

Whole Body MRI: Non-oncological Musculoskeletal Applications

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Abstract

Purpose of the Review Whole-body MRI is an emerging imaging technique on continuous evolution, used in many oncologic indications and introduced more recently in rheumatologic and systemic disorders. In this article, we review the recent musculoskeletal applications of this technique outside the field of cancer.

Recent Findings Whole-body MRI, with its high sensitivity to bone marrow and soft-tissue alterations, and ability of extensive body coverage, is progressively regarded as an effective and powerful imaging tool for the detection, staging, and monitoring under treatment of many rheumatic diseases and systemic pathologies affecting the musculoskeletal system. Disease specific imaging protocols have been designed.

Summary Whole-body MRI is an appealing, non-irradiating tool emerging in musculoskeletal imaging. It is becoming the imaging of choice in several non-oncologic indications, and its application field is on continuous expansion.

Keywords Whole-body MRI · Rheumatism · Bone · Muscle · Joints · Spondylarthritis

Introduction

MRI provides excellent tissue contrast, high spatial resolution, and uses no ionizing radiation. All this makes it an appealing modality in children, young adults, and pregnant patients, and in patients suffering from chronic diseases, oncologic or not, for whom repeated imaging examinations are required.

Whole-body MRI (WBMRI) emerged over the last 20 years as a new promising imaging tool, combining extensive body coverage with the high soft-tissue contrast and exquisite sensitivity to bone marrow disorders.

WBMRI applications first targeted the detection of bone marrow involvement in patient with solid tumors, multiple myeloma and lymphoma [1–3]. With the development of the technique, its indications are progressively extended to the assessment of systemic non-oncologic pathologies affecting the musculoskeletal system [4–6].

The diagnostic performance of the technique has been optimized by adapting the most sensitive sequences and their recent developments (3D technique, diffusion-weighted MRI (DWI), Dixon technique,...) for whole-body coverage. And also by combining these sequences with more specific approaches targeting disease specific lesions or involved anatomic areas [7]. This combination allows an “all tissues” diagnostic approach.

Bone marrow and entheses, muscles and fascias, tendons and sheaths, nerves and vessels can now be evaluated at the scale of the whole-body during one single examination obtained in a reasonable time.

This article highlights the recent developments of WBMRI in non-oncologic disorders. It underlines its roles,

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paralleling those played by the technique in oncology, i.e., disease detection, assessment of severity and staging, decision of treatment initiation, and evaluation of response to this treatment [8•, 9].

Non-Oncological Indications

Non-oncological indications of WBMRI can be subdivided into rheumatologic diseases and non-rheumatologic disorders.

Ankylosing spondylitis (AS), psoriatic arthritis, rheumatoid arthritis (RA), polymyalgia rheumatica, systemic sclerosis, aseptic chronic recurrent multifocal osteitis (CRMO), and the “synovitis, acne, pustulosis, hyperostosis, osteitis” (SAPHO) syndrome are among the most studied rheumatological indications for WBMRI.

Non rheumatologic diseases include multifocal bone, muscular, and neuro-vascular pathologies.

Technical Bases

WBMRI has expanded the limited anatomic fields of view previously used in MRI studies from limited coverage of the pelvic joints, spine or peripheral joints, to the thoracic wall, the shoulder and pelvic girdles, as well as to the peripheral joints and entheses.

In inflammatory arthritis and diffuse muscle, bone, joint, nerve or vessel diseases, WBMRI can really cover the body from “head to toes”. This coverage may be limited “from eyes to thighs” in axial rheumatisms. In rheumatologic applications, imaging protocols typically include whole-body coronal T1 and STIR sequences and whole-spine sagittal T1 and STIR sequences. Disease specific sequences or anatomic planes may be added, such as high resolution oblique coronal coverage of sacro-iliac joints in AS or psoriatic arthritis, of the anterior chest wall in the SAPHO syndrome, transverse slices in muscle disease [9].

