Commenter	Section	Priority	Issue	Proposal	Committee Discussion	Resolution (w Rationale if rejected)
Nancy Obuchowski, PhD	4.2	M	I don't think you can expect the slope to be exactly one. You should give guidance about how far from one is acceptable.	Require actors to construct a 95% CI for the slope. The CI should lie between 0.95 and 1.05.	small sample size-> could go 0.95 and 1.05.	follow suggestion from Nancy?
Nancy Obuchowski, PhD	4.2	M	You have appropriately required actors to assess linearity and the magnitude of the slope, but the claims are strongly dependent on the wCVs. You need to include an assessment of the wCV and criteria for whether the actor has/nas not met the	Is it possible to perform test-retest on the DROs?	how did dsc solve the problem-> static R2* phantom, propagate the errors from T1 to ktrans (into appendix).	do a sensitivity calculation for ktrans from T1, see how good the software reproduces T1, try to relate to slope for DRO T1 values. We could reference the work from c. lavini (https://linkinghub.elsevier.com/retrieve/pii/S0730725X14003117) which did such an analysis.
Nancy Obuchowski, PhD	2.3	L	You don't mention the assumptions/justifications underlying the last two claims	Add in your justification for the last two claims.	state that we assume ktrans to be linear in the claims? look at other profiles.look at DSC	include statistical assumptions into claim description.
Nancy Obuchowski, PhD	2.2	L	It is awkward having three claim 2s.	Would it help to identify the three claim 2s as 2a, 2b, and 2c?	should not all be claim 2. Use a,b and c.	change claim label to 2a, 2b, and 2c.
Steven Sourbron, PhD	Exec Summary	M	Ktrans is not a model specific parameter. It is a physiological parameter that measures the rate of uptake of an indicator into the extravascular space.	N/A	ktrans is a true (physiological biomarker), but there is no way to validate -> use 1999 method to calcualte as gold standard and describe it in this section.	Check Mark's suggested edit
Steven Sourbron, PhD	Exec Summary	M	Remarkably	I would temper the language a bit. To demonstrate a potential of a new method you don't need methods that are reproducible in clinical practice.	soften the language (promising for 30 years)	
Steven Sourbron, PhD	Exec Summary	M	clinical research	drug development needs to be mentioned.	add drug development (pre-clinical?)	
Steven Sourbron, PhD	Exec Summary	M	independent of imaging platforms	For clinical practice, I agree. For basic research, not necessarily. If I have one centre that is able to produce accurate Ktrans measurements (and can prove that) then that one centre can produce valuable basic research even if no other centre in the world can replicate it.	which starategy was used to compile the profile - literature search - commitee agreement - public comment agreement	

Steven Sourbron, PhD	Exec Summary	M	consensus by the DCE-MRI Committee	Can you outline the processes by which consensus was achieved? How many people are on the committee, what are their backgrounds, and how did you make sure their views were heard? Also: it would useful to make it clear in the document which recommendations are evidence based and which are consensus based.	- positively confirm by "co-authors" via email? - add information about writing process.	The profile is based on a literature search for test re-test data in DCE incoroporating all publications matching (see https://docs.google.com/document/d/1uSwz2d9b9mon2MKSMCftXWYu-KZ-7LftKkhgjiZv45s/view for details.) There was only very limited yield for test-retest data but those for brain and prostate were used to define a claim for a biomarker change. Additionally, more recent non test-retest publications were and BC expert knowledge was used to extend the recommendations to state-of-the-art parameters. The consensus was reached by the biomarker comitttee which is open to all interested scientiests and physicians. Additionally, we contacted known experts in the field.
Steven Sourbron, PhD	2.1	M	contrast agent transfer constant	The values of Ktrans depend on the indicator used. Is the profile relevant for all indicators? If not, which?	- specific about contrast (doesn't apply eovist/primovist) - we don't expect substantial difference in pharmacokinetics for the commonly used agents (Dotarem, Gadovist, Multihance, look up details)	sentence added:The profile refers to DCE-MRI using standard extracellularcontrast agents (e.g. Dotarem, Gadovist, Prohance), and not using liver-specific agentes (e.g. primovist)
Steven Sourbron, PhD	2.2	M	(glioblastoma multiforme,194 GBM)	Does this mean the claim can only be trusted if a biopsy is available to confirm the tumor type?	- could this be applied to different tumors? - paper does not only apply to GBM but also to (lower grade) gliomas (Jim) - adjust claim with gliomas...high grade gliomas grad 3 and 4	This is a not so simple question: if either a system has a similar ktrans or if the statistics are independent of ktrans, it is not necessart to know the tissue is a true GBM.
Steven Sourbron, PhD	3.6	M	Recommended for this purpose is the variable flip angle method	Why? Considering the issues with accuracy - would it not be better to use Look Locker? E.g. the prostate can easily be covered in realistic scan times	- address why vfa in the profile	text added: The VFA is fast and 3D, and can therefore have exactly the same coverage and resolution of the DCE scan.

Steven Sourbron, PhD	3.6	M	A sufficient temporal resolution is important for a valid quantitative DCE examination	Why? This claim is about Ktrans, not perfusion or vascularity. I would think a slower injection combined with a slower acquisition would be a better approach. Fast injection + rapid sampling is only important if you are also interested to measure other parameters from the same scan.	- address other applications (like Breast, Liver) - rework - reword (ambigious now)	discuss in the group on 28 March: Ktrans is only valid in a very theorectical setting. Looking at the contast agent curves, it is obviousl that you will obtain varying ktrans when reducing the sampling resoultion (I once made a ISMRM poster for this, perhaps there is also a publication somewhere).
Steven Sourbron, PhD	3.6	M	spatial resolution should be sufficient	If you are going for a measured VIF, it should also be sufficient to resolved the vessel lumen. This is usually the more constringent requirement. It also means you need to be careful about slab positioning to avoid inflow effects. If you are using a reference VIF then these constraints can be dropped, which then gives you more freedom in sequence optimization. The choice of VIF approach determines the optimal acquisition protocol.	- should be sufficient for the lumen of the feeding vessel (is an individual VIF is used) - use sagital sinus to correct max concentration (in brain) - sufficient: acquired voxels are smaller than the vessel lumen - in prostate: illiac artery? 14 mm (men) / 11 mm (women)	- add a general comment (one or two sentences) - point out the correct vessel for different organs? - look for publications for recommentation
Steven Sourbron, PhD	3.6	M	NIST phantom	The NIST phantom is head sized. Should protocols for prostate & breast be modified (FOV, matrix etc) to fit the phantom? Or can they be run as they are (from my experience, not).	- could work for prostate (except for FOV) - mention if profile (if NIST does not provide adjusted versions of the profile) -	NIST has an extremity phantom:added the sentence A head and an extremity T1 and T2 arrays phantoms are available at present .
Steven Sourbron, PhD	3.6	M	T2* effect	T2* and signal non-linearity are not the same effect (more importantly, do not have the same solution).	- separate into T1 - T2* (depends on EchoTime) - only in the peakk concentration - take the shortest possible echo time	- make recommendations about echo time - think about in/out phase - look at publications? - FA as high as SAR allows - lower dose - recommend population averaged VIF? - use recommentations in tables below? - describe for non-physicst

