Radiology

Oncologically Relevant Findings Reporting and Data System (ONCO-RADS): Guidelines for the Acquisition, Interpretation, and Reporting of Whole-Body MRI for Cancer Screening

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Acknowledging the increasing number of studies describing the use of whole-body MRI for cancer screening, and the increasing number of examinations being performed in patients with known cancers, an international multidisciplinary expert panel of radiologists and a geneticist with subject-specific expertise formulated technical acquisition standards, interpretation criteria, and limitations of whole-body MRI for cancer screening in individuals at higher risk, including those with cancer predisposition syndromes. The Oncologically Relevant Findings Reporting and Data System (ONCO-RADS) proposes a standard protocol for individuals at higher risk, including those with cancer predisposition syndromes. ONCO-RADS emphasizes structured reporting and five assessment categories for the classification of whole-body MRI findings. The ONCO-RADS guidelines are designed to promote standardization and limit variations in the acquisition, interpretation, and reporting of whole-body MRI scans for cancer screening.

Online supplemental material is available for this article.

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Learning Objectives:

After reading the article and taking the test, the reader will be able to:

- List cancer predisposition syndromes for which whole-body MRI is recommended for cancer screening
- Describe the standard whole-body MRI protocol for cancer screening
- Discuss the classification of abnormal findings into categories according to their likelihood of being oncologically relevant

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Several guidelines recommend the use of whole-body MRI for cancer screening in individuals with cancer predisposition syndromes. In Li-Fraumeni syndrome (LFS), whole-body MRI is indicated annually along with contrast-enhanced brain MRI (and breast MRI in adult women) as the techniques of choice for children and adults (1–4). Screening using whole-body MRI is also recommended for children and adults with hereditary paraganglioma and pheochromocytoma syndromes (5), whereas annual whole-body MRI from the age of 6 years is recommended in patients with constitutional mismatch repair deficiency syndrome (6) and from the age of 8 years in those with hereditary retinoblastoma (7). Whole-body MRI is also used in patients with neurofibromatosis for detecting the number, volume, and distribution of neurofibromas (8). The National Comprehensive Cancer Network recently suggested that there was a need to develop practice guidelines for introducing whole-body MRI as a method for detecting malignant peripheral nerve sheath tumors (9).

However, there is no recommendation on data acquisition methods for whole-body MRI when performed for cancer screening in individuals with cancer predisposition syndromes in terms of MRI protocols, including machine use, coil set-ups, imaging sequences, and anatomic coverage. Likewise, there is no consensus regarding the reading of screening whole-body MRI scans, nor on the reporting of examinations including how to deal with any abnormalities found.

Abbreviations

ADC = apparent diffusion coefficient, DW = diffusion weighted, LFS = Li-Fraumeni syndrome, ONCO-RADS = Oncologically Relevant Findings Reporting and Data System

Summary

This Oncologically Relevant Findings Reporting and Data System, or ONCO-RADS, consensus on whole-body MRI for cancer screening proposes standard protocols for higher-risk individuals.

Essentials

- Whole-body MRI for cancer screening is recommended by international guidelines for cancer predisposition syndromes.
- Standard and short acquisition protocols for whole-body MRI include anatomic and diffusion-weighted sequences, which can be completed in 50 minutes and 30 minutes, respectively.
- Standardized acquisition protocols and structured reporting will support clinical deployment, training, and research in whole-body MRI for cancer screening.

A meta-analysis by Ballinger et al published in 2017 (10), which described the use of whole-body MRI for baseline cancer screening in 13 study cohorts including patients with LFS from different age groups (children and adults alike), showed that most studies included T1-weighted, T2-weighted, or diffusion-weighted (DW) sequences. T1- and T2-weighted sequences were used in 12 of the 13 studies, whereas DW imaging was used in 11. Despite similarities among protocols used in the literature, there exists inherent interpretive variability of whole-body MRI examinations, as noted by Greer et al (7) in their review published in 2017, and the adoption of templates in standardized reporting is therefore encouraged. Only the UK Magnetic Resonance Imaging Screening in Li Fraumeni Syndrome, or SIGNIFY, study on the use of whole-body MRI for cancer detection in adults with LFS made use of a structured reporting template, providing separate assessments for each body region, to which six numeric scores from 0 to 5 were assigned (11). The numeric score summarized the final impression of the radiologist regarding the oncologic relevance of the findings observed and provided the basis for subsequent interventions related to the study (no follow-up required vs additional imaging and/or biopsy). In the same study, the choice of the appropriate investigation for suspicious lesions or incidental findings was discussed in a cross-center video-linked multidisciplinary team meeting.

There is also emerging interest in using whole-body MRI for cancer screening in asymptomatic individuals in the general population, with a review of 12 studies that included more than 6000 asymptomatic individuals reporting an average rate of histologically verified cancers of 1.1% (12). In addition, we note that thousands of whole-body MRI examinations are currently being performed worldwide in self-referred asymptomatic individuals within health check-up programs in the attempt to meet the growing demand for wellness checking. However, it is not known whether this application of whole-body MRI is beneficial, or even potentially harmful due to an increase of unnecessary additional imaging, biopsies, and anxiety, because there is a lack of randomized trials with long-term follow-up.

Likewise, there is no recommendation on image acquisition and reporting of whole-body MRI for cancer screening in asymptomatic individuals, or in the management of findings, which is crucial for any screening program. Only a few studies described the classification of abnormal findings into categories, but the categorization systems have been heterogeneously applied (ranging from two to five categories, with some studies evaluating the impact of findings on management) (11,13–22). Similarly, the experience on the management of whole-body MRI findings is limited, with some authors referring cases with potentially oncologically relevant findings to multidisciplinary tumor boards (11,14,19,21) while others take direct responsibility for the onward management of cases (17,20,22).

Acknowledging the increasingly important role of whole-body MRI for cancer screening in individuals with cancer predisposition syndromes, an international multidisciplinary expert panel of radiologists and a leading geneticist with subject expertise in cancer screening convened to discuss the technical standards, interpretation criteria, and limitations of whole-body MRI for cancer screening in individuals with cancer predisposition syndromes. The Metastasis Reporting and Data System for Prostate Cancer, or MET-RADS-P, guidelines on the use of whole-body MRI for metastasis evaluation in prostate cancer (23) and the Myeloma Response Assessment and Diagnosis System, or MY-RADS, guidelines on the use of whole-body MRI for the assessment of involvement by myeloma (24) were used as models to formulate the standards for whole-body MRI use in cancer screening.

The Oncologically Relevant Findings Reporting and Data System (ONCO-RADS) recommendations are designed to promote standardization and diminish variations in the acquisition, interpretation, and reporting of whole-body MRI scans obtained for cancer screening in individuals with cancer predisposition syndromes. As a future direction, these recommendations may be adapted for use in asymptomatic individuals in the general population, with specific modifications that consider the differences in cancer prevalence.

The specific aims of the ONCO-RADS recommendations are to *(a)* establish minimum acceptable technical parameters for whole-body MRI data acquisition for cancer screening in high-risk patients and asymptomatic individuals in the general population; *(b)* develop standardized data collection methods that enable detailed descriptions of the abnormal findings across multiple anatomic regions; *(c)* assign the likelihood of malignancy of abnormal findings by using a five-category assessment score to direct further management; *(d)* enable data collection for outcome evaluations in the context of clinical trials; *(e)* provide training and educational materials for radiologists on whole-body MRI reporting for cancer screening to limit the variability of imaging interpretations; *(f)* enhance communication with and between radiologists and with referring clinicians; and *(g)* promote quality assurance and research in whole-body MRI for cancer screening.

