QIBA Profile:

SPECT-CT: Estimating the Concentration of ^{99m}Tc Based Imaging Biomarkers in Large and Small Volumes of Interest

(Short Title: ^{99m}Tc SPECT-CT)

Stage: B. Version for public comment

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90 # Change Log:

This table is a best-effort of the authors to summarize significant changes to the Profile.

Date	Sections Affected	Summary of Change
2015.10.10	All	Major cleanup based on comments resolved in the Process Cmte. Also had to remove a few hundred extraneous paragraph styles.
2015.10.21	All	Approved by Process Cmte
2015.11.04	2 (Claims) 3 (Requirements)	Incorporating the more refined form of the claim language and referenced a separate claim template. Added Voxel Noise requirement to show example of the linkage between the requirement and the assessment procedure.
2015.12.16		Minor changes to remove reference to "qualitative" measurements, fix reference to guidance and clean some formatting.
2016.01.06	1, 3.8.1	Rewording to avoid the term "accuracy".
2017.05.12	1, 2, 3, 5, AppE	Explain profile stages. Update Claim examples to match guidance. Add Clinical Interpretation subsection to separate that topic from general discussion of the claims. Add Discriminatory text example. Add Section 3 activity requirement subsections with examples for Site Conformance, Staff Qualification, Product Validation, Protocol Design (some of these are to disentangle activities that happen at different times, i.e. product validation, protocol design and patient image acquisition, that were previously entangled Add Conformance Section 5. Add Checklist appendix with requirements regrouped by actor.

Date	Sections Affected	Summary of Change
2015.12.11	all	agreement to start profile in 3Q2016 after stabilizing first SPECT profile in neurodegenerative imaging
2016.05.15	all	Mozley sketches first draft based on neuroimaging profile
2016.07.24	all	clean up of simple line edits; prior draft preserved
2016.11.04	all	Mozley & Dewaraja: general strategy reviewed and revised
2016.11.05	all	Moz: Revisions
2016.11.30	all	Presentation at QIBA breakout session; breakdown of tasks
2017.01.02	all	Edits/revisions by Yuni
2017.11.14	all	Edits/revisions by Yuni
2017.11.25	all	Copy & past into new QIBA template of 2Q2017
2017.11.29	all	Progress during f2f meeting at RSNA 2017 in Chicago
2017.12.17	all	Moz: Attempt to regain version control to reflect current consensus
2018.01.13		Moz: trivial line edits

2018.01.19	Most	Miyaoka: cut and paste generic text sections from ioflupane SPECT profile to ^{99m}Tc SPECT profile.
2018.05.13		Clean up prior to f2f meeting at RSNA HQ
2018.05.13	Acquisition & Recon (Section 3.9 & 3.10) Calibration Factor and validation of absolute quantification (Section 4.7)	Yuni
2018.05.14	Image Analysis (Section 3.13)	Robert
2018.07.10	General Cleanup	Robert
2018.08.06	Sections 3.6, 3.7, and 3.8	Miyaoka: Draft text for Sections 3.6, 3.7 and 3.8
2018.10.08	Sections 3.5, 3.6, 3.8, 3.9 and 3.11	Robert: Rearranged sections in tables to be follow profile guidelines provided by Kevin O'Donnell
2018.11.28	All Sections 3.X	Robert, Dennis, Brian, Charles, Johannes
2019.01.15	Sections 3.X	Robert, Moz, Yuni, John D
2019.02.12	All Sections	Robert cleans up formatting, deletes resolved comments
2019.02.12	All Sections	BC addresses & deletes most comments
2019.03.12	All Sections	BC addresses highlighted issues in document
2019.04.10	Sections 3 & 4	BC addresses technical comments
2019.04.11		Line editing
2019.08.15		Line Editing
2019.09.10	All Sections	Line Editing and conformance table editing
2019.10.08	All Sections	General clean up
2019.10.21	All Sections	Final clean up
2020.02.11	All Sections	Response to reviewers
2020.02.12	All Sections	Group edit: response to reviewer comments
2020.03.11	All Sections	Group edit: response to reviewer comments
2020.04.14	All Sections	Group edit: response to reviewer comments

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Open Issues:

The following issues are provided here to capture associated discussion, to focus the attention of reviewers on topics needing feedback, and to track them so they are ultimately resolved. In particular, comments on these issues are highly encouraged during the Public Comment stage.

Q. Acquisition of the Diagnostic: The field needs a method for determining minimal acceptable counts and optimal counts. A. Ground work by the neuro-SPECT task force was funded, and completed. It should be applicable to other isotopes in extracranial tissues, e.g., metastatic liver masses, pulmonary nodules, etc. Briefly, random Poisson sampling techniques were applied to remove counts from long acquisitions until the minimum number of counts required to achieve the maximum confidence in the measurands was characterized. From the minimum number of counts, the radiopharmaceutical specific count rate, and the contrast, the minimum acquisition time can be estimated for each pharmaceutical. Corroboration for ^{99m}Tc is still pending.
Q. Context-specific scalar values of bias are currently uncertain. We note that there are a range of claims in the literature. We expect the reproducibility of estimates of bias to continue varying as new hardware (e.g., CZT detectors, novel pinhole collimator geometry, innovations in in-line CT, etc.), and signal processing algorithms rapidly evolve. A. Proposal to obviate the issue of bias for some users by developing a constrained measurand based on a "background tissue" in some contexts, e.g., normal hepatic parenchyma for liver metastases, striatal muscle for many cell surface receptors that are not found in muscle (e.g., folate receptors in lung tumors compared to the count density in the infraspinatus muscle) or antigens (e.g., PSMA target density in pelvic lymph nodes compared to count density in gluteal muscles). However, reference tissues are known to present hazards in many situations, so it will be incumbent on each user to qualify them on a case-by-case basis.
Q. There are multiple methods for segmenting target tissues from their surrounding background tissues. A. The biomarker committee can easily envision that several strategies will produce sufficient precision and bias for segmenting the SPECT images. The committee can also imagine that the CT Volumetry committee might provide methods based on the in-line CT that can be co-registered to the corresponding SPECT scans. However, segmentation is known to be precarious, and can convey substantial variance and bias. Enterprises claiming conformance based on distinctions between target and background will need to describe their own methods for segmentation and present their own evidence of qualification for the method.
Q. Standards: solid (e.g., ^{57}Co) or fillable phantoms (e.g., with $^{99m}TcO_4$) A. There is emerging evidence that "pocket phantoms" can reduce the risk of scanner drift in longitudinal studies. But with regards to using phantoms to confirm a lack of bias in cross-sectional measurands, no decisions have been made. Risks associated with fillable phantoms are under discussion. There are only vague plans to develop solid phantoms in the future, or adapt anthropomorphic CT phantoms to include liquid or solid radionuclide sources of known activity.
Q. Measurand: specific binding ratio (target-to-background ratio) or percent injected dose per mL or kBq/mL?

A. Consensus is preference for absolute quantification in terms of kBq/CC. There is, nevertheless, a constituency that prefers to make target-to-background ratio (TBR) a co-primary, as it might be better suited for some contexts, such as multi-center trials.

Closed Issues:

The following issues have been considered closed by the biomarker committee. They are provided here to forestall discussion of issues that have already been raised and resolved, and to provide a record of the rationale behind the resolution.

Q. Is this template open to further revisions? A. Yes. This is an iterative process by nature. Submit issues and new suggestions/ideas to the QIBA Process Cmte.
Q. Must this profile be limited to only ^{99m}Tc, or can we add other isotopes, such as ^{123}I, ^{67}Ga, ^{177}Lu, and many others? A. Only ^{99m}Tc at this time. The profile would become too cumbersome if we included other isotopes. Too many cases and caveats would need to be added, e.g., "if septal penetration from a high energy gamma ray in low abundance, then all these many, many extra steps . . ." This workforce may consider other isotopes if this profile succeeds in achieving a status of technically confirmed. Alternatively, this workforce will cooperate with a new task force or biomarker committee that has the bandwidth to create another profile.

1. Executive Summary

The quantification of ^{99m}Tc labeled biomarkers can add unique value in many different settings, ranging from clinical trials of investigation new drugs to the treatment of individual patients with marketed therapeutics. For example, goals of precision medicine include using companion radiopharmaceutical diagnostics as just-in-time, predictive biomarkers for selecting patients to receive targeted treatments, customizing doses of internally administered radiotherapeutics, and assessing responses to treatment.

This Profile describes quantitative outcome measures that represent proxies of target concentration or target mass in topographically specific volumes of interest (VOIs). These outcome measures are usually expressed as the percent injected dose (i.e., radioactivity) per mL of tissue (%ID/mL), a standard uptake value ratio (SUVr), or a target-to-background ratio (TBR). In this profile, targeting is not limited to any single mechanism of action. Targeting can be based on interaction with a cell surface protein, an intracellular complex after diffusion, protein-mediated transport, endocytosis, or mechanical trapping in a capillary bed, as in the case of transarterial administration of embolic microspheres. Regardless, the profile focuses on quantification in well-defined volumes of interest.

Technetium-99m based dopamine transporter imaging agents, such as TRODAT, share similar quantitative analysis as the predecessor profile on ^{123}I-ioflupane for neurodegenerative disorders. (See www.qibawiki.rsna.org) Cancer has often been used as the base case for many of the QIBA profiles, but the intent is to create methods that can be useful in other therapeutic areas where diseases are characterized by spatially-limited anatomical volumes, such as lung segments, or multifocal aggregations of targets, such as white blood cell surface receptors on pulmonary nodules in patients with sarcoidosis. Neoplastic masses that can be measured with x-ray computed tomography (CT) or magnetic resonance imaging (MRI) are the starting point for quantitative assessment of ^{99m}Tc-based radiotracers. However, the intent of this effort is to create a profile that can be extrapolated to diseases in other therapeutic areas that are also associated with focal, or multi-focal pathology, such as pulmonary granulomatous diseases of autoimmune or infectious etiology, non-oncological diseases of organs such as polycystic kidney disease, and the like.

The criteria for measurability are based on the current resolution of most SPECT-CT systems in clinical practice, and are independent of criteria for measurability in other contexts. For this SPECT profile, conformance requires that a “small” VOI must be greater than 30 mL to be measurable. It is understood that much smaller VOIs can sometimes exhibit high conspicuity on SPECT, but these use cases are beyond the scope of this profile and will not be tested for conformance in this version. It is left to individual stakeholders to show the extent to which they can achieve conformance when measuring VOIs less than 30 mL.

The detection of smaller changes during clinical trials of large groups can be achieved by referring to the QIBA companion guidance on powering trials.

The Claims (Section 2) asserts that compliance with the specifications described in this Profile will

(1) produce cross sectional estimates of the concentration of radioactivity [kBq/mL] in a volume of interest (VOI) or a target-to-background ratio (TBR) within a defined confidence interval (CI), and

(2) distinguish true biological change from system variance (i.e., measurement error) in individual patients or clinical trials of many patients who will be studied longitudinally with ^{99m}Tc SPECT

agents. Both claims are founded on observations that target density varies between patients with the same disease as well as within patients with multi-focal disease.

The Activities (Section 3) describes the requirements that are placed on the **Actors** who need to achieve the Claim. Section 3 specifies what the actors must do in order to estimate the amount of radioactivity in a volume of interest, expressed in kBq/mL (ideal) or as a TBR (acceptable) within a 95% CI surrounding the true value. Measurands such as %ID/mL are targets for nonclinical studies in animal models that use terminal sacrifice to establish ground truth for imaging studies. TBRs can be precarious, as the assumptions that depend on the physiology of the background regions matching the volume of interest can be hard to accept sometimes. It is up to each individual stakeholder to qualify the background regions used in their own use case. This profile qualifies only a few in some very limited contexts as examples.

The Assessment Procedures (Section 4) for evaluating specific requirements are defined as needed. The requirements are focused on achieving sufficient accuracy and avoiding unnecessary variability of the measurements. The clinical performance target is to achieve a 95% confidence interval for concentration in units of kBq/mL (kilobequerels per milliliter) or %ID/mL (percent injected dose per milliliter) or TBR with both a reproducibility and a repeatability of +/- 8% within a single individual under zero-biological-change conditions.

This document is intended to help clinicians base decisions on these biomarkers, imaging staffs generating measurements of these biomarkers, vendors who are developing related products, purchasers of such products, and investigators designing trials to be able to make informed decisions based upon accurate and reproducible SPECT derived biomarkers.

Note that this document only states requirements to achieve the claims, not “requirements on standard of care” nor compliance with any particular protocol for treating participants in clinical trial settings. Conformance to this Profile is secondary to properly caring for patients or adhering to the requirements of a protocol.

QIBA Profiles addressing other imaging biomarkers using CT, MRI, PET and Ultrasound can be found at www.qibawiki.rsna.org .

2. Clinical Context and Claims

Clinical Context

Theranostic pairs can be produced in several ways. Classic examples include the detection of neoplastic thyroid disease with a low energy photon emitting isotope of iodine, ^{123}I, or ^{99m}Tc-pertechnetate, and subsequent treatment with a relatively high energy, particle emitting isotope, ^{131}I. This profile focuses on diagnostics and companion diagnostics that are radiolabeled with ^{99m}Tc regardless of a companion therapeutic. Emphasis is placed on theranostics for which the method of localization by the companion diagnostic is expected to be the same as the corresponding therapeutic. Physical examples include capillary embolization after transarterial infusion of macroaggregated albumin (MAA) or ceramic beads, and compound molecules built by conjugating either diagnostic radioisotopes or therapeutic agents to "targeting" pharmacophores that bind specific cell surface proteins. Therapeutic agents could be a radiotherapeutic that emits high energy alpha or beta particles, or a chemotherapeutic. Targeting pharmacophores now in the clinic or in development include, but are not limited to, antibodies, antibody fragments, and small molecules, such as the peptide receptor agents. Companion therapeutics include both drugs and radiotherapeutics. Although this profile describes only ^{99m}Tc diagnostics, analogous examples in clinical practice include ^{111}In-Octreoscan or ^{68}Ga-DOTATATE, which can be paired with chemotherapeutics such as a somatostatin receptor antagonist (e.g., Octreotide, Sandostatin, others) or radiotherapeutics (e.g., ^{177}Lu [DOTA0, Tyr3] Octreotate (^{177}Lu-DOTATATE, or Lutathera). Theranostic pairs might help address several major health problems. This profile assumes stakeholders have proven companion imaging diagnostics that have ĺpharmacokinetic profiles that are similar enough to their companion therapeutics to be accepted as qualified proxies for the eventual distribution of the therapeutics. It further assumes that any deviations from ideal concordance can be measured and accounted for. It should also be recognized that this profile can be used for quantifying diagnostics when there are no companion therapeutics per se, as in the case of quantifying regional lung perfusion as a pre-surgical criterion for segmentectomy or pulmonary air valve placement.