The T1 sequence provides basic anatomic information and identifies structural changes in entheses and subchondral bone, or fatty infiltration in chronic muscle disorders.

The STIR sequence, and alternatively T2 images acquired using the Dixon technique, are highly sensitive for the detection of bone marrow edema adjacent to enthesitis, disc or joint disorders, for the detection of active inflammation in the synovium, muscles and fascias, and for the detection of fluid in bursae and joints. The need for contrast material injection in T1-weighted sequences has almost systematically been replaced by this use of STIR sequences [10]. The adjunction of diffusion-weighted sequences, as those used in oncological indications, is currently evaluated in research protocols.

The first steps have been made towards standardization of acquisitions and of reporting WBMRI examinations paralleling the recommendations established in oncology [11•, 12].

Ankylosing Spondylitis (AS)

In AS, WBMRI provides a global evaluation of both the inflammatory involvement and the structural changes affecting axial and peripheral entheses, sacro-iliac joints (SIJ), disco-vertebral junctions, and peripheral joints and tendons [13]. “Local” MRI of the SIJ and spine has been demonstrated to be the method of choice, most often sufficient, for early diagnosis of AS, as it can detect enthesitis, the hallmark of the disease, and bone marrow edema within the subchondral bone of the SIJ surface or adjacent to vertebral endplates, which indicate early-stage AS, preceding structural skeletal changes [14]. According to the Assessment of SpondyloArthritis International Society criteria, MRI detection of bone marrow edema neighboring the SIJ is considered a key criterion for the positive diagnosis of AS [15].

The most commonly involved skeletal areas in AS are the spine, especially its lower thoracic and lumbar segments and the SIJ [16]. However, WBMRI has revealed the frequent involvement of areas which are typically ignored during clinical examination and during limited MRI studies [17]. It has shown the frequent involvement of non-axial sites, affected in more than half of AS patients [13]. It has demonstrated the frequent observation of synovitis and enthesitis in the hips and knees [18, 19]. The heels and ankles can be affected by Achilles enthesitis, ankle joint tenosynovitis, and plantar fasciitis. It also showed the frequent involvement of the gleno-humeral joints, acromioclavicular joints, scapular entheses, including the insertions of the deltoid onto the acromion and of the supraspinatus onto the greater tuberosity of the humerus [20].

While high resolution MRI of the SIJ is sufficient for a positive diagnosis of AS in the vast majority of cases, WBMRI may play a diagnostic role in rare patients with negative SIJ MRI but strong clinical suspicion [6]. Another important indication of WBMRI is developing in patients with advanced disease and ankylosed SIJ and spine, in whom it allows identification of peripheral activity and evaluation of treatment needs [6]. WBMRI may provide quantitative indices of inflammation affecting the SIJ, the spine, the peripheral joints and entheses, which can be monitored to assess treatment response in patients with AS [21•].

In some cases, in which discrimination of axial inflammatory rheumatisms from diffuse idiopathic skeletal hyperostosis (DISH) or degenerative joint disease (DJD) can be challenging, WBMRI can contribute to correct a diagnosis by revealing discriminating features of AS such

