Radiology

ORIGINAL RESEARCH • SPECIAL REPORT

The QIBA Profile for MRI-based Compositional Imaging of Knee Cartilage

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X.L. supported by the National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases (R01AR077452).

Conflicts of interest are listed at the end of this article.

See also the editorial by Kijowski in this issue.

Radiology 2021; 301:423–432 • https://doi.org/10.1148/radiol.2021204587 • Content codes: HP MR

MRI-based cartilage compositional analysis shows biochemical and microstructural changes at early stages of osteoarthritis before changes become visible with structural MRI sequences and arthroscopy. This could help with early diagnosis, risk assessment, and treatment monitoring of osteoarthritis. Spin-lattice relaxation time constant in rotating frame (T1ρ) and T2 mapping are the MRI techniques best established for assessing cartilage composition. Only T2 mapping is currently commercially available, which is sensitive to water, collagen content, and orientation of collagen fibers, whereas T1ρ is more sensitive to proteoglycan content. Clinical application of cartilage compositional imaging is limited by high variability and suboptimal reproducibility of the biomarkers, which was the motivation for creating the Quantitative Imaging Biomarkers Alliance (QIBA) Profile for cartilage compositional imaging by the Musculoskeletal Biomarkers Committee of the QIBA. The profile aims at providing recommendations to improve reproducibility and to standardize cartilage compositional imaging. The QIBA Profile provides two complementary claims (summary statements of the technical performance of the quantitative imaging biomarkers that are being profiled) regarding the reproducibility of biomarkers. First, cartilage T1ρ and T2 values are measurable at 3.0-T MRI with a within-subject coefficient of variation of 4%–5%. Second, a measured increase or decrease in T1ρ and T2 of 14% or more indicates a minimum detectable change with 95% confidence. If only an increase in T1ρ and T2 values is expected (progressive cartilage degeneration), then an increase of 12% represents a minimum detectable change over time. The QIBA Profile provides recommendations for clinical researchers, clinicians, and industry scientists pertaining to image data acquisition, analysis, and interpretation and assessment procedures for T1ρ and T2 cartilage imaging and test-retest conformance. This special report aims to provide the rationale for the proposed claims, explain the content of the QIBA Profile, and highlight the future needs and developments for MRI-based cartilage compositional imaging for risk prediction, early diagnosis, and treatment monitoring of osteoarthritis.

Online supplemental material is available for this article.

Advances in MRI technology have revolutionized cartilage imaging from morphologic assessment to compositional analysis. MRI-based compositional cartilage biomarkers such as spin-lattice relaxation time constant in rotating frame (T1ρ) and T2 values provide quantitative measures used for early detection of cartilage damage (1–3). T1ρ is an MRI sequence developed for use in musculoskeletal imaging research and not in widespread clinical use. T1ρ is sensitive to proteoglycan content of cartilage, whereas T2 is more sensitive to water and collagen content and orientation of collagen fibers. The measures have also been used to predict and monitor incidence and progression of osteoarthritis (4–7) while also assessing response to interventions, such as cartilage repair and osteotomy (8–11). Nevertheless, MRI-based compositional cartilage biomarkers have not been used widely in clinical practice. Instead, they have been used mostly for cross-sectional and longitudinal research studies (12–14). A major issue preventing the transition to clinical application is a lack of standardization, which includes patient preparation, image acquisition, and image analysis, to reduce measurement variability and achieve comparable outcomes with different scanners.

To overcome technical limitations and to better standardize quantitative imaging biomarkers, the Radiological Society of North America launched Quantitative Imaging Biomarkers Alliance (QIBA) in 2007. QIBA aims to "improve the value and practicality of quantitative imaging biomarkers by reducing variability across devices, sites, patients, and time" (15) and to "unite researchers, healthcare professionals and industry to advance quantitative imaging and the use of imaging biomarkers in clinical trials and clinical practice" (16). The primary output of QIBA committees are quantitative imaging documents based on validated and standardized imaging biomarkers called Profiles. A Profile makes performance claims. Claims are summary statements of the technical performance of the quantitative imaging biomarkers being profiled on the basis of currently accepted standards. A Profile also defines the groundwork activities, clinical context, and appropriate compliance procedures to achieve the claims.

Abbreviations

QIBA = Quantitative Imaging Biomarkers Alliance, T1ρ = spin-lattice relaxation time constant in rotating frame

Summary

This article summarizes the claims and procedures of the Musculoskeletal Biomarker Committee Profile of the Quantitative Imaging Biomarkers Alliance for standardized MRI-based cartilage compositional imaging (spin-lattice relaxation time constant in rotating frame, or T1ρ, and T2).

