Whole Body MR: Techniques and Staging in Oncology - How To

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Imaging in Oncology

- Extent of disease and staging
- Response to treatment
  - Early assessment of response to treatment may allow more individualized therapy
- Surveillance
- Complications
  - Osteonecrosis
  - Infection
- Cancer predisposition syndromes screening
<table>
<thead>
<tr>
<th>Condition</th>
<th>Associated neoplasms</th>
<th>Surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>NF type I</td>
<td>Optic nerve glioma, neurofibromas, leukemia (especially juvenile myelomonocytic leukemia and myelodysplastic syndromes, MPNST (lifetime risk of 8%–13%), GIST (lifetime risk of 6%), pheochromocytoma (1%), rhabdomyosarcoma, neuroblastoma</td>
<td>Annual physical examination; annual ophthalmologic examination in early childhood (to age 5 y); regular developmental assessment and blood pressure monitoring; appropriate monitoring by a specialist according to CNS, skeletal, or cardiovascular abnormalities</td>
</tr>
<tr>
<td>Beckwith-Wiedemann syndrome</td>
<td>Wilms tu (40%–43%), hepatoblastoma (12-20%), adrenocorticalca, neuroblastoma, rhabdomyosarcoma</td>
<td>Abdominal US every 3 mo to age 7 y; measurement of serum AFP level every 3 mo to age 4 y; daily abdominal examination by the caretaker at the discretion of the caretaker or parent; abdominal examination by a physician every 6 mo</td>
</tr>
<tr>
<td>MEN 1</td>
<td>Parathyroid gland adenomas (65%–90%), pancreatic neuroendocrine tumors (50%–70%), and anterior pituitary gland adenomas (25%–65%)</td>
<td>Screening starting at age 5–10 y, including measurement of fasting glucose, calcium, PTH, insulin, prolactin, and IGF1 levels; annual pancreatic US; pancreatic and pituitary MR imaging every 3–5 y; yearly abdominal CT or MR imaging and head MRI</td>
</tr>
<tr>
<td>MEN 2</td>
<td>2A: Medullary thyroid cancer (100%), pheochromocytoma (50%), and parathyroid adenomas or hyperplasia (25%)</td>
<td>Prophylactic thyroidectomy by age 5 y for MEN 2A and in the 1st year for MEN 2B; surveillance includes annual measurement of catecholamine levels for pheochromocytoma and MRI every 3 y</td>
</tr>
<tr>
<td>Li-Fraumeni Syndrome</td>
<td>osteosarcoma, soft-tissue sarcoma, leukemia, breast cancer, brain tumors, melanoma, and adrenal cortical tumors</td>
<td>For adrenocortical carcinoma, US of the abdomen and pelvis every 3–4 mo, complete urinalysis every 3–4 mo, and blood work (measurement of ESR, LDH, BHCG, AFP, 17-OH progesterone, testosterone, androstenedione, and DHEAS levels) every 4 mo; for breast cancer, monthly breast self-examination (starting at age 18 y), biyearly clinical breast examination, and annual mammography starting at age 20–25 y; for rhabdomyosarcoma and osteosarcoma, annual total-body MRI</td>
</tr>
<tr>
<td>von Hippel-Lindau Syndrome</td>
<td>hemangioblastoma, clear cell renal cell carcinoma, adrenal pheochromocytoma, islet cell tumors, endolymphatic sac tumor, papillary cystadenoma of the epididymis</td>
<td>For retinal hemangiomas, annual ophthalmologic evaluation and visual field testing starting around age 2 y; for CNS hemangioblastomas, MRI of the brain and spine every 2 y starting in early adolescence; for renal conditions, annual abdominal US starting at age 5 y; for pancreatic carcinoma, abdominal CT or MRI starting at age 20 y; for pheochromocytoma, frequent blood pressure monitoring and measurement of urinary catecholamine levels or plasma metanephrine levels every 1–2 y starting at age 2 y</td>
</tr>
</tbody>
</table>

41 WB-MRI in 25 survivors of hereditary RB

8 WB-MRI with abnormal findings

3 with benign abnormalities
- Hemangioma
- Minor marrow abnormality
- Fibroids
- No further work up required

5 with abnormalities suspicious for malignancy
- 5/5 required dedicated imaging
- 3/5 required biopsy

- Osteosarcoma (2)

- Benign findings (3)
  - Chondroblastoma
  - Spondylolysis
  - Osteonecrosis

<table>
<thead>
<tr>
<th>Modality</th>
<th>~ Cost</th>
<th>~ Radiation Effective Dose (mSv) §</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole body MRI*</td>
<td>$4600</td>
<td>0</td>
</tr>
<tr>
<td>WB Bone scan ($^{99}$mTc-MDP)</td>
<td>$2400</td>
<td>4</td>
</tr>
<tr>
<td>PET CT (FDG)</td>
<td>$2500-4000</td>
<td>6.5</td>
</tr>
<tr>
<td>MIBG (I-123)</td>
<td>$4800</td>
<td>4.5</td>
</tr>
<tr>
<td>Skeletal survey</td>
<td>$1200</td>
<td>1.8</td>
</tr>
</tbody>
</table>

*WB MRI: Billed as chest/abdomen/pelvis

WB MRI in Oncology—Why?

