Commenter	Section	Line #	Priority	Issue	Proposal	Committee Discussion	Resolution (w Rationale if rejected)	Status
See http://qibawiki.rsna.org/index.php/Public_Comment_Process for more guidance on the comment resolution process						*OK = No action requested	17	OK
						*Done = Profile update completed	42	Done
Andrea Falkoff, MBA	Section 2, Discussion	175	L	I believe there is a correction needed here 'However, if cartilage composition changes size beyond these limits, you can be 95% confident there has been a true change in the size of the tumor'. I don't think 'tumor' is the correct reference.	Instead of referencing 'tumor' I believe it should be 'lesion' or change in cartilage loss	thank you for catching this	typos will be corrected	done
Andrea Falkoff, MBA	3.1.2 Specification	210	L	Typo in 'radiologist': 'Shall undergo documented training by qualified physicist/radiolgist..'	Shall undergo documented training by qualified physicist/radiologist..'	thank you for catching this	typos will be corrected	done
Andrea Falkoff, MBA	3.5.2 Specification	340	L	Typo in 'rest': 'Need to make sure that patient rest 30 minutes before...'	Need to make sure that patient rests 30 minutes before...'	thank you for catching this	typos will be corrected	done
Andrea Falkoff, MBA	3.6 Image Data Acquisition	355	L	Fig 1 typo in Siemens: 'The MAPSS-based T1ρ and T2 imaging sequence is available as research prototype by the three major 360 MR vendors including GE, Simens and Philips.'	The MAPSS-based T1ρ and T2 imaging sequence is available as research prototype by the three major 360 MR vendors including GE, Siemens and Philips.'	thank you for catching this	typos will be corrected	done
Yuxi Pang, PhD	NA	NA	L	To reduce an MR relaxation metric variability across the multi-site studies, it is better to limit the number of acquisition variables as small as possible. This is particularly true for the proposed T1rho and T2 mapping. Given that T2 could be treated as a "specific" T1rho with a spin-locking amplitude (ω_1/2π) of zero, T2 could be, in theory, derived from T1rho "dispersion" (by curve fitting) using only the proposed T1rho sequence. Here are two arguments for considering the removal of the proposed CPMG-based T2 mapping sequence. First, for clinical MR scanners, the durations of the employed RF pulses in composite (i.e. 90x180y90x) CMPG sequence cannot be considered "negligible", and thus a TE-correction scheme was introduced by assuming a constant T1/T2 ratio. It is well-known that T1 is mostly constant in human knee cartilage; however, T2 is orientation-dependent due to the magic angle effect (MAE). Therefore, the proposed TE-correction will introduce some spatially dependent systematic errors. Second, the "spin-locking" effect in the proposed T2 mapping has never been discussed. As an interval between the centers of two adjacent 180 pulses becomes shorter, CPMG pulse will behave increasingly like a spin-locking sequence. It is unclear to what extent that the proposed T2 mapping approaches to T1rho measurements. REFERENCES 1.Wyatt C, Guha A, Venkatachari A, Li XJ, Krug R, Kelley DE, Link T, Majumdar S. Improved differentiation between knees with cartilage lesions and controls using 7T relaxation time mapping. J Orthop Transl 2015;3(4):197-204. 2.Kim J, Mamoto K, Lartey R, Xu K, Nakamura K, Shin W, Winalski CS, Obuchowski N, Tanaka M, Bahroos E. Multi-vendor multi-site T1ρ and T2 quantification of knee cartilage. Osteoarthritis and Cartilage 2020.	In short, it would become more efficient and accurate to derive both T2 (ω_1/2π=0) and T1rho (ω_1/2π=500Hz) using only one pulse sequence (MAPSS T1rho) by varying only ω_1 in image data collection (keeping TSL constant).	Using only one 180 refocusing pulses for T2 prep would significantly underestimate T2 in vivo due to diffusion effect, field inhomogeneity etc. And these are reasons that CPMG becomes the 'gold standard' method for T2 measures in the field. During the committee discussion, Dr. Pang also mentioned the idea of characterizing T1rho dispersion and then extrapolate T2 from it. It is an attractive idea, which however needs further development and validation. For the potential "spin-locking" effect in CPMG sequence, Santry et al suggested 'These findings demonstrate that the conditions for spin locking with the CPMG sequence are satisfied in tissues (include leg muscle which has similar T2 compared to cartilage) for Tcp (time between 180 refocusing pulses) <= 0.25ms' . The time interval between 180 refocusing pulses in MAPSS T2 is approximately 5ms, which is much larger than 0.25ms, and thus the SL effect would be minimal. Ref: Santyr GE, Henkelman M, Bronskill MJ. Variation in measured transverse relaxation in tissue resulting from spin locking with the CPMG sequence. J Magn Reson 79, 24-88, 1988. Sensitivity tests have been performed to evaluate potential bias introduced by T2 variation to the corrected TE and consequently fitted T2. In the paper by Kim et al OAC 2020, T1/T2=40 (assuming T1=1.2s and T2=30ms) was used. Sensitivity test was performed assuming T2=60ms. With this doubled T2, the CV of fitted T2 btw T1/T2=40 and T1/T2=20 is less than 0.6%, suggesting minimal bias that will be introduced to the fitted results through assumed T1/T2 values and corrected TEs.	no action needed per committee discussion	done
Yuxi Pang, PhD	3.8	NA	M	Another comment is about T1rho/T2 image data interpretation (Part 3.8). Although this Profile avoids the "controversial topic", i.e. what does T1rho/T2 really measure in cartilage? it is necessary to advise the perspective users to take MAE into account when evaluating the longitudinal changes of cartilage composition. Specifically, for the intra-subject T1rho/T2 changes, MAE is anticipated to be small when the same imaging protocol is always followed. However, for inter-subject T2/T1rho changes, cautions should be excised when interpreting the results even the same imaging protocol is used. This is because that the potential orientation-dependent factors, e.g. varied femoral bone shapes, may play a role in the observed changes in T2 values (or T1rho values to a less extent).	None provided	The focus of the profile is to make recommendations on data acquisition and processing of cartilage T1rho and T2 measures. The specific mechanism of T1rho and T2 relaxation time in cartilage is a topic with active research in the field, which is not the focus of this profile. Magic angle effect will introduce variation in T1rho and T2 measures and the discussion on MAE will be added in the profile.	The discussion below has been added to Section 3.7.1. Magic angle effect, or the orientation dependency to collagen fibers, have been observed in T2 and T1rho imaging (1-3). The orientation dependency is less in T1rho imaging due to the spin-lock compared to T2 imaging (4), and such orientation dependency diminished at spin-lock frequency higher than 1KHz (2) or 2KHz (4). Consistent knee and feet positioning during data acquisition and matched-region analysis during data processing are strategies to minimize the effect of magic angle effect on data interpretation. 1. Li X, Cheng J, Lin K, Saadat E, Bolbos RI, Jobke B, et al. Quantitative MRI using T1rho and T2 in human osteoarthritic cartilage specimens: correlation with biochemical measurements and histology. Magn Reson Imaging. 2011;29(3):324-34. 2. Wang N, Xia Y. Anisotropic analysis of multi-component T2 and T1rho relaxations in achilles tendon by NMR spectroscopy and microscopic MRI. J Magn Reson Imaging. 2013;38(3):625-33. 3. Shao H, Pauli C, Li S, Ma Y, Tadros AS, Kavanaugh A, et al. Magic angle effect plays a major role in both T1rho and T2 relaxation in articular cartilage. Osteoarthritis Cartilage. 2017;25(12):2022-30. 4. Akella SV, Regatte RR, Wheaton AJ,	Done

