Nuclear Medicine in Pediatric Sarcomas

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Introduction

- Most common pediatric sarcomas:
  - Osteosarcoma
  - Ewing sarcoma
  - Rhabdomyosarcoma

Key Points :
Nuclear Medicine in Pediatric Sarcomas

- **Identify optimal biopsy site**
- **Initial Staging**:
  - FDG-PET/CT or PET/MR is recommended for initial staging to detect distant metastases.
  - Detect systemic disease & metastases
- **Assessment of Neoadjuvant Therapy and Treatment Response**:
  - FDG-PET/CT can help evaluate response to neoadjuvant treatments and
  - planning subsequent therapies in neoadjuvant settings.
  - identify residual metabolic activity.
- **Detection of Bone Metastases**:
  - FDG-PET/CT has high sensitivity for detecting bone metastases in pediatric sarcomas.
- **Restaging and detecting recurrence**
- **Surveillance**

Complement anatomical imaging MRI/CT

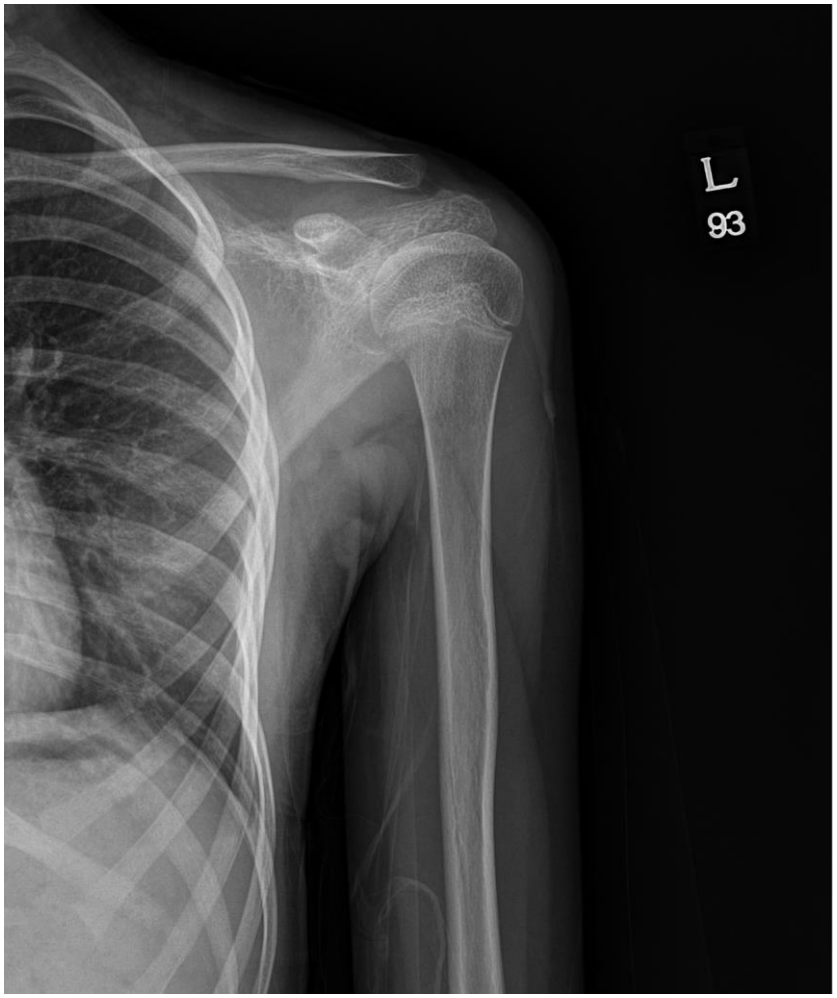
Staging

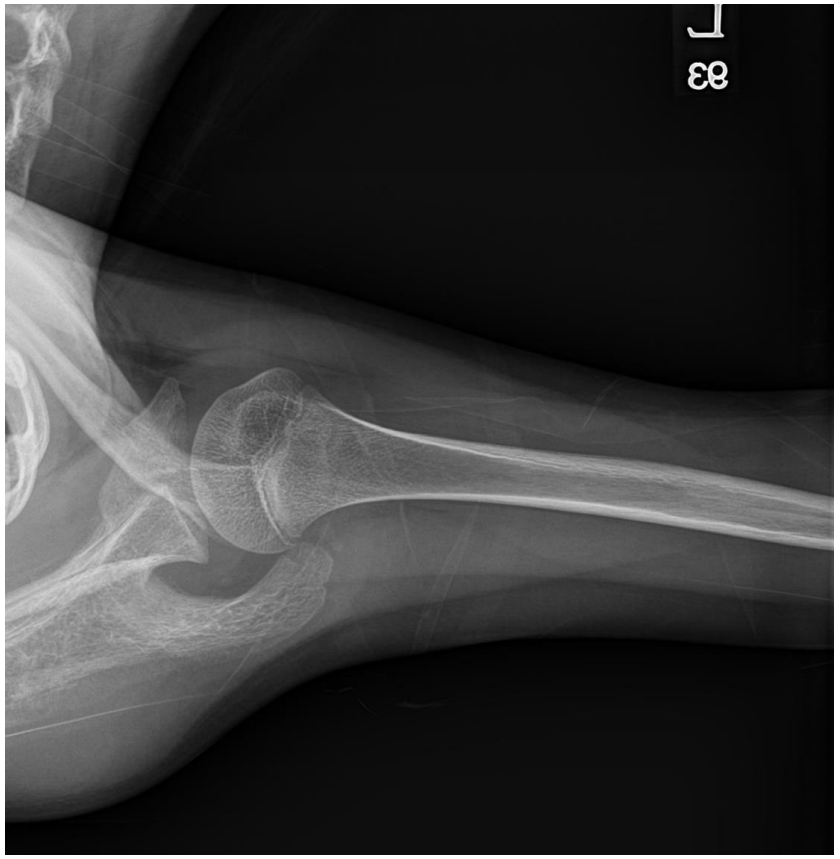
- MRI: local tumor extent
- Chest CT: pulmonary metastases
- **FDG-PET/CT: systemic staging**
  - Soft tissue & bone metastases detection
  - Bone Metastases Detection:
    - High sensitivity for detecting bone metastases.
    - Bone Scan : alternative when needed
    - Bone Scan: alternative if PET unavailable

Initial Workup: ES, OS,RS

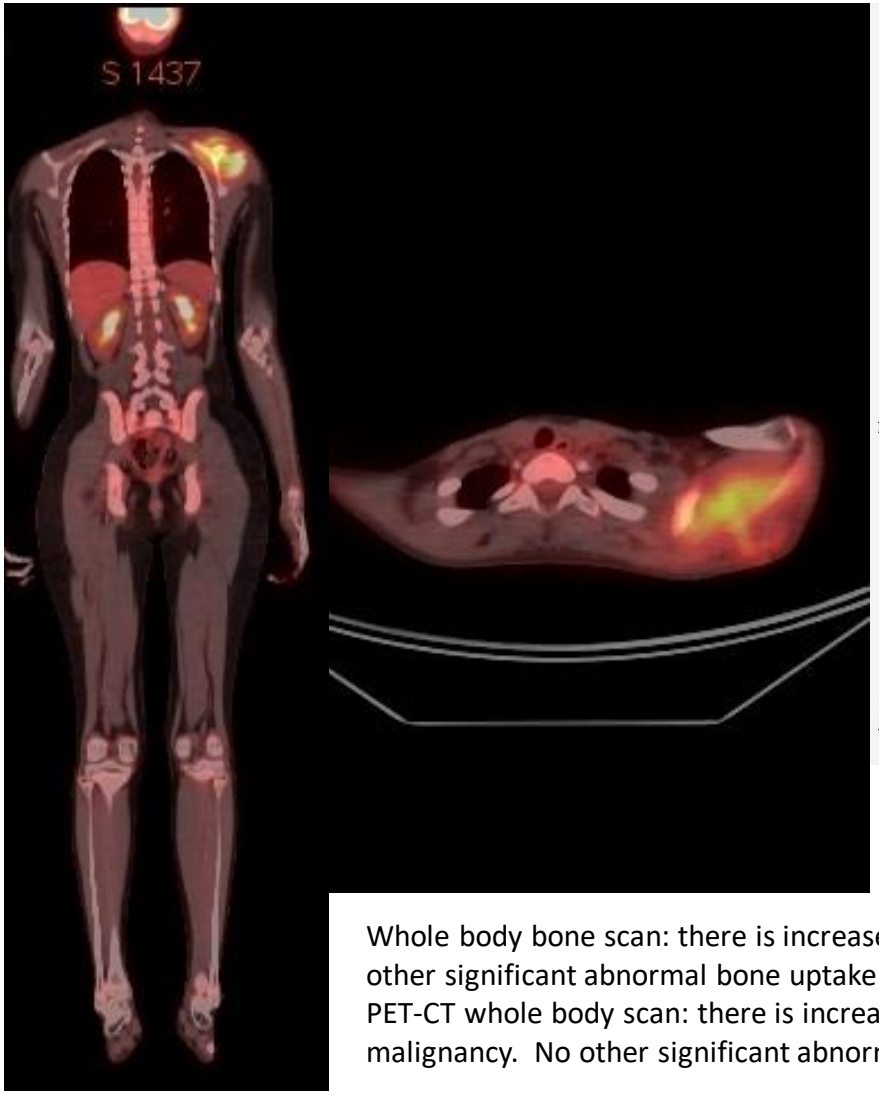
NCCN Guideline:

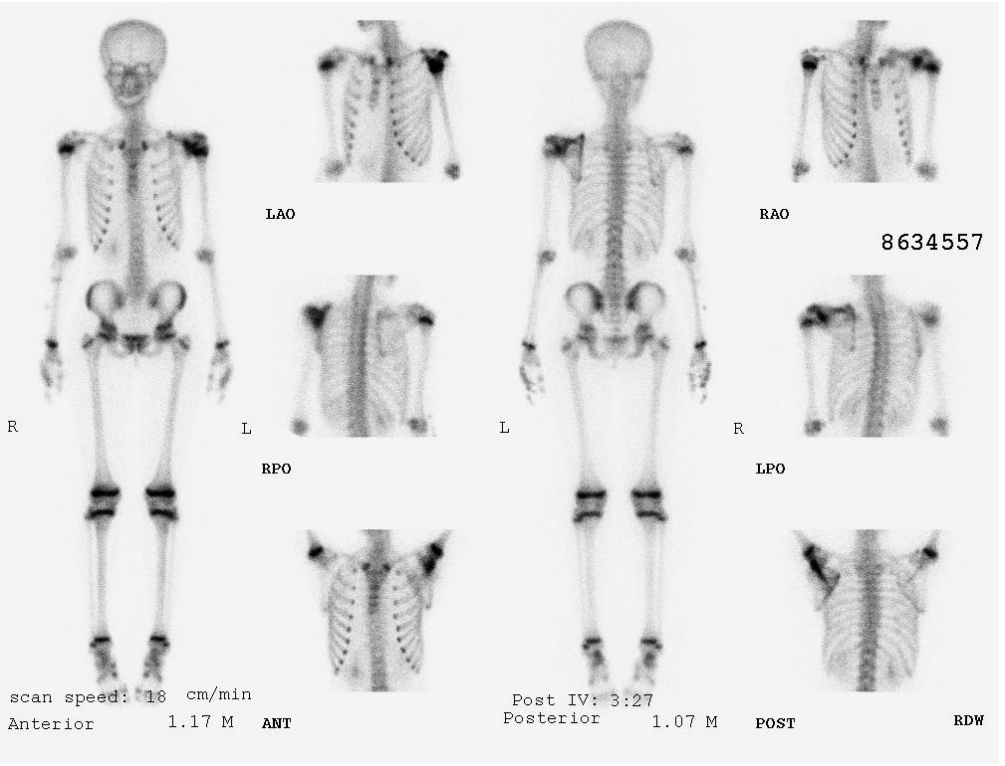
FDG PET/CT or bone scan



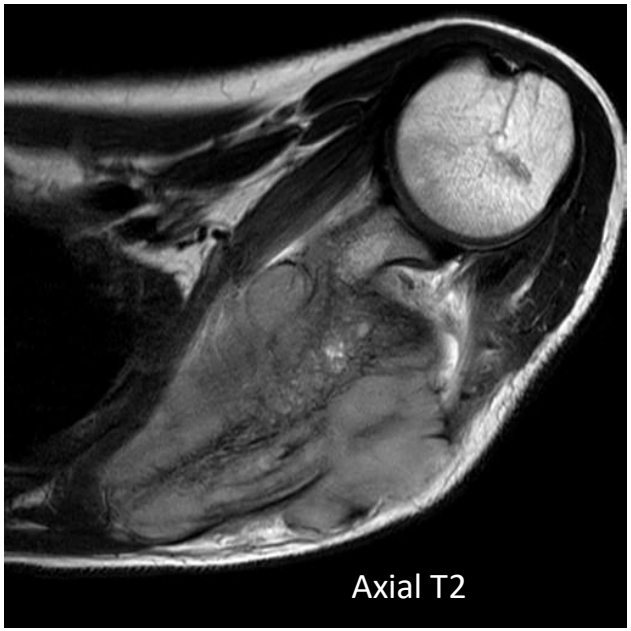


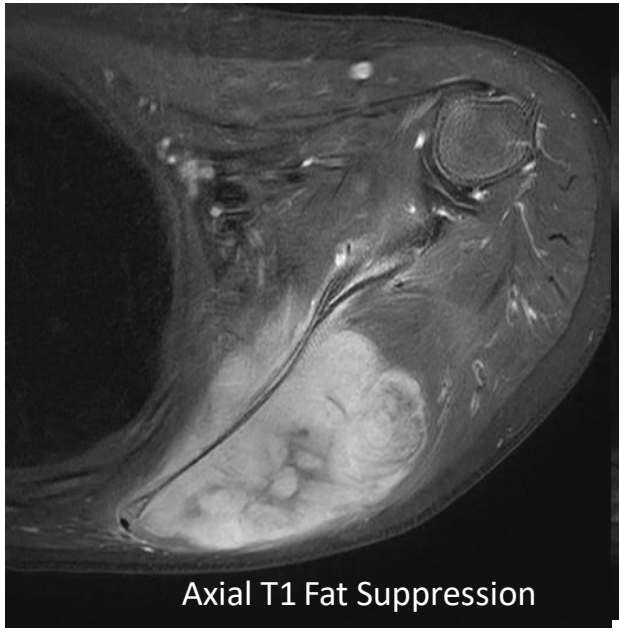
There is aggressive (moth-eaten) osteolytic lesion involving the left scapula, mainly its spine.