Steven Sourbron, PhD	3.6	M	longer TRs	The problem with long TR is more about temporal resolution, not so much T1 weighting	- vendor specific (option in Siemens for changing FA or TR, no such option on Philips)	TR has everything to do with T1 weighting: comment ignored
Steven Sourbron, PhD	3.6	M	Repetition Time (0018, 0080)	Does this work for all vendors? I thought in Siemens you need to check the echo spacing.	- should be echo-spacing (on Siemens) - (0018, 0080) - for 2D sequences. - Discussion: should not be included into the profile - if, then include as caveate for 2D - add a note that if 2D sequences are used, the TR is not necessarily the "true" TR. - on Siemens (- do not use to set the time interval - use echo-spacing	Move comment to appendix
Steven Sourbron, PhD	3.6.2	M	Imaging sequencing: 3D fast spoiled gradient recalled echo or equivalent	Are you allowing radial golden-angle sequences? If so some notes need to be added in the reconstruction part as it gives flexibility on the temporal resolution	hendrik: no, this would be too technical for most readers.	there is a footnote at page 21 about Kspace sharing, defereed as "2". I have addede this "2" in all the three tables at the voice "GRE sequence or equivalent: check this.
Steven Sourbron, PhD	3.10.2	M	Requirement: "...image registration prior..."	I would advocate model-driven registration (Buonaccorsi MRM 2007; 58: 1010) instead. Here MoCo and Ktrans mapping are done simultaneously.	hendrik: this is technically challeging. Keep in mind that this not a profile for physicists and programmers but rather for clinical people and hospitals. Most tools do this stepwise and the important point here is to point out the requirement of a montion correction. Personally, I think that a comnbined approach smoothes some of the spatial pharamacokinetic information. Is there a scientific result suggesting the superiority of this appoach?	By combining ktrans model and motion, we might have a flatten the contrast agent curves since higher ktrans might be more 'expensive' for the optimization used in motion correction. It's complicated and would add unknown influences (and would make reproduciblity even more complicated when using differen software packages). We might think of a footnote for this.
Steven Sourbron, PhD	3.11	M	volume-to-volume artefacts	They also need to check for inflow effects in the VIF location (if a subject specific VIF is used). If the vessel is bright before contrast injection, the quantification cannot be trusted.	hendrik: indeed, this should be mentioned.	mention inflow effects when selecting a roi to determine VIF.

Steven Sourbron, PhD	3.12	M	mevis lab website	I am sensing a conflict of interest at play. Why mention Mevislab and no other tools?	hendrik: yes, we should add some more tools here: ImageJ, ...	Look up a representative list of (non-commercial) software tools
Steven Sourbron, PhD	3.13.1	M	Algorithmic steps for parametric image calculation	C and E don't need to be done sequentially. It's OK and probably better to package them up in a single forward model SI(Ktrans, VIF, T10) and fit in one step)	hendrik: good point. With variations in sequences used, the step wise procedure also has advantages. Perhaps we could change the order to make clear that C and E could be combined.	Change order for steps to clearify that step C and E could be combined into one. Keep as seperate steps to keep Appendix C readable. Also adjusted order in Appendix C
Steven Sourbron, PhD	3.14.2	M	How to deal with ROI selection in follow-up studies?	What if the tumor has shrunk or grown? Should the same ROI ideally be used as in the first scan, or should it be changed to the new tumour size? This is important because the claim is written in terms of Ktrans changes.	hendrik: yes, this should be at least discussed. For now, the radiologist should identify corresponding tumor areas manually. Size is probably alreadt assessed by the recist-criteria. Ktrans should reflect the changes in permeability/perfusion. Averaging in the active tumor reagion is seems to be reasonable.	Mention role for radiologist until automatic solution is available. Should be the Radiologist rather then the operator, mentioned in "Image Analysis"
Steven Sourbron, PhD	4.2	M	The VIF can be obtained from the lowest row in the images	How do I validate a software package that does automated VIF selection making use of anatomical features? This may well have advantages in terms of repeatability but is likely to fail on the DRO.	hendrik: this is an issue with the desing of the DROs and can not be covered by the profile. As soon as we have a more sophisticated DRO, we will include it here.	Add a footnote about possible improvements for the DRO?
Qing Yuan	Open Issues	Medium	For parallel imaging, the word “minimize” is confusing, should be clearly specified.	N/A	hendrik: Agreed. What about 'avoided'? Would that make more sense?	hendrik: change minimized to avoided
Qing Yuan	Open Issues	High	The ROI for DCE-MRI should be segmented from post-contrast DCE images. Most likely all DCE images are co-registered prior to generating parametric maps. ROIs defined on post-contrast DCE images can be easily copied and pasted to parametric maps to extract quantitative results.	N/A	- look in Appendix C if it mentions co-registration it might be overlooked	Added comment in Image Analysis
Qing Yuan	1	Medium	N/A	consider to introduce GKM & eGKM	hendrik: agreed, add Reference in section 1	included in executive summary

Qing Yuan	2.1	Medium	Should include MR scientists	N/A	hendrik: it's kind of intergrated into "image analyst" and "acquisition device", see line 264.	Added "scientists"
Qing Yuan	2.2	Medium	GKM and eGKM need definitions. AIF should be VIF. Why are there 3 Claim 2 for Prostate?	N/A	hendrik: yes, there should be 2. I should check the numbers!	hendrik: consider separating eGKM and GKM. added defintion of eGKM in executive summary. Someone adjusted aif to vif. There is a claim for 1.5 and 3.0 T and GKM and one for 3.0T an eGKM
Qing Yuan	2.3	Medium	the definition of Ktrans is confusing	N/A	hendrik: that's the definition from Tofts et al, 1999 (flow and permeability limited). Do you know a more simple version? Use definition from Tofts:	Removed the extra part at the end since it seemed like it was from a previous version
Qing Yuan	2.3	Low	missing “of” in “Example of clinical interpretation…..”	N/A	agreed	add "of"
Qing Yuan	3.1	Medium	Should include MR scientists	N/A	we replace Physicist with MR Scientist.	Added "Scientist"
Qing Yuan	3.1.1	Low	replace “technician” with “technologist”	N/A	yes, check english language!	
Qing Yuan	3.4.1	Medium	Parallel imaging is discussed here, which is coil-related. It’d be more relevant to point out the phased-array or multi-element coils should be used to enable parallel imaging acquisition.	N/A	discuss type of coil?	
Qing Yuan	3.5.1	Low	delete the repeated “the”	N/A	ok	
Qing Yuan	3.6.1	Medium	consider to make it consistent by using T1 or R1 mapping throughout the profile	N/A	agreed, use T1 instead of R1	
Qing Yuan	3.6.1	Medium	It is a valid concern about signal stead state for the VFA scans. However, image analyst needs to make sure the image analysis tools, especially commercially available software, can use the correct images for R1 mapping.	N/A	do a more general comment on t1 input data (technologist should check validity of T1 data)	Good point but should be clear for someone capbale of setting up these seqeuences. It's a bit beyond this profile ...
Qing Yuan	3.6.1	Medium	define Ca	N/A	agreed	

