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SLN Profile:

Small Lung Nodule Volume Assessment and

Monitoring in Low Dose Chest CT Screening

Technical Guidance Document

April 13, 2026

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This document is a continuation of the RSNA/QIBA CT Small Lung Nodule Profile that has been improved and refined by the Small Lung Nodule Profile guideline group (slnprofile.org). The American Lung Association and QMIC supports and endorses this initiative.

1.0 Executive Summary

This document outlines guidance recommended by the SLN Profile for Small Lung Nodule Volume Assessment and Monitoring in Low Dose CT Screening. This Profile focuses on improving the consistency and reliability of quantitative CT volume measurements for solid lung nodules, aiding in the management of screen-detected nodules and optimizing patient care. This Profile provides a framework to ensure reliable and consistent CT imaging results across different imaging platforms and clinical sites.

The SLN Profile aims to achieve a useful level of performance for a specific biomarker. It consists of:

1. The Claim (Section 2): Describes the biomarker performance.
2. Conformance Checklist (Section 3): Outlines activities that generate the biomarker and sets requirements for Actors (Radiographers/technologists).

This Profile focuses on the accuracy and precision of quantitative CT volumetry for solid lung nodules between 6-10 mm in diameter. It sets requirements for:

- Acquisition Devices
- Technologists/Radiographers
- Radiologists
- Image Analysis Tools

These requirements cover various activities, from equipment quality assurance to image analysis, aiming to achieve accurate measurements and reduce unnecessary variability. The Profile provides two sets of claims:

1. 95% confidence intervals for volumetric measurements of 6-10 mm solid lung nodules.
2. Guidance on:
 - Percentage of volumetric change needed to confirm true solid lung nodule growth with 95% confidence.
 - 95% confidence interval for volumetric size change measurements.

This document is a resource for clinicians, imaging staff, vendors, purchasers, and researchers involved with pulmonary nodule volume measurements. This Profile document includes a conformance test that can be performed to test the fundamental imaging performance characteristics of the CT scanner to be used at a clinical site.

Note: This Profile sets requirements to achieve the claim, not standards of care. Patient care always takes precedence over meeting Profile goals.

2.0 Clinical Context and Claims

Clinical Context

This Profile focuses on quantifying volumes and volume changes of solid lung nodules with a longest bi-dimensional diameter between 6 mm and 10 mm.

Claims

When all relevant staff and equipment conform to this Profile, the following claims are supported:

Claim 1: Nodule Volume

For a measured nodule volume Y , the 95% confidence interval for the true nodule volume is $Y \pm (1.96 \times Y \times CV)$, where CV is the Coefficient of Variation from Table 1.

Claim 2: Nodule Volume Change

a) A measured nodule volume percentage change X indicates a true change if $X > (2.77 \times CV1 \times 100)$, with 95% confidence.

b) For volume measurements $Y1$ and $Y2$ at two time points, with corresponding CVs ($CV1$ and $CV2$) from Table 1, the 95% confidence interval for volume change $Z = (Y2 - Y1) \pm 1.96 \times \sqrt{[Y1 \times CV1]^2 + [Y2 \times CV2]^2}$.

Claim Conditions

These claims are valid when:

- The nodule is completely solid
- Nodule longest dimension is 6-10 mm at the first time point
- Nodule's shortest diameter is at least 60% of its longest diameter
- Nodule is measurable at both time points
- Interpolation is used for CV values between provided table values

Table 1. Coefficients of Variation (CV)

Nodule Diameter (mm)	Nodule Volume (mm ³)	CV	95% CI Limits (mm ³)	Minimum Detectable Difference
6	113	0.290	± 64	80.4%
7	154	0.227	± 68	62.8%
8	268	0.186	± 98	51.6%
9	382	0.159	± 119	43.9%
10	524	0.138	± 142	38.3%
11	697	0.123	± 168	34.0%
12	905	0.111	± 196	30.6%
13	1150	0.101	± 227	27.9%
14	1437	0.093	± 261	25.6%
15	1767	0.086	± 296	23.7%

For a more detailed explanation of the clinical context, including the benefits and challenges of low-dose CT for lung nodule measurement, please refer to the full discussion in Appendix A.