Key Results

- Cartilage spin-lattice relaxation time constant in rotating frame (T1ρ) and T2 are measurable with 3.0-T MRI with a within-subject coefficient of variation of 4%–5%.
- A measured increase or decrease in T1ρ and T2 of 14% or more indicates a minimum detectable change, which can be used for defining response and progression criteria for quantitative cartilage imaging.
- If only an increase in T1ρ and T2 is expected (progressive cartilage degeneration), then an increase of 12% represents a minimum detectable change.

The QIBA Musculoskeletal, or MSK, Committee aims to standardize the application of T1ρ and T2 imaging as biomarkers for the quantification of cartilage composition. To implement this task, the QIBA MSK Committee has worked on requirements and recommendations for acquisition devices, technologists, radiologists, reconstruction software, and image analysis tools involved in study participant handling, image acquisition, image data reconstruction, image quality assurance, and image interpretation. The requirements are focused on achieving sufficient reproducibility for the longitudinal evaluation of cartilage composition by using different MRI scanners.

This report provides a concise summary of the QIBA MSK Committee Profile on MRI-based compositional cartilage biomarkers and describes its claims. This report also includes potential implications for clinical patient care and research including clinical trials and epidemiologic observational studies, and future directions in this field.

Current State and Challenges of Cartilage Compositional Imaging

Osteoarthritis is the most common type of arthritis and a major health concern for our aging population, with prevalence of 33.6% in adults older than 65 years (17). Disease burden of osteoarthritis is multifaceted and includes direct, indirect, and intangible costs related to pain, disability, and reduced quality of life (18). To our knowledge, we do not have an efficacious drug therapy for this debilitating and progressive disease. Thus, the development of reproducible biomarkers for risk assessment, early diagnosis, and monitoring of osteoarthritis has a considerable impact at personal and public levels.

The Kellgren-Lawrence grading system, accepted by the World Health Organization in 1961, remains the current reference standard to diagnose osteoarthritis. It is based on radiographic findings of osteophytes and joint space narrowing as indirect evidence of cartilage loss (19). Over the last 2 decades, noninvasive compositional cartilage imaging by using MRI has been developed and used extensively, mostly in research settings. MRI has become the imaging modality of choice for cartilage assessment because of its ability to depict a wide spectrum of structural and compositional features of tissues. Thus, MRI is a central component of large-scale longitudinal epidemiologic studies such as the Osteoarthritis Initiative, or OAI, and the Multicenter Osteoarthritis Study, or MOST.

Typically, osteoarthritis-related changes at MRI are assessed with morphologic analysis (20) but this assessment has drawbacks, including subjective evaluation and diagnosis at advanced disease stages when cartilage loss has already occurred. To address these limitations, quantitative imaging biomarkers for assessing cartilage compositional changes at a prestructural stage have been developed. Several techniques have been developed, such as T2/T2* mapping (21–27), T1ρ measurements (23,27–30), delayed gadolinium-enhanced MRI in cartilage (31,32), sodium imaging (33), glycosaminoglycan chemical exchange saturation transfer (34,35), and diffusion MRI (36,37). These techniques analyze the cartilage mainly by providing information regarding water content, collagen integrity, and proteoglycan content (38).

Among all the available techniques for MRI-based compositional cartilage imaging, T2 and T1ρ mappings have become widely accepted with the largest body of literature. Multiple studies, mostly at the knee, have reported promising data regarding the validity, reproducibility, ability to monitor interventions, and ability to predict symptomatic osteoarthritis for T2 (21–27) and T1ρ (23,27–30). Other compositional cartilage imaging techniques overall have been studied less rigorously because they are newer and their advanced technical requirements limit them to a handful of research institutions.

In clinical practice, there are still tangible concerns regarding the standardization of compositional cartilage imaging techniques for longitudinal examinations, particularly regarding the use of different scanners from the same or different vendors. In addition, to our knowledge, no reference values for T2 and T1ρ have been established to define cartilage as normal or abnormal. These shortcomings have limited the utility of the biomarkers to clinical research, such as longitudinal clinical trials. Thus, addressing them is crucial before these imaging approaches can be used as reliable and reproducible tools in clinical practice (12–14). These issues are mainly the results of specific scanner features, sequence protocols (including image noise, spatial resolution), and different technologies from multiple vendors (including data reconstruction, correction). These are addressed in the QIBA MSK Profile and its claims.

Profile Claims

The QIBA Profile summarizes test-retest variability and minimum detectable change (the smallest change over time that can confidently declare a true change) of cartilage T2 and T1ρ values in claims 1 and 2.

Claim 1

Test-retest variability (nonlongitudinal) of cartilage T2 and T1ρ values are measurable at the knee with a within-subject coefficient of variation of 4%–5%. This claim applies to 3.0-T scanners from the same vendor (2,23,25,27,39).

