Introduction

The human body has ever attracted different scientific areas in terms of finding methods of how to systematically and reproducibly analyze its constituents on a micro- and macroscopic level. Due to technical progress and new modalities, the concept of body composition profiling (BCP) has gained increasing interest in recent years and has thus experienced various ways of assessment and definition (1). BCP in its broadest sense describes the composition and distribution of the large compartments in the human body—muscles, adipose tissue, parenchymal organs, bones and blood (2). Magnetic resonance imaging (MRI) with its optimal soft tissue resolution and inherently high contrast between fat and water is an ideal modality for the assessment of adipose tissues and muscle without the use of ionizing radiation. This review article intends to give an overview of BCP emphasizing qualitative and quantitative MR imaging concepts in the assessment of adipose and muscle tissues.

Methods for BCP

Dual-energy X-ray absorptiometry (DEXA)

The interest in BCP has started a long time before the invention of MR and imaging in general, an exemplary development was the invention of the body mass index (BMI) in the nineteenth century. However, the need for measures of BCP beyond BMI was early noticed among the radiologic community, and CT-derived volume estimations have been first described as early as in 1984 (3). Dual-energy X-ray absorptiometry (DEXA) is a modality well known for its usability in the setting of osteoporosis quantification. However, DEXA proved comparably well for volume assessment of different body compartments by using only a very limited amount of radiation (0.5 µSv) (4). To date, DEXA is the most popular imaging technique...
Table 1 Exemplary whole-body MRI protocol for sarcopenia assessment (partially adopted from Morone et al. 2017)

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Acquisition direction</th>
<th>Field of view</th>
<th>Slice thickness</th>
<th>Examination region</th>
<th>Target acquisition time</th>
<th>Specials</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D or 2D T1-weighted gradient-echo Dixon (two-point)</td>
<td>Axial (or coronal acquisition)</td>
<td>Largest available (usually $50 \times 50 , \text{cm}$)</td>
<td>5–7 mm</td>
<td>Whole-body</td>
<td>~10 min</td>
<td>No coil needed. Recommended use of breath-hold sequences</td>
</tr>
<tr>
<td>T1-weighted multi-echo Dixon</td>
<td>Axial</td>
<td>Adapted to thigh size (both sides)</td>
<td>2–3 mm</td>
<td>Mid-thigh (10–20 slices)</td>
<td>~2 min</td>
<td>Multi-channel body coil. $T_2^*$ corrected multi-echo images may improve accuracy</td>
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Computed tomography (CT)

CT allows for the attenuation-based depiction of body compartments with high resolution. Besides, it facilitates the segmentation of muscle cross-sectional areas per slice as well as for 3D volume segmentation, e.g., calculation of total muscle mass. As attenuation data are scaled in relation to water (HU 0) and thus comparable among different scanners, a threshold-based approach is applied, typically at a range of around −30 to 150 Hounsfield Units (HU) as segmentation mask (12,13). Unlike DEXA, muscle segmentation also allows for macroscopic morphologic assessment of muscle quality. Within the segmented muscle cross-sectional areas, myosteatosis is identified by streaks of negative HU values and fatty infiltration lowers muscle attenuation as fat voxels by definition have negative HU values (13). However, muscle and fat volume segmentation is time-consuming, which is why CT currently focusses on muscle quantity assessment extrapolated from a single slice, most commonly at the level of the third or fourth lumbar vertebra (13). There is large-scale research that has recently been investigating the automation of muscle areas in CT, enhancing its diagnostic yield in terms of whole-body muscle volume assessment. As for other radiological demands, automation enhanced by artificial intelligence algorithms has already demonstrated the potential for muscle mass segmentation (14). However, the use of CT for this task is naturally associated with substantial radiation dose and therefore usually limited to a specific population and indication, limiting its role for longitudinal observations (5,15).

