

# RADY 401 Case Presentation

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# Focused patient history and workup

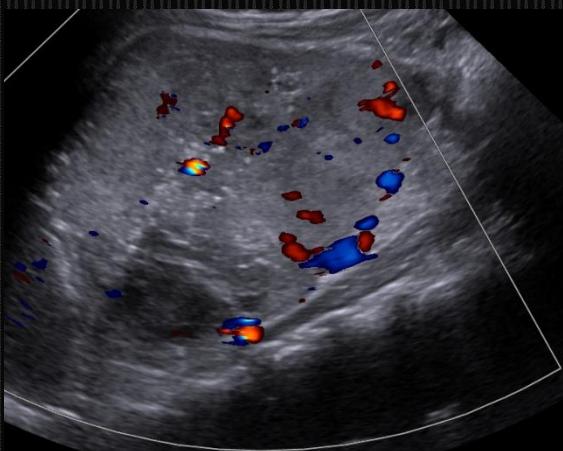
- 4 yo F w/ 1 month history of abdominal pain and pallor presented to outside ED for worsening abdominal pain and fatigue.
- Has also complained of knee/leg pain for 1.5 years
- Vitals unremarkable
- Physical exam remarkable for pallor and hepatosplenomegaly
- Labs: WBC 5.1, ANC 2.7, Hgb 5.1, Plt 120, AST 134, ALT 63, LDH 4026, Uric acid 6.6
- Transferred to UNC for further workup

# List of imaging studies

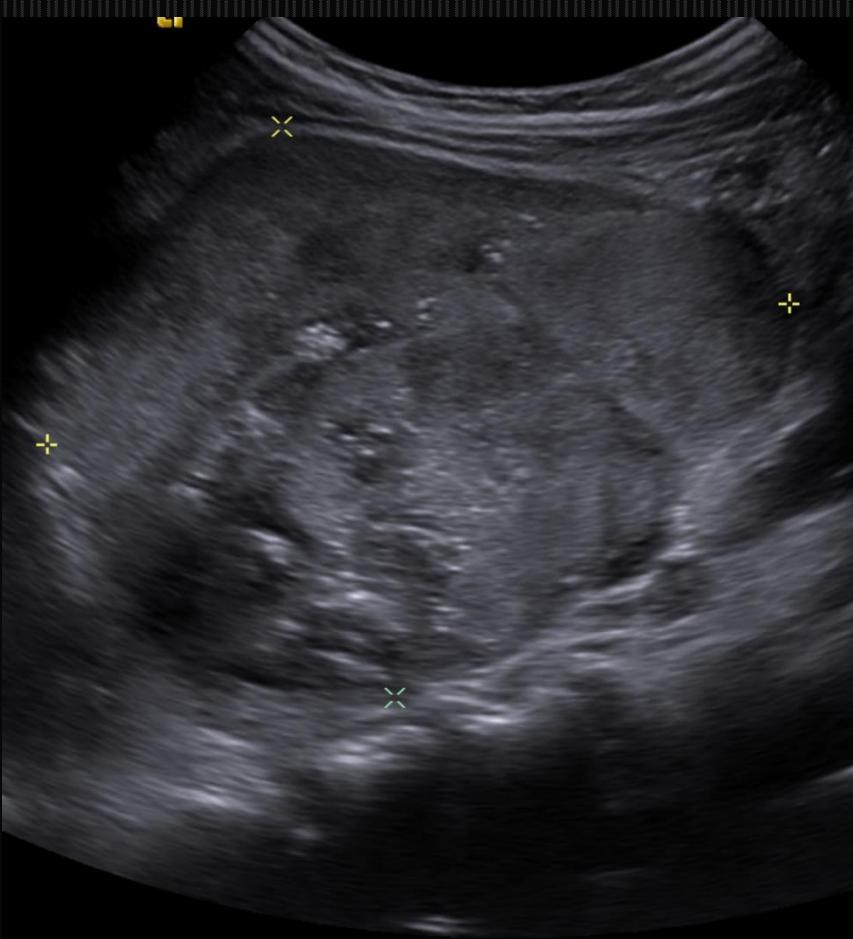
- Abdominal ultrasound
- Chest x-ray (unremarkable)
- CT chest abdomen and pelvis w/ contrast
- MIBG scintigraphy I-123 MIBG (Metaiodobenzylguanidine)

# Abdominal Ultrasound

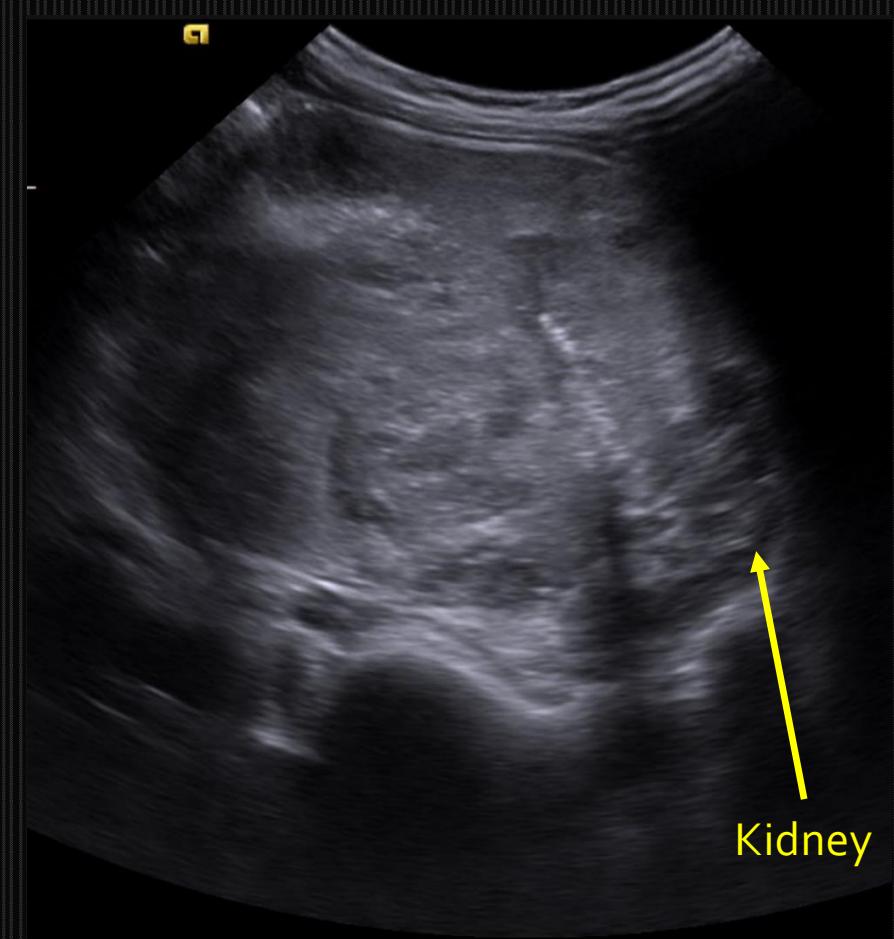
Findings?