Conformance to this Profile <u>by all relevant staff and equipment</u> supports the following claim(s):

Claim 1: Cross sectional. Calibration.

Claim 1A: Absolute Quantification. For a target volume > 30 mL with a contrast ratio of more than 2-to-1 in an image with more than 2 million counts, empirical evidence shows the within subject coefficient of variation (wCV) is less than 8% (0.08). When these conditions hold, for a measured concentration of radioactivity of Y in units of kBq/mL or %ID/mL, a 95% confidence interval* for the true activity concentration is $Y \pm 1.96 \times 0.08 \times Y$.

For example, if the concentration of radioactivity is measured to be 4 kBq/mL after the correction for any known bias as described below, then the 95% CI for the true concentration is (4-0.63)-to-(4+0.63), or [3.37-to-4.63] kBq/mL.

*The CI is constructed from an estimate of the within-subject coefficient of variation, under the assumption of negligible bias.

The assessments described in Section 4 need to be performed to verify that the system meets the total error requirements listed above, such as a wCV $\leq$ 8%, which includes assessments of

actors' measurement bias and precision. The above claim assumes that any known bias has already been corrected and the remaining bias is <5%. For example, if an actor knows that their activity concentration measurements are consistently 20% too low, then they should logically adjust all the activity concentration measurements by increasing the values by 20%. This assumes that operators have applied quantitative calibration as described in Section 4.7. If the bias is volume-dependent (partial volume effects) then a target volume dependent adjustment should be made, for example by using recovery coefficients determined by phantom measurements.

Claim 1B: Target-to-Background Ratio (TBR). For a target volume > 30 mL, for a measured TBR of Y, a 95% confidence interval for the true uptake ratio is $Y \pm 1.96 \times 0.08 \times Y$. For example, if striated muscle has been qualified as a defensible background region for a tumor imaging agent, and a tumor-to-muscle ratio is 2.5:1, then the 95% CI for the true target tissue-to-muscle ratio is (2.5-0.39) to (2.5+0.39) or [2.11 to 2.89].

*****The CI is constructed from an estimate of the within-subject coefficient of variation.

This form of the claim does not require correcting for the bias if, but only if, the percent bias associated with the measurement of the target tissue is adequately similar to the percent bias associated with the background.

Claim 2: Longitudinal Changes Within Subjects

Claim 2A: Longitudinal detection of change. A measured change in concentration or TBR of Δ% indicates that a true change has occurred with 95% confidence if Δ is larger than the estimated repeatability coefficient (RC)*. In practice this means that for an activity concentration of Y at timepoint T1, the change at timepoint T2 must exceed 2.77 x wCV x Y, which for a wCV of 0.08 is 0.22 x Y

*The estimated repeatability coefficient (RC) is defined below.

Claim 2B: Amount of change. If Y_1 and Y_2 are the measurements of concentration or TBR at two time points, a 95% confidence interval for the true change is

$$Y_2 - Y_1 \pm 1.96 \times \sqrt{(Y_1 \times 0.08)^2 + (Y_2 \times 0.08)^2}$$

Note: This claim assumes that the bias at both the time points was the same, and thus cancels out (in other words, that the slope of a regression line of measured versus true values of concentration or TBR is one).

Caveats of Context. These claims hold when:

- Volumes of interest (VOIs) are greater than 30 mL
- The target to background ratio in the VOIs are at least 2-to-1
- Background regions have been qualified by the user as fit-for-purpose, e.g., the cerebellum has been qualified as an adequate background region for dopamine transporter imaging agents, such as ^{99m}Tc-TRODAT. The attributes of an ideal background region include the following, and must be substantiated for each use case by the user:

  - Easily demarcated with a relatively simple verbal description
  - Large (>30 mL, preferably >100 mL)
  - Same biological properties as the target, including blood flow and perfusion, or a known method of compensating for any differences
  - Same tissue density as the target (e.g., it should have nearly the same ADC on MRI or nearly the same HU on CT as the target)
  - The background VOI contains no target tissue
  - The sum of these attributes is such that measurements produce high (>85%) intra- and inter-rater reliability

- Radioactivity represents specific localization in the target tissue of interest, and not a mechanistically unrelated phenomenon, such as excretion into the gallbladder, binding unintended receptors on normal tissues, etc.
- Anatomical imaging, such as x-ray computed tomography (CT) or magnetic resonance imaging (MRI), has already ruled out other causes of radiotracer accumulation, e.g., excretion into a surgically constructed urinary bladder;
- The patient has not been taking drugs or nutritional supplements that can transiently influence the measurements, such as multivitamins in the case of folate receptor imaging, or somatostatin in the case of SSR imaging;
- The patient does not have a deformity or condition that prevents proper positioning in the scanner, such as a severe kyphosis;
- The patient can tolerate the imaging procedures well enough to prevent motion from confounding the acquisition;
- The administration of the radiopharmaceutical is not confounded by infiltration of the dose;
- The uptake of tracer doses within the region of interest can be considered to be constant over the time of data acquisition, unless saturating doses of the pharmacophore are co-administered;
- And other such conditions, which, in the opinion of the professional staff, confound the examination.

Discussion

The primary measurand, or outcome measure, is the absolute concentration of radioactivity in a volume of interest (VOI). It may be expressed in units of kBq/mL or %ID/mL. Alternatively, when qualified by the user, target-to-background ratios (TBRs) obtained in properly selected target tissues, e.g., a neoplastic mass, a sarcoid nodule, an infected lymph node, etc., and a properly selected background region, e.g., a muscle group or a volume of normal liver. While research studies sometimes include the TBR for other structures and backgrounds, such as the bone marrow for companion therapeutics that can cause bone marrow suppression, measurements in each of these regions are beyond the scope of this profile.

The TBR is defined as the count density in a volume of interest (VOI) divided by the count density in the reference region and is roughly equivalent to the binding potential (BPnd) using a reference region as estimate of non-displaceable uptake in the target tissue.

Ideal reference regions will vary with context, and in some situations, there will be no appropriate reference region, in which case only absolute quantification will suffice. Sometimes choices will be limited by tissues in the same field of view as the target tissue. For example, it might be necessary to use paraspinous muscle when assessing a retroperitoneal target at the level near the diaphragm, or normal liver when evaluating a liver metastasis. Acceptability might need to be established by each enterprise; this profile will focus on striatal muscle and normal liver.

An alternative outcome measure is the fraction of the injected activity per unit volume in a VOI expressed in units of kBq/mL. It might be an ideal outcome measure in some settings.

Additionally, with advances in SPECT-CT technology the use of standardized uptake values (SUV), traditionally used in PET, is now emerging in clinical SPECT applications.

These claims are based on estimates of the within-subject coefficient of variation (wCV) for concentration or TBRs. In the claim statement, the CI is expressed as Y ± 1.96 × Y × wCV. The claim assumes that the wCV is constant for each component of the target tissue (e.g., Target Lesion 1 is the same as Target Lesion 2, etc.) in the specified size range, and that there is negligible bias in the measurements (<5%). For estimating the critical % change, the % Repeatability Coefficient (%RC) is used: 2.77 × wCV × 100.

The +/- 22% (i.e., 2.77*0.08) boundaries can be thought of as “error bars” or “noise” around the measurement of TBR change. If an operator measures change within this range, it cannot be certain that there has really been a change. However, if a TBR changes beyond these limits, then an observer can be 95% confident there has been a true change in the TBR, and the perceived change is not just measurement variability. Note that this does not address the biological significance of the change, just the likelihood that the measured change is real.

Clinical interpretation with respect to the magnitude of true change:
The magnitude of the true change is defined by the measured change and the error bars (+/- 22%). If an operator measures the TBR to be 3.0 at baseline and 1.5 at follow-up, then the measured change is a 50% decrease in TBR (i.e., 100x(3.0 – 1.5)/3.0). The 95% confidence interval for the true change in TBR is is $(1.5 - 3.0) \pm 1.96\sqrt{(1.5 \times 0.08)^2 + (3.0 \times 0.08)^2}$, or [-2.01, -0.99], which represents a 33% to 67% decrease in TBR.

Clinical interpretation with respect to longitudinal progression or response:
A change in concentration or TBR that exceeds the lower or upper bound of the Repeatability Coefficient indicates there is a 95% probability of true change in the status of the disease or condition. The medical implications of changes that are greater than the bounds of the confidence interval are beyond the scope of this profile.

Discrimination between patients or groups based on cross sectional calibration claims must be qualified for each use case. This profile characterizes the measurements, but does not describe their medical meaning in any particular context.

3. Profile Activities

The Profile is documented in terms of "Actors" performing "Activities". Equipment, software, staff or sites may claim conformance to this Profile as one or more of the "Actors" in the following table.

Conformant Actors shall support the listed Activities by conforming to all requirements in the referenced Section.

Section 3 Table 1: Actors and Required Activities

Actor	Activity	Section
Site	Site conformance	3.0
Acquisition Device	Product Validation	3.2
	Pre-delivery	3.3
	Image Data Acquisition	3.9
	Image Data Reconstruction	3.10
Reconstruction Software	Product Validation	3.2
	Pre-delivery	3.3
	Image Data Reconstruction	3.10
Image Analysis Tool	Product Validation	3.2
	Pre-delivery	3.3
	Image Analysis	3.13
Radiologist	Staff Qualifications	3.1
	Subject Selection	3.7
	Subject Handling	3.8
Physicist	Periodic QA	3.5
	Imaging Protocol Design	3.6
	Image Data Reconstruction	3.7
	Image QA	3.8
Technologist	Periodic QA	3.5

	Imaging Protocol Design	**3.6**
	Subject Handling	**3.8**
	Image Data Acquisition	**3.9**
	Image Data Reconstruction	**3.10**
	Image QA	**3.11**
	Image Distribution	**3.12**
	Image Analysis	**3.13**

The requirements in this Profile do not codify a Standard of Care. They only provide guidance intended to achieve the stated Claim. Failing to conform to a "shall" declaration in this Profile could be a protocol deviation. Although deviations could invalidate the Profile Claim, such deviations may be reasonable and unavoidable, and the imaging professionals or supervising physicians are expected to do so when required by the best interest of the patients or research participants. How study sponsors and others decide to handle deviations for their own purposes is entirely up to them.

3.0. Site Conformance

This activity involves establishing the overall conformance of an imaging site to this Profile. It includes criteria to confirm the conformance of each of the participating Actors at the site.

3.0.1 DISCUSSION

A site conforms to the Profile if each relevant actor conforms to each requirement assigned in the Activities of the Profile. Activities represent steps in the chain of preparing for and generating biomarker values (e.g. product validation, system calibration, patient preparation, image acquisition, image analysis, etc.).

Since a site may assess conformance actor by actor, a checklist document is available in Appendix E which extracts, for convenient reference, all the requirements in this Profile and regroups the requirements by Actor.

Sites may be able to obtain a QIBA Conformance Statement for some actors (e.g. Acquisition Devices) attesting to their conformance to this Profile, rather than the site having to confirm conformance themselves.

3.0.2 SPECIFICATION

Parameter	Actor	Specification
Acquisition Devices	Site	Shall confirm all participating acquisition devices conform to this Profile.
Reconstruction Software	Site	Shall confirm all participating reconstruction software conforms to this Profile.
Image Analysis Tools	Site	Shall confirm all participating image analysis tools conform to this Profile.
Radiologists	Site	Shall confirm all participating radiologists conform to this Profile.
Physicists	Site	Shall confirm all participating physicists conform to this Profile.
Technologists	Site	Shall confirm all participating technologists conform to this Profile.

3.1. Staff Qualification

This activity involves evaluating the human Actors (Radiologist, Physicist, and Technologist) prior to their participation in the Profile. It includes training, qualification or performance assessments that are necessary to reliably meet the Profile Claim.

3.1.1 DISCUSSION

These requirements, as with any QIBA Profile requirements, are focused on achieving the Profile Claim. Evaluating the medical or professional qualifications of participating actors is beyond the scope of this profile.

3.2. Product Validation

This activity involves evaluating the product Actors (Acquisition Device, Reconstruction Software, and Image Analysis Tool) prior to their use in the Profile (e.g. at the factory). It includes validations and performance assessments that are necessary to reliably meet the Profile Claim.

3.2.1 DISCUSSION

Performance measurements of specific protocols are not addressed here. Those are included in Section 3.6.2.

SPECT camera will meet standards specified by relevant or appropriate standards organizations. Systems will have passed initial acceptance testing and follow a quality control program.

3.2.2 SPECIFICATION

Parameter	Actor	Requirement
Acquisition Protocol	Acquisition Device	Shall be capable of storing protocols and performing scans with all the parameters set as specified in Section 3.6.2 "Protocol Design Specification".
	Acquisition Device	Shall prepare a protocol conformant with Section 3.6.2 "Protocol Design Specification" and validate that protocol as described in Section 3.6.2.
Image Header	Acquisition Device	Shall support imaging start time
Image Header	Acquisition Device	Shall support recording in the image header (Image Comments (0020,4000) or Patient Comments (0010,4000)) information entered by the Technologist about the acquisition.
Reconstruction Protocol	Reconstruction Software	Shall be capable of performing reconstructions and producing images with all the parameters set as specified in Section 3.6.2 "Protocol Design Specification".
Reading Paradigm	Image Analysis Tool	To meet the longitudinal claim shall be able to present the reader with both timepoints side-by-side for comparison when processing the second timepoint. Shall re-process the first time point if it was processed by a different Image Analysis Tool or Radiologist.
Target Activity Concentration or Target to Background Ratio	Image Analysis Tool	Shall be validated to compute Target Activity Concentration or Target to Background Ratio with accuracy within 8% of the true activity concentration or TBR. See Section 4.8 Assessment Procedure: Target Activity Concentration or Target to Background Computation.

Parameter	Actor	Requirement
Target Activity Concentration or Target to Background Ratio Repeatability	Image Analysis Tool	Shall be validated to achieve volume activity concentration change repeatability with: • an overall repeatability coefficient of less than or equal to 22%* (assuming best estimate of CV is 8% then RC = 2.77*8% see [ref, NO, 2016]).
Confidence Interval of Result	Image Analysis Tool	Shall calculate and make available to the operator the 95% confidence interval for target change based on the equation: $(Y_2 - Y_1) \pm 1.96 \times \sqrt{(Y_1 \times CV_1)^2 + (Y_2 \times CV_2)^2}$ Where Y_1 and Y_2 are the measurements of concentration at timepoints 1 and 2, CV_1 and CV_2 , the within-object coefficient of variation for Y_1 and Y_2, is 8%.