Qing Yuan	3.6.2	Medium	There is no spacing between slices (i.e. slice gap) in 3D acquisition. The description in the tables is very vendor-specific, which should be made more general. Use “pixel size” instead of “pixel spacing”. “Images in Acquisition” is confusing. Just use “Number of slices” instead.	N/A	agreed	"pixel spacing" -> "pixel size" "images in acquistion" -> "number of slices"
Qing Yuan	3.6.2	High	Table for Brain: spoiled gradient echo is a low-SAR sequence. Provide reference for the concern of SAR limits. Field strength should be 1.5 or 3T.	N/A	could not find SAr, but add 3T to table	
Qing Yuan	3.6.2	Medium	Table for Prostate: the coil selection is confusing. Phased-array surface coil is commonly used with or without endo coil. I’m not aware of the situation of using endo coil only.	N/A	looks ok no	Agreed. Chaned sequence of coils in text.
Qing Yuan	3.6.2	Medium	Table for Breast: delete Tofts in footnote. The unit for temporal resolution cannot be square of second.	N/A	Should be GKM, rework footnote.	GKM replaced. But it is not sec square but a ref to footnote 2. However I cannot remove the 2 without deleting the footnote
Qing Yuan	3.7.1	Low	delete “based on kidney function”, which is covered in Line 448.	N/A	agreed	
Qing Yuan	3.7.1	Medium	GBCA should be defined in Line 449. “ACR Manual on Contrast Media” should be mentioned as guideline in this session.	N/A	resolve GBCA, Qing will send reference	Added line about the ACR manual
Qing Yuan	3.9.2	Medium	delete “torso phased-array” in the Table. It does not apply to all anatomies covered in this profile.	N/A	makes sense	Removed
Qing Yuan	3.10.2	Medium	image registration in DCE-MRI is usually accomplished by image analysis software, not by image reconstruction on scanner.	N/A	make sense, motion correction is not part of MRI reconstruction	Added "image analysis software"
Qing Yuan	3.11.1	Medium	typo “analyst”. “pulsatory effect” does not apply to all anatomies covered in this profile, should change it to a more general word, such as image artifacts.	N/A		Typo fixed, changed to imaging artifacts with phase-encoded motion artifacts as an example
Qing Yuan	3.13.1	Low	or use population average VIF	N/A	make sense, include sentence	

Qing Yuan	3.13.2	Medium	what is “a fixed set of image contrasts”?	N/A	make sure to be consistent with other suggestions on roi definition.	windowing level
Qing Yuan	3.14.1	Low	change “AIF” to “VIF”	N/A	agreed	Fixed 2019.01.20 but re-occured multiple times ... should keep this up-to-date
Qing Yuan	3.14.2	Medium	FOV coverage for lesion is usually not a problem. Instead, the coverage in slice direction should be confirmed.	N/A	extend to 3D (or look up general language for complete coverage)	"The FOV shall completely cover the lesion in both the transverse and slice directions."
Qing Yuan	4.1.2	Medium	R2 value is mentioned here. Is there any recommendation on this? Or reference?	N/A	depending on seqeunce, check reference	Changed at some point
Qing Yuan	Appendix B	Low	change “is” to “was”	N/A	agreed	A couple instances
Qing Yuan	Appendix B	Medium	verify TR and TE values	N/A	is probably 3.7-4.1 ms; flip angle 12° or 15°; TE = 1.3 - 1.4 ms, check reference	Was missing dashes, also cleaned up this section in general
Qing Yuan	Appendix C	Medium	unless a specific publication is given for breast, I’d move Elastix to the first paragraph of this section. For prostate, pre-MRI prep, such as using Levsin or Glucagon, is worth mentioning since not all sites use the endorectal coil.	N/A	make sense the way it is written now	Good point
Qing Yuan	Appendix C	Low	to avoid confusion, specify “the T1 mapping series should be acquired immediately…”	N/A	agreed	Already done
Qing Yuan	Appendix C	Low	error in equation the a1 (alpha) in the denominator should be aj.	N/A	correct! Replace 1 with j	Fixed, citation: https://journals.sagepub.com/doi/pdf/10.1177/1748301816656288
Qing Yuan	Appendix C	Low	change SI(t) and SI(0) to S(t) and S(0) to match Line 978.	N/A	Replace SI with S	There was another place with the same difference
Qing Yuan	Appendix C	Medium	should be equation (4)?	N/A	correct, replace 1 with 4.	There are a lot of issues with equations numbers so I will go ahead and fix them all
Qing Yuan	Appendix C	Medium	verify the equation #	N/A	some extra equation (8) in line 1024, change (1) to (10) in line 1019	There was an extra equation number appended to it for some reason
Qing Yuan	Appendix C		ve is the volume fraction of EES, not EES itself	N/A	agreed	Fixed, in appendix E currently though

Qing Yuan	Appendix C	High	post-contrast images usually demonstrate lesions very well. ROIs defined on post-contrast images or the ones with motion correction match the locations on parametric maps. If ROIs are drawn on the whole lesion, i.e., more than one slices, matching the locations from a different series may not be possible.	N/A	discussed above: Row 34	intermediate slices might not be present in morphological slices
Qing Yuan	Appendix D	Low	in addition to the abbreviations listed here, all abbreviations should be defined in the profile when used first time	N/A	agreed	Will go through and double check
Qing Yuan	Site Checklist	Medium	Table number for R1 performance needs to be given	N/A	add table number	referenced Table 3.6.1 and added an acceptable error level there.
Qing Yuan	Image Analyst Checklist	Low	for “Lesion location”, change to “ROI-averaged analysis”, “voxel-by-voxel analysis”. For “Artifact sources”, remove “CT”.	N/A	CT-volumes at the end of the table, remove.	
Qing Yuan	General comment	Medium	1) Chrome should be recommended for accessing all links, since some of them do not work with internet explorer. 2) No Claims for Breast, Head & Neck. No scanning specification is recommended for Head & Neck.	N/A	- check for Head and Neck in profile and remove if not fitting - No GKM for breast but important application of DCE.	1) IE has <1% of browser usage now since its discontinuation so this can be implied 2) Added in Appendix C(A)

Rianne van der Heijden	Open questions	High	ROIs need to be delineated on anatomical images, not on the parameter map	Do you mean also not on the raw DCE images? To avoid registration issues, which are quite frequent in other body parts than the brain, it would be best to draw ROIs on the raw DCE images. This way, registration of the individual DCE time points is the only registration needed. This is only possible if the acquired DCE images have a high enough resolution of course. Furthermore, I am not sure whether each kind of ROI should have an inter-observer variability measured. If a certain ROI is known to be reliable, for instance knee cartilage, this should be enough. In the case of a known high variability, consensus between two observers would be a better solution. In the case of automatic ROI drawing, a proportion of the ROIs should be checked visually to ascertain quality.	- use the first (non-contrast image) - inflamation as a new target - knee embolisation - anatomical structure sufficient for definition. - use fit-quality to be included into the roi definition -- difficult in bone -- might not work in tissues other than brain -- might be influenced by model results	