For detailed examples and clinical interpretations of Claims 1 and 2, please refer to Appendix B. A web-based calculator for computing the equations in the Claims is available at <https://services.accumetra.com/NoduleCalculator.html>.

3.0 Clinical Site Conformance Checklist

This checklist provides a streamlined approach for clinical sites to achieve conformance with this Profile. It is designed to be applicable across different regions, including Europe and the USA. The checklist is divided into two main sections: Preparation and Performance. Each step indicates the responsible actor(s) in parentheses.

For detailed technical information on Profile requirements, please refer to Section 4.

Preparing for Lung Nodule Measurement

1. CT Scanner and Lung Nodule Analysis Software Verification (**Radiologist**)

☐ 1.1 Verify that the CT scanner model is approved for use in your region.

☐ 1.2 Verify that the volumetric software name and version are approved for use in your region.

2. CT QA and Lung Screening Protocol Verification (**Medical Physicist, Technologist/Radiographer**)

☐ 2.1 Establish and save a CT lung cancer screening protocol

☐ 2.2 Scan a reference object using the saved protocol

☐ 2.3 Obtain a passing automated CT image quality report

Performing Lung Nodule Measurement

4. CT Data Acquisition, Lung Nodule, and Segmentation Verification (**Radiologist**)

☐ 4.1 Verify same CT scanner and protocol used for follow-up scans

☐ 4.2 Confirm no IV contrast was used

☐ 4.3 Verify nodule characteristics (solid, 6-10mm longest diameter at baseline, $\leq 1/3$ attached)

- ☐ 4.4 Check for absence of significant artifacts and excessive noise
- ☐ 4.5 Verify absence of segmentation errors

Note: You can use the approved nodule calculator for measurement error guidance

Note: Specific regional requirements (e.g., CTDIvol limits) should be incorporated into the relevant steps as needed.

4. Profile Activities

This Profile outlines the activities necessary for proper lung cancer screening to achieve the applicability of the profile claims. It is organized by key actors involved in the screening process. Each actor is responsible for specific activities that contribute to the overall quality and consistency of the screening process. Figure 1 provides a quick overview of how the different activities for CT tumor volumetry are sequenced. The following table (Table 2) outlines the actors and their required activities, with references to detailed specifications in subsequent sections.