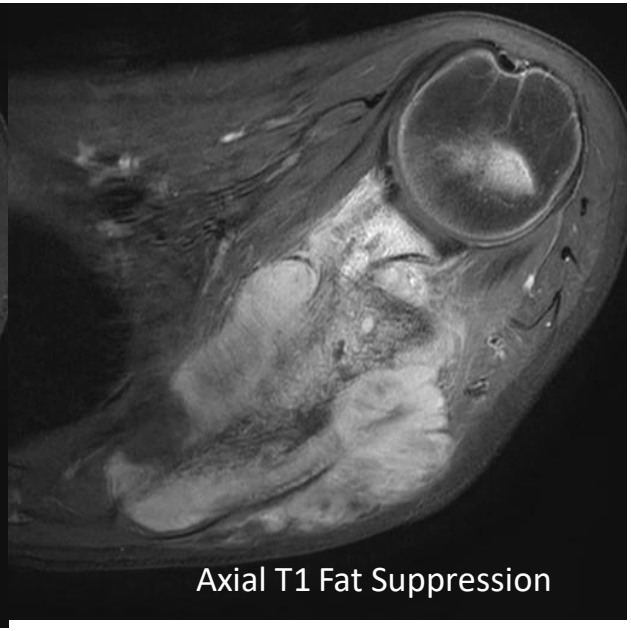




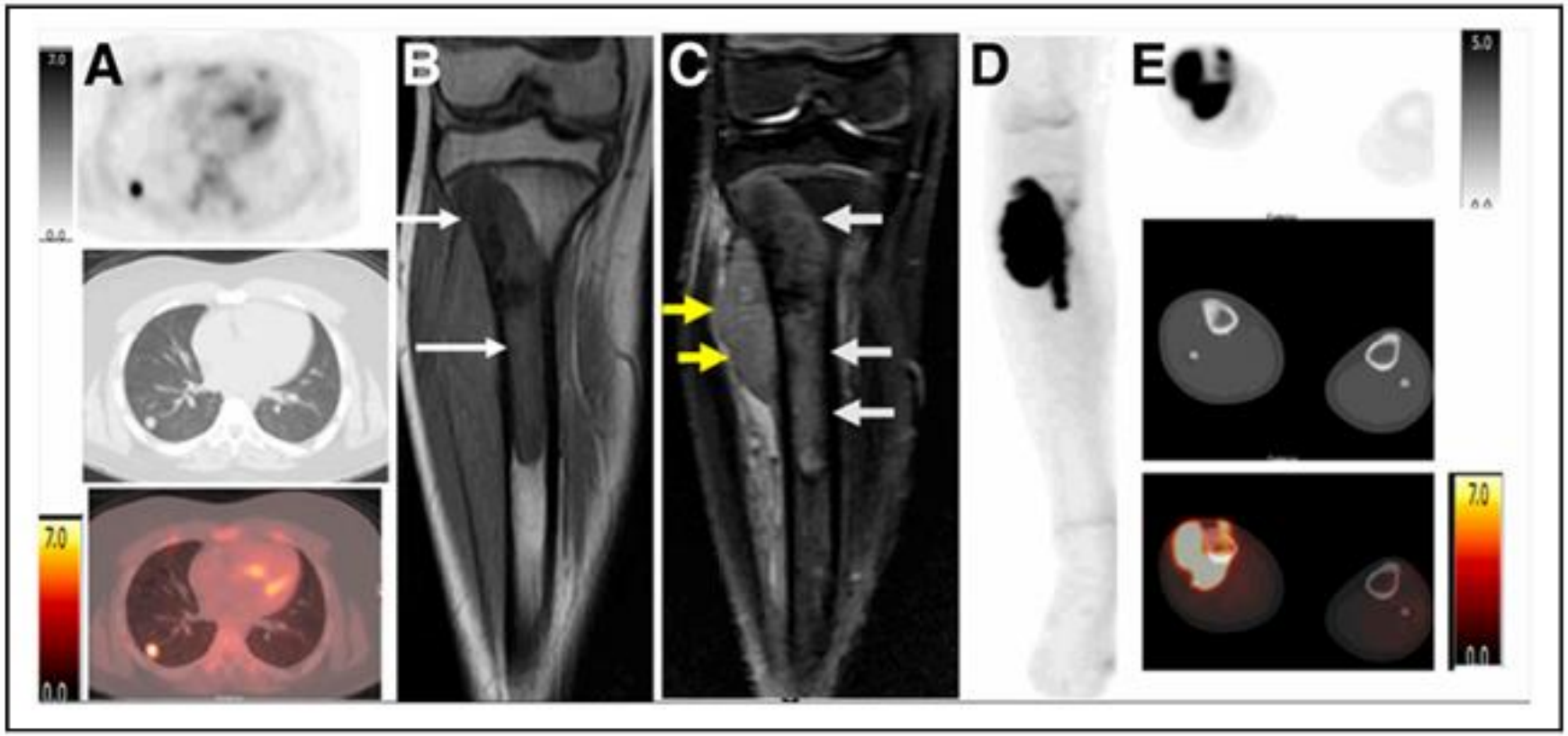
Whole body bone scan: there is increased radiotracer uptake in the left scapula, suspicious for malignancy. No other significant abnormal bone uptake to suggest skeletal metastasis.
PET-CT whole body scan: there is increased FDG uptake in the soft tissue mass involving left scapula, suggestive of malignancy. No other significant abnormal FDG uptake to suggest distant metastasis



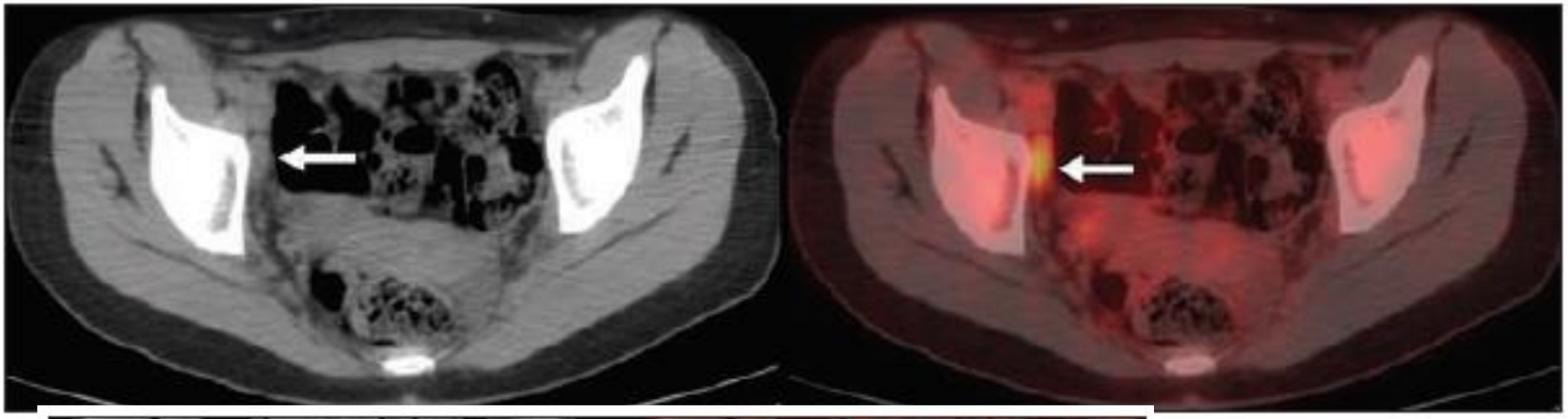


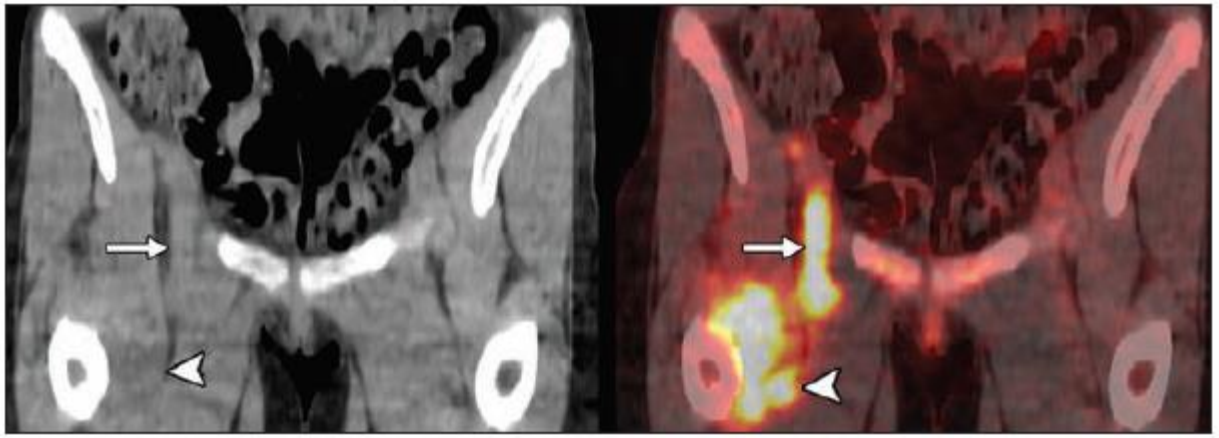


Extensive soft tissue mass (9.5 X 6 X 7.6 cm) involving left scapula (including acromion and coracoid) with invasion of the supraspinatus, infraspinatus, and subscapularis muscles. This mass shows diffuse high signal with low signal striation on T2 WI, prominent enhancement, and diffusion restriction. No definite osteoid matrix/calcification in soft tissue component.
Multiple borderline lymph nodes in left supraclavicular fossa and axillary area.
Edematous changes at supraspinatus, infraspinatus, and teres minor muscles.

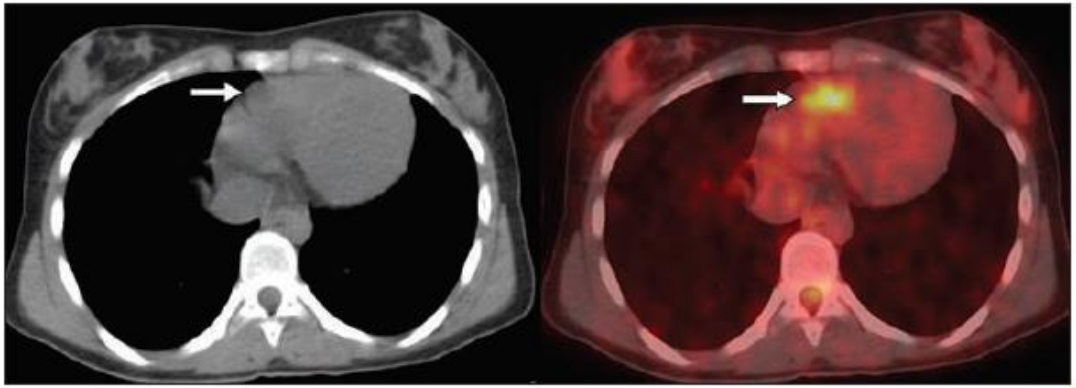


A13-y-old boy with right leg pain. (A) 18F-FDG PET CT shows 1-cm nodule with markedly elevated uptake in right lower lobe (SUVmax,6.7)
Hypointense signal on coronal T1 MR image shows tumor extending from tibial metaphysis through proximal third of right tibia (arrows). (C) Coronal T2 short-tau inversion recovery MR image shows intermediate signal within intramedul lary component of tumor (white arrows), corresponding to hypointense T1 signal, and hyperintensity in soft-tissue component lateral to tibia (yellow arrows). (D) 18F-FDG PET/CT anterior maximum intensity-projection view shows intense uptake in the proximal aspect of the right distal lower extremity. (E) 18F-FDG PET axial emission image (top), transmission CT bone window (middle), and PET/CT image (bottom) show intense though irregularly increased uptake of 18F-FDG in both bone and soft-tissue components of tumor (SUVmax,15.TM).





