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PICTORIAL ESSAY

Paediatric Whole-body Magnetic Resonance Imaging and its Role in Oncological and Non-oncological Cases

ER Mohd Rusli[1], F Mohd Zaki[1], AHZ Samsudin[2], L C-Khai[3], EY Hing[1], H Alias[3], H Abdul Hamid[1]

[1]Department of Radiology, Universiti Kebangsaan Malaysia Medical Center, Jalan Yaacob Latif, 56100 Kuala Lumpur, Malaysia
[2]Department of Radiology, Hospital Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia
[3]Department of Paediatrics, Universiti Kebangsaan Malaysia Medical Center, Jalan Yaacob Latif, 56100 Kuala Lumpur, Malaysia

INTRODUCTION

Magnetic resonance imaging (MRI) is a favourable diagnostic tool compared with other imaging modalities due to its high soft tissue contrast and spatial resolution in detecting pathologies. Most importantly, it is free of ionising radiation, making it suitable for the paediatric population, especially in those who require repeat imaging.[1-3]

Approximately 27% of paediatric oncological cases present with metastases. The consequent needs for long-term follow-up and frequent imaging with either computed tomography (CT) scan or positron emission tomography (PET-CT) will increase the cumulative radiation dose over time.[4-7] Whole-body MRI (WBMRI) has been advocated since the early 1990s to ensure optimum whole-body imaging surveillance with comparable diagnostic accuracy to that of CT and PET-CT.[8] This paper discusses and illustrates the role of WBMRI in oncological and non-oncological cases.

IMAGING TECHNIQUES

There are a few radiological modalities available for paediatric oncological cases, each with limitations. Conventional CT and PET-CT scans provide wide body coverage but patients are exposed to ionising radiation. Ultrasound is preferred for its non-ionising radiation property but is operator-dependent and the area of

Correspondence: *Dr F Mohd Zaki, Department of Radiology, Universiti Kebangsaan Malaysia Medical Center, Jalan Yaacob Latif, 56100 Kuala Lumpur, Malaysia*
Email: drfaizah@ppukm.ukm.edu.my

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examination is limited. With technological advancement, WBMRI can produce high image resolution for locoregional and distant staging assessment.

Imaging techniques and best image quality depend on the magnetic field strength, coil system, and pulse sequences. A comparison by Mohan et al[9] of 1.5-T and 3-T MRI machines concluded that 1.5-T MRI produced superior image quality, structural visibility, and fewer artefacts. There was a higher risk of developing susceptibility artefacts, dielectric shading, and motion artefacts with 3-T MRI even though it has a higher signal-to-noise ratio and contrast-to-noise ratio compared with 1.5-T.[2] Nevertheless both machines were comparable for detecting pathology.[9] The current technical standard for WBMRI includes a dedicated multi-channel, multi-element surface coil system, allowing imaging of any part of the body at a particular time without having to move the coil system.[2] Unfortunately, not all centres have this technology so the protocol has to be tailored for each case to gain the best image possible.[8,10]

Pulse sequences including short tau inversion recovery (STIR), T1-weighted, diffusion-weighted images, and magnetic resonance angiography have been discussed at great length.[2] STIR sequence is the most frequently used sequence and has been adopted by our institution since 2015 since it provides homogenous fat suppression with higher sensitivity for detection of abnormalities. It can identify lesions even in the hypercellular red bone marrow of a young child compared with T1-weighted imaging alone.[2,10] The slice thickness should be <4.0 to 5.0 mm for good image quality.[8]

Scanning time in the paediatric population is another consideration. On average, a single examination takes 30 to 60 minutes, similar to bone scintigraphy.[10] Imaging in the axial plane will increase lesion detection by 10% but will also increase the table time.[10] In our institution, we take an average 30 minutes of table scan time with most patients requiring oral or intravenous sedation. Additional sequences are also added to increase diagnostic accuracy.

