Whole Body MRI and Diffusion Weighted Images in Pediatric Oncology: Lymphomas and Several Others Tumors

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Abstract Cancer in a pediatric population represents the majority of non-related to trauma deaths. In most developed and emerging countries there is a need for early and accurate imaging detection, usually with fast examinations protocols, and no or low radiation exposure to avoid a secondary radiation induced neoplasia. The advance of magnetic resonance imaging techniques permitting the use of whole body images on oncology patients and multifocal diseases and the use of diffusion weight images DWI techniques allow additional metabolic information for WB-MRI with growing evidence that the disease metabolic activity is correlated with cellularity in some tumors. This permits DWI sequences and suggests tumor activity with the therapy response as an alternative to PET-CT. WB-MRI has proved to be more sensitive than scintigraphy in detecting both marrow and non-marrow involvement on lymphoma patients and can be a very good alternative to those who cannot undergo a PET-CT. Other small cell neoplasms such as Ewing family, neuroblastoma and some sarcomas also have been effectively evaluated by WB-MRI. On palliative care patients, WB-MRI plays a role on detecting lesions that can cause pain or pressure over vital structures. In conclusion, WB-MRI has been proved an extremely useful method

on multifocal diseases and oncology with the same routine MR contraindications and should be, respecting the limitations inherent to any radiology method, accepted as another powerful tool especially in pediatric oncology. It can be used to avoid radiation exposure related disease and could be more available to these patients.

Keywords WB-MRI · Whole body · Magnetic resonance imaging · DWI · Pediatric · Oncology

Introduction

Cancer in a pediatric population represents the majority of non-related to trauma death in most developed and emerging countries. It has an estimated cure rate of 70 %, and needs an early and accurate imaging detection, usually with fast examinations protocols, and no or low radiation exposure avoiding a secondary radiation induced neoplasia [1–5, 6•, 7].

WB-MRI Use in Pediatrics

To reach these requirements along with the advance of magnetic resonance imaging (MRI) techniques since 2004, the use of Whole Body (WB) images has been increasing on oncology patients and multifocal diseases [8] as a new alternative to the gold standard PET-CT which provides full body information despite radiation exposure and low availability [6•] (Fig. 1). Other advances such as the use of diffusion weight images (DWI) technique in MRI also allowed additional metabolic information for WB-MRI. [9–11].

Since the advent of 1.5 Tesla systems with an automated moving table and a large field-of-view (FOV) (500 mm)

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Fig. 1 *Right* Whole body MRI of a Hodgkin Lymphoma staging T2 showing a left cervical mass (*arrowhead*) and a pulmonary metastasis (*arrow*), same findings were observed on CT (*left*)

[12, 13] total body MRI use has been increasing. A number of different studies [14–21] evaluated several MRI sequences, and only the inversion recovery, such as STIR (Short Tau Inversion Recovery) were in unanimity among their protocols, as it is sensitive to diseases when compared to other sequences [14, 15], and exhibits image properties of a mix of proton density, T1, T2 with inherent fat suppression [22] (Fig. 2). Even despite its lacking measurement of the disease activity and usually has a persistent abnormal signal on scar/inflammatory reactions [23–25], STIR has proved feasible for a number of pathologies and has shown to be more accurate than bone scan [26]. It was validated by the American College of Radiology appropriateness criteria in the year 2000 [27].

There is growing evidence that disease metabolic activity is correlated with cellularity in some tumors [28, 29] which permits diffusion weighted images (DWI) sequences and suggests the tumor activity and therapy response as an alternative to PET-CT on this issue. DWI technique relies on water Brownian motion modified by the interaction of cell membranes and macromolecules. DWI creates images from water motion restriction and its degree of restriction is inversely proportional to the cellularity and membranes integrity, and it can be measured by the ADC (apparent diffusion coefficient) [30–33]. The inverse relationship between ADC (recording as low as the more restricted water Brownian motion by cells) and SUV (used on PET-CT that

Fig. 2 Normal STIR whole body image with properties of a mix of proton density, T1, T2 with inherent fat suppression

records higher if more glucose is consumed by cellular activity) has been demonstrated by Mori et al. [34] and Ho et al. [35] for malignant tumors [9] (Fig. 3).

Fig. 3 Neuroblastoma 4 pretreatment total body MR, side by side STIR (*left*) and DWIBS (*right*) showing left adrenal mass, paravertebral bilateral and cervical nodes, and abnormal bone marrow signal, as neuroblastoma is a hypercellular tumor, water diffusion is restricted in generating a high signal on diffusion weighted images

Diffusion images have to be reconstructed from multiple axial 3D data with background suppression (DWIBS) creating a maximum intensity projection 3D image, which can have an inverted gray scale applied to display similar to PET images for the clinicians' comfort in interpretation [36] (Fig. 4).

Most authors, especially concerning adults, also include T1 sequences out of phase [37], on an orthogonal plane, as a radiology rule to accurately determine the lesion. Usually a sagittal image series is added to the most commonly used coronal planes [38•]. Other authors determine that WB-MRI should target to have the maximum body coverage within the shortest time and minimum sequences regardless of the “two orthogonal planes rule” [22].