Table 1: Sequence Components for Whole-Body MRI

Sequence No.	Sequence Description	Standard Protocol	Short Protocol
1	Whole spine: sagittal T1-weighted TSE with 4–5-mm-thick sections	Yes	No
2	Whole spine: sagittal T2-weighted imaging with fat suppression (preferably STIR), 4–5-mm-thick sections	Yes	Yes
3	Whole body: axial T1-weighted GRE imaging with Dixon technique, 5-mm-thick contiguous sections, multiple stations. Fat and water image reconstructions are mandatory and should be used to generate fat fraction maps (fat fraction = fat/(fat + water) × 100%)	Yes (vertex to feet)*	Yes (vertex to midthighs)*
4	Whole body: axial T2-weighted TSE without fat suppression, 5-mm-thick contiguous sections, multiple stations	Yes (vertex to feet)*	Yes (vertex to midthighs)*
5	Whole body: axial DW images (*b* values, 50–100 sec/mm^2 and 800–1000 sec/mm^2), STIR fat suppression, 5-mm-thick contiguous sections, multiple stations; ADC calculations with mono-exponential data fitting; coronal MPR with *b* value of 800–1000 sec/mm^2†; 3D MIP reconstructions of highest *b*-value images‡	Yes (vertex to feet)*	Yes (vertex to midthighs)*
6	Brain: axial T2-weighted imaging with FLAIR technique, 4–5-mm-thick contiguous sections	Yes	Yes
7	Lung: T1-weighted GRE VIBE with short echo time (<1.5 msec), <3 mm contiguous sections	Yes	Yes

Note.—ADC = apparent diffusion coefficient, DW = diffusion weighted, FLAIR = fluid-attenuated inversion recovery, GRE = gradient echo, MIP = maximum intensity projection, MPR = multiplanar reconstruction, STIR = short inversion time inversion-recovery, 3D = three-dimensional, TSE = turbo spin echo, VIBE = volumetric interpolated breath-hold examination.

* Axial imaging with 5-mm-thick sections may be chosen to match section thickness of DW imaging to facilitate image review. Imaging of lower limbs is not required in patients with hereditary paraganglioma and pheochromocytoma syndromes.

† Images obtained with *b* values of 800–1000 sec/mm^2 from all diffusion imaging stations are grouped and reconstructed as contiguous two-dimensional coronal 5-mm-thick sections.

‡ Whole-body three-dimensional maximum intensity projection images, displayed as rotating images, using an inverted gray scale.

Whole-Body MRI Data Acquisition and Analysis

Imaging Protocol

Imaging can be performed with 1.5- or 3-T scanners, provided that good image quality can be ensured over the entire scan volume.

The "standard" protocol for whole-body MRI is designed for individuals at higher risk, including those with cancer predisposition syndromes. It includes whole-spine sagittal T1- and T2-weighted imaging with fat suppression (preferably short inversion time inversion-recovery due to the large field of view) and axial T1-weighted, T2-weighted, and DW images, with anatomic coverage extending from the vertex to feet, including proximal upper limbs. Note that T1-weighted acquisitions can be performed using the Dixon technique, allowing relative fat fraction images to be calculated from fat only (F) and water only (W) reconstructions, using the following formula: [F/(F+W)] × 100. Relative fat fraction images can aid in the detection of bone abnormalities and facilitate the characterization of soft-tissue abnormalities (eg, adrenal lesions, dermoid cysts) and other incidental diagnoses such as fatty infiltration of the liver. Axial T2-weighted imaging with fluid-attenuated inversion recovery for brain and gradient-echo T1-weighted high-spatial-resolution imaging for lung assessments are always performed. This standard protocol should be completed within 50 minutes (Table 1). However, the standard protocol should be customized as required for other specific at-risk anatomic areas according to the underlying predisposition conditions (eg, additional contrast-enhanced brain sequences should be added in patients with LFS, neurofibromatosis, constitutional mismatch repair deficiency syndrome, and hereditary retinoblastoma or additional imaging examinations should be performed in distal upper limbs), thus increasing examination times. Conversely, imaging of brain and lower limbs is not required in patients with hereditary paraganglioma and pheochromocytoma syndromes (7).

A "short" protocol is proposed for cancer screening in the general population. Compared with the standard protocol, whole-spine sagittal T1-weighted imaging is not performed (as the likelihood of bone metastases is extremely low in the general population). The anatomic coverage for axial T1-weighted, T2-weighted, and DW images is of shorter length, extending from the vertex to midthighs, including the proximal upper limbs, for time savings. This protocol can be considered analogous to the core protocols recommended for metastasis detection in advanced prostate cancer (Metastasis Reporting and Data System for Prostate Cancer) (23) and multiple myeloma (Myeloma Response Assessment and Diagnosis System) (24), with minor modifications, and can be completed within 30 minutes (Table 1, Fig 1). Optional detailed images of the prostate gland in older men using T2-weighted and high *b*-value DW images may be considered (25).

The administration of contrast material is avoided as much as possible in the standard protocol because of medical and public concerns regarding gadolinium deposition in the brain and other