EIBALL - Mr. Jonathan Clark	NA	NA	NA	The profile provides important recommendations for one of the most active areas in MSK imaging research - quantitative, compositional, MR for knee cartilage - particularly for longitudinal multi-centre trials. Although the profile is also intended to apply for clinical practice, there is no solid evidence regarding utility of such techniques for routine clinical care.	None provided	These are good points. However, it is noted that there is a T2 mapping product sequence which is used by clinicians.	No action requested	OK
EIBALL - Mr. Jonathan Clark	NA	NA	NA	Two specific biomarkers, T2 and T1rho mapping, are proposed, both of which seem to be reasonable choices based on the currently literature. However, sensible alternative techniques for compositional cartilage MRI are available (e.g. GagCEST, sodium MRI, dGEMRIC, and few others) with active research going on in each of these methods. There is insufficient mentioning of the pros and cons of T2 and T1rho relative to these alternatives, and a solid motivation for the choice of T2 and T1rho as the proposed biomarkers is lacking.	A more balanced introduction with overview of available techniques is encouraged.	Alternative sequences were not discussed in much detail as limited reproducibility data is available. (Also response to Garry Gold's comment)	Expand introduction to include other sequences	done
EIBALL - Mr. Jonathan Clark	NA	NA	NA	A very specific pulse sequence (MAPPS), currently a research sequence, is proposed for T2- and T1rho mapping. Although the involvement of Siemens, GE and Philips in ultimately incorporating this sequence in their systems is applauded, it is somewhat concerning that the sequence is currently not generally available to researchers world-wide. The sequence currently only is available through bilateral collaborations with authors of the profile, with the support of vendors.	None provided	This is correct and a current limitation of this technology. However, information about access to this research sequence from different vendors is available in the profile.	No action requested	OK
Richard J Martin, JD (on behalf of AAPM)	NA	P4 L74	NA	Physicists are involved in designing/optimizing the protocols	They should be listed among impacted stakeholders here.		add physicists	done
Richard J Martin, JD (on behalf of AAPM)	NA	P5 L80	NA	11-14% precision seems a little too much. This value appears to be derived from Appendix B and most of those references are old references.	We recommend against using the precision of 11-14%	11-14% is the minimum detectable difference in T2 and T1rho values in a single patient in longitudinal scans, which can be used as a basis for defining response/progression criteria for quantitative cartilage imaging. Clinical trials with larger sample sizes could potentially detect smaller differences based on the sample size, inter-subject and within-subject coefficient of variations. will add updated references in Appendix B	change according to Nancy's comments in the Majid's paper -added 9-12% if only increase is expected (claim is one-sided), and added the following to Important considerations and limitations under the Claims: '11-14% (two-sided) or 9-12% (one-sided) is the minimum detectable difference in T2 and T1rho values in a single patient in longitudinal scans, which can be used as a basis for defining response/progression criteria for quantitative cartilage imaging. Clinical trials with larger sample sizes could potentially detect smaller differences based on the sample size, inter-subject and within-subject coefficient of variations.' Added updated references in Appendix B	done
Richard J Martin, JD (on behalf of AAPM)	NA	P5 LL80, 81	NA	For the same manufacturers, different scanner models may have to use different parameters because the hardware and software are different. For example, 60cm vs. 70cm bore size, different Slew rate and Gradient performance, old software vs. new software.	Reference 5 in Appendix B should support this claim.	The difference slew rate and gradient performance will result in different min TR and TE in the readout, which however has minimal effect on T1rho and T2 quantification using MAPSS structure. For other parameters as listed in Table 3, including Matrix, number of slices, slice thickness, FOV, BW, TSL and prep TE, the same parameters shall be set up and used among different scanners used in one study/trial.	Added discussion in Section 3.6	done
Richard J Martin, JD (on behalf of AAPM)	NA	LL89, 90	NA	The goal of this document appears to be for clinical practice and that point should be clearly stated.	Please clarify "While the emphasis is on clinical trials, this process is also intended to apply for clinical practice."	change wording	modify as suggested	done
Richard J Martin, JD (on behalf of AAPM)	NA	P7 LL134-137	NA	Both claims of T2 and $T1_\rho$ variations are within 4~5%, however, there are not many vendors providing $T1_\rho$ methods.	Please specify how you can achieve this goal in general clinical practice.	using sequences by manufacturers, as outlined	acknowledge as a limitation - contact details provided - will in the future modify profile once manufacturer's provide this as a commercial product	done
Richard J Martin, JD (on behalf of AAPM)	NA	P8 LL159	NA	Lack of reference values for your calibration phantom of T2 and $T1_\rho$.	Please provide reference values for your calibration phantom of T2 and $T1_\rho$.	new phantom	no reference values at this stage, new phantom from NIST will have reference values, will be provided once phantom is finalized (expected in 2021)	done
Richard J Martin, JD (on behalf of AAPM)	NA	P8 L161	NA	The impact of segmentation on T2 and $T1_\rho$ values is obvious.	Please clarify whether the software has been validated.	The variations of T1rho and T2 values with different time of recovery, views per segment, with and without parallel imaging accelaration have been tested in Ref 3 (Kim et al OAC 2020). Average CV =0.4% was reporting, suggesting minimal variations with changes in these parameters.	add discussion in 3.6.1	done
Richard J Martin, JD (on behalf of AAPM)	NA	P10 L191	NA	Missing actors in Table 1	In Table 1, add physicists or MRI scientists to install WIP sequences or tools, check the QC,and verify the T2 and $T1_\rho$ values.		add physicists	done
Richard J Martin, JD (on behalf of AAPM)	NA	P11 L197		Clarification needed...	Please clarify "how study sponsors and others decide to handle deviations...". Specify what kind of deviations.	deviations were discussed	we added the following text to the profile: "...such as changes in the acquisition or image analysis protocols..."	done
Richard J Martin, JD (on behalf of AAPM)	NA	P12 L238		We question whether "A R01 grant...." should be included in this profile now.		remove R01 grant and reword as funded study	remove R01 grant and reworded as funded study	done
Richard J Martin, JD (on behalf of AAPM)	NA	P13 LL240-245			In the table, we suggest changing “MR Physicist” to “MR Scientists/Physicist.”		done	done
Richard J Martin, JD (on behalf of AAPM)	NA	P13 LL240-245		In the table, there are a lot of segmentation tools.	It should state the specific image analysis tool.	no standardized segmentation tools	require performance - see comment 23	done
Richard J Martin, JD (on behalf of AAPM)	NA	P14 L255		Term used.	“ACR Phantom” should be changed to “small ACR phantom” or “ACR phantom for knee coil.”		done	done
Richard J Martin, JD (on behalf of AAPM)	NA	P14 L260		We question whether human volunteer studies should be performed before and after changes.		remove human volunteers, only calibration phantoms		done
