Whole-Body MRI in Children and Adolescents – S1 Guideline

Ganzkörper-Magnetresonanztomografie im Kindes- und Jugendalter – S1-Leitlinie

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ABSTRACT

Whole-body MRI is an imaging method that uses advanced modern MRI equipment to provide high-resolution images of the entire body. The goal of these guidelines is to specify the indications for which whole-body MRI can be recommended in children and adolescents and to describe the necessary technical requirements.

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ZUSAMMENFASSUNG

Die Ganzkörper-Magnetresonanztomografie (GK-MRT) ist eine bildgebende Methode, welche unter Nutzung fortgeschrittener Verfahren moderner MRT-Geräte eine hochaufgelöste Darstellung des gesamten Körpers ermöglicht. Ziel dieser Leitlinie ist es, Indikationen zu benennen, bei denen die GK-MRT im Kindes- und Jugendalter empfohlen werden kann, und dafür notwendige, technische Voraussetzungen zu beschreiben.

1. Introduction

Whole-body MRI is an imaging method that uses advanced modern MRI equipment to provide high-resolution images of the entire body [1 – 5]. In principle, under these conditions, the image quality and image contrast of examinations of the head and torso do not differ when age- and indication-adapted protocols are additionally used [1, 3 – 7]. However, a loss of spatial resolution in the region of peripheral joints must be taken into consideration. Whole-body MR-angiography is possible [8]. Whole-body MRI can be performed at a field strength of 1.5 as well as 3 Tesla [9]. The examination time depends on the number of selected image contrasts and additional equipment- and measurement protocol-dependent parameters and can therefore vary greatly. Particularly in children and adolescents, the protocol must be adjusted to the particular medical issue in order to limit the examination time.

MRI is the method of choice for evaluating the local finding in solid tumors in children and adolescents. However, it is increasingly also performed as whole-body MRI in systemic staging [3, 6, 7, 10 – 33]. In particular, the focus is on osteomedullary metastases here [22, 23, 26, 32, 34 – 37]. In hereditary syndromes with increased tumor incidence, whole-body MRI will play an even greater role in screening in the future [38 – 46]. In addition to malignant solid tumors, a series of non-malignant diseases, e. g. of a rheumatic origin, require systemic staging via imaging. The goal is to use whole-body MRI to differentiate between local and advanced systemic disease and possibly to detect previously clinically silent regions [47 – 56]. The search for an inflammatory focus is also an indication for whole-body MRI [57].

Whole-body MRI is in competition with other radiology methods, particularly computed tomography (CT), positron emission tomography in combination with CT (PET/CT) or MRI (PET/MRI), and scintigraphy, which are all associated with relevant radiation exposure. Therefore, in general, whole-body MRI can always be used when one of the methods specified above can be eliminated while still providing at least equivalent diagnostic information or when whole-body MRI can provide complementary information [7, 12, 14 – 17, 19, 20, 23, 27, 32, 35 – 37, 43, 47, 48, 50, 51, 53 – 56, 58 – 68].

In the last two decades, the diagnostic accuracy of whole-body MRI for various pediatric diseases has been investigated primarily in comparison to other imaging methods and superiority compared to conventional imaging methods apart from lung imaging has been shown [15, 27, 32, 35, 36, 52, 54, 55, 64]. However, due to the lack of large prospective and randomized studies, whole-body MRI does not have a high level of evidence.

According to the guidelines commission, the high sensitivity of the method results in a risk of overdiagnosis particularly in the case of incidental findings or suspected pathologies when the diagnostic report is created without sufficient pediatric radiology experience. Since whole-body MRI can be used effectively in all age groups, comprehensive knowledge of the normal maturation of organ systems is a major requirement for optimal quality and evaluation of findings.

The goal of these guidelines is to specify the indications for which whole-body MRI can be recommended in children and adolescents and to describe the necessary technical requirements.