Rianne van der Heijden	question 2	High	population vs patient specific	I do agree that the patient specific VIF is the best option, but most of the times the temporal resolution is not good enough. Otherwise the population vif is better than literature vif. Though, VIF choice also depends on the question you want to answer. In case of a follow up of individual patients the patient specific vif is needed to adequately detect individual changes. In case of comparison of a group of patients with a group of controls, the population average is more reliable.	- population averaged was most reliable in knee osteoatrithis - look at profile text, should be adjusted	Open questions resolved and deleted.
Rianne van der Heijden	1	Medium	DCE MRI for cancer	Besides cancer, it can also be used to study inflammation. There are several studies in knee rheumatoid artritis and osteoarthritis, which I can provide if requested.	- was discussed above	To be added in a later document
Rianne van der Heijden	2.2	High	articles on reproducibility of DCE-MRI	I do know articles on DCE-MRI reproducibility in the knee, for instance: Reproducibility of DCE-MRI time-intensity curve-shape analysis in patients with knee arthritis: A comparison with qualitative and pharmacokinetic analyses	- was discussed above	To be added in a later document
Rianne van der Heijden	3.6	Medium	scan duration	If also reliable measurement of ve/kep is needed, scan time should also include the wash out period. This can take up a long time in some instances. I understand Ktrans is the parameter on which the focus lies, but I think it should be good to add a statement about ve/kep.	- muscoletrally you need longer acquisition times - wait until extravasation started in tissue - depends on ktrans range? - or state that ist should be highly perfused tissue	ve/kep is not part of the claims and not considered a biomarker

Rianne van der Heijden	3.8	Medium	hematocrite measurements	Should it also be added that hematocrite should be measured, especially in individual follow up studies?		Hematorit should be an issue for pubulation averaged VIFs.
Professor James O'Connor (EIBALL)	Overall Profile	High	Overall, the profile is in a very mature state. It is well written and clear. The clinical context (section 2), profile activities (section 3), assessment procedures (section 4), conformance (section 5) and appendices are laid out in a logical and detailed manner.	The specific comments to follow are largely minor, but are provided to address certain points prior to public consultation.	Thank you.	
Professor James O'Connor (EIBALL)	Open question 1	Low	Concerning 'How to delineate ROIs for DCE-MRI':	We agree that T1W and T2W images should be the first choice. However, it is possible that motion occurs between these anatomical images being acquired and the dynamic series being acquired, either due to physiologic motion (more typically in chest and abdomen), or in the case of the focus in this profile (brain, prostate) due to patient movement. Guidance is required for dealing with such patient movement – can the dynamic series be used in this scenario to delineate the ROI?	- use B-Value image (500) - hirachical approach? - T1 - ... - ... - deliniate on anatomy and early dynamics - depends on organ - add to open issue section - anantomical image (e.g., t1 and t2w)	Open questions removed, discussed in appendix C
Professor James O'Connor (EIBALL)	2	Low	a) where Ktrans can be considered a true PD biomarker of the therapy mechanism of action (e.g. reporting on an anti-vascular drug targeting the vasculature) and b) where Ktrans is a non-specific downstream biomarker (e.g. reporting on non-specific actions of a cytotoxic chemotherapy).	It may be worth distinguishing two conceptually different scenarios in therapy evaluation.	- pharmacodynamc biomarker - 'downstream biomarker' - could be used for both - clinical application? - monitor non-antiangiogenic therapies? - Prof O'Connor will write some explaining lines and send them to Susan	- ktrans is measuring (somehow) vasculature - already resolved

Professor James O'Connor (EIBALL)	2	Low	What is the rationale for the 'true change' threshold being 95% for claim 2b and 105% for claim 2c? It is not clear where these numbers come from, unlike the thresholds for claim 1 and claim 2a, which are explained in lines 246-249.	Clearly state rationale for values	check for latest public comments	See comments from Nancy (Row 10/11)
Professor James O'Connor (EIBALL)	2	Low	More generally, it is surprising that there is such little repeatability data on DCE-MRI from clinical studies of brain tumours and prostatic tumours. How generalizable are the data, when considering: a) the small numbers (e.g. N=11 for glioma), b) dependence on just one study for glioma and two studies for prostate, c) the fact that tumour type may vary between the reference studies cited in the profile and populations in studies that hope to use the profile, and d) the fact that some studies relied on are nearly 20 years old and had protocols performed on machines that are now obsolete?	Provide more info on this	- just one glioma study - Prof O'Connor could provide some test-retest data for liver or colorectal metastasis - Summary of ongoing studies	
Professor James O'Connor (EIBALL)	2	Low	The above make a clear rationale for more studies of repeatability. If extra studies do get performed and published in the next few years, do QIBA plan to update the profile?	Provide info	- should have an update (claim more complicated) - European Radiology test-retest on rheumatic athritis -	Of course ;-)
Professor James O'Connor (EIBALL)	2	Low	There is no minus sign before the 65%. This is discrepant from line 241 where the reduction in Ktrans is cited as -105%.	Fix	check for latest public comments version	

Professor James O'Connor (EIBALL)	3	Low	We appreciate that this figure is only illustrative, but this seems to have two issues. The brain requirement for true change in Ktrans is +/- 21%. Therefore, it is illogical that the bar chart for the responder is set at 10% +/- 5%. Further, a responder would have a reduction in Ktrans, so should the axis have negative numbers?	Address	- good point - need to correct -	Adjusted Diagram
Professor James O'Connor (EIBALL)	3.5	Low	Is annual QA with phantom scanning frequent enough?		- once a month, reasonable - depends on machine/vendor - once a week resonable - personal / scan time available - more frequent during sudy?	write: annualy or more frequent dependent on scanner or personal availablity
Professor James O'Connor (EIBALL)	3.5	Low	Many investigators would argue that it is essential that patients undergoing sequential repeated scanning are imaged on the same machine for their multiple visits. Is the phrase 'strongly recommended' itself strong enough?		- should be used for one patient - emphasis on different scanners - need to point out in profile - explain in the profile the problem / a possible risk - weight arguments (availality vs reprodicibility) - claim definition on the same machine!!	Point out problem (also in the claims)
Professor James O'Connor (EIBALL)	3.11	Low	Does the image QA of 'imaging parameters' include checking that T1 values are within the published reference range? This is not explicitly mentioned in section 3.11 but is an important part of DCE-MRI QA/QC.		- site specific T1 (e.g., breast, ..)? - check T1 value for tissue of interest?	- should be in the profile! Add a sentence, add to image QA (by Radiologist/Physician).
Professor James O'Connor (EIBALL)	3.11	Low	Focus is on QA only and does not include QC. Is there a need to discuss QC in the profile?		- reach out to Mike Boss about this.	I see some has been added
Youngkyoo Jung	3.5.1	Medium	It is somewhat unclear what routine QC processes are.	An example, like weekly and annual ACR QC procedures, could be provided.	- QC is described in line 369 and below	
Youngkyoo Jung	3.6.1	Low	Appendix H is missing in the document.		- Yes. Missed to update the appendix header, should be Appendix F	D,F,G -> D,E,F