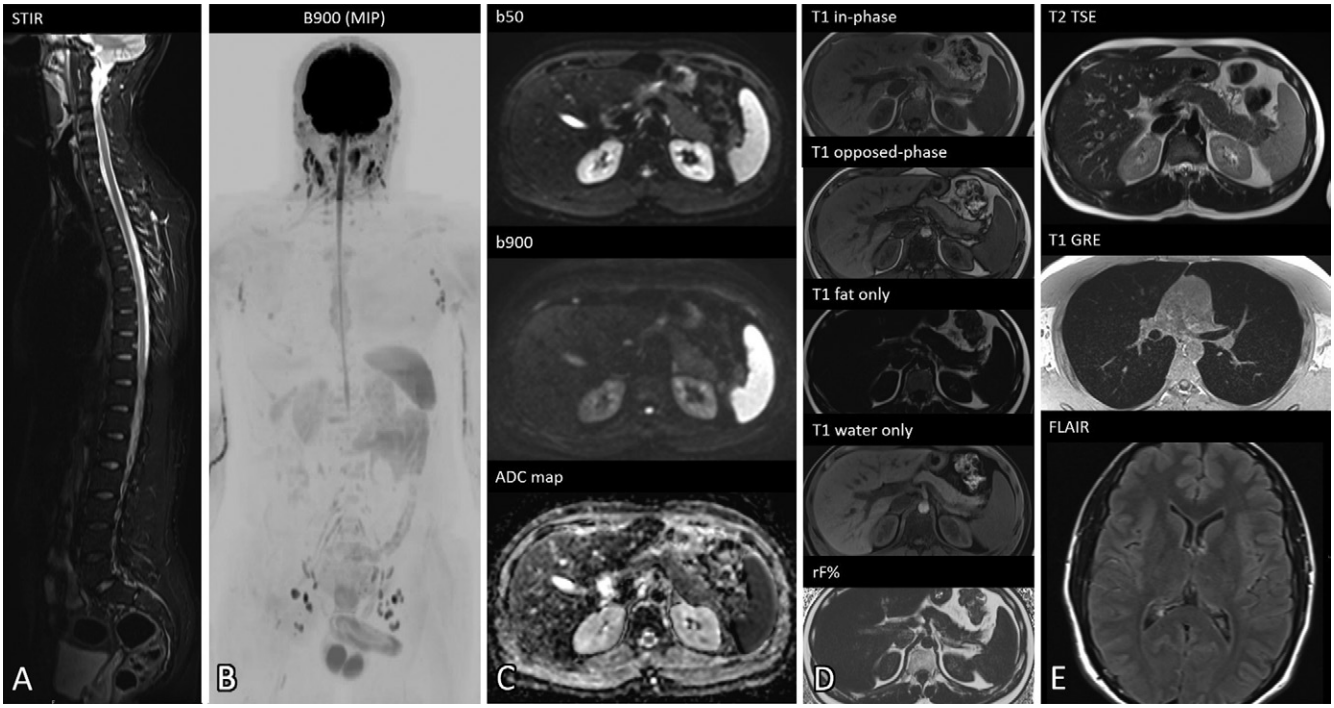


Figure 1: MRI scans illustrate the typical short protocol for a whole-body MRI examination (30 minutes). Images were obtained in a 30-year-old man from the general population. No previous screening tests had been performed, and there was no personal history of cancer and a positive family history of cancer (maternal grandfather). *A,* Sagittal short inversion time inversion-recovery (STIR) T2-weighted turbo spin-echo image of the spine. Loss of cervical lordosis is observed. *B,* Diffusion-weighted (DW) image with *b* value of 900 sec/mm^2 (B900) stack was reconstructed as a three-dimensional maximum intensity projection (MIP) image and displayed using an inverted gray scale. Coronal MIP image shows no bone lesions. Note that the low signal intensity in the brain, spleen, spinal cord, and testicles is a normal finding, as are the small but prominent lymph nodes in the neck, axilla, and groin. *C,* Axial DW images obtained with *b* values of 50 sec/mm^2 (b50) and 900 sec/mm^2 (b900) and corresponding apparent diffusion coefficient (ADC) map. No abnormal findings are detected in this section at the level of the upper abdomen. *D,* In-phase, opposed-phase, fat-only, and water-only images from axial T1-weighted gradient-recalled echo MRI with Dixon technique and relative fat fraction map (rF%). No abnormal findings are detected in this section at the level of the upper abdomen. *E,* Axial T2-weighted turbo spin-echo (TSE) image at the level of the upper abdomen, gradient-recalled echo (GRE) T1-weighted image of the lung, and T2-weighted fluid-attenuated inversion recovery (FLAIR) image of the brain. No abnormal findings are detected in any of the images shown. Given the low prevalence of cancer, no deviation from the standard short protocol is needed for this asymptomatic individual from the general population.

body tissues (26) and the discomfort related to intravenous injections, unless it is needed to enhance diagnostic accuracy or when there is a requirement for investigating additional body parts (eg, brain, soft-tissue mass, or breast evaluations in LFS, as discussed earlier). For the same reasons, the administration of contrast material should always be avoided in the short protocol due to the lower prevalence of malignant cancer in the general population.

Clinical Information

Ideally, a medically trained professional should meet with the patient or individual before the whole-body MRI examination to *(a)* carefully collect family history and pertinent medical history data; *(b)* evaluate previous tests and assess the need for additional screening tests (breast mammography, fecal occult blood test or colonoscopy, prostate-specific antigen test, etc) as per national guidelines; *(c)* assess whether the individual has any major sign or symptom of an underlying disease at the time of the whole-body MRI examination; *(d)* consider adding dedicated MRI subprotocols if relevant clinical data emerge when collecting pre-MRI clinical information or advise an alternative imaging test specific to the clinical data collected, if appropriate; *(e)* explain the expected frequency of abnormalities, their usual nature, and limitations of whole-body MRI and the next steps regarding results and further investigations that may be necessary for shared decision making; and *(f)* obtain written informed consent for additional testing procedures including blood tests for tumor markers and/or genetic tests if appropriate (27).

The use of a questionnaire facilitates uniformity of practice, as well as prospective data collections within clinical trials (Appendix E1 [online]). In addition to institution-specific explanations regarding the MRI examination, we recommend the inclusion of specific information relating to the use of whole-body MRI for cancer screening, including limitations of the method (Appendix E2 [online]).

Assessing Whole-Body MRI Scans

Image interpretation must not rely on the analysis of a single type of image, but multisequence evaluations should be undertaken of all DW images (low *b*-value and high *b*-value images and apparent diffusion coefficient [ADC] maps) in conjunction with the anatomic T1- and T2-weighted images and relative fat fraction images, using image linking and scrolling workstation facilities and coregistration tools as diagnostic aids.

Radial maximum intensity projections of high *b*-value images displayed by using the inverted gray scale are useful for fast

Table 2: Examples of Possible False Findings for Cancer according to Anatomic Region

Region	False-Positive Findings	False-Negative Findings
Bones	Fractures, osteoarthritis, infection, bone infarcts, hemangiomas, enchondromas, ganglion cysts, focal red marrow, isolated bone marrow islands, artifacts around metal implants	Background bone marrow hypercellularity (due to young age, anemia or high-altitude living), sparse tumor cell infiltration pattern (eg, smoldering multiple myeloma), focal lesions with dense matrix mineralization, areas of body movement (eg, ribs and sternum), skull vault and base lesions
Head	Non-specific white matter signal changes, lymphoid tissue hypertrophy (eg, nasopharynx, oropharynx)	Small primary tumors and/or metastases within brain, small meningiomas, small primary tumors within nasopharynx and oropharynx
Neck	Reactive lymph nodes, nerve and ganglia, thyroid nodules	Thyroid cancers <1 cm, lesions arising in organs that normally show hyperintensity at diffusion imaging (eg, salivary glands, hypopharynx, and larynx)
Chest	Inflammatory lung nodules, reactive lymph nodes (eg, sarcoidosis), nerve and ganglia, proteinaceous breast cysts, breast fibroadenomas	Solid lung nodules <5 mm, pure ground-glass lung nodules <1 cm, small mediastinal lesions (due to cardiac and respiratory movement), nodal stations within the mediastinum and lung hilum, mucinous breast cancer, small breast cancers and in situ carcinomas
Abdomen	Hemangiomas, nerve and ganglia, reactive lymph nodes	Small lesions with unfavorable histomorphic cell type (eg, clear cell renal cell carcinoma, tubulocystic renal cell carcinoma, hepatocellular carcinoma), metastases with mucinous deposits (eg, from mucinous colorectal carcinoma, mucinous ovarian cancer, and mucinous breast cancer) or with melanin rich deposits (eg, melanoma), lesions arising in organs that normally show hyperintensity at diffusion imaging (eg, spleen, adrenal glands, gastrointestinal wall)
Pelvis	Low flow and/or thrombosed varices, nerves and ganglia, reactive lymph nodes, gas artifacts to the bowel, adnexal masses	Lesions arising in organs that normally show hyperintensity at diffusion imaging (eg, testis, gastrointestinal wall), tumors with mucinous deposits (eg, mucinous colorectal carcinoma, mucinous ovarian cancer), small ovarian tumors
Limbs	Intramuscular hemangiomas, nerve, and ganglia, including neuromas, varices	Small soft-tissue sarcomas

localization of any potential abnormal findings (23,24). These images can display disease within both the soft tissues and the bone, but they should not be used alone for interpretation because false-positive and false-negative findings can occur (eg, due to T2 shine-through, respiratory motion signal dephasing, or sparse disease patterns) (28,29). Any potential abnormality should always be correlated with ADC maps and morphologic T1- and T2-weighted images.

Serial examinations of maximum intensity projection comparisons can be facilitated by using windowing techniques; for example, by maintaining similar window width between studies but adjusting the window level to normal tissues such as muscle or subcutaneous fat for each time point.

The evaluation of source images obtained with DW sequences at *b* values of 800–1000 sec/mm^2 is based on comparing high *b*-value image intensity to adjacent muscle signal intensity, but assessments of ADC maps are numeric (unit: $\times 10^{-3}$ mm^2/sec or μm^2/sec). The definitions for hypointense and hyperintense signal on high *b*-value DW images is subjective but can be gauged by using adjacent muscle as the reference background tissue (29–31).

It must be emphasized that not all hyperintense bone (32,33) and soft-tissue lesions on high *b*-value images are malignant (Table 2). Strategies for mitigating against false-positive hyperintense areas at DW imaging include direct correlations with morphologic appearances including T1-weighted, T2-weighted, and Dixon images, relative fat fraction images (34,35), ADC values, and computed ultrahigh *b*-value images (if reconstructed).

On the other hand, the absence of hyperintense bone and soft-tissue lesions on high *b*-value images does not completely exclude the presence of cancer, as there are multiple causes of false-negative findings in all anatomic regions, as detailed in Table 2 (34,36–41). It must be noted that the pixel size, using a 256 × 256-mm matrix at a whole-body field of view of 400–440 mm, can be 1.5–2 mm for T1- and T2-weighted sequences, respectively. For DW imaging, pixel sizes are on the order of 3–4 mm. The use of 5-mm-thick sections further compounds partial volume averaging effects. The resulting spatial resolution is much less than what is achievable with routine CT scans (range, 0.8–1 mm), potentially affecting the detection of lesions smaller than 5 mm.