MRI

Parallel to advantages in the application of CT for BCP tasks, MRI has gained comparable importance in the assessment of body compartments, muscle mass, and associated anthropometric measures. The technique is free of ionizing radiation and therefore allows repetitive scans in specific longitudinal observations. Furthermore, free from several technical biases or errors in DEXA and CT, MRI has been validated to reliably measure body compartments (16,17), and to perform this task at high accuracy, given a range of quantitative error of 1.1% to 4.4% (18). This error may also depend on basic acquisition parameters, such as the use of surface or body coils or other protocol decisions (e.g., continuous moving table acquisition; see Table 1 for exemplary protocol) with implications on signal-to-noise ratio and acquisition time. This must be considered and handled individually, as an error of a few percent may be negligible for certain populations and indications while playing a significant role in e.g., monitoring examinations of athletes. In any case, despite its validity and reliability, MRI currently faces difficulties in availability and ease of use in terms of data assessment. The big advantage of muscle assessment by MRI, namely acquisition of whole-body data,
Figure 1 Multiplanar coronal reconstructions of composed (A) fat- and (B) water-only images, as derived from scanner, from an axially acquired T1-weighted whole-body MRI gradient echo sequence using two-point Dixon technique. The images are from a clinically indicated examination of a 34-year-old female patient with mild overweight. The images were post-hoc labor-intensively segmented manually, as shown in the (C) color-coded segmentation image.

demands technically difficult and still time-consuming post-processing. Manual segmentation, as shown in Figure 1 takes several hours (depending on the volume, accuracy, and detail of segmentation) but is currently not ready-for-use in clinical practice. Numerous automated methods intend to ease whole-body segmentation (20-22), but except for very limited proprietary examples, the majority of BCP assessment by whole-body MRI is currently performed in research settings employing artificial intelligence for advanced segmentation tasks with promising results (Figure 2).

Standard Spin-Echo MR imaging

The different MR behavior of macroscopic and cellular fat and water has been extensively described since the very beginnings of animal and clinical MR research (23). Obvious differences in T1- and T2 relaxation times paved the way for qualitative interpretations of fat and water components in tissue and organs in current clinical MR imaging. In acute reactions, muscle tissue usually experiences edematous changes associated with an increase
in water and volume, followed by a decrease in water with atrophy and fatty infiltration in chronic changes. While edema can be depicted on fluid sensitive T2-weighted usually fat-saturated sequences, muscle volume and fatty infiltration can be best seen on non-fat saturated T1 or T2-weighted sequences. Goutallier et al. were the first to describe fatty infiltration grades of the shoulder rotator cuff muscles on a five-point scale, depending on the amount of visually perceivable intramuscular fat on CT images (24). This simple and straightforward concept has been adopted also in MR imaging of the shoulder and different other regions of the body (25,26). Some studies have however also investigated semi-quantitative methods to quantify muscle atrophy and fat infiltration (26,27). According to Davis et al., mere cross-sectional muscle area measurements are more reproducible than semi-quantitative grading with Goutallier classification (28). Advanced quantitative segmentation algorithms in 2D or 3D are able to determine fat content and percentage of a muscle area or volume (29).

In addition to muscular volume and fat content assessment, MRI theoretically enables statements about muscle quality regarding muscle fiber type composition based on differences in relaxation times. The relative composition of muscular fiber types I and II, also known as slow- and fast-twitch fibers, determines the functional profile of a muscle and impacts on relaxation behavior. This was until recently only investigated by dissection. Already more than thirty years ago, MRI demonstrated to be excellent for the correlation with pathology in a small cohort (30). However, the underlying principles of tissue differences in T1 and T2 times have been thoroughly investigated throughout the last decades and were shown to be dependent on a wide spectrum of influencing factors. Especially edematous changes and sex/age-related differences have a substantial impact on fiber type composition derived from MR relaxation times (31,32). In fact, the non-specificity of muscular T1 and T2 times limits the ability to reproducibly determine fiber type composition in clinical routine. More recent investigations have however presented encouraging approaches utilizing quantitative
methods of diffusion-weighted MR (q-space imaging) and were able to differentiate different muscles (by their fiber composition) in mice (33).