Youngkyoo Jung	3.6.2	Medium	Constant prescan parameters are also important as well.	Prescan parameters, such as Tx and Rx gains, could be ensured if vendor specific tags are provided.	- really needed? In case of variable flip angle? - Cristina will look up in the profile (and propose some text if not), the rescaling factors are not Tx or Rx for Philips. - Contact the commenter - use user defined rather shortest.	Should only incude parameters which would also be noted in an MRM or JMRI publication. Should note standard/common dicom parameters
Youngkyoo Jung	3.9.1	Medium	Specific procedures to ensure constant pre-scan calibration could be described.	A possible example is "If an option to choose manual or auto pre-scan is available, it is advisable to run a sequence with the highest flip angle with auto pre-scan first and run the others, including DCE scan, with manual pre-scan to ensure constant pre-scan parameters."	- sounds reasonable, need to be looked up - needed in day-to-day scanning or sequence development/ - is this an option on the scanner (if a vfa is predefined)? - could be included in the profile	Added the suggested sentence
Tsutomu Inaoka, MD, PhD	N/A	N/A	I have checked the documents of DCE-MRI Quantification (DCEMRI-Q). I think it is very great work. The contents are very nice and there should be no problems.	N/A		
Yoshifumi Kuroki, MD, PhD	3.6.2	Medium	Acquisition of at least 5 dynamics (phases) minutes of post injection is longer than the criteria based on PI-RADS version 2.1.	Acquisition of at least 3 dynamics (phases) minutes of post injection is better.	- does this apply to the model based (Tofts) analysis? - does not address ktrans as a biomarker.	contact commenter but do not add to profile
Daniel Margolis	2.2	Low	There are 3 claims for prostate DCE, where the higher field strength requires a much greater change in the pharmacokinetic parameter to suggest a biologic change. This is counterintuitive and confusing, and an unsophisticated reader might question the veracity or accuracy of this claim.	Consolidate Claim 2 into a single "configuration."	- agreed that this is confusing, but based on test-retest publications - publications describing test-restest are mentioned in the discussion section - comment on possible reasons: B1 error, differences in AIF definition	add description or reasoning to profile

Daniel Margolis	Open Issues	Low	The last Q/A suggests that view sharing should not be used but that there is insufficient information regarding radial and compressed sensing acquisitions. However, justification for discouraging view sharing is lacking	View sharing along with radial acquisition and compressed sensing should be listed as having insufficient information to provide a recommendation.	- add view sharing in this Q/A section - reference section in the profile discussing view sharing	Fixed by somebody, footnote added
John Jordan, MD	Open Issues	High	N/A	Regarding segmentation and delineation, the gold standard is manual segmentation, although potentially time-consuming with inter- and intra-observer variability. And this may affect precision, therefore, it is urged that automated methods be considered, or at least deployed in parallel. Ultimately these would be faster with less variability, but longer 'training periods' may be required, and applicability to other systems and data sets may be problematic. Nevertheless, this appears to be the direction needed for progress for development of more precise, reproducible biomarkers and metrology.	- beyond scope of the profile - use most consistent method (over timepoints) - is also discussed later in the profile - to broad for DCE-profile especially for different organs/tumors - different software might produce results even more different than manual segmentation - very disease related in DWI, no real segmentation method	This was part of the open issue section and had been closed (as mentioned in the closed section).

John Jordan, MD	Open Issues	High	Regarding dosage and relaxivity, the standard dose is 0.1 mmol/kg, in the absence of robust data indicating otherwise, reducing dose may reduce the sensitivity for accurate delineation of tumors and/or their changing features with treatment/time. Repeatability is another issue that could be further compromised. While GDD is of concern, I would be cautious for the initial development of the biomarker in the absence of robust evidence that can validate the utility of reductions in dose.	N/A	- should we mention dose reduction in the profile - beyond the scope of the profile? - look up publications using lower dose for quantitative? - cristina will look for publication	This was part of the open issue section and had been closed (as mentioned in the closed section).
John Jordan, MD	Open Issues	High	Parallel imaging may be less problematic at 3T, but the risk of decreased signal to noise, potential variability among scanners, and reconstruction artifacts, make this technique less desirable when seeking to establish precise and reproducible biomarkers. Agree that its use should be minimized particularly in neuroimaging.	N/A	- in agreement with the profile? - contact commenter to be sure.	This was part of the open issue section and had been closed (as mentioned in the closed section).
Jinnan Wang	3.6.2	Medium	For limiting TR less than 5ms in prostate imaging. At 1.5T, this would prevent the use of Dixon imaging	By relaxing the requirement to 7 ms, Dixon imaging would be supported	- good point - important for breast, brain or breast? - EchoTime? - InversionRecovery based? - Ask Scott Reader (PDFF) or commenter? - Hendrik will contact commenter and look up details of Dixon	Added a note about this
Jinnan Wang	2.2	Medium	All claims explicitly suggest using an individual AIF. But the referenced publications used population-based or study-averaged AIF. Also, in other sections of the profile, population-based AIFs are declared acceptable.	To remove the restriction to using an individual AIF.	- check in the publications Peled et al., 2015(?)	Sections 3.12 and 3.13 in particular address more population-based VIF (AIF).

Jinnan Wang	4.2	Low	The QIDW actually offers a variety of DCE DROs. None of them matches the description, though (lowest sigma in the Tofts_v12 set is 2).	Please clearly mark which dataset should be used.	confusing language: two types of DROs, one for t1 and one for dce. t1 has sigma=2 (version v03) and dce has sigma=5 (v12). Reach out to Dan Barboriack for details.	fix language. Reach out to Dan. Give a more general description on where to find the data. Coordinate with QIDW?
Jinnan Wang	4.2	Medium	The T1 map and analysis are based on a T1 of 1000 ms. Note for Claim 2, DCE-MRI in the prostate, that the T1 of prostate gland tissue is more in the order of 2000 ms.	Please reconcile.	Refering to the DRO? As Dr Wang. In Peled et al, 2018, the estimate for T1 is 1434 ms.	Look up related T1 paper from Andrey et al. Reach out to Dr wang about details? -> valid comment, reached out to Dan Barboriak and got tools to generate prostate specific T1 Maps, will prepare accordingly to Issue above.
Jinnan Wang	4.2	Low	General comment: It may be adequate to add a hint to turn off any co-registration options in the analysis software, as it could introduce undesired deformations with synthetic data.	As stated.	Important point. Should be stated in the assessment section.	Added sentence about motion correction
Jinnan Wang	4.2	Low	General comment: The analysis software download link is actually not called "ODET" but "QIBA evaluate tool" right now	Please update.	we'll adjust the name.	Changed to "QIBA DRO Evalulation Tool (QDET)"
Jinnan Wang	2.2	Low	A general comment for the document, sometimes a field strength of 3T is referred to as “3T” and sometimes as “3.0T”. The referenced section/line is the first incidence in the document.	We suggest to harmonize and use “3T” throughout the document	We agree and will use 3T.	Switched 3.0T to 3T
Richard J Martin, JD (AAPM)	Exec Summary	N/A	This language appears to break from the QIBA protocol.	N/A	Only published data? QIBA has endorsed this comment.	sounds reasonable, should be an ongoing effort to get some more basis from publications. Studies should be encouraged.
Richard J Martin, JD (AAPM)	2.1		Word choice	Consider “active surveillance” or “active monitoring” in lieu of “watchful waiting.”		change to active surveilance
Richard J Martin, JD (AAPM)	2.1	N/A	Regulatory agencies (i.e., FDA) are part of the target audience as well given the list and language already there.	N/A	we included Gov. officials but could add agencies as well.	
Richard J Martin, JD (AAPM)	2.1	N/A	Regarding Tofts modeling: For a VIF extracted from MR images, time delays between VIF and tissue DCE curves likely exist, which affects perfusion estimation.	Please specify how to identify and handle the time delay. The time delay could be pre-estimated or incorporated in modeling. Please identify what methods are recommended.	We addressed this in line 1028 and would recomment using a pre-modelling correction by shifting the VIF. Should we include the other possibility as well? We could look up publication on this recommendartion, though.	Add reference to appendix for model details in line 175.