2. Key recommendations

whole-body magnetic resonance imaging can be used to examine the extent of malignant and non-malignant systemic diseases in children and adolescents.	yes	10/10
to obtain clinically useful diagnostic information, age- and indication-adapted protocols should be used, and the findings should be reported by radiologists with pediatric radiology experience.	yes	10/10
additional examinations using other imaging methods can be indicated.	yes	10/10

3. Comments

3.1 Indications (▶ Table 1)

3.1.1 Malignant tumors

Based on the available data regarding some malignant entities in children, there are indications for whole-body MRI which can completely replace, minimize, or supplement the need for further imaging. However, to date, whole-body MRI is typically not included as a staging tool in treatment studies of the national and international oncological societies (GPOH, SIOP). Nonetheless, it can be assumed that whole-body MRI will be taken into consideration in the future in the further development of protocols. The indications can still be adapted to the available study protocols and whole-body MRI can be performed as a complementary method.

For Hodgkin lymphoma (HL), the use of 18F-FDG-PET/CT is specified for nodal and extranodal staging as well as for treatment monitoring. Whole-body MRI can be performed in this phase on a supplementary basis, particularly when diagnostic CT was not performed during PET/CT [27]. The importance of diffusion-weighted imaging (DWI) in the evaluation of treatment response is still a topic of research. A decrease in diffusion restriction is to be interpreted as an indication of treatment response [28, 33]. Generally valid criteria for assessing complete remission and limit values for the apparent diffusion coefficient (ADC) have not yet been defined. Moreover, the extent of the diffusion restriction in the interim control seems to have prognostic significance [28] and indicates the residual tumor load with very high sensitivity [33]. Whole-body MRI can provide comprehensive information and can therefore be recommended for further follow-up after completed treatment to check for recurrence and for monitoring treatment-associated complications (e. g. osteonecrosis) [58].

If PET/CT is not performed, non-Hodgkin lymphoma (NHL) generally represents an indication for whole-body MRI, particularly when higher stages (Ann-Arbor classification > 2), a primary extranodal manifestation (e. g. bones) or CNS involvement is suspected [11 – 13, 18, 31, 33, 69]. Diffusion restriction seems to be more pronounced in aggressive NHL than in HL [70]. In the case of large cell B-cell lymphoma, it was able to be shown that

▶ **Table 1** Possible indications for whole-body MRI

diagnosis	issue
malignant tumors	staging, tumor extent, restaging, and follow-up
langerhans cell histiocytosis (LCH)	staging, unifocal vs. multifocal, treatment monitoring
avascular osteonecrosis (AVN)	extent and severity, detection of asymptomatic findings
chronic non-bacterial osteomyelitis (CNO/NBO/CRMO)	unifocal vs. multifocal, "silent lesion", treatment monitoring
fever syndromes	focus, extent of changes, tumor exclusion
syndromes and genetic predisposition with increased tumor risk	extent of changes, tumor screening
battered child syndrome	no standard; in addition to evaluation of extent of injuries, particularly soft tissues and organ involvement (refer to guidelines on imaging in the case of suspicion of child abuse)

the risk for tumor progression or for recurrence is significantly higher when MRI detects bone marrow involvement and random biopsy is negative [14]. For the post-therapeutic phase, the same recommendations as for HL apply.

In the case of soft-tissue sarcomas (e. g. rhabdomyosarcomas), osteosarcomas and Ewing sarcomas, local cross-sectional images of the tumor are already available in many cases. If this is not the case, whole-body MRI can be supplemented by local MR images with additional sequences and imaging planes corresponding to the GPOH study specifications [7, 24]. The main advantage of the method is that the response to neoadjuvant treatment in metastasized tumors can be identified in a single examination and the primary tumor can be detected prior to local treatment. In the case of metastasized Ewing sarcoma, a retrospective analysis was able to show that systematic irradiation of all primary osteomedullary metastases detected with whole-body MRI ensures a significantly higher survival rate compared to a comparable collective [22]. While bone and bone marrow involvement can be evaluated in most studies with higher accuracy compared to bone scintigraphy [23, 26, 36, 37] and soft-tissue findings and brain metastases can be evaluated with high accuracy [20, 35], the use of MRI to detect lung metastases remains controversial [35]. Therefore, the indication for chest CT must be determined as a function of the tumor entity and treatment situation.