**Chemical-shift MR imaging**

The principle of chemical shift imaging is based on different precession frequencies of water and fat protons at a certain magnetic field strength. This allows acquiring in- and opposed-phase images where proton spin magnetization vectors at two different echo times (i.e., two-point technique) are either in equal or opposed direction to each other. Respective signal intensities can then be used to additionally generate fat and water images (Figure 1), resulting in four different image contrasts in total. This principle was first described by Dixon in 1984 (34) and is nowadays widely used in clinical imaging. The Dixon technique due to its robustness, in general, does offer homogeneous fat-saturation over a large field of views, as well as fast MR imaging of large target volumes, e.g., whole-body (wb) MR imaging when used with gradient-echo sequences (35-37). However, limitations have to be considered, as especially fast two-point Dixon sequences are prone to B0-magnetic field inhomogeneity (38). There are however different strategies in reducing this error. On one hand, multi-echo Dixon techniques compensate for these inhomogeneities, allowing to accurately quantify fat content in any image voxel through fat-fraction maps where the grey value of each pixel is proportional to its respective fat-percentage (39). This technique is most widely used for quantification of liver steatosis and has shown to be comparable to a histologic reference standard (40,41). The same technique has also been applied to muscle imaging and in a recent study fatty infiltration of rotator cuff muscles was quantified with isotropic fat-fraction maps from multi-echo 3D-Dixon sequences and correlated with post-operative outcome measures (42), indicating the direction of advanced muscle quality assessment with quantitative MR imaging. On the other hand, certain methods for B0-magnetic field inhomogeneity reduction focus on the use of prospective and retrospective intensity inhomogeneity correction. Exemplarily, Andersson et al. proposed a self-calibrating correction method that allows for the processing of raw as well as normalized images with regard to B0 magnetic field inhomogeneities (43).

In addition to the plain large-scale separation of mainly fat and water containing body compartments, precise assessment of intra- and intermuscular fat can be obtained with higher spatial resolution. Though sometimes misleadingly used synonymously, these two quantitative descriptors of adipose tissues are defined as presence of macroscopic fat within/between fibers of one muscle (i.e., real fatty muscle infiltration, also named “interstitial fat”) and of adipose tissue that accumulates between muscle groups underneath the deep fascia, respectively (44,45). While intramuscular fat is more difficult to image, these types of fat deposition are known to be associated differently with several physiologic and pathologic conditions. For example, intramuscular fat content is twice as high after spinal cord injury, compared to healthy controls (46). On the other hand, intermuscular fat is sometimes referred to as “bad” adipose tissue, as it correlates stronger with visceral adipose tissue and is hence linked to the metabolic disease spectrum, and furthermore serves as a good predictor of insulin sensitivity (47). Moreover, over the past two decades, different groups have demonstrated quantitative changes of intramuscular fat in diseases from the spectrum of neuromuscular disorders, most commonly muscular dystrophies (48). Dahlqvist et al., for example, proved that fat fraction derived by chemical shift imaging of paraspinal and other muscles in facioscapulohumeral dystrophy patients, correlated with clinical and genetic disease markers, even when symptoms did not (49). Another group used three-point Dixon for quantification of intramuscular fat fraction in Duchenne muscular dystrophy. The result was a stronger correlation with a validated disease severity score than any other tested clinical examinations, such as isokinetic dynamometry of the knee extensor strength (50).

Dixon technique cannot only generate fat- and water-images but can also define precise quantitative water and fat fraction maps on a voxel basis. This represents a major benefit compared to CT (51,52) where a certain attenuation/HU value is attributed to each voxel based on the integral of the respective constituents. Hence, the potential fat contribution to a certain attenuation value of one single voxel cannot be clearly identified (53). As the presence of fat even in one small voxel is though known to improve specificity in lesion characterization (53), detection of intravoxel, and more specifically intracellular fat, is of utmost importance and used in several clinical scan protocols, e.g., for liver imaging (54,55), as well as in research settings (56,57).