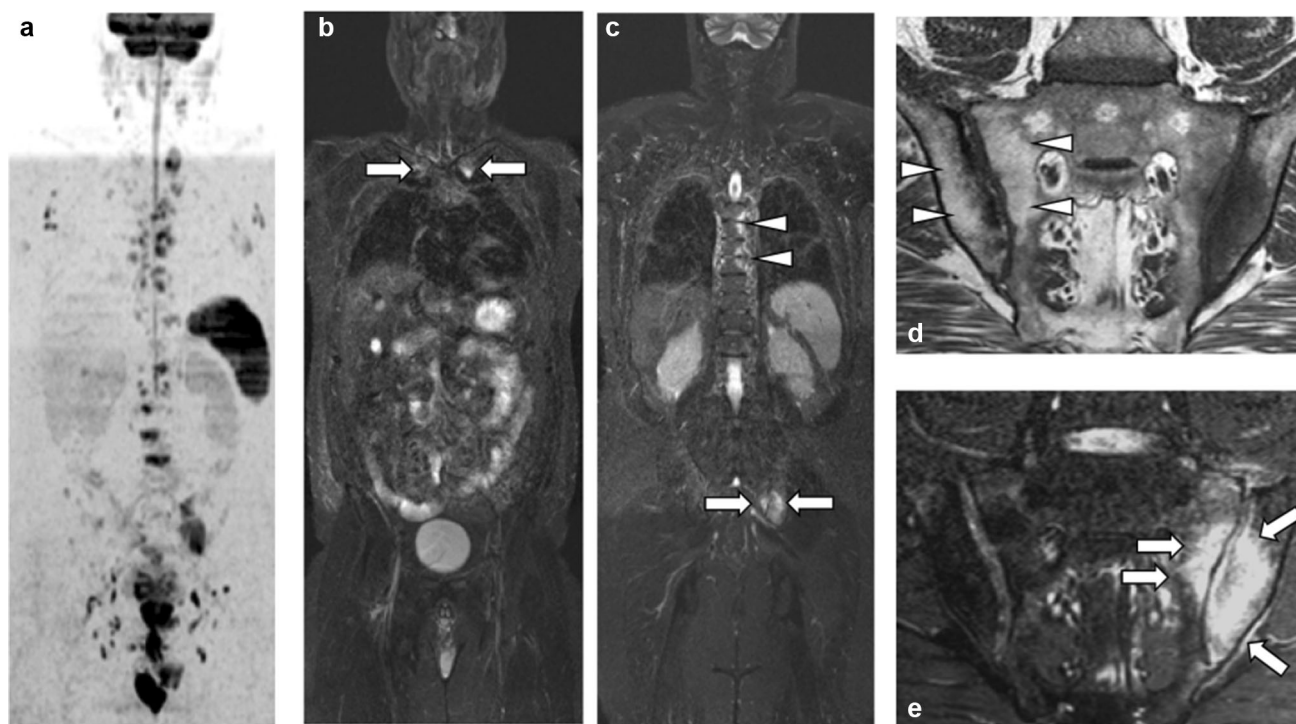


Fig. 1 WBMRI images in a 50-year-old male patient with long history of diffuse pain but newly diagnosed AS. Whole-body DWI sequence (MIP view, inverted grey scale) (**a**) shows multifocal abnormalities, mainly involving disco-vertebral junctions, sterno-clavicular joints and SIJ (note that the spleen, axillar and inguinal lymph nodes, and testes are “physiological” observations on DWI images). Coronal STIR MR images (**b**, **c**) show high signal intensity

suggestive of active inflammation at the level of sterno-clavicular joints (arrows in **b**), of midthoracic vertebral endplates and costo-vertebral junctions (arrowheads in **c**), and left SIJ (arrow in **c**). Oblique coronal T1 (**d**) and STIR (**e**) MR images show typical association of “structural” fatty involvement of the subchondral bone adjacent to the right SIJ (arrowheads in **d**) and active inflammation adjacent to the left SIJ (arrows in **e**)

as edema or fat infiltration of suchondral bone adjacent to the SIJ, inflammation of the posterior vertebral elements inflammatory lesion, and facet joints ankylosis [22].

WBMRI highlights distinctive features between AS and degenerative disease affecting the spine, SIJ and pelvic or scapular girdles, which may help in the sometimes difficult diagnosis between these conditions. For example, subtle edema adjacent to SIJ or disco-vertebral junctions may result in nonconclusive examinations. In these patients, the detection of manubrio- and chondro-sternal joint involvement or hip synovitis on WBMRI strongly favors the diagnosis of AS against those of DISH or DJD [23•]. DWI sequences have a very promising role in this setting, offering more effective distinction between inflammatory lesions and degenerative changes than conventional STIR sequences and providing an “at a glance” vision of global disease activity (Fig. 1) [23•].