In the case of embryonal tumors, there is certain evidence for the use of whole-body MRI to diagnose neuroblastomas [10, 15, 20, 21, 32, 71]. Depending on the risk group (low, intermediate, high) and stage (INSS, International Neuroblastoma Staging System), whole-body MRI is helpful and indicated in every phase of the disease. Low stages (locally limited tumor growth) and absence of chromosomal aberrations (amplification of the MYCN oncogene or deletions of the short arm of chromosome 1) usually do not represent an indication. Whole-body MRI is to be viewed as additive and/or complementary to ^{123}I MIBG (metaiodobenzylguanidine) scintigraphy and replaces additionally necessary skeletal scintigraphy [21, 32]. The local tumor extent can be evaluated pretherapeutically with respect to the IDRFs (image-defined risk factors) of the INGRSS (International Neuroblastoma Risk Group Staging System) with an adapted examination protocol. In particular, whole-body MRI is suitable for determining the extent in different compartments and for detecting metastases [6, 20]. Current data show that there is a connection between the decrease in diffusion restriction and treatment response [72]. In the case of occult tumors in opsoclonus-myoclonus syndrome (OMS), ^{123}I MIBG (metaiodobenzylguanidine) scintigraphy can be negative in up to 57 % of cases if a ganglioneuroma is present [73]. Therefore, whole-body MRI is to be preferred as a search method, particularly due to the lack of radiation exposure [10].

3.1.2 Langerhans-cell histiocytosis (LCH)

The detection of multifocal and/or multisystemic lesions has significant consequences for treatment and follow-up. Whole-body MRI is more sensitive regarding bone marrow infiltration than X-ray-based methods or skeletal scintigraphy and 18-F-FDG-PET [52, 55, 56]. The primary involvement of the bone marrow and typically rapid osteodestruction explain the reduced sensitivity of scintigraphy. In general, whole-body MRI can be advantageous in primary staging due to the simultaneous detection of extraskeletal manifestations including CNS involvement [52, 56]. The low specificity of MRI should be taken into account in consideration of methodological aspects in the evaluation of extent and treatment response [52] in order to avoid unnecessary or excessive treatment.

3.1.3 Avascular osteonecrosis (AVN)

More avascular necrosis than clinically suspected is seen under steroid therapy or in combination with high-dose chemotherapy [58, 74, 75]. Conventional imaging is negative in the early stages [58, 74, 75]. The severity and location (e. g. subchondral) are important criteria for determining whether surgical therapy is necessary [58, 74, 75]. Therefore, in the case of a corresponding risk constellation, whole-body MRI is indicated.

3.1.4 Chronic non-bacterial osteomyelitis (CNO)

Whole-body MRI can detect symptomatic as well as clinically silent manifestations, e. g. in the spine, in one examination with high sensitivity and thus accelerates the diagnosis of multifocality based on typical findings [53, 62]. Up to 45 % more lesions are detected than in the clinical examination [47, 49]. The detection

rate is significantly better compared to conventional radiological imaging [54]. Compared to skeletal scintigraphy, whole-body MRI is even significantly more sensitive in relation to symptomatic regions [64]. DWI can be used for differential diagnosis with respect to malignant processes [59]. Moreover, in particular, treatment response and any necessary intensification of medication-based therapy are relevant indications for whole-body MRI [49, 50].