Fi
PE
(a
no
stasis detected on ^{18}F-FDG
n FDG-avid lymph node
addition of FDG PET. Lymph



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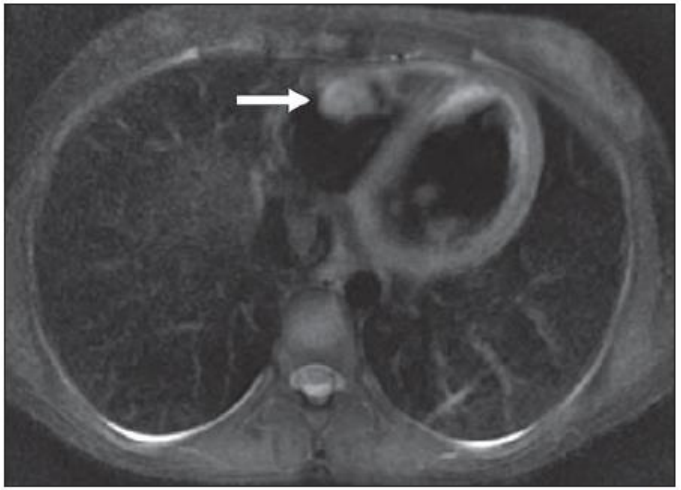


RS:
Regional lymph nodes

- MRI+ FDG PET/CT or PET/MRI for evaluating locoregional lymph nodes.
- Pathological lymph nodes>15 mm
- Any FDG positive lymph node with a short axis<15 mm should be considered suspicious, with FDG positivity defined as uptake greater than normal liver FDG uptake without a known physiological explanation

Prognosis

- Prognosis: High SUV values in FDG-PET/CT are associated with higher tumor grade, tumor aggressiveness and poorer prognosis.

FDG-PET/CT in Osteosarcoma Prognosis

- SUVmax reduction after chemotherapy correlates with histologic response

- Predicts progression-free and overall survival

Prognostic Value in Rhabdomyosarcoma

- Complete metabolic response after therapy linked to better survival

OS:
PREDICTION OF OUTCOMES

- **SUVmax at baseline and after NCT**, could predict progression-free survival and OS

- SUVmax of over **2.5** after NCT is associated with worse progression-free survival

- SUV declined after NCT, which reflected the histologic response

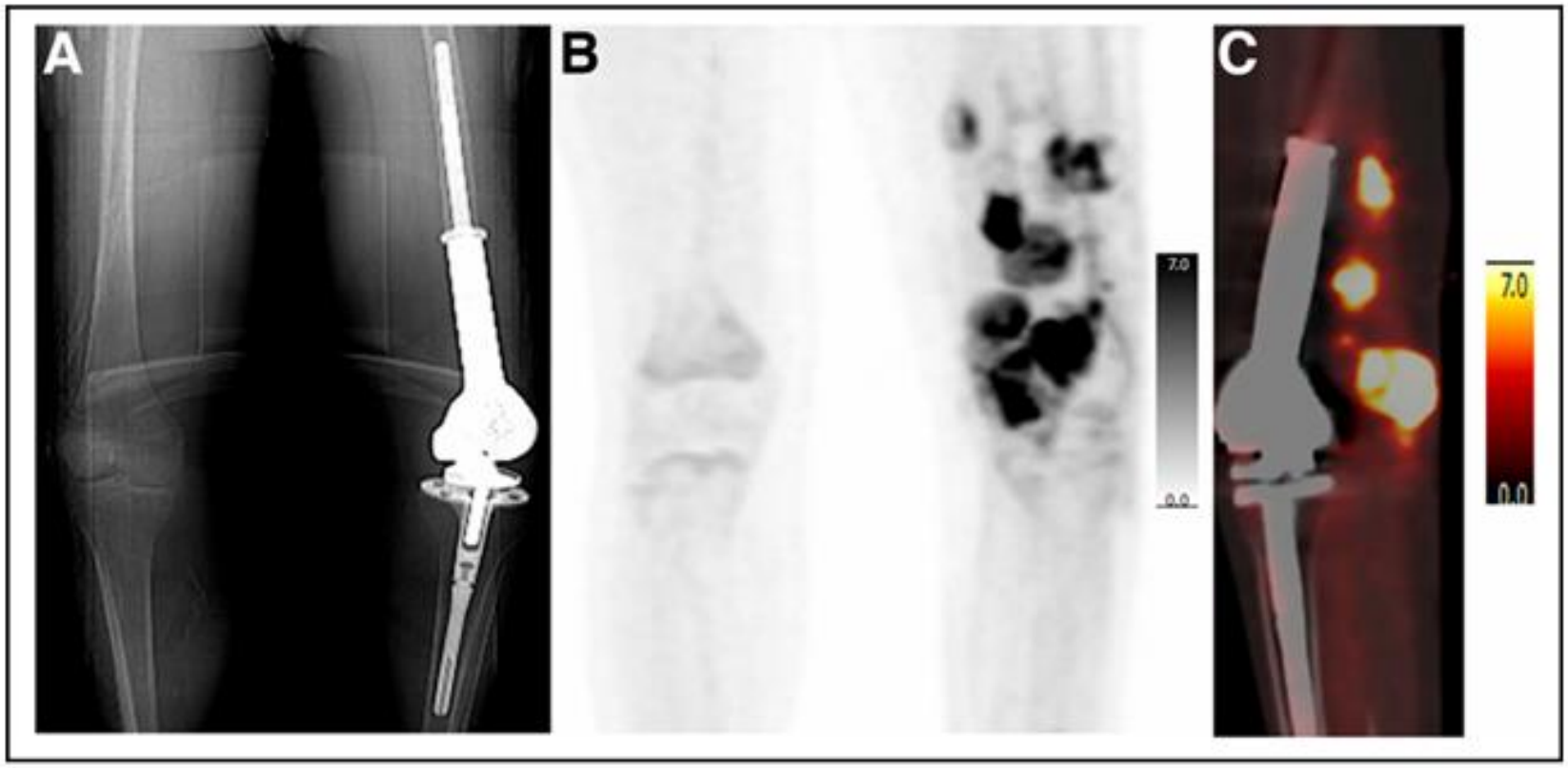
OS:
PREDICTION OF RESPONSE TO NCT

- Predicting the histologic response of tumor **during NCT** may be a better option than doing so after completion of NCT in the clinic because the latter is too late to modify the NCT regimen

- SUVmax after **1cycle of NCT** can also predict the histologic response with an accuracy of 92.9% using a cutoff of 3.2

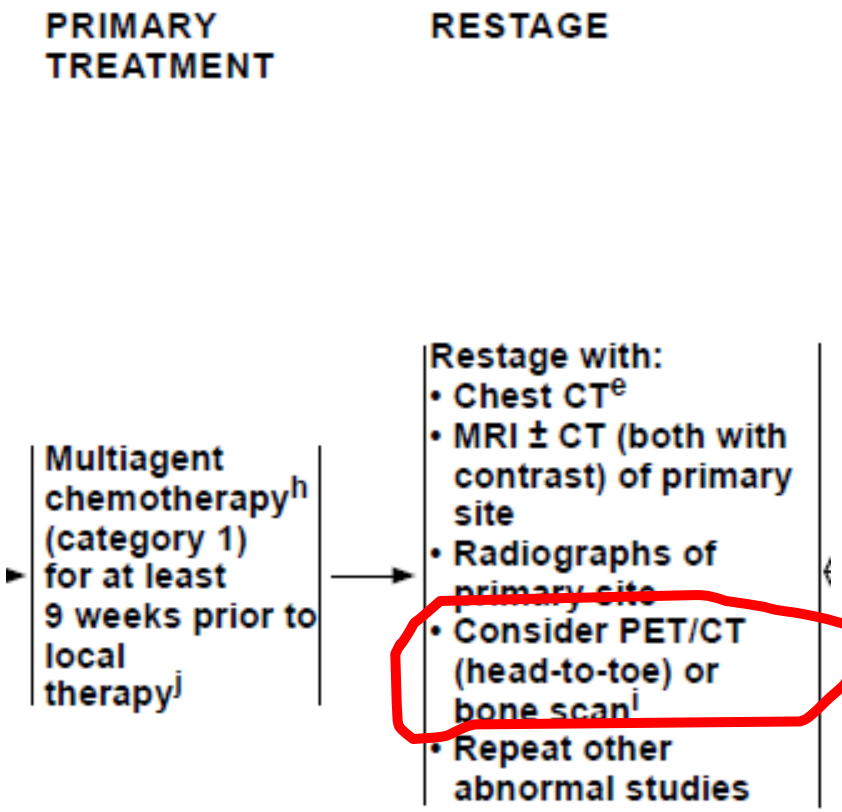
RECURRENT DISEASE

- excellent diagnostic performance, with pooled sensitivity and specificity rates of 91% (95% CI, 81% to 96%) and 93% (95% CI, 87% to 97%), respectively



15-y-old boy with history of osteosarcoma in left femur and limb-sparing procedure on left lower extremity. (A) Topogram from attenuation-correction CT shows rotating-hinge modular prosthesis in left distal femur and left knee. (B) Anterior maximum-intensity projections shows multiple areas of markedly elevated uptake in left lower extremity. (C) PET/CT sagittal view of left leg shows numerous soft-tissue nodules with intense uptake posterior to prosthesis (SUVmax, 20.3).