**Diffusion-weighted imaging and MR spectroscopy**

Apart from chemical shift (Dixon-technique) imaging,
different groups have also assessed muscle quality utilizing diffusion-weighted and diffusion-tensor imaging (DTI) (58-60). In the example of rotator cuff muscles, quantitative fat fractions, as well as different DTI-derived parameters, were shown to highly correlate with age-related alterations, which were undetectable by visual reading. The findings were also supported by naturally higher interreader agreements, compared to the readers’ rating according to the Goutallier classification system (61). Other groups were also able to show significant correlations between standard DTI measures and functional tests of muscle quality, such as Klupp et al. by comparing paraspinal muscular DTI parameters with measures from an isokinetic dynamometer (62). DTI may also help determine muscle integrity or recovery from bundle tears that can be nicely illustrated by additional tractography but until now DTI has not found its way to large scale applications in clinical routine and largely remains a research tool.

MR spectroscopy attempts to quantify tissue constituents on a molecular level, usually based on H1-proton signals. While there is a large body of literature about MR spectroscopy application in fat quantification and other tasks of liver imaging (63,64), the technique has also proven its usability in neuroradiologic as well as musculoskeletal settings. In musculoskeletal radiology, standard proton-based MR spectroscopy has mostly been used for the analysis of tumor lesions but also shows significant correlations with the metabolic status of muscular tissue (65). MR spectroscopy does not only allow to assess lactate concentration after muscle exertion (66) but can also accurately determine fat content in a certain volume of interest (VOI). However, this is associated with considerable sample error as a consequence of VOI position variance (67). Only small changes in the VOI position may have a huge impact on accurate fat quantification. The additionally rather long acquisition times and the need for a prospective acquisition, further prevent large scale use of this technique beyond scientific studies. While MR spectroscopy has existed even before clinical MR imaging and is still often considered as the gold standard of volumetric fat quantification (68,69), current clinical investigations predominantly focus on chemical shift imaging (70). Nonetheless, MR spectroscopy is still used frequently in research settings, also due to recent discoveries in the field of in-vivo muscle function assessment with 31-P-spectroscopy (71,72). This has recently allowed for the accurate assessment of muscular metabolic changes in different diseases, revealing altered pH levels at rest and under exercise in nephropathic type 1 diabetes mellitus patients (73), or identifying three different disease phases in facioscapulohumeral dystrophy (74).

**Texture analysis and advanced post-processing**

Among musculoskeletal experts as well as in all other radiologic subspecialties advanced methods of image pattern analysis, termed texture analysis (TA) (75), have been investigated with significant implications on clinical outcome. Pattern recognition may help to find new biomarkers that better correlate with clinical outcomes compared to mere qualitative ratings, e.g., percentage gradings of fatty muscle infiltration (76,77). Moreover, isotropic MR sequences allow for the acquisition of detailed large volume datasets, e.g., of whole muscle groups or even whole-body MR data sets allowing for 3D volume assessment pattern recognition of fatty muscle infiltration, e.g., of the psoas muscle (78). TA may thus produce more reproducible and sophisticated biomarkers of muscle quality than mere qualitative ratings of radiologists.

**Clinical applications of MRI for BCP: the present**

The currently used concepts of BCP assessment differ by large regarding technical (i.e., imaging modality) and clinical conditions (i.e., heterogeneity of definition) and are therefore of limited comparability. Despite the trending character of whole-body imaging, it is currently believed that this is one of the main-restricting factors for further clinical applications in metabolic/geriatric settings as well as in oncologic disease monitoring (79).