3.1.5 Rheumatic diseases and fever syndromes

MRI is one of the main methods used for the objective evaluation of inflammatory activity and joint destruction for various rheumatic diseases in clinical studies. Therefore, scoring systems were developed both for rheumatoid arthritis and for psoriasis arthritis [76]. With respect to the use of whole-body MRI in adults with rheumatic arthritis, there is an initial consensus report from the Outcome Measures in Rheumatology (OMERACT) MRI Working Group in which a scoring system for whole-body MRI was proposed based on a systematic literature review [76, 77]. In contrast, studies on children and adolescents are rare [2]. Characteristic whole-body MRI findings for juvenile spondylarthritis have been described [60] and it was shown that it is possible to identify enthesitis in comparison to clinical findings and additional information regarding the spine and pelvis can be obtained [78]. It can be assumed that this is in agreement with the data for adults also for other types of rheumatoid arthritis [76]. The detection of extraskeletal findings in the brain, soft tissues, musculature is of great importance for a series of additional autoinflammatory diseases. An excellent correlation with clinical parameters was found for juvenile dermatomyositis and polymyositis and additional information regarding treatment success was generated over the course of the disease [61]. Moreover, targeted muscle biopsy could be performed with the help of whole-body MRI [51]. Whole-body MRI is also indicated when clinical and laboratory findings differ or when multifocality can only be detected on a limited basis with other methods. Fever syndromes and unclear inflammatory constellations indicating a systemic disease, an undetected focus, or a previously unknown malignant process are indications for whole-body imaging. Whole-body MRI without radiation exposure is to be viewed here as an alternative to PET/CT [57]. However, comparative studies are not currently available.

3.1.6 Syndromes with increased tumor risk

Whole-body MRI is fundamentally suitable in asymptomatic patients with hereditary tumor syndromes to determine the development of a solid tumor as already shown for Li-Fraumeni syndrome [38, 40]. Whole-body MRI is also recommended for other syndromes [39, 79 – 81]. In the case of neurofibromatosis type 1, the tumor load of plexiform neurofibromas detected on whole-body MRI correlates with the development of a malignant peripheral nerve sheath tumor (MPNST) [42, 46]. However, the differentiation between symptomatic plexiform neurofibromas and MPNST remains problematic [44]. Moreover, the value of intervals and use of additional imaging methods (e. g. 18F-FDG-PET) must be evaluated [44]. This also seems reasonable for other syndromes.

3.1.7 Battered child syndrome

While brain MRI is the most sensitive method to evaluate bleeding, ischemia, and axonal damage caused by non-accidental trauma, whole-body MRI currently cannot be recommended as the sole standard imaging method in battered child syndrome. The major advantage of being able to perform comprehensive diagnostic imaging in a single examination [82] is offset by the insufficient sensitivity of whole-body MRI with only coronal STIR sequences with respect to the typical skeletal findings, particularly in infants [83]. (AWMF Guidelines 064 – 014 imaging in the case of suspicion of child abuse).

3.2 Technical requirements

Automatic table movement, the connection of multiple array coil elements that completely cover the body and simultaneous signal acquisition through independent receiving channels are basic requirements for performing successful high-resolution whole-body MRI [1 – 4, 6]. A large field of view (FOV) in the Z-direction (e. g. 500 mm) including homogeneous fat saturation is relevant for the visualization of the desired volume and the lower number of acquisition blocks results in a shorter examination time. In addition, parallel imaging in all 3 spatial directions, automatic table movement and coil selection are necessary for quick examinations. The slightly overlapping coronal scans at several stations are automatically combined to whole-body images.

3.3 Proposed protocols

Since the diagnostic value of MRI depends on the selected sequences and sequence parameters but the examination time affects patient comfort, a modular sequence pool structure consisting of a basic module and expanded sequences is essential (▶ **Table 2**, example of a whole-body MRI protocol from the pediatric radiology department at the University Hospital Tübingen) [1 – 4, 6, 84]. The modular concept allows adjustment of the protocol to the particular indication. At the same time, the reproducibility and comparability are improved.