Richard J Martin, JD (on behalf of AAPM)	NA	P14 L272		Specify how to measure the eddy current and how to perform the gradient calibration.	Provide instructions.	The committee will revise the lanaguage and will not recommend that the site measures eddy current or performs gradient calibration. Per recommendations from the OAI paper (Schneider et al 2008), measurements such as ghosting shall be performed. The MR system characteristics that were found to affect the ghost level were mechanical vibration and eddy currents. If the measures exceed the set threshold (for example ghosting level > 0.5%), a service call shall be made.	Rewording as ''Measurements should include signal-to-noise ratio (SNR), signal uniformity, spatial accuracy, and ghosting as suggested in (6, 7)"	done
Richard J Martin, JD (on behalf of AAPM)	NA	P15 LL290-295		Specify how to define the calibration factor.	We suggest using the phantom data or volunteer data to define the calibration factor.	NIST phantom and volunteers work in progress	limitation - needs new phantom	done
Richard J Martin, JD (on behalf of AAPM)	NA	P16 L300			We recommend listing the subject selection conditions.	add more detailed subject selection	change language	done

Richard J Martin, JD (on behalf of AAPM)	NA	P17 LL320-323		It seems the activities before the exam affect T2 and $T1_\rho$ values significantly.	Please specify whether the environment temperature is also affected. Please list the difference if there is no seated position prior to the scan for 30 minutes.	No studies in the literature reported changes with and without seated position for 30 mins prior to MR scans. Taylor et al reported ~7% changes in T1rho with daily activities. Although T1rho and T2 values are affected by temperature, as shown in the abstract by Hardy et al, the committee did not think the environment temperature in the scanner room will have a noticeable direct effect on body temperature nor T1rho and T2 values.	added refererence on T1rho and T2 changes with loading (running or daily activities). Added discussion in the temperature paragraph, information from Peter Hardy's poster was added and the poster was referenced.	done
Richard J Martin, JD (on behalf of AAPM)	NA	P19 L380		MSME is a product for T2 mapping on most of MRI scanners, but the final values here are different among different vendors.	Please specify whether this is because of the fitting methods or scanning parameters or the sequence design. This document gives the scanning parameters. We recommend providing the offline fitting/post processing method for different vendors.	The difference was because different fitting methods by different vendors but also different software/hardware imperfection on each MR systems as the sequence is known to prone to bias introduced by stimulated echo due to imperfect refocusing and magnetization transfer, as discussed in 3.6.1. It was not sure whether this needs to be implemented as this sequence is not recommended in this profile (although it has been discussed as an option if MAPSS sequence is not accessible)	none taken, given that this sequence was not recommended in the profile.	done
Richard J Martin, JD (on behalf of AAPM)	NA	P25 L484			Please give the recommendation clearly rigid vs. non-rigid registration.	add more details and references for registration	added more details and two more references for registration	done
Richard J Martin, JD (on behalf of AAPM)	NA	P26 L495		In the table, it states to perform the segmentation manually, however, in the text, a lot of places reference only semi-automatic segmentation.	Please clarify.	manual for focal lesions	Table 1 was modified and manual was removed for global analysis	done
Richard J Martin, JD (on behalf of AAPM)	NA	P33 L662		Do not say “new surface coil.”	We recommend saying “new coil” or “new knee coil.”		"surface" was removed and replaced by "knee"	done
Richard J Martin, JD (on behalf of AAPM)	NA	P33 L672		Should be $T1_\rho$, not T1p.	Make update	typo	corrected	done
Garry Gold, MD, PhD (Stanford)	NA	NA		I wanted to bring to your attention an important point around pulse sequences for T1rho and T2. Although MAPSS has been widely used and is the most published method, there are many methods out there of rapid T1rho and T2 acquisition. Different groups and different platforms have different methods. My own group has use many different acquisition methods, and more are under development to improve acquisition speed, resolution, or other factors. Instead of specifying MAPPS as the recommendation specifically, can we say something like “T2 and T1rho data acquired with XX resolution, etc. that shows repeatability similar to the MAPSS method”? That leaves space for continued development and application to machine learning and AI methods to the field. Ultimately, we’d like these methods to be widely available and its possible that GE, Philips, and Siemens may adopt other methods for T2 and T1rho in product in the future.	Add other available methods or methods under development.	The reason the committee made the recommendation on MAPSS in the current profile, after much discussion, is because as you pointed out that MAPSS is the most published 3D T1rho and T2 method, and because it is the only sequence that has published data on inter-site and inter-vendor reproducibility and the QIBA claims are based on these reproducibility data. QIBA profiles recommend specific acquisition protocols that have been applied in multiple studies, have solid reproducibility data and are straightforward for potential future users to follow. The committee also agreed that other availabe methods and methods under development without intersite intervendor reproducibility data yet shall be added to discussion.	We will add in the Discussion other available methods or methods under development, but without intersite intervendor reproducibility data. Research is in flow and the committee can provide updates in future profiles to include the newer sequences especially if the vendor come up with some products and intersite reproducibility data is available.	done
Takatoshi Aoki, Tsutomu Inaoka (Japanese QIBA)	NA	NA		Thank you very much for your E-mail of September 12, 2020. We have read the profile. We think that it is absolutely fine. Thank you again for giving me this kind of opportunity. We look forwarding to your ongoing support.	none provided	n/a	none required	OK
Frank W. Roemer, MD	3.7	458/459	M	Segmentation from high Resolution 3D GRE MRI	„The segmentation shall be overlaid to T1ρ and T2 maps”- While agreeing that this should be ideal in reality this is a very challenging task that needs co-registration particularly as the 3D GRE images have much higher resolution /thinner slices compared to the T2 or T1rho images. Sugges to add word “ideally” as first word of sentence.	Segmentation using T1rho and T2 MAPSS sequences. Preferred method is using high resolution preferred MENSA-GE and DESS-Siemens, which are good concerning spatial resolutionand and contrast (or alternatively fat sat CUBE - but this may not be as good).	Protocol will be modified: DESS/MENSA are recommended (different vendor implementations) as they provide good spatial resolution and contrast - MAPSS should not be used for segmentation. "Ideally" will be added to the protocol.	ok
Frank W. Roemer, MD	3.7	Fig. 2	L	yellow marking for lateral femur should not nclude anterior subregion/anterior lateral trochlea but only central and	re-draw Image marking for lateral femur	need to correct Figure 2	Figure 2 was corrected.	ok