- No ionizing radiation
- Excellent soft-tissue contrast resolution
- Can be used to evaluate local tumors and metastatic disease in the same sedation or general anesthesia
- Primarily used to assess the bone marrow
Weaknesses

• Lack of specificity (eg: NB and MIBG)
• Lung parenchyma assessment for metastatic disease
• Detection of calcification within neoplasms
• Cost
• Sedation for young children
TECHNICAL INNOVATIONS

• Rolling table platform → allows the patient to be moved in stages through the magnetic bore
• Multiple-phased array coils → improve resolution
• Parallel imaging techniques
Sliding table and repositioning surface coil approach

Protocol/Technique

- Series of images acquired in successive stations
- The number of stations is a function of the FOV and the patient’s size
- Series are merged craniocaudally using post-processing software
- Some authors recommend respiratory gating for the trunk and antiperistaltic drugs for the abdomen
- Planes
  - Coronal: More intuitive, easier to compare to other modalities
  - Axial: More sensitive
  - Sagittal: Only spine
- Sequences ➔ No consensus about which combination of sequences provides the highest diagnostic accuracy while maintaining reasonable time efficiency
- Most authors do not use IV gadolinium
<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th># of pts</th>
<th>Disease/s</th>
<th>Protocol/Techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daldrup-Link et al</td>
<td>2001</td>
<td>39</td>
<td>Ewing, OS, lymphoma, RMS, Melanoma, LCH</td>
<td>Cor T1 SE (all pts) Sag T1 SE (spine, all pts) Cor STIR (10 pts)</td>
</tr>
<tr>
<td>Mazumdar et al</td>
<td>2002</td>
<td>7</td>
<td>RMS, Ewing, NB</td>
<td>Cor T1 TSE Cor STIR</td>
</tr>
<tr>
<td>Laffan et al</td>
<td>2004</td>
<td>10</td>
<td>Leukemia, lymphoma, NB, LCH, cystic angiomatosis</td>
<td>Cor STIR Sag STIR (spine)</td>
</tr>
<tr>
<td>Kellenberger et al</td>
<td>2004</td>
<td>8</td>
<td>Lymphoma</td>
<td>Cor FSE STIR</td>
</tr>
<tr>
<td>Kellenberger et al</td>
<td>2004</td>
<td>140</td>
<td>Malignancy (solid and hematogeneous), LCH, hemangiomatosis, vasc. malformations</td>
<td>Cor FSE STIR</td>
</tr>
<tr>
<td>Goo et al</td>
<td>2005</td>
<td>36</td>
<td>NB, lymphoma, RMS, granulocytic sarcoma</td>
<td>Cor STIR Sag T1 (spine)</td>
</tr>
<tr>
<td>Goo et al</td>
<td>2006</td>
<td>9</td>
<td>LCH</td>
<td>Cor STIR Sag STIR Cor T1 FS post Gd</td>
</tr>
<tr>
<td>Kumar et al</td>
<td>2008</td>
<td>26</td>
<td>Ewing, NB, RMS, granulocytic sarcoma</td>
<td>Cor STIR Sag T1 (spine)</td>
</tr>
<tr>
<td>Punwani et al</td>
<td>2010</td>
<td>26</td>
<td>Lymphoma</td>
<td>Cor STIR-RARE Axial STIR-RARE</td>
</tr>
<tr>
<td>Punwani et al</td>
<td>2013</td>
<td>39</td>
<td>Lymphoma</td>
<td>Cor STIR-RARE Axial STIR-RARE DWI (b value: 0, 300 and 500)</td>
</tr>
<tr>
<td>Kembhavi et al</td>
<td>2014</td>
<td>34</td>
<td>NB, PNET, RMS</td>
<td>Cor STIR Cor T1</td>
</tr>
</tbody>
</table>
Expected bone marrow changes