Strategies for mitigating against false interpretations in bone and soft tissues include direct correlations with morphologic appearances on T1-weighted, T2-weighted, and Dixon images, relative fat fraction images (34,35), and ADC maps. For reference, the ADCs of normal bone marrow are generally less than 600–700 μm^2/sec and those of viable tumor lie between 700 and 1400 μm^2/sec (41–43). ADCs of malignant tumors in soft tissues are usually less than 1000 μm^2/sec.

ADC measurements should only be obtained from lesions when water is detectable on DW images (all *b*-value images should be examined to detect the presence of water signal), otherwise the ADCs will be erroneous, reflecting mainly the noise

Table 3: Clinical Reporting Template

Clinical Reporting Template	Notes
Indication	
Statement regarding the individual's risk state	Individuals with cancer predisposition syndromes, asymptomatic subject of general population
Previous examinations	Prior imaging studies including date, modality, and anatomic coverage
Technique: standard or short protocol, additional sequences and deviations	Artifacts and their likely effect on imaging; in-line (ADC maps) and off-line (relative fat fraction, MIP, MPR)
Findings	
Each abnormal finding should be assigned to one of the seven anatomic regions	Bones, head, neck, chest, abdomen, pelvis, limbs
ONCO-RADS category for each abnormal finding	
1	Normal
2	Benign finding highly likely
3	Benign finding likely
4	Malignant finding likely
5	Malignant finding highly likely
Other findings	Even if not suspicious for cancer, other findings should be included if considered important for an individual's health; anatomic variation should also be annotated
Conclusion and management	
Summary statement	The presence or the absence of any lesions suspicious for cancer
If findings of ONCO-RADS categories 1 and 2 are reported in individuals in the general population	The individuals are considered at low risk of cancer; no specific follow-up is required
If findings of ONCO-RADS categories 1–2 are reported in higher-risk individuals or category 3 is reported in individuals in the general population	The individuals are considered at intermediate risk of cancer; in higher-risk individuals, whole-body MRI should be repeated at the appropriate time, according to guidelines; in individuals in the general population, clarification of findings including other specific imaging tests is required
If findings of ONCO-RADS categories 3–5 are reported in higher-risk individuals or if ONCO-RADS 4–5 categories are reported in the general population	The individuals are considered at high risk of cancer; further investigations with or without histologic examination are recommended

Note.—ADC = apparent diffusion coefficient, MIP = maximum intensity projection, MPR = multiplanar reconstruction, ONCO-RADS = Oncologically Relevant Findings Reporting and Data System.

in the images. Thus, ADC (and fat fraction maps) should not be measured in dense sclerotic bone lesions without signal intensities detectable on DW images. Similarly, fat-containing lesions, hemorrhagic lesions, and melanin-rich deposits can have erroneous ADCs. The mere absence of tissue signal intensity on high (800–1000 sec/mm^2) *b*-value images does not invalidate a tissue from ADC measurements, provided that signal intensity is detectable on lower *b*-value images, as it may occur in cystic lesions or mucin containing cancers.

We also recognize that there are limitations to the ADC cut-off values presented earlier, which are partly related to the fact that ADCs depend on the choice of *b* values of DW images used for their calculations (hence, the constraints on the recommended choices of *b* values in the protocol suggested for Metastasis Reporting and Data System for Prostate Cancer, Myeloma Response Assessment and Diagnosis System, and ONCO-RADS). ADCs also depend on the diffusion time achievable with DW sequences (which is dependent on sequence waveforms and imager specifications). Aside from imaging parameters, ADC images are also influenced by additional factors, which are related to patients and caused by susceptibility effects (eg, metal implants, air-tissue interfaces) or related to motion and technique and caused by the specifications of the MRI unit, including magnetic field strength, gradients, and coils (29).

Where there are deviations from the recommended *b* values due to machine, software, or technical factors, then institutions can determine their muscle-normalized high *b*-value signal intensity and ADC cut-off values for normal tissue and malignant lesions, as described by Padhani et al (31).

Structured Reporting

Relevant previous and/or concurrent imaging studies and reports should be available at the time of image assessments. Previously obtained whole-body MRI scans (if any) and their reports should also be available. Radiologists should be familiar with the normal range of appearances on their equipment as these can vary slightly among MRI scanners. They should also be aware of the range of imaging artifacts that may be encountered (34).

It must be understood that exclusion of a malignant tumor can never be absolute; it is important that the individuals undergoing whole-body MRI and all those involved in their management recognize the limitations of whole-body MRI investigations, just like any other imaging or medical tests. A statement of limitations should also be integrated into the report. Radiologists working in

Table 4: Examples of the Most Frequently Observed Abnormal Findings in the Head, Neck, and Chest

ONCO-RADS Category	Head	Neck	Chest
Category 1, normal finding	Normal	Normal	Normal
Category 2, benign finding highly likely	Diffuse white matter alterations, diffuse mucosal thickening of paranasal sinuses, pharynx and/or larynx, arachnoid cysts	Nonsuspicious thyroid nodule <1 cm (in individuals <35 y),* nonsuspicious thyroid nodule <1.5 cm (in individuals ≥35 y),* lipoma	Lung nodules <6 mm,† thymic hyperplasia, pericardial cysts, lipoma
Category 3, benign finding likely	Isolated white matter alterations, focal mucosal thickening of paranasal sinuses, pharynx and/or larynx	Nonsuspicious thyroid nodule ≥1 cm (in individuals <35 y),* nonsuspicious thyroid nodule ≥1.5 cm (in individuals ≥35 y)*	Lung nodules 6–8 mm,† pneumonia, pleural effusion
Category 4, malignant finding likely	Brain lesion(s) suspicious for cancer (primary or metastatic)	Thyroid nodule(s) (solid), salivary gland solid lesion	Lung nodules >8 mm, mediastinal mass
Category 5, malignant finding highly likely	Brain lesion(s) with aggressive features, very suspicious for cancer (primary or metastatic)	Thyroid nodule(s) with aggressive features, very suspicious for cancer	Lesions with aggressive features, very suspicious for cancer, to lung, mediastinum
Other findings, including anatomic variations	Hydrocephalus, hemorrhage, cavum septum pellucidum, cavum vergae, mega cisterna magna, Chiari malformations	Thyroglossal duct cyst	Pneumothorax, thoracic aortic aneurysm, azygos lobe, thoracic aorta variants (eg, right-sided aortic arch, double aortic arch)

Note.—The threshold for assigning ONCO-RADS categories should be adapted to the individual's risk category (general population or higher risk including cancer predisposition syndromes). ONCO-RADS = Oncologically relevant findings Reporting and Data System.

* From reference 46.

† From reference 47.

multidisciplinary teams are best placed to educate other caregivers on the potential advantages and limitations for specific indications.

Structured clinical and tabulated template reporting should be undertaken for each examination (Table 3). The structured textural whole-body MRI report should be composed of the indication for imaging, technique, findings, and conclusions and management.

Indication.—It should be explicitly stated that the whole-body MRI examination was performed for cancer screening. A statement regarding the individual's risk state is required, specifying whether the examination was performed in a higher-risk individual or in an asymptomatic individual from the general population. In higher-risk individuals, the syndrome or risk condition should be named if known, including prior treatments and current clinical-pathologic status. History of prior cancers and their treatment should be recorded.

If images from previous whole-body MRI examinations or other imaging studies are available, they should be noted. When comparisons are made with previous images, the dates of and anatomic regions scanned in previous studies should be indicated.

Technique.—Details of the technique and anatomic coverage (standard or short protocol) should be reported, including contrast material administration if used and whether dedicated regional imaging was performed. Important deviations in techniques and artifacts should be noted, along with their causes (eg, metal implant artifacts, patient movements from pain, reception coil nonusage or failure), and their likely effect on imaging interpretation should be specifically stated.

If specific solutions for improving image quality have already been noted, then these should be documented so the same image adjustments are performed at subsequent whole-body MRI examinations. The in-line (ADC maps) and off-line (eg, relative fat fraction images, maximum intensity projections, multiplanar reconstructions) reconstructions performed may also be noted.