Frank W. Roemer, MD	3.8.1	Table1 and Figure 4	M	normative values grouped for KL0 and 1	Current understanding likely implies that KL0 and 1 should be treated as separate stages of pre-OA. While KL0 implies no signs of OA on the X-ray KL1 includes presence of an equivocal osteophyte and may be considered early disease. Prevalence of morphologic cartilage damage (e.g. as scored by SQ assessment) is higher in KL1 than 0. Would suggest to present and aim at displaying KL0 and 1 as separate entities.	Table refers to WORMS 0 and 1, not KL 0 and 1.	no modification required.	OK
Frank W. Roemer, MD	4.1.3	Feature extractio n beyond T2 and T1rho values	M	relevance of exploring additional data extraction	Please see example publications (and others) by Joseph et al Arthritis Res Ther. 2011;13(5):R153. doi: 10.1186/ar3469. or recent PNAS paper by Kundu et al Proc Natl Acad Sci U S A. 2020 Sep 21:201917405. doi: 10.1073/pnas.1917405117	Texture analysis of cartilage T2 maps - should we include this	add to discussion - provide good additional information but are not well standardized - include studies - discuss problems.	OK
Gregory Chang, MD	Image Data Analysis	480	L/M	Since the document also addresses clinical trialists, rheumatologists, orthopedists, it would be helpful to direct them toward software that can perform the image analysis.	Provide short list of software that can do the image analysis, e.g. Siemens MapIT, Matlab, etc.	Vendors have inline reconstruction of T2 maps such as GE Cartigram, Siemens MapIt, and Philips T2 mapping . But no product available by manufacturers for cartilage segmentation	add to discussion - provide good additional information but are not well standardized - include studies - discuss problems, also added Cartigram from GE, MapIt from Siemens, and T2 mapping from Philips	ok
Gregory Chang, MD	Image Data Analysis	465	L/M	Semi-automatic or automatic segmentation software is mentioned.	It would be great to also list software for the segmentation, if different from above.	see above		ok
Gregory Chang, MD	Image Data Acquisition	380	L/M	Should the recommendation for number of echoes be mentioned?	Specify recommended number of echoes.	minimum of 4 echos is recommended - as shown in Table 3, default - for reproducible measurement of mono-exponential decay components 4 echos is minimum	4 echos is minimum - can be increased up to 8 - 4 echos is default - reproducibility for 4 echos is good - 8 may provide more in depth information about cartilage degradation - but this active area of research- was added to discussion 3.6.1	ok
Gregory Chang, MD	Installation	220	L/M	Even different model 3T scanners from the same vendor could demonstrate variation in measurements. Rheumatologists and orthopedists may not be aware.	Clarify that even within a vendor, different model 3T scanners could increase variability in measurements.	same vendor and field strength scanners have variability in measurements	highlight this in profile - different models from same vendor and different machines, same model have differences	ok
Flavia Cicuttini, PhD, MSc	General comment	N/A	H	The approach presented in this document is a very good general approach and guideline.	However it may need to be acknowledged that if there is the need to examine change, groups who do work on the same machine, using a standard protocol and measurement approach may be able to assess the state of the cartilage and detect clinically significant changes using modifications of the approach presented.	good point where should we acknowledge this - our claim is longitudinal	This comment was added to the discussion	Ok

Flavia Cicuttini, PhD, MSc	N/A	145	N/A	The Claim requires presence of a significant amount of cartilage to be present and that there is no significant loss of cartilage volume and there are no major defects in the measured area. In order to focus on subjects with less severe cartilage loss, analyses should be restricted to patients with Kellgren-Lawrence (KL) Score of 0-2.'	KL 2 can be associated with significant cartilage loss. The authors need to provide evidence that the Claim is valid in the setting of KL2.	Heterogeneity of cartilage damage in KL2 knees and recent research work by Roemer et al were discussed.	Limitations with KL 2 knee inclusion were added in the claims section both in the "Important considerations and limitations" and "discussion" sections": While KL Score 0-2 knees are recommended to be included it needs to be considered that patients with KL2 knees not infrequently have regions with full thickness cartilage loss. According to work by Roemer et al. approximately 25% of knees with KL2 have wide-spread full thickness cartilage loss in the medial femoro-tibial joint compartment (mFTJ) and 11% in the lateral femora-tibial joint compartment (lFTJ) {Roemer, 2021 #1555}. Regarding absence of cartilage damage 20% of KL2 knees do not exhibit any cartilage damage in the mFTJ, while these numbers are 40% for the lFTJ and 15% for the patella-femoral joint compartment (PFJ). One third of KL2 knees exhibit only minimal cartilage damage in the MFTJ. Given the heterogeneity of cartilage damage in KL2 knees, radiography as an instrument to define which patients should undergo compositional cartilage imaging has limitations which need to be acknowledged.	OK
Flavia Cicuttini, PhD, MSc	N/A	175	N/A	The 11-14% boundaries can be thought of as "error bars" or "noise" around the measurement of compositional change. If you measure change within this range, you cannot be certain that there has really been a change. However, if cartilage composition changes size beyond these limits, you can be 95% confident there has been a true change in the size of the tumor	Is 'tumor' a typo? Also can the authors clarify the difference between identifying true change in an individual compared to average change that may be detected across 2 groups eg in a clicnal trial.	tumor was corrected - needs a biostatistician - changes in a clinical trials may be smaller	address clinical trial issue - can detect smaller changes- this was added under" Important considerations and limitations".	ok
Flavia Cicuttini, PhD, MSc	General comment	N/A	N/A	This is an important and timely document.	N/A			ok
Samuel A. Einstein, PhD	2	146	H	The studies supporting the claims are based on phantoms and a few healthy volunteers (i.e. no pathology, implants, poor positioning due to patient discomfort, etc.), yet these claims seem to be applied to the clinic. How can you justify these claims in a clinical setting based on the limited data in the references?	N/A	larger studies underway	will be addressed with new studies that are work in progress	ok
Samuel A. Einstein, PhD	3.2	217	M	Additional requirements for hardware specifications needed	Please provide additional requirements for hardware specifications such as for the RF amplifier and gradient performance.	varies from scanner - no specific requirements	if the sequence runs on scanner there is no need to specify RF and gradient details	ok
Samuel A. Einstein, PhD	3.3.1	288	M	Won't partial pressure of oxygen changes also have a significant effect on T2 if bacteria start growing in the agarose when stored at room temperature?	N/A	The committee acknowledged it is a viable concern. Comments from NIST: Agar (which consists of agarose + agaropectin) is susceptible to bacterial growth. For the proposed phantom, we use agarose (not agar) with GdCl3 and EDTA. EDTA is used here to complex with the GdCl3 and prevent breakdown of the agarose bonds (which would cause the gel to degrade). EDTA is also considered a bacterial growth inhibitor. Additionally, the preparation process involves elevated temperatures to above those used for pasteurization and renders the gels free from bacteria. We use Good Manufacturing Processes (GMP) to ensure all parts and supplies are clean and free of contaminants when assembling the phantoms. This prevents potential recontamination of the gels. Finally, the gels are placed in clean storage tubes with a tight seal. NIST has successfully used this protocol to create agarose + Gd-EDTA gels that remained free of bacteria growth at +3 years (to date). At the same time that the samples are prepared for the phantom, samples will be prepared in NMR tubes. The T1, T2, and T1rho relaxation times will be measured on the NIST NMR system at the initial time point (just after the gels are made) and at a minimum a subset of the samples will be remeasured each six months for an anticipated duration of 2-3 years.	No action required	done