Color flow



LUQ Sagittal

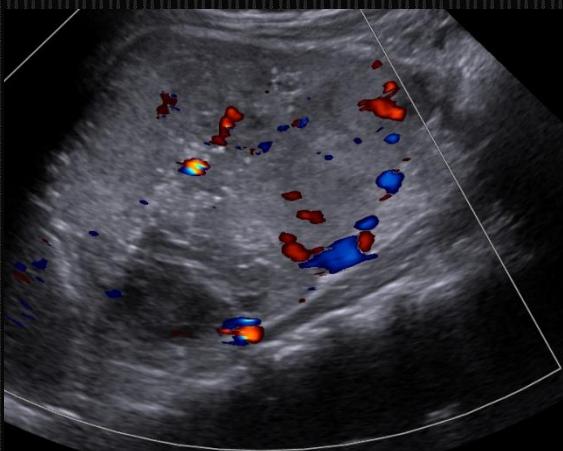


LUQ Transverse

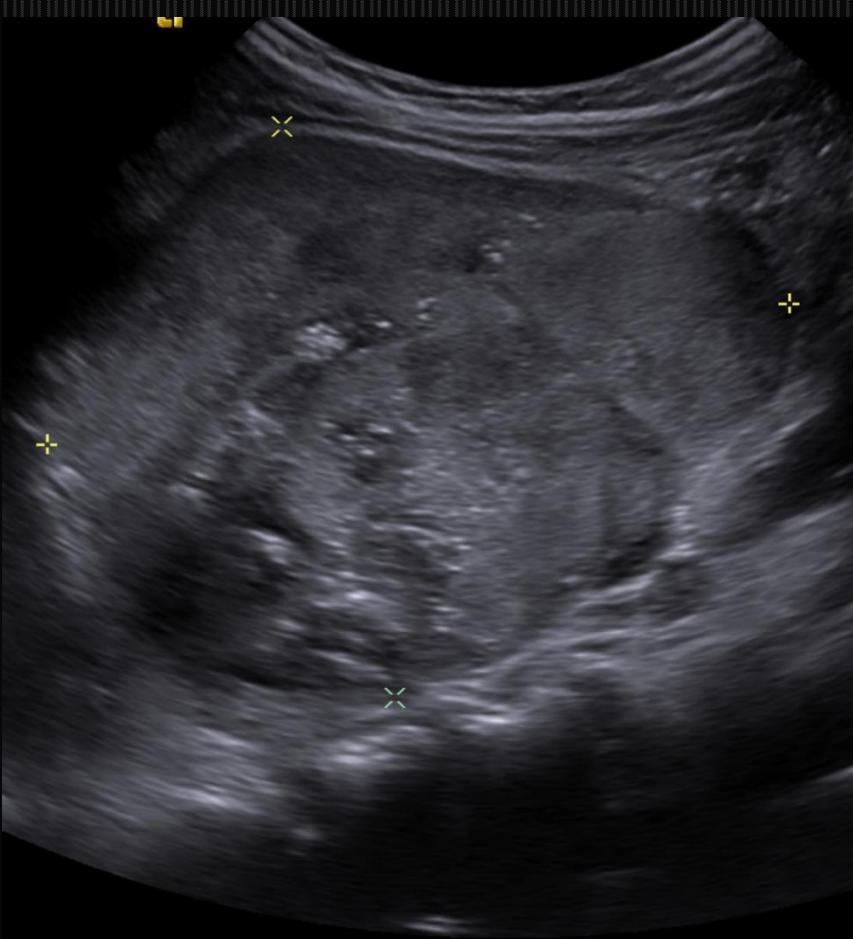
# Abdominal Ultrasound

## Findings:

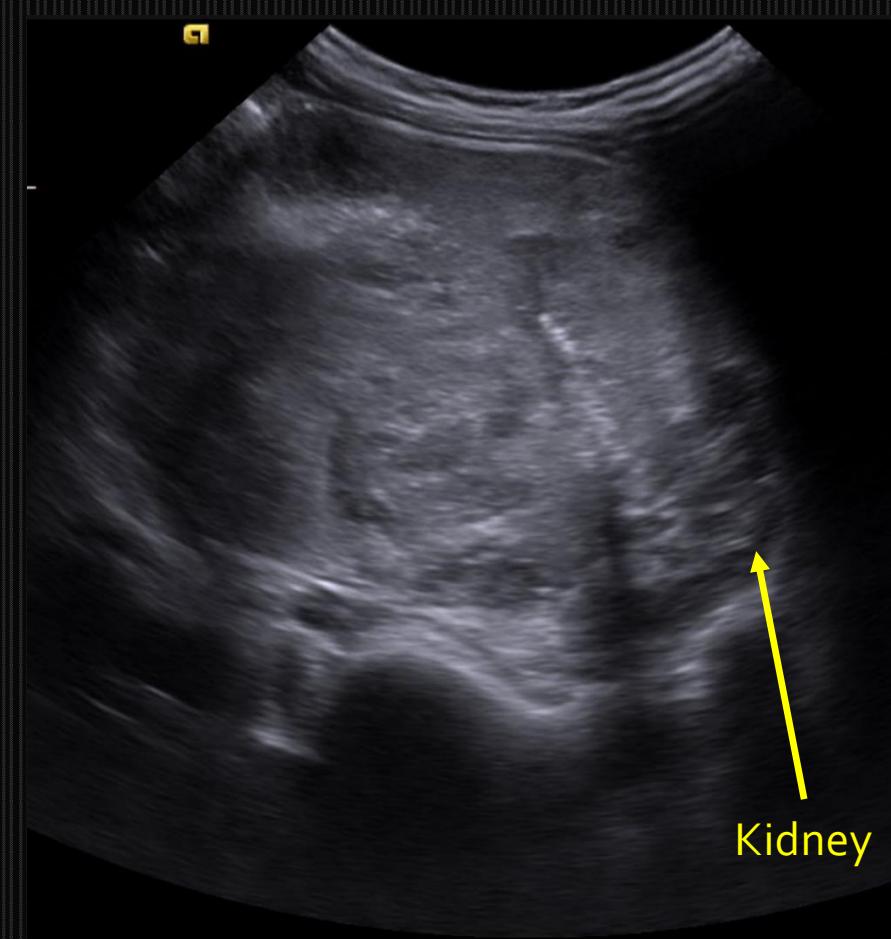
- $7.6 \times 7.8 \times 9.3$  cm left juxtarenal mass, heterogenous in echotexture and vascular



Color flow



LUQ Sagittal



LUQ Transverse

# Abdominal Ultrasound

Findings?