Clinical Application

Lymphoma

Lymphoma is the third leading cause of malignancy in children following brain tumours and leukaemia.[10-12] Recently, the Society of Pediatric Radiology (SPR) has recommended WBMRI as an alternative to contrast-enhanced CT thorax, abdomen, and pelvis.[13] PET-CT nonetheless remains a vital imaging modality to assess tumour and treatment response.[10,12-14] In our institution, PET-CT is done during follow-up as per the current recommendation and results correlated with those of WBMRI to determine the metabolic activity of the lesions. WBMRI can recognise both nodal (98% sensitivity and 99% specificity) and extranodal disease (91% sensitivity and 99% specificity). MRI has been shown to be capable of detecting lymph nodes >12 mm with a sensitivity of 92.0% and specificity of 99.9%.[11,14] According to Guimarães et al,[14] WBMRI with coronal STIR sequence is more sensitive in detecting marrow involvement in the initial phase of the disease than other conventional imaging.

The downside of MRI includes its inability to identify malignant nodes <1 cm and to discriminate between lymphomatous bony infiltration and therapy-induced marrow signal abnormalities.[11] Some of our patients presented with nodal and others with extranodal disease (Figure 1).

Neuroblastoma

Neuroblastoma is the most common extracranial solid tumour in children, accounting for about 6% of cases and approximately 15% of cancer deaths in children.[3] It arises from the sympathetic chain and metastasises to the bone, lymph nodes, liver, and skin.[3,10] In the past, CT and metaiodobenzylguanidine (MIBG) scintigraphy together with bone marrow aspiration were essential to diagnose and assess neuroblastoma, but MRI is increasingly being utilised for regional disease.

Although WBMRI in neuroblastoma has not been fully evaluated, a small study by Goo[2] revealed that it has higher sensitivity than MIBG and CT in detecting bone metastases.[10] In our centre, we perform an MIBG scan for all new lesions detected on WBMRI, especially in MIBG-positive cases (MIBG scintigraphy was a baseline investigation before treatment) before proceeding with biopsy. Two cases with neuroblastoma are shown (Figures 2 and 3).

Langerhans Cell Histiocytosis

Langerhans cell histiocytosis (LCH) is mainly a disease of childhood, occurring at a median age of 30 months and affecting the reticuloendothelial system; bone marrow, liver, spleen, lymph node, and lungs.[3,15] The disease varies from a unifocal bone lesion to a multisystemic disorder.[8,10] In the past, plain radiograph and bone scintigraphy were performed for diagnosis and follow-up,