STIR image interpretation should be fast and take approximately 5 min, even though there can be a large amount of images, and the detection of signal alteration occurs as a binary process of normal or abnormal MR signal [39], letting there be longer interpretation times for complicated studies that require comparison or presents multiple lesions (Fig. 5).

Fig. 4 Neuroblastoma 4 with inverted gray scale DWIBS, there is a proportional correlation between restricted diffusion due to tumor cell membranes and tumoral activity, therefore, inverted gray scale images can be used to make this sequence friendlier to clinicians as it seems similar to PET reconstructions

The use of WB-MRI for pediatric oncology is well established with a comparable sensitivity to PET-CT of 96 % for malignancy detection and a 100 % detection of bone lesions [40•], detecting more metastasis on 17 % of cases studied by Schlemmer et al. [41], when compared to CT.

Pediatric Malignancies

Lymphoma

Lymphoma is the third most common malignancy in pediatrics accounting for more than 10 % of cancer on childhood [5]. Staging both Hodgkin and non-Hodgkin lymphoma involves the search for bone marrow involvement present at up to 16 % of whose that can be missed at plain radiography [42]. WB-MRI has proved to be more sensitive than scintigraphy detecting both marrow and non-marrow involvement [17] and can be a very good alternative to patients who cannot undergo a PET-CT [43]

Fig. 5 Localized STIR images of a lymphoma treatment follow up, there is a good therapy response, different to other total body scan follow up images that can be evaluated by a localized series generated before reconstruction

during its important staging because even the iliac crest blind biopsy can be negative reflecting the patchy bone marrow involvement pattern [44] (Fig. 6).

The use of STIR WB-MRI for following treatment cannot clearly differentiate residual lesions or scars when present as inflammatory, and traumatic bone lesions also exhibit high signal intensity on STIR images [23–25], so larger DWI studies has been carried out to prove the preliminary results of its importance due to the relationship between cellularity, water diffusion restriction and disease activity on lymphoma patients [45•]. It might help to improve WB-MRI acceptance by clinicians as an alternative to PET-CT during the diagnostic work-up and follow up [36] (Figs. 7, 8).

Neuroblastoma and other small cell neoplasm

Other small cell neoplasms such as Ewing family, neuroblastoma and some sarcomas also has been effectively evaluated by WB-MRI [22]. Neuroblastoma, the most common extra cranial malignance in children, has established image-defined risk factors during its primary evaluation [46–48] and studies showed similar findings of sensibility and specificity on both CT and MR [49]. Early therapy response can be very well evaluated by WB-MRI,

Fig. 6 Patchy bone marrow involvement pattern of Hodgkin lymphoma on bilateral tibial, femoral, iliac and humeral bone marrow, visualized on both STIR and DWIBS sequences

Fig. 7 Right humeral late metastasis workup of a rhinopharynx carcinoma demonstrated by STIR and DWIBS sequences

possibly even better than I-MIBG [18], but, unfortunately, late therapy evaluation has the same limitation as lymphomas in dealing with scar and residual disease [38••].

Fig. 8 DWIBS and STIR total body lymphoma 8-month healing follow up. Notice the complete disappearance of the mediastinal mass on DWIBS even the remains of little scar high signal on the STIR

sequence. The patient confirmed complete cure with other tests including PET-CT, assuring the DWIBS signal loss value.

Fig. 9 Bilateral leukemia renal infiltration, a diffuse high bone marrow signal can also be noticed by DWIBS sequences

DWI also found significant difference of the ADC map of neuroblastoma compared to ganglioneuroma and ganglioneuroblastoma, adding probably a new utility for this sequence on WB-MRI following further studies [50].

WB-MRI can also be used to evaluate patients with metastasis of unknown primary tumors [51] that can happen in up to 10 % of patients with bone metastasis [52]. Laffan et al. [16] found unsuspected neuroblastoma, leukemia and lymphoma in a pediatric population that had no primary diagnosis (Fig. 9). Despite the search for suspected tumors, incidental findings that have clinical importance affecting the management were reported. Jaremko et al. [53], when studying neurofibromatosis, were able to find unsuspected avascular necrosis, insufficiency fractures, a secondary tumor other than neurogenic among other less important conditions.

For palliative care patients, WB-MRI plays a role for detecting lesions that can cause pain or pressure over vital structures. Geitung et al. [54] had findings on these patients that changed the treatment for 40 %, and determined that palliative patients could benefit from WB-MRI where PET-CT might be too much.

Conclusion

In conclusion WB-MRI has been proven to be an extremely useful method for multifocal diseases and oncology with the same routine MR contraindications. It should be, respecting the limitations inherent to any radiology method, accepted as another powerful tool, especially in pediatric oncology, avoiding radiation exposure related disease and being more available to these patients.

Compliance with Ethics Guidelines

Conflict of Interest Dr. Jose Luiz de Oliveira Schiavon declares no potential conflicts of interest. Dr. Henrique Manoel Lederman is a section editor for *Current Radiology Reports*.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of major importance

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