Sagittal

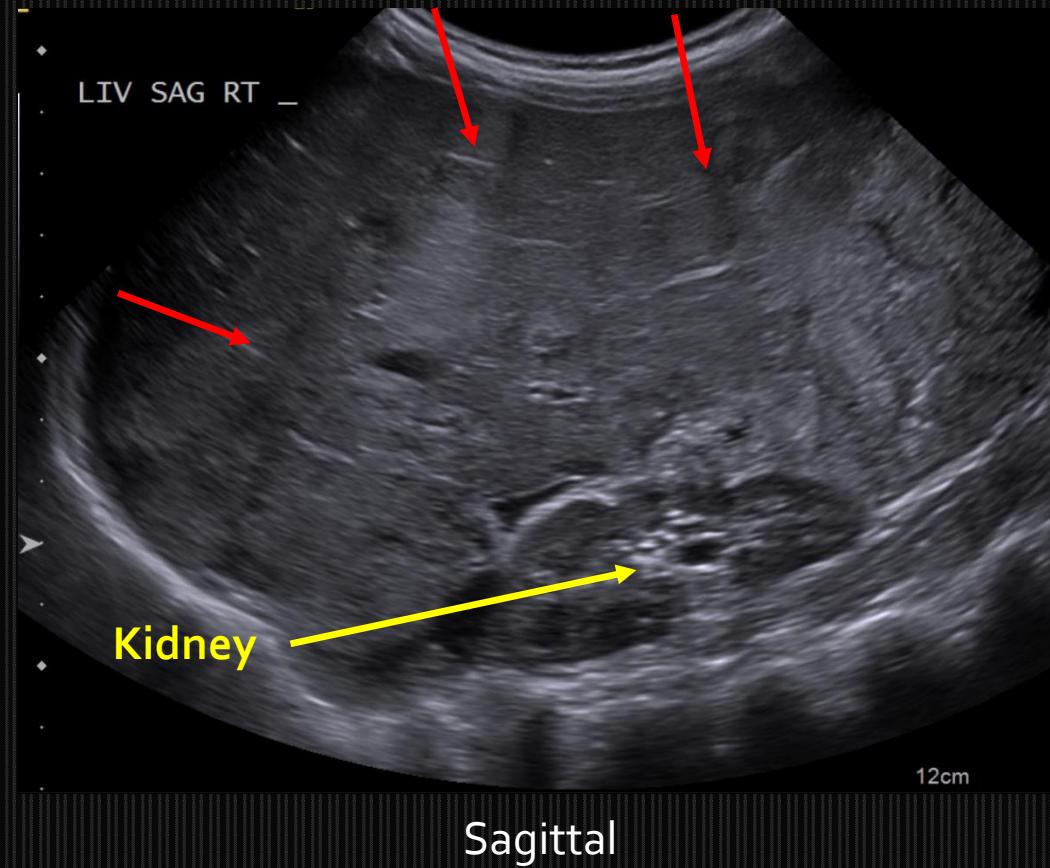


Transverse

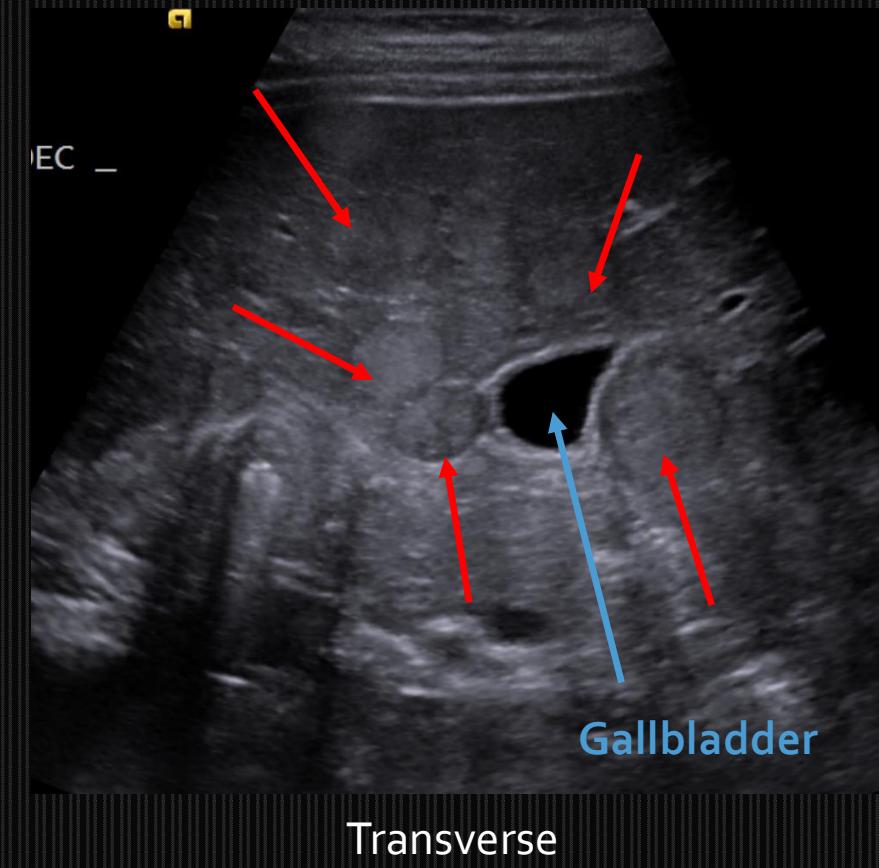
# Abdominal Ultrasound

## Findings:

- Hyperechogenic masses/mets throughout liver parenchyma
- Enlarged liver (13.8 cm sagittal)
- Normal appearing right kidney