Samuel A. Einstein, PhD	3.3.2	294	M	N/A	Please consider adding the ACR definition of MR scientist as a potential physicist qualification.	scientist was changed to physicist		ok
Samuel A. Einstein, PhD	3.6	355	M	This looks like a high-SAR sequence.	Please provide typical SAR values and, if typical SAR is high, recommendations for reducing SAR if necessary (e.g. should the flip angle be reduced? Matrix reduced? What won't affect the relaxation time constant measurement?).	The local extremety SAR using the transmit/receive knee coil and recommended MAPSS protocol with spin-lock frequency at 500Hz is <20% of the safety limit. When the body transmit and receive-only flex coil is used, at some systems, the MAPSS will not able to run at SL frequency at 500Hz, either due to SAR exceeding safety limit or RF amplifier fault. In such case, it is recommended to reduce the SL frequence to 400Hz. It needs to be noted T1rho values will decrease with SL frequency of 400Hz as compared to 500Hz. Again, it is strongly recommended to keep consistent coil and protocol for data collection for each single study. In MAPSS-T1rho-T2 mapping sequence, the read out is gradient echo acqusition with small flip angle trains. We do not recommend to reduce flip angle or matrix to reduce SAR.	add discussion in 3.6.1	done
Samuel A. Einstein, PhD	3.6.2	409	M	I may be missing something obvious, but I don't see a spin-lock frequency recommendation. Are you using 500 Hz? Or adiabatic pulses?	Please provide missing info	500Hz or 400Hz (for flex coil if 500Hz doesnot work) is recommended based on studies in the literature	Spin-lock frequency of 400Hz or 500Hz is added to Table 3	done
Eric Y Chang, MD	3.3	289	M	"Temperature has a significant impact on relaxation times." Recommend a little expansion of this sentence. Preceding paragraphs describe numeric results in reasonable detail, but this sentence just cites personal communication without detail provided as to what constitutes "significant impact." Ref 9 is a 36 year old article that only covers up to 100 MHz (although the recommended field in the document s 3T). Some questions include: what is the recommended Zone IV temperature range? Within this range could there be "significant" differences in results, and for which of the measures? Also, is there a usual temp difference between Zones IV and the lower Zones? Finally, what about differences in temperature in the patients? Intra-articular temps in the knee in OA patients can range from 30.1 - 36.9C (95% CI). (Ref: Ammer K. Temperature of the huma knee - a review. 2012 Therm Int)	Proposed changes are included in documentation of issue <-------	Peter Hardy - address temperature issue in more detail - was published as AAPM abstract - implement in profile - discussion with Michael Boss - older literature from John Gore	added details in 3.3.1 on effect of temperature of relaxation time with results from Hardy's abstract and more references	done
Eric Y Chang, MD	3.8.1	512	M	Why is the lower portion of the age range specifically set at 20?	Set at 18	age	age was changed	done
Eric Y Chang, MD	4.2	666	L	N=40 "normal subjects." Perhaps better to keep consistent with line 659 where it state a group of "healthy volunteers."	Change to "healthy volunteers"		changed language to healthy volunteers	done
Jason Kim, PhD	3.3	255	M	Concern about shelf-life from phantom supplier; Is there not a time for breakdown of agarose? How many uses does the phantom have?	The supplier of phantom should establish a lifetime for the phantom and/or re-calibration process	Question for NIST was discussed, overlaps with comment 56.	see above - comment 56	done
Jason Kim, PhD	3.3	260	M	Regarding coils and other equipment: Perhaps the indication for the profile (or another specification in the future) should be directly specifically toward knee OA? This would help lock the type of acceptable coils and other equipment	focus on a specific indication; this would be aligned for an FDA approval possibly?	specify that claims apply to the knee	Title was changed to include knee	done

Jason Kim, PhD	3.5	320	L	Clarificaiton on seated position for 30 minutes	Clarify if patient can walk to the scanner? Or seated the entire time??	patient can walk to scanner, prescanning before T1rho/T2 includes 10-15 minutes morphological imaging which adds to rest time but may increase motion artifacts.	walking to the scanner and acquisition of morphological sequences before T1rho/T2 sequences was added to the profile.	done
Jason Kim, PhD	3.5	325	L	What is the spec of the sandbag?	Adding some details of sandbags would minimize variation	sandbags are standard MRI equipment	more detailed information was provided	done
Jason Kim, PhD	3.8	505	H	Reference interval is critical	Disagree that the reference interval is out of scope. Even if the ideal population is not captured, some effort should be placed to establish a reference interval.	reference database would require an additional study - reference data available for OAI study	is beyond the scope of the profile, but required to clinically apply the technology	done
Jason Kim, PhD	4.1.1	630	M	List of acceptable hardware/software should be identified.	Make a list of acceptable hardware/software; If list is not comprehensive to cover all users, the users should use "at-risk" or better yet repeat the various verif/valid studies to show equivalence (and submit to qiba group to expand list)	MR scanners- software - coils - analysis software - needs more detail - focus needs to be on phantoms - limited literature	more detail about MRI scanners and NIST phantom was added (under 4.1.1. imaging equipment and 3.2. Installation)	done
Ashley Williams	2	175	L	"site of tumor"	fix this typo?	typo	corrected	done
Ashley Williams	3.4.1	315	M	effects of metal artifact(s) from metal implants, surgical hardware, shrapnel, etc on calculated T1rho, T2 values or on high-res GRE morphology images	guidance needed on how to handle interpretation of relaxometry values in presence of metal artifacts	metal artifact - depends on implants titanium, ceramic may work - steel and cobalt-chromium should be excluded - ACL reconstruction - parts of the knee may need to be excluded -	added to profile: compartments that are affected by metal artifacts shall be excluded during data analysis.	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	2	134-143	M	Definition of CV	Specify how CV's are defined (ROI size, topographical location, tissue depth, joint surface, etc.)	CV are defined using mean values from defined cartilage compartments	added specifics that CV will be calculated using mean values from cartilage compartments as defined in section 3.7	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	2	161	M	cartilage segmentation	Provide argument for using only semiautomatic/automatic segmentation. Automatic segmentation tools are time efficient, but not necessarily always more accurate than manual segmentation, which is still considered the gold standard. Minimum requirements (performance, reproducibility) for the dedicated software should be added	we can include manual, semi-automatic and automatic segmentation and define required reproducibility of 1.5-2.2% from Stehling paper as a requirement.	