Priority	Line #	Section #
L	various	
L	various	
H	1	1
	62	1
	62	1
	62	1
	62	1
	62	1
	62	1
	62	1
	62	1
	63	1
	63	1
	63	1
	63	1
	63	1
	64	1
	64-65	1
	65	1
	67	1
	67	
	68	1
	68	
	73	1
	73	

	88	1
	93	1
	93	1
	93	1
	94	1
	99	2
M	100	
		2
		2
		2
	101	2
	101	2
	101-102	2
	119-120	2
	126	2
	141	2
	163	2
L	169	

	170	2
M	172	
L	172	
	173	2
	174	
M	174	
	174	2
	182	2
	185	2
M	190	
	192	2
L	193	
	195	3
	195	3

L	197	
	203	
	215	
	215	3
	219	3
L	220	
	220	3
	229	3
	230	3
	243	3.1.1
	248	3.1.1
	252	3.1.1
	252	3.1.1
M	252-254	3.1.
	255	3.1.1
	255	3.1.2
	255	3.1.2
	255	3.1.2
	255	3.1.2
	255	3.1.2
L	256	
L	256	
L	256	

	263	3.1.3
	265	3.1.3
	265	3.1.3
	265	3.1.3
	267-279	3.1.3
	282	3.1.3
	284	3.1.3
	284	3.1.3
	285	3.1.3
	286	3.1.3
	286	3.1.3
M	288	
M	288	
M	288	
	288	3.1.4
	288	3.1.4
	288	3.1.4
	289-385	3.2
	292	3.2.1
	304	3.2.1

	304	3.2.1
	315	3.2.1
	315	3.2.1
	320	3.2.1
	320	3.2.1
	320	3.2.1
	320	3.2.1
	320	3.2.1
	325	3.2.1
	325	3.2.1
	325	3.2.1
	330	3.2.1
	386	3.2.2
M	388	3.2.2
M	388	3.2.2
M	389	3.2.2
	390	3.2.2
	390	3.2.2
	390	3.2.2
	390	3.2.2
	393	3.2.2

	387	3.2.3
	387	3.2.3
	387	3.2.3
	387	3.2.3
	387	3.2.3
M	389	3.2.3
	390	3.2.4
	390	3.2.4
	393	3.3.1
	436	3.3.2
	436	3.3.2
	436	3.3.2
	436	3.3.2
	437	3.3.2

	441	3.4.1
	447	3.4.1
	454	3.4.1
	456	3.4.2
	456	3.4.2
	456	3.4.2
	457	3.4.2
	458	3.4.2
L	459	
L	474	
L	495	
M	497	
M	497	
L	497	
M	497	
L	497	
L	497	
	503	4.1
	505	4.1
	505-510	4.1
	507	4.1
	507	4.1
	509	4.1

510	4.1
514	4.1
514	4.1
515	4.1
540-545	4.2
541	4.1
545	4.2
546	4.2
550	4.2
550	4.2
552	4.2
560	4.2
564	4.2
565	4.2
568	4.2

	568	4.2
	569	4.2
	578	4.2
	585	4.3.1
	585	4.3.1
L	586	
L	590	
	590	4.3.1
	595	4.3.1
L	597	
L	597	
L	597	
	600	4.3.1
	605	4.3.1
	606	4.3.1
L	608	
	608	4.3.1
L	612	
L	614	
M	623	
L	633	
L	635	
		4.3.3
		4.3.3

		4.3.3
		4.3.3
	638	4.4
L	640	
	657	4.4.1
	660	4.4.1
	660	4.4.1
	665	4.4.1
L	687	
L	690	
	698	4.4.3
	726	4.4.3
	730	4.5
	737	4.5.1
	741	4.5.2
	746	4.5.3
	747	4.5.3
	779-780	Appendix B
	784-785	Appendix B
	798	Appendix C
	804	Appendix C

Issue

Some places say shall, some places say "must"
Both cross-section and cross section in use. Makes searching for things unreliable.
The group should be congratulated on this important work.

document needs to define (C)CTA at first use and in title if this term is retained.

However, I do not understand why C is used in front of CTA. At first I thought that it meant cardiac, but the scope of the document clearly includes carotid arteries and could apply to aortic and peripheral arteries as well.
cross-out: Currently
cross-out: clinical application of (C) CTA and atherosclerosic imaging
cross-out: as a
inserted: CT angiography (CTA)
inserted: a
inserted: widely--available (hyphen)
inserted: , non-invasive
inserted: , (comma after coronary vascular disease)
inserted: arteries,
inserted: technique
inserted: the (before assessment)
cross-out: the (before plaque structure)
inserted: best
cross-out: best medical treatment of revascularization
this needs qualification. It is NOT first line for acute symptoms with abnormal ECG or positive enzyme tests, where the patient need to be sent to the cath lab for probable intervention.
cross-out: carotid
inserted: luminal
cross-out: add further biomarkers
inserted: use additional biomarkers in clinical practice that are
cross-out: becoming
inserted: it can become

A critical parameter for therapeutic decision making is percent areal stenosis. To determine this, the lumen area is required to be determined at a normal arterial segment and at the location of the narrowing. Standardization of this is essential. The point of narrowing can be easily determined as the location of the smallest area, but how should the area at the "normal" location be determined, especially for arteries that naturally narrow distal to their origin. This is an important point to be resolved.

cross-out: basing
inserted: making
inserted: based
inserted: , (after products)
Section 2 is far too long; discusses background and medical issues that are not needed and not always correct. This should be shortened to about 2 paragraphs. Look at other profiles for guidance.
The intention of this section is long the lines of "Measurement X is used to assess Y"

In the claim section (section 2), the unit for bias is the same as the measurand. However, according to the assessment section (section 4.3.3), natural log transformation is suggested to be applied to the measurements before assessing the linearity and bias. It is unclear whether it is the bias or the percent bias that would be a constant for the whole range of measurand.
In addition, the specification for the image analysis tool (section 3.5.2) specifies that for the parameter “composition”, the slope for calcified area and LRNC area only needs to be within 1±0.5 and 1±0.8, respectively. The error bar for the slope are quite wide and the bias would no longer be constant if the slope deviates too much from 1.