Psoriatic Arthritis and Juvenile Arthritis

In psoriatic arthritis, WBMRI may be helpful in diagnosis as well as in response evaluation. It is perfectly suited for identifying, quantifying, and monitoring juxta-articular

bone damage, synovitis, soft-tissue involvement, and enthesitis [24]. The ability to cover all entheses within the body makes WBMRI a promising “one-step” imaging modality in patients with psoriatic arthritis.

Optimized protocols are being developed to cover the upper extremities in WBMRI studies obtained in patients with peripheral rheumatism: the hands can be positioned behind the back or on the belly during acquisitions on the trunk, the feet may be studied with specific sequences [25].

Because of these capabilities and its lack of ionizing radiation, WBMRI also becomes the preferred initial modality for early diagnosis, staging, and response evaluation of juvenile rheumatism [26, 27•].

Rheumatoid Arthritis (RA)

Rheumatoid arthritis (RA) mainly affects the peripheral joints as hands and feet, but can also affect other joints, entheses and tendons. The role of WBMRI in RA remains investigational. An early study by Axelsen et al. suggested that inflammation is identified more frequently with WBMRI than with clinical examination and that the

technique allows evaluation of the total inflammatory load in only one MRI study [28]. Additionally, WBMRI can assess the evolution of RA throughout treatment and can confirm response by demonstrating a decreasing inflammation count [29•]. These studies suggest the possibility of using WBMRI as a more objective tool than clinical examination or sonography for assessing and monitoring RA. Future WBMRI studies should focus on optimizing coverage and developing quantitative imaging parameters.

Polymyalgia Rheumatica

Polymyalgia rheumatica is a rheumatologic disease characterized by pain and stiffness affecting scapular and pelvic girdles and showing non ambiguous response to corticosteroids.

WBMRI may play diagnostic role in this condition. Its high resolution may help the clinician to distinguish polymyalgia rheumatica from rheumatoid arthritis [30]. WBMRI also has a prognostic value: the observation of an extracapsular inflammation pattern in the pelvic region identifies a subset of polymyalgia rheumatica patients who are better responders to gluco-corticoid treatment [30].

CRMO and SAPHO

Chronic recurrent multifocal osteitis (CRMO) that affects children and adolescents and the “synovitis, acne, pustulosis, hyperostosis, osteitis” syndrome (SAPHO) that affects adults share multifocal aseptic osteitis as a main common feature. The etiology of both diseases is unclear, and some consider CRMO as the pediatric form of SAPHO [31].

Multifocal skeletal involvement is the common key finding. Skeletal lesions are typically suggesting osteitis observed at different stages, active and chronic, relapsing and remitting, but also clinical and subclinical [32]. The large coverage and high sensitivity of WBMRI can detect this multifocal asynchronous involvement by the disease, reveal the different stages of the lesions and uncover subclinical lesions allowing early treatment and prevention of complications like vertebra plana in children. The involvement of long bones of the lower limbs in children, spine, sterno-costo-clavicular regions and sacro-iliac joints in adults is highly suggestive (Fig. 2).

In brief, WBMRI allows exhaustive identification of skeletal involvement, both in axial and peripheral locations, and has a better performance than clinical evaluation. Its extensive identification of skeletal involvement lead to its adoption as a substitute to irradiating techniques such as radiographs and bone scintigraphy [33, 34•, 35].