Added reproducibility from paper below as a requirement in 3.7. Image Data Analysis (A novel fast knee cartilage segmentation technique for T2 measurements at MR imaging--data from the Osteoarthritis Initiative. Stehling C, Baum T, Mueller-Hoecker C, Liebl H, Carballido-Gamio J, Joseph GB, Majumdar S, Link TM. Osteoarthritis Cartilage. 2011 Aug;19(8):984-9. doi: 10.1016/j.joca.2011.04.002. Epub 2011 Apr 12.)	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	2	169-177	L	Reference needed	Provide reference or justification	provide updated reference for Kim et al multivendor paper	add paper: Multi-vendor multi-site T1ρ and T2 quantification of knee cartilage. Kim J, Mamoto K, Lartey R, Xu K, Nakamura K, Shin W, Winalski CS, Obuchowski N, Tanaka M, Bahroos E, Link TM, Hardy PA, Peng Q, Reddy R, Botto-van Bemden A, Liu K, Peters RD, Wu C, Li X. Osteoarthritis Cartilage. 2020 Dec;28(12):1539-1550. doi: 10.1016/j.joca.2020.07.005. Epub 2020 Jul 30.	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	2	176	L	Discussion of tumor?	Seems irrelevant for the topic. Change to "compositional change" etc	Already addressed	Typo has been corrected	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.3	254-255	H	Phantom specs	Technical specifications of the calibration phantom (content, description) should be included here for phantom fabrication	add phantom sepcifics	Phantom specifications were added to the profile	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.3	257	M	Automated software specs	Add what should be the requirements specifications of the automated software to be used (not only refererence to commercial software)	this is currently research - no commercial tools	none required	OK
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.5	326	M	Landmarks not defined	Add examples of landmarks	the profile referred to landmarking during MR scans. Not specific landmarks.	Reworded the lanaguage to avoid confusion	Done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.6	344-345	H	Unique sequence for T2/T1rho	Although standardization should be the ultimate aim, restrainining the choice to only one sequence for T1rho and T2 quantitation is a too strict requirement. The use of MAPSS could be recommended as preferred approach, however it should be acknowledged that other methods are acceptable as well if certain criteria are met. Is MAPSS available for 1.5 T systems as well? Even though the recommended field is 3 T, there is no reason for not using 1.5 T scanners for cartilage T2 mapping	Please see response to comment 40. MAPSS is available at 1.5T	language added	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.6	355	L	Typo	There is a typo in the figure legend of Figure 1: "simens" should be "siEmens"	typo	Typo has been corrected.	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.6	369,371	L	Reference to wrong table	Table referred to in the text should be table 3, not table 1	incorrect Table number	Table number corrected	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.3	276	L	Add reference	Cartilage locations with specific abbreviations used, could add ref #25 to Eckstein here to provide info on the abbreviations	location of regions - line 303 in current version	reference was added	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.6.2	396	L	Missing reference to table	Add reference to Table 2 in the text		Reference to Table 2 added in the text.	done

Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.6.3	406	H	Parameters for T2/T1rho sequences	Some general recommendation for parameters for conventional multi echo spin echo and spin lock sequences, including instructions on TR and range/min/max TE/TSL values, and spin-lock amplitute (sensitivity to cartilage degeneration varies with frequency)	included in Table 3 for MAPSS parametes. OAI protocol is recommened to use for MESE	Information was added in Table 3, and in discussion 3.6.1 for MESE	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.6.3	439	L	Typo	Simens --> Siemens	typo	Typo has been corrected.	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3	464	M	Reconstruction of relaxation maps	"With or without noise components". This, the use of, or not using noise should be very precisely defined, as well as the exact way of handling noise, as this will affect the fitted data values.	This is a viable comment. However currently there is no conensus on optimized fitting algorithm for cartilage T1rho and T2 especially regarding how to handle the noise component. More studies are needed in the field. Could cite this paper as a discussion of various ways to fit data to derive a relaxtion time when the signal comes from multi-element coils. Hardy PA, Andersen AH. Calculating T2 in Images from a Phased Array Receiver. Magn Reson Med. 2009;61(4):962-9.	more discussion and references are added to section 3.7.1 regarding fitting methods	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.7	466	H	Definition of compartments	1. Definitions of the regions are too vague. In figure 2, the images on the left are not showing any anatomical landmarks, while in the images on the right there are no lines indicating buondaries between regions. 2. The proposed regions are way too large, resulting in averaging out most of the local changes and reduced sensitivity to early cartilage degeneration. At least load-bearing cartilages should be divided and alternative approaches should be mentioned (e.g. Hunter DJ et al. Evolution of semi-quantitative whole joint assessment of knee OA: MOAKS (MRI Osteoarthritis Knee Score). Osteoarthritis Cartilage. 2011;19(8):990-1002. doi: 10.1016/j.joca.2011.05.004. Hannila I et al. Topographical variation of T2 relaxation time in the young adult knee cartilage at 1.5 T. Osteoarthritis Cartilage. 2009;17(12):1570-5. doi: 10.1016/j.joca.2009.05.011.) Division into layers (i.e. superficial and deep halves) should also be mentioned.*	Figure 2 was changed and regions were better defined, may need some more detailed definitions of regions, also added Eckstein definitions - should we subdivide femoral region - weight-bearing/non-weight-bearing deep and superficial cartilage layers	leave recommendation as is, but discuss additional regions, refer to MOAKS, Eckstein subcompartments, reproducibility for larger compartments, subdivision may decrease reproducibility, which would also impact the claims. This was added in 3.7.1 discussion	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.8	531	L	Missing reference to table	Add reference to the Table in the text		reference was added	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.8	531	L	Significant decimals	number of significant digits seems too high	Table was taken from publication	left as is	OK
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.8	535	L	Missing reference to figure	Add reference to the figure 4 in the text		reference to Fig. 4 was added	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.8	562	L	Missing reference to figure	Add reference to the figure 5 in the text		reference to Fig. 5 was added	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.8	566	M	"The table" is referred	Figure caption refers to an unnumbered / inexistent table. The reference should be removed, or the table added.		substituted table with figure	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.8	595	L	Missing reference to figure	Add reference to the figure 6 in the text		reference to Fig. 6 was added	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	3.8	595	L	Risk calculator	It is not clear how the risk calculator tool fits with the purpose of this claim, it seems rather handwaving	this part of the discussion of 3.8. Image Data interpretation and how T1rho and T2 can be used in the future - similar to FRAX for BMD measurements	none required	Ok