Finally, for poolability analysis, it is suggested that assessor uses 4.5 mm of the vessel size as a cutoff to form two subgroups. It is not clear how this specific requirement is selected. Explanation should be provided to justify this suggestion. If there is a vessel size below which the claims do not hold, the range of vessel size, especially the lower bound, should be included in the claim.
The Profile is for atherosclerosis in both coronary artery and carotid. However, cardiac motion for the small vessels representing coronary artery is not accounted for in the bias and linearity assessment procedures. If the motion is negligible for the analytical performance of the measurements, its absence should be justified. Otherwise, the potential issue of cardiac motion should be discussed and accounted for.

With childhood obesity and diabetes rates increasing, and the increasingly poor diet, atherosclerotic disease is becoming increasingly prevalent in children and young adults. There is no need to constrain the population in this sentence. The next point emphasizes the particular relevance to the elderly.
cross-out: for our aging population
this sentence is not grammatically correct
define at first use, not here
define {plaque imaging association with acute chest pain}
If you are going to spell out the acronym for some trials, do it for all trials {MESA}
insert: , (comma after e.g.)
Don't need to re-iterate inside the claim what conformance means. That's the purpose of the rest of the

insert: , (comma after Profile)
Range and Bias column values are likely in the stated units
This table says burden units are Ratio; Appendix D says None.
on what data are these expectations based ?

Or - is this the tolerance that you want a method to achieve in order to meet the profile??

If so, based on what clinical premise? How was it determined that this level of bias and variation is acceptable for making clinically appropriate decisions?
I'm not sure what this first bullet means. So the range, bias and variability values are somehow related to the

put a footnote on every table where an abbreviation is used. Readers should not have to look back to find out the meaning of an abbreviation.
cross-out: comma after LRNC area

alignment of image data with histology data is notoriously inexact as the tissue slicing distorts and tears the vessel and plaque. Also, unless a bone histomorphometry technique is used, traditional plaque histology is performed first by decalcifying the vessel so that the histological slicing can be performed (calcium is too hard for routine slicing equipment). In essence, histology is a very poor source of truth. Micro CT should be used on intact segments of vessels. This will provide absolute measures of volume for comparison to 3D measurements of the segmented plaque regions.

BREAKPOINT IN TEAM REVIEW ON 7/29/2019

Are vendor components the first three actors in Table 3-1? And is this permission to conform to only a narrow range? And presumably this refers to the range values in the table
arteries walls are < 1 mm to about 2 mm thick in healthy individuals. In patients with mild to moderate disease, wall thickness may be a few additional mm. Thus measurement of maximum wall thickness will require an underlying capability to resolve sub mm distances. The ranges of bias and variation given in the claims Table (which should be numbered and titled) are too big, in my opinion, to give clinically meaningful measurements of wall thickness or to differentiate normal vs diseased regions.

Not clear what "point-wise wall thickness" means. And largest within the lesion implies moving along the vessel to find the max.
spell out QA in table
The physicist is involved in far more than image reconstruction. He or she selects the optimized acquisition and reconstruction protocols, after participating in the equipment selection, installation, acceptance testing and quality assurance program. They are further involved in establishing the best parameters for analysis software and for confirming results against phantoms, when possible. Technologists are the first line for Image QA as they often screen for inadequate images prior to sending to PACS. They are also often the actor performing the quantitative measurements, sometimes in a dedicated 3D or post-processing lab.

"Conformant Actors shall support the listed Activities by conforming to all requirements in the referenced Section." but the section reference column has been omitted
add a comma after e.g.
this is not mentioned in Table 3.1 {refers to "managing the equipment performance related specifications"}
highlighted "managing the equipment performance related specifications"
the raw data is not image data. They are attenuation measurements.
If the profile doesn't have longitudinal claims, probably don't need some of this text.
poor grammar
Algorithms ~~which~~ that
for example,
it is important to
all scan geometries on clinical systems are 3rd generation. Not clear what is meant here. axial vs helical scanning shouldn't make a lot of difference here. Image reconstruction algorithm is likely the bigger effect.
a discussion is needed about centering to the thorax as a whole, and not trying to center about the heart. For proper dose modulation and kV selection, the thorax needs to be center both in the A/P and in the L/R
kV settings of the patient is not written correctly ... This whole sentence needs help.
Placement of comas confuses intention of paragraph. While grammatically correct this section could be clearer.

not clear if you are saying nitrates should be given routinely, occasionally (if so, which patients), etc. For longitudinal studies, the same technique must always be used.

Also, what about beta blockers and optimal heart rate. Metal artifacts are discussed but motion artifacts are much more relevant, especially for the right coronary or at high heart rates.
any recommendation here about weight-based protocols? what does consistent to baseline mean if this is the first scan or a cross sectional study? A more appropriate benchmark is a range of CT numbers within the left again - give a CT number range. Enhancement of the vessel is a critical parameter for accurately resolving the lumen boundaries and also for having sufficient contrast with respect to lipids or calcium. Without giving the imaging physician clear guidance on the necessary contrast enhancement to be achieved, there is no "target" for the physician to aim for to ensure "appropriate" conspicuity.
what about arms above head - arms along side can cause issues with artifacts also. what recommendations for when you can't remove the metal (pacemaker leads, stents)?
not really sure what you mean with mid-axillary. What you want is for the coronal laser to lie at the midline of the AP dimension of the thorax at the location of the heart.
this is establishing routine use of nitro. What ramifications does this have on the need for nursing or physician personnel, neither of whom are guaranteed to be at the scanner.