Claim 2

A measured increase or decrease in T2 and T1ρ of 14% or more indicates that a minimum detectable change has occurred with 95% confidence on longitudinal scans. If only an increase in T2 and T1ρ is expected (ie, progressive cartilage degeneration), then an increase of 12% represents a minimum detectable change.

The claims are focused on these specific measurements because of their relevance for clinical practice and clinical trials, and availability of published supporting literature. The practical implication of the claims is to establish a measurement assay (4%–5%) for test-retest reliability of T2 and T1ρ measurements. Also, claim 2 provides the minimum detectable difference in T2 and T1ρ values in a single patient in longitudinal scans, which can be used as a basis for defining response and progression criteria for quantitative cartilage imaging. Clinical trials with larger sample sizes could potentially detect smaller differences on the basis of the sample size, and intersubject and within-subject coefficient of variations.

Considerations for the Profile Claims to Be Valid

The following several conditions should be considered for the claims to be valid:

1. The claims are for knee cartilage only. There are only a few studies that use T1ρ and T2 at the hip, with less standardization of measurements. The hip may be added at a later stage.
2. The claims require most of the morphologic structure of the cartilage to be normal without marked cartilage loss or major defects. Therefore, analyses should be restricted to patients with a Kellgren-Lawrence score of 2 or less at baseline.
3. These claims are on the basis of semiautomatic or automatic cartilage segmentation by using dedicated analysis software.
4. The claims are applicable for single and multicenter studies by using the same 3.0-T MRI scanner model, type, and imaging protocol. We do not anticipate that the claims will be met for scanners from different manufacturers at this point.
5. The claims require use of calibration phantoms to confirm consistency of measurements.

Derivation of the Claim

Test-retest reproducibility and variability of T2 and T1ρ values have been reported in a number of publications

Table 1: Publications on Test-Retest Variability Included in the Derivation of the Profile Claims

Publication	Biomarker*	Repeatability Parameter	Parameter Value†	Cited in Article	MRI Sequence	Note
Glaser et al 2006 (41)	T2	RMS CV	3.6	Table 1	Fat-saturated ME TSE	At seven different points, patellar cartilage evaluated
Li et al 2008 (42)	T1ρ	CV	1.7–8.7	Table 2	3D MAPSS	Use of two phantoms at two different points
Mosher et al 2011 (23)	T2, T1ρ	RMS CV	6.6–12.0 (T2); 5.7–13.6 (T1ρ)	Table 6	T2 MSME 3D T1ρ balanced FFE	At four points, data from ACRIN-PA 4001 multicenter trial
Schneider et al 2013 (25)	T2	RMS CV	1.5–5.4, 2.1–3.9‡	Table IIB page 4	T2 MSME	Longitudinal (8 years) monthly QA from the OAI study on two different phantoms, four locations and single scanner type
Li et al 2014 (40)	T2, T1ρ	RMS CV	5.2 (T2), 5.3 (T1ρ)	Page 4	Combined MAPSS T1ρ and T2§	At four different points, single scanner, location, and phantom
Jordan et al 2014 (30)	T2, T1ρ	RMS CV	6.4, 9.3, 10.7 (T2); 4.6, 6.1, 6.0 (T1ρ)‖		DESS (T2) CubeQuant (T1ρ)	At four different points, single scanner and location
Li et al 2015 (27)	T2, T1ρ	RMS CV		Table 3, Figure 5	Combined MAPSS T1ρ and T2§	
Single-site study						
Part 1			Phantom 0.7–1.6 (T2), 0.6–1.2 (T1ρ), participant 0.8–1.6 (T2), 1.0–2.1 (T1ρ)			Long-term reproducibility: monthly phantom and participants

Table 1 (*continues*)

Table 1 *(continued)*: Publications on Test-Retest Variability Included in the Derivation of the Profile Claims

Publication	Biomarker*	Repeatability Parameter	Parameter Value†	Cited in Article	MRI Sequence	Note
Part 2			Phantom 0.1–0.5 (T2), 0.4–2.3 (T1ρ); participant 1.8–2.7 (T2), 1.5–2.3 (T1ρ)			Variation with different MRI systems: phantom at four scanners, participants at two scanners
Part 3			Phantom 0.6–1.8 (T2), 0.4–1.1 (T1ρ); participant 0.2–2.2 (T2), 1.4–3.8 (T1ρ)			Variation with different coils: two phantoms, participants using two coils
Multisite study			3.2–5.3 (T2), 2.3–3.9 (T1ρ)			Single scanner and coil at three sites (monthly up to 8 months), phantom and participants
Kim et al 2020 (39)	T2, T1ρ	CV		Tables 2, 3	Combined MAPSS T1ρ and T2§	
Single-site study						Three vendors, phantom and human participants
Part 1			Phantom 1.1–3.0 (T1ρ), 1.8–3.3 (T2)			
Part 2			Participant 1.6–3.9 (T1ρ), 1.4–4.1 (T2)			
Multisite study						Three vendors, phantom and human participants at four sites
Part 1			Phantom 5.2 (T1ρ), 6.5 (T2)			
Part 2			Participant 8.1 (T1ρ), 10.1 (T2)			

