Whole-body MR in children with cancer

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Whole-body MR in children with cancer: Applications & possible impact on treatment and prognosis

• Introduction
  – imaging technique
• Applications
  – review of scientific literature
• Conclusions
  – impact on treatment and prognosis?
Introduction
WB-MRI

sliding table platform → multiple stations → reconstruction
WB-MRI

or

vertex – toe  (head)neck – groin
WB-MRI

• WB-MRI is usually performed at 1.5T
  – higher field strengths (esp. when including functional imaging)
    • B0, B1 inhomogeneities
    • susceptibility artifacts

• Coils
  – Integrated quadrature body coil
  – Phased array surface coils
WB-MRI

*Single non-integrated vs. Whole-body surface coil technology*
WB-MRI

• Slice direction
  – coronal
  – axial (neck, thorax, abdomen)
  – sagittal (spine)

• Breathing technique
  – free breathing
  – thorax and abdomen:
    • breath-hold (T1) or respiratory triggering (STIR)
    • navigator techniques
Sequences

• T2 STIR
• T1/T2-weighted FSE/TSE
• Fat Sat T1/T2 (SPIR, SPAIR, mDIXON, ...)
• ceT1-weighted FSE/GE
• DWI
• ....

• Depending on clinical indication!
DWIBS
Diffusion weighted Whole body Imaging with Background body signal Suppression

Takahara T et al, Radiation Medicine 2004;22(4):275-282
Applications
Clinical applications

- Bone marrow imaging (metastases)
- Lymphoma
- Histiocytosis
- Neuroblastoma
- Cancer predisposition syndromes
- ...

Bone Marrow (protocol)

Chemical shift/oppose phase imaging

DWI (b1000)

ADC

sSTIR
Bone marrow imaging (metastases)

- systematic review (age < 21y)
  - 5 studies including
  - 132 patients (96 patients with solid tumors)
- patient groups & used reference tests were heterogeneous
  - unclear or high risk of bias
- sensitivity: 82-100%
- positive predictive value: very variable
  - influenced by the used reference standard

Smets AM et al, Pediatr Radiol 2018;48:241-252
Bone marrow imaging (metastases)

• WB-MRI vs. PET/CT
  – 13 patients, neuroblastoma
  – WB-DWIBS (b800), visual assessment only
  – reference: $^{123}$I-MIBG scintigraphy, bone scintigraphy, and CT

• Sensitivity, specificity, overall accuracy, PPV, NPV:
  – PET/CT: 90.7, 73.1, 80.3, 70.1, and 91.9%
  – WB-DWIBS: 94.7, 24.0, 53.0, 46.4 and 86.7%

• high incidence of false-positive findings on WB-MRI (75.9%)

Bone marrow imaging (metastases)

- MRI vs. PET-CT
  - 20 patients with Ewing sarcoma (112 osseous lesions), age 5-29y
  - T1 & STIR, coronal & sagittal
  - reference: histopathology or expert panel (all available data)
- 39% of metastases on MRI missed by PET-CT!
  - extensive active hematopoietic bone marrow
  - chemotherapeutic treatment
  - lesions smaller than 10 mm
- Patient-based: 92.3% concordance (one false-positive PET-CT)

Lymphoma (protocol)
Lymphoma (protocol)
Lymphoma Staging

• very good agreement between WB T2 STIR and PET/CT (sens., spec., kappa (k))\(^1,2\):
  – nodal sites: 93-98%, 98-99%, 0.91-0.97
  – extranodal sites: 89-91%, 99-100%, 0.91-0.94

• WB-MRI (STIR & DWI) superior to contrast enhanced CT\(^3\)
  – sens. 95.5% vs. 86.4%

• no additional value of DWI to conventional MRI sequences\(^1,4\)

1 Punwani S et al, Radiology 2010;255:182–190
2 Littooij AS et al, Eur Radiol 2014;24:1153–1165
3 Regacini R et al, Pediatr Radiol 2018;48:638–647
Lymphoma Staging

