History of fractures, trauma, osteomyelitis, arthritis, neoplasm, metabolic bone disease
- History of therapy that might affect the results of bone scintigraphy (e.g. antibiotics)
- History of surgery (e.g. presence and location of orthopaedic hardware) that might affect the results of bone scintigraphy
- History of renal abnormalities

#### *Before and after injection*

If available and permitted by national regulations, a local anaesthetic cream can be used prior to venepuncture, to reduce discomfort [37]. Regardless of whether local anaesthetic is used or not, the venous access should be established in advance. Toilet-trained children should be asked to urinate immediately before delayed imaging and

should be encouraged to drink plenty of fluids during the waiting time and for at least 24 hours after radiopharmaceutical administration to lower the radiation burden.

Sedation is usually not required for a technically satisfactory examination [38], but children who have painful conditions such as osteomyelitis or septic arthritis should be given adequate doses of an appropriate analgesic, and in some patients who cannot or do not want to cooperate mild sedation might be necessary. Some centres use intranasal or per-rectal midazolam, which might help in reducing extreme anxiety. Nevertheless, if sedation is used, it must follow national and local hospital guidelines. When sedation is used the child will have oral fluid intake restricted and will also not micturate spontaneously; under such circumstances delayed images (see section D. [Image acquisition](#)) or the placement of a bladder catheter may be necessary to visualize the pelvis adequately.

#### Radiopharmaceutical

Several  $^{99m}\text{Tc}$ -labelled radiopharmaceuticals are available for bone scintigraphy:

- Medronate (methylene diphosphonate, MDP)
- Oxidronate (hydroxymethylene diphosphonate, HMDP or HDP)
- Diphosphonopropanedicarboxylic acid (DPD)

The injected activity should be adjusted to the patient's weight according to the latest version of the EANM dosage card [39], an online calculator is available on the EANM website to determine the appropriate dose ([https://www.eanm.org/scientific\\_info/dosagecard/dosagecard.php?navId=548](https://www.eanm.org/scientific_info/dosagecard/dosagecard.php?navId=548)). Recommended injected activities for  $^{99m}\text{Tc}$ -MDP imaging based on the dosage EANM card [39] are listed in Table 1. The minimum activity is 40 MBq. The maximum activity may be limited by national regulations.

#### Radiation dose

The estimated absorbed radiation doses to various organs in healthy subjects following administration of  $^{99m}\text{Tc}$ -labelled phosphates and phosphonates according to the ICRP Publication 80 [40] are set out in Table 2. The radiation burden is calculated assuming a 3-hour bladder void. If the bladder needs to be emptied more frequently by encouraging oral fluid intake, then the above radiation doses will be reduced.

#### Image acquisition

A single- or dual-head gamma camera equipped with a low-energy, high-resolution collimator is most frequently used (energy window centred over the 140 keV photo-

peak of  $^{99m}\text{Tc}$ ). Multiphase bone scintigraphy includes blood-flow images, immediate blood-pool images, and delayed images. The blood-flow images are a dynamic sequence of planar images of the area of greatest interest obtained as the tracer is injected. The immediate (blood-pool or soft-tissue phase) images include one or more static planar images of the areas of interest or a whole-body image (recommended), obtained immediately after the flow portion of the study and completed within 10 min of injection of the tracer. If appropriate, the blood-flow images can be omitted, and the time used to obtain better quality blood-pool images. Blood flow and whole-body blood-pool images are most helpful for evaluation of suspected active infection or inflammation, and are recommended in older children with, for example, polyarthritis. Delayed images, planar or tomographic [35], should nevertheless include the whole body [17], but may be limited to the areas of interest only in uncooperative children. They are usually acquired 2–5 h after injection. If necessary, additional delayed images may be obtained up to 24 h after tracer injection.

#### Positioning of the child

During image acquisition the child has to lie absolutely still; cooperative parents are a great help. For neonates and small children, scheduling the delayed images in the normal day-time sleeping period is the ideal. For older children pleasant surroundings, entertainment such as the option to watch a film or listen to a story during the imaging procedure, and an appropriate attitude towards the child have proved to be most effective for immobilization. The use of a vacuum mattress and/or sand bags with Velcro straps can support the fixation, ensuring that the distance between child and collimator is not increased by the fixation material.

It is recommended to do all imaging with the child lying down. If a dual-head gamma camera system is used it is important to position the posterior head as close as possible to the child. Placing the anterior head too close may frighten the child. Exceptions include imaging of hands or elbows in larger children where the child may do better sitting in front of the horizontal camera with the lower forearms positioned directly on the collimator. The child may also sit on a parent's lap if necessary.