Note.—CV = coefficient of variation, DESS = dual echo steady state, FFE = three-dimensional T1⩾ fast field-echo, MAPSS = magnetization-prepared angle-modulated partitioned k-space spoiled gradient-echo snapshots, ME = multiecho, MSME = multislice multiecho, OAI = osteoarthritis initiative, QA = quality assurance, RMS = root-mean-square, TSE = turbo spin echo, T1⩾ = spin-lattice relaxation time constant in rotating frame, 3D = three-dimensional.

* Relaxation time (msec).

† Data are percentages.

‡ Outer compartment and inner compartment of the knee phantom, respectively.

§ Modified magnetization-prepared angle-modulated partitioned k-space spoiled gradient-echo snapshots T1⩾ quantification sequence (27).

‖ Short, moderate, and long-term variability, respectively.

(25,27,30,40). Details of the claims were derived from extensive review of the literature (Table 1) and two recent meta-analyses (2,3). Comparing repeatability of measurements from different studies is complicated by lack of standard imaging protocols and heterogeneity in methodologic analyses. Therefore, the proposed claims are mainly consensus claims that have not yet been substantiated by studies that strictly conform to the specifications in the Profile. The expectation is that data will be collected from future studies and/or field testing, and changes will be made to the Profile accordingly.

A further complication when comparing publications is the difference in scanner systems, and single versus multiple sites of imaging. Most of the published literature uses a single scanner system (23,40–42). Schneider et al (25) reported data on the basis of the Osteoarthritis Initiative study by using the same scanner model at different sites. Li et al (27) reported test-retest reproducibility of T2 and T1ρ at single and multiple sites by using same scanner system, coils, and imaging protocols. Recently, Kim et al (39) used different MRI scanner systems at multiple sites to report reproducibility of T2 and T1ρ. Studies also vary in terms of internal validation of measurements with phantom imaging and different MRI sequences used for T2 and T1ρ imaging (Table 1).

Global or regional segmentation of cartilage for measurement of T2 and T1ρ values also varied between publications. Whereas Mosher (23) and Li et al (40) reported values on a five-regions-of-interest segmentation system, Jordan et al (30) used a 10-regions-of-interest segmentation of the knee. Glaser (41) reported reproducibility of T2 value only on the patellar cartilage.

Table 2: Profile Structure of QIBA Musculoskeletal Biomarker Committee

Structure
Part 1: Executive summary
Part 2: Clinical context and claims
Part 3: Profile activities
3.1 Staff qualification
3.2 Installation
3.3 Periodic QA
3.4 Study participant selection
3.5 Study participant handling
3.6 Image data acquisition
3.7 Image data analysis
3.8 Image data interpretation
Part 4: Assessment procedures
4.1 T1ρ and T2 measurements of cartilage
4.2 Test-retest conformance study
References and Appendices A–E

Note.—MSK = musculoskeletal, QA = quality assurance, QIBA = quantitative imaging biomarker alliance, T1ρ = spin-lattice relaxation time constant in rotating frame.

Clinical Interpretation

An increase in T1ρ and T2 measurements represents progressive cartilage degeneration, driven by risk factors for osteoarthritis such as obesity (43), previous injury (44), and excessive physical activity (45,46). The smaller the amount of increase in these measurements, the less cartilage degeneration is observed. Of note, cartilage injury related to marathon running has been shown to be reversible, with increase in T2 value after the marathon and normalization over 3 months (47).

Profile Structure

Table 2 lists the overall structure and activities of the Profile. Each section describes recommendations necessary to achieve the Profile claims. Here we provide a brief overview of the steps and recommendations. Some critical information necessary to achieve the Profile claims are presented as appendices and checklists.