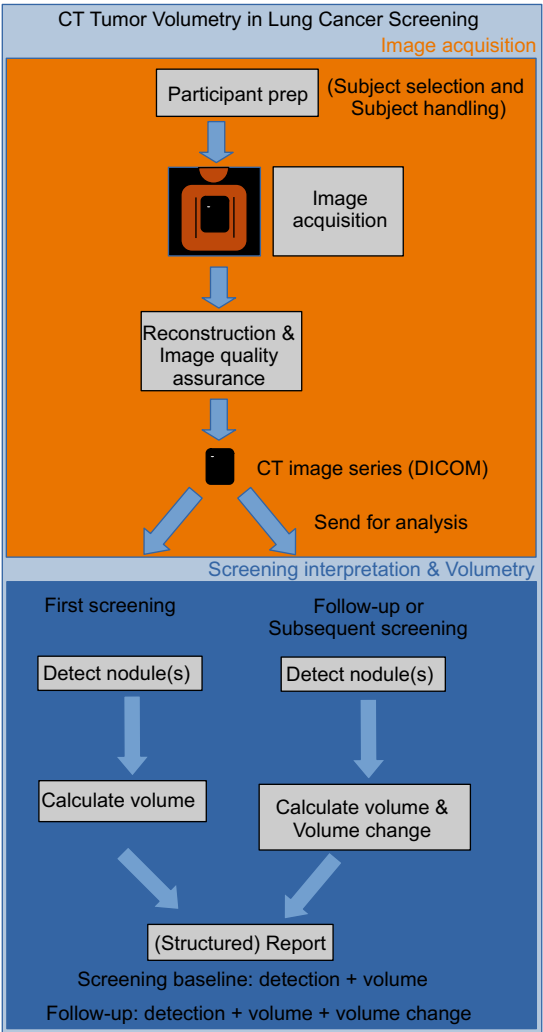


Figure 1: CT Tumor Volumetry - Activity Sequence

Table 2: Actors and Required Activities

Actor	Activities	Section
Acquisition Device	Product Validation	4.1
Image Analysis Tool	Product Validation	4.1
Radiographer	Staff Qualification, Protocol Design, Subject Handling, Image Data Acquisition, Image Data Reconstruction, Image Quality Assurance	4.2, 4.4, 4.6, 4.7, 4.8, 4.9
Radiologist	Staff Qualification, Protocol Design, Subject Selection, Subject Handling	4.2, 4.4, 4.5, 4.6
Medical Physicist	Equipment Quality Assurance, Protocol Design, Image Data Acquisition	4.3, 4.4, 4.7
Referring Clinician	Subject Selection	4.5
Image Analyst	Staff Qualification, Image Data Acquisition, Image Quality Assurance, Image Analysis	4.2, 4.7, 4.9, 4.10

Note: Successful implementation of this Profile requires a team effort. Each actor must perform their respective activities as outlined in the table above to ensure the overall quality and consistency of the lung cancer screening process.

4.1. Product Validation

This activity evaluates the Acquisition Device and Image Analysis Tool prior to their use in the Profile. It includes validations and performance assessments necessary to reliably meet the Profile Claim.

4.1.1 Discussion

- Performance measurements of specific protocols are addressed in section 4.4.2.
- CT scanners should have a minimum of 16 detector rows to ensure:
 - Adequate scan duration (entire lung in a single breath-hold)
 - Sufficient z-axis resolution
 - Appropriate radiation dose management
- Scanners with fewer than 16 detectors and pitch high enough to allow the entire lung to be scanned in a single breath hold may result in Z-axis resolution that is inadequate for nodule volumetry in some patients [26].

4.1.2 Specification

Table 3: Product Validation - Actors and Requirements

Parameter	Actor	Requirement
Number of Detector Rows	Acquisition Device	Shall have 16 or more detector rows.
Acquisition Protocol	Acquisition Device	Shall be capable of storing and performing scans with parameters specified in section 4.4.2. Shall prepare and validate a protocol conformant with section 4.4.2.
Image Header	Acquisition Device	Shall record actual values for tags listed in section 4.4.2 in the DICOM image header.
Reading Paradigm	Image Analysis Tool	Shall present images from both time points side-by-side for comparison.
Change Calculation	Image Analysis Tool	Shall calculate change as the difference in volume between two time points relative to the earlier time point, expressed in mm ³ .
Scientific Validation	Image Analysis Tool	Shall have appropriate scientific validation, including measurement linearity, coefficient of variation, and zero bias.

4.2. Staff Qualification

This activity evaluates the human Actors (Radiologist, Medical Physicist, Radiographer, and Image Analyst) prior to their participation in the Profile. It includes training, qualification, or performance assessments necessary to reliably meet the Profile Claim.

4.2.1 Discussion

- These requirements focus on achieving the Profile Claim, not evaluating medical or professional qualifications.
- In clinical practice, the Radiologist interpreting the examination often will be the Image Analyst.
- In some clinical practice situations and research settings, the image analyst may be a non-radiologist professional.
- Analyst Training should be appropriate for the setting and purpose of the measurements, covering topics such as:
 - Generation and components of volumetric CT images
 - Principles of image reconstruction and processing
 - Technical factors influencing quantitative assessment
 - Relevant CT anatomy
 - Definition of a nodule
 - Image artifacts

4.2.2 Specification

Table 4: Staff Qualification - Actors and Requirements

Actor	Specification
Radiologist	Shall fulfill qualifications required by national or regional radiology boards, including: - Certification by the appropriate national radiology board - Appropriate licensing - Documented experience in CT interpretation - Compliance with continuing education requirements
Radiographer	Shall fulfill qualifications required by national or regional radiography boards, including: - Certification by the appropriate national radiography board - Appropriate licensing - Documented training and experience in performing CT - Compliance with continuing education requirements
Medical Physicist	Shall fulfill qualifications required by national or regional medical physics organizations, including: - Certification by the appropriate national medical physics board - Appropriate licensing - Documented experience in CT physics - Compliance with continuing education requirements
Image Analyst	Shall undergo documented training in performing CT image volumetric analysis of lung nodules in lung cancer screening by a radiologist having qualifications conforming to the requirements of this profile. Note: If the Image Analyst is a Profile-conformant Radiologist, additional training is not required.