With the child in a lying position, lateral imaging of the skull should include the arm of the same side. Oblique views of the ribs can be obtained with the child in a lying position with the camera rotated to an oblique angle. For adequate visualization of the hips, knees and fibula, the feet should be turned inward with the toes close together (radiographic neutral position). If the child cannot be positioned in the radiographic neutral position, the child should be placed in as symmetrical a position as possible for the initial images of the

**Table 1** Recommended activities for  $^{99m}\text{Tc}$ -MDP based on the EANM dosage card [39]

Weight (kg)	$^{99m}\text{Tc}$ -MDP activity (MBq)	Weight (kg)	$^{99m}\text{Tc}$ -MDP activity (MBq)
3	40	32	255
4	40	34	270
6	60	36	280
8	75	38	295
10	95	40	310
12	110	42	320
14	125	44	335
16	140	46	350
18	155	48	360
20	170	50	375
22	185	52–54	395
24	200	56–58	420
26	215	60–62	445
28	225	64–66	470
30	240	68	490

The dosage recommendations should be taken in the context of “good practice“ of nuclear medicine and do not substitute for national and international legal or regulatory provisions. The national diagnostic reference levels should not be exceeded.

whole body. Additional spot views should then be recorded to, for example, separate the tibia and fibula by rotating the detector without moving the child.

To detect lesions in the feet, images in the plantar, dorsal and lateral projections are required. If a child has difficulty lying still or If a child is unable to lie still for any reason or

**Table 2** Absorbed dose to various organs in healthy subjects following administration of  $^{99m}\text{Tc}$ -labelled phosphates and phosphonates according to ICRP Publication 80 [40]

Organ	Absorbed dose per unit activity administered (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	0.0021	0.0027	0.0039	0.0058	0.011
Bladder	0.048	0.060	0.088	0.073	0.13
Bone surfaces	0.063	0.082	0.13	0.22	0.53
Brain	0.0017	0.0021	0.0028	0.0043	0.0061
Breast	0.00071	0.00089	0.0014	0.0022	0.0042
Gallbladder	0.0014	0.0019	0.0035	0.0042	0.0067
Stomach	0.0012	0.0015	0.0025	0.0035	0.0066
Small intestine	0.0023	0.0029	0.0044	0.0053	0.0095
Colon	0.0027	0.0034	0.0053	0.0061	0.011
Heart	0.0012	0.0016	0.0023	0.0034	0.0060
Kidneys	0.0073	0.0088	0.012	0.018	0.032
Liver	0.0012	0.0016	0.0025	0.0036	0.0066
Lungs	0.0013	0.0016	0.0024	0.0036	0.0068
Muscles	0.0019	0.0023	0.0034	0.0044	0.0079
Oesophagus	0.0010	0.0013	0.0019	0.0030	0.0053
Ovaries	0.0036	0.0046	0.0066	0.0070	0.012
Pancreas	0.0016	0.0020	0.0031	0.0045	0.0082
Red marrow	0.0092	0.010	0.017	0.033	0.067
Skin	0.0010	0.0013	0.0020	0.0029	0.0055
Spleen	0.0014	0.0018	0.0028	0.0045	0.0079
Testes	0.0024	0.0033	0.0055	0.0058	0.011
Thymus	0.0010	0.0013	0.0019	0.0030	0.0053
Thyroid	0.0013	0.0016	0.0023	0.0035	0.0056
Uterus	0.0063	0.0076	0.012	0.011	0.018
Other organs	0.0019	0.0023	0.0034	0.0045	0.0079
Effective dose (mSv/MBq)	0.0057	0.0070	0.011	0.014	0.027

there is a need for differentiation of activity, for example, in the renal pelvis or the ribs, spot images of the spine or thorax can be acquired in a sitting position. A radionuclide side marker should always be used to identify the extremities.

#### *Flow images*

There is debate as to the usefulness of the first phase study. These guidelines do, however, recommend acquisition of the first phase especially in children with primary malignant bone tumours or clinical suspicion of localized bone disease. When flow images are acquired, the camera should be positioned over the region of interest before tracer injection. At least 30 frames should be obtained in a 64×64 or greater matrix at 1–3 s per frame.

#### *Blood-pool (tissue phase) images*

Blood-pool images should be acquired immediately after the flow portion of the study and completed within 10 min of tracer injection, for approximately 3–5 min per image. After 10 min, some activity may be apparent in the skeleton. Blood-pool images are usually obtained in a 128×128 or greater matrix, with a count density of approximately 300,000 counts per image (150,000–200,000 counts per image may be adequate for the extremities). In children under the age of 4 years, high-quality blood-pool images of the whole body can be obtained acquiring overlapping static images, each of 3 min duration, starting with the area most likely to show pathology and finishing with the area least likely. In older children a whole-body image is recorded at a scan speed of 25 to 30 cm per minute).