Sagittal

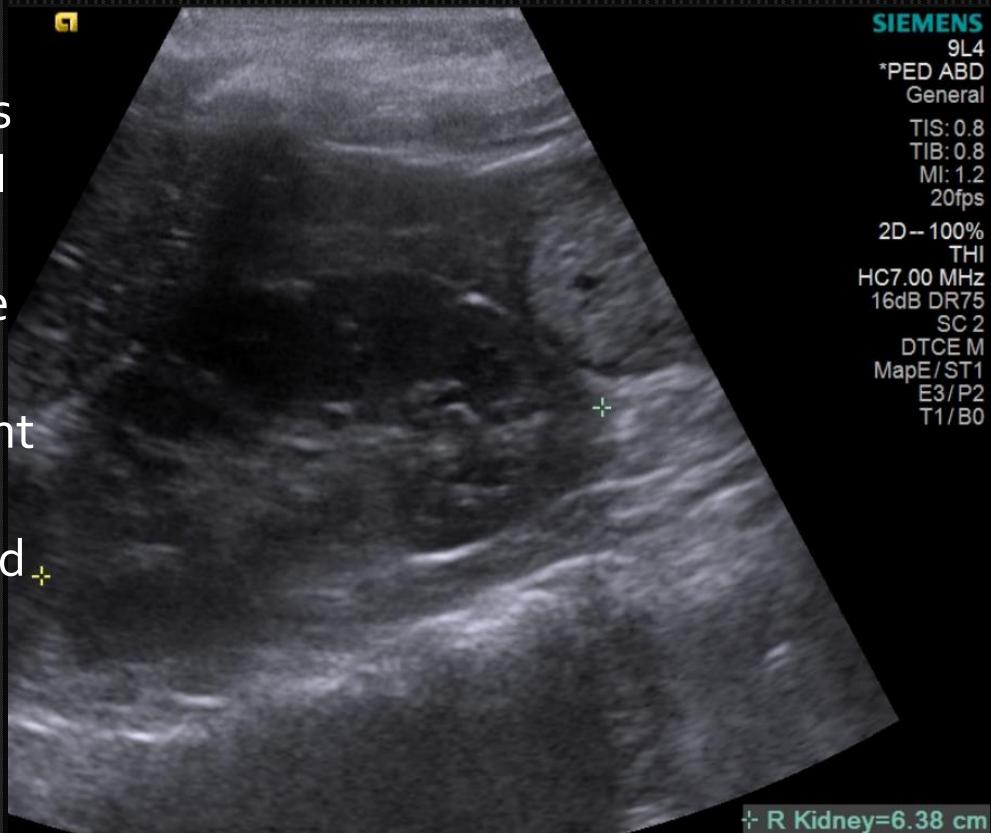


Transverse

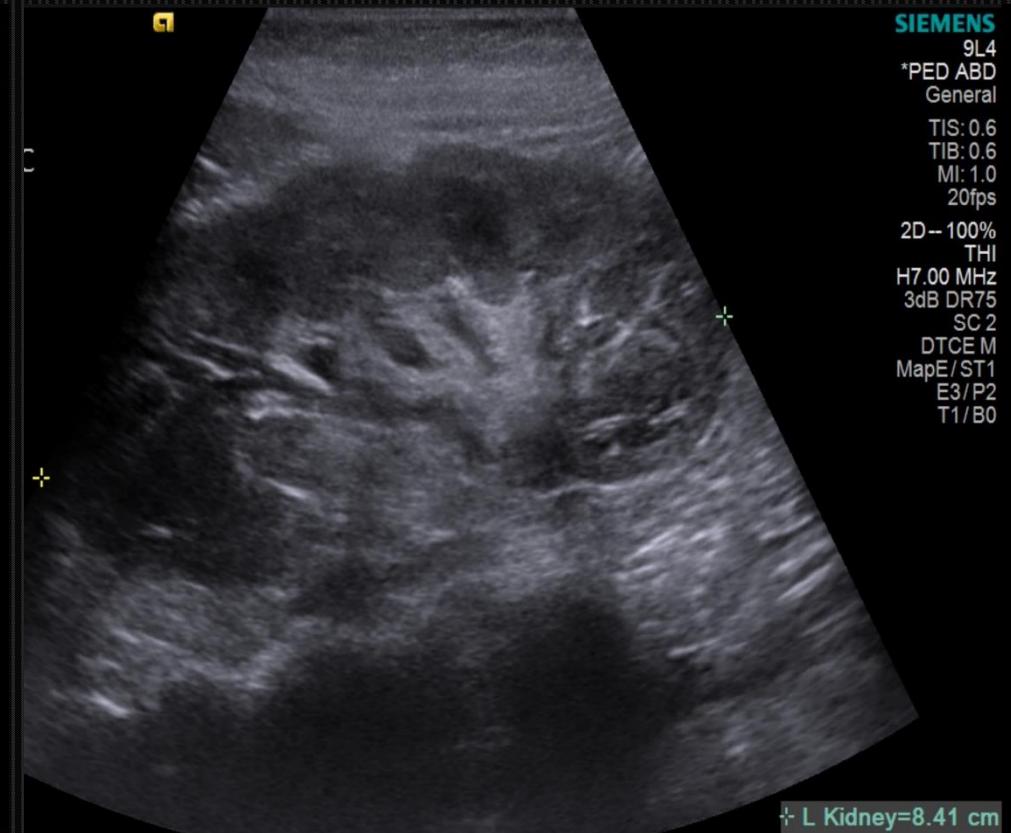
# Abdominal Ultrasound

## Findings:

- Normal kidneys
- NB: Mean renal length for a patient this age is 7.9 cm +/- 2x 0.5 cm. The right kidney may be under measured due to the adrenal mass.



Right



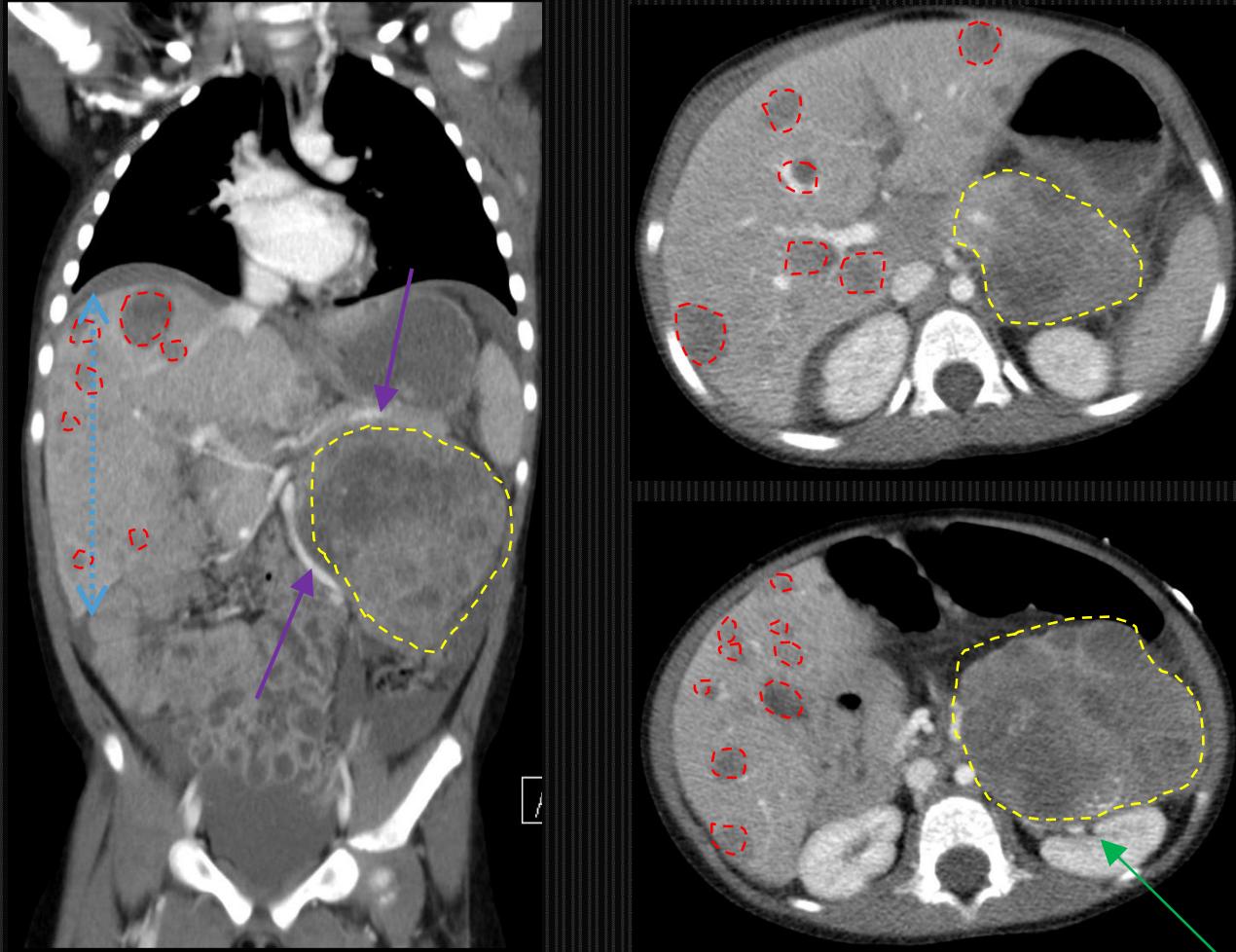
Left

# CT Chest Abdomen & Pelvis



Findings?