ES



Use the same imaging technique that was performed in the initial workup

Restaging

- Chest imaging
- MRI of primary site with or without CT and plain radiography.
- Head-to-toe FDG-PET/CT or bone scan can be used for restaging depending on the imaging technique that was used in the initial workup.

Surveillance

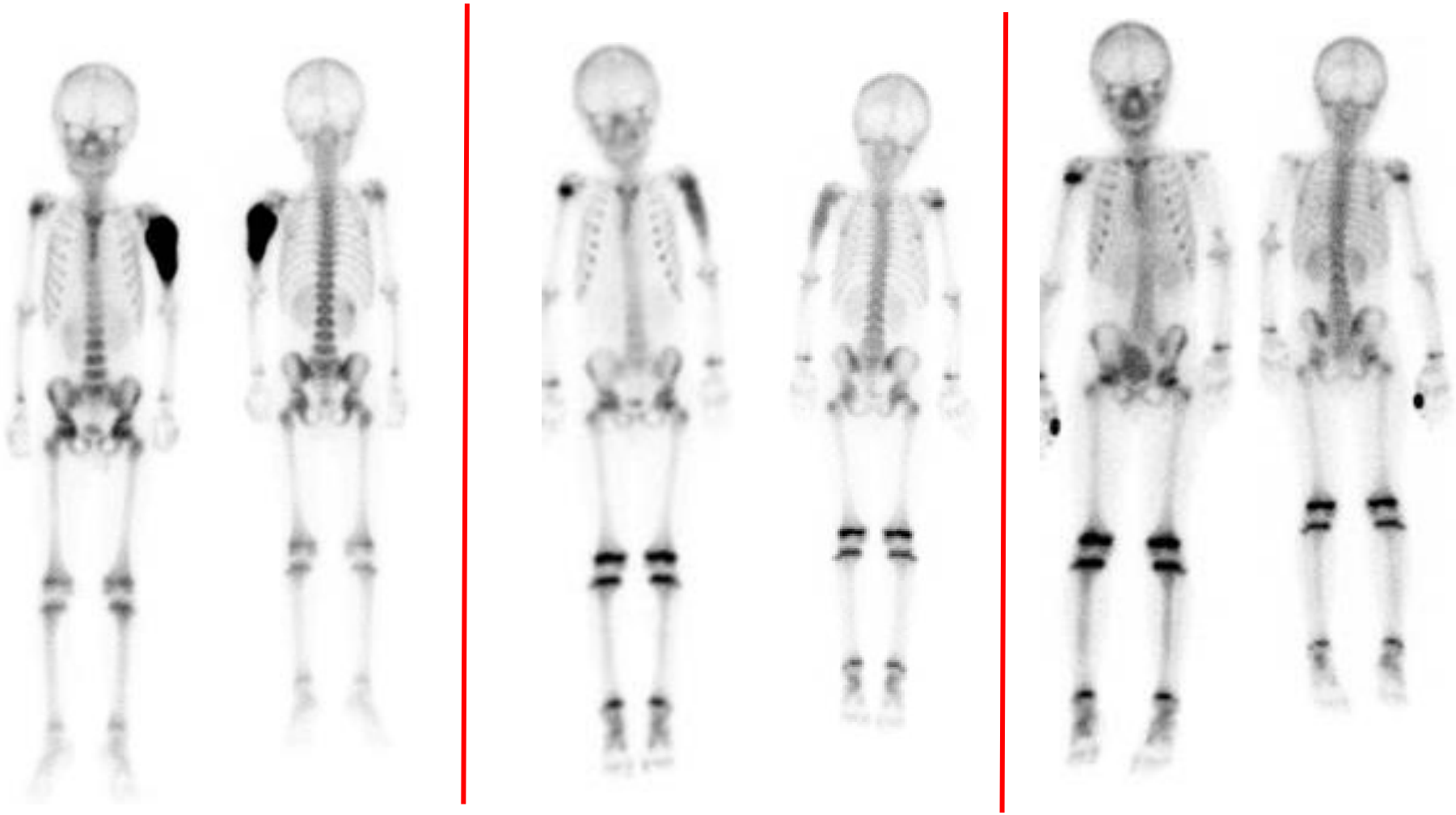
- Physical examination,
- CBC and other laboratory studies (as indicated)
- MRI with or without CT, and plain radiographs of the primary site
- Chest imaging (x-ray or CT) is recommended every 3 months.
- FDG-PET/CT or bone scan can be considered as appropriate.

Bone Scan

(whole Body Bone Scan)

- a valuable aid for clinical management Ewing sarcoma/OS,…

- nonspecific increased uptake of the bone-seeking agent both at
    - the primary site
    - metastatic sites



Bone Scan

(whole Body Bone Scan)

- FDG PET/CT:
  - Superior to bone scan for skeletal metastases (88% vs 37%)
  - Useful in bone marrow involvement

FDG-PET/CT in Osteosarcoma Staging

- Higher sensitivity than bone scintigraphy (95% vs 76%)

- Superior for bone metastasis detection

FDG-PET/CT in Rhabdomyosarcoma

- More sensitive than bone scan & marrow biopsy

- Superior for lymph node and bone metastases

FDG PET/CT

- High sensitivity and specificity
  - Primary site
  - Bone metastases

  - Soft tissue lesions
  - Skip lesions
  - BM
  - LNs

Bone Scan or FDG PET/CT

- **High concordance**

- FDG-PET and bone scan had a **high level of agreement** in detecting osseous metastatic disease (examination-based concordance rate 98%)

Bone Scan or FDG PET/CT

- Some disagreement when evaluating specific regions of patients with osseous metastatic disease
  - While bone scans identify areas of osteoblast activity
  - FDG-PET scans identify areas of glucose metabolism

  - Skull

  - Soft tissue lesions
  - Skip lesions
  - BM
  - LNs

Bone Scan or FDG PET/CT

- Some studies :FDG-PET to be slightly superior to bone scan for screening for osseous metastatic disease
  - **Lytic or sclerotic**
- Both imaging modalities to provide complimentary information