Profile Activities

This section of the Profile organizes details on qualification, installation, quality assurance, study participant handling, image acquisition, image analysis, and data interpretation in a pipeline that extracts quantitative imaging biomarkers with the specifications described in the Profile claims. Site, equipment, staff, and software should claim conformance to this Profile as the "actors" (Table 3) supporting the listed "activities." Table 4 is an example of three components of parameter, actor, and requirements for periodic quality assurance. The requirements in this Profile do not codify a standard of care and only provide guidance intended to achieve the stated claims. Failing to conform to a "recommendation" in this Profile is a protocol deviation. Although deviations invalidate the Profile claims, such deviations may be reasonable and unavoidable, and the radiologist or supervising physician is expected to do so when required in the best interest of the patient or research participant.

Table 3: Profile Activities: Actors and Required Activities

Activity	Section
Site	
Staff qualification	3.1
Installation	3.2
Acquisition device	
Installation	3.2
Periodic QA	3.3
Study participant handling	3.5
Image data acquisition	3.6
Technologist	
Staff qualification	3.1
Periodic QA	3.3
Study participant handling	3.5
Image data acquisition	3.6
Image analysis	3.7
Radiologist	
Study participant selection	3.4
Study participant handling	3.5
Image analysis	3.7
Data interpretation	3.8
Image analysis tool	
Image analysis	3.7

Note.—QA = quality assurance.

Table 4: Specifications for Periodic Quality Assurance by Staff and Acquisition Device

Actor	Requirement
Calibration	
Technologist, MRI Physicist	Recommend performing calibration monthly using T1ρ and T2 and ACR phantom. Recommend recording the date and time of the calibration for auditing.
Acquisition device	Calibration phantom should be suitable for performing the calibration factor assessment. Recommend recording the most recent calibration factor for use in subsequent activities.
Qualification	
Physicist	Recommend QA to be overseen by a qualified medical physicist as defined by AAPM.

Note.—AAPM = American Association of Physicists in Medicine, ACR = American College of Radiology, QA = quality assurance, T1ρ = spin-lattice relaxation time constant in rotating frame.

Table 5: Suggested MRI Protocol for all Vendors with Sequences for Cartilage Segmentation and T1ρ and T2 Measurement

Acquisition Device and Technologist Parameter	Requirement	
	High-Spatial-Resolution Sequence	3D T1ρ and T2 MAPSS Sequence
Field strength	3.0 T	3.0 T
Acquisition sequence	DESS/SPGR/MFFE/3D-FSE	3D T1ρ and T2 MAPSS
Coil type	Transmit/receive phased array, ≥8 channels	Transmit/receive phased array, ≥8 channels
Acquisition time (min)	6–8	6–12*
Matrix (frequency × phase)	~384 × 300	256–320 × 128–160
No. of sections	96–160	24–32
Section thickness (mm)	0.7–1.0	3–4
Field of view (mm)	140–160	140–160
Flip angle (degree)	10–25	VFA
TE (msec)	Min, 3–6	Min, 2–4
TR (msec)	Min, 8–15	Min, 6–9
Bandwidth (Hz/pixel)	~186	~400
TSL/prepared TE (msec)		
T1ρ	NA	0/10/40/80
T2	NA	0/10/30/60

Note.—Magnetization-prepared angle-modulated partitioned k-space spoiled gradient echo snapshots (MAPSS) has a total of seven echo images; one time of spin lock/prepared echo time combined T1ρ and T2 mapping echo followed by three additional echoes for T1ρ and three additional echoes for T2. DESS = double echo steady state, FSE = fast spin echo, GE = gradient echo, MFFE = multiecho steady state free precession, NA = not appliable, SPGR = spoiled gradient recalled, TE = echo time, 3D = three-dimensional, TR = repetition time, TSL = time of spin lock, T1ρ = spin-lattice relaxation time constant in rotating frame, VFA = variable flip angle.

* For four to eight echo images.

Installation of Pulse Sequences, Coils, Phantoms, and Segmentation Software

We recommend performing installation and initial validation according to manufacturer-defined procedures and specifications. Pulse sequences are based on the recommendations of the published cross-calibration study (39) (details are listed in the Image Data Acquisition section). To achieve the Profile claims of reproducibility, our recommendations for installation include the following:

1. For reproducible knee positioning, at a minimum, use knee quadrature transmit eight-channel phased-array receiver coils or eight-channel phased array flex coil with positioning device.
2. Use identical coils for repeated longitudinal measurements.
3. Use a calibration phantom to cross-calibrate repeated measurements across scanners and different sites and to assess reproducibility of T1ρ and T2 measurements.
4. Install semi-automatic or automatic segmentation software that allows reproducible segmentation of the cartilage.