Findings.—All abnormal findings should be assigned to one of the following seven anatomic regions: bones, head, neck, chest, abdomen, pelvis, and limbs.

Each abnormal finding should be described using free text and given an assessment category from 1 to 5, assessing the likelihood of being oncologically relevant, with the following five categories: ONCO-RADS category 1, normal finding; ONCO-RADS category 2, benign finding highly likely; ONCO-RADS category 3, benign finding likely; ONCO-RADS category 4, malignant finding likely; and ONCO-RADS category 5, malignant finding highly likely.

The presence of findings important for an individual's health (eg, aortic or intracranial aneurysm, pneumonia, hydrocephalus) should be annotated in the report and listed under "other findings" only if they are not clearly related to an underlying neoplasm. Any finding that may be related to an underlying neoplasm (eg, subacute vertebral compression fracture) should be assigned

Table 5: Examples of the Most Frequently Observed Abnormal Findings in the Abdomen and Pelvis

ONCO-RADS Category	Abdomen	Pelvis
Category 1, normal finding	Normal	Normal
Category 2, benign finding highly likely	Hemangioma (liver and spleen), cyst and hemorrhagic cyst <30 mm (kidney),* angiomyolipoma (kidney), adenoma (adrenal gland), steatosis (liver), lithiasis (gallbladder), lipoma	Benign prostatic hyperplasia (prostate), simple adnexal cyst ≤3 cm (postmenopausal),† simple adnexal cyst ≤5 cm (premenopausal), hemorrhagic adnexal cyst ≤5 cm (premenopausal),† ovarian fibroid,† uterine leiomyoma, para-ovarian cyst, luteal body
Category 3, benign finding likely	Solitary liver nodule ≥10 mm, solid likely focal nodular hyperplasia or adenoma, complex cyst (kidney), hemorrhagic cyst >30 mm (kidney),* pancreatic cyst ≤2.5 cm‡	Thickening of colorectal wall, simple adnexal cyst >3 cm (postmenopausal),† simple adnexal cyst >5 cm (premenopausal),† hemorrhagic adnexal cyst (postmenopausal),† hemorrhagic adnexal cyst >5 cm (premenopausal)†
Category 4, malignant finding likely	Lesion(s) suspicious for cancer in liver (solid nodules), kidney (solid lesion or cystic lesion with solid component),* pancreatic cyst with worrisome features (≥3 cm, thick wall, mural nodule, main pancreatic duct >7 mm)‡	Lesion(s) suspicious for cancer to uterus (eg, focal endometrial thickening), prostate (impeded diffusion and hypointensity on T2-weighted image in the peripheral zone), colon and rectum, simple adnexal cyst ≥10 cm, adnexal cyst with solid tissue, thick irregular septa, papillary projections, locules with different signal intensity†
Category 5, malignant finding highly likely	Lesion(s) with aggressive features in liver, kidney, pancreas, pancreatic cyst with high-risk features (solid component within the cyst, main pancreatic duct >10 mm, common bile duct dilatation)‡	Lesion(s) with aggressive features, very suspicious for cancer, to uterus, ovary, prostate, colon and rectum
Other findings, including anatomic variations	Abdominal aortic aneurysm, pancreas divisum, annular pancreas accessory spleen, inferior vena cava variants (persistent right posterior cardinal vein, persistent left supracardinal vein, retro-aortic left renal vein)	Fluid collection, uterine duplication anomalies (eg, uterus didelphys, bicornuate uterus septate uterus)

Note.—The threshold for assigning ONCO-RADS categories should be adapted to the individual's risk category (general population or higher risk including cancer predisposition syndromes). ONCO-RADS = Oncologically Relevant Findings Reporting and Data System.

* From reference 48.

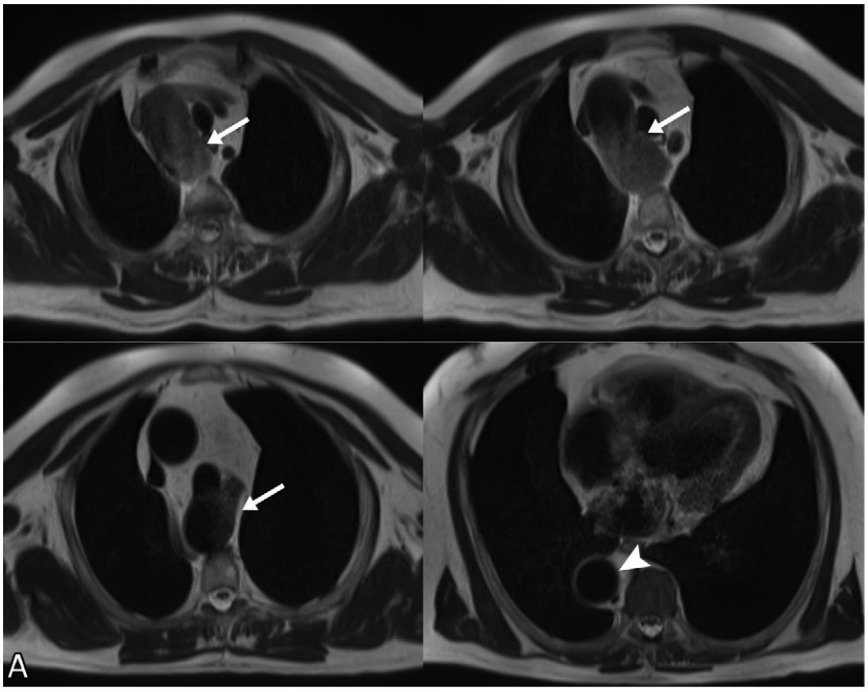
† From reference 49.

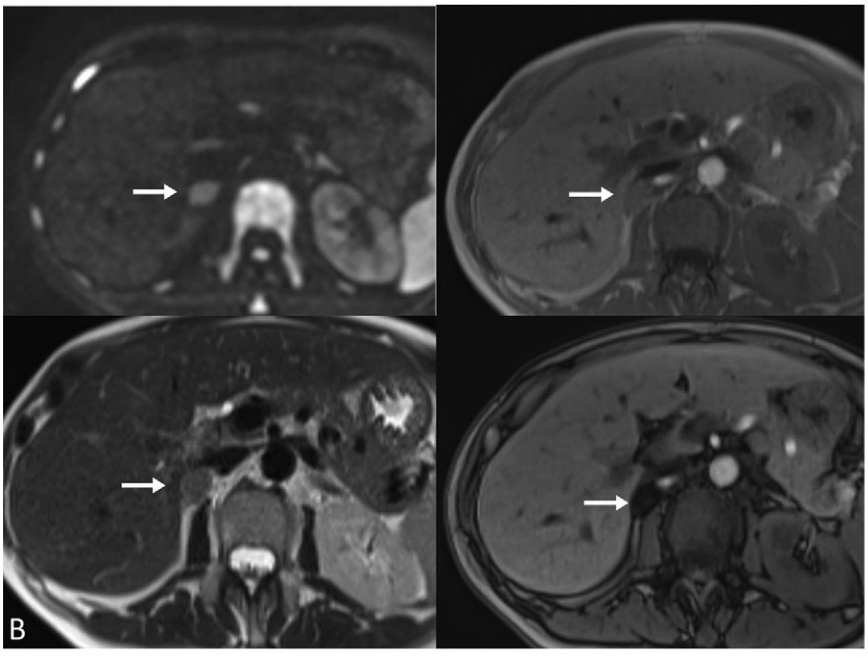
‡ From reference 50.