Fig. 2 WBMRI in a 14-year-old girl presenting clinically symptomatic bone lesions in the right knee. Coronal T1 (a) and STIR (b) images reveal profound bone marrow edema (arrows) in the distal metaphyses and epiphyses of both femurs, in the proximal and distal metaphyses of both tibias, on the right calcaneus and the lateral extremity of the left clavicle (arrows). Ill-defined edemalike osseous lesions predominantly affecting periphyseal regions of the lower limbs in a symmetrical fashion—most of which are asymptomatic—are highly suggestive of chronic recurrent multifocal osteomyelitis (CRMO)

Systemic Sclerosis

Systemic sclerosis (scleroderma) usually involves the musculoskeletal system in a multifocal and symmetrical fashion. Deep and vital organs’ involvement conditions the prognosis of the disease, but the clinician lacks “markers of disease severity”, particularly to assess the efficacy of treatments. WBMRI has proven effective to identify involvement of muscles, subcutaneous tissue, joints, tendons and ligaments, showing a higher sensitivity than biological and clinical scoring systems (Fig. 3) [36, 37]. WBMRI has a huge potential for the non-invasive evaluation and effective follow-up of this disease [38].

A combined PET/MRI approach has been suggested by Sauter et al. [39], where FDG-PET can detect active mediastinal lymphadenopathy, and WBMRI is used for detecting esophagus involvement, allowing an exhaustive evaluation of the complex expression of the disease.

Multifocal Bone Disorders

WBMRI has been showed to be a valuable imaging tool for detection and evaluation of many multifocal bone diseases.

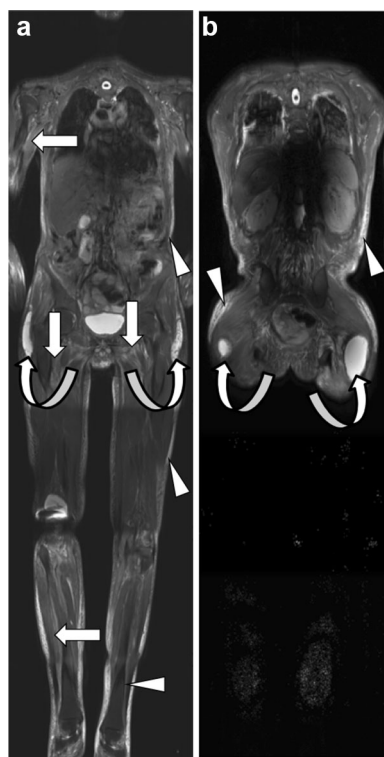


Fig. 3 WBMRI images in a 46-year-old man suffering from a severe form of diffuse systemic sclerosis with myocardial, esophageal and lung involvement, presenting diffuse tendon friction rubs, tenosynovitis, and reduced range of motion in all joints. Coronal STIR MR images (**a**, **b**) show extensive musculoskeletal involvement with concurrent diffuse infiltration of subcutaneous tissue (arrowheads), muscles (arrows), and severe bilateral paratrochanteric bursitis (curved arrows). Note the presence of pleural and pulmonary involvement (**b**). Quantitative evaluation of these parameters is currently evaluated as biomarker of disease severity to evaluate response of experimental therapies (in this case oral glucocorticoids, mycophenolate mofetil and methotrexate)

Multifocal epiphyseal infarcts, observed mostly in *systemic osteonecrosis* related to gluco-corticoid intake, or other conditions like lupus, sickle cell anemia, alcoholism, leukemia, and lymphoma are a recent indication of WBMRI.

Avascular necrosis of the epiphysis can have devastating consequences for the joint, especially if not detected at early stages. WBMRI enables an early diagnosis of pre-clinical ischemic lesions within epiphyses in patients at risk, and also the detection of subclinical lesions in patients with some symptomatic joints [40, 41, 42••].

WBMRI can also be used to characterize *multifocal skeletal dysplasias*. When used at diagnosis, it can identify unsuspected lesions outside of the limited field of view of

usual MRI examinations [43]. In a report on the characterization of dysplasia epiphysealis hemimelica (DEH), also known as Trevor's Disease, Volders et al. found that WBMRI allows the identification of a DEH distribution pattern and has a clear therapeutic impact as it demonstrates additional, unknown lesions [43].