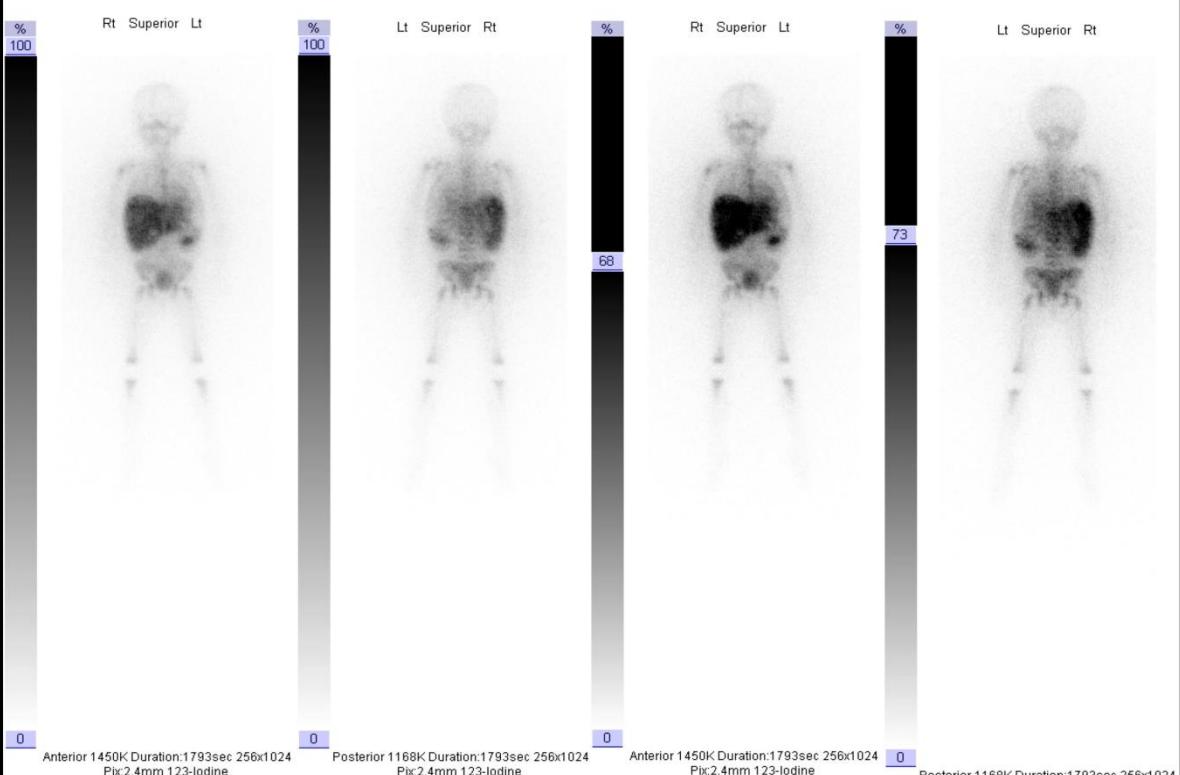
# CT Chest Abdomen & Pelvis



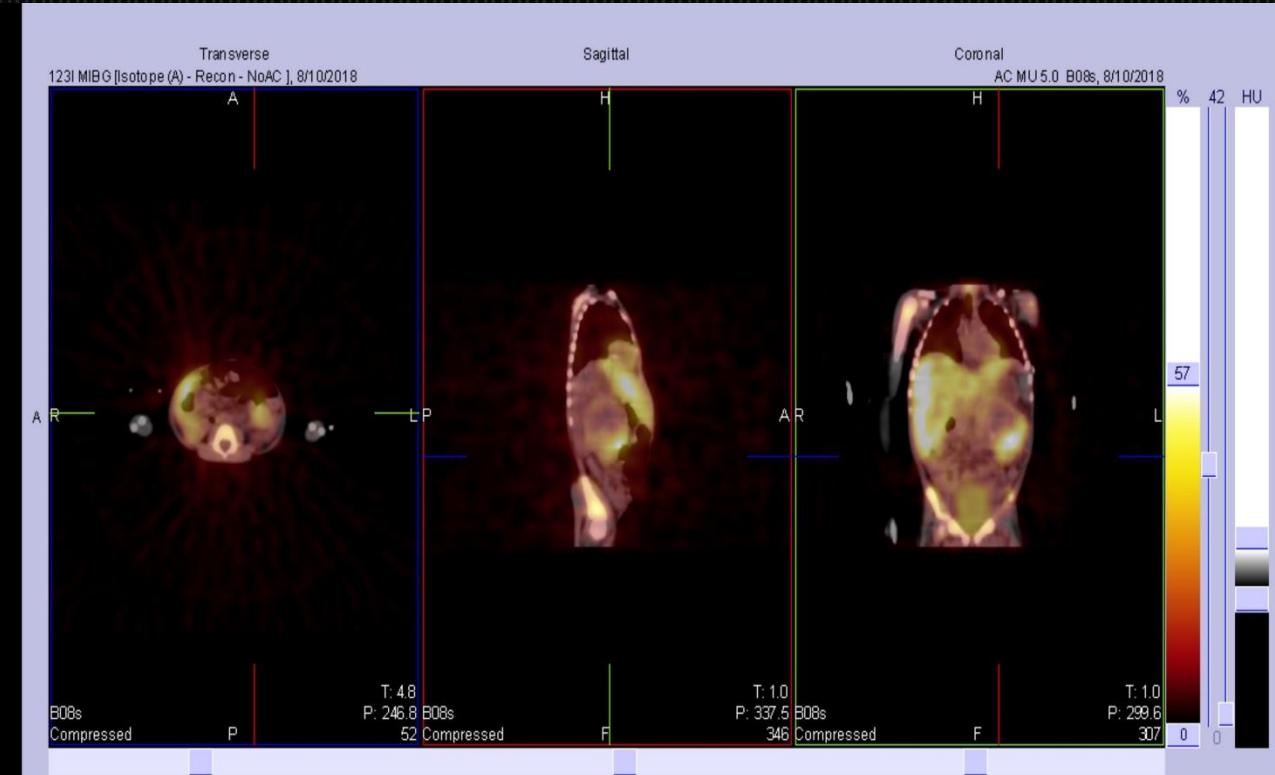
## Findings:

- **Enlarged liver (13 cm)** with numerous hypodense **mets**
- **Large mass in LUQ** with multiple internal calcifications and heterogenous enhancement
- Note: mass does not arise from the left kidney, but exerts **mass effect** on left kidney
- **Compression and displacement** of left renal vasculature posteriorly and inferiorly and superior **displacement** of splenic vessels
- Findings suggestive of **metastatic neuroblastoma**