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	4.1.1	631	M	Field dependence	It might be worth to mention that relaxation times are field dependent	T1rho and T2 relaxation time and field strength	we added to 4.1.1. that relaxation times are field dependent	done
Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	4.2	675	M	upper bound of wCV?	Check the conformance criteria. Less-than 5% seems conformant if target is between 4-5%	not sure what is meant here	none required	ok

Miika Nieminen, Mikko Nissi, Evelina Lammentausta, Victor Casula (OARSI)	Appendix B	780	H	Two more publications	The findings of two recent systematic reviews and meta-analyses should be considered: Atkinson HF et al. MRI T2 and T1ρ relaxation in patients at risk for knee osteoarthritis: a systematic review and meta-analysis. BMC Musculoskelet Disord. 2019;20(1):182. doi:10.1186/s12891-019-2547-7 MacKay JW et al. Systematic review and meta-analysis of the reliability and discriminative validity of cartilage compositional MRI in knee osteoarthritis. Osteoarthritis Cartilage. 2018;26(9):1140-1152. doi: 10.1016/j.joca.2017.11.018.	MacKay reference was included in our previous discussion, both references were discussed	references were added to Appendix B	done
James MacKay | james.w.mackay@uea.ac.uk	Title page, 1	6, 74	L	Prefer term 'osteoarthritis' to degenerative joint disease which is a little vague	Change 'degenerative joint disease' to 'osteoarthritis'	definition of osteoarthritis based on KL and clinical findings	exchange degenerative disease with (early) osteoarthritis (OA is a serious disease, FDA paper white paper, OARSI, add to background)	done
James Mackay, MBBCHIR, MRCP	1, 2	78, 135-6	H	Does the reproducibility of 4-5% refer to global, compartmental or laminar (e.g. superficial, deep) values? One would expect reproducibility to worsen with more granular analyses	Clarify what type of analysis the 4-5% refers to.	probably best to use global and the 6 major compartment measurements	global and 6 major compartments - add discussion - subcompartments including laminar analysis	done
James Mackay, MBBCHIR, MRCP	2	139-40	M	Suggest a caveat is added here or elsewhere to clarify that many studies have demonstrated bidirectional changes in T2/T1r with increasing degeneration (particularly with more granular compartmental/subcompartmental analyses) and so one-sided analyses should only be performed with caution	Add caveat regarding the indiscriminate use of one-sided analyses given likelihood of bidirectional change	bi-directional changes have been seen with more advanced degneration	focus on early osteartheritis - while early progression is more likely associated with increase in T2/T1rho, decrease may be seen (abstract from Felix Eckstein's group) and decrease will also be seen with treatment/intervention (studies from Stanford, NBA, ISMRM abstracts), bi-directional change is included in the profile, added under claims, Important considerations and limitations	done
James Mackay, MBBCHIR, MRCP	2	180	M	Similar to comment 3, should at least acknowledge that we frequently see concurrent increases and decreases in T2/T1r in different regions of the same knee There is sound biological rationale for this: in early osteoarthritis the synthesis of proteoglycan and type II collagen actually increases (dx.doi.org/10.1016/S1063-4584(97)80013-1). In addition, disruption of the normal cartilage structure may cause a counterintuitive increase in the amount of bound water molecules by increasing the number of accessible hydrophilic binding sites (dx.doi.org/10.1016/j.rcl.2009.04.003).	acknowledge that we frequently see concurrent increases and decreases in T2/T1r in different regions of the same knee in clinical studies	heterogeneity of collagen metabolism was discussed	discussion was included, under claims, Important considerations and limitations	done
James Mackay, MBBCHIR, MRCP	3	221-2	H	In my experience the flexible coils demonstrate improved image quality compared to some rigid coils. They also permit simultaneous bilateral imaging. If including this statement, the QA data needs to be included to justify.	Remove statement on flexible coils not being recommended or provide supporting data	flexible coils - statements about coils may need to be less rigorous - caveats - technical parameters (transmit/receive vs receive only) requires change in technical parameters - SAR issues	provide additional information - flex coil can be used - but need to meet conformance, discussion was included under 3.2. Pulse sequences, coils, phantom and segmentation software	done
James Mackay, MBBCHIR, MRCP	3	265-6	M	Bland-Altman analysis would be preferrable here. A t-test would not tell you anything about the magnitude of any systematic difference between different hardware/software settings, which Bland-Altman analysis would	Change Student's t-test to Bland-Altman analysis	Nancy's comment - repeatability using phantom - variance/mean - measure wCV for each tube/ B-A-plots true value on x-axis and - y axis ->measurements variability - wCV should be below a certain measurement (3%)	added Bland-Altman analysis	done
James Mackay, MBBCHIR, MRCP	3	320	M	I have found defining what constitutes 'exercise' difficult to define, and is something which study participants often ask about. For exampe, is walking/cycling to their MRI appointment ok? How much 'exercise' is too much? Perhaps we could try to define this a little more here	Clarify what is meant by 'should not have exercised'	Patients should not have exercised on the day of the exam (no high impact sports and no running, no exercise gym). They should not have performed any unusual, atypical physical activities (such as a marathon or an extended hike) 48 hours before the MRI examination	discussion was added under 3.5 Subject handling	done
James Mackay, MBBCHIR, MRCP	3	375-385	M	Could also mention qDESS sequence here which allows simultaneous acquisition of morphological data and T2 maps 'for free'	Mention qDESS sequence	devoted a paragraph	qDESS sequence was included in the profile	done
James Mackay, MBBCHIR, MRCP	3	455-65	M	Should we provide thresholds for implausible values (e.g. T2 > 100 msec) or poor fits (e.g. r-squared < 0.8) above/below which pixels should be excluded from analysis	Consider specifying exclusion thresholds for implausible values/poor fits	will add	added to profile	done
Dimitrios Karampinos, PhD	3.6.1	380	M	Multi echo spin echo sequences (MESE) are introduced. Beyong the OAI protocol, MESE sequences remain the most widely available sequences for T2 mapping in all platforms, but they have known issues with sensitivity to stimulated echoes as highlighted in the text. The text does not provide a clear recommendation on whether MAPSS should be the only sequences used for T2 mapping.	Some more clear statements on the use of the MESE for cartilage T2 mapping should be included.	MESE vs MAPSS- previous discussions - MAPSS is recommended as the preferred method based on reproducibility evaluation. Other sequences including MESE may be used when MAPSS T1ρ and T2 are not accessible, provided the Test-Retest Conformance can be met.	lanaguage added in 3.6.1	done