Richard J Martin, JD (AAPM)	2.1	N/A	This QIBA profile may be used for voxel-by-voxel perfusion modeling. Some perfusion-mapping techniques incorporate spatial regularization to enforce perfusion image smoothness.	Specify how these techniques can be clinically evaluated and used.	clearify to reader, dependent on situation/application. Add to the appendix.	Addressed in 3.10 and 3.13 (added special footnote there)
Richard J Martin, JD (AAPM)	3	N/A	N/A	We suggest that use of "MR Scientist" within this document echo the definition (and requirements) as outlined by the ACR.	https://acrsupport.acr.org/support/solutions/articles/11000060916-general-personnel-requirements-medical-physicists-mr-scientists-for-ct-mri-nuclear-medicine-and-pe	look up definition and requirement of the acr.
Richard J Martin, JD (AAPM)	3.1	N/A	N/A	Clarify whether phantom scanning can be performed by MR physics/scientist "assistants."		Phantom scanning setup needs to be oversighted by a Physicist but an be conducted by an assistant. The evaluation of the phantom data should be conducted by the Physiscist.
Richard J Martin, JD (AAPM)	3.5	N/A	Not modifying during a longitudinal study makes sense for research.	We recommend that the document address clinical use of DCE and long-term follow-up of patients. This is the important question here.	There will be changes in hard and software. Could only be applied in a short and specific study. Ask manufacurer if there are changes in acquisition to be excpected. Redo a site qualitfication for major changes in hard or software.	Adjusedd text accordingly
Richard J Martin, JD (AAPM)	3.6	N/A	Regarding Image Protocol: A MR scanner usually has memory size limit for an acquisition.	Specify how to make the compromises between image resolution, temporal resolution, image size, temporal length in the protocol.	shouldned be a problem with mordern scanners.	To my (Hendriks) Knowledge, In DCE the constraints because of temporal resolution are usually much more limiting than the storage capabilities of the scanner (Memory has been growing quite rapidly for most computer systems in recent years.
Richard J Martin, JD (AAPM)	3.6	N/A	VIF typically has a sharp peak on the first pass.	Specify whether it is necessary to capture the very peak for accurate DCE quantification. Does that put a requirement on temporal resolutions of DCE MRI in relation to imaging sites?		Text about need to have a VIF peak has been added in two places in 3.6

Richard J Martin, JD (AAPM)	3.6	N/A	What is the speed of bolus injection? When to start DCE MR Acquisition after the injection starts? An appropriate starting time would save memory space for dynamic data rather than baseline data. This may depend on the location of bolus injection and site for DCE MRI.	Please specify.	see 3.4	0.1 mmol/kg rate? 5 baseline timepoints, rate?
Richard J Martin, JD (AAPM)	3.6	High	There are longitudinal study limitation comments again without guidance on how to treat real patients.	Please include this guidance.	- when should you worry? - consult manufacturer if they expect changes affecting DCR-MRI - should not be a problen if assessement procedures pass succesfully(?) - documenting of image post-processing by the manufacturer - multi center study(?) -switch off new image improvment features (ask manufacturer)	Discussed in 3.5
Richard J Martin, JD (AAPM)	3.6	N/A	While we generally agree there is a need to assess drift, the action limits provided are not well defined. For example, you do not identify what a marked deviation is.	Please define.	add reference to assesment procedure R1/T1 mapping.	very old, probably not an issue nowadays? Look for publications. Not important for DCE because of large signal change because of CA. No need to worry.
Richard J Martin, JD (AAPM)	3.6	N/A	There is a reference to DCE trial, but no guidance for clinical use.	Please provide this guidance.	- the paragraph should be removed, probaly leftover form the old profile. - is R1/T1 mapping described in the assessment procedures sufficient to ensure stability?	Added guidance for clinical use.
Richard J Martin, JD (AAPM)	3.6	N/A	N/A	Consider using “contrast agent” instead of an abbreviation here.	agreed!	Agreed

Richard J Martin, JD (AAPM)	3.6	N/A	Is it worth discussing impact of TE selection on signal (T2*) in this section?	- Discussed for 3T in 423, include as possible changed paramter in discussion in next paragraph. - T2* Covered by phantom? - consider different patients in protocol design - discussing with Cristina - could be a problem in blood - dicussed in the Arterial Input Function? - we specified 4 ms in Table - add section about minimum TE as mentioned in the tables - is there a threshold for acceptable T2* i.e. EchoTime? - get back to Trevor about this.		Added discussion about TE, CA concentration and T2*
Richard J Martin, JD (AAPM)	3.6.2	N/A	N/A	Consider “proprietary” for DICOM tags that are not public instead of leaving empty. It tells the user they are there and to look for them, and points to industry a need for more public tags.	- which ones are meant? left out are number of dynamic phases, baseline phases and temporal resolution. - give acquisition time tag - GE uses TriggerTime (has a dicom tag) - is there a dicom tag for number of phases - add tags like acqiusition time and Trigger time with a footnote on how to derive this information	add tags like acqiusition time and Trigger time with a footnote on how to derive this information
Richard J Martin, JD (AAPM)	3.6.2	N/A	We believe field strength of 1.5T is being pushed in the document even though 3T is standard of practice for both brain and prostate.	If DCE cannot be done at 3T for these two anatomies with confidence, maybe DCE should not be done at all outside of controlled studies.	- if one takes B1 seriously... - define specifications	Discussed in Appendix on B1 mapping
Richard J Martin, JD (AAPM)	3.6.2	N/A	Terminology	Consider "interpolation" in table as opposed to “zero fill”	-cristina agrees, change to interpolation.	Changed to interpolation