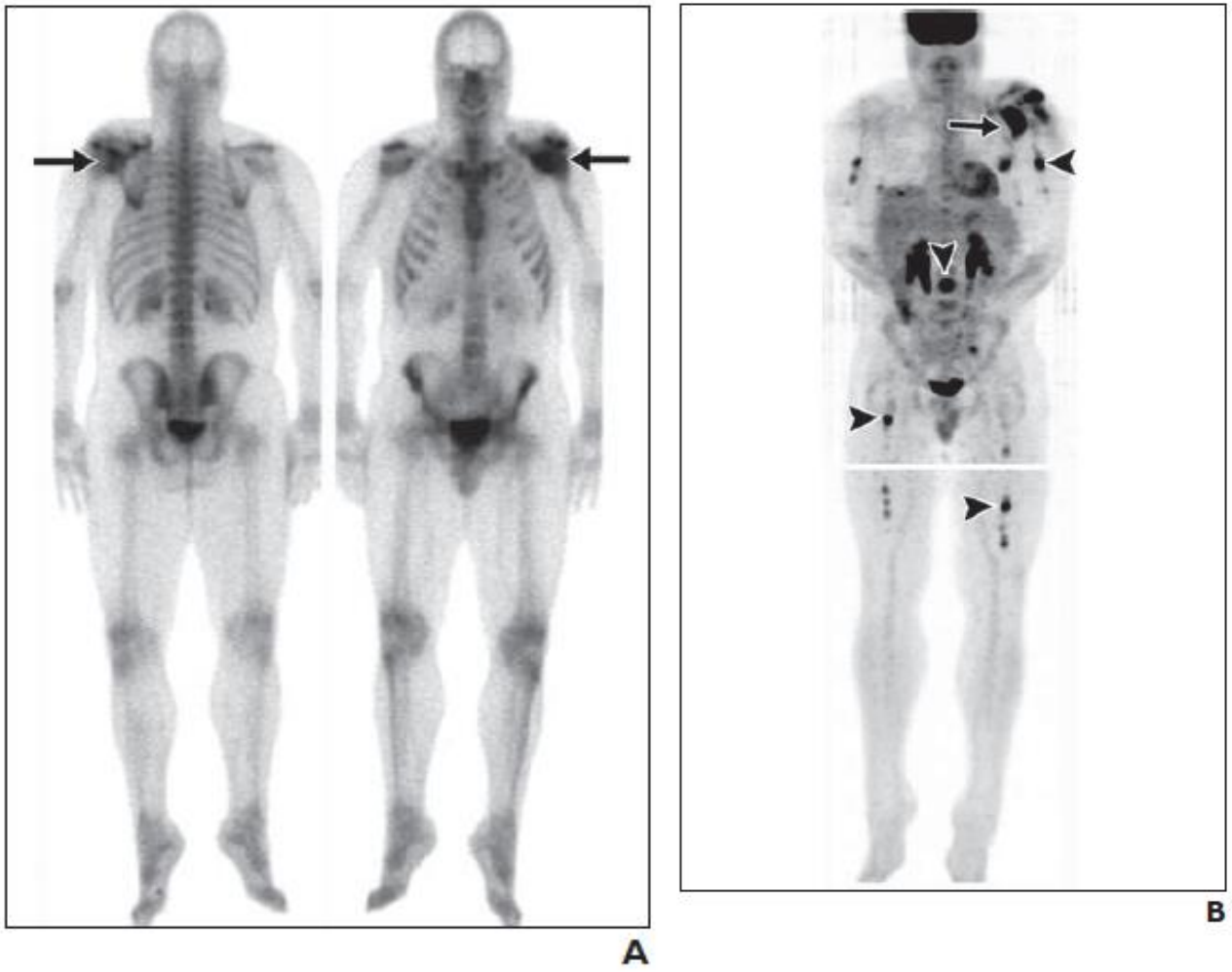


Fig. 1—32-year-old man with Ewing sarcoma (ES) with bone metastases detected on 18F-FDG PET/CT but not bone scan.
A, Posterior and anterior planar bone scan images show abnormal MDP uptake in left scapula representing primary ES (*arrows*).
B, FDG PET/CT maximum intensity projection image shows not only abnormal uptake in left scapula primary ES (*arrow*) but also multiple osseous metastases (*arrowheads*) in spine and upper and lower extremities.

Primary malignancy was lytic on CT (not shown).

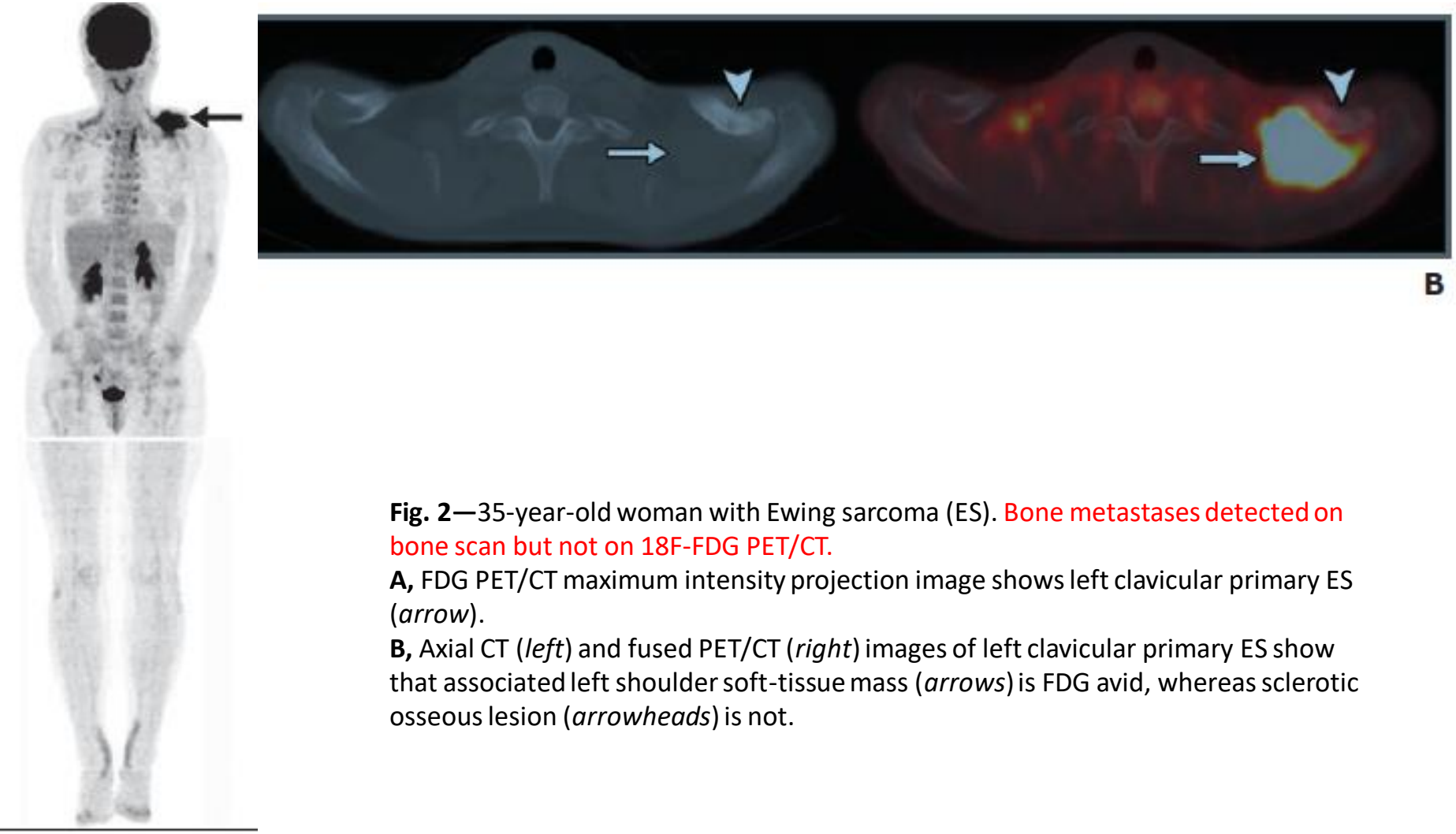
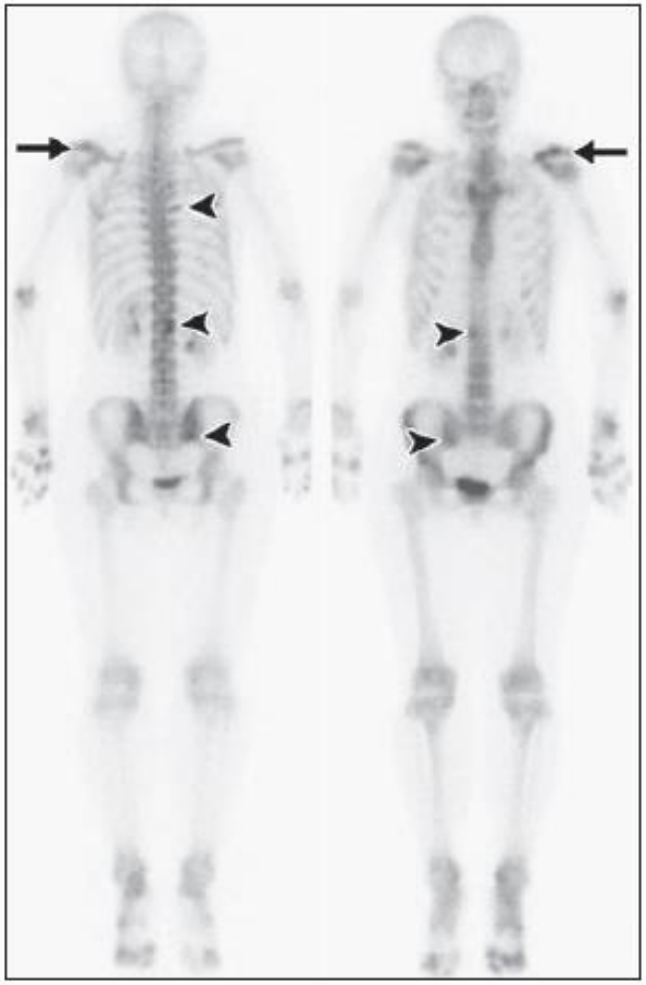


Fig. 2—35-year-old woman with Ewing sarcoma (ES). Bone metastases detected on bone scan but not on 18F-FDG PET/CT.

A, FDG PET/CT maximum intensity projection image shows left clavicular primary ES (*arrow*).

B, Axial CT (*left*) and fused PET/CT (*right*) images of left clavicular primary ES show that associated left shoulder soft-tissue mass (*arrows*) is FDG avid, whereas sclerotic osseous lesion (*arrowheads*) is not.