- WB-MRI vs. multi-modality reference standard:
  - 50 pediatric patients
  - cSTIR, DWI, tT2/STIR, tce T1
  - reference: all imaging and clinical investigations (incl. PET/CT), long-term follow up

- **44%** discordance for full patient staging (TPR, FPR and kappa)
  - nodal disease: 91%, 1%, 0.93
  - extranodal disease: 79%, < 1%, 0.86

1Latifoltojar A et al, Eur Radiol 2019;29:202–212
Lymphoma

*Early response assessment*

- early recognition of chemotherapy response or failure
- PET/CT recommended as imaging technique of first choice
  - not officially outside clinical trials
  - good in identifying treatment failure
  - negative PET does not guarantee good prognosis!\(^1\)
- several (pilot) studies using WB-MRI
  - inconclusive results
  - presence/absence of inverse correlation ADC vs. SUV

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\(^1\)Adams HJ et al, Br J Haematol 2015;170:356-366
Lymphoma

Early response assessment

• WB-MRI vs. multi-modality reference standard:
  – 50 pediatric patients
  – cSTIR, DWI, tT2/STIR, tce T1
  – reference: all imaging and clinical investigations (incl. PET/CT), long-term follow up

• WB-MRI response classification:
  – correct in 25/38 evaluable patients (66%)
  – underestimating response in 26% ($\kappa = 0.30$, 95% CI 0.04–0.57)

¹Latifoltojar A et al, Eur Radiol 2019;29:202–212
Histiocytosis (protocol)

cT1

cSTIR

cce T1 fatsat

DWI (b800)

ADC

sSTIR
Histiocytosis

• mostly small studies
  – 2-15 patients
  – cSTIR and (ce) cT1-weighted sequences
• compared to skeletal survey & bone scintigraphy\textsuperscript{1,2}:
  – additional bony lesions
  – extra-osseous disease involvement

\textsuperscript{1}Goo HW et al, Pediatr Radiol 2006;36:1019–1031
\textsuperscript{2}Steinborn et al, RoFo 2008;180:646–653
Histiocytosis

• WB-MRI vs. PET/CT:
  – 15 patients (21 scans)
  – STIR, (ce) T1-weighted sequences (cor, sag, trans)
  – reference: histopathology, follow-up imaging

• overall sensitivity and specificity:
  – WB-MRI: 87%, 47%
  – PET/CT: 67%, 76%

• main limitation MRI: false-positive findings (follow-up)!

Histiocytosis

• Combined MRI/PET analysis improved sensitivity
  – decreasing false-negative rate of PET (primary staging)
  – decreasing false-positive rate of WB-MRI (follow-up, larger lesions)

Histiocytosis

- WB-MRI vs. Skeletal survey vs. Bone scintigraphy:
  - 46 patients, initial staging
  - STIR (cor, sag), cT1-weighted (fatsat), ce 3D T1-weighted (fatsat)
  - reference: clinical and follow-up imaging (consensus 2 radiologist)
- sensitivity, accuracy (concordance rate):
  - WB-MRI: 99%, 0.98
  - Skeletal survey: 56.6%, 0.91
  - Bone scintigraphy: 38.4%, 0.83
- no significant difference in false-positive rates!

Neuroblastoma (protocol)

cT2 STIR (whole body)

c3D T2
tT1 fatsat
ce tT1 fatsat
DWI (b800)
ADC
sT1
sSTIR
Neuroblastoma (protocol)
Neuroblastoma