- Entire skeleton is hematopoietic at birth
- Red marrow in adults typically located in the spine and pelvis, and, to a lesser degree, in the metaphyses of the proximal long bones
- Adult pattern of red marrow distribution is reached in the early 20s
- Marrow transformation to fatty marrow predictable fashion
  - From the fingers to the shoulders and from the toes to the hips
  - Within each bone fatty marrow transformation begins in the epiphyses
    - Epiphysis become fatty 6 months after appearance of ossification center
  - Within the shaft of the long bones fatty marrow transformation begins at the diaphysis and proceeds towards the metaphyses
Fluid sensitive sequences

- Most pediatric studies ➔ coronal STIR; acquisition time: 2-4 min per station
- Highly sensitive to bone and soft tissue abnormalities due to short inversion time ➔ eliminates fat signal
- Fat suppression in STIR more robust and homogeneous than on T2 FS. Fat suppression in STIR is superior with metallic hardware, off isocenter imaging, and imaging near curved air and soft tissue interfaces
- STIR typically requires longer acquisition times with increased noise and decrease in spatial resolution compared with T2-weighted FSE sequences
- If using T2 FS ➔ TE >60 milliseconds; avoid the intermediate PD FS sequences (commonly used in joint imaging) ➔ TE in the range of 40 to 50 ms ➔ may decrease lesion conspicuity
Fluid sensitive sequences

• STIR → Increased conspicuity of marrow lesions compared to T2 FS

• Most path tissue → rich in protons (prolonged T1 & T2 relaxation times) → High signal on STIR

• Certain organs have a physiological STIR hypersignal (lymph organs: spleen, thymus, Waldeyer’s ring and kidneys) → lesions are visible in relative hyposignal

• Osteoblastic lesions may be missed

• Signal of other substances with a short T1 relaxation time is also reduced (blood, liquid protein, melanin and gadolinium) → NEVER pursue STIR after Gadolinium
Regarding the administration of intravenous (IV) gadolinium for Whole Body MR imaging, which one of the following statements is correct?

A. IV gadolinium should be administered immediately after the localizing sequences.

B. IV gadolinium should be administered only if diffusion weighted images are obtained.

C. IV gadolinium is usually administered to enhance visualization of pathologic lesions.

D. IV gadolinium is usually not required for whole body MR imaging. If administered, the STIR sequence should be performed after the administration of IV gadolinium.

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T1-weighted sequences

- Typically used to search for bone lesions in adults
- Bone marrow malignancies and mets → typically isointense to hypointense to muscle in a confluent pattern replacing the normal marrow fat signal
- Advantages
  - Good spatial resolution
  - Short acquisition times
- In-phase & out-of-phase imaging → faster BUT less sensitive than spin echo
  - Preservation of a component of internal fat is a typical feature of a benign bone marrow process
  - Out-of-phase imaging shows signal dropout in red marrow secondary to intravoxel fat and water
  - In adults helps to differentiate benign osteoporotic and malignant compression fractures of the spine
In 2004, Takahara et al reported on the use of “DWIBS” → diffusion weighted imaging with background body signal suppression

DWIBS sequence is performed with heavy diffusion weighting \( (b = 1000 \text{ sec/mm}^2) \) and fat suppression using an inversion or chemical shift–selective pre-pulse, such as STIR

Multiple thin axial slices with a high number of signal averages are acquired during free breathing

The axial source DW images may be reconstructed in the coronal plane and the gray scale may be inverted to resemble PET images. This is convenient for analyzing the distribution of primary lesions and their metastases

DWIBS is primarily used qualitatively to depict restricted diffusion, therefore apparent diffusion coefficient (ADC) values are typically not determined. Because DWIBS is a free-breathing technique, ADC measurements of moving organs may be less accurate, less reproducible, and may differ from conventional breath hold or respiratory triggered DWI
Not only malignant tumors show diffusion restriction. Some normal structures show restricted diffusion and DWIBS should be interpreted in conjunction with anatomic sequences:

- normal lymph nodes, lingual and palatine tonsils, salivary glands
- brain, spinal cord, peripheral nerves
- Spleen, adrenals, kidneys, ureters, gallbladder, bowel, ovaries, testicles, prostate and bone marrow

DWIBS is very sensitive to magnetic field heterogeneities → distortion artifact in almost all patients. Most conspicuous in air-soft tissue and soft tissue-bone interfaces, e.g. in the lower neck, shoulders and lung apices.

Motion artifacts may occur around the diaphragm, heart and bowel. Lesions may be either missed or overestimated in these areas.

In adults, DWIBS aids in bone metastasis detection → restricted diffusion, display high signal with high b-values.

However, DWIBS is hard to adequately assess in pediatric patients → may exhibit normal foci of restricted diffusion in their skeletons (particularly lumbar spine and pelvis → potential misdiagnosis).