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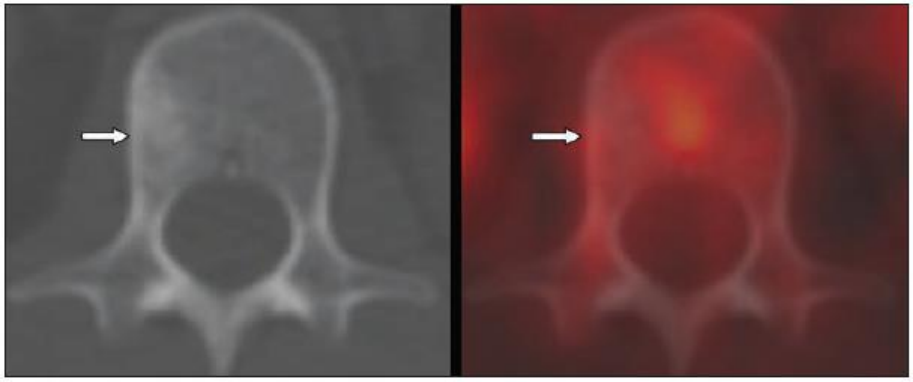
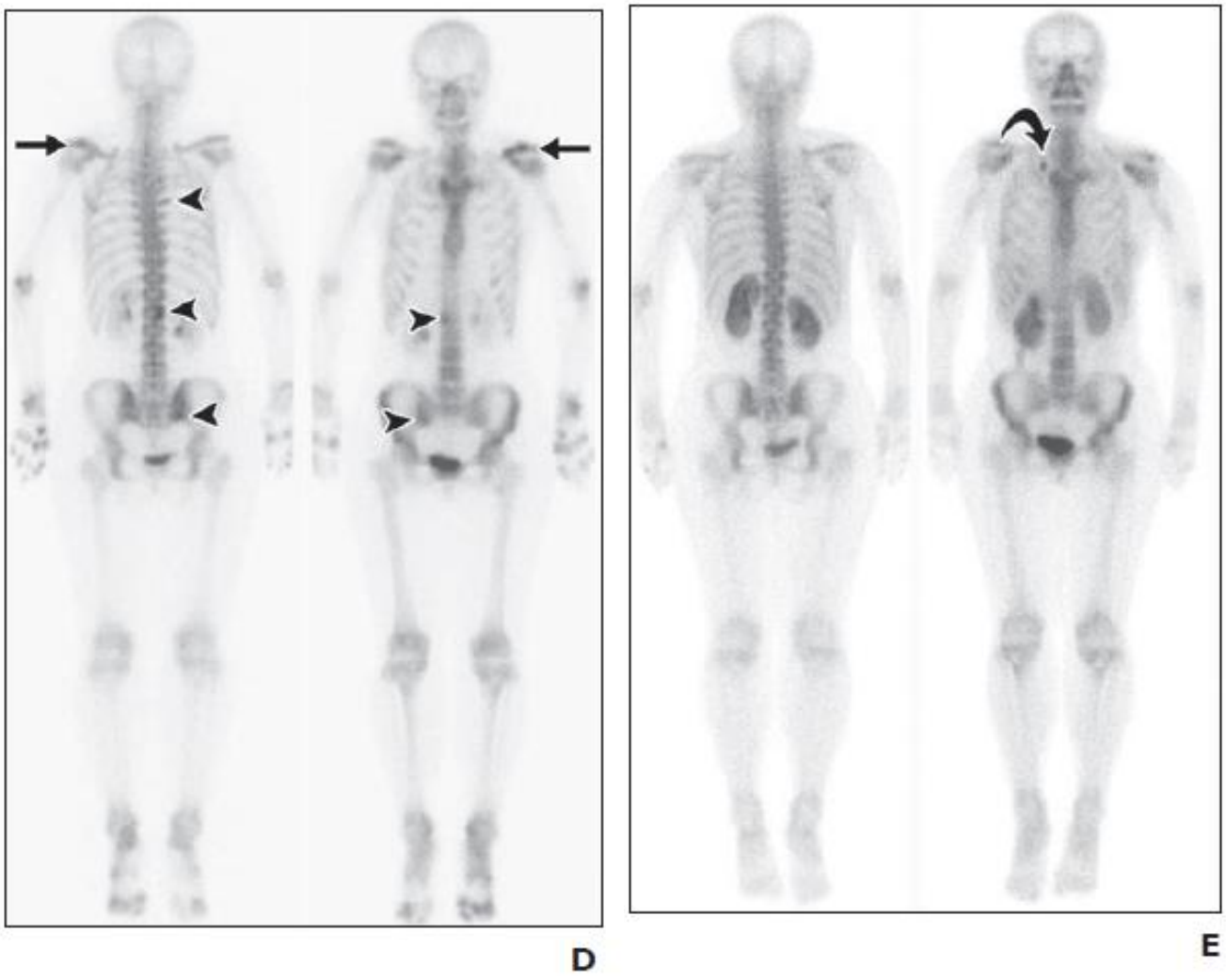


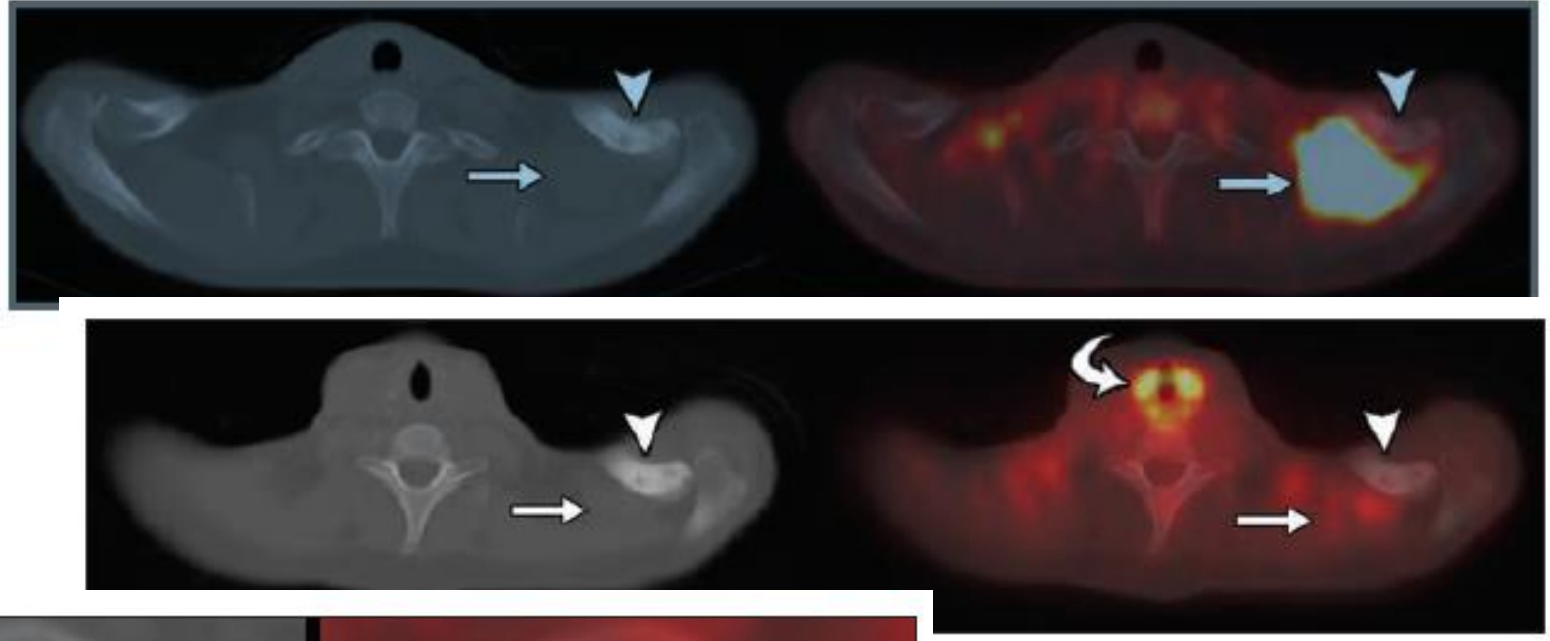
C

C, Axial CT (*left*) and fused PET/CT (*right*) images of L1 vertebral body show non–FDG-avid mild sclerosis (*arrows*), considered nonspecific on PET/CT.

D, Posterior and anterior planar MDP bone scan images show not only left clavicular primary ES (*arrows*) but also multiple osseous metastases (*arrowheads*) in L1 vertebral body, posterior right rib, and right ilium.



E, Repeat bone scan after chemotherapy shows resolution of MDP-avid metastases. MDP is seen in right chest wall MediPort catheter (*curved arrow*).