Staging & response assessment

# Neuroblastoma

## Imaging Defined Risk Factors (MRI, CT)

### Descriptions of IDRFS

<table>
<thead>
<tr>
<th>Anatomic Region</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple body compartments</td>
<td>Ipsilateral tumor extension within two body compartments (i.e., neck and chest, chest and abdomen, or abdomen and pelvis)</td>
</tr>
<tr>
<td>Neck</td>
<td>Tumor encasing carotid artery, vertebral artery, and/or internal jugular vein</td>
</tr>
<tr>
<td></td>
<td>Tumor extending to skull base</td>
</tr>
<tr>
<td></td>
<td>Tumor compressing trachea</td>
</tr>
<tr>
<td>Cervicothoracic junction</td>
<td>Tumor encasing brachial plexus roots</td>
</tr>
<tr>
<td></td>
<td>Tumor encasing subclavian vessels, vertebral artery, and/or carotid artery</td>
</tr>
<tr>
<td></td>
<td>Tumor compressing trachea</td>
</tr>
<tr>
<td>Thorax</td>
<td>Tumor encasing aorta and/or major branches</td>
</tr>
<tr>
<td></td>
<td>Tumor compressing trachea and/or principal bronchi</td>
</tr>
<tr>
<td></td>
<td>Lower mediastinal tumor infiltrating costovertebral junction between T9 and T12 vertebral levels</td>
</tr>
<tr>
<td>Thoracoabdominal junction</td>
<td>Tumor encasing aorta and/or vena cava</td>
</tr>
</tbody>
</table>

### Thoracoabdominal junction

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor encasing aorta and/or vena cava</td>
</tr>
<tr>
<td>Tumor infiltrating porta hepatitis and/or hepatoduodenal ligament</td>
</tr>
<tr>
<td>Tumor encasing branches of superior mesenteric artery at mesenteric root</td>
</tr>
<tr>
<td>Tumor encasing origin of celiac axis and/or origin of superior mesenteric artery</td>
</tr>
<tr>
<td>Tumor invading one or both renal pedicles</td>
</tr>
<tr>
<td>Tumor encasing aorta and/or vena cava</td>
</tr>
<tr>
<td>Tumor encasing iliac vessels</td>
</tr>
<tr>
<td>Pelvic tumor crossing sciatic notch</td>
</tr>
<tr>
<td>Intraspinal tumor extension (wherever the location) provided that more than one-third of spinal canal in axial plane is invaded, the perimedullary leptomeningeal spaces are not visible, or the spinal cord signal intensity is abnormal</td>
</tr>
<tr>
<td>Infiltration of adjacent organs and structures</td>
</tr>
<tr>
<td>Pericardium, diaphragm, kidney, liver, duodenopancreatic block, and mesentery</td>
</tr>
</tbody>
</table>

*Source.* -- Reference 8. Conditions that should be recorded but are not considered IDRFS are multifocal primary tumors, pleural effusion with or without malignant cells, and ascites with or without malignant cells.

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Neuroblastoma

• WB-MRI vs. I-123 MIBG scintigraphy\(^1\)
  – 28 patients (50 scans, 22 staging/28 follow-up)
  – (ce) T1-weighted, T2-weighted, STIR (cor, sag, transv)
  – reference: histopathology, follow-up imaging (≥ 6 months)

• Sensitivity and specificity:
  – WB-MRI: 69%, 85%
  – I-123 MIBG: 86%, 77%
  – combined analysis: 99%, 95%

\(^1\)Pfluger T et al, AJR Am J Roentgenol 2003;181(4):1115–1124
Neuroblastoma (lymph node metastases)

- WB-MRI vs. PET/CT
  - 13 patients, neuroblastoma
  - WB-DWIBS (b800), visual assessment only
  - reference: $^{123}$I-MIBG scintigraphy, bone scintigraphy, and CT
- Sensitivity, specificity, overall accuracy, PPV, NPV:
  - PET/CT: 100, 98.7, 98.9, 95.0, and 100%
  - WB-DWIBS: 94.7, 85.3, 87.2, 62.1, and 98.5%

Neuroblastoma

• role of DWI in differentiating subtypes?\textsuperscript{1,2}
  – 15 & 19 patients
  – (ce) T1, T2, STIR, DWI (b50, b400, b800)
  – NB (10/15), GNB (2/1), GN (4/3)