Diagnosis and staging of the skeletal involvement in *sarcoidosis* and *multifocal eosinophilic granulomas* are another “niche” indication for WBMRI (Fig. 4) [44, 45]. While histology remains the reference standard, WBMRI may be useful in detecting concurrent bone, muscle, and lymph node involvement, as well as quiescent or healed lesions, and for monitoring active lesions when they heal [46, 47].

Patients with *hereditary multiple exostosis*, also named hereditary osteochondromatosis, have a risk of malignant transformation of the lesions and may require continuous follow-up. WBMRI is an effective tool to detect all lesions, in a single exam, especially the osteochondromas that are not accessible to clinical exam as in the trunk, and to follow them over time [48]. Other complication of the disease (mass effect on muscles, vessels, nerves, bursitis,...) may also be observed.

Finally, WBMRI has a potential role in the staging and follow-up of *polyostotic fibrous dysplasia*. It represents a reliable substitute to radiographs, especially in children. Ferreira et al. suggest that, following the initial radiographic readings, WBMRI can be used to monitor the disease to reduce the risk of radiation complications. WBMRI may observe progression phases of the disease and detect complications in symptomatic patients [49].

Multifocal Muscular Diseases

This category encompasses several diseases mainly affecting muscles, but also other tissues, i.e., myositis, polymyositis, fasciitis, and dermatomyositis.

In these multifocal inflammatory muscle disorders and related diseases, WBMRI is now used to confirm muscle involvement, assess its severity and its activity (Fig. 5). It provides clues in the differential diagnosis of the diseases based on the distribution of lesions within the body, and upon the demonstration of associated subcutaneous or fascial involvement in case of dermatomyositis [50]. WBMRI distinguishes “edematous” active from “fatty” quiescent muscle lesions. It can highlight the involvement of muscles that are difficult to assess by clinical