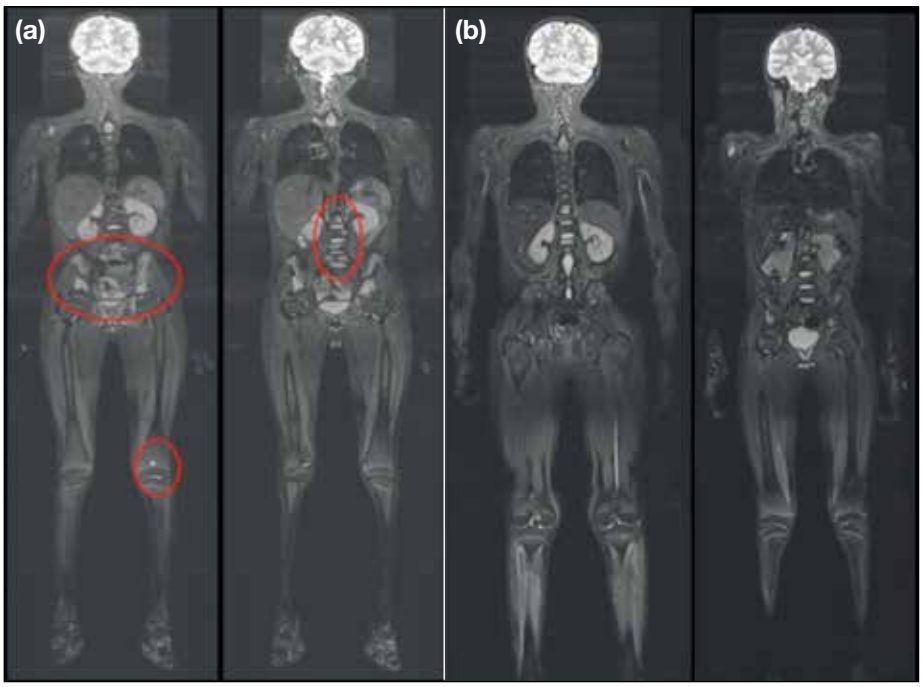

Figure 1. A 12-year-old boy with stage 4 diffuse large B cell lymphoma. Scan performed (a) after 2nd cycle of chemotherapy and (b) 3 months later; showing significant reduction in the multiple hyperintense marrow lesions at iliac, thoracolumbar spine and distal left femur metaphysis (circles in [a]) during the interval scan.

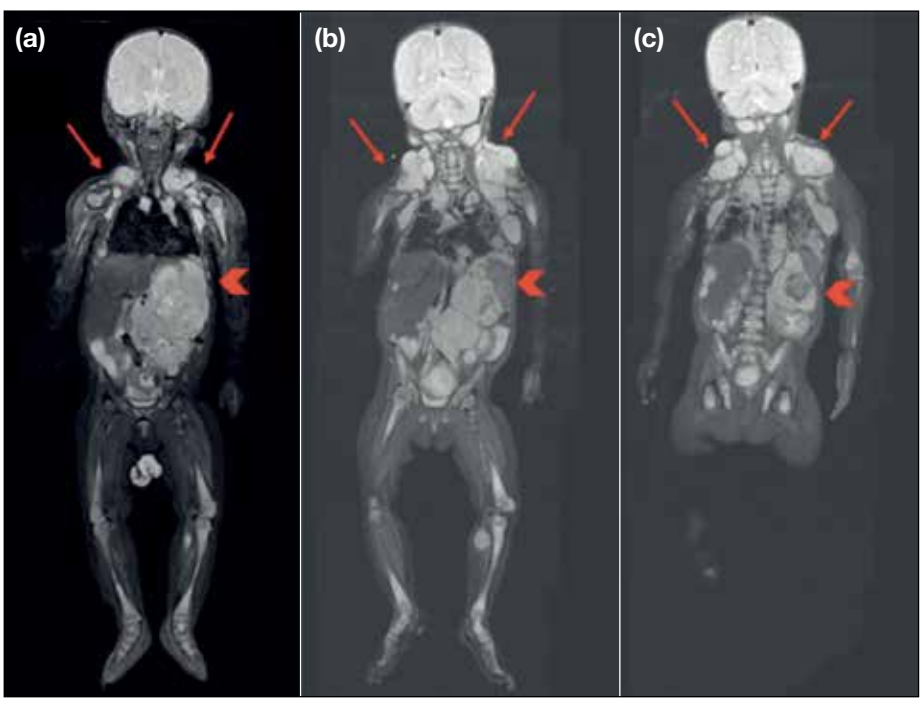

Figure 2. A 5-month-old girl diagnosed with infantile neuroblastoma. Scan performed (a) at diagnosis, (b) 2 months post-chemotherapy and (c) 4 months later; showing increasing and decreasing sizes of bilateral supraclavicular lymph nodes (arrows) between the scanning intervals with progressively smaller left suprarenal mass (arrowheads).

but clinicians are now more inclined to utilise WBMRI as it can detect both skeletal and extraskeletal lesions.[10] It is important to stage the disease before treatment commences, since the presence of more than one lesion will impact treatment decisions, i.e., intralesional corticosteroid versus systemic chemotherapy.[3,8]

According to Goo et al,[16] concurrent T1 post-contrast sequence is more beneficial in differentiating solid from cystic lesions than STIR sequence alone. The solid lesion will commonly show avid or peripheral enhancement on post-contrast images.[3] Nonetheless difficulty arises in distinguishing residual lesions post-treatment from