Note: Specific qualifications may vary by country within Europe. Actors should comply with their national and local regulations and standards.

4.3. Equipment Quality Assurance

This activity involves quality assurance of imaging devices not directly associated with a specific subject. It includes calibrations, phantom imaging, and performance assessments necessary to reliably meet the Profile Claim.

4.3.1 Discussion

- Focus is on ensuring the acquisition device is aligned/calibrated/functioning normally.
- Conformance requires adherence to:
 - Relevant national or regional regulations (e.g., EU medical device regulation 2017/745 (MDR))
 - Equipment performance evaluation procedures of national radiology accreditation programs
 - Manufacturer's quality control procedures

- Annual technical performance evaluation by a qualified medical physicist
- Daily quality control monitoring of water CT number, standard deviation, and artifacts
- Regular preventive maintenance by a qualified service engineer

4.3.2 Specification

Table 5: Equipment Quality Assurance - Actors and Requirements

Parameter	Actor	Specification
Quality Control	Medical Physicist	Shall perform quality control procedures consistent with those generally accepted for routine clinical imaging.
Quality Control	Medical Physicist	Shall adhere to installation and periodic quality control procedures specified by the scanner manufacturer and relevant national accreditation programs.
Maintenance	Medical Physicist	Shall ensure that preventive maintenance is conducted and documented by a qualified service engineer at intervals recommended by the scanner manufacturer.

Note: Specific requirements may vary by country within Europe. Actors should comply with their national and local regulations and standards.

4.4. Protocol Design

This activity involves designing acquisition and reconstruction protocols to reliably meet the Profile Claim.

4.4.1 Discussion

- Protocol Design typically occurs at the imaging site, but sites may use protocols developed elsewhere.
- Specifications focus on resulting dataset characteristics rather than specific techniques.
- In CT screening for lung cancer, minimizing radiation dose is crucial.
- CTDIvol ≤ 3 mGy is generally sufficient for a standard-sized person (170 cm, 70 kg; as defined by ICRP Publication 89 (2002)).
- Variability in CT nodule volumetry using low dose techniques is comparable to that of standard dose techniques [14, 17, 18, 27, 28].
- Automatic Exposure Control is optional but should be consistent with baseline if used.
- Reconstructed Slice Thickness: Should be small relative to the size of the smallest nodules detected. Thinner sections are preferable to reduce partial volume effects and improve accuracy [11-13, 36].
- Reconstruction Kernel should be medium smooth to medium sharp without edge enhancement.

4.4.2 Specification

Table 6: Protocol Design - Actors and Requirements

Parameter	Actor	Specification	DICOM Tag
Acquisition Protocol	Radiologist and Radiographer	Shall prepare a protocol meeting the specifications in this table. Shall ensure	

		radiographers are trained on profile requirements.	
Nominal Tomographic Section Thickness (T)	Radiologist and Radiographer	Shall set to achieve reconstructed slice thickness ≤ 1.25 mm.	Single Collimation Width (0018,9306)
Reconstruction Protocol	Radiologist and Radiographer	Shall prepare a protocol meeting the specifications in this table. Shall ensure radiographers are trained on profile requirements.	
Reconstructed Image Thickness	Radiologist and Radiographer	Shall set to ≤ 1.25 mm.	Slice Thickness (0018,0050)
Reconstructed Image Interval	Radiologist and Radiographer	Shall set to $\leq$ Reconstructed Image Thickness (no gap, may overlap).	Spacing Between Slices (0018,0088)
Resolution	Radiologist, Radiographer, and Medical Physicist	Shall validate that the protocol achieves: • 3D PSF sigma ellipsoid volume $\leq 1.5\text{mm}^3$ • Z PSF sigma $< 2\times$ in-plane PSF sigma	
Edge Enhancement	Radiologist, Radiographer, and Medical Physicist	Shall validate that the protocol does not result in edge enhancement $> 5\%$.	
HU Deviation	Radiologist, Radiographer, and Medical Physicist	Shall validate that the protocol results in CT HU value deviation < 35 HU for Air and Acrylic materials.	
Voxel Noise	Radiologist, Radiographer, and Medical Physicist	Shall validate that the protocol achieves standard deviation ≤ 50 HU for homogeneous Air and Acrylic materials.	
Spatial Warping	Radiologist, Radiographer, and Medical Physicist	Shall validate that 3D image acquisition results in Spatial warping < 0.3 mm Root Mean Square Error (RMSE).	