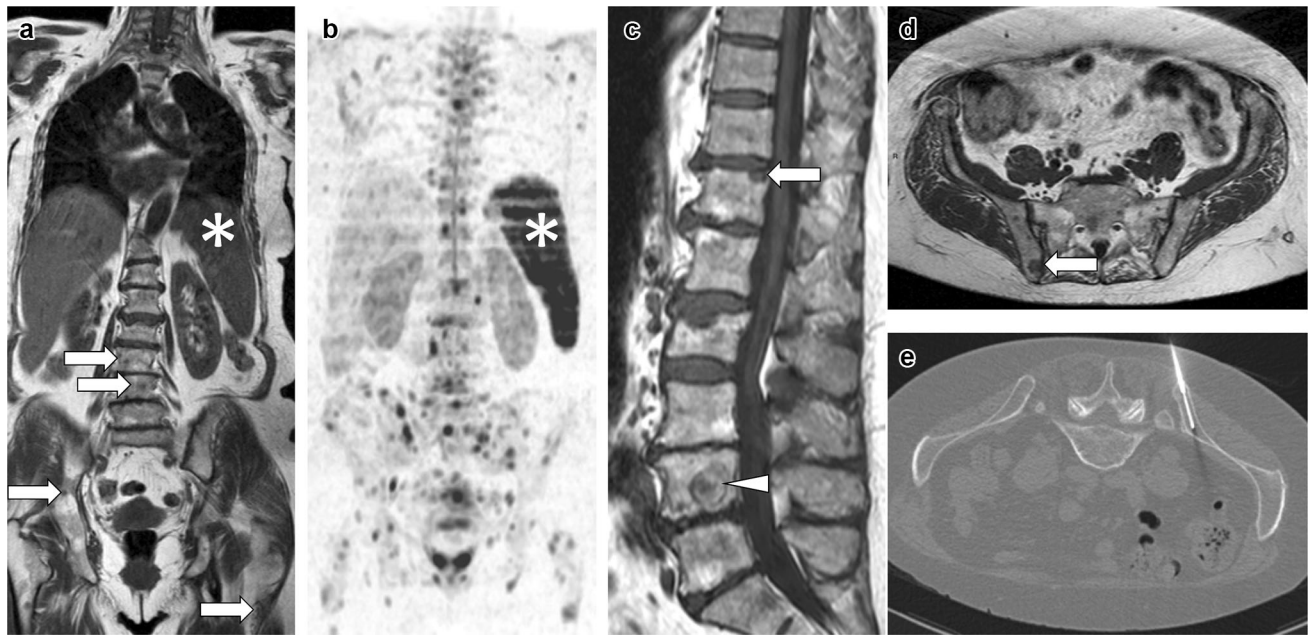


Fig. 4 WBMRI images in a 43-year-old female presenting with sarcoidosis. Coronal T1 (**a**) and diffusion-weighted (**b**) MRI images show multiple bone lesions (arrows in **a**) involving the whole skeleton, more conspicuous on the DWI image. Note the splenomegaly (asterisks). Sagittal T1 (**c**) MR image shows the concurrent observation of active (low signal on T1, T12 location, arrow) and

more quiescent (predominantly fatty high signal on T1, L4 location, arrowhead). Transverse T1 MR image of the pelvis (**d**) was used to choose an active lesion (right iliac crest, arrow) which served as biopsy target. CT guided (**e**) biopsy brought the diagnosis of sarcoidosis. All lesions resolved after corticoid therapy

examination and may detect occult malignancies since dermatomyositis and polymyositis can be paraneoplastic conditions [51].

Another major role of MRI in these conditions is to identify a site of active pathology and guide a surgical biopsy for definitive histological diagnosis.

Neuro-vascular Diseases

The sensitivity to soft-tissue lesions and extensive anatomic coverage of WBMRI enable the staging of multifocal or extensive vascular and neurological diseases. In neurofibromatosis, WBMRI including both anatomic and functional sequences allows the detection and characterization of lesions, disease follow-up, and is evaluated for the detection of malignant transformation [52]. WBMRI was found to be preferable to whole spine MRI, due to its superiority for the evaluation of tumor burden [53]. Multiparametric WBMRI also provides information on the

growth pattern, dynamics, and extent of nerve sheath tumors, becoming the reference standard for identifying neurofibromatosis-associated nerve sheath tumors [54].

Conclusion

WBMRI has been introduced in clinical practice for the study of a growing number of non-oncologic musculoskeletal disorders, providing advances in the work-up and management of these diseases. The technique allows for an early diagnosis, assessment of therapeutic response, and offers clear advantages compared to previous imaging modalities, including absence of ionizing radiation and of contrast injection, and convenience for the patient. It allows a global skeletal, articular, and soft-tissue work-up in one step.

The number of its indications is rapidly increasing, in rheumatologic, bone, skeletal muscle, neurologic, and vascular disorders.