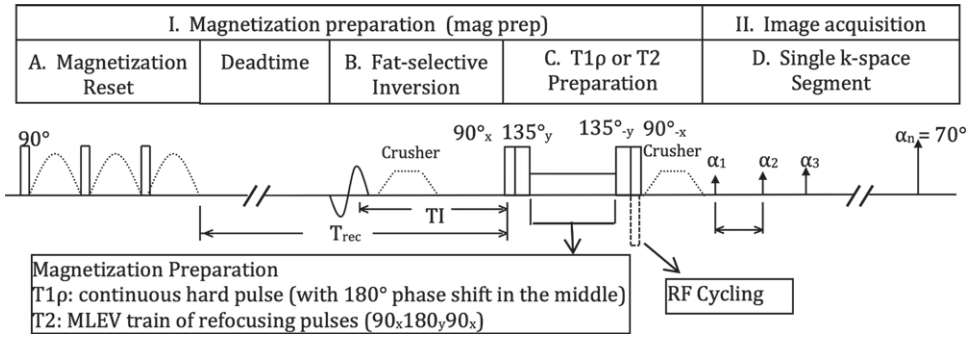

Figure 1: The magnetization-prepared angle-modulated partitioned k-space spoiled gradient echo snapshots–based spin-lattice relaxation time constant in rotating frame (T1ρ) and T2 imaging sequence is available as a research prototype by the three major MRI vendors including GE Healthcare, Siemens Healthineers, and Philips Healthcare Solutions. MLEV = Malcolm Levitt composite-pulse decoupling sequence, RF = radiofrequency.

Image Data Acquisition

Our recommendations (Table 5) for image data acquisition include the following:

1. T1ρ and T2 sequences are recommended to be based on the magnetization-prepared angle-modulated partitioned k-space spoiled gradient-echo snapshots acquisition (Fig 1).
2. High-spatial-resolution three-dimensional gradient-echo sequences are recommended (48) for registration with T1ρ and T2 sequences and to perform reliable and reproducible cartilage segmentation. In particular, fast acquisition double echo, dual-echo steady state, and multi-echo