What about heart rate and beta blockers to ensure the lowest heart rate and lowest risk of motion artifacts? This would have serious implications for nursing and physicians presence during the exam.

What about optimal phase of the RR cycle?
Row Contrast - Is consistency with baseline relevant?
Row Intravenous Contrast - are contrast parameters different that contrast protocol?
Row Nitrates - "within 5 minutes of the start of the acquisition" is a bit ambiguous.

coronary CTA
need to be consistent with acronyms. Also, since this is a coronary section, why not just say CTA?
coronary CTA
I agree that these are important issues. Do all QIBA protocols provide such descriptive guidance on who to acquire the best data for measurement accuracy? This seems like a how to guide for performing good coronary CTA. Is that expected for QIBA protocols, which I thought were more about standardizing the measurements once a data set is in had, even if the data are suboptimal.
{section is highlighted in pink in reference to Breath Holding} - refers to next comment
above you called this bolus tracking, assuming that the reader understood what that was. Why are you not using the same terminology here? you want to be consistent throughout the document. Someone might wonder if you mean something different here if you don't use the same wording.
with the use of lower tube potentials than 120 kV, a CT number of 180 HU will correspond to very different concentrations of iodine. At lower tube potentials, this means that the scan will trigger very early, often well before the contrast enhancement in the left ventricle (and hence the coronaries) reaches its maximum. This can lead to inconsistent enhancement and even the scan ending before all the dye is injected. The scan certainly won't be temporally centered within the plateau of the enhancement curve. The threshold must be specific to define all acronyms!
scan delay times are patient specific and affected by heart rate, patient size, etc. They also depend on the threshold for triggering.
clarify that you mean radiation dose and not iodine contrast dose
clarify that you mean radiation dose and not iodine dose. The sentence makes sense with either interpretation
Row Heart Rate - What is the pass/fail for this requirement?

Row ECG Gating - shouldn't iterative reconstruction be in the protocol design rather than subject handling?

Row ECG Gating - So Prospective is a SHALL but Retrospective may be required? So if I don't use Prospective do I conform or not?
with dual source systems, a temporal resolution as good as 66 ms can be achieved, allowing motion-artifact-free images of even the right coronaries at considerably higher heart rates. The heart rate will also impact the optimal acquisition phase suggested in the next row.
iterative reconstruction can produce non-linear effects and also blur out low contrast structures, such as clots and lipids. Further, some IR methods have been shown to impact the accuracy of segmentation and CT numbers. One examples in the literature demonstrated that the coronary calcium scores changed when IR was used instead of FBP. Accuracy of a biomarker trumps using the "lowest possible radiation exposure" and thus advice to use IR or otherwise push the dose "too low" is not appropriate.
prospective gating at what phase?
this entire section reads like an attempt at an abbreviated tutorial on CT imaging. Any user of a profile on obtaining quantitative biomarkers should already be an expert in qualitative imaging and should not need such a primer, which is not relevant to defining an actual profile for a biomarker. The draft profile is extremely long and unfocused in terms of reproducible and unbiased quantitation of measured data. Yes, it is important that the underlying data be of high enough quality to make an unbiased measurment, but as noted above, the profile needs to focus on defining the characteristics of a "good" data set and not on the dependencies of the data on with modern high-frequency generators, the adjective "peak" for tube potential is meaningless and is being abandoned. Additionally, one should not use a unit of measure as a noun. The term tube potential should be used throughout unless you are giving a numerical value followed by a unit (kV)
software version

of course this is not always possible as equipment and SW upgrades occur. Even within one practice, patients can be triaged to different scanners as scheduling systems rarely (ever?) look to see what equipment was used on a prior exam. Thus this recommendation is somewhat optimistic. A discussion of cross-over methods would be useful to provide guidance on how to map data from one system to data on another system
they are not available at this time, either. The new DICOM supplement for CT protocols will greatly facilitate this, but no manufacturer has adopted it yet. (2)
this paragraph seems to have longitudinal research studies in mind ("participating sites"). For clinical patient management, each measurement should be accurate in its own right, within tolerances, so that any data point can stand on its own merit for clinical are. (3)
agree completely, yet so much of the prior text was rather prescriptive regarding acquisition methodology. What is needed is to define the characteristics of an adequate dataset. (5)
please use the quantity name (noun) and not the units (6, 8)
please define all acronyms throughout the document (7, 9)
performance targets for the measurands? How does one verify that in patients in the absence of reference truth? Performance targets for the data are measurable and verifiable and these should be given in this profile. N and T have not been defined. (11)
text crossed out - (12) (13)
IEC standards have required this for many years now. This is not a true statement for most installed systems capable of cardiac CT. (14)
time (15) - after acquisition
I have NEVER heard this phrase since the dawn of MSCT. It must be a vendor specific term. I don't think it is appropriate to note every permutation of parameter name. The IEC name is the standardized name that all vendors should be using (16) -- {in reference to Nominal Tomographic Section Thickness}
iterative reconstruction methods produce non-linear spatial resolution values that are dependent on the contrast over an edge. Values will be superior over high contrast edges relative to low contrast edges, especially for edges with contrast levels below about 20 HU. you will need to define the contrast level that you mean and the specification for that contrast. (1)
Row Acquisition Protocol – seems unlikely physician will prepare a protocol for each encounter.