Nonetheless, MRI may be a very promising BCP assessment method for the future. So far, there is exciting literature on the correlation of MR BCP data with clinical indications and their disease outcomes. Apart from using MR data for evaluation of normal healthy populations (80), athletes or elderly patients (81), it is also significantly associated with classic outcome parameters, e.g., mortality and common laboratory tests, e.g., tumor markers in oncologic (58,82) and metabolic (83-86) patients. In terms of drug-monitoring, studies have demonstrated both positive (87) and negative (88) drug effects on MR-derived BCP measures. Large-scale prospective biobank trials have furthermore had first achievements in phenotyping by imaging, e.g., by linking different BCP types with increased risk of type II diabetes or coronary heart disease (89).
Sarcopenia

The most interesting application may however be in the field of sarcopenia. The term sarcopenia, originating from the Greek for “loss of flesh” (sarx penia) is a condition determined by the loss of muscle volume and force and is believed to correlate with higher mortality in geriatric patients among all disease-specific cohorts. Furthermore, sarcopenia seems to be linked to higher mortality, as discovered by an opportunistic screening study in a cross-sectional elderly population (13,90).

This condition is defined by three diagnostic criteria: anatomic changes (as reduced calf circumference); loss in muscle quality; decrease physical strength (as reduced grip strength and/or walking speeds). According to recently revised guidelines published by the European Working Group on Sarcopenia in Older People (EWGSOP), sarcopenia in the elderly patient per definition is “probably” present when muscle strength is reduced, “confirmed” by a reduced muscle quality or quantity (depending on the modality in use, e.g., ASMM in MRI), and is believed to be “severe” when physical performance is in addition significantly reduced (91,92). The EWGSOP recommends MRI as one of the imaging modalities to evaluate the confirmation criteria, i.e. muscle quantity or quality. In the last version, the guidelines specifically recommend the utilization of MRI for measuring appendicular skeleton muscle mass, or its related index (ASMMI) for height-adopti

MRI and BCP: challenges and future

An increasing number of prospective investigations demonstrated interesting results for whole-body MRI for muscle and fat evaluation. Similarly, the topic of muscle quality and BCP assessment with MRI has gained increasing attention, as shown by a doubled number of publications focusing on fat volume assessment in MRI in the last five years (22).

Since on one hand, MR is valid, reliable and reproducible for the assessment of muscle quality and quantity, and on the other hand, first prospective studies have shown promising results for application in preventive medicine and disease (or therapy) monitoring, the time is now to leverage the technique on a clinical routine level.

As typical for novel techniques, several sources of systematic errors and difficulties may be challenging. First, as previously described, data quality and validation are necessary for multi-center comparison. Substantial differences in data acquisition may be corrected post-hoc in academic settings but are important limitations to introduce these techniques in routine clinical practice. It is therefore important to establish and provide clinicians and non-academic imaging experts with normative values of BCP measures, specific for races, age and sex and with

Common qualitative and quantitative measures of BCP in WB-MRI are as follows:

(I) Fat-related volumes:
- Visceral adipose tissue volume (VAT);
- Subcutaneous adipose tissue (SCAT);
- Pericardial adipose tissue.

(II) Muscle-related volumes:
- Total muscle volume;
- Appendicular skeleton muscle mass (ASMMI).

(III) Muscle quality parameters:
- Intermuscular adipose tissue (IMAT) at mid-thigh level;
- Total cross-sectional area of visualized muscles at the L3 level;
- Total cross-sectional area of psoas muscle at the L4 level.

(IV) Anthropometric and other measures:
- Patient height;
- Circumferences (abdominal, thigh, calf);
- Liver fat fraction.

from a single slice (98,99) may prove beneficial for the use of BCP profiling and muscular assessment with MRI.

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Figure 3 Quantitative methods of muscle quality assessment in MRI. Apart from regular anthropometric measures and cross-sectional area segmentation of (A,E) fat-only- and (B,F) water-only-maps, MRI also allows for sub-visual assessment of muscle quality, e.g., utilizing (C,G) absolute fat-fraction, and (D,H) water-fraction-maps for analysis of e.g., intra- and intermuscular adipose tissue (arrow in A and E). The images of the two top rows (A,B,C,D) show a mid-thigh slice of axial whole-body scans of a healthy 23-year male student who does on average 6 to 7 hours of sports activities per week. Images (E,F,G,H) show analog representative images of an 82-year-old male individual (sportive activity unknown) with markedly increased areas of intermuscular adipose tissue and in comparison, mild atrophy of the muscular circumference.