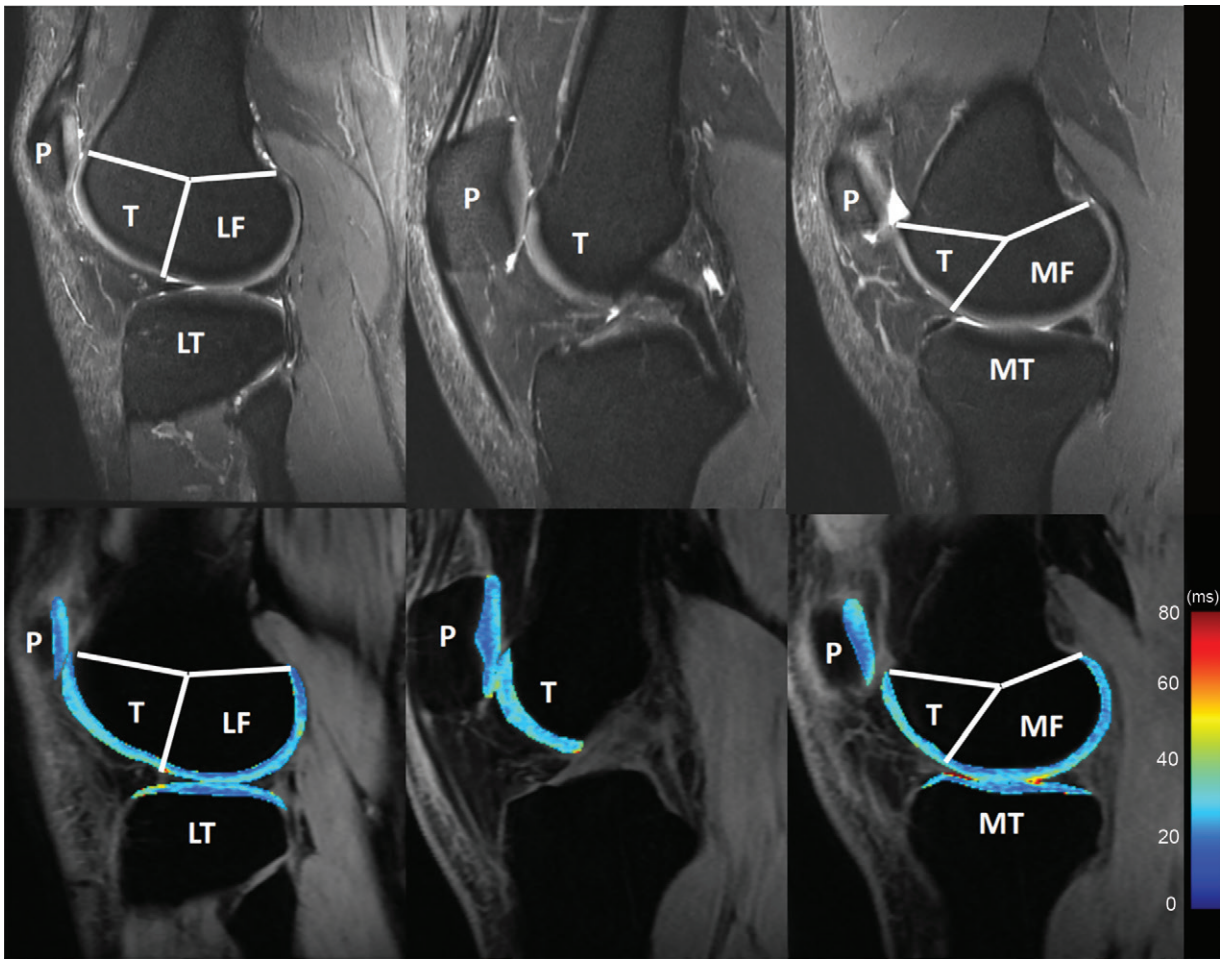

Figure 2: Knee cartilage compartments with anatomic labels implemented in lateral (left side), central (middle), and medial (right side) MRI obtained with an intermediate weighted fat-saturated fast-spin-echo sequence (top row) and a spin-lattice relaxation time constant in rotating frame (T1ρ) magnetization-prepared angle-modulated partitioned k-space spoiled gradient echo snapshots sequence (bottom row, T1ρ maps). Study was performed without administration of intravenous gadolinium-based contrast material. The lateral femur (LF)/medial femur (MF) and lateral tibia (LT)/medial tibia (MT) can be further divided into subcompartments on the basis of meniscus anatomy according to Eckstein et al. Source.—Reference 53. P = patella, T = trochlea.

in steady state acquisition sequences provides superior contrast between cartilage and fluid for segmentation.

3. It is recommended to scan the calibration phantom by using geometric structures included in the phantom for the high-spatial-resolution imaging for registration and cartilage segmentation.

The magnetization-prepared angle-modulated partitioned k-space spoiled gradient echo snapshots technique has been validated in multisite multivendor studies (27,39,42) and has a combined T1ρ and T2 mapping capability (40). Multisection multiecho sequences have been used to measure cartilage T2 value (49). Whereas multisection multiecho sequences have good reproducibility across different sites for one vendor (25), statistically significant differences in T2 measures have been reported between vendors (10%–25%) (50). Multisection multiecho sequences are also prone to variations introduced by stimulated echoes and magnetization transfer effects (51). Three-dimensional fast spin-echo sequences (such as CUBE and sampling perfection with application optimized contrasts by using different flip-angle evolution, known as SPACE) have been used for cartilage segmentation but tend to have signal loss in the deep cartilage layers (52).

Image Data Analysis and Interpretation

The following are our recommendations on image analysis and interpretation:

1. Global, knee compartment-specific, and focal (lesion-specific) cartilage analysis should be performed.
2. Semiautomatic or automatic segmentation software could be used. Six knee compartments are defined in Figure 2. The femoral and tibial compartments can be further divided into subcompartments on the basis of meniscus anatomy (53).
3. The region of interest could be manually drawn around areas of cartilage repair and evolving cartilage lesions for lesion-specific analysis (54). Surrounding cartilage should be segmented and used as a control region. "Surrounding" cartilage should include all the remaining and clearly distinguishable cartilage in one of the six knee compartments.

Table 6: Specifications for Imaging Requirements and Procedures

Parameter	Actor	Requirement
Imaging requirement	Scientist/physicist	As outlined in section 3.2 of the Profile, installation and initial functional validation is recommended to be performed according to manufacturer's defined procedures and specifications including specific guidelines for the MRI scanner include coils, sequences, and calibration phantom. The preferred field strength is 3.0 T.
Imaging procedure	Technologist/MRI operator	MRI technologists or other site personnel performing T1ρ and T2 MRI acquisition should be MRI-certified according to site-specific local or institutional requirements. These individuals should be trained or have prior experience in conducting T1ρ and T2 MRI acquisition as outlined in section 3.6 of the Profile. A standard imaging phantom for standardized image acquisition and processing procedures is required.

Note.—T1ρ = spin-lattice relaxation time constant in rotating frame.

4. The segmentations obtained should be overlaid on the first echo of the T1ρ- and T2-weighted images after registration.
5. Mean and standard deviation of T1ρ and T2 values should be measured for each defined compartment and the average of all compartments (55).

Image data interpretation will focus on longitudinal changes of the cartilage composition on the basis of the claims of the Profile. A large-scale normative cartilage T2 value database specific to age, sex, and body mass index is available on the basis of data from the Osteoarthritis Initiative (56). Currently, to our knowledge, there is no T1ρ and T2 normal reference database with the sequences proposed in this Profile. Development of a normal reference database is beyond the scope of this Profile but would be the next step in the clinical implementation of T1ρ and T2 measurements.