Young children → extensive interindividual variation. Asymmetric patterns may be normally seen in nearly 50% of the cases.

Beware of growth plates → restricted diffusion.
Illustrative cases
An 11-year-old female with large retroperitoneal mass subsequently proved on biopsy to be neuroblastoma
Neuroblastoma

- Most common extracranial solid malignant tumor in children. Majority (~70%) arise in the abdomen (adrenal gland or paravertebral sympathetic ganglia). Metastases occur to cortical bone and bone marrow, lymph nodes, liver, and skin.
- In 2005 Goo et al showed that in 13 children with NB, WB MRI had a higher sensitivity for detection of bone metastases than MIBG and CT (100%, 25%, and 10%, respectively), but poor positive predictive values for detection of skeletal and extraskeletal metastases in comparison with MIBG.
- Imaging plays an important role in establishing diagnosis, defining resectability and determining presence of metastatic disease. Role of WB MRI in NB is yet to be fully evaluated in larger studies.
- In 2009, the International NB Risk Group published a new staging system and risk classification for NB, shifting the attention to pretreatment staging from initial imaging findings and the identification of imaging-defined risk factors (previously focus was on surgical/path findings).
- Protocols traditionally use a combination of CT, MIBG and bone marrow biopsy to evaluate local and distant disease spread, however, regional MRI is playing an increasing role.
- MIBG limitations:
  - Failure to detect bone marrow disease (needs bone marrow biopsy to complete staging)
  - Lack of MIBG avidity in 6-10% of the cases
  - Loss of MIBG avidity at relapse
  - Suboptimal visualization of liver lesions
- PET and PET CT and PET-CT also play a role in the imaging of NB, usually for cases of non-MIBG avidity.
A 10-month-old female presenting with a large right inguinal mass and subsequently diagnosed with extra renal rhabdoid sarcoma.
Sarcomas and other Solid Tumors

- Increasing role of WB MRI for the staging of other solid pediatric neoplasms such as Ewing sarcoma, osteosarcoma, and rhabdomyosarcoma, with studies demonstrating similar and often increased sensitivity for detection of bony metastatic disease in comparison with traditional staging techniques.

- Main limitation of MRI in this setting → limited ability to detect subcentimeter pulmonary nodules. More recent adult studies have shown good sensitivity for detection of nodules >6mm.

- Additional limitations of WB MRI:
  - Assessment of lymph node involvement
  - Differentiation between viable and residual non-viable tumor
  - Detection of calcified lesions
You are shown a stitched image from a whole-body MRI of a 12-year-old with after treatment of stage II Hodgkin disease. Which one of the following is the MOST likely etiology of the abnormalities?

A. Infection
B. Metastasis
C. Granulocyte colony stimulating factor (GCSF) therapy
D. Osteonecrosis
E. None of the above
Osteonecrosis

- Corticosteroid therapy, alone or in combination with other chemotherapy → most important predisposing factor in the development of osteonecrosis in the treatment of malignancy
  - To control for graft-versus-host disease, nausea and vomiting
  - For immunosuppression in patients who have undergone hematopoietic stem-cell transplant

- Higher risk → survivors of leukemia and lymphoma → osteonecrosis of the weight-bearing joints 1/3 of patients with ALL

- Osteonecrosis involving at least 30% of the articular surface of the hip → worse outcome → predictive of articular surface collapse in 80% of cancer patients within 2 years of presentation, with approximately 50% of requiring arthroplasty

- Symptoms of osteonecrosis correlate with the extent of subchondral involvement and the size of the lesion
Conclusion

- With advancements in technology WB-MRI can now be used on a routine basis and the role of this modality in pediatric oncology is expanding.

- WB-MRI offers a radiation-free alternative to scintigraphy and CT for diagnosis, staging and surveillance. Its role with respect to nuclear medicine needs to be determined. The number of studies demonstrating similar efficacy are increasing.

- WB-MRI is superior to scintigraphy and PET-CT in the detection of bone, brain and liver lesions but remains inferior for the detection of lymphadenopathy and pulmonary lesions.

- Currently, most recommended WB MRI protocol in the setting of metastatic work up include: coronal STIR, axial diffusion and sagittal STIR of the spine. This protocol is a compromise between the detection sensitivity of skeletal and visceral metastases and a reasonable acquisition time.

- The incorporation of diffusion-weighted sequences into WB MRI protocols may lead to use the modality in combination with or instead of PET, which involves substantial radiation.

- Targeted and homogenous studies are still needed to specify the role of WB-MRI in each type of pediatric neoplasm, at the time of the diagnosis or during surveillance. In this way, the technical parameters may be optimized and standardized for each indication.
Thank you for your attention!