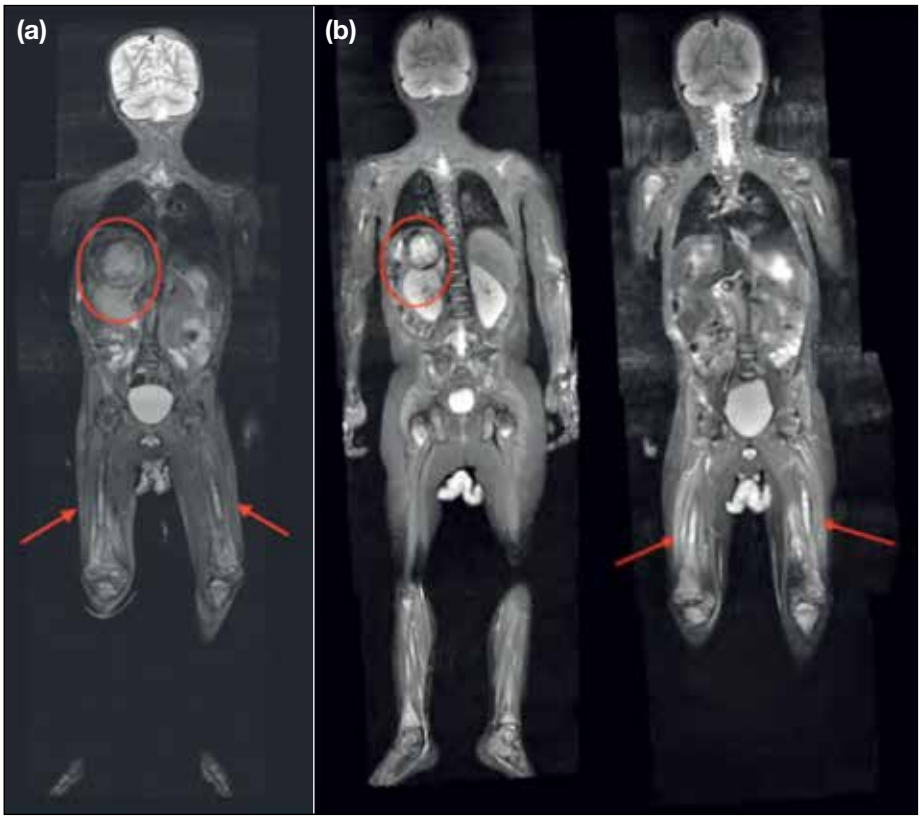

Figure 3. A 4-year-old boy with stage 4 neuroblastoma. Scan performed after (a) 2 cycles of chemotherapy and subsequently (b) 2 months later; showing smaller right suprarenal mass (circles) with unchanged hyperintense marrow lesions in bilateral femurs (arrows).

active lesions so functional imaging techniques such as PET-CT, diffusion/perfusion MRI or MRI spectroscopy are employed.

Although PET-CT has higher accuracy than plain radiograph and bone scintigraphy, WBMRI is the modality of choice to identify vertebral lesions.[10,16] Twelve cases diagnosed with LCH underwent WBMRI at our centre (Figure 4).

Chronic Recurrent Multifocal Osteomyelitis

Chronic recurrent multifocal osteomyelitis is a rare condition first described in 1972. Affected children will present with nonspecific musculoskeletal pain and swelling. Imaging is required to exclude underlying malignancy.[17]

Compared with PET and bone scintigraphy, WBMRI is superior at identifying multifocal oedematous lesions as they appear hyperintense on the STIR sequence. In a cohort study by Leclair et al,[18] an average of two lesions was found in all 16 patients, mainly located at the epimetaphyseal region of the long bones. These lesions are usually ill-defined and asymmetric.[18] No such case was encountered at our centre.