Note: See section 5.1. Technical Evaluation Methods

4.5. Subject Selection

This activity describes criteria and procedures for selecting appropriate imaging subjects to reliably meet the Profile Claim.

4.5.1 Discussion

- Pulmonary Symptoms: Subjects should be asymptomatic or at baseline for cardiac and pulmonary symptoms. Acute or subacute abnormalities could interfere with nodule volume measurements or breath-holding compliance.
- Recent Medical Procedures: Procedures like bronchoscopy, thoracic surgery, or radiation therapy may cause parenchymal lung abnormalities that could invalidate Profile Claims.
- Oral Contrast: Residual contrast from gastrointestinal imaging may cause artifacts interfering with quantitative nodule assessment.

- Chronic Abnormalities: Conditions such as pulmonary fibrosis may affect nodule volume measurement accuracy and invalidate Profile Claims.

4.5.2 Specification

Table 7: Subject Selection - Actors and Requirements

Parameter	Actor	Requirement
Medical Procedures	Referring Clinician	Shall schedule scanning prior to or at an appropriate time, following procedures that could alter the attenuation of the lung nodule or surrounding lung tissue.
	Radiologist	Shall confirm appropriate timing of scan relative to medical procedures.
Pulmonary Symptoms	Referring Clinician	Shall delay scanning for a time period that allows resolution of potential reversible CT abnormalities if pulmonary symptoms are present.
	Radiologist	Shall confirm absence of acute pulmonary symptoms or appropriate baseline status.

Note: If these conditions cannot be met, measurements may not be of sufficient quality to fulfill the Profile Claims.

4.6. Subject Handling

This activity involves handling each imaging subject at each time point to reliably meet the Profile Claim.

4.6.1 Discussion

- Intravenous Contrast: Not used for CT lung cancer screening [29]. Its use may affect volume quantification [30, 31] and invalidates Profile Claims.
- Artifact Sources: Radiographers should evaluate for and remove external metallic objects that may produce artifacts.
- Subject Positioning: Consistent positioning is important to reduce variation in x-ray beam hardening, scatter, and nodule orientation [32, 33].
 - Supine with arms overhead
 - Sternum over table midline
 - Midaxillary line at widest part of gantry
- Breath Holding: Scans should be performed during maximal inspiration to reduce motion artifacts and improve segmentation [21, 34, 35].
 - Live breathing instructions strongly recommended
 - Practice round before scanning is advised

4.6.2 Specification

Table 8: Subject Handling - Actors and Requirements

Parameter	Actor	Requirement
Intravenous contrast	Analyst, Radiologist	Shall not use images with intravenous contrast for quantitative nodule volumetry in lung cancer screening or follow-up.
Artifact sources	Radiographer	Shall remove or position potential sources of artifacts to avoid

		degrading reconstructed CT volumes.
Subject Positioning	Radiographer	Shall position the subject consistent with baseline.
Table Height & Centering	Radiographer	Shall adjust table height for mid-axillary plane to pass through gantry isocenter. Shall be consistent with baseline.
Breath holding	Radiographer	Shall instruct subject in proper breath-hold and start acquisition shortly after full inspiration. Shall ensure breath hold state is consistent with baseline.

4.7. Image Data Acquisition

This activity involves the acquisition of image data for a subject at either time point, including details necessary to reliably meet the Profile Claim.