Row In-Plane Spatial Resolution – also likely inefficient to re-validate the protocol for each encounter.
Row Scan Duration – this was in CTVol to deal with breath holds over the length of the lung – do you have the same issue for carotids and coronary artieries?
highlight - please define your terminology {in reference to f50 value} (2)
line pairs per mm (3)
this should be called pixel noise as you are focusing all measurements in terms of 2D (area). Noise is measured in a 2D matrix of pixels having no thickness. The tissue represented by a pixel value has a 3rd dimension, but the CT numbers, whose values you are evaluating, do not.
one thing that is not clear is that, so far, the focus has been on CTA, which looks at the lumen and uses iodine. A measurand that is listed is calcium area, yet calcium is routinely measured in the absence of iodine (a non-contrast scan). Noise requirements may not need to be the same for these two scan types and measurands. Further, lumen area is notoriously compromised in the presence of dense calcifications due to blooming of the bright calcium into the less bright iodine, making the lumen appear smaller than it is. Conversely, for low density calcium, the brighter iodine signal of the lumen in a contrast-enhanced scan can bloom into the calcium, altering the calcium area. These are important limitations for making unbiased and repeatable measurements.
g (4)

this value arbitrarily disqualifies a large number of good cardiac CT systems.
again, this is arbitrary and exclusionary. to cover a 12 cm typical cardiac volume, this is a 3 sec scan! The contrast plateau can be longer than this. What is wrong with a 5 sec scan? a 6 sec scan? etc.
is revolution the correct term? Not rotation?
awkward wording. Please rephrase. {regarding "shall enable with trigger set…}
here you use an adjective (diastolic) byt below you use a noun (systole). Review by a professional scientific editor is needed.
You have given specific instructions for particular ECG gating. However, this scanner dependent and the parameters you have provided would be suboptimal for some scanners in current use.

this is the first discussion of carotids. Also, what about the aorta or pheripheral vessels, who also require quantitation of lumen stenosis and sometimes plaque or calcium burden

all of these protocol parameters are being prescribed by the imaging physician. The imaging physicist would be involved as he or she is often more familiar with many of the technical trade-offs in performance that occur when these parameters are varied. All protocol parameters should be determined with a protocol team, which should include an imaging physician, physicist and technologist. (e.g., the physician is unlikely to know all the various settings on different makes and models of scanners and software versions, which the tech and physicist will know). Both ACR and TJC require that protocols be established and reviewed by this team, all of whom are
as above, this discussion section is too long for this profile. It is an overly simplified primer on the fundamentals of CT. References to more precisely written articles or textbooks should be provided instead for those users who need such a tutorial. The QIBA profiles should not be cluttered with this didactic material. This section should be reduced to no more than one moderate paragraph that directs the reader to the appropriate sources.
why not less than 0.5 mm is the noise is controlled? These would give even more accurate information and there are scanners that now do this.
ummm - for clarity of terminology - the in-plane dimension of a voxel is the pixel size. You have focused primarily on area measurements and mention that 3D (volumetric) values can be determined from those. Such 3D measurements woiuld take into account the voxel depth, which has been established above as the reconstructed image thickness. The term pixel should be used here, not voxel.
see comments in 3.2.2 about the terminologies used here.

More importantly, these parameters can only be determined after the reconstruction has been performed. The reconstruction parameters completely establish these values. Thus these parameters can't be specific or assess in 3.2.2 as no reconstruction methodology or parameters have yet been defined there.

That is, there are no values for these parameters that are a function of only the acquisition. They are determined by both the acquisition and reconstruction.
it should be noted that these values are for a specific size phantom and do not define the noise that can be anticipated in patients. Previous noise standards have been defined for coronary artery calcium assessment as a function of patient size. By assigning a target noise value for a single phantom size (20 cm ACR CT phantom), will the noise be appropriate across a range of patient sizes?
the physicist is particularly essential to the process of selecting the correct reconstruction parameters. For example, many scanners provide reconstruction kernels (filters) that enhance edges. These alter CT number accuracy. Even though this filter is discussed in the tutorial material above, it is left out of this specification table! Without the correct filter, ALL quantitative measurements will be wrong and they certainly won't be

these primarily need to be measurable characteristics of the image data and not the parameters used to acquire and recon the data.
time of exam interpretation? {refers to reporting time}
this comment is only relevant for longitudinal studies. what about checking adequate enhancement for a single clinical study. And - what constitutes consistent? Within 20 HU? Within 50 HU? Consistent at what point in the artery? Left main? Carotid bifurcation?
refer to marked-up AAPM version for crossed-out text and insertions, table 3.4.2, specification
inserted text: (e.g., arms down at sides), or equipment issues (e.g., ring artifacts) (comment 11, table 3.4.2)
important to note absolute requirements for any given exam (i.e., when only one exam is available, when exams are performed in a different manner but the biomarker information is still needed for each time point) as well as requirements to match the baseline when longitudinal studies are performed and compared.
patient can be perfectly still but cardiac or swallowing motion (ie motion not under patient control) can still cause problems. Patient motion usually implies non-compliance/gross motion. I suggest just calling this Motion
I don't know what phase of enhancement means. There is a phase within the cardiac cycle where images are acquired and reconstructed, but the enhancement is not phasic.
Will all measurements involve a lesion (i.e. no measurements of regular vessels?)

The sentence would benefit from some punctuation/clarification.
Does support matching mean matching patients, or matching vessels, or matching vessel cross-section locations, or something else?
Row Vessel Structure – seems more likely this will be done once during a product validation activity than during the image analysis for every patient.