Cancer Predisposing Syndrome

Children with cancer predisposing syndrome (neurofibromatosis type 1, Beckwith-Wiedemann syndrome, multiple endocrine neoplasias, Li-Fraumeni syndrome, von Hippel-Lindau syndrome, and familial adenomatous polyposis) are at significant risk of developing cancer due to its familial inheritance.[3,10,14] They require regular screening that should include a physical examination, blood analysis, urinalysis, and imaging.[10]

According to Greer et al,[19] WBMRI is now recommended in these children due to its head-to-toe coverage with no additional radiation risk, making it more favourable than CT or PET-CT. It is a potential screening technique that can improve patients' long-term outcome while reducing the tumour burden by identifying the tumour at the earliest and most curable stage due to its high sensitivity and specificity.[3,20] Furthermore, the SPR recommends WBMRI as a replacement for skeletal survey radiograph and bone scintigraphy in assessment of osseous LCH.[13]

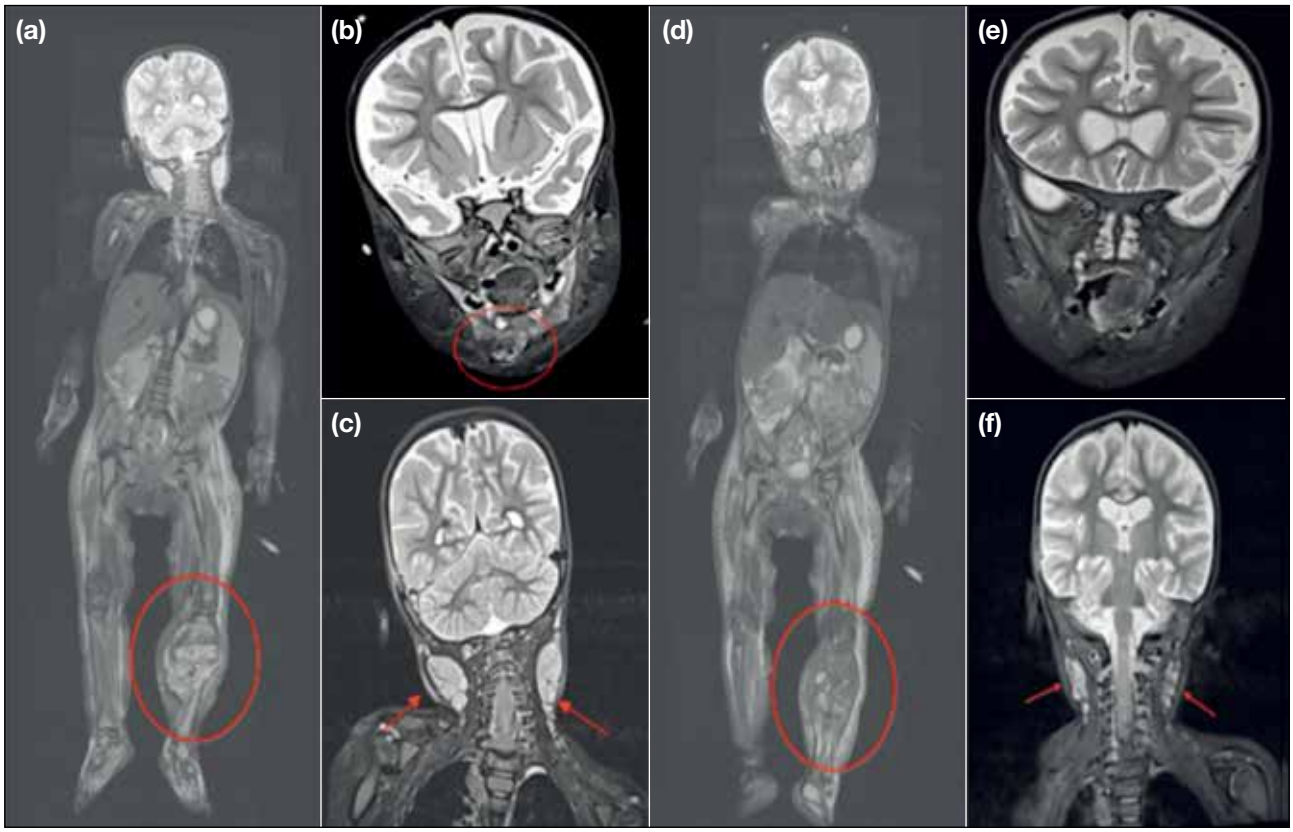

Figure 4. A 22-month-old girl with Langerhans cell histiocytosis. Scan performed (a, b, and c) at diagnosis and (d, e, and f) 4 months later; showing smaller soft tissue mass at the proximal left tibia (circles in [a] and [d]), right mandible (circle in [b]), and bilateral cervical lymph nodes (arrows in [c] and [f]).