Dimitrios Karampinos, PhD		410	M	N/A	It would be useful to include some statements regarding the use of parallel imaging and compressed sensing for T2/T1rho mapping, as they are nowadays mainstream tools for accelerating image acquisitions across platforms.	parallel imaging is a standard - we can recommend this in the discussion - acceleration factor of 2 in phase direction were commonly used, if higher acceleration factors (with compressed sensing) are used make sure that claims are met	discuss below are added in 3.6.1 Parallel Imaging for image acquisition is recommended to reduce acquisition time. Accelaration factor of 2 in phase direction has been used in studies in the literature. Higher acceleration factor may be used with improved coil structure. Promising results have been demonstrated using compressed sensing to accelerate cartilage T1ρ and T2. Accuracy and precision need to be evaluated when advanced accelerating techniques are applied.	done

Feliks Kogan | fkogan@stanford.edu	Not Provided	219-222	ot Provide	"As coils have a significant impact on signal and measurements quadrature transmit/(minimum) eight-channel phased-array receive coils shall be used. In order to meet the claims identical coils need to be used for repeated, longitudinal measurements. Conventional flexible coils are not recommended as reproducibility was found to be limited unless special holders to improve reproducibility are used (Unpublished QA Data)"	I would say this should be amended to reflect a measure of SNR. Coil variation (like all other factors) is important in terms its effect on data noise. Thus, a measure of repeatability is of importance (as stated in the claims 1 and 2), rather than the coil used. I disagree with a blanket statement that flexible coils are not to be used. In fact, we have found that our 16 channel Extremity Coils shows considerably increased SNR (and reproducibility) compared to even the QED 18 Ch T/R Coils. Further, Dr. Li's work has shown this in reference (5) where she showed improved SNR and reduced fitting error using a receive only 16ch flex coil compared to a T/R 8Ch knee coil.	flex coil can be used - but need to meet conformance / reproducibility listed in claims	Langauge added in 3.2. also see above - comment 101	done
Feliks Kogan, PhD	Not Provided	Not Provided	Not Provided	Not Provided	I wonder if it is worth splitting up how longitudinal and cross-sectional studies are discussed in the profile. In particular because (1) T2 and T1rho are still primarily used for longitudinal changes and (2) there is a lack of literature supporting the use of T2/T1p for cross sectional studies across sites (and as you know better than most, is very difficult to do between systems not to mention vendors)	cross-sectional vs longitudinal studies - claim is longitudinal --there are studies across different sites/vendors but still limited at this stage in the field for cross-sectional claims -- Arthritis Foundation - Osteoarthritis Cartilage. 2015 Dec;23(12):2214-2223, Osteoarthritis Cartilage. 2020 Dec;28(12):1539-1550	claim is longitudinal, discussion is added under image data interpretation	Ok
Feliks Kogan, PhD	Not Provided	Not Provided	Not Provided	I bring this up largely because the notion of a QIBA profile that states that MAPSS as a standardized sequence for longitudinal studies seems a bit limiting. We are obviously biased but we use qDESS for robust and SNR efficient T2 mapping That sequence has similarly been disseminated across dozens of sites, is available on all three major vendors and is hopefully also being productized. I'm not saying that is the right way or that it should be included as well, rather that we want make sure not to restrict development in our research field. Similarly, if someone comes up with improvements to mapss such as better sampling trajectories, incorporation of CS, etc… I hope that those will be accepted (assuming they are properly vetted). Please dont take this as opposition to MAPSS, I am fully supportive of all of your efforts to make this more widely available and with proper parameters. What Im hoping to avoid is getting a paper rejected because we didnt use the standardized QIBA sequence for T2 analysis or comments on grant that state why do we need better imaging methods when there is MAPSS	i.With all that said, as the utility of these quantitative methods is largely based around detection of longitudinal changes, I would suggest the addition to the profile that states the choice of T2/T1rho sequence should ensure: 1.That intra-subject repeatability is in-line with Claim 1a and 1b (<5% CV) 2.Methods are appropriate markers of T2 and T1rho, respectively 3.Maybe some statement about minimum image (for long TE) SNR to help guide selection of parameters ii.This will ensure that QIBA will used to help us build better methods to improve T2/T1rho imaging as well as for people who dont have research agreements and cant use MAPSS and are thus using more rudimentary sequences.I believe that new methods that improve speed, accuracy or robustness offer to improve utilization of these methods and should be adapted as long as they uphold the standard of repeatability in order to detect longitudinal changes	discuss sequences - base recommendations on reproducibility, validation, SNR - we have included other sequences the discussion - also the committee acknowledged that there are different stages of imaging biomarker development, initial technical development, standardization etc. The profile focuses on standardization and recommended MAPSS based on reproducibility as discussed previously. The profile can get updated with more technical development in the field.	discussion about sequences was added	done
Feliks Kogan, PhD	3.8	Not Provided	ot Provide	Cross-sectional comparison - Section 3.8 - Data Interpretation is a bit confusing to me. The profile states that, "Based on the claim of our profile data interpretation will focus on longitudinal changes of cartilage composition." However, the discussion focuses on Z-score analysis from the OAI (using a method that is at different that the suggested QIBA Profile) Current methods, even utilizing the same sequence, have shown poor reproducibility across sites and vendors. Until inter-site and inter-vendor reproducibility can be shown, it's hard to see the utility of a Z-score from a single scan and seems beyond what can currently be scoped for this initiative. (The discussion presented was self limited in the OAI study with a set vendor/coil/sequence and has not been reproduced or validated outside of the data in that study)	With that said, cross-sectional analysis or z-score has potentially the most clinical utility. I wonder if the profile can scope what needs to happen to enable cross-sectional analysis in clinical studies	discussion about use of cross-sectional data interpretation - "However, reference databases are not part of QIBA profiles, and we believe that this is beyond the scope of our profile. In the discussion we have included previous studies that describe a reference database for T2 measurements and a risk score."	see above, comment 109, beyond the scope of the claim	done
Feliks Kogan, PhD	Not Provided	666	Not Provided	Test-Retest Conformance - Line 666 - "In order to test this assumption, N=40 normal subjects will be imaged, with each subject imaged twice on the same day (and additionally, some of these subjects may return for a third scan within one week)." This seems like a high bar. Is N=40 necessary or can this be done with a much lower burden? Also, is conformance in a single region or for global knee cartilage.	N/A?	Test-Retest Conformance Study - number of subjects (n=20) needed - line 771, which regions - global cartilage? Number of subjects depends on quality of the site, and wCV. Can be done at different sites to check feasibility. difficult to balance practical and statistical issues.	number of subjects was reduced to 20 in Test-Retest Conformance Study	done
Feliks Kogan, PhD	Not Provided	662	Not Provided	"New surface coils" - I assume this surface is not needed here.	Alternatively could state 'radiofrequency' coils	this was already removed	This was removed, instead we used Knee coils.	ok