Row Vessel Structure – The text “noting that the full 95% confidence intervals (not only the point estimates) shall meet or exceed the indicated specifications when tested over range as given in Claims section” seems to be about how to come up with the numbers that you compare to the table, so the text would fit better inside the referenced 4.3 procedure. Would also allow you to elabourate on the meaning a bit more.
Row Basis of Volume Results – what is this referring to? All the measurands seem to be 1D or 2D (thickness, area)
Row Provenance Records – what does “identity” mean here? What qualifies as a “step taken”? What does the visual query or the programmatic query have to do? And how does this requirement support the claim?
Row Result Verification –
Row Result Verification – do you prefer margin contours or segmentations?
this section needs to be redone completely
define - What you mean here is the spatial frequency at which the amplitude of the MTF (not "contrast") is 50% of the amplitude at the zero frequency (which should be 1 for a properly normalized MTF).
text crossed out - refer to marked-up AAPM version for crossed-out text and insertions {Assement Procedure: In-plane Spatial Resolution}
describes the ability of an imaging system to faithfully produce a signal that is an accurate representation of an input signal of a specific spatial frequency. An MTF value of 1.0 at a given spatial frequency means that the output signal is identical to the input signal. (comment 9) {refers to crossed-out text}
this definition is not correct (comment 10)
this is not correct. Spatial frequency is given in terms of line pairs per mm. A line pair includes a bar and a space, each of which is considered a detectable object (you need to see both the bar and the space). That means that for 1 line pair/mm, you have 2 objects/mm so each resolvable object is 0.5 mm. The equation is thus 1 / [lp/mm x 2] (comment 12)

this is not correct. Spatial frequency is given in terms of line pairs per mm. A line pair includes a bar and a space, each of which is considered a detectable object (you need to see both the bar and the space). That means that for 1 line pair/mm, you have 2 objects/mm so each resolvable object is 0.5 mm. The equation is thus 1 / [lp/mm
this is one phantom that can provide a sharp edge for measurement of an edge response function, which can be used to calculate an MTF curve, but there are many others. Further, MTF curves are typically performed by scanning a very thin wire.

Above, the MTF for a tissue contrast level and air were required. Very few phantoms have an edge with a tissue (about 40 HU) contrast level. The CTAP phantom has either an approx. -80 HU level or a +120 HU level. Use of low contrast edges will result in very noise data and are subject to much greater uncertainty, or else lower resolution if blurring is used to reduce the noise in the curve.

Also, the MTF for lower contrast edges will vary with IR algorithm and strength. Wires all have high contrast.

We recommend that the high contrast spatial resolution (MTF) be all that is measured using an object/air edge or an MTF wire.
there is no AAPM TG233 phantom. Report 233 details evaluations that can be performed with many different
Refer to marked-up AAPM version for crossed-out text
Refer to marked-up AAPM version for crossed-out text and insertions
there is no such thing as a TG233 phantom.
Refer to marked-up AAPM version for crossed-out text and insertions (comments 5-9) Pixel, pixel, tube
the std dev of pixel values reflects the variation in the measurement of CT number in a 2D matrix. It is therefore pixel noise, not voxel noise.
this is a term that applies to one specific reconstruction method from one specific manufacturer and is therefore not general. While the text dose note that this is an example, the specific vendor terminology should be excluded.

Further, radiation dose levels need to be quantified in terms of scanner output (CTDIvol) and not mA and kV (again, please refer to the quantity and not the unit).

Finally, BMI is not the best surrogate for patient attenuation, as patients carry their weight in very different regions. What about a tiny woman with very large breasts? She will have an overall normal BMI but very high attenuation over the heart. What about a man with a very large belly due to metabolic syndrome and hence has a pretty high BMI, but is not very muscular and has a lower attenuating thorax?

Patient attenuation should always be measured at the location of the scan, preferably with water equivalent diameter. If that is not readily done, than lateral dimensions at the scan location should be performed by the
A much more robust approach would be to include a generic technique chart, whereby the tube current and tube potential are presented with respect to a reference technique for a reference size, much as is done on the image gently website.
these instructions don't need to be included. Any tech or physicist who operates a CT system knows to warm it up and runs cals before the start of a measurement session
inserted text: image (comment 1)
inserted text: pixel (comment 2)
why? what would you do with the info? (comment 3)
inserted text: several different (comment 5)

s that are representative of the patient population for which the scan and measurements will be performed, (comment 6)
as a function of size is too vague. would this have to be every cm? every mm? something like 20, 30, 40 and 50 cm diameter would cover necks and legs through very large torsos (comment 7)
inserted text: pixel (comment 8)
Not at all realistic for an imaging site to do this test unless the phantom is provided, and if phantom is provided, there will likely be an issue with contrast agent dehydrating and crystalizing. Is there any reason the authors would expect that this should vary dramatically from scanners and protocols that meet the conformance requirements? If not, a small group could establish expected bias and linearity values by scanning the same phantom on a number of scanners and using different protocols. (comment 9)
Figure 4.1. (comment 10)
Most of these assessment procedures are written in terms of an assessor. Who is the registrant? Is this saying that the assessor shall obtain a set of phantom scans that meet the following requirements, either by scanning them locally or by obtaining them from another source such as the QIDW?
Is “scanner settings” the same as “acquisition protocol” used elsewhere?