3.3. Pre-delivery

This activity describes calibrations, phantom imaging, performance assessments or validations prior to delivery of equipment to a site (e.g. performed at the factory) that are necessary to reliably meet the Profile Claim.

3.3.1 DISCUSSION

The Acquisition Device should be held to the same standard whether it is a mobile unit or a fixed installation; a mobile gamma camera may require additional calibration to achieve proper performance.

Any CT data (used for image correction) should be encoded in CT or Enhanced CT Image Storage SOP Class.

3.3.2 SPECIFICATION

Parameter	Actor	Requirement
Release Testing	Acquisition Device	Shall pass all manufacturing in-process and release testing criteria
File Format	Acquisition Device	Shall encode SPECT raw data in the DICOM Nuclear Medicine Image Storage SOP Class.
	Reconstruction Software	Shall encode SPECT reconstructed data in the DICOM PET Image Storage SOP Class.
	Image Analysis Tool	Shall support the DICOM NM and PET Image SOP Class.

3.4. System Acceptance Tests

This activity describes calibrations, phantom imaging, performance assessments or validations following installation of equipment at the site that are necessary to reliably meet the Profile Claim.

3.4.1 DISCUSSION

Acceptance tests are performed on systems when they are installed in order to 1) ensure that they meet the performance criteria set forth in the purchasing process, and 2) establish a baseline for evaluation of performance over time. Thereafter, the performance tests described in Section 3.3 shall be performed at the interval prescribed, or after any major repair. At the very least, acceptance tests shall include the intrinsic uniformity, system uniformity, planar spatial resolution, and center of rotation tests described in Section 3.3, although they will typically be more substantive than this.

A number of documents (for example, see those produced by the ACR, the AAPM and the IAEA listed in the Reference Section) give specific guidance as to how to conduct acceptance testing.

A qualified medical physicist shall perform the tests. Alternatively, the tests may be performed by properly trained individuals approved by the medical physicist. The test results shall be reviewed by the qualified medical physicist and properly documented.

3.5. Periodic QA

This activity describes calibrations, phantom imaging, performance assessments or validations performed periodically at the site, but not directly associated with a specific subject, that are necessary to reliably meet the Profile Claim.

3.5.1 DISCUSSION

A number of documents from several authoritative bodies (e.g., ACR, IAEA, AAPM, NEMA, IPEM, IEC) have been produced that give specific guidance as to how to conduct the tests described below. The list represents a minimum of set of performance measures that should be monitored on a regular basis. Manufacturers' recommendations and institutional policy may require additional or more frequent tests.

A qualified medical physicist shall perform these tests. Alternatively, the tests may be performed by properly trained individuals, such as a nuclear medicine technologist, who has been authorized by a supervising medical physicist. The test results must be reviewed by the qualified medical physicist and properly documented.

Overall system performance confirms system ability to quantify objects of interest in test phantom large enough to avoid significant partial volume effects or other losses due to resolution (see Figure 3.10-1). This test can also be performed for a small VOI placed in a uniform region of the object away from the edges such that edge effects and partial volume effects are minimized.

Note that some specifications that follow come from IAEA Human Health Series 6.

3.5.2 SPECIFICATION

Parameter	Actor	Requirement
Quality Control Results	Physicist	Values for the listed tests shall be compared with those obtained at acceptance and the action levels established at the time of acceptance testing.
SPECT Calibration Factor	Physicist	Shall determine and record the SPECT Calibration Factor (at least quarterly and consistent with manufacturer recommendation). See 4.7 Assessment Procedure: SPECT Calibration Factor
Time Synchronization	Physicist	Shall confirm daily that all device clocks are synchronized to within ± 1 minute.
Intrinsic Uniformity	Physicist	Shall confirm not less than quarterly that the intrinsic uniformity from a ^{99m}Tc point source is within 4% in the UFOV. See 4.1 Assessment Procedure: Intrinsic Uniformity
System Uniformity	Physicist	Shall confirm daily that the system uniformity from a ^{99m}Tc or ^{57}Co source is within 4% in the UFOV. See 4.1b Assessment Procedure: System Uniformity
Planar Spatial Resolution	Physicist	Shall confirm semiannually that the planar FWHM spatial resolution from the collimators used for ^{99m}Tc imaging is less than 8mm. See 4.2 Assessment Procedure: Planar Spatial Resolution.
Center of Rotation (COR)	Physicist	Shall confirm not less often than semiannually that the mean value of the COR offset does not exceed 1/2 pixel (typically 2 mm) when measured at the center and edges of the FOV. Shall confirm the position of Y=0 axis and the Y gain are the same for all heads in a multi-head system.
Photon Energy Analyzer	Physicist	Shall confirm that the accuracy of the photon energy analyzer is within manufacturer specifications. Ideally, confirmation will be performed every day the instrument is used to make measurements.
SPECT -CT Alignment	Physicist	Shall confirm that the SPECT-CT alignment is within the manufacturer specifications. The target is to confirm registration not less than semi-annually.
Overall System Performance	Physicist	Shall confirm percent bias is 5% or less of the true concentration. See 4.8 Validation of Absolute Quantification Capability: Phantom Study. This should be done not less than annually.

3.5.3 ANCILLARY EQUIPMENT

This activity describes calibrations, performance assessments or validations performed periodically at the site, but not directly associated with a specific subject nor the SPECT-CT system, that are necessary to reliably meet the Profile Claim.

Radionuclide Calibrator

The following guidelines are collected from ANSI standard N42.13.2004 and IAEA Technical Report Series TRS-454. All requirements assume measurements on unit doses of ^{99m}Tc and that calibration sources are in the 'syringe' geometry (i.e., no bulk doses).

The Constancy test ensures reproducibility of an activity measurement over a long period of time by measuring a long-lived source with known activity.

The Accuracy test ensures that the activity values determined by the radionuclide calibrator are correct and traceable to national or international standards to within reported uncertainties. This can be accomplished either through NIST or equivalent (e.g., from a nuclear pharmacy with established traceablity).

The Linearity test confirms that, for an individual radionuclide, the same calibration setting gives the correct readout over the full range of use for that radionuclide calibrator.

Parameter	Actor	Requirement	DICOM Tag
Constancy	Technologist	Shall be evaluated daily (or after any radionuclide calibrator event) using a NIST-traceable (or equivalent) ^{99m}Tc, ^{137}Cs, or ^{57}Co radionuclide calibrator standard and confirmed that net measured (and decay-corrected) activity differs by no greater than ±2.5% from the standard value.	
Accuracy	Technologist	Shall be evaluated annually (or after any radionuclide calibrator event) with a NIST-traceable (or equivalent) ^{99m}Tc standard or simulated ^{99m}Tc radionuclide calibrator standard (if available). Shall confirm that the measured (and decay-corrected) activity differs by no greater than ±2.5% from the standard value.	
Linearity	Technologist or Radiation safety officer or Qualified Medical Physicist	Shall be evaluated quarterly (or after any radionuclide calibrator event) using either ^{18}F or ^{99m}Tc and shall be within ±2.5% of the true value over an operating range of 37 to 1110 MBq (1 to 30 mCi). The true value is determined by a linear fit (to the log data) over the same operating range.	

Clocks and timing devices

The SPECT scanner computer and all clocks in an imaging facility used to record activity/injection measurements shall be synchronized to a standard time reference to within ± 1 minute. These include

any clocks or timekeeping systems that are connected with a subject's ^{99m}Tc study, in particular those associated with the radionuclide calibrator, the injection room, the scanner, and the acquisition computer(s). The synchronization of all clocks (to date, time of day, and time zone) shall be achieved using the Consistent Time Integration Profile as defined in the IHE IT Infrastructure Technical Framework. The Consistent Time Profile requires the use of the Network Time Protocol (NTP; www.NTP.org). In locations where access to an international standard clock signal is not possible, then all clocks shall be synchronized with a smart phone that is able to pick up a satellite time signal shortly prior to the start of study activities. Synchronization shall be confirmed prior to each study, and shall be monitored at least weekly as part of the ongoing QA program. In addition, clocks shall be inspected immediately after power outages or civil changes for Daylight Savings Time (North America) or Summer Time (Europe).

Parameter	Actor	Requirement	DICOM Tag
Scanner and site clocks	Approved personnel	SPECT scanner computer and all clocks in an imaging facility used to record activity/injection measurements shall be synchronized to a standard time reference to within ± 1 minute. Synchronization shall be verified daily and after power outages or civil changes for Daylight Savings Time or Summer Time.	

3.6. Imaging Protocol Design

This activity involves designing acquisition and reconstruction protocols for use in the Profile. It includes constraints on protocol acquisition and reconstruction parameters that are necessary to reliably meet the Profile Claim.

3.6.1 DISCUSSION

The Profile considers Protocol Design to take place at the imaging site, however, sites may choose to make use of protocols developed elsewhere.

The approach of the specifications here is to focus as much as possible on the characteristics of the resulting dataset, rather than one particular technique for achieving those characteristics. This is intended to allow as much flexibility as possible for product innovation and reasonable adjustments for patient size and target region (e.g., torso versus head), while reaching the performance targets. Again, the technique parameter sets in the Conformance Statements for Acquisition Devices and Reconstruction Software may be helpful for those looking for more guidance.

Planar spatial resolution (defined as the full width at half maximum (FWHM) of a line source in air). Planar spatial resolution directly correlates with the best tomographic spatial resolution. Planar spatial resolution is set by the collimator used, the distance the source is from the collimator, the radio-isotope being imaged and the intrinsic spatial resolution of the detector. The planar spatial resolution shall be <8 mm full width at half maximum (FWHM) for a line source in air at a distance of 10 cm from the collimator.

Number of view angles (defined as the total number of projections collected over 360°). Depending upon the vendor the standard number of view angles is 120 or 128 (i.e., 60 or 64 stops per head for a dual-headed camera). The purpose for the number of view angles is to support the desired spatial resolution of the reconstructed image. The number of view angles usually approximates the number of spatial bins in the projection dataset and should be selected to support the angular sampling requirements of the image reconstruction technique.

Detector orbit (defined as the geometrical path that the detectors take around the patient). Whenever available, detector auto-contouring shall be used to minimize the distance between the subject and the imaging detectors as they orbit around the patient. If auto-contouring is not available, then an elliptical orbit that minimizes the distance between the subject and the imaging detectors is recommended.

Time per frame (defined as the dwell time at each angular position of the detectors during SPECT data acquisition. The minimum time for frame is determined by the minimum number of counts needed to be acquired to support the quantitative imaging requirements. As specified in Section 3.9.1, the minimally acceptable number of counts is at least 2 million for each SPECT imaging field of view, to minimize the impact of image noise on the quantitative estimate for the volume of interest. Please note that the recommended number of minimum counts is for quantitation of objects greater than 30 mL in volume. Minimum number of counts for low contrast and/or smaller objects may need to be higher to provide adequate signal to noise ratio for detection (i.e., Rose criteria [Adler 2017]). For a two headed SPECT camera, the number of projection time frames corresponds to ½ the number of projections (i.e., 128 angular bins corresponds to 64 time frames). The time per frame can be determined from the following formula:

(2,000,000 / total system cps) / (number of time frames).

Image voxel size (defined by the in-plane and axial dimensions of the image) to support quantitatively accurate estimates of tracer uptake. Ideally, the cross-sectional size of a voxel would be 4-8 times smaller than the diameter of the volume being measured to minimize the bias in the voxel counts due to coarse sampling of the object. A matrix size and zoom factor that gives a pixel size of one-third to one-half the expected spatial resolution shall be used. Typically, a 128 x 128 matrix and pixel size of no larger than 5 mm is needed to meet this profile's specifications. When imaging structures in the brain that do not occupy the full imaging area of the SPECT detectors, it is recommended to use a zoom factor, as smaller voxel sizes should support more accurate quantitative assessment of structures of interest.

Reconstruction Characteristics influence the noise, texture and quantitative accuracy of the reconstructed image. Characteristics here refer to the type of reconstruction algorithm (e.g., filtered back projection (FBP), iterative, artificial intelligence, etc., as long as they meet conformance specifications) and different corrections applied to the images (e.g., attenuation and scatter correction and resolution recovery). Resolution recovery can increase contrast and spatial resolution; however, it can also lead to ringing artifacts at object borders that can negatively impact the quantitative accuracy of the images. For iterative image reconstruction (i.e., MLEM or OSEM) the physicist/radiologist must determine the number of updates to use (e.g., #OSEM updates = #iterations * # updates) during image reconstruction. Finally, if deemed necessary a post reconstruction filter can be applied to the image, either to reduce image noise or to enhance boundaries between objects.

3.6.2 SPECIFICATION

Parameter	Actor	Requirement
Acquisition Protocol	Physicist	Shall prepare an acquisition protocol to meet the specifications in this table
Planar spatial resolution	Physicist	Using the collimator that will be used for the imaging protocol, the planar spatial resolution shall be <8 mm for a line source in "air" at a distance of 10 cm from the collimator.
Number of view angles	Technologist	Shall be either 120 or 128 depending upon the recommendation of the camera vendor.
Detector orbit	Technologist	Detector auto-contouring shall be used when available. When auto-contouring is not available, elliptical detector orbit will be used where the arc of the orbit is set to minimize the distance between the patient and the detector.
Acquisition time per frame	Physicist	The acquisition time per projection angle shall be determined by the minimum number of counts required for the study; and the current imaging detector count rate. The formula to calculate time per frame is included above.
Image voxel size	Physicist	Shall select a number of spatial bins in order to achieve a voxel size that is not larger than the spatial resolution divided by 2. The voxel size shall not be more than 5 mm.
Reconstruction Protocol	Physicist	Shall prepare a protocol to achieve quantitatively accurate image. More details about the image reconstruction protocol are provided in Section 3.10. Shall use a reconstruction technique that achieves 90% recovery coefficient for a 30 ml object.

Parameter	Actor	Requirement
CT Technique: Protocol Design	Technologist / Physician / Medical Physicist	A team comprising a Technologist / Physician / Medical Physicist shall ensure that CT techniques protocols are designed such that dose exposure is the lowest radiation dose necessary to achieve the objective. Protocols defined by Image Gently and Image Wisely shall be used where feasible. The protocol shall be recorded and documented.
	Technologist	The technologist shall ensure that the CT dose conforms to the dose prescribed by the supervising physician or protocol.