Metastasis

WBMRI can be utilised to assess malignant solid tumours as it has a higher if not similar degree of sensitivity and specificity to PET or CT.[6,10,14] About 10% of patients with bone metastases have an unknown primary and this too can be assessed by WBMRI.[21] MRI generally has a sensitivity of >90% in detecting bone metastases and this further increases when STIR sequence is performed along with T1-weighted sequence.[12,14] We have scant experience in performing WBMRI on soft tissue sarcoma as it is not a standard imaging protocol for treatment assessment. Furthermore, sarcoma rarely presents with disseminated disease. However, the SPR recommends WBMRI, particularly in disseminated disease.[13]

Examples of malignant solid tumours in childhood encountered in our centre include rhabdomyosarcoma (Figure 5), Ewing sarcoma, osteosarcoma (Figure 6) and primitive neuroectodermal tumours.[6,10]

Figure 5. A 14-year-old boy with alveolar rhabdomyosarcoma of the left hypothenar muscle. Whole-body magnetic resonance imaging performed 4 months after completion of chemotherapy showing abnormal hyperintense marrow signal in the left iliac bone, left acetabulum, left iliac and left gluteus intermedius muscle (circle) suggestive of metastases.

Figure 6. An 11-year-old girl with distal right femur osteosarcoma on chemotherapy. Scan performed (a-d) at diagnosis and (e-h) 3 months later; showing disease progression with enlarging primary lesion in the distal right femur extending to the knee joint and proximal tibia (arrows in [a] and [e]). The intramedullary lesions in the distal left femur (circle in [a]), proximal left tibia (circles in [b] and [f]), L5 vertebrae (circles in [c] and [g]) and proximal right femur (arrows in [d] and [h]) appear more heterogeneous with similar characteristics to the primary lesion. Fixed flexion deformity of the right knee caused the inability to 'stitch' the images.

Imaging Pitfalls

There are some pitfalls related to WBMRI. One is the need to apply an individual coil rather than a dedicated body coil resulting in the inability to stitch together the final images.[2] This problem is frequently encountered in our centre. Distortion of a patient's normal anatomical position will also affect the post-processing images as shown in Figure 6.

Although STIR sequence is advantageous, it is unfortunately not specific in detecting malignancy. Other disease processes including infection and inflammation will also appear hyperintense on STIR making it difficult to differentiate post-treatment oedema from residual tumour.[22] At our centre, when a new lesion is encountered, especially in the bone, we will characterise it depending on its morphology. If the lesion is small with no aggressive features (e.g., no cortical erosion, periosteal reaction or soft tissue component), the lesion will be regarded as nonspecific and likely benign. Closer imaging follow-up within 3 to 4 weeks is then advised. Other sequences including diffusion-weighted images and T1-post contrast are also employed to increase the image quality and image detection but at the expense of time.[2]

The effects of treatment such as radiation and chemotherapy also limit WBMRI, further confounded by the constantly developing nature of children's bones. Understanding the normal physiology of bone metabolism and bone development is crucial to avoid misdiagnosis.[13,23]

Previous literature indicated that WBMRI was less sensitive in the detection of lung lesions so CT thorax remains the modality of choice in the assessment of lung metastases in oncological patients such as those with sarcoma.[13,24]

CONCLUSION

The paediatric population is radiosensitive. WBMRI is the modality of choice given its ionising radiation-free property making it suitable for repeated imaging. Although it may be time-consuming, the benefits appear to outweigh the disadvantages due to its high sensitivity and specificity compared with conventional imaging.

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