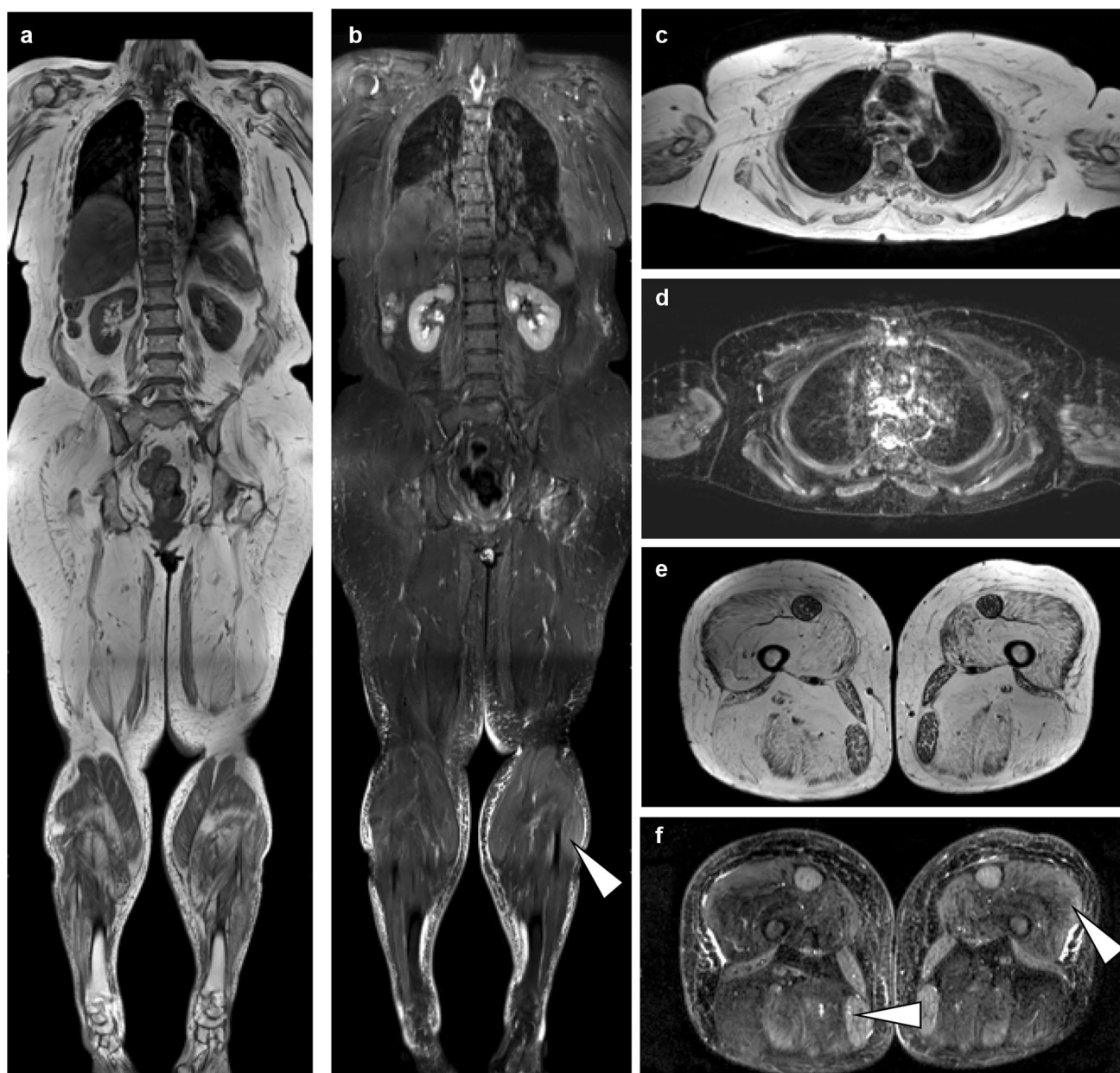


Fig. 5 WBMRI images in a 73-year-old female woman with longstanding polymyositis (more than 30 years) presenting with diffuse muscle weakness, dysphagia and dyspnea. Coronal T1 (a) and STIR (b) MR images show severe atrophy and fatty involution of multiple muscles with predominating trunk and thigh involvement.

Compliance with Ethical Guidelines

Conflict of interest Elie Barakat, Maria Stoenoiu, Ihsan Moslemi, Marie Faruch, Perrine Triqueneaux, and Frédéric E. Lecouvet each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

Transverse T1 (c, e) and STIR (d, f) MR images at the level of chest (c, d) and thighs (e, f) show fatty involution of most muscles, although moderate high signal intensity on STIR images suggest disease activity within several relatively preserved muscles (arrow-heads), which was confirmed by a biopsy

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