# MIBG



Planar Scintigraphy



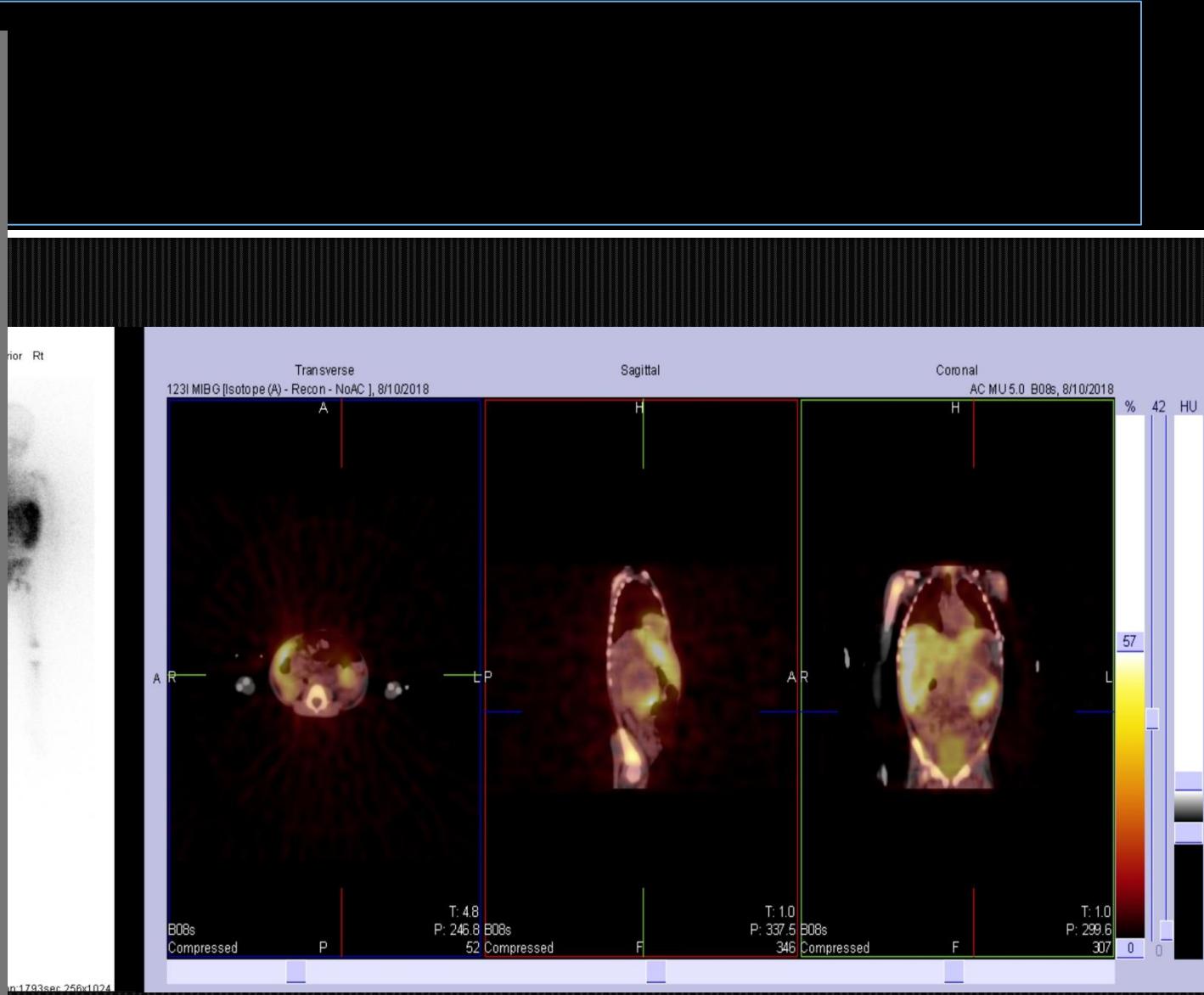
SPECT/CT



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## - SPECT= Single photon emission computed tomography

- Heterogenous mass in LUQ → avid radiotracer uptake in periphery, and less avid regions centrally and medially
- Diffuse uptake in liver consistent with metastatic disease involving the liver
- Diffuse osseous uptake involving the pelvis, spine, and appendicular skeleton (most of the femurs and the proximal humeri and tibia).
- No pulmonary nodules.
- MIBG avid left upper quadrant mass and hepatic lesions, with diffuse osseous uptake are consistent with metastatic neuroblastoma



SPECT/CT

# Additional workup and patient treatment

- Liver biopsy demonstrated metastatic neuroblastoma with unfavorable histology (The sections show a small round blue cell tumor. In order to further evaluate the tumor a panel of immunohistochemical stains was performed. The tumor is strongly and diffusely positive for synaptophysin. The tumor is negative for CD99, CD45, WT1, and myogenin. The morphology and immunophenotype are consistent with metastatic neuroblastoma)
- Bone marrow was biopsied demonstrating involvement by metastatic neuroblastoma, >90% of marrow space bilaterally
- Cytogenetics pending
- Started on ANBL1531 treatment protocol with cyclophosphamide and topotecan

# Discussion: Neuroblastoma

- Can arise anywhere throughout sympathetic nervous system<sup>1</sup>
- Most commonly adrenal gland (40%), abdominal (25%)<sup>1</sup>
- Presentation- abdominal mass/pain, bone pain, anemia, back pain, subcutaneous nodules, Horner syndrome, systemic symptoms, etc<sup>1</sup>
- Distant mets at presentation seen in 60-70% of children with abdominal neuroblastoma—bone marrow, lymph nodes, liver, skin, less commonly lungs and brain<sup>2</sup>

# Discussion: Neuroblastoma

- Ddx: Wilms' tumor, hepatoblastoma, lymphoma, rhabomyosarcoma
- Diagnostic evaluation<sup>1</sup>
  - Labs: urine vanillylmandelic acid, homovanillic acid (also useful for monitoring)
  - Definitive diagnosis: biopsy of 1° tumor or bone marrow biopsy/aspirate

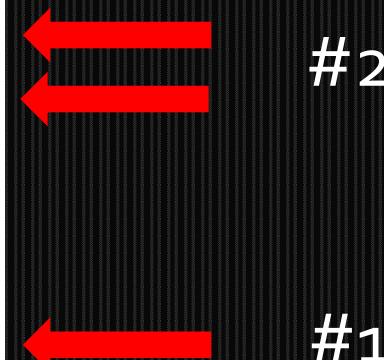
# Discussion: What imaging to order first?

Date of origin: 1998  
Last review date: 2014

**American College of Radiology  
ACR Appropriateness Criteria®**

**Clinical Condition:** Palpable Abdominal Mass

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen with IV contrast	9	Use of intravenous contrast may help better delineate the mass.	⊕⊕⊕
MRI abdomen without and with IV contrast	9	Use of intravenous contrast may help better delineate the mass.	O
CT abdomen without IV contrast	8	Use of intravenous contrast may help better delineate the mass.	⊕⊕⊕
MRI abdomen without IV contrast	8		O
US abdomen	7	This procedure may be appropriate as a first imaging examination for certain abdominal masses in adults (eg, superficial). Usually this is the first examination in pediatric and pregnant patients.	O
CT abdomen without and with IV contrast	6	This procedure without, followed by with, contrast may be useful in cases in which enhancement pattern of mass may help differentiate or further characterize the lesion.	⊕⊕⊕⊕
X-ray abdomen	5	This procedure is a simple and inexpensive way to evaluate bowel for obstruction or constipation as the cause of the mass.	⊕⊕



# Discussion: Imaging Studies

- Initial imaging with chest and abdominal radiographs, skeletal films or abdominal ultrasound usually performed to investigate presenting symptoms<sup>2</sup>
- Because of variability in origin and metastatic disease, multi-modality imaging is required for staging<sup>2</sup>
  - CT or MRI
  - $^{123}\text{I}$ -MIBG