this sentence is poorly worded. Please define what is meant by scanner settings representative of clinical practice. (comment 12)
For section 4.3.1, a phantom was introduced for structural measurand assessment. However, it is not clear if the phantom is commercially available. The specifications for fabricating similar phantoms are not clear. For instance, line 595 mentioned an example material for vessel phantom with a density of 1.06g/ml and it is not clear how much density tolerance one may allow for making such phantoms.
Which manufacturer? Phantom, scanner, Analysis tool?
What do you mean by subset? – do only 4 of the phantoms? Or do 6 but for the last one have a tube length D of 70mm instead of 80mm?
So if someone documents their “reduced scope” e.g. just one phantom, do they still conform?
one or more (comment 1)
) (comment 2)
this experimental setup is rather poor and misses key aspects. why vegetable oil? what size of a "box" should be used? Should tube current modulation be used for this test? how about ECG gating? (comment 3)
If “scan parameters” is the same as “acquisition protocol” used elsewhere, lets converge on “acquisition
what makes a variation for a scan parameter "admissible"? (comment 4)
What does it mean “recording how requirements as described in Image Analysis Activity have been met”?
Consider being specific about what the assessor is required to segment.
Section 4.3.2 and 4.3.3 have stopped referring to the four specific measurements been assessed. As a result the text doesn’t line up. E.g. I see how maximum wall thickness might be measured by micrometer, but I don’t see how lumen area, wall area, and plaque burden would be.
Why have small vessel and large vessel subgroups been introduced? They do not seem to appear elsewhere.
What does “assess the ability to pool the results” require the assessor to do?
For section 4.3.3, it is not clear why natural log is needed.
For section 4.3.3, regarding linearity assessment, statistical significance or non-significance alone of the parameters in the quadratic curve does not tell what the deviations from linearity are. One good alternative assessment of linearity is to evaluate the deviations from the best-fitted line. We suggest the profile committee consider the following references: EP06-A “Evaluation of the linearity of quantitative measurement procedures: A statistical approach; Approved Guideline (2003).”, and Tholen DW. Alternative statistical techniques to evaluate linearity. Arch. Pathol Lab Med. 1992; 116(7) :746-756

For section 4.3.3, discussing the linearity assessment, it is not clear why the targets need to be divided into vessel subgroups at the cutoff of 4.5 mm.
The profile mentions the use of histology for evaluating the accuracy of measurements in section 4.3.3. This session is written in a way suggesting that using histology is the only or best method for that purpose. However, using histology is only applicable for ex-vivo based assessment, and the method itself is not optimal due to the need for registration and other limitations. The Profile should mention that using histology is only one approach and there are might be alternative approaches such as the use of IVUS as a reference imaging modality or the use of dual energy CT for plague material decomposing toward potentially classifying plaques as calcified or non-calcified. Such alternative approaches would certainly need to be validated for their use, which also applies for
If I understand this right – this procedure would require CT imaging of 90 pathology samples and to then determine the bias and linearity of the imaging and analysis process. This again – is not at all feasible for an imaging site to do. This seems more appropriate for a group of scientists to do with a the same sample set on a variety of scanners and with a variety of image analysis tools to produce expected bias and linearity – unless there is reason to think that some scanners or image analysis tools that meet the requirements of the conformance statement might behave dramatically differently. (comment 1)
It doesn't say which "tissue characteristics" it evaluates.

For section 4.3.3, line 657 suggests "correlate histology cross-sections with locations in the CT image volume". This is not a trivial procedure, and it is not clear if there are validated and accessible methods/tools that one may use. Although an "acceptable method" (line 657) was provided, it is not clear how that "acceptable method" was validated and whether the tool is publicly available. No reference was provided.

this sentence is very poorly written. (comment 1)
raw CT can cause confusion, as it could be mistaken for raw CT data, i.e., CT projection data. "primary CT images" may be a more suitable term here. (comment 2)
should the goal of a QIBA profile be to suggest HOW to mitigate these limitations? (comment 3)
What does "recording how requirements have been met" mean?
Edit which segmentation? Does the preceding "perform analysis" require segmentation? Line 663 mentions scrupulously avoiding use of the analysis tools segmentations. Otherwise they don't seem to be mentioned.
If o (comment 1)
cross out: coverage probability (comment 1)
the names used for these assessment procedures are not consistent. the first one talks about vessel structure bias and linearity, and evaluates either a reader or an analysis tool. In this one the same is done for variability, but the title is centered around the reader/analysis tool. A consistent approach should be used. (comment 2)
inserted: the (comment 4)
incomplete or otherwise poorly structured sentence (comment 5)
sentence poorly written - this is common throughout the document. a careful editing of the document is
See highlighted text (comment 7)
phantoms may be used to evaluate not only acquisition, but also reconstruction and post processing. moreover, their use applies beyond longitudinal studies described here. (comment 1)
you are including in the appendix several definitions, such as "lesion definition variability", that are never used anywhere in the text. (comment 3)
what is the purpose of this table? are those values meant to be references for each measurement? if so ranges should be provided, and the expected accuracy of the measurement be indicated. (comment 1)
are these examples? how are these values taken? (comment 3)

where are all these numbers taken from? a range would be more appropriate. also, pixel size alone is not an accurate description of image resolution detail. for example, reconstructed CT images with very small pixel size may have very poor spatial resolution if an excessively smooth reconstruction kernel is used. (comment 4)
On its own, the appendix is a bit ambiguous whether maximum thickness it is max radially or max along the vessel. Is the centerline relevant?

Typo in title. Also would consider inclusion of other relevant CCTA measures such as contrast density difference and specifying 3D plaque burden

Proposal

When must means shall, use shall.

Decide on cross-section or cross section and use consistently (I prefer cross-section)

The plaque characteristics discussed are very limited for the assessment of the coronary arteries, my area of expertise. In coronary artery assessment it is routine to assess atherosclerotic plaque in a three dimensional manner. This is important because of the small size of the plaques and their eccentric and complex nature. A 2 dimensional assessment will significantly limit reproducibility in coronary artery plaque assessment. In particular, plaque volume (total, calcified, non calcified and low attenuation) is one of the most important parameters in studies assessing quantitative plaque assessment in the coronary arteries to date. Plaque volume and plaque burden calculated from plaque and vessel volume are the most frequent parameters being used in current research studies. Therefore, the proposed parameters are not really representative of current or future research or clinical practice in the coronary arteries. Include 3 dimensional volumetric assessment of atherosclerotic plaque.