Table 6: Examples of Most Frequently Observed Abnormal Findings in the Bones and Limbs

ONCO-RADS Category	Bones	Limbs
Category 1, normal finding	Normal	Normal
Category 2, benign finding highly likely	Hemangioma, cyst, fat-poor bone marrow, bone island, enchondroma, healed fractures	Intramuscular hemangioma, lipoma
Category 3, benign finding likely	Bone lesion(s) with nonspecific features	Soft-tissue lesion(s) with unspecific features
Category 4, malignant finding likely	Bone lesion(s) suspicious for cancer (primary or metastatic)	Soft-tissue lesion(s) suspicious for cancer (primary or metastatic)
Category 5, malignant finding highly likely	Bone lesion(s) with aggressive features, very suspicious for cancer (primary or metastatic)	Lesion with aggressive features, very suspicious for cancer
Other findings, including anatomic variations	Fracture, transitional vertebrae (eg, lumbarization of S1, sacralization of L5)	Intramuscular hematoma

Note.—The threshold for assigning ONCO-RADS categories should be adapted to the individual's risk category (general population or higher risk including cancer predisposition syndromes). ONCO-RADS = Oncologically Relevant Findings Reporting and Data System.





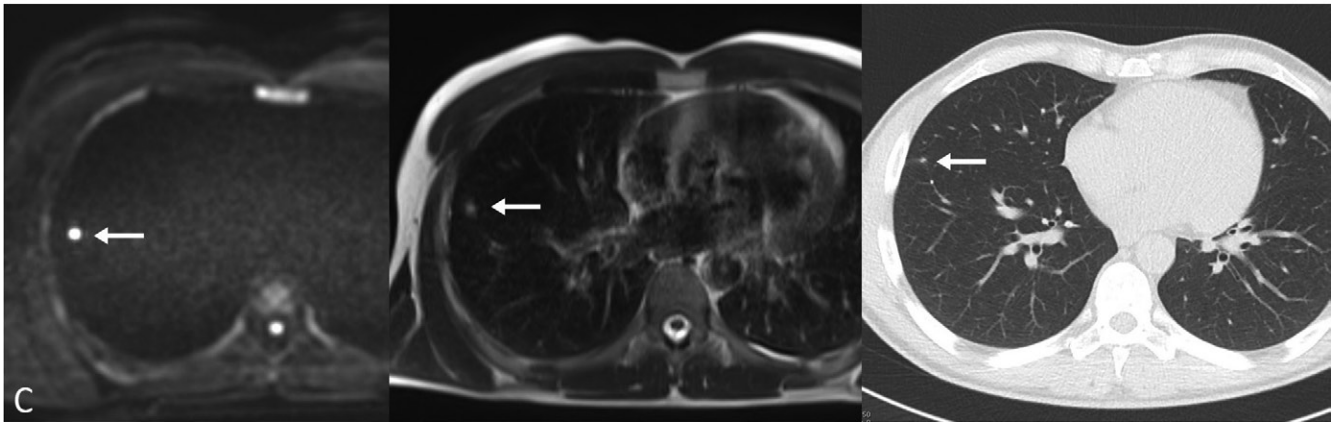


Figure 2: Imaging findings for each Oncologically Relevant Findings Reporting and Data System (ONCO-RADS) category. *A*, T2-weighted MRI scans in a 72-year-old man from the general population. The man had a negative fecal occult blood test and low serum prostate-specific antigen level (2.6 ng/mL); no other screening tests had been previously performed. Normal findings (ONCO-RADS category 1) were reported in all anatomic regions, and the man is considered to have low likelihood of cancer. No follow-up is therefore required. However, an anatomic variation was detected in the chest. Images of the chest at different levels show a right-sided aortic arch coursing to the right of the trachea (arrows) and of the spine (arrowhead). No follow-up is required. *B*, Images in a 50-year-old man from the general population. The man had a low prostate-specific antigen level (2.2 ng/mL); no other screening tests had been performed previously. MRI scans show a 15-mm lesion in the right adrenal gland (arrows). The lesion is moderately hyperintense on high *b*-value (900 sec/mm^2) diffusion-weighted (DW) image (top left), is hypointense on T2-weighted image (bottom left), and shows signal drop out on the opposed-phase T1-weighted Dixon image (bottom right) compared with the in-phase T1-weighted Dixon image (top right). These findings are consistent with the presence of intracellular fat, which is considered diagnostic of an adenoma. The lesion is therefore categorized ONCO-RADS category 2, and the man is considered to have low likelihood of cancer. No follow-up is therefore required. *C*, Images in a 45-year-old man from the general population. No previous screening test had been performed. The man is a former smoker and has hypertension. The man has a positive family history for cancer (father, brother). High *b*-value (900 sec/mm^2) DW image (left) and T2-weighted image (middle) show a 7-mm nodule (arrow) in the right lower lobe of the lung. The nodule was categorized as ONCO-RADS category 3, and the man is considered to have intermediate likelihood of having cancer. Clarification of fading is needed; according to the Fleischner Society guidelines (47), and CT at 6 months was requested. CT scan (right) shows a reduction in the size of the lung nodule (arrow), consistent with its benign nature *(Fig 2 continues)*.

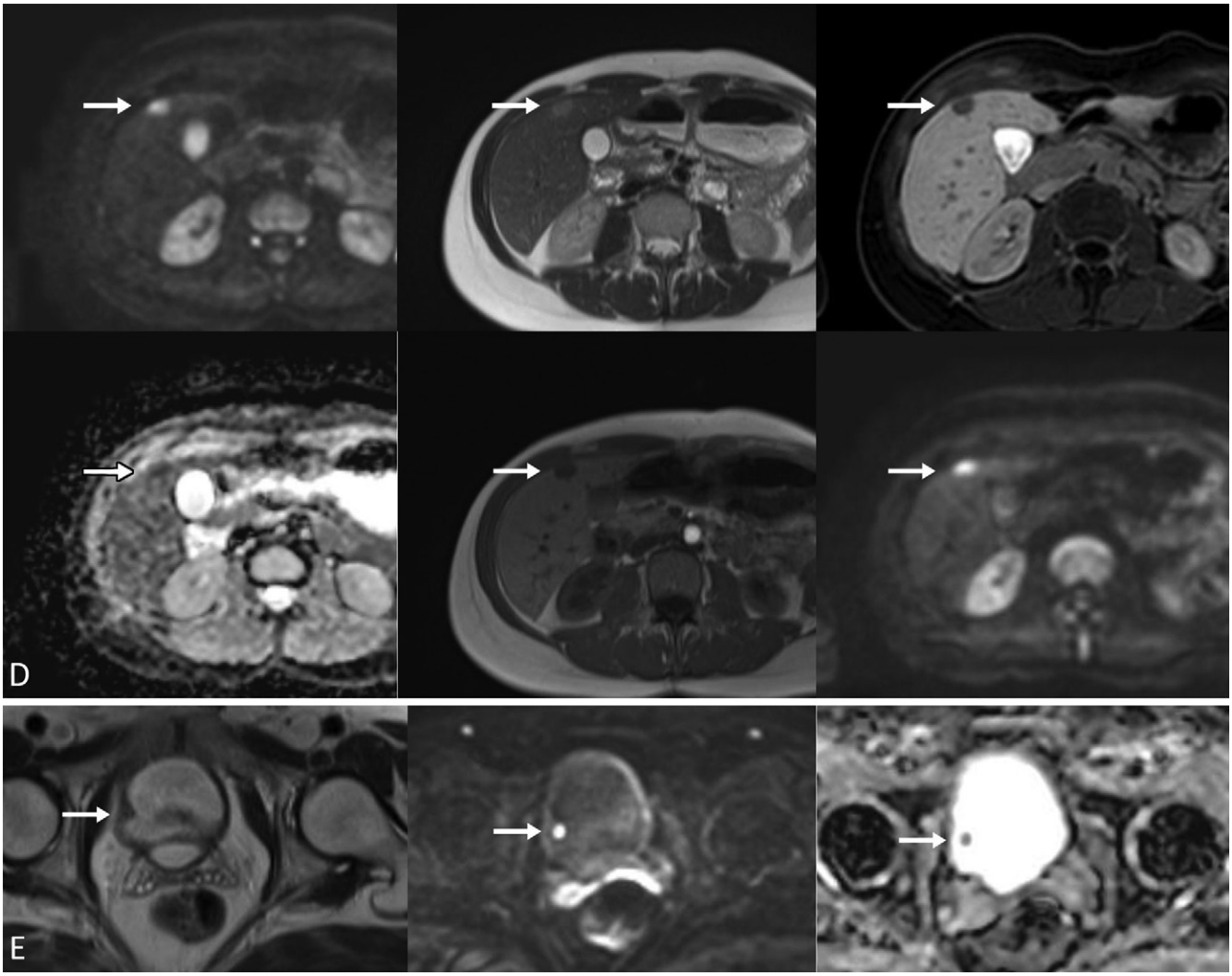
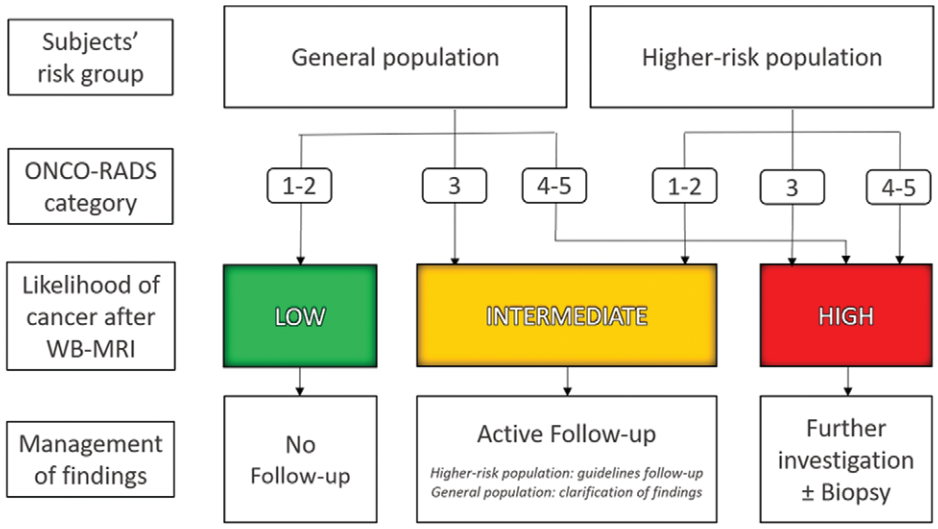