appropriate inter-scanner comparability. Furthermore, comparable post-hoc evaluation by automated segmentation software will be important to guarantee data validity. With respect to scan comparability, different groups have made efforts in the recent past to demonstrate excellent multi-center reproducibility as well as reproducibility between different field strengths. On one hand, scan protocol harmonization and user training may be crucial to achieving acceptable reproducibility of manually assessed quantitative measures (100). However, semi-automated assessment, which will be of increasing importance, requires even more sophisticated strategies to allow for multi-scanner and -center comparison. Karlsson et al. therefore demonstrate an accurate and reproducible segmentation method based on
non-rigid multi-atlas registration of muscle volumes (101), which is also used by a large vendor specialized in body compartment assessment.

Another challenge is the huge amount of MRI data per whole-body scan. A typical whole-body MRI produces 400 to 500 images per composed series (e.g., in-phase, opposed-phase, fat-only- or water-only-images). Without robust and fast automated segmentation solutions, BCP assessment with whole-body MRI will be very time consumption up to several hours per patient, which is far more than an average clinical radiologist is allowed to spend for one examination. Alternatives to whole-body solutions may, however, focus on the investigation of data reproducibility that is derived from representative single- or few-slice segmentations. The most representative single slice region of whole-body compartments is believed to be on a lumbar spine level. More specifically, Schweitzer et al. suggest the level of the third lumbar vertebra as optimum in terms of reproducibility and correlation with body compartments (102). As mentioned before, likewise approaches may be a legitimate strategy for a restricted spectrum of clinical tasks, e.g., initial sarcopenia assessment in an opportunistic screening setting. However, the aspect of reduced accuracy must be considered carefully for the majority of clinical demands. Most importantly, more recent studies have proven the inferiority of single-slice technique compared to whole-body compartment assessment, and this method furthermore lacks the required reproducibility for e.g., longitudinal studies, as demonstrated by recent CT-, and more recently MR-related investigations (103,104). Another strategy in assessing these large data amounts is the utilization of automatic registration and segmentation algorithms. Especially within the last few years and rising with the use of artificial intelligence in radiology, several groups have made efforts in testing different segmentation concepts for whole-body imaging, muscle and fat compartment assessment. While the first studies mostly focused on CT images, an increasing body of literature has recently focused on automated segmentation of different regions and for different radiologic subspecialties in MR and CT as well. A recently published review article describes 408 included original papers that aimed to automatically segment tissue (20). For the musculoskeletal system, Dice similarity coefficients around 0.9 are currently being achieved (20). While most of these applications are limited to research questions, it may be expected, that also due to improvements of expertise among the radiologic community regarding implementation of machine learning these algorithms will be part of clinical routine soon.

The acquisition itself has been usually tested in quite homogeneous populations that were able helping to acquire flawless imaging (or else excluded from many studies). However, whole-body muscle assessment is usually performed using a composition of many smaller acquisition stacks. At the levels of the trunk, these series are usually acquired performing breath-holds, not seldom for up to 20 seconds. This is not only challenging in elderly patients due to their reduced functional lung capacities but may remain impossible for intensive care unit patients, a cohort where BCP has significant implications on their nutritional therapy and outcome (95). Even CT has been investigated scarcely for monitoring of nutritional status (105).

Finally, the main challenge remains in the interpretation of image-based results. Sarcopenia is confirmed by imaging findings; however, disease severity is based on physical examination and tests that relate to patients’ physical activity. Since normative values may vary throughout different populations and among various types of body constitution (94), the interpretation of relatively low or high measures of muscle quality or volumes is difficult and requires awareness among diagnostic radiologists. Premature use of pathologic ranges may cause false-positive diagnoses with all its consequences, e.g., cost-intensive patient careers and uncertainty of healthy individuals.

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Footnote
Conflicts of Interest: The authors have no conflicts of interest to declare.

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