#### *Delayed (skeletal phase) images*

Routine delayed images are usually obtained from 2–5 h after injection. Whole-body bone scintigraphy can be accomplished with multiple overlapping images (i.e. spot imaging) or with continuous images (i.e. whole-body scan) obtained in anterior and posterior views with a high-resolution or ultrahigh-resolution collimator. The first option is recommended in children younger than 4 years of age. When spot views are used as the primary method of acquiring bone images, the areas of bony skeleton covered by the spot views must overlap to avoid missing regions of the skeleton.

The first spot view of the axial skeleton, usually the chest, is acquired for approximately 500,000 to 1 million counts. The remaining spot views are then acquired for the same time as the first view, or using as a rule of thumb the following parameters

- 50–100 kcounts for hands and feet
- 100–200 kcounts for the knees
- 300 kcounts for the skull

Spot images may be obtained in a 128×128 or 256×256 matrix. Whole-body views are usually obtained in a 256×1024 or greater matrix, with the following suggested parameters:

- Scan speed 8 cm/min from 4 (or 5) to 8 years of age
- Scan speed 10 cm/min from 8 to 12 years of age
- Scan speed 12 cm/min from 12 to 16 years of age
- Scan speed 15 cm/min over 16 years of age

or total imaging time 30 minutes.

#### *SPECT images*

In some patients, SPECT imaging is helpful in determining the presence, location and extent of disease. SPECT imaging should be performed as recommended by the gamma camera manufacturer. Typical acquisition and processing parameters with a single-head gamma camera are 360° circular orbit, 60–120 steps, 128×128 or greater matrix, and 10–40 s per stop. An equivalent total number of counts should be acquired if continuous acquisition is used.

#### *Pinhole collimator images*

A pinhole collimator may be used if very high-resolution images of a specific area are necessary for the evaluation of relatively small anatomic structures such as the hips (for slipped capital epiphysis, for example), hands or feet [41]. The resolution of the pinhole collimator is inversely related to the diameter of the aperture (typically between 2 and 5 mm). The closer the pinhole to the bone, the greater the magnification. Approximately 75,000–100,000 counts should be obtained for pinhole collimator views. Zoom magnification or a converging collimator may also be used to improve resolution, particularly when small structures are being imaged. The physician interpreting the image must be informed when collimators such as a pinhole, which introduce distortions, are used.

#### *Hybrid imaging*

If SPECT/CT scanners are used attention must be paid to the additional radiation dose of the CT portion the scan, and the CT acquisition should be strictly limited to the body segment of interest. The radiation burden varies dramatically depending on the patient's age and the CT settings, as shown, as an example, in Table 3 (where the volumetric anthropomorphic CT dose index, CTADI<sub>vol</sub>, is used instead of the volume CT dose index) [42]. Hence, CT settings should be individually adjusted according to the patient's age and BMI. If the CT scan is only used for attenuation correction, kVp values as low as 80 and mAs values below 10 result in adequate attenuation correction in children [15]. In performing hybrid

**Table 3** Radiation doses (CTADI<sub>vol</sub> in milligray) from CT scans in relation to patient age, tube voltage, and tube current [42]

Phantom	Measurement no.	Tube voltage (kVp)	Tube current (mA)				
			10	20	40	80	160
Newborn	1	80	0.42	0.85	1.69	3.39	6.78
	2	100	0.80	1.60	3.21	6.41	12.83
	3	120	1.26	2.53	5.05	10.10	20.20
	4	140	1.77	3.53	7.06	14.13	28.25
1-year-old	1	80	0.37	0.74	1.47	2.94	5.88
	2	100	0.70	1.40	2.80	5.59	11.19
	3	120	1.11	2.22	4.45	8.89	17.78
	4	140	1.57	3.14	6.28	12.56	25.11
5-year-old	1	80	0.33	0.66	1.32	2.65	5.30
	2	100	0.64	1.28	2.55	5.10	10.20
	3	120	1.02	2.04	4.08	8.16	16.31
	4	140	1.46	2.91	5.83	11.66	23.32
10-year-old	1	80	0.30	0.60	1.19	2.38	4.76
	2	100	0.58	1.16	2.32	4.64	9.27
	3	120	0.92	1.84	3.67	7.35	14.69
	4	140	1.32	2.63	5.26	10.52	21.04

imaging, then, the purpose of the CT part (attenuation, anatomical localization or diagnosis) must be clear.