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3.7. Subject Selection

This activity describes criteria and procedures related to the selection of appropriate imaging subjects that are necessary to reliably meet the Profile Claim.

3.7.1 DISCUSSION

The subject selection is based upon the health needs of the patient. Specific inclusion and exclusion criteria for each subject are established by the study design protocol. In the case of clinical research protocols, all patients must provide informed consent to participate in the study. In general, there will not be any discrimination between the inclusion of men or women in the studies. Likewise, in general, there will be no exclusions based upon race. Some procedures require the subjects be adults (i.e., 18 years old or older).

3.7.2 SPECIFICATION

Parameter	Actor	Requirement
Subject Selection	Referring health care provider	Shall refer subject for the quantitative imaging procedure.
Inclusion criteria	Health care provider (nurse, physician or technologist)	Shall go over health records with subject to verify subject meets inclusion criteria for the imaging exam.
Exclusion criteria	Health care provider (nurse, physician, or technologist)	Shall go over health records with subject to verify that subject does not meet an exclusion criteria for the study. Shall perform a pregnancy test in women of childbearing potential

3.8. Subject Handling

This activity describes details of handling imaging subjects that are necessary to reliably meet the Profile Claim, specifically with regard to preparation, injection, SPECT scan acquisition, follow up instructions, and other logistics occurring on the scanning day.

3.8.1 DISCUSSION

All procedures shall conform to good clinical practices regarding the provision of information to the patient about the risks, benefits, logistics, and reasonable expectations concerning the imaging activities.

Administration of radiotracer. In most cases administration of radiotracer will be intravenous. In some exams administration may be by another route, such as intra-arterial, subcutaneous, intra-tumoral, intrathecal, et cetera. Administration of radiotracer will be by a certified nuclear medicine technologist or nuclear medicine physician. The dose of the radiotracer is measured in a dose calibrator with the time of the measurement recorded before administration to the patient.

Radiotracer uptake. Each procedure will have a standard uptake period for the distribution and accumulation of the radiotracer in the tissue of interest. For some studies imaging commences immediately after dose administration (e.g., lung perfusion, testing for hepatic lung shunting before radioembolization, etc.). Other studies can require a minimum of 2.5 hours before imaging after drug administration. For studies where the subject is not injected on the imaging table, they will usually be requested to void their bladder before positioning on the imaging table.

Subject positioning. In general, subject will be asked to lie Supine/Arms Up on the imaging table. It is important to promote consistency in patient positioning (especially in the case of longitudinal studies). Depending upon the organ/tissue of interest, the subject will be positioned Feet First in the scanner. Positioning wedges and/or pillows under the knees is recommended for the comfort of the patient and also to minimize patient movement (which can lead to artifacts in the images) during the imaging study. Additional artifact sources, in particular metal and other high density materials, can shield the activity and produce artifacts in the reconstructed image. The subject shall remove artifact sources from their person, if feasible. The imaging technologist will position the subject in imaging system based upon instruction from the overseeing physician.

Instructions to subject during acquisition. In general, SPECT data acquisition is done during free breathing. In the case of imaging with a SPECT and multi-slice CT camera, patients will usually be required to hold their breathe during the CT portion of the study. To promote patient compliance, performing a practice round of breathing instructions before imaging is strongly recommended. For the SPECT portion of the study, patients shall be instructed to take shallow regular breathes during the the data acquisition. In addition to shallow regular breathing, patients will be asked to remain as still as possible during the SPECT data acquisition and to also try not to move between the SPECT and CT data acquisitions.

3.8.2 SPECIFICATION

Parameter	Actor	Requirement
Administration of radiotracer	Health care provider (nurse, physician, or technologist)	Shall administer radiotracer to subject.
Radiotracer uptake	Technologist	If an uptake period is required shall instruct the subject on the length of the uptake period and if there are any activity restrictions (e.g., no food). Shall monitor the length of the uptake period.
Subject positioning	Physician	Shall specify the subject's imaging volume of interest. Shall also determine if imaging should be done over one or more fields of view.
	Technologist	Shall position the subject on the imaging table and setup the imaging system to acquire data over the appropriate imaging volume of the subject.
Table height and centering	Technologist	Shall adjust the table height for the mid-axillary plane to pass through the isocenter. Shall position the patient such that the

Parameter	Actor	Requirement
		"sagittal laser line" lies along the sternum (e.g., from the suprasternal notch to the xiphoid process).
Breathing instructions	Technologist	Shall instruct the subject in proper breath-hold for CT portion of study if CT image is being acquired. Shall instruct the subject on proper shallow breathing technique during SPECT data acquisition to minimize breathing motion artifacts.

3.9. Image Data Acquisition

This activity describes details of the data acquisition process that are necessary to reliably meet the Profile Claim. It may also include calibrations, performance assessments or validations during acquisition that are necessary to reliably meet the Profile Claim.

3.9.1 SCANNER ACQUISITION MODE PARAMETERS

We define acquisition mode parameters as those that are specified by the Technologist at the start of the actual SPECT-CT scan. These parameters do not include aspects of the acquisition that occur earlier (e.g., injected activity) or later (e.g., reconstruction parameters) in the overall scan process.

SPECT Acquisition

The SPECT acquisition is performed on a properly calibrated SPECT-CT system with at least two imaging heads fitted with collimators as described in the specifications below. Single headed SPECT systems are not recommended**.** Parallel-hole collimators with manufacturer specified (or measured according to NEMA standards) planar system resolution of < 8 mm FWHM (in 'air' at 10 cm distance) shall be used. Low Energy High Resolution (LEHR), and Low Energy Ultra-High Resolution (LEUHR) collimators, typically meets the resolution requirement. Of course, there might be other collimators designs that could meet conformance standards that are not widely used today, such as some variants of fan-beam collimators, multi-hole pin hole collimators, etc.

Once the patient is placed on the imaging table it is important to have the radius of the rotation as small as possible. This may be particularly challenging in patients with degenerative spine disease or other orthopedic problems affecting posture. The acquisition is adequately performed in continuous mode or step and shoot mode with angular sampling every ~3 degrees collecting photopeak counts (140 keV +/- 10% or less) into a 128 x 128 matrix . Acquisition time is set to acquire a minimum of 2 million counts in the field of view from all projections provided the target to background ratio is at least 2 to 1 (for higher ratios, less counts may be adequate) for a target object >30 mL. Typically this requires 10-30 minutes of total scan time, remembering that the longer the acquisition time, the more likely it is the patient will move. In step and shoot mode, the acquisition time per frame can be calculated by dividing the number of counts needed per projection view (e.g., 2 million counts/number of projection views) by the average count rate for the anterior and posterior views and then rounding up to the number of seconds up to the nearest integer. For continuous mode acquisition, the minimum acquisition time is determined by dviding 2 million counts by the average counting rate for the anterior and posterior views and rounding

the number of seconds up to the nearest integer. Note that the recommended number of minimum study counts is for quantitation of objects greater than 30 mL in volume. Minimum number of counts for smaller object size may need to be higher, but are not within the scope of this profile.

3.9.2 SCANNER SPECIFICATION

Parameter	Actor	Requirement
Acquisition Protocol	Technologist	Shall select a protocol that has been previously prepared and qualified for this purpose (See Section 3.6.2 "Protocol Design Specification"). Shall report if any parameters are modified beyond the specifications in Section 3.6.2 "Protocol Design Specification".
Collimator	Technologist	Shall use a collimator that provides planar system resolution of < 8 mm FWHM (in 'air' at 10 cm distance) for ^{99m}Tc.
SPECT acquisition mode	Imaging center and its applicable standard operating procedures	The key SPECT acquisition mode parameters shall be specified in a manner that is expected to produce comparable results regardless of the scanner make and model. The key parameters are: **Rotational radius**: shall be the smallest possible. Auto contouring shall be used if available. **Energy windows:** The photopeak window shall be set at 140 keV ± 10% (126 – 154 keV) or as recommended by the system manufacturer. Lower energy scatter window adjacent to the photopeak shall be set in the range ± 5 to 15% or as recommended by the manufacturer. **Angular sampling:** 360 degree coverage with angular sampling of not less than 120 views shall be used (<= 3 degree increments). Step-and-shoot is typically used, but continuous mode can be used to provide shorter total scan time. **Total counts** When possible, the scan duration shall be adjusted to obtain > 2 million total counts detected in the photopeak window. The total number of counts may be acquired in a single revolution when scanning relatively stationary distributions of radioactivity, but shall be broken down into multiple revolutions when the biokinetics are unduly fast compared to the scan duration, just so long as the counts per rotation do not drop too low to violate the

Parameter	Actor	Requirement
		assumptions driving the reconstruction method, such as OSEM. **Matrix and pixel size**: A matrix size and zoom factor that gives a pixel size of one-third to one-half the expected spatial resolution shall be used. Typically, a 128 x 128 matrix and pixel size of no larger than 5 mm.
	Technologist	The technologist shall set up the acquisition, acquire the data, and store the data.
SPECT Acquisition	Technologist	Shall watch the patient to make sure the patient does not move during the data acquisition.

CT Acquisition

For the CT component of the SPECT-CT scan, this Profile only addresses the aspects related to the quantitative accuracy of the SPECT image. The focus is on attenuation correction and anatomical localization only. This profile does not describe a diagnostic CT scan. When CT is used for attenuation correction only, the CT can be performed with tube current time product down to 10 mAs and when used for anatomic localization, the CT can be performed with 30 – 60 mAs (with 110-130 kVp, pitch 0.8-1.5). If anatomic localization includes CT-based organ and lesion segmentation higher mAs values may be used.

The CT acquisition parameters shall be selected based on Image Wisely guidelines (see http://www.imagewisely.org/imaging-modalities/nuclear-medicine/articles/ct-protocol-selection) and availability on the scanner.

Parameter	Actor	Requirement
CT Acquisition mode	Imaging center and its applicable standard operating procedures	The key CT acquisition mode parameters (kVp, mAs, pitch, and collimation) shall be specified in a manner that is expected to produce comparable results regardless of the scanner make and model, and with the lowest radiation doses consistent for the role of the CT scan: correction for attenuation and for localization. The CT acquisition mode shall utilize the protocol that delivers the lowest possible amount of radiation dose to the subject (e.g. a relatively low dose protocol) that retains the quantitative accuracy of corrections for attenuation.
	Technologist	The key CT acquisition mode parameters (kVp, mAs, pitch, and collimation) shall be set as specified by study protocol and used consistently for all subject scans.

3.10. Image Data Reconstruction

This activity describes criteria and procedures related to producing images from the acquired data that are necessary to reliably meet the Profile Claim.

3.10.1 DISCUSSION

Reconstruction is performed on the projection data following a quality control check of the sinogram to assess for any motion and potential artifacts.

Images must be reconstructed using iterative (e.g., OSEM or conjugate gradient) or equivalent high quality methods that incorporate image degrading physical factors in the reconstruction model. Iterative methods allow for more accurate and complete compensation for attenuation, scatter and resolution effects compared with analytical methods.

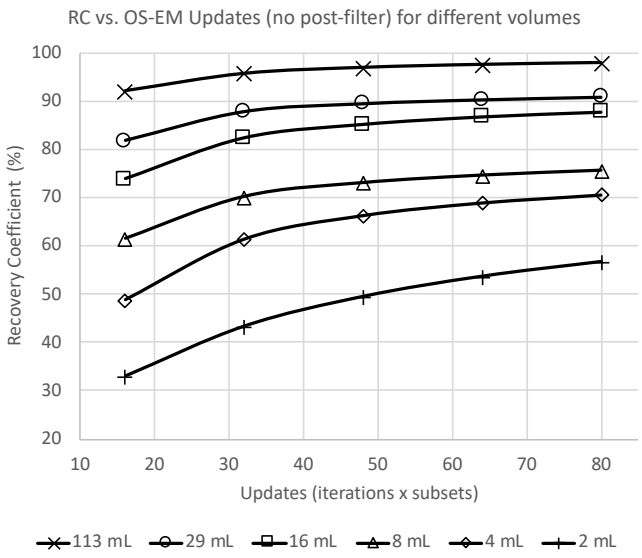
Reconstructed images must be corrected for attenuation. The patient specific non-uniform attenuation coefficient map must be generated from a co-registered CT. The attenuation coefficients can be included in the system matrix of the iterative reconstruction model. Measured attenuation maps obtained from CT images shall have the attenuation values translated so that they are appropriate for 140 keV and be registered to the emission images with an accuracy of better than 2 mm.

Reconstructed images must be corrected for scatter. The most practical and widely used method is the triple-energy-window (TEW) scatter correction, which reduces to a dual-energy window method in the case of ^{99m}Tc because the upper energy window is not needed (due to lack of higher energy emissions). Other more sophisticated methods include scatter modeling methods (e.g., ESSE [Frey, 1996]) or Monte Carlo-based ([Dewaraja 2006, Beekman 2002]) methods. For iterative reconstruction, the scatter

compensation should be incorporated as an additive term in the reconstruction model in order to obtain the best noise properties.

When quantifying mean activity in a VOI, collimator-detector-response (CDR) compensation also known as resolution recovery, a large number image updates (typically > 60 depending on the contrast with the background), and little or no post-reconstruction filtering is recommended in order to reduce partial volume effects. The recommendation of > 60 updates (OS-EM iterations times subsets) is partially based on the phantom results of Figure 1, but ideally such studies should be performed by the user as the number of iterations for convergence will depend on factors other than volume (for example, sphere-to-background ratio, compensation methods used for scatter and reconstruction parameters). In some cases, a smaller number of iterations and some post-reconstruction low-pass filtering can be useful to help control noise and its effects on the regional activity estimates. As the volume of the target increases, less updates are needed for convergence (Figure 1). The ringing artifacts associated with CDR compensation [Rahmim 2013] and any impact on quantification shall be evaluated when determining whether to include this. Explicit partial volume compensation, such as the use of recovery coefficients, can be considered for the mean activity concentration or target to background ratio if incomplete count recovery is evident. This is particularly relevant for structures in the lower end of the volumes considered in this profile (i.e., ~ 30 mL).

If pre-or post-reconstruction low-pass filtering is applied to the images it is important that the filter be linear across the count ranges. It is desirable that reconstructed images be saved in such a way as to preserve as much dynamic range (numeric precision) as possible and avoid truncation of voxel values. Storing scale factors needed to convert the images to activity concentration units is encouraged.