A whole-body image using high-resolution fat-saturated T2-weighted sequences (e. g. STIR) with slice thicknesses of 3 – 4 mm in coronal orientation should be acquired in every case. To avoid possible limitations regarding diagnostic accuracy due to partial volume effects, additional acquisitions in transverse orientation, e. g. using T2-weighted and fat-saturated or STIR sequences, should be performed in the region of the head and neck as well as the torso [1 – 4, 6, 84]. Sequences with radial k-space acquisition and/or breathing navigator to reduce motion artifacts in the region of the torso are recommended here. Sequences or reconstructions in sagittal orientation are necessary in the case of issues regarding the axial skeleton. Expansion of the protocol to include diffusion-weighted and/or T1-weighted sequences before and after contrast administration is to be planned with consideration of the benefits. Dixon sequences are advantageous here. In the case of solid tumors, this addition can be expected to result in improvement of the diagnostic reliability.

Apart from whole-body examinations, local regions (brain, facial bones and neck, upper abdomen and pelvic organs, spine)

▶ **Table 2** Example of a whole-body MRI protocol from the pediatric radiology department of the University Hospital Tübingen (according to 6).

modules	region	sequence type	orientation and phase-encoding direction	basic matrix (without interpolation in readout direction)	comments
basic module	whole-body	2 D STIR TSE/FSE	coronal FH	384	position hands on the abdomen in MSK issues
	head and neck	2 D STIR TSE/FSE	transverse AP	384	caudal to aortic arch
	thorax	2 D T2w TSE/FSE with fat saturation with breath trigger	transverse AP	384	when possible, radial K-space sampling
	abdomen and pelvis	2 D T2 TSE/FSE with fat saturation with breath trigger	transverse AP	384	when possible, radial K-space sampling
DWI	Whole-body	2 D EPI (SPAIR) 2b values 50 and 900 s/mm^2	transverse AP	128	coronal MPR ADC map calculation of a high b-value >1200 s/mm^2
contrast agent contrast-enhanced sequences	whole-body	3 D T1w GRE (VIBE) with fat saturation or Dixon	transverse AP	288 – 320	when possible, scans during breath-hold coronal MPR
optional additional sequences and local imaging (brain, facial bones, upper abdominal organs, spine, extremities) depending on the issue					

DWI = diffusion-weighted image; STIR = short T1 inversion recovery; TSE = turbo spin echo; FSE = fast spin echo; EPI = echo planar imaging; GRE = gradient echo; VIBE = volumetric interpolated breath-hold examination; SPAIR = spectral attenuated inversion recovery; FH = feet head; AP = anterior posterior.

can be investigated without restriction using the requirements regarding equipment and coil configuration specified under point 3.1 [1 – 4, 6]. This must be taken into consideration particularly in the case of children and adolescents who can only be examined under anesthesia or sedation when additional examinations can consequently be eliminated. The extension of the examination time should then be weighted in relation to the elimination of additional imaging methods [7].

The majority of protocol recommendations for whole-body MRI in children and adolescents have a fixed field of view (FOV), resolution matrix and slice thickness and thus a fixed voxel size [1 – 4, 6, 40, 84]. However, as is typical in pediatric MRI, these sequence parameters should be adapted to the various body sizes from infant to toddler and child to adolescent since the spatial resolution is extremely important for diagnostic reliability [85]. This is even more important when only one slice plane is acquired. Therefore, the following procedure can be helpful: starting from a typical resolution matrix (256^2–384^2), the voxel size is reduced by adjusting the FOV and by moderately adjusting the slice thickness to a smaller body size resulting in relatively constant anatomical resolution/image information. However, the associated signal loss must be compensated (e. g. increase in phase oversampling or signal averaging), resulting in an extension of the acquisition time. Therefore, an optimal compromise between tolerable SNR loss and measurement time should be found. It is advantageous that the number of blocks/stations in the Z-direction and thus the total acquisition time can be reduced based on the body geometry of small children. The use of predefined protocols optimized to body size and length facilitate adaptation to the daily routine.

Conflict of Interest

The authors declare that they have no conflict of interest.

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