#### Interventions

In children who cannot empty their bladder for any reason and in whom delayed images are logistically difficult, a bladder catheter may be necessary to visualize the pelvis adequately.

**Table 4** Recommended activities based on the current EANM dosage card for two- and three-dimensional <sup>18</sup>F-fluoride PET [39]

	Weight (kg)	Activity (MBq)		Weight (kg)	Activity (MBq) 2D	
		Two-dimensional	Three-dimensional		Two-dimensional	Three-dimensional
	3	26	14	32	189	102
	4	30	16	34	200	108
	6	44	24	36	207	112
	8	55	30	38	218	118
	10	70	38	40	229	124
	12	81	44	42	237	128
	14	92	50	44	248	134
	16	104	56	46	259	140
	18	115	62	48	267	144
	20	126	68	50	277	150
	22	137	74	52–54	292	158
	24	148	80	56–58	311	168
	26	159	86	60–62	329	178
	28	167	90	64–66	348	188
	30	178	96	68	363	196

The dosage recommendations should be taken in the context of “good practice” of nuclear medicine and do not substitute for national and international legal or regulatory provisions. The national diagnostic reference levels should not be exceeded.

#### Processing

The images should be processed before the child has left the department. Dynamic images should be reframed to 2- or 3-s images. For SPECT image processing check for movement and use a filter, which moderately increases the contrast and does not smooth the data too much. Details depend on the camera and computer interface used. Transverse, sagittal and coronal slices should be reconstructed in relation to the body axis. In some cases (e.g. lower spine) reorientation in relation to the organ axis might be necessary. The slice thickness should be equal to the resolution of the camera system. SPECT/CT acquisition must be checked carefully for movements that occurred between the CT scan and the SPECT scan

#### Quality control/pitfalls

If possible (depending of the child’s condition), the child should be in a straight and symmetrical position for all images. Separate visualization of the epiphyseal plates of the tibia and fibula and the radius and ulna is essential for a high-quality bone scan. The quality of the bone scan can be judged by the sharpness of the appearance of the epiphyseal plates of the femora, tibiae and fibulae. For good visualization of the pelvis the bladder should be empty.

The vertebrae and ribs should be clearly identified one by one. Interpretation of the images should always be done with knowledge of the results of plain radiography, ultrasonography and MRI, and of the clinical history (for example, a long period of immobilization can lead to decreased bone uptake of the radiotracer; similarly in

sympathetic reflex dystrophy the painful limb is generally the hypoactive one). Knowledge of the normal appearance of the skeleton at different ages is important. Another pitfall is a lack of increased uptake in osteomyelitis in which increased intraosseous pressure leads to reduced perfusion.

A thorough knowledge of possible normal variants, such as age-dependent ossification (for example, the normal synchondrosis of the posterior pubic ramus [43]), reduces the risk of false-positive statements. The "shine-through" of activity from the costochondral junctions in posterior views of the thorax should not be mistaken for multiple rib fractures.

### <sup>18</sup>F-Fluoride PET

PET using <sup>18</sup>F-fluoride is an emerging alternative to conventional scintigraphy for evaluation of bone metabolism. <sup>18</sup>F-Fluoride is a bone-seeking agent that shows the favourable characteristic of high bone uptake in the setting of rapid blood clearance. The resulting high bone-to-background ratio in a short time together with the high sensitivity of modern PET scanners allows the acquisition of high-resolution images starting 15 to 30 min after administration of the radiopharmaceutical and completed within 1 h of injection, compared to several hours for <sup>99m</sup>Tc-MDP imaging [4]. The radiation dosimetry of <sup>18</sup>F-fluoride bone scans has been reported to be similar to that with <sup>99m</sup>Tc-MDP imaging [44, 45]. Recommended injected activities based on the current EANM dosage card [39] for two- and three-dimensional <sup>18</sup>F-fluoride PET are listed in Table 4. In the evaluation of benign bone disease, encouraging results have been reported for the use of <sup>18</sup>F-fluoride in the evaluation of back pain in adolescents [45], imaging of condylar hyperplasia [46], and evaluation of suspected child abuse [47].

Although excellent results with <sup>18</sup>F-fluoride for the detection of bone metastases have been reported in adults with higher sensitivity than conventional bone scintigraphy [48], published data in paediatric oncology are scarce and further studies are necessary to confirm that sensitivity is also higher in the paediatric age group and to evaluate the impact on clinical management.

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