• significantly difference in ADC NB vs. GNB/GN
  – considerable overlap
  – ADC cutoff ≤ 1.05 (1.1\textsuperscript{1}): sens. 100%, spec. 93,8\%\textsuperscript{2}

\textsuperscript{1}Gahr N et al, Eur J Radiol 2011;79(3):443–446
\textsuperscript{2}Peschmann AL et al, Eur Radiol Exp 2019;30:6
Neuroblastoma

• role of DWI in predicting outcome?\(^1\)
  – 19 patients
  – (ce) T1, T2, STIR, DWI (b50, b400, b800)
  – NB (15), GNB (1), GN (3)
• low baseline ADC predictive of tumour progression/relapse
  – ADC ≤ 0.80
• during therapy:
  – increasing ADC predictive of relapse-free survival
  – decreasing ADC indicator of poor prognosis

\(^1\)Peschmann AL et al, Eur Radiol Exp 2019;30:6
Cancer Predisposition Syndrome (protocol)
Cancer Predisposition Syndrome (protocol)
Cancer predisposition syndromes

• Whom to screen?¹
  – risk >5% in first two decades
  – risk 1-5% in rapidly progressive/aggressive cancers

¹Brodeur GM et al, Clin Cancer Res 2017;23:e1–e5
Cancer predisposition syndromes

• AACR Pediatric Working Group recommendations:
  – Li–Fraumeni syndrome, NF1, NF2 with schwannomatosis, hereditary retinoblastoma, constitutional mismatch repair deficiency syndrome and hereditary paraganglioma pheochromocytoma syndrome
  – (DICER1 syndrome, rhabdoid tumor predisposition syndromes and Rothmund–Thomson syndrome)
• imaging protocol depends on type of predisposition syndrome!

¹Greer ML, Pediatr Radiol 2018;48:1364–1375
Cancer predisposition syndromes

- 25 patients, hereditary retinoblastoma
- WB-MRI (1-5): T1, T2 STIR (transv, sag)
- reference: biopsy or dedicated MRI
- results:
  - 5 suspicious bone lesions: 2 malignant, 3 benign
  - 1 interval osteosarcoma
  - sens. 66.7%, spec. 92.1%

1Friedman DN et al, Pediatr Blood Cancer 2014;61(8):1440–1444
Cancer predisposition syndromes

- 24 patients, cancer predisposition syndromes
- WB-MRI: T1, T2, STIR (cor, ax), T2 HASTE (cor, sag, ax)
- reference: biopsy and follow-up
- Results:
  - 9 suspicious lesions (2 high-risk, 2 moderate risk, 2 low-risk); only 1 proven malignancy
  - sens. 100 % (95 % CI 6–100 %), spec. 94 % (82–98 %), NPV 94 %, PPV 25%

Anupindi SA et al, Am J Roentgenol. 2015;205(2):400–8
Cancer predisposition syndromes

• main limitations:
  – potential risk of false-positive findings
  – high percentage of incidental findings!

• interpretation reserved to expert radiologists
  – appropriate risk stratification
  – minimize unnecessary additional imaging/interventions

1 Friedman DN et al, Pediatr Blood Cancer 2014;61(8):1440–1444
2 Anupindi SA et al, Am J Roentgenol. 2015;205(2):400–8
Conclusions
Conclusions

• no or mostly small (pilot) studies
  – < 25 patients
  – largest cohorts: lymphoma (50), LCH (46)

• no standardization of imaging protocols
  – definition of WB-MRI

• contradictory results
Conclusions

• Good radiation free alternative for anatomical imaging (staging)
  – lymphoma, LCH, neuroblastoma (IDRFs)

• Bone marrow metastases
  – high incidence of false-positive/normal findings

• Screening
  – potential risk of incidental/false-positive findings

• Response assessment & prognosis?
  – underestimation of response (lymphoma, LCH)
  – prediction of outcome (neuroblastoma)