# Discussion: Imaging Studies

Figure 13

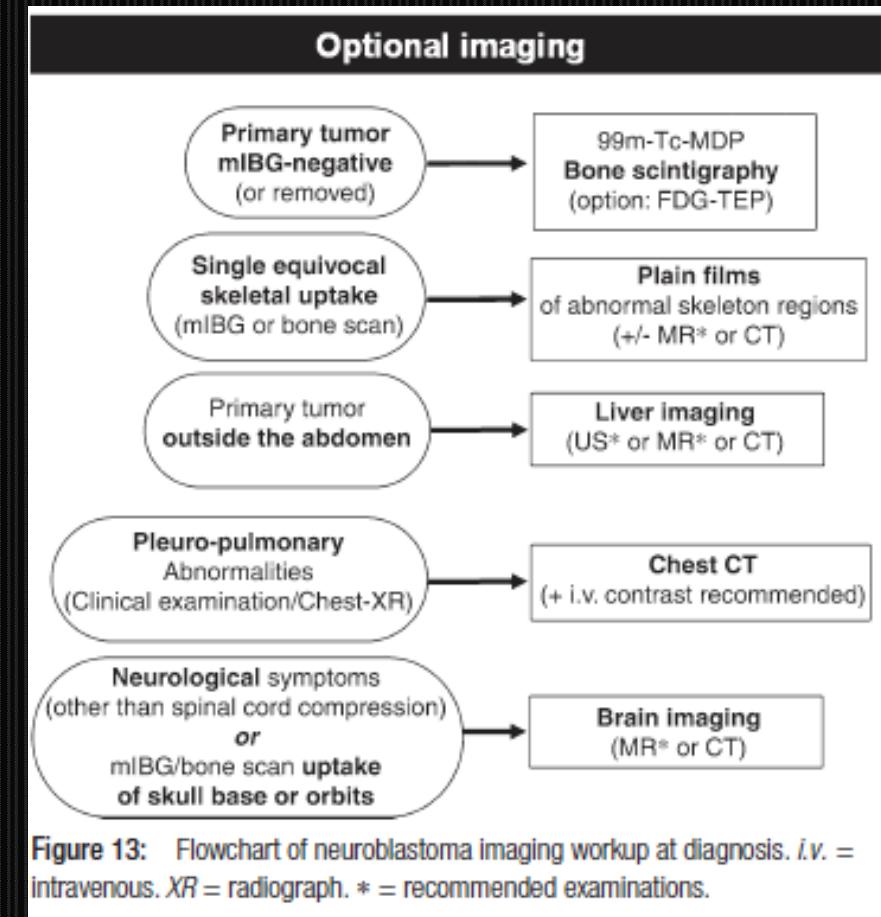
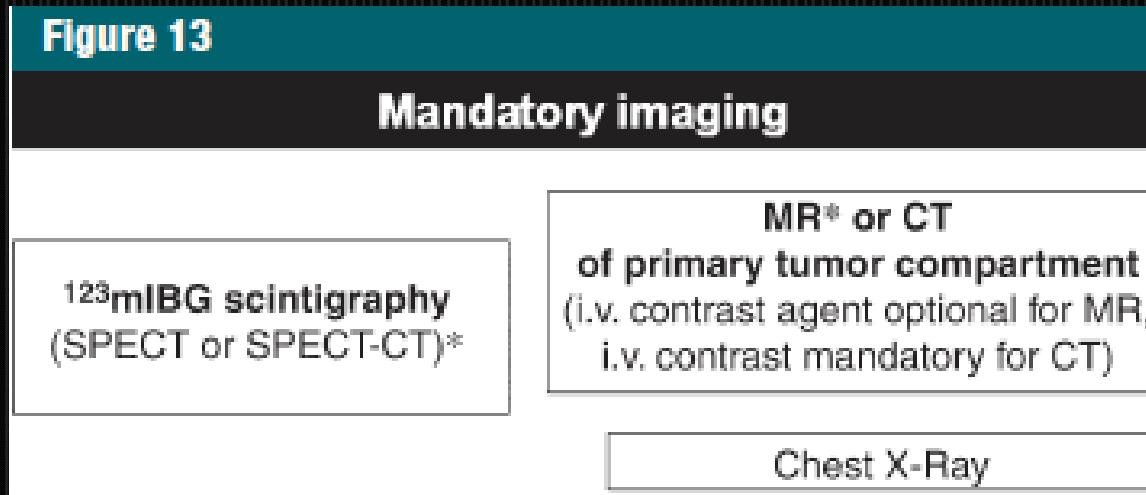
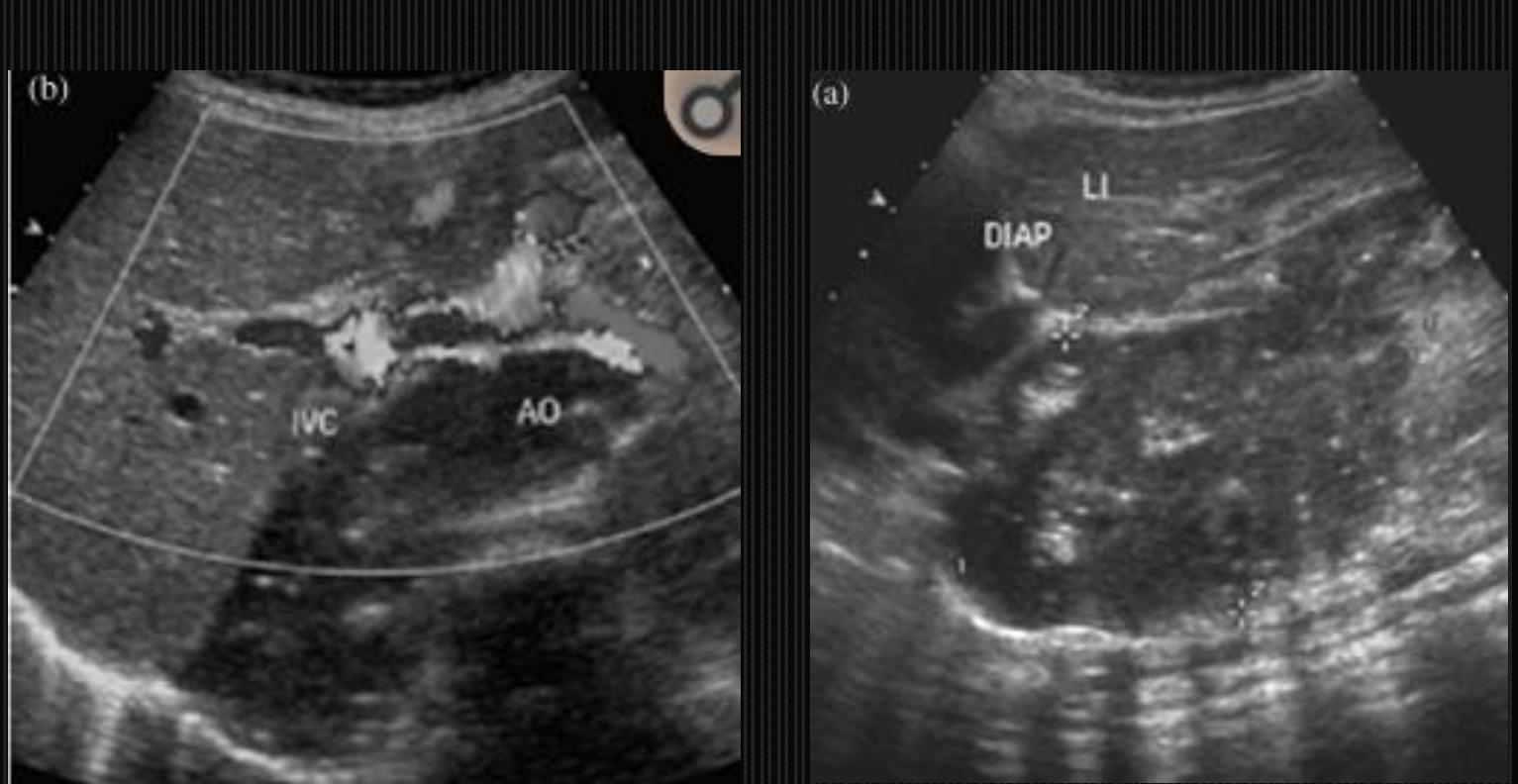


Figure 13: Flowchart of neuroblastoma imaging workup at diagnosis. *i.v.* = intravenous. *XR* = radiograph. \* = recommended examinations.