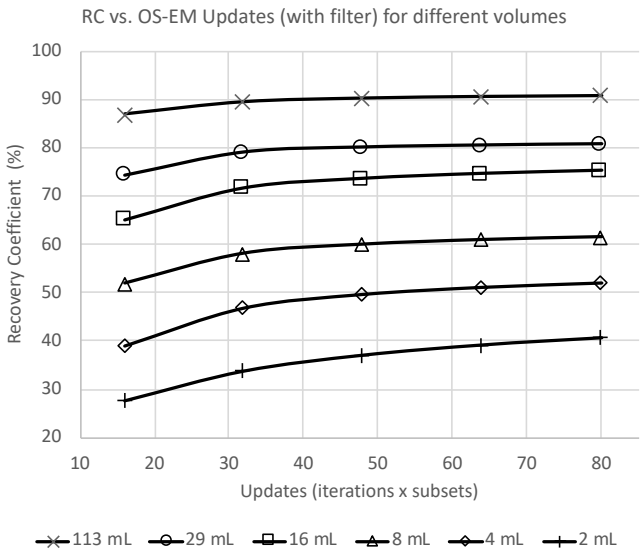


Figure 3.10-1. Counts recovery as a function of OS-EM updates from a ^{99m}Tc phantom study performed on a SPECT-CT system with low-energy high resolution collimators. The sphere-to-background activity concentration ratio was 8:1 and the sphere VOIs were defined on CT. All reconstructions included attenuation, energy-window based scatter and CDR compensation and was performed without (left) and with (right) a 8.4mm Gaussian post-filter.

3.10.2 SPECIFICATION

Parameter	Actor	Requirement
SPECT image Reconstruction	Technologist	Shall run iterative reconstruction as specified by study protocol.
SPECT matrix/voxel size	Technologist	The Technologist shall perform the image reconstruction such that the matrix, slice thickness, and reconstruction zoom shall yield a voxel size of ≤ 5 mm (same as projection bin size) in all three dimensions, although not necessarily isotropic. The final size shall not be achieved by re-binning, etc., of the reconstructed images.
Correction: attenuation	Technologist	CT-based attenuation correction shall be included in the reconstruction.
Correction: Scatter	Technologist	Scatter correction shall be used. Dual energy window (DEW) or equivalent is recommended.
Collimator detector response modeling	Technologist	Shall be used if available.
Image Reconstruction Updates	Technologist	Shall be 60 updates (iterations times subsets) or more depending on target-to-background activity concentration ratios and the target size. For large organs such as the liver fewer updates are needed for convergence.
Stored Reconstructed Image	Camera Manufacturer	Reconstructed images shall be stored in such a way as to preserve the image dynamic range.

3.11. Image QA

This activity describes criteria and evaluations of the images that are necessary to reliably meet the Profile Claim.

3.11.1 DISCUSSION

Many factors can adversely influence image quality, and degrade quantification. Some of these problems can be inferred from a qualitative assessment of the images by an experienced operator, such as a nuclear radiologist. An example of an adverse event is a bad dose administration (i.e., dose infiltration occurs). If this happens the profile will not hold.

3.11.2 SPECIFICATION

The normative list below is based on the recommendations from several national and international guidance documents.

Parameter	Actor	Specification
Patient motion Frequency	Technologist	Shall view cine of projection data or vendor software tool to determine if patient moved during scan. With guidance from physician shall determine if scan needs to be reacquired.
Injection site	Technologist	Shall observe counting rate during data acquisition to make sure counting rates are close to what is expected for the exam. If counts are low, shall image the injection site to make sure there is little to no extravasation at the injection site. If dose infiltration occurs dose claims will not hold.
SPECT-CT alignment	Technologist	Shall make sure SPECT and CT images are properly aligned for proper attenuation correction and also for image fusion (and in some cases, for segmentation).
Image artifacts	Technologist	Shall view reconstructed image to make sure that there are no artifacts present. Artifacts can be caused by patient motion, SPECT-CT misalignment, metal in the FOV, etc.

3.12. Image Distribution

This activity describes criteria and procedures related to distributing images that are necessary to reliably meet the Profile Claim.

3.12.1 DISCUSSION

Discussions of archiving and distributing SPECT data often mention 'raw data'. This is an ambiguous term as it can refer to: scanner raw data (i.e., sinograms) or image raw data. To avoid confusion, the term raw data shall not be used without making it clear which form is under discussion.

Scanner raw data include the sinograms as acquired from the SPECT scanner, i.e., a list of planar projection images, one image for each acquired angle and energy window. This is always a single DICOM file containing projections images grouped by acquisition energy window. These projections can be analyzed by the Image Data Reconstruction Software.

Image raw data is the image data exactly as produced by the reconstruction process by the Image Data Reconstruction Software, i.e., a stack of DICOM slices/files constituting a SPECT image volume with

no processing other than that occurring during image reconstruction. This is always a stack of DICOM slices/files constituting a SPECT image volume that can be analyzed on one or more of the following: SPECT scanner console, SPECT image display workstation, PACS system, etc.

Post-processed image data are images that have been transformed after reconstruction in some manner, including but not limited to: smoothing, image zoom, rotation/translation, resampling, spatial normalization, interpolation, slice averaging, MIP, etc. This is typically a stack of DICOM slices/files constituting a SPECT image volume that can still be analyzed on one or more of the following: SPECT scanner console, SPECT image display workstation, PACS system, etc.

For distributing and archiving at the local site or imaging core lab (if relevant), the most important data are the reconstructed images, i.e., the image raw data, and post processed image data including averaged images if any. In the unlikely event that the scanner raw data (which shall be archived by the local site) is required for later reprocessing; this should be made clear in the protocol. Should scanner raw data be archived, all information needed for proper reconstruction and attenuation correction shall be kept in DICOM files.

3.12.2 SPECIFICATION

Parameter	Actor	Requirement
Image Distribution	Technologist	The original projections (sinogram) images (scanner raw data), shall always be archived at the local site. The reconstructed SPECT images (image raw data), along with all required corrections, and CT images shall always be archived at the local site. If processed SPECT images are required, they shall be archived as separate secondary datasets. If scanner raw data need to be archived for future reprocessing, this shall be defined prospectively in the Protocol.

3.13. Image Analysis

This activity describes criteria and procedures related to producing quantitative measurements from the images that are necessary to reliably meet the Profile Claim.

3.13.1 DISCUSSION

The Image Analyst using computer workstation analysis tools shall perform the specified measurements. The two quantitative measurands are radioactivity concentration in units such as kBq/mL or %ID/mL and target to background ratio (TBR) for a user specified target and background. To reduce the confounding effects of partial volume, all object volumes of interest (VOI) must be greater than 30 mL with a preference of background VOIs greater than 100 mL. The profile describes the data analysis methodology.

The absolute quantitative activity measures kBq/mL and %ID/mL require a scaling (calibration) factor to convert reconstructed image cps to activity . This scaling factor, in units such as cps/MBq, may be determined from a planar sensitivity measurement or from a reconstructed SPECT image of a uniform phantom as detailed in Section 4.7. Some newer SPECT-CT systems come with an ‘in-built’ calibration

procedure and this can be followed to obtain an image in activity concentration units such as Bq/mL. For most vendor systems, the image analyst will either have to input the pre-determined sensitivity of the system (i.e., cps/MBq) to obtain the image in activity concentration units or will have to perform the counts-to-activity conversion offline. In addition, absolute quantitative activity measures may require corrections for physical decay of ^{99m}Tc during acquisition and dead time associated with the detector and acquisition electronics. These corrections are sometimes included in the vendor software, but if not can be performed offline by the image analyst.

TBR semi-quantitation maybe determined from reconstructed images with output reported as counts. Since the TBR is a dimensionless variable the image for analysis does not need to be converted to kBq/mL. Further since dead time and radioactive decay are scalar corrections to the complete image data set they need not be applied when determining TBR.

Input Data:

The output images from Image Reconstruction are considered the input for Image Analysis. Once stored on the analysis workstation the image data will be processed for region of interest image analysis as described below. The original input data will be maintained as a separate file and will be stored along with the processed data for image analysis. In addition to output images from Image Reconstruction, physical phantom and digital reference object images may also be used as input for Image Analysis to validate the Image Analysis and workstation tools. As detailed in Section 4.8 the physical phantoms include anthropomorphic phantoms with organ inserts and lesion inserts (i.e., >30mL) that can be placed in the background or large organs such as liver and lungs. In addition, circular/elliptical cylindrical phantoms or the NEMA IQ phantom can be used with large spherical or cylindrical inserts (i.e., >30 mL) as the target volume. Finally, custom lung phantoms can be used for evaluating absolute activity concentration or TBR for phantoms designed to test quantitative corrections in objects that span the densities of normal to emphysemic lung (i.e., -650 to -970 HU).

Volume of Interest Selection:

The output images from Image Reconstruction are considered the input for Image Analysis and VOI placement. VOIs can be manually defined (usually on anatomical images and then applied to co-registered SPECT) by the image analyst or VOIs can be semi-automatically defined directly on the SPECT image using analysis workstation VOI drawing tools (e.g., threshold-based, gradient-based, etc.). There are several review articles on image segmentation in emission tomography [ref Hatt 2017, Zaidi 2010]. Although these focus on segmentation of PET images for external beam radiotherapy application, the methods are also applicable to SPECT. Because of the relatively poor spatial resolution, VOI definition directly on the SPECT image can be challenging. Methods based on thresholding the SPECT counts are practical, and a fixed threshold of ~ 40% is often used. However, the optimal threshold level varies with target size, shape, contrast as well as the imaging parameters, hence a fixed threshold can result in substantial errors. If SPECT thresholding is used, a practical alternative to fixed thresholding is to generate a curve of optimal threshold level vs. volume from phantom measurements. Then, using *an a priori* estimate of the target volume of the patient, the threshold level can be selected from the phantom calibration curve. The VOI can also be defined on the co-registered CT of the SPECT-CT. However, since the CT of SPECT-CT is acquired without contrast and in low-dose mode it is not of diagnostic quality, hence lesion/organ boundaries may not be well visualized. Mis-registration between SPECT and CT due to movement between the sequential scans and respiratory motion will impact the quantification when

CT-defined VOIs are applied to the SPECT. In addition, if a diagnostic quality CT or MR image is available, the VOIs may be drawn on this image and transferred to the SPECT-CT image following CT-CT co-registration. Manual contouring on anatomical images is time consuming and require the involvement of a radiologist at some level, especially in the case of lesions.

There are several other more advanced image segmentation methods that have been developed to address some of the limitation of thresholding the emission image and manual contouring on the anatomical image. One such method that is available in commercial software is based on calculating the intensity gradient between a voxel and surrounding voxels to locate sharp changes in intensity values (edges) in the emission image. An advantage of the gradient based method over threshold based methods is that the uptake near boundaries do not need to be uniform. Other more sophisticated segmentation algorithms include learning based methods based on extracted image features and joint segmentation (co-segmentation) on multimodality imaging exploiting the information in both anatomical and functional images that can be complementary. However, most of these methods based on advanced algorithms are not yet available in commercial software packages for nuclear medicine imaging applications. These methods have been summarized in a recent review article [Hatt, 2017]

3.13.2 SPECIFICATION

Parameter	Actor	Requirement
Absolute Activity Concentration (kBq/mL)	Image Analyst	Analysis Workstation Shall have a suitable monitor of appropriate size and pixel density for diagnostic viewing of medical images. Shall be placed in a room with in room lighting appropriate for image data analysis and interpretation (i.e., a radiology reading room). Shall have appropriate computation power and memory to carryout VOI data analysis.
		Post processed image for data analysis Image for data analysis shall be reconstructed in accordance with parameters as described in Section 3.10.
		VOI software analysis tools Using analysis workstation tools, volumes of interest shall be placed on the object of interest. Activity concentration shall be reported as the mean activity for the VOI or the maximum activity concentration for the VOI.
Absolute Activity Concentration (%ID/mL)	Image Analyst	Analysis Workstation Shall have a suitable monitor of appropriate size and pixel density for diagnostic viewing of medical images. Shall be placed in a room with in room lighting appropriate for image data analysis and interpretation (i.e., a radiology reading room). Shall have appropriate computation power and memory to carryout VOI data analysis.
		Post processed image for data analysis Image for data analysis shall be reconstructed in accordance with parameters as described in Section 3.10.
		VOI software analysis tools

Parameter	Actor	Requirement
		Using analysis workstation tools, volumes of interest shall be placed on the object of interest. Activity concentration shall be reported as the mean activity concentration in the VOI times 100% divided by the injected activity.
Target to Background Ratio	Image Analyst	Analysis Workstation Shall have a suitable monitor of appropriate size and pixel density for diagnostic viewing of medical images. Shall be placed in a room with in room lighting appropriate for image data analysis and interpretation (i.e., a radiology reading room). Shall have appropriate computation power and memory to carryout VOI data analysis.
		Post processed image for data analysis Image for data analysis shall be reconstructed in accordance with parameters as described in Section 3.10.
		VOI software analysis tools Using analysis workstation tools, volumes of interest shall be placed on the object of interest and the reference tissue. Mean activity or count rate concentration is extracted for each region. The target to background ratio shall be reported as the counts concentration (mean counts or counts divided by volume) of the target VOI divided by the counts concentration in the background VOI
Certify VOI	Qualified professional	Shall either (1) agree with region boundaries, (2) reject boundaries and return for reprocessing, or (3) make revisions “on the fly” as indicated.

3.14. Image Interpretation

This activity describes criteria and procedures related to clinically interpreting the measurements and images that are necessary to reliably meet the Profile Claim.

3.14.1 DISCUSSION

In the USA, under the Centers for Medicare & Medicaid Services’ Medicare Improvements for Patients and Providers Act of 2008 (MIPPA), the American College of Radiology (ACR) is required to validate compliance with accreditation requirements on advanced diagnostic imaging service facilities. Facilities should refer to the tool kit available on the ACR website at the bottom of the Breast MRI, CT, MRI, Nuclear Medicine and PET Accreditation Program pages located at http://www.acraccreditation.org/modalities/mri

These documents will help facilities gather and organize information for periodic the site surveys.

Some of the most common items that are not found during a survey are the following:

- Policies for primary source verification, verifying that personnel are not included on the Office of Inspector General's exclusion list and a consumer complaint notice that gives the patients contact information for the ACR (one can be found on our website at http://www.acr.org/~/media/ACR/Documents/Accreditation/PatientNotice.pdf .
- Documentation of initial qualifications, continued education and continued experience for the interpreting physician and medical physicist. Self-documentation is not acceptable.