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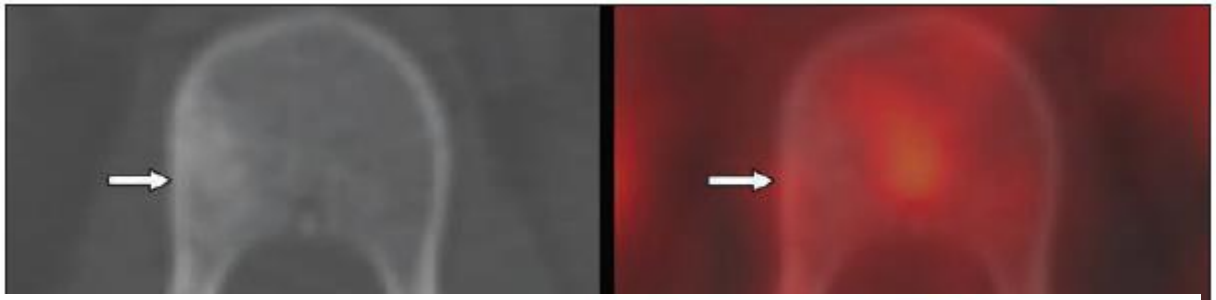

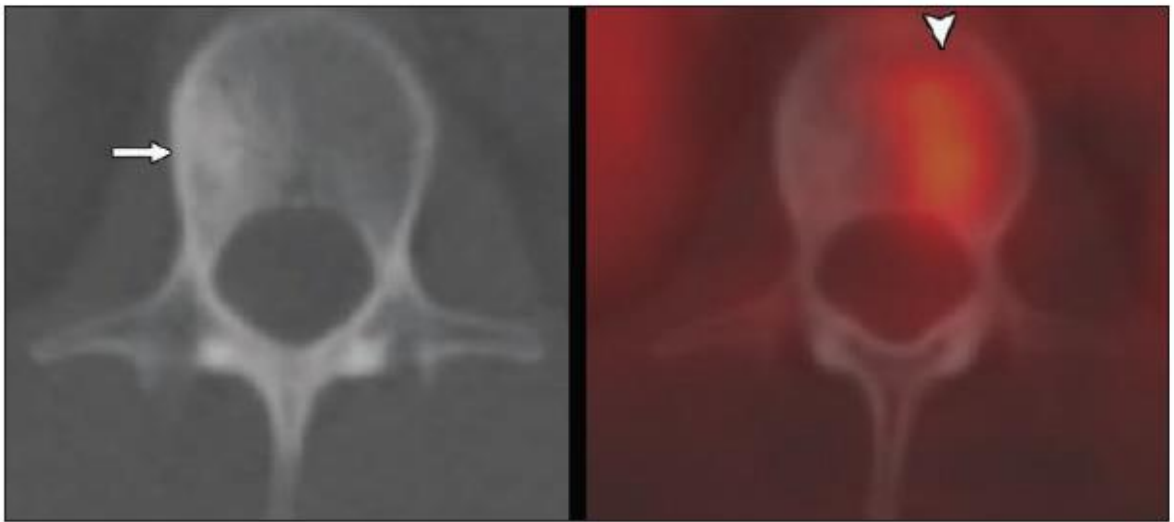

F, Postchemotherapy axial CT (*left*) and fused PET/CT (*right*) images show resolution of FDG-avid left shoulder mass (*arrows*). Non–FDG-avid sclerotic clavicular lesion remains (*arrowheads*). Physiologic FDG avidity is seen in vocal cords (*curved arrow*).

G, Postchemotherapy axial CT (*left*) and fused PET/CT (*right*) images show increased sclerosis of L1 vertebral body (*arrow*) consistent with healing of osseous metastases. FDG-avid bone marrow repopulation in left aspect of vertebra (*arrowhead*) is absent in healing metastasis

FDG PET/CT and MDP Bone Scan in Ewing Sarcoma

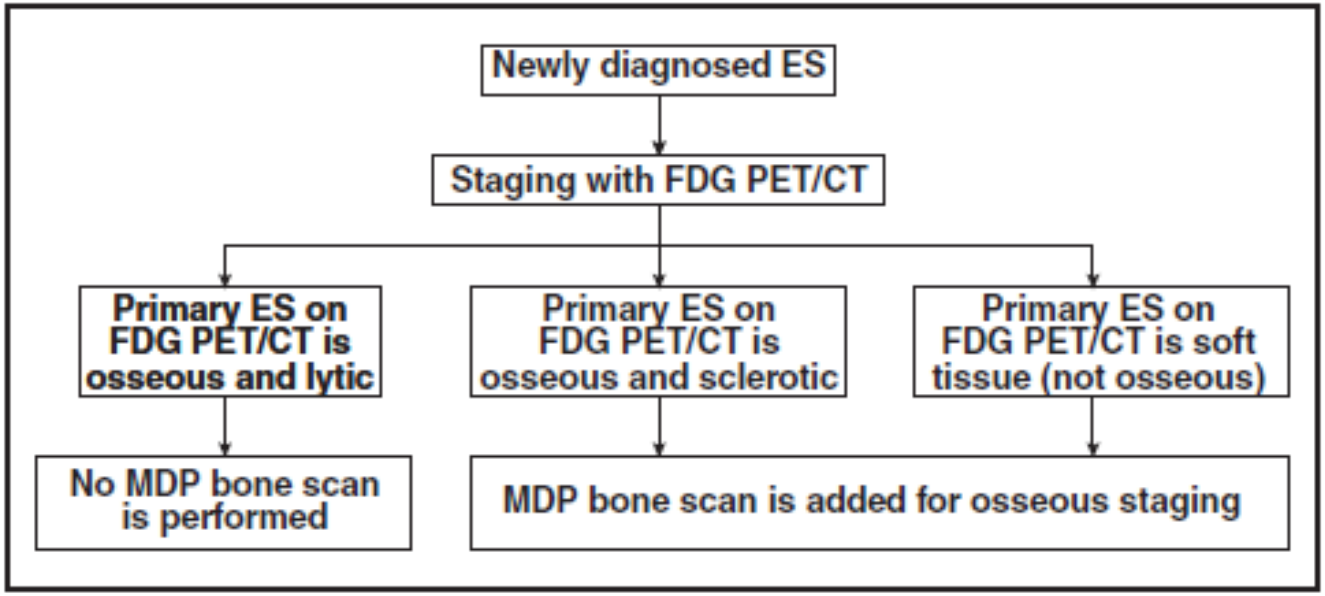

Fig. 5—Proposed algorithm for staging of newly diagnosed Ewing sarcoma (ES) with ^{18}F-FDG PET/CT and methylene diphosphonate (MDP) bone scan.


THANK YOU

Table 3 Summary of recommendations for imaging in paediatric rhabdomyosarcoma

	Induction therapy Cycles 1–9			Maintenance therapy HR: 6 or 12 cycles VHR: 12 or 24 cycles
	Staging	During	End of induction	
Imaging of the tumour site(s)[a]	•	After cycles 3, 9 (after 6 in case of distant metastatic disease — very high risk group)		HR: After cycles 6, 12 VHR: After cycles 6, 12, 18, 24
Chest CT[b]	•	If positive after 3 cycles, repeat after cycle 6	If positive at staging, repeat at end of induction treatment	As clinically indicated
FDG PET/CT or PET/MRI[c]	•	As per local practice After cycle 3 for HR/VHR patients in FDG PET substudy Recommended to repeat in case of FDG PET positive lymph nodes or FDG PET positive distant metastases at diagnosis until negative		

FDG PET [F-18]2-fluoro-2-deoxyglucose positron emission tomography, *HR* high risk, *VHR* very high risk

[a] MRI is recommended for all anatomical regions

[b] Repeat chest CT is recommended only if there is pulmonary involvement at baseline

[c] FDG PET/CT or PET/MRI is the investigation of choice; otherwise, as per local practice. Use same mode of investigation throughout the study. Children with FDG-PET-positive lymph nodes or FDG-PET-positive distant metastases at diagnosis are recommended to have repeat FDG PET scans until negative (or in case of another explanation of persisting FDG PET avidity, e.g., post irradiation)

Table 2 [F-18]2-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) visual scoring system: Deauville-like 5-point scale

Score	Definition
1	No uptake
2	Uptake ≤ mediastinum
3	Uptake > mediastinum but ≤ liver
4	Uptake moderately more than liver uptake, at any site
5	Markedly increased uptake at any site and/or new sites of disease

RS:
Response assessment in upfront treatment

- early response assessment and assessing the initial response after 2–3 courses of chemotherapy,
- re-assessing the disease status before local therapy in case of distant metastatic disease (after course 6),
- at end of induction chemotherapy, after every 6 cycles of maintenance therapy and
- at completion of therapy

- FDGPET/CT or PET/MR imaging: value of this modality in both identifying sites of disease and measuring tumor response.
- Children with FDG-avid lymph nodes or FDG-avid distant metastases, with a Deauville score 4–5 at diagnosis, are recommended to have repeat PET scans after every three cycles until negative (FDG uptake in previously positive nodes is decreased to activity in or below normal liver parenchyma, as visually read based on Deauville criteria).

- In general, children with FDG negative lymph nodes or metastases do not need further FDG PET/CT or PET/MR