# Discussion: Imaging Findings

- Ultrasound<sup>2</sup>
  - Heterogenous solid lesions, mostly echogenic
  - Calcifications are common- coarse or fine
  - Anterior displacement of aorta and IVC



Cancer Imaging. 2005; 5(1): 116–127<sup>2</sup>

# Discussion: Imaging Findings

- CT<sup>2</sup>
  - Large, heterogenous, lobulated soft-tissue masses that show heterogenous or little enhancement
  - Calcifications seen in 85% of abdominal and 50% of thoracic cases
  - Diffuse infiltration or focal hypodensities seen with liver involvement
  - Can show displacement of organs and vasculature



Cancer Imaging. 2005; 5(1): 116–127<sup>2</sup>

# Discussion: Imaging Findings

## ■ MRI<sup>2</sup>

- Heterogenous with variable enhancement pattern, prolonged T<sub>1</sub> and T<sub>2</sub> relaxation times with low signal intensity on T<sub>1W</sub> and high signal intensity on T<sub>2W</sub>.
- Can identify cystic and hemorrhagic areas, but not calcifications

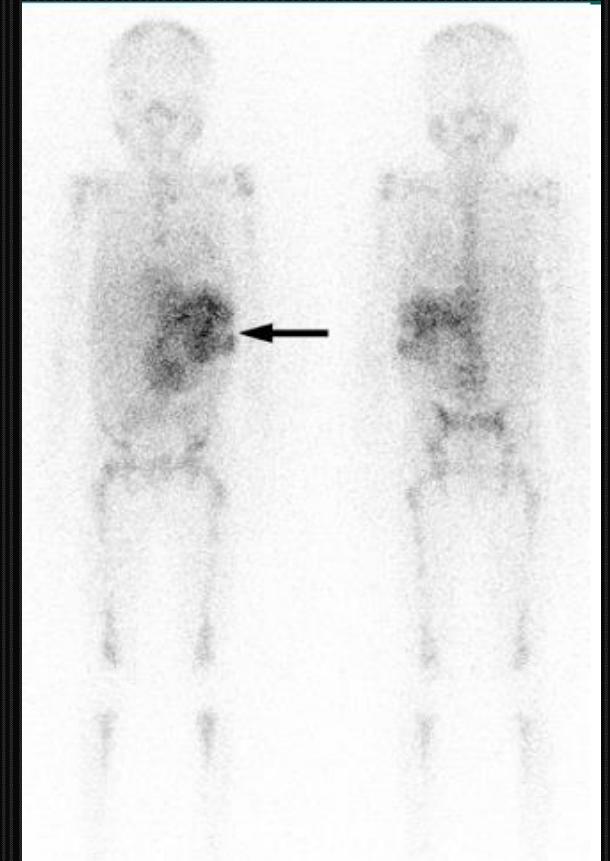


Cancer Imaging. 2005; 5(1): 116–127<sup>2</sup>

# Discussion: Imaging Findings

## ■ MIBG

- Analogue of catecholamine precursors, concentrated in neuroblastic cells and sympathetic tissue<sup>2</sup>
- High sensitivity (88%) and specificity (99%) in detecting 1° tumor and metastatic involvement in >90% of patients<sup>2</sup>



Radiology. 2011 Oct;261(1):243-57<sup>4</sup>

# Discussion: Staging

**Table 1.** Image-Defined Risk Factors in Neuroblastic Tumors

Ipsilateral tumor extension within two body compartments
Neck-chest, chest-abdomen, abdomen-pelvis
Neck
Tumor encasing carotid and/or vertebral artery and/or internal jugular vein
Tumor extending to base of skull
Tumor compressing the trachea
Cervico-thoracic junction
Tumor encasing brachial plexus roots
Tumor encasing subclavian vessels and/or vertebral and/or carotid artery
Tumor compressing the trachea
Thorax
Tumor encasing the aorta and/or major branches
Tumor compressing the trachea and/or principal bronchi
Lower mediastinal tumor, infiltrating the costo-vertebral junction between T9 and T12
Thoraco-abdominal
Tumor encasing the aorta and/or vena cava
Abdomen/pelvis
Tumor infiltrating the porta hepatis and/or the hepatoduodenal ligament
Tumor encasing branches of the superior mesenteric artery at the mesenteric root
Tumor encasing the origin of the coeliac axis, and/or of the superior mesenteric artery
Tumor invading one or both renal pedicles
Tumor encasing the aorta and/or vena cava
Tumor encasing the iliac vessels
Pelvic tumor crossing the sciatic notch
Intraspinal tumor extension whatever the location provided that:
More than one third of the spinal canal in the axial plane is invaded and/or the perimedullary leptomeningeal spaces are not visible and/or the spinal cord signal is abnormal
Infiltration of adjacent organs/structures
Pericardium, diaphragm, kidney, liver, duodeno-pancreatic block, and mesentery
Conditions to be recorded, but <i>not</i> considered IDRFs
Multifocal primary tumors
Pleural effusion, with or without malignant cells
Ascites, with or without malignant cells

Abbreviation: IDRFs, image-defined risk factors.

**Table 2.** International Neuroblastoma Risk Group Staging System

Stage	Description
L1	Localized tumor not involving vital structures as defined by the list of image-defined risk factors and confined to one body compartment
L2	Locoregional tumor with presence of one or more image-defined risk factors
M	Distant metastatic disease (except stage MS)
MS	Metastatic disease in children younger than 18 months with metastases confined to skin, liver, and/or bone marrow

J Clin Oncol. 2009 Jan 10;27(2):298-303<sup>5</sup>

## Descriptions of Original INSS Tumor Stages

### Tumor Stage Description

- |    |  |
|----|--|
| 1  | Localized tumor with complete gross excision, with or without microscopic residual disease; representative ipsilateral lymph nodes negative for tumor microscopically. Nodes attached to and removed with the primary tumor may be positive.                                       |
| 2A | Localized tumor with incomplete gross excision; representative ipsilateral nonadherent lymph nodes negative for tumor microscopically  |
| 2B | Localized tumor with or without complete gross excision, with ipsilateral nonadherent lymph nodes positive for tumor; enlarged contralateral lymph nodes negative microscopically  |
| 3  | Unresectable unilateral tumor infiltrating across the midline (beyond the opposite side of the vertebral column) with or without regional lymph node involvement, or midline tumor with bilateral extension via infiltration (unresectable) or lymph node involvement              |
| 4  | Any primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs (except as defined for stage 4S disease)  |
| 4S | Localized primary tumor (as defined for stage 1, 2A, or 2B disease) with dissemination limited to skin, liver, and/or bone marrow (limited to infants younger than 1 year, marrow involvement of less 10% of total nucleated cells, and MIBG scan findings negative in the marrow) |

Radiology. 2011 Oct;261(1):243-57<sup>4</sup>

**INRGSS:** pre-op staging  
**INSS:** post-op staging + prognosis<sup>4,6</sup>



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# Cost and Radiation Dose

Study	Cost <sup>7</sup>	Effective Radiation Dose <sup>9</sup>
Chest Radiography	\$29 - \$472	0.1 mSv
Abdominal Ultrasound (duplex)	\$436 - \$1,404	0 mSv
CT Chest (w/ contrast)	\$440 - \$2,464	7 mSv
CT Abdomen and Pelvis (w/ contrast)	\$512 - \$5,055	10 mSv
MRI Abdomen	\$935 - \$4,136	0 mSv
MIBG Scintigraphy	\$1,454 - \$5,241 <sup>8</sup>	3.5 mSv <sup>10</sup>

# Neuroblastoma: Summary

- Can arise anywhere from sympathetic nervous system, but most commonly from adrenal gland.
- Abdominal US first-line imaging for palpable abdominal mass
- Required imaging: CXR, CT/MRI of primary tumor compartment, MIBG scintigraphy
- Imaging is important for staging and treatment planning

# References

1. Shohet DI, Nuchtern JG. Clinical presentation, diagnosis, and staging of neuroblastoma. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2018.
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