In Japan, the European Union, and other regions, professional health care providers shall meet, and maintain, standards set by their local regulatory authorities for the practice of medicine with unsealed radioactive material.

Visual image assessment is performed to assess he adequacy of the acquisition for a quantitative endpoint. Checks for the integrity of the acquired data include looking at the projection data for signs of patient motion. Checks for the integrity of the reconstruction include proper alignment between SPECT and CT when CT is used for attenuation correction or VOI placement. Also check for metal artifacts if CT is used with SPECT.

4. Assessment Procedures

To conform to this Profile, participating staff and equipment ("Actors") shall support each activity assigned to them.

To support an activity, the actor shall conform to the requirements (indicated by "shall language") listed in the specifications table of the activity subsection in Section 3.

Although most of the requirements described in Section 3 can be assessed for conformance by direct observation, some of the performance-oriented requirements cannot, in which case the requirement will reference an assessment procedure in a subsection here in Section 4.

Formal claims of conformance by the organization responsible for an Actor shall be in the form of a published QIBA Conformance Statement. Vendors publishing a QIBA Conformance Statement shall provide a set of "Model-specific Parameters" describing how their product was configured to achieve conformance. Vendors shall also provide access or describe the characteristics of the test set used for conformance testing.

4.1. Assessment Procedure: Intrinsic Uniformity

This procedure can be used by a vendor or an imaging site to assess the uniformity of images from an acquisition device detector. Planar Uniformity is assessed in terms of the integral uniformity and differential uniformity of pixel values when imaging a uniform source.

Additional guidelines for this procedure are available from authoritative bodies such as IAEA, AAPM, NEMA, IPEM, IEC.

The assessor shall suspend a small point source of ^{99m}Tc above the uncollimated gamma camera at a distance of five times the diagonal distance of a rectangular detector. The assessor shall acquire a flood image with count densities of at least 10,000 counts per pixel (about 30 million total counts for a 64x64 matrix). The image shall be visually assessed for variations in count density, noting any areas that clearly stand out. The assessor shall measure and record the integral uniformity and differential uniformity as defined in the above-mentioned guidelines.

4.1b. Assessment Procedure: System Uniformity

This procedure can be used by a vendor or an imaging site to assess the uniformity of images from the combined system of a detector and a collimator in an acquisition device. System Uniformity is assessed in terms of the integral uniformity and differential uniformity of pixel values when imaging a uniform source.

Additional guidelines for this procedure are available from the manufacturer and authoritative bodies such as IAEA, AAPM, NEMA, IPEM, IEC.

The assessor shall prepare a flood source using either ^{99m}Tc or ^{57}Co following the guidelines recommended by system manufacturers. The assessor shall place the flood source in contact with, or as close as possible, to the face of the collimator that will be used for ^{99m}Tc imaging and acquire 10 - 30 million total counts. Innovative alternatives may be used as long as these techniques are in conformance with the QIBA specifications for uniformity. The image shall be visually assessed for variations in count

density. The assessor shall measure and record the coefficient of variation, integral uniformity and differential uniformity as defined in the above-mentioned guidelines.

4.2. Assessment Procedure: Planar Spatial Resolution

This procedure can be used by a vendor or an imaging site to assess the planar spatial resolution of the acquisition device. Planar Spatial Resolution is assessed in terms of the Full-Width Half-Max (FWHM) of a line spread function.

Additional guidelines for this procedure are available in NEMA NU 1-2012 for measuring system spatial resolution without scatter.

The assessor shall fill a capillary tube with an inside diameter < 1 mm with ^{99m}Tc to an active filled length of at least 120mm. The assessor shall position the tube 100mm from the face of the collimator in air and along the axis of measurement. The assessor shall acquire an image, with the collimators routinely used for ^{99m}Tc studies, and measure the FWHM of the line spread function as outlined in NEMA NU 1-2012.

4.3 Assessment Procedure: Center of Rotation

Center of rotation performance can be assessed by following the NEMA guidelines for measuring system alignment of gamma camera tomographic systems. The mean value of the COR offset shall not exceed 1/2 pixel (typically 2 mm) when measured at the center and edges of the FOV. Position of Y=0 axis and the Y gain shall be the same for all heads in a multi-head system.

4.4 Assessment Procedure: Tomographic Uniformity

As a SPECT technique, ^{99m}Tc imaging requires correction for photon attenuation within the body to be accurately quantified. CT-based attenuation correction is recommended. It is important to assess that the correction for attenuation is being applied appropriately. It is also important to assess that center of rotation corrections are fit for purpose. With such potential sources of error, it is important for all trials that transaxial plane uniformity is assessed. This can be achieved by acquiring a high count (~15 million counts) SPECT acquisition of a cylindrical phantom filled with ^{99m}Tc solution. Following reconstruction with corrections applied for attenuation and possibly scatter, a profile about 3 cm wide shall be placed through the center of rotation of the phantom, and the resulting count distribution visually assessed for the appropriateness of CT or calculated attenuation correction. A correctly applied attenuation correction should yield a flat profile other than image noise.

The performance of the system with such tests may change following any detector changes or recalibration, and for SPECT after mechanical changes made to the system, and shall therefore be checked after such actions have been performed.

4.5 Assessment Procedure: Voxel Noise in the Reference/Background Compartment

Target to Background Ratio (TBR) calculations involve the regions of interest of the target (e.g., tumor) and also a background region (e.g., liver or soft tissue). Noise levels and bias in the background region can have an impact on the uncertainty in TBR.

Image noise levels in this region shall be measured using an appropriate phantom with a uniform area to assess image 'noise' by means of the coefficient of variation (CV). The CV is also known as the relative standard deviation (%RSD), which is expressed as a percentage and is defined as CV = (SD / Mean) x 100, for the voxel values within a specified volume of interest (VOI). The phantom shall be scanned using the minimal time per projection/view angle specified in the trial protocol or using the routinely applied time per projection/view angle in the local clinical setting. Moreover, image reconstruction methods and settings shall equal those specified in the trial protocol or equal those routinely applied in the local clinical setting. A volume of interest (VOI) shall be positioned entirely within the phantom's uniform area, with its size and position chosen to match that used to quantify TBR. The CV of the total counts in the volume of interest thus determined shall be recorded and the upper bound of the 95% CI for the CV should be <8%. If the upper 95% confidence bound for the CV is above 8%, the acquisition parameters should be adjusted accordingly.

Parameter	Entity/Actor	Requirement
Planar Uniformity QC	Technologist	At least quarterly and following detector changes, calibrations and/or software upgrades the uniformity of detector response to a uniform flux of radiation of ^{99m}Tc should be assessed. Daily, or at least on the day of a trial subject, the collimated uniformity of the detectors using collimators to be used for ^{99m}Tc imaging should be assessed using a ^{99m}Tc or ^{57}Co source. For both measurements, uniformity should be measured and assessed in accordance with local regulatory requirements.
SPECT uniformity QC	Technologist or Medical Physicist	At least quarterly and following detector changes, calibrations and/or software upgrades, the SPECT uniformity should be measured using acquisition parameters defined in the clinical protocol trial.

4.6 Assessment Procedure: Motion & Artifacts

After acquisition and before reconstruction review of projection data in cine mode and sinograms shall be used for an initial determination of scan quality, patient motion, and artifacts. Cine review of planar images will show up patient motion along the axis of rotation. A horizontal reference line overlying the image can be used to assess motion. Sinogram review will reveal transverse patient motion as discontinuities in the sinusoidal form of shapes included within the image.

The acquisition can also be performed as a dynamic SPECT (for example, six 5 minute frames) to better assess motion. After reviewing the sinograms of each rotation only those frames where significant motion is not evident are summed for the reconstruction, excluding projection data with patient motion.

4.7 SPECT Scanner Sensitivity (Calibration Factor) for Absolute Quantification

This procedure can be used by a vendor, physicist, or imaging site to assess the Calibration Factor (*CF*) of the SPECT imaging system. The *CF* to convert count rates to activity is specific to acquisition conditions such as collimator and energy windows as well as to the reconstruction method and parameters. Therefore, the calibration study should be performed using the same imaging and reconstruction conditions that will be used for patient studies. In SPECT, the conversion from counts to activity by scaling by the *CF* is typically performed by the user and applied offline (outside of the system software). With some recent SPECT-CT systems that have quantitative image formation capabilities the reconstructed image is available in activity concentration units as in PET-CT. In this case, the manufacturer determined *CF* or camera sensitivity is embedded in the software and the user is required to perform periodic tests with a long-lived source to verify consistency.

The *CF* is assessed by imaging a large (to avoid partial volume effects) phantom filled uniformly with a known activity concentration of ^{99m}Tc, *c* (in MBq/mL). Following reconstruction with corrections specified in Section 3.10, the count rate, *R* (in cps), is measured in a large VOI of volume *V* (in mL) placed in a uniform area at the center of the phantom image to avoid edge effects. For a 20 cm diameter phantom, e.g., the VOI may be defined by a 15 cm diameter ROI. Then the *CF* in units of cps per unit activity (cps/MBq for example)is:

$$CF = \frac{R}{c * V} * f_1 * f_2$$

where the product $c * V$ is the true activity in the VOI. The terms $f_1$and $f_2$are correction factors that accounts for the decay during the time delay t_1 between the time that the true activity concentration was measured and the start time of the phantom acquisition and for the decay during the acquisition time t_{acq}, respectively.

$$f_1 = e^{\lambda t_1} \qquad \text{and} \qquad f_2 = \frac{\lambda t_{acq}}{1 - e^{-\lambda t_{acq}}}$$

where λ is the physical decay constant. The activity concentration used in the above calibration measurement should be determined with high accuracy using a traceably calibrated instrument (see Section 3.9.3). The activity concentration in the phantom should be sufficient to yield ~ 5 – 30 kcps per detector head. The ^{99m}Tc activity needed to achieve this is 185 – 370 MBq.

In order to match the calibration geometry to the patient geometry as much as possible, spherical or organ shaped inserts in phantoms are sometimes used to determine calibration factors for lesions and organs. The ready availability of 3D printing technology has facilitated the use of such inserts [Tran-Gia and Lassman 2018; Finocchiaro et al, 2019; Price et al, 2019]. This potentially reduces the impact of

imperfect compensation for scatter and attenuation. It is also possible to use a planar point-source measurement in 'air' (attenuation and scatter free conditions) for the camera sensitivity measurement instead of a SPECT acquisition with a phantom. A calibration factor from a planar point source based measurement is valid for SPECT only when perfect correction for image degrading factors (e.g. scatter, attenuation) is available. Since this is typically not the case, the phantom based calibration is preferred over a planar point-source measurement, although the latter measurement is much more practical to perform in a busy clinic environment. If all corrections are perfect, the calibration factor determined with different source geometries should give the same value. The camera sensitivity should be verified periodically although modern SPECT-CT systems have been shown to be very stable. A retrospective study analyzing sensitivity calculated as part of a patient gamma camera imaging protocol performed over 4 years has reported a variability of 2.3% for the CF [Anizan, 2014].

Although a physical phantom measurement is preferred, it is also possible to calibrate the system using Monte Carlo simulated projection data if a well validated (for the particular system) code is available and if the camera parameters to include in the Monte Carlo model is known with high accuracy.

4.8 Validation of Absolute Quantification Capability: Phantom Study

The accuracy and precision of the absolute quantification can be assessed by imaging a phantom filled with a known activity concentration of ^{99m}Tc. Ideally, an anthropomorphic phantom with fillable organ and lesion inserts (30 mL and larger) should be used for the validation study, but if not available a uniform phantom with fillable spheres and background can be used. The phantom used to assess quantification should be different from the phantom used to determine the calibration factor in Section 4.7. Activity distributions and target-to-background activity concentration ratios (TBR) used to fill the phantom should be clinically relevant. Additionally, the activity concentration used to fill the phantom should be chosen such that sufficient counts are obtained with a reasonable acquisition time. For example, the 10L elliptical phantom with 6 spheres ranging from 2 to 100 mL (Figure 1) and sphere-to-background ratio of 8:1 filled with a total [^{99m}Tc] activity of 370 MBq (10 mCi) results in a photopeak count rate of ~ 10 kcps per detector of a typical SPECT system with LEHR collimators and a 5/8 inch NaI(Tl) crystal. Hence an acquisition with 15 seconds per projection view will result in ~150 kcps per view.

The SPECT acquisition and reconstruction of the validation phantom should be performed with the same acquisition parameters (e.g. same collimator, same energy window settings) and reconstruction parameters (e.g. same number of effective iterations, same corrections for image degrading physical factors , same post-filtering) used for the above (Section 4.7) described calibration phantom study. Then, the SPECT estimated activity concentration (in units such as MBq/mL) for a large volume, V_{VOI}, is:

$$c_{SPECT} = \frac{R_{VOI}/V_{VOI}}{CF}$$

Where $R_{VOI}$is the count rate (in cps) of reconstructed counts within the VOI (in mL). The target volumes ('lesions', 'organs', etc.) can be segmented manually on the CT of the SPECT-CT or can be defined by other segmentation methods summarized in Section 3.13. The background should be defined in a

uniform activity region away from boundaries. The segmentation and VOI definition for the phantom study should be performed using the same method used in patient studies.

If using a relatively small volume for the validation test, such as a 'hot' sphere with a volume < 30 mL, corrections for partial volume effects will be needed. The simplest such correction is to scale the SPECT estimated activity concentration, determined using the equation above, by a pre-determined volume-dependent recovery coefficient. Recovery coefficients are typically determined by a SPECT acquisition of a multi-sphere phantom with:

$$Recovery\ Coefficient_{VOI} = \frac{SPECT\ estimed\ activity\ concentration\ in\ VOI}{True\ actvity\ concentration\ in\ VOI}$$

The phantom study should be performed with similar acquisition, reconstruction and quantification procedure as in the patient study. The recovery coefficients are plotted as a function of sphere volume and a fit function is obtained for recovery as a function of volume. This function is used to determine the recovery coefficient for the target VOI in the patient study. This approach, though practical, is an approximation because partial volume effects depend on factors other than volume (e.g. shape, target-to-background).

If the quantity of interest is the TBR, the absolute quantification step where counts are scaled by the CF can usually be omitted if the recovery coefficients in the target and the background are sufficiently similar. The segmentation of the background VOI definition can be performed in the same manner as for absolute quantification. The TBR is the mean counts (or count concentration) in the target divided by the mean counts in the background.