We recommend that the leading (C) be removed from the entire document.

Add a sentence along those lines.
Most of the current paragraphs are interesting background but could move to a Background Annex.

Could just say "Conformance to the Profile …"

Clarify whether variability is also in those units or in SD, etc.
None is probably better.

Clarify
Consider mentioning in the discussion that the Measurements listed in the table are formally defined in Appendix D

Clarify

Define it once in Appendix D rather than in several places.

Reword or put back the Section reference

Remove.

"As with the use of similar scan settings, during different visits of the patient to overcome potential differences due to different kV settings, consistent centering of the patient avoids unnecessary variation in the behavior of dose modulation algorithms during scan."

Rephrase or remove
Use one phrase
Clarify if this means before, after or either.

Clarify whether you pass if the heart rate is 70BPM but you tried to get 65, or whether you fail if the heart rate is above 65, in which it's not really targeting, it's achieving.
Move

Clarify

Would be better to have a protocol design activity which is done only once, rather than as part of the activity for each encounter.

Validation could be part of the protocol design activity.
If not, consider dropping the requirement (or replacing it with something more apt) – same in next table

Add something along the lines of "or at heart rate appropriate for scanner according to SCCT guidelines"

Might want to refer to the measurement location rather than the lesion? Same for several rows

Clarify

Move to product validation activity. Same for several of the other rows in this table.

Move text into 4.3. (Same type of comment for a couple following rows)

Remove Basis of Volume Results?

Clarify text or consider dropping.

tool-> Image Analysis Tool
Use one or the other consistently or make a clear distinction.

Clarify

If so, lets converge on “acquisition protocol”. It will also make it easier to find the relevant “requirements of this Profile” it is expected to meet.

Clarify
Clarify

Clarify

See above

Be more specific.

Reference specific measurements rather than generalizing.

Remove?
Clarify/remove

Do something like section 4.3.

Clarify what details shall be recorded to be conformant.
Clarify

Maybe add an introductory sentence or two. E.g. All measurements are taken at a chosen perpendicular cross-section of the vessel. This produces a roughly circular lumen area (representing the blood channel) and an annular wall area (presenting the vessel wall, including plaque, calcium and other attached materials). Need to be clear which area for Calcified and LRNC

Change title to "Measurement Definitions and Units". Define contrast density difference as "Maximum percent change in HU across a lesion" and 3D plaque burden as plaque volume/vessel volume

Disposition

Replaced as suggested.

Adopted "cross-section" more consistently.

We agree as to the importance of 3D, and had attempted to express this but it was too subtle based on unique but detailed aspects of the validation procedure which obscured out intent. We have now explictly included these measurements at all relevant places in the Profile.

Now (C)CTA is replaced by CTA at all occurrrences.

Simplified paragraph to avoid unnecessary detail, providing greater focus on the actual measurands beign considered explicitly.

We decided that Stenosis not be in the Profile explictly, rather focusing on underlying measurements that are more objective. The specific question of reference which is you mention is an a question extensively covered by NASCET and ECST. QIBA's contribution is to add area measurement (rather than being limited to diameter), but leave the topic of reference for these other works. We have also added soem explanation of this rationale into the Profile so as to be more explanatory.

Replaced as suggested.

Simplified to focus on the most relevant portion.

Simplified to focus on the most relevant portion, and incorporated Appendix D directly into body.

The natural log was specified in error and has been removed. The performance claims and specifications are intended to be consistently in the original scale, rather than in percent, across the document.

Each version of the Profile captures a snapshot of the state of the art. The first step to improvement is to be explicit on the performance - not all participants in the plaque morphology field may yet be able to identify their actual performance, and out hope is that this work by QIBA can provide incentives for more of them to reach that. Then, over successive revisions, the Profile can specify increasing performance as the state of the art improves.
This text was removed as unnecessary.

This is handled in two ways: first, there are specifications for the application of ECG gating, temporal resolution, and bounds and conditions on heart rate in the coronary specific section. Also, we make explcit QA for motion artifact to be reviewed prior to analysis. In future, claims regarding scan-rescan repeatability are not yet in scope but we expect that they will be needed in an ammended Profile and this issue will be formally assessed at that time.

Simplified to focus on the most relevant portion.

Simplified to focus on the most relevant portion.
Simplified to focus on the most relevant portion.
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Simplified to focus on the most relevant portion.
Simplified to focus on the most relevant portion.
Simplified to focus on the most relevant portion.
Simplified as suggested.

Simplified to focus on the most relevant portion.
Yes, the units are the same (the original scale).
Now use "unitless ratio" in both places.
Explanatory footnote as to boty source of current figures, and status of the Profile development at various stages, has been added.

Clarified.
Incorporated Appendix D directly into body.

Expanded acronym.

This variability in the validation process is essential, so we have left it in as essential to an objective validation.
Despite the issues, histology is the proper standard. MicroCT is a self-referential comparator that is not defined extrinsic to CT imaging, as it cannot appreciate cell type and morphology as histology can. Hence the approach is to mitigate the issues you correctly identify in the use of histology, rather than to believe it can be avoided.

Clarified.

Whereas we agree that ideally it would be great to resolve to sub-mm distances, the claimed performance does not adequately support improvement to clincial practice. Wall disease routinely increases the thickness by at least 1 or 2 mm, and often by 3 or even 4 in extreme remodeling associated with the most dangerous plaques. Overstatement of this requirement, while well intended, can provided a needless sense that invasive intravascular techniques are needed, which is not the case. Even more detrimental, the invasive techniques are themselves inferior with regard to tissue characterization (IVUS in particular, which demonstrates poor agreement with histology). Our goal is to more properly establish what is and isn't possible by CTA, and in parallel to help focus the community on what is most important to achieve and provide insight into what the relative merits of different techniques are.
Incorporated Appendix D directly into body.