Richard J Martin, JD (AAPM)	3.6.2	N/A	N/A	Consider striking "as many slices as possible" because it is not really ideal.	-as many slices as the time resolution allows -consider region of insterest, perhaps spatial resolution -suggestion "cover the field of view, could tumor or whole brain, depending on study" -**sufffcient number of slices to cover the region of interest while mentaining the spatial and temporal resolution**	Changed accordingly.
Richard J Martin, JD (AAPM)	3.6.2	N/A	If in-plane voxel limit is just <2mm, suggest that.	We recommend putting matrix afterward and state variable to achieve spatiotemporal resolution and a typical value.	-not sure which row in the tables was addressed, ask Trevor. Pixel Spacing?	Agreed
Richard J Martin, JD (AAPM)	3.6.2	N/A	N/A	Please correct typo: "The acquisition plan[e]."		Corrected
Richard J Martin, JD (AAPM)	3.6.2	N/A	N/A	Comment on flow compensation usage and/or obliquity in discussion of plane selection.	In Row "Imagin Plane" Column "Requirement", change plan to plane.	Suggested to avoid plane perpendicular to feeding vessel or use a population averaged VIF.
Richard J Martin, JD (AAPM)	3.6.2	N/A	N/A	We recommend mentioning explicitly that T1 VFA desired to be same (or nearly so) sequence and parameters as dynamic.	mentioned in text? Maby handy in text also? Yes? Could be "Ideally" rather than "must" since interpolation might be applied possible.	Added another footnote to state this.
Richard J Martin, JD (AAPM)	3.6.2	N/A	NSA or NEX superfluous in requirement and different than other specifications.	Recommend using just >=1.	- specifications for other organe (brain / breast)? --> **ask Trevor**	
Richard J Martin, JD (AAPM)	3.6.2	N/A	Should temporal resolution be about 10s or less than 10s?	N/A	less than 10 s	
Richard J Martin, JD (AAPM)	3.6.2	N/A	Prostate field strength is 1.5T or 3.0T, brain is 1.5T.	N/A	ask Caroline. See line 128...	Added 3T for brain
Richard J Martin, JD (AAPM)	3.6.2	N/A	Prostate stands out with T1 VFA having the lowest upper FA recommendation. This seems odd.	N/A	we recommend 25 for the DCE sequence, could be 25 for maximum flip angle for prostate. Look at publication from Amita (Table 3, Reference 38, 36, 39, 46) and Peled. Mark will look up references. Look up common T1 of prostate tissue.	Looked up in literature and corrected upper value to 20˚

Richard J Martin, JD (AAPM)	3.6.2	N/A	There is a breast specification, but no profile claims.	We recommend including for consistency.	- There is no test-retest study for breast. but Breast is a common application for DCE and we hope to see test-retest. - perhaps postpone the discussion	Described in the text that DCE for breast is frequently used but there is no test-retest data. Hoping that some time in the future will bring this data, we gave a best-practice MRI protocol from literature.
Richard J Martin, JD (AAPM)	3.6.2	N/A	The actor is only physic technologist in entire table. This is superfluous.	Just state in title.	- could be removed, depend on template style for qiba profiles. We could add a note in the caption and remove the column. We should aks Kevin....	Added comment after the "Specification" header and deleted the table "Actor" column
Richard J Martin, JD (AAPM)	3.6.2	N/A	All 3 tables use same rows.	We suggest putting DICOM TAG with field name, then using columns for anatomy (brain, prostate, breast). When there is no difference between them, consider merging cells. This suggestion might also help with some of the haphazard specification formatting throughout.	-good point, but should be discussed in a broader round.	This was the table desgin in an older version. To improve readablitity, we introduced per-site tables for users to have an easy overview over theit requirements.
Richard J Martin, JD (AAPM)	3.6.2	N/A	Is entire breast coverage really a requirement (i.e., neoadjuvant monitoring)?	N/A	- it's a point. Should be tabled for a lareger round.	We describe the most common sequences in Breast MRI. We are not aware of a recent study using a smaller field of view. Thich is probably caused by the clinical value for staging (i.e., missing additional lesions)
Richard J Martin, JD (AAPM)	3.6.2	N/A	Images in acquisition: bringing up ACR is confusing here. It makes sense when diagnostic breast, but not in all cases. Also, now have to look at all the other parameters for ACR. Not sure about need for ACR compliance (in the same way there is a disclaimer for PIRADS).	N/A	- it's confusing. Should be tabled for a lareger round.	These guidelines are designed for diagnosis of breast cancer using morphology and slow dynamics. DCE might require some deviations from this. Remove? Add footnote?
Richard J Martin, JD (AAPM)	3.7	N/A	Consistency	Throughout the document, stick with GBCA acronym or toss it, but do not use multiple references to contrast agent.	- agree, stick GBCA	We need to specify the difference between GBCA and normal CAs w/o Gad ... so maybe stick with either CA or GBCA (if we want to be more specific for toxicities etc.)
Richard J Martin, JD (AAPM)	3.7.2	N/A	Contrast is prescribed by a physician/radiologist. Accordingly, the actor role(s) are not quite right or convoluted by combining contraindication and technical	N/A	- ordered by the physician - checked py person administering - technologist should confirm that patient has no contraindication for Gd	reword table accordingly

Richard J Martin, JD (AAPM)	3.9.1	N/A	General thought: is use of a power injector FDA cleared generally for DCE or is this off-label use?	If off-label, need to communicate this?	- we always thought it was approved , need to check. - check with DSC group - use google/ fda page - injection speed? - call up vendor, ask field rep.	- check if approved -> FDA has no direct approval but it's cleared for contrast application which is conducted with comparable parameters.
Richard J Martin, JD (AAPM)	3.9.1	N/A	These VFA => Dynamic and coverage principles should be consistent with the VFA and DCE acquisition tables. In fact, best if presented prior to.	N/A	- clearify later - put in both places - should be in the table! - but a sentence in the protocol design section	- add in table as a footnote - add in seciont protocol design
Richard J Martin, JD (AAPM)	3.10.1	N/A	This language might be ambiguous. Is the guidance that surface coil intensity corrections based on image intensity not be used, but corrections based on measured array-coil sensitivity profiles can (or 'should') be used?	Please clarify. We recommend specifying "image intensity" or "generalized image intensity" to make sure it is clearly distinguished.	- image intensifty (post processing) based correction vs coil sensitivity (reconstruction) based correct. - combine coil sensitivity and reconstuction in sentence l523 - add another sentence for image post-processing - mention vendor specific details (option names, affected sequences, ...). - Zarah will contact Siemens, trevor will ask Philips and Hendrik will reach out to GE about post-processing filters in DCE	Looks like it has been changed
Richard J Martin, JD (AAPM)	3.10.2	N/A	We believe the spatial misregistration segment is not clear. Presume motion correction needed before T1 mapping too and registration between T1 and DCE as well.	Please clarify.	- should include T1 mapping and T1 to DCE alignement - motion correcion vs image registration (first more commonly used)	
Richard J Martin, JD (AAPM)	3.11.1	N/A	N/A	Please correct typo: analy[s]t.	agreed, already corrected in working version	
Richard J Martin, JD (AAPM)	3.11.1	N/A	N/A	Figure 2 - it would be helpful to see examples relevant to the anatomic profiles outlined in this document. It seems liver has disappeared from the document.	- need some artifacts for organs presented in the profile: breast: phase encoding?, susceptibility in breast, scan database of image artifatcs, shunts/valve in brain imaging - Ask Mark Shiroshi and Harrison	Added motion from brain scan provided by Mark Shiroishi. Copyright images of other artifacts were difficult to obtain (and are still welcome)