Repeat scans to determine bias and precision of activity estimate: Once the phantom is prepared with the desired filling ratios, 20 SPECT scans using the imaging/acquisition parameters specified in Section 3.9 should be performed with re-positioning after each scan. Each scan should be set up to achieve ~ 2 - 5 million total (all views) counts. With the example filling ratios and activities described above this will take ~ 5 min per scan. Image reconstruction should be performed as specified in Section 3.10. Then, for each of the repeat scans the SPECT estimated activity concentration c_{SPECT} should be determined for each of the target and background VOIs using the above equation. The bias in the activity concentration for each VOI is calculated as:

$$\%bias = 100 * \frac{c_{true} - \bar{c}_{SPECT}}{c_{true}}$$

$$\widehat{Var_b} = \frac{\sum(b - \hat{b})^2}{N}$$

Where $\bar{c}_{SPECT}$is the mean value of the SPECT estimated activity concentration from the repeat scans, the $c_{true}$is the true activity concentration used to fill the volume, and $\hat{b}$ is the mean bias over the VOIs. Similarly, the bias in the TBR can be found. The assessor shall calculate the 95% CI for the bias (i.e., *b*) as $\hat{b} \pm t_{\alpha=0.025,(N-1)df} \times \sqrt{\widehat{Var}_b}$, where $t_{\alpha=0.025,(N-1)df}$ is from the Student's t-distribution with α=0.025 and (N-1) degrees of freedom.

For conformance testing, upper and lower 95% confidence intervals for the bias of the SPECT activity concentration and for the bias of TBR must be calculated. The lower bounds must be >-5% and the upper bounds must be <5% in order to be conformant with claims 1A and 1B.

For each case, the assessor shall calculate the SPECT estimated activity concentration and the TBR (denoted Y_i), where *i* denotes the *i*-th case. Let X_i denote the true value for the i-th case. The assessor shall fit an ordinary least squares (OLS) regression of the Y_i's on X_i's. A quadratic term is first included in the model to rule out non-linear relationships: $Y = \beta_o + \beta_1 X + \beta_2 X^2$. If $|\beta_2| < 0.5$, then the assessor shall fit a linear model: $Y = \beta_o + \beta_1 X$, and estimate R^2. For conformance with claim 2B, the absolute value of the estimate of β_2 should be <0.50 and R-squared (R^2) should be >0.90.

The assessor shall also calculate the 95% CI for the slope as $\widehat{\beta_1} \pm t_{\alpha=0.025,(N-2)df}\sqrt{\widehat{Var}_{\beta_1}}$. It is assumed in claim 2B that the regression slope equals one. Thus for conformance to claim 2B, the 95% CI for the slope should be completely contained in the interval 0.95 to 1.05.

For conformance testing the within-subject Coefficient of Variation (wCV) of the activity concentration and TBR should be calculated for each of the targets. The wCV is the relative standard deviation (standard deviation of the replicate measurements divided by their mean) estimated from the multiple scans:

$$\%wCV = \sqrt{(\sum_{i=1}^{N}(Var_i/\bar{Y}_i^2)/N)} \times 100,$$

where Var_i is the estimated variance of the replicate measurements for case i, $\bar{Y}_i$ is the mean of the replicate measurements for case i, and N=20 here.

Estimate the % Repeatability Coefficient as $\widehat{\%RC} = 2.77 \times \%wCV$. For conformance testing, upper 95% confidence bound for the wCV of the SPECT activity concentration and for the wCV of TBR must be calculated. These upper bounds must be <8% in order to be conformant with the four claims.

5. Conformance

To conform to this Profile, participating staff and equipment (Actors") shall support each activity assigned to them in Table 1 in Section 3.

To support an activity, the actor shall conform to the requirements (indicated by "shall language") listed in the Specifications table of the activity. Each activity has a dedicated subsection in Section 3. For convenience, the Specification table requirements have been duplicated and regrouped by actor in the form of a checklist in Appendix E.

Some requirements reference a specific assessment procedure in Section 4 that shall be used to assess conformance to that requirement.

If a QIBA Conformance Statement is already available for an actor (e.g. your analysis software), you may choose to provide a copy of that statement rather than confirming each of the requirements in that Actors checklist yourself.

Formal claims of conformance by the organization responsible for an Actor shall be in the form of a published QIBA Conformance Statement.

Vendors publishing a QIBA Conformance Statement shall provide a set of "Model-specific Parameters" (as shown in Appendix D) describing how their product was configured to achieve conformance. Vendors shall also provide access or describe the characteristics of the test set used for conformance testing.

References

AAPM, Report No. 177

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Appendices

Appendix A: Acknowledgements and Attributions

Appendix B: Background Information

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Appendix C: Conventions and Definitions

Appendix D: Model-specific Instructions and Parameters

Appendix E: Conformance Checklists

QIBA Checklist:

SPECT ^{99m}Tc Quantitation for Large and Small Volumes of Interest

INSTRUCTIONS

This Checklist is organized by "Actor" for convenience. If a QIBA Conformance Statement is already available for an actor (e.g. your analysis software), you may choose to provide a copy of that statement rather than confirming each of the requirements in that Actors checklist yourself.

Within an Actor Checklist the requirements are grouped by the corresponding Activity in the QIBA Profile document. If you are unsure about the meaning or intent of a requirement, additional details may be available in the Discussion Section of the corresponding Activity in the Profile.

Conforms (Y/N) indicates whether you have performed the requirement and confirmed conformance. When responding **N**, please explain why.

Site Opinion is included during the Technical Confirmation process to allow you to indicate how the requirement relates to your current, preferred practice. When responding **Not Feasible** or **Feasible, will not do** (i.e. not worth it to achieve the Profile Claim), please explain why.

Since several of the requirements mandate the use of specific assessment procedures, those are also included at the end to minimize the need of referring to the Profile document.

Feedback on all aspects of the Profile and associated processes is welcomed.

Site checklist	**Page 2**
Acquisition Device checklist	**Page 3**
Image Analysis Tool checklist	**Page 4**
Radiologist checklist	**Page 6**
Physicist checklist	**Page 9**
Technologist checklist	**Page 10**

SITE CHECKLIST

Name of Site Checked:

Parameter	Conforms (Y/N)	Requirement	Site Opinion
Site Conformance (Section 3.0)			
Acquisition Devices		Shall confirm all participating acquisition devices conform to this Profile.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Reconstruction Software		Shall confirm all participating reconstruction software conforms to this Profile.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image Analysis Tools		Shall confirm all participating image analysis tools conform to this Profile.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Radiologists		Shall confirm all participating radiologists conform to this Profile.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Physicists		Shall confirm all participating physicists conform to this Profile.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Technologists		Shall confirm all participating technologists conform to this Profile.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible

ACQUISITION DEVICE AND RECONSTRUCTION SOFTWARE CHECKLIST

Acquisition Device(s) Checked - Make/Model/Version:

Parameter	Conforms (Y/N)	Requirement	Site Opinion
Acquisition Device			
Product Validation (Section 3.2)			
Acquisition Protocol		Shall be capable of storing protocols and performing scans with all the parameters set as specified in Section 3.6.2 "Protocol Design Specification".	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Shall prepare a protocol conformant with Section 3.6.2 "Protocol Design Specification" and validate that protocol as described in Section 3.6.2.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image Header		Shall support imaging start time.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Pre-delivery (Section 3.3)			
Release Testing		Shall pass all manufacturing in-process and release testing criteria.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
File Format		Shall encode SPECT raw data in the DICOM Nuclear Medicine Image Storage SOP Class.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image data acquisition (Section 3.9)			
SPECT Acquisition Mode		The key SPECT acquisition mode parameters shall be specified in a manner that is expected to produce comparable results regardless of the scanner make and model. The key parameters are:	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Rotational radius: shall be the smallest possible. Auto contouring shall be used if available.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Energy windows: The photopeak window shall be set at 140 keV ± 10% (126 – 154 keV) or as recommended by the system manufacturer.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible

Parameter	Conforms (Y/N)	Requirement	Site Opinion
		Lower energy scatter window adjacent to the photopeak shall be set in the range ± 5 to 15% or as recommended by the manufacturer.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Angular sampling: 360 degree coverage with angular sampling of not less than 120 views shall be used (<= 3 degree increments). Step-and-shoot is typically used, but continuous mode can be used to provide shorter total scan time.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Total counts When possible, the scan duration shall be adjusted to obtain > 2 million total counts detected in the photopeak window. The total number of counts may be acquired in a single revolution when scanning relatively stationary distributions of radioactivity, but shall be broken down into multiple revolutions when the biokinetics are unduly fast compared to the scan duration.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Matrix and pixel size: A matrix size and zoom factor that gives a pixel size of one-third to one-half the expected spatial resolution shall be used. Typically, a 128 x 128 matrix and pixel size of no larger than 5 mm.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
CT Acquisition Mode			□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
			□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image data reconstruction (Section 3.10)			
Stored Reconstructed Image		Reconstructed images shall be stored in such a way as to preserve the image dynamic range.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Reconstruction Software			
Produce Validation (Section 3.2)			
Reconstruction Protocol		Shall be capable of performing reconstructions and producing images with all the parameters set as specified in Section 3.6.2 "Protocol Design Specification".	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Pre-delivery (Section 3.3)			
File Format		Shall encode SPECT reconstructed data in the DICOM PET Image Storage SOP Class.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible

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IMAGE ANALYSIS TOOL CHECKLIST

Image Analysis Tool(s) Checked - Make/Model/Version:

Parameter	Conforms (Y/N)	Requirement	Site Opinion
Product Validation (Section 3.2)			
Reading Paradigm		To meet the longitudinal claim shall be able to present the reader with both timepoints side-by-side for comparison when processing the second timepoint.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Shall re-process the first time point if it was processed by a different Image Analysis Tool or Radiologist.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Target Activity Concentration or Target to Background Ratio		Shall be validated to compute Target Activity Concentration or Target to Background Ratio with accuracy within 8% of the true activity concentration or TBR.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		See Section 4.8 Assessment Procedure: Target Activity Concentration or Target to Background Computation.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Target Activity Concentration or Target to Background Ratio Repeatability		Shall be validated to achieve volume activity concentration change repeatability with: an overall repeatability coefficient of less than or equal to 22%* (assuming best estimate of CV is 8% then RC = 2.77*8% see [ref, NO, 2016]).	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Confidence Interval of Result		Shall calculate and make available to the operator the 95% confidence interval for target change based on the equation: $(Y_2 - Y_1) \pm 1.96 \times \sqrt{(Y_1 \times CV_1)^2 + (Y_2 \times CV_2)^2}$ Where Y_1 and Y_2 are the measurements of concentration at timepoints 1 and 2, CV_1 and CV_2 , the within-object coefficient of variation for Y_1 and Y_2, is 8%.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Pre-Delivery (Section 3.3)			
File Format		Shall support the DICOM NM and PET Image SOP Class.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible

RADIOLOGIST CHECKLIST

Note: The Radiologist is responsible for the protocol parameters, although they may choose to use a protocol provided by the vendor of the acquisition device. The Radiologist is also responsible for ensuring that the protocol has been validated, although the Physicist actor is responsible for performing the validation. Protocol design should be done collaboratively between the physicist and the radiologist with the ultimate responsibility to the radiologist. Some parameters are system dependent and may require special attention from a physicist.

Radiologist(s) Checked:

Parameter	Conforms (Y/N)	Specification	Site Opinion
Imaging Protocol Design(Section 3.6)			
Acquisition Protocol		Shall prepare an acquisition protocol to meet the specifications in this table.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Subject Selection (Section 3.7)			
Subject Selection		Shall refer subject for the quantitative imaging procedure.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Inclusion Criteria		Shall go over health records with subject to verify subject meets inclusion criteria for the imaging exam.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Exclusion Criteria		Shall go over health records with subject to verify that subject does not meet an exclusion criteria for the study. Shall perform a pregnancy test in women of childbearing potential.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Subject Handling (Section 3.8)			
Administration of Radiotracer		Shall administer radiotracer to subject.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Subject Positioning		Shall specify the subject's imaging volume of interest. Shall also determine if imaging should be done over one or more fields of view.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image Analyst (Section 3.13)			
Certify VOI		Shall either (1) agree with region boundaries, (2) reject boundaries and return for reprocessing, or (3) make revisions "on the fly" as indicated.	□ Routinely do already □ Feasible, will do □ Feasible, will not do

Parameter	Conforms (Y/N)	Specification	Site Opinion
			□ Not feasible

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PHYSICIST CHECKLIST

Note: The role of the Physicist actor may be played by an in-house medical physicist, a physics consultant or other staff (such as vendor service or specialists) qualified to perform the validations described.