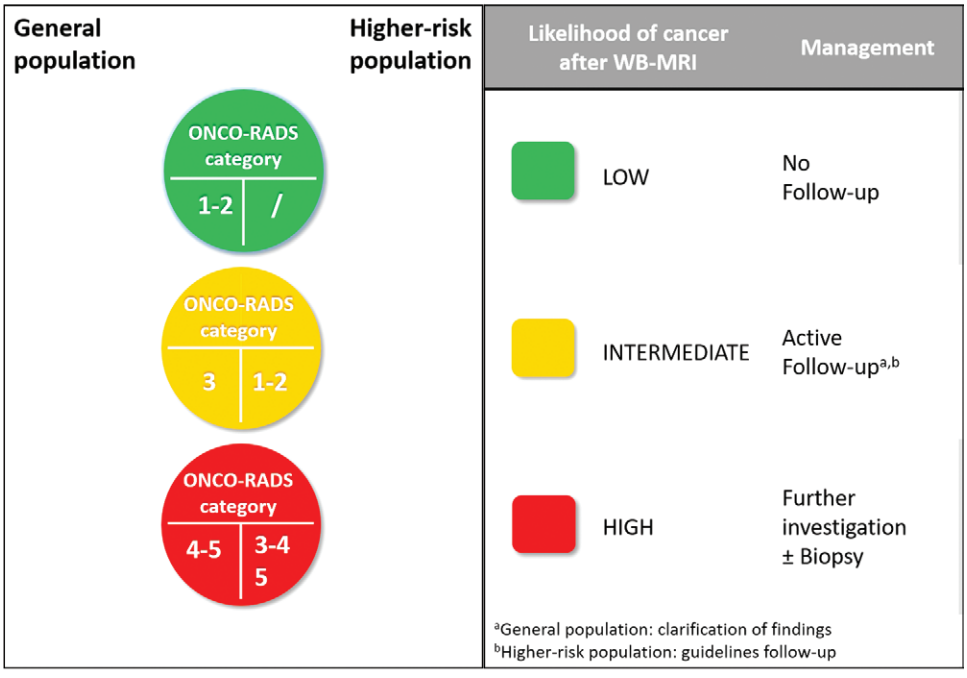
Figure 2 *(continued):* *D*, MRI scans in a 45-year-old woman with Li-Fraumeni syndrome (LFS). The woman had a history of breast cancer, acute myeloid leukemia, anaplastic astrocytoma, basal cell skin carcinoma, and high-grade pleomorphic sarcoma of the trapezius muscle. Images from whole-body MRI show a 15-mm lesion (arrows) in the fifth liver segment. The lesion is hyperintense on high *b*-value DW image (900 sec/mm^2) (top left), with an average apparent diffusion coefficient (ADC) of approximately 1100 μm^2/sec (bottom left), mildly hyperintense on T2-weighted image (middle image, top row), and hypointense on T1-weighted image (middle image, bottom row). After the whole-body MRI examination, the lesion is considered of uncertain nature, either a malignant lesion (most probably a liver metastasis) or a benign lesion (most probably an atypical hemangioma). Given the risk group of the individual (woman with LFS), the lesion is categorized as ONCO-RADS category 4 and the woman is considered as high likelihood of having cancer. A further investigation with MRI with hepatobiliary contrast material was performed, in which the lesion does not show typical enhancement features of hemangioma (early, peripheral, globular enhancement) and is hypointense on T1-weighted image acquired in the hepatobiliary phase (top right image). A liver biopsy was then recommended, but the woman refused to undergo biopsy. Whole-body MRI scan obtained 12 months after the first whole-body MRI examination (bottom right image) shows that the size and MRI characteristics of the lesion are stable. *E*, MRI scans in a 57-year-old man from the general population with a negative fecal occult blood test and low serum prostate-specific antigen level (0.5 ng/mL); no other screening tests had been performed previously. The man is a heavy smoker (>25 cigarettes per day) and has a positive family history for urinary bladder cancer. Images show an 8-mm right lateral bladder wall lesion (arrows). The lesion is hypointense on T2-weighted image (left), is hyperintense on high *b*-value (900 sec/mm^2) DW image (middle), and has low ADC on the corresponding ADC map (right). The lesion is categorized as ONCO-RADS category 5, likely a nonmuscle invasive bladder cancer (uninterrupted low signal intensity line on T2-weighted image representing muscularis integrity), and the man is considered to have high likelihood of cancer. The patient underwent transurethral resection of the bladder lesion, with the histologic diagnosis of pTa noninvasive papillary carcinoma.

an ONCO-RADS category according to suspicion of malignancy. It is extremely important to emphasize that the criteria for assigning the clinical significance of abnormal findings to an ONCO-RADS category should be different between higher-risk individuals and those in the general population because of the different probability of having cancer (pretest probability).

Higher-risk individuals have a higher prevalence of cancer. For example, individuals with known or suspected cancer predisposition syndromes can have a lifetime risk of developing cancer approaching 100% in some syndromes (44,45), and the likelihood of cancer being present at their first whole-body MRI screening ranges from 4.3% to 32% (11,13–22). Therefore, for higher-risk individuals, radiologists must maximize their sensitivity when assigning ONCO-RADS categories to the lesions found, so as not to miss early cancers. On the other hand, in the general population, individuals who undergo



a.



b.

Figure 3: **(a)** Flowchart of risk-based management pathways of abnormal findings and **(b)** summary of risk management pathways. When asymptomatic individuals from the general population are diagnosed with findings of Oncologically Relevant Findings Reporting and Data System (ONCO-RADS) categories 1–2, they are considered to have low likelihood of cancer and no follow-up is required. When higher-risk individuals are diagnosed with findings of ONCO-RADS categories 1–2 or when members of the general population are diagnosed with findings of ONCO-RADS category 3, they are considered to have intermediate likelihood of cancer and active follow-up is planned, as follows: In higher-risk individuals, whole-body MRI should be repeated at the appropriate time, according to guidelines, whereas in members of the general population, appropriate clarification of findings including other specific imaging tests is required. When higher-risk individuals are diagnosed with findings of ONCO-RADS categories 3–5 or when members of the general population are diagnosed with findings of ONCO-RADS categories 4–5, they are considered to have high likelihood of cancer and further investigations with or without histologic examination are recommended. WB = whole body.

whole-body MRI for cancer screening have a low prevalence of cancer, in the range of 1%–2% (12). For these individuals, a higher specificity threshold should be applied when assigning ONCO-RADS categories to lesions to limit additional testing, biopsies, and anxiety.