Richard J Martin, JD (AAPM)	3.11.2	N/A	N/A	Specify how contrast administration should be 'documented' (agent name, volume, rate, etc.)?	Agreed. But where? dicom? Gauge diameter? In a study, it should be part of the study setup (with perhaps need for deviations). Address in the profile to motivate manufactuers?	Add to section 3.9: Could be part of the analysis software? Propose dicom tags (fields in the MRI software. @Rianne will bring this up in OSIPI. Add to profile to motivate manufacturers to identify a solution. 1. Solution: add this to dicom, contact dicom people. 2. Include into analysis or evaluation software 3. Use Excel/paper 4. Use SOP
Richard J Martin, JD (AAPM)	3.13	N/A	Guidance on research, but no guidance on practice.	Please include additional guidance.	- document? check use phantoms and DROs? - bias and precision,	- check 'yourself' with the DRO and the R1 phantom - in the future there might be some recommendations - include in profile if not already present
Richard J Martin, JD (AAPM)	3.13	N/A	Is motion compensation needed for T1 VFA? T1 map to DCE?	N/A	Depending on organ/site: not much for brain or prostate. Would be needed for breast/liver/	- this part of the profile for dynamic series: add for T1-mapping as well - add "dynamic and t1 mapping data" in line 611 - or, perhaps better in 612
Richard J Martin, JD (AAPM)	3.14	N/A	Regarding Image Interpretation: Can DCE estimated perfusion parameters relate to actual physical measurements of perfusion? Are there phantom results validating DCE perfusion parameters?	dicussed in other sections 2.1. The lack of a dynamic phantom should be mentioned there as well. We also avoided to name ktrans a trye physical measure. We stated that it is model based.	This is a difficult issue. DCE-Perfusion is influenced by different types of perfusion (you probably know the flow and permeability limited). There are flow phantoms available though mainly for large flow system (e.g.., cardiac) and not for tumor tissue we're interested in. There is a phamtom by harrison kim. But to mu knowledge, there is no one simulating the permeaniit processes in tumor tissue.	- I remember this was discussed in another section (This is about image interpretation). I'll look this up. - A section about phantoms would probably be beneficial.
Richard J Martin, JD (AAPM)	3.14.1	N/A	AIF vs VIF	Please be consistent throughout.	agreed (Hendriks suggestion)	Replaced AIF with VIF
Richard J Martin, JD (AAPM)	3.14.2	N/A	Artefacts vs artifacts	Please be consistent throughout.	agreed (Hendriks suggestion)	corrected
Richard J Martin, JD (AAPM)	3.14.2	N/A	What is meant by statement that routine anatomic image shall document slab location? Is this a requirement to somehow visualize the slab on a reference image and save it? It appears to be overly prescriptive.	If kept, you might need a graphic to demonstrate what is meant. In fact, this is generally true for image requirements throughout.	- sounds extravagant but means something obviously done every time: chanage to something like "Acquire a reference anatomically image putting the dce volume in an anatomical perspective. Make sure this is also send to pacs.	make more clear in Table 3.14.2 (e.g. the routinly acquired anatomical images shall be used to identify the slab position).

Richard J Martin, JD (AAPM)	4.1.1	N/A	N/A	Please correct typo: requirements [from]?	agreed (Hendriks suggestion)	Done
Richard J Martin, JD (AAPM)	4.1.2	N/A	This is a serious issue, but users need to be aware that the dynamic acquisition for DCE does not “see” the T1 of an arbitrary IR sequence used for T1 validation, it sees the same T1 used for VFA T1 mapping as long as the parameters are not varied too far from the DCE acquisition. Also, it is important to note that applying a correction schema to the T1 maps, but not to the DCE images, is likely to be problematic.	N/A	- good point. We should probably mention TR based methods or give a detailed description about IR mapping - same goes for the correction applied. I think we mentioned that T1 maps should not be "improved" with algorithms (other than B1 correction which should also be applied to the DCE-Images) this already discussed someplace else.	- look up section about T1 mappping correction (should be 3.9 or 3.6,) - propose discussion about IR-mapping or switch to TR-mapping - make clearer that IR is meant for the calibration measurements on the phantoms and not the clinical imaging
Richard J Martin, JD (AAPM)	4.1.3.1	N/A	B1 mapping guidance for knee and breast appear to be outside the scope of this document. Exceeding the scope of the guidance happens often in the current version of the document. As a result, it becomes very difficult to relate Claims to "supplementary guidance and best practices."	N/A	I think we decided no to focus on the knee in the current profile. It is unclear to me why the reviewer stated that breast is outside the scope as it has been named in these sentences. I think he rases a more general point, which is indeed an issue, but I think we are not able to give more guidance than we do at the moment, certainly noy pertaining B1 mapping.(RH) ------- -Mention shimming (Philips) in Appendix F (and make reference in original section	The differences in Knee and breast are mentioned to illustrate the importance of B1 maps for all DCE-applications.
Richard J Martin, JD (AAPM)	Appendix B	N/A	N/A	Although the Claims being made off “old” protocols is concerning, you might re-word this statement to state that the proposed guidance uses these studies as "minimum" bars and presents practices that the authors believe would further decrease the variance and/or increase the accuracy of DCE based on their experience and expertise in this area.	Agree (RH)	reworded more optimistically

Richard J Martin, JD (AAPM)	Appendix C	N/A	Breast and H&N included are in this part of the review, but no claims are made in rest of document.	N/A	This was because there was no (t enough) reproducibility data on these body parts, was not it? (RH)	There was no test-retest data for breast but we considered breast mri of high importance in DCE-MRI and wanted to give guidelines disregarding missing test-retest-data. Will add a footnote in Claim definition.
Richard J Martin, JD (AAPM)	Appendix C	N/A	If ROI is to be prescribed from an anatomical scan, should that scan prescription match that of the DCE acquisition?	This should probably be stated somewhere because in practice it is rarely done.	Agreed, how to handle? We do it often when we want to examine a certain part of the knee to understand pathophysiology. Normally we acquire a detailed anatomical scan next to the DCE and register them. Might be not an issue for the tissues this proposal focuses on. Therefore, we could think of leaving it out to avoid misunderstanding(RH)	While this is relevant to smaller regions of interest, this would not be feasible for larger organs and tumors. Added a qualifying statement.
Michael Kin Kuok Lam	3.6.1	High	Is 2 dynamics really necessary for building up steady state in VFA series? Tried both phantom and patient scans on various Siemens scanners - no significant difference could be observed on the T1 maps	Validation of the statement / supporting literature is needed. The VFAs are most probably multi-averaged - could it be responsible for the observations? Implications: 1. Shorter examination time; 2. B1 correction could be done inline on Siemens scanners if dynamics is not needed, this saves further work - a workflow that can be easily implemented in non-academic centres	True that when using a standard FFE sequence the K space will be acquired from high to low (K value), and steady state can be reached before center K space. This might not be true for TFE. So, My experience is that it is needed, but I cannot think of any reference	- look for a publication? - look at presentation from Ed