Assessment Procedures and Conformance

Procedures to assess test-retest conformance are in Appendix E1 (online). Table 6 depicts specifications for imaging requirements and procedures.

Limitations

First, the variability among vendors, centers, MRI scanners, and patients could limit the reproducibility of the claims of this Profile. Second, open source semiautomated or fully automated cartilage segmentation data set and analysis software is lacking, which may further increase variability among different centers.

Future Developments and Conclusions

Multiple studies and technological advancements that can be implemented in the next version of this Profile are under development. Compositional cartilage MRI data sets are available through the Osteoarthritis Initiative (57) and other multicenter studies (27). Moreover, continuous advances in technology (58,59) have made it feasible to take a stepwise approach to bringing quantitative cartilage imaging to the clinic. Further studies that provide normative data and cutoff values for MRI-based cartilage biomarkers to define abnormal cartilage compositional values and disease burden are required. Many of these studies are currently underway or in the planning stage:

1. A National Institutes of Health and National Institute of Arthritis and Musculoskeletal and Skin Diseases–funded multicenter calibration study is underway to standardize cartilage compositional MRI sequences across different vendor platforms. This will help to establish reproducibility of T1ρ and T2 values across different sites and vendors.
2. Also funded through the National Institutes of Health and the National Institute of Arthritis and Musculoskeletal and Skin Diseases, a calibration phantom is being developed to obtain reference measurements with T1ρ and T2 that makes data comparison between different sites and vendors feasible.
3. Development of single "best suited" and vendor-independent high-spatial-resolution three-dimensional MRI sequence for cartilage segmentation and registration is another goal of the QIBA MSK Biomarker Committee to further improve reproducibility and standardization of MRI cartilage composition.
4. Machine learning–based image reconstruction algorithms are being developed for automatic cartilage segmentation, cartilage lesion detection, and differentiation of different musculoskeletal anatomies (58,60–65).

Successful accomplishment of the claims of this Profile and these four steps will expedite establishing normative data and cutoff values for MRI-based cartilage biomarkers to define pathologic structure (12). Large-scale validated quantitative biomarker data could be used to improve risk prediction models for clinical use such as the Tool for Osteoarthritis Risk Prediction model developed on the basis of study participant characteristics, knee radiographs, and MRI data (66).

The current version of the Quantitative Imaging Biomarkers Alliance (QIBA) Profile for MRI-based cartilage compositional imaging provides practical recommendations for standardized cartilage compositional imaging, which can be used clinically, for research, and for developing drugs. The proposed claims could be used for longitudinal clinical evaluation and research (67). We acknowledge that it is challenging to follow the proposed claims outside specialized scientific and research centers at this time. However, we believe that with recent advancements in MRI techniques, artificial intelligence and deep learning–based algorithms are promising tools to overcome these

obstacles that will be available in the near future. This Profile will be updated periodically on the basis of emerging data and advances in technology. We believe QIBA Profiles including the presented work provide roadmaps for implementation of quantitative imaging in clinical practice and a robust foundation for technology advancements and precision medicine.

Acknowledgments: We thank all the individuals and institutions that provided us with their invaluable comments on the publicly available version of the MSK QIBA Profile. We are particularly grateful for the assistance and diligent support provided by the RSNA staff and QIBA leaderships.

Author contributions: Guarantors of integrity of entire study, M.C., X.L., A.G., T.M.L.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, M.C., X.L., A.G., J.A.C., T.M.L.; clinical studies, M.C., A.G.; experimental studies, M.C.; statistical analysis, M.C., N.A.O.; and manuscript editing, all authors

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Disclosures of Conflicts of Interest: M.C. disclosed receiving the RSNA R&E Research Scholar Grant. **X.L.** disclosed no relevant relationships. **A.G.** disclosed consultancies from Pfizer, AstraZeneca, Regeneron, Novartis, MerckSerono, TissueGene; stock/stock options from BICL; is member of the *Radiology* editorial board. **N.A.O.** disclosed money paid to author's institution from RSNA because the author is a statistical consultant for QIBA through a contract between Cleveland Clinic and RSNA. **J.A.C.** disclosed consultancies from Pfizer, Covera, Globus, Simplify Medical; disclosed travel/accommodations/meeting expenses from Carestream, Image Analysis Group; disclosed that author is a deputy editor for *Radiology*, associate editor for *Arthritis and Rheumatology*. **E.H.O.** disclosed no relevant relationships. **T.M.L.** is member of the *Radiology* editorial board.

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