Other findings, including those not suspicious for cancer, should be included if considered important for an individual's health (eg, aortic and intracranial aneurysm, pneumonia, vertebral collapse, hydrocephalus). The presence of anatomic variations should also be noted.

Examples of frequently observed abnormal findings are shown in Tables 4–6. Figure 2 shows examples of findings for each ONCO-RADS category in multiple body regions.

Conclusions and management.— A clear summary of the overall assessment of the individual's status indicating the likely presence or the absence of any lesions suspicious for cancer should be presented along with the necessary actions for the investigations of relevant findings if demonstrated.

A blank standardized report is given in Appendix E3 (online), and an example of a report in an asymptomatic individual in the general population can be found in Appendix E4 (online).

Managing ONCO-RADS Findings

Standardized management of relevant findings fills a critical gap for using whole-body MRI for cancer screening. Given the high sensitivity of whole-body MRI, its successful adoption depends on having the multisystem knowledge needed to manage the entire range of findings generated by a whole-body MRI examination.

When an ONCO-RADS category is assigned to a finding, the management pathways should consider the population cancer prevalence (higher-risk or general population) (Fig 3). For example, a liver lesion that looks like as a typical hemangioma is classified as ONCO-RADS category 2. This will require follow-up in an individual at higher risk, whereas no follow-up is needed for an asymptomatic individual in the general population. Greater attentiveness to imaging findings should

therefore be adopted for higher-risk populations owing to the higher pretest probability of having malignant cancer, whereas the established guidelines for the management of incidental findings should be used for asymptomatic individuals in the general population. Examples of such guidelines include those for lung nodules (47), renal cysts (48), and incidental findings on abdominal and pelvic CT and MRI scans (52), including pancreatic cysts (50), thyroid nodules (46), and adnexal masses (49). The radiologist who reports whole-body MRI examinations should have in place specific referral pathways for all discovered likely relevant findings.

Treatment of individuals with low likelihood of malignancy after whole-body MRI.—When normal findings of ONCO-RADS category 1 or abnormal findings of ONCO-RADS category 2 are reported in asymptomatic individuals in the general population, they are considered to have a low likelihood of cancer and no specific follow-up is required. In this group, annual screening with whole-body MRI is considered optional and may be offered in addition to standard screening tests to people who may like to undergo annual check-ups. On these occasions, ONCO-RADS category 2 findings should be reviewed for confirmation of stability.

Treatment of individuals with intermediate likelihood of malignancy after whole-body MRI.—When ONCO-RADS category 1–2 findings are reported in the higher-risk population, the individuals should be still considered at intermediate likelihood of cancer and whole-body MRI should be repeated at the appropriate time, according to guidelines. In addition, when ONCO-RADS category 3 findings are reported in asymptomatic individuals in the general population, they are also considered at intermediate likelihood of having cancer. Although most of these findings are likely to be benign, appropriate clarification of findings, including the use of other targeted imaging tests, is required; the timing and the imaging technique and further follow-up should be explicitly stated, depending on radiologic judgments, and be consistent with guidelines of good practice (46–50,52).

Treatment of individuals with high likelihood of malignancy after whole-body MRI.—When abnormal findings of ONCO-RADS categories 3–5 are reported in higher-risk individuals and ONCO-RADS categories 4–5 are reported in the general population, the asymptomatic individuals are considered at high likelihood of cancer and further investigations with or without histologic examination are therefore recommended. Reports should specify which further investigations are needed, according to the radiologist's judgment in line with common guidelines and good practices (46–50,52) (Fig 3).

Limitations

There are limitations to our approach. Whole-body MRI examinations are more challenging to perform and evaluate with 3-T scanners, with unique artifacts (eg, dielectric effect, T1 shortening in bone marrow altering bone marrow appearances, greater susceptibility effects on bone marrow signal intensities of diffusion images, and chemical shift artifacts). With current whole-body MRI technology, whole-body MRI protocols do not cover the lower arms. If clinically needed, additional MRI examinations specific to the arms and legs should be performed. Although improved in the past years, lung evaluations with MRI are still challenging. Pure ground-glass lung nodules (eg, atypical adenomatous hyperplasia or early adenocarcinomas), which may be malignant, as well as small nodules (<5 mm) may be missed. However, it should be noted that in population lung CT cancer detection programs, lung nodules smaller than 6 mm are in general not investigated (47). Similar limitations can occur for the detection of prostate cancers. With the whole-body MRI protocol, only larger cancers can be detected and focused prostate cancer studies are needed (25). In the absence of intravenous contrast material administration, which is considered mandatory only in patients with LFS, neurofibromatosis, constitutional mismatch repair deficiency syndrome, and hereditary retinoblastoma, it is not possible to confidently detect small brain lesions or small meningiomas with whole-body MRI.

It must be noted that whole-body MRI examinations are not performed to assess skin and subcutaneous tissues, which are best evaluated clinically, and that there are other blind spots for whole-body MRI, including the gastrointestinal tract, breast, and cervix. However, these are not necessarily major drawbacks because whole-body MRI is never recommended as a substitute to the standard screening tests, which include fecal occult blood testing or colonoscopy, mammography, and cervical smears.

As currently designed, the ONCO-RADS imaging protocols are only for cancer detection. Any other information regarding nononcologic diseases (eg, neurologic, cardiovascular, orthopedic diseases) may be limited.

Reader expertise is important for the successful use of whole-body MRI for cancer screening. Anupindi et al (53) proposed that whole-body MRI examinations must be reported by radiologists with sufficient experience in oncologic MRI. We have also emphasized that oncologic expertise at the multiorgan level is a fundamental prerequisite for successful whole-body MRI reporting. However, there is no consensus regarding the number of examinations a radiologist should report to be considered as having sufficient expertise to report screening examinations.

Finally, ethical concerns exist for cancer screening with whole-body MRI in the general population. Given the high frequency of abnormal findings, importance should be given to the possible repercussions on the postscreening quality of life and anxiety. In two studies, Schmidt et al noted that individuals in the general population who underwent whole-body MRI for cancer screening had short-term distress while awaiting results (6 weeks) (51) but showed no significant differences in quality of life or in depressive symptoms during long-term follow-up (2.5 years), regardless of whether they were diagnosed with potentially relevant findings (2188 individuals) or not (2232 individuals) (54). In countries with limited MRI equipment, the use of whole-body MRI for general cancer screening may be an unjustified use of resources adding to disparities in the allocation of health care resources. Any future implementation of whole-body MRI for cancer screening should consider also such

potential ethical and arising legal issues arising from whole-body MRI limitations.

Conclusion

The Oncologically Relevant Findings Reporting and Data System (ONCO-RADS) is designed to stratify the risk of having malignant tumors in individuals undergoing whole-body MRI for cancer screening, by enabling the categorization of abnormal findings. Categorizations of oncologically relevant findings facilitate subsequent treatment. ONCO-RADS recommendations fulfill the need to promote standardization and diminish variations in the acquisition, interpretation, and reporting of whole-body MRI for cancer screening. The system is designed for guiding clinical care but has the potential for incorporation into clinical trials. ONCO-RADS requires validation within clinical trials, including assessments of reproducibility and integration with other biomarkers in the setting of cancer screening. We suggest that ONCO-RADS should be evaluated in prospective studies of whole-body MRI for cancer screening in different populations to evaluate the frequency of malignancy within the ONCO-RADS categories. Long-term prospective studies should evaluate the utility of whole-body MRI for maintaining health by means of timely interventions for malignant disease and record at the same time over-investigations that could adversely impact quality of life.

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