Done (and throughout the document).
The table itself, as well as descriptions of physicist and technologist now use the phrasing from the comment.

Simplified wording.

Done.
Removed.
Removed.
Removed paragraph as unecessary.
Removed as suggested.
Unnecessary phrase removed.
Done.
Done.
Added.
Unnecessary phrase removed.

Re-worded for clarity.

Consistency is required.
Changed to protocol

Use of acronyms now consistent across Profile.

Simplified the text.

Reworded as per suggestions.

Moved.

The whole section has been shortened and simplified, based on the review comments and representign our agreement that the section text was too long, incorrect in many cases, and missed the papoint that the specification tables are where requirements belong rather than in discussion sections.

The shortening of the discussion section now makes it more obvious that the protocol design activity which is done only once, rather than as part of the activity for each encounter.

Dropped.

Fixed.
Renamed throughout document.

We highly agree. That's why the validation procedures of section 4 (4.3, 4.4, and 4.5) are important to have a histological basis, an objective truth standard not subject to the limitations mentioned. Some suppliers have started to turn their focus to objetive validation to move beyond the issues with analysis methods that do not mitigate these effects. We hope that our work in QIBA increasingly draws attention to this and improves the state of the art broadly.

Fixed.

Fixed the discrepancy.

Added as suggested.

Agree that these other arteries also need this. This version of the Profile decided to start here, but we could extend to other arterial beds as the community requires.

Changed to physicist.

The gratutitous text has been removed for a much smaller section.

Actors changed to physicist.

Improved per reviewer suggestions.

Changed.

There is an introductory sentence that indicates image analysis involves quantitative assessment of vessel structure and tissue composition of plaque morphology within a target vessel, lesion, or vessel subtree.
Improved.
Clarified.

Agreed, but in any case these are the requirements to be met. It is overly complex to create a separate activity for product validation. The requirements are correct as stated, and the assessment procedures are identified as to how to do it.
It is important to note here rather than the subordinate procedure, as many actors will only read down to this level. Specifically, only the Image Analysis Tool vendors will spend time with the procedure, but all actors need to know how to interpret statements on these specifications.

This was confusing in the original vesion as the 3D measurands were not expliclty listed. Now they are.
Dropped the row, it is a good practice rather than a requirement.

Fixed.
Replaced by "segmentations".

Material is removed.

Removed.

Re-stated as per reviewer suggestions.

Fixed.
The section now makes it more explicit that the procedure is intended to be done by the Image Analysis Tool vendor.

Fixed.
Removed this unnecessary language.

Clarified.

Phantoms may become commercially available, and the specificatiosn for them may be iumproved over successive versions of the Profile.

Clarified.
Clarified.

Clarified.
Reworded.
Added.
Subsequent versions of Profile can further improve this.

“Acquisition protocol” now used consistently.
Clarified.
Now more specific in each section.

The section is written accurately, and would allow for generalization in later versions of the Profile.

Removed as suggested.

Removed.

This was errant text that has been removed.

Despite the difficulty of applying it, histology is an objective standard that is tied to actual tissue. IVUS is a poor subsitute, as it itself has not been validated (and attempts to do so have shown the limitaitons in the ultrasound signal that prevent its ever demonstrating substantial objective validation). Use of micro CT as a reference for CT is self-referential; the standard needs to be defined by a modality separate from, not a different version of, the modality being assessed.

Clarified that it is for the Image Analysis Tool vendor.

The section is written accurately, and would allow for generalization in later versions of the Profile.

The committee judges that the best contribution it can make is to establish the importance of objective validation. Over time, the commercial availability of assessment tools will be increase. For this version fo the Profile, it is sufficient to outline at least one acceptable method.

Broke it up for clarity.
Used better word choice.

Yes, it is critical to express this explicitly.
Clarified.
Removed errant paragraph.

Fixed.
Fixed.
More consistent naming now adopted.

Inserted.
Clarified.
Clarified.
improved
We agree. This was an old paragraph that was leftover and is now removed.

The unused defintions have been removed.

The appendix has been re-named and a more explanatory paragraph added to introduce the table and its purpose.
See comment above.

See footnotes beneath the table.

Added an explanatory paragraph as suggested to introduce.

The term "measurand" is taken from standard metrology usage to describe what is measured, whereas a "measurment" is one such result of measuring the measurand. Regarding addition of contrast density, this is neither needed nor preferred, as a quantitative imagign biomarker is one that may be validated against an external truth standard not dependent on radiological presentation. The measurands adopted by the profile have this key characteritic and are tied to the biology through extensive literature.

Comment from
Mr. O'Donnell
Mr. O'Donnell
Comments from a few separate reviewers (details in cell BP)

AAPM reviewers

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Mr. O'Donnell

FDA reviewers

FDA reviewers

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2019-04-26 12:53:42	2019-04-26 12:39:06	2019-04-26 12:53:42	876	69.25.25.2	Chrome

2019-05-16 16:51:06	2019-05-15 12:56:13	2019-05-16 16:51:06	100493	192.231.86.244	Chrome

Mac http://qibawiki.rsna.org/index.php
/Profiles

Windows	http://qibawiki.rsna.org/index.php/Profiles	15630834	Complete	Atherosclerosis Biomarkers by (C) CTA - 2019	Seth A Cole	scole-t@acr.org

Mac http://qibawiki.rsna.org/index.php
/Profiles

15723374	Complete	Atherosclerosis Biomarkers by (C) CTA - 2019	Michelle Williams

15723374	Complete	Atherosclerosis Biomarkers by (C) CTA - 2019	Michelle Williams

15728082 Complete Atherosclerosis Biomarkers Alan Kwan
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