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Physicist(s) Checked:

Parameter	Conforms (Y/N)	Requirement	Site Opinion
Periodic QA (Section 3.5)			
Quality Control Results		Values for the listed tests shall be compared with those obtained at acceptance and the action levels established at the time of acceptance testing.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
SPECT Calibration Factor		Shall determine and record the SPECT Calibration Factor (at least quarterly and consistent with manufacturer recommendation). See 4.7 Assessment Procedure: SPECT Calibration Factor.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Time Synchronization		Shall confirm daily that all device clocks are synchronized to within ± 1 minute.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Intrinsic Uniformity		Shall confirm quarterly that the intrinsic uniformity from a ^{99m}Tc point source is within 4% in the UFOV. See 4.1 Assessment Procedure: Intrinsic Uniformity.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
System Uniformity		Shall confirm daily that the system uniformity from a ^{99m}Tc or ^{57}Co source is within 4% in the UFOV. See 4.1b Assessment Procedure: System Uniformity.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Planar Spatial Resolution		Shall confirm semiannually that the planar FWHM spatial resolution from the collimators used for ^{99m}Tc imaging is less than 8mm. See 4.2 Assessment Procedure: Planar Spatial Resolution.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Center of Rotation (COR)		Shall confirm semiannually that the mean value of the COR offset does not exceed 1/2 pixel (typically 2 mm) when measured at the center and edges of the FOV.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Shall confirm the position of Y=0 axis and the Y gain are the same for all heads in a multi-head system.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible

Parameter	Conforms (Y/N)	Requirement	Site Opinion
Photon Energy Analyzer		Shall confirm (typically daily) that the accuracy of the photon energy analyzer is within manufacturer specifications.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
CT Attenuation Map Registration		Shall confirm (typically daily) that the attenuation maps are registered to the SPECT images within the manufacturer specifications.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Overall System Performance		Shall confirm percent bias is 5% or less of the true concentration. See 4.8 Validation of Absolute Quantification Capability: Phantom Study.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Linearity		Shall be evaluated annually (or after any radionuclide calibrator event) using either ^{18}F or ^{99m}Tc and shall be within ±2.5 % of the true value over an operating range of 37 to 1110 MBq (1 to 30 mCi). The true value is determined by a linear fit (to the log data) over the same operating range.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Scanner and Site Clocks		SPECT scanner computer and all clocks in an imaging facility used to record activity/injection measurements shall be synchronized to a standard time reference to within ± 1 minute. Synchronization shall be verified daily and after power outages or civil changes for Daylight Savings Time or Summer Time.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Imaging Protocol Design (Section 3.6)			
Acquisition Protocol		Shall prepare an acquisition protocol to meet the specifications in this table.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Planar Spatial Resolution		Using the collimator that will be used for the imaging protocol, the planar spatial resolution shall be <8 mm for a line source in “air” at a distance of 10 cm from the collimator.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Acquisition time per frame		The acquisition time per projection angle shall be determined by the minimum number of counts required for the study; and the current imaging detector count rate. The formula to calculate time per frame is included above.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image Voxel Size		Shall select a number of spatial bins in order to achieve a voxel size that is not larger than the spatial resolution divided by 2. The voxel size shall not be more than 5 mm.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Reconstruction Protocol		Shall prepare a protocol to achieve quantitatively accurate image. More details about the image reconstruction protocol are provided in Section 3.10. Iterative image reconstruction	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible

Parameter	Conforms (Y/N)	Requirement	Site Opinion
		with attenuation and scatter correction are recommended over filtered backprojection.	
CT Technique: Protocol Design		A team comprising a Technologist / Physician / Medical Physicist shall ensure that CT techniques protocols are designed such that dose exposure is the lowest radiation dose necessary to achieve the objective. Protocols defined by Image Gently and Image Wisely shall be used where feasible. The protocol shall be recorded and documented.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image Analyst (Section 3.13)			
Absolute Activity Concentration (kBq/mL)		Analysis Workstation: Shall have a suitable monitor of appropriate size and pixel density for diagnostic viewing of medical images. Shall be placed in a room with in room lighting appropriate for image data analysis and interpretation (i.e., a radiology reading room). Shall have appropriate computation power and memory to carryout VOI data analysis.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Post processed image for data analysis: Image for data analysis shall be reconstructed in accordance with parameters as described in Section 3.10.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		VOI software analysis tools: Using analysis workstation tools, volumes of interest shall be placed on the object of interest. Activity concentration shall be reported as the mean activity for the VOI or the maximum activity concentration for the VOI.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Absolute Activity Concentration (%ID/mL)		Analysis Workstation: Shall have a suitable monitor of appropriate size and pixel density for diagnostic viewing of medical images. Shall be placed in a room with in room lighting appropriate for image data analysis and interpretation (i.e., a radiology reading room). Shall have appropriate computation power and memory to carryout VOI data analysis.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Post processed image for data analysis: Image for data analysis shall be reconstructed in accordance with parameters as described in Section 3.10.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		VOI software analysis tools:	□ Routinely do already

Parameter	Conforms (Y/N)	Requirement	Site Opinion
		Using analysis workstation tools, volumes of interest shall be placed on the object of interest. Activity concentration shall be reported as the mean activity concentration in the VOI times 100% divided by the injected activity.	□ Feasible, will do □ Feasible, will not do □ Not feasible
Assessment Procedure: Voxel Noise in the Reference/Background Compartment (Section 4.5)			
Planar Uniformity QC		At least quarterly and following detector changes, calibrations and/or software upgrades the uniformity of detector response to a uniform flux of radiation of ^{99m}Tc should be assessed.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Daily, or at least on the day of a trial subject, the collimated uniformity of the detectors using collimators to be used for ^{99m}Tc imaging should be assessed using a ^{99m}Tc or ^{57}Co source.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		For both measurements, uniformity should be measured and assessed in accordance with local regulatory requirements.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
SPECT Uniformity QC		At least quarterly and following detector changes, calibrations and/or software upgrades, the SPECT uniformity should be measured using acquisition parameters defined in the clinical protocol trial.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible

TECHNOLOGIST CHECKLIST

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Technologist(s) Checked:

Parameter	Conforms (Y/N)	Specification	Site Opinion
Periodic QA (Section 3.5)			
Time Synchronization		Shall confirm daily that all device clocks are synchronized to within ± 1 minute.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Intrinsic Uniformity		Shall confirm quarterly that the intrinsic uniformity from a ^{99m}Tc point source is within 4% in the UFOV. See 4.1b Assessment Procedure: System Uniformity.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
System Uniformity		Shall confirm daily that the system uniformity from a ^{99m}Tc or ^{57}Co source is within 4% in the UFOV. See 4.1b Assessment Procedure: System Uniformity.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Center of Rotation (COR)		Shall confirm semiannually that the mean value of the COR offset does not exceed 1/2 pixel (typically 2 mm) when measured at the center and edges of the FOV.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Shall confirm the position of Y=0 axis and the Y gain are the same for all heads in a multi-head system.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Photon Energy Analyzer		Shall confirm (typically daily) that the accuracy of the photon energy analyzer is within manufacturer specifications.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
CT Attenuation Map Registration		Shall confirm (typically daily) that the attenuation maps are registered to the SPECT images within the manufacturer specifications.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Scanner and Site Clocks		SPECT scanner computer and all clocks in an imaging facility used to record activity/injection measurements shall be synchronized to a standard time reference to within ± 1 minute. Synchronization shall be verified daily and after power outages or civil changes for Daylight Savings Time or Summer Time.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Constancy		Shall be evaluated daily (or after any radionuclide calibrator event) using a NIST-traceable (or equivalent) ^{99m}Tc, ^{137}Cs, or ^{57}Co radionuclide calibrator standard and confirmed that net measured (and decay-corrected) activity differs by no greater than ±2.5 % from the standard value.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible

Parameter	Conforms (Y/N)	Specification	Site Opinion
Accuracy		Shall be evaluated monthly (or after any radionuclide calibrator event) with a NIST-traceable (or equivalent) ^{99m}Tc standard or simulated ^{99m}Tc radionuclide calibrator standard (if available). Shall confirm that the measured (and decay-corrected) activity differs by no greater than ±2.5 % from the standard value.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Linearity		Shall be evaluated annually (or after any radionuclide calibrator event) using either ^{18}F or ^{99m}Tc and shall be within ±2.5 % of the true value over an operating range of 37 to 1110 MBq (1 to 30 mCi). The true value is determined by a linear fit (to the log data) over the same operating range.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Imaging Protocol Design (Section 3.6)			
Number of View Angles		Shall be either 120 or 128 depending upon the recommendation of the camera vendor.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Detector Orbit		Detector auto-contouring shall be used when available. When auto-contouring is not available, elliptical detector orbit will be used where the arc of the orbit is set to minimize the distance between the patient and the detector.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
CT Technique: Protocol Design		A team comprising a Technologist / Physician / Medical Physicist shall ensure that CT techniques protocols are designed such that dose exposure is the lowest radiation dose necessary to achieve the objective.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Protocols defined by Image Gently and Image Wisely shall be used where feasible.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		The protocol shall be recorded and documented.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		The technologist shall ensure that the CT dose conforms to the dose prescribed by the supervising physician or protocol.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Subject Handling (Section 3.8)			
Administration of Radiotracer		Shall administer radiotracer to subject.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible

Parameter	Conforms (Y/N)	Specification	Site Opinion
Radiotracer Uptake		If an uptake period is required shall instruct the subject on the length of the uptake period and if there are any activity restrictions (e.g., no food). Shall monitor the length of the uptake period.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Subject Positioning		Shall position the subject on the imaging table and setup the imaging system to acquire data over the appropriate imaging volume of the subject.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Table Height and Centering		Shall adjust the table height for the mid-axillary plane to pass through the isocenter.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Shall position the patient such that the “sagittal laser line” lies along the sternum (e.g., from the suprasternal notch to the xiphoid process).	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Breathing Instructions		Shall instruct the subject in proper breath-hold for CT portion of study if CT image is being acquired. Shall instruct the subject on proper shallow breathing technique during SPECT data acquisition to minimize breathing motion artifacts.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image Data Acquisition (Section 3.9)			
Acquisition Protocol		Shall select a protocol that has been previously prepared and qualified for this purpose (See section 3.6.2 "Protocol Design Specification").	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Shall report if any parameters are modified beyond the specifications in section 3.6.2 "Protocol Design Specification".	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Collimator		Shall use a collimator that provides planar system resolution of < 8 mm FWHM (in ‘air’ at 10 cm distance) for ^{99m}Tc.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
SPECT Acquisition Mode		The technologist shall set up the acquisition, acquire the data, and store the data.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
SPECT Acquisition		Shall watch the patient to make sure the patient does not move during the data acquisition.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
CT Acquisition Mode		The key CT acquisition mode parameters (kVp, mAs, pitch, and collimation) shall be set as specified by study protocol and used consistently for all subject scans.	□ Routinely do already □ Feasible, will do □ Feasible, will not do

Parameter	Conforms (Y/N)	Specification	Site Opinion
			□ Not feasible
Image Data Reconstruction (Section 3.10)			
SPECT Image Reconstruction		Shall run iterative reconstruction as specified by study protocol.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
SPECT Matrix/Voxel Size		The Technologist shall perform the image reconstruction such that the matrix, slice thickness, and reconstruction zoom shall yield a voxel size of ≤ 5 mm (same as projection bin size) in all three dimensions, although not necessarily isotropic. The final size shall not be achieved by re-binning, etc., of the reconstructed images.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Correction: Attenuation		CT-based attenuation correction shall be included in the reconstruction.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Correction: Scatter		Scatter correction shall be used. Dual energy window (DEW) or equivalent is recommended.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Collimator Detector Response Modeling		Shall be used if available.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image Reconstruction Updates		Shall be 60 updates (iterations times subsets) or more depending on target-to-background activity concentration ratios and the target size.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		For large organs such as the liver fewer updates are needed for convergence.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image QA (Section 3.11)			
Patient Motion Frequency		Shall view cine of projection data or vendor software tool to determine if patient moved during scan. With guidance from physician shall determine if scan needs to be reacquired.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		With guidance from physician shall determine if scan needs to be reacquired.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Injection Site		Shall observe counting rate during data acquisition to make sure counting rates are close to what is expected for the exam.	□ Routinely do already □ Feasible, will do

Parameter	Conforms (Y/N)	Specification	Site Opinion
			□ Feasible, will not do □ Not feasible
		If counts are low, shall image the injection site to make sure there is little to no extravasation at the injection site.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
SPECT-CT Alignment		Shall make sure SPECT and CT images are properly aligned for proper attenuation correction and also for image fusion.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image Artifacts		Shall view reconstructed image to make sure that there are no artifacts present. Artifacts can be caused by patient motion, SPECT-CT misalignment, metal in the FOV, etc.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image Distribution (Section 3.12)			
Image Distribution		The original projections (sinogram) images (scanner raw data), shall always be archived at the local site.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		The reconstructed SPECT images (image raw data), along with all required corrections, and CT images shall always be archived at the local site.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		If processed SPECT images are required, they shall be archived as separate secondary datasets.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		If scanner raw data need to be archived for future reprocessing, this shall be defined prospectively in the Protocol.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Image Analyst (Section 3.13)			
Absolute Activity Concentration (kBq/mL)		Analysis Workstation: Shall have a suitable monitor of appropriate size and pixel density for diagnostic viewing of medical images. Shall be placed in a room with in room lighting appropriate for image data analysis and interpretation (i.e., a radiology reading room). Shall have appropriate computation power and memory to carryout VOI data analysis.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Post processed image for data analysis: Image for data analysis shall be reconstructed in accordance with parameters as described in Section 3.10.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		VOI software analysis tools:	□ Routinely do already

Parameter	Conforms (Y/N)	Specification	Site Opinion
		Using analysis workstation tools, volumes of interest shall be placed on the object of interest. Activity concentration shall be reported as the mean activity for the VOI or the maximum activity concentration for the VOI.	□ Feasible, will do □ Feasible, will not do □ Not feasible
Absolute Activity Concentration (%ID/mL)		Analysis Workstation: Shall have a suitable monitor of appropriate size and pixel density for diagnostic viewing of medical images. Shall be placed in a room with in room lighting appropriate for image data analysis and interpretation (i.e., a radiology reading room). Shall have appropriate computation power and memory to carryout VOI data analysis.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Post processed image for data analysis: Image for data analysis shall be reconstructed in accordance with parameters as described in Section 3.10.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		VOI software analysis tools: Using analysis workstation tools, volumes of interest shall be placed on the object of interest. Activity concentration shall be reported as the mean activity concentration in the VOI times 100% divided by the injected activity.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Target to Background Ratio		Analysis Workstation: Shall have a suitable monitor of appropriate size and pixel density for diagnostic viewing of medical images. Shall be placed in a room with in room lighting appropriate for image data analysis and interpretation (i.e., a radiology reading room). Shall have appropriate computation power and memory to carryout VOI data analysis.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		Post processed image for data analysis: Image for data analysis shall be reconstructed in accordance with parameters as described in Section 3.10.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
		VOI software analysis tools: Using analysis workstation tools, volumes of interest shall be placed on the object of interest and the reference tissue. Mean activity or count-rate concentration is extracted for each region. The target to background ratio shall be reported as the counts concentration (mean counts or counts divided by volume) of the target VOI divided by the counts concentration in the background VOI.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Certify VOI		Shall either (1) agree with region boundaries, (2) reject boundaries and return for reprocessing, or (3) make revisions “on the fly” as indicated.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
Assessment Procedure: Voxel Noise in the Reference/Background Compartment (Section 4.5)			
Planar Uniformity QC		At least quarterly and following detector changes, calibrations and/or software upgrades the uniformity of detector response to a uniform flux of radiation of ^{99m}Tc should be assessed. Uniformity should be	□ Routinely do already □ Feasible, will do □ Feasible, will not do

Parameter	Conforms (Y/N)	Specification	Site Opinion
		measured and assessed in accordance with local regulatory requirements.	□ Not feasible
		Daily, or at least on the day of a trial subject, the collimated uniformity of the detectors using collimators to be used for ^{99m}Tc imaging should be assessed using a ^{99m}Tc or ^{57}Co source. Uniformity should be measured and assessed in accordance with local regulatory requirements.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible
SPECT Uniformity QC		At least quarterly and following detector changes, calibrations and/or software upgrades, the SPECT uniformity should be measured using acquisition parameters defined in the clinical protocol trial.	□ Routinely do already □ Feasible, will do □ Feasible, will not do □ Not feasible

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