4.7.1 Discussion

- CT scans should ideally be performed on the same platform (manufacturer, model, and version) for an individual subject to reduce variation.
- Consistency with baseline scans is crucial for reducing potential sources of variance.
- Image header recordings of key parameter values facilitate meeting and confirming consistency requirements.
- Anatomic Coverage:
 - Baseline scan: entire volume of the lungs (apex through base)
 - Nodule measurement: full nodule plus 5 to 10 mm of lung region above and below
- For recommended dose levels and justification, see Section 4.4 Protocol Design.
- Pitch should not exceed 2.0 for single x-ray tube CT acquisitions or equivalent for dual-source technology.

4.7.2 Specification

Table 9: Image Data Acquisition - Actors and Requirements

Parameter	Actor	Requirement
Acquisition Protocol	Radiographer, Radiologist	Shall select a protocol previously prepared and validated for this Profile (See section 4.4.2 "Protocol Design Specification").
Scan Duration	Radiographer	Shall perform the scan in a single breath hold.
Consistency	Radiographer	Shall ensure that follow-up scans use the same CT scanner model and acquisition protocol settings.

4.8. Image Data Reconstruction

This activity involves the reconstruction of image data for a subject at either time point, including criteria and procedures necessary to reliably meet the Profile Claim.

4.8.1 Discussion

- Reconstructed data must remain consistent with baseline acquisitions (see Section 4.7).
Reconstruction Field of View: Set to the widest diameter of the lungs, consistent with baseline [11, 12].
- [11-13, 36].
- Reconstructed slice thickness and reconstruction kernel settings shall follow the validated protocol defined in Section 4.4.
- Reconstruction Interval: Contiguous or overlapping (50% overlap may provide better accuracy [37]).
- Reconstruction Algorithm Type: Both filtered back projection and iterative reconstruction are acceptable [16-18, 28, 38, 39].

4.8.2 Specification

Table 10: Image Data Reconstruction - Actors and Requirements

Parameter	Actor	Specification	DICOM Tag
Reconstruction Protocol	Radiographer	Shall select a protocol previously prepared and validated for this purpose (See section 4.4.2).	
Reconstruction Field of View	Radiographer	Shall ensure FOV spans full extent of thoracic and abdominal cavity, consistent with baseline.	Reconstruction Field of View (0018,9317)
Reconstructed Image Thickness	Radiographer	Shall apply the reconstruction interval defined in the validated protocol (see Section 4.4.2) and ensure it is consistent with baseline (no gaps, overlap if specified).	Slice Thickness (0018,0050)
Reconstruction Interval	Radiographer	Shall apply the reconstruction interval defined in the validated protocol (see Section 4.4.2) and ensure it is consistent with baseline (no gaps, overlap if specified).	Spacing Between Slices (0018,0088)
Reconstruction Kernel	Radiographer	Shall select the reconstruction kernel defined in the validated protocol (see Section 4.4.2) and ensure the same kernel is used at all time points.	Convolution Kernel (0018,1210), Convolution Kernel Group (0018,9316)

4.9. Image Quality Assurance

This activity involves evaluating the reconstructed images prior to image analysis, including image criteria necessary to reliably meet the Profile Claim.

4.9.1 Discussion

- Factors affecting image quality and nodule volume measurements include:
 - Motion artifacts
 - Dense object artifacts
 - Thoracic disease processes

- Nodule contact with anatomic structures
- The Profile Claims do not apply to nodules affected by image quality deficiencies that impair overall nodule measurability.

4.9.2 Specification

Table 11: Image Quality Assurance - Actors and Requirements

Parameter	Actor	Requirement
Motion Artifacts	Radiographer, Image Analyst	Shall confirm images are free from motion artifacts.
Dense Object Artifacts	Radiographer, Image Analyst	Shall confirm images are free from artifacts due to dense objects or anatomic positioning.
Thoracic Disease	Image Analyst	Shall confirm images are free from disease processes affecting nodule measurability.
Nodule Margin Conspicuity	Image Analyst	Shall confirm nodules are sufficiently distinct from and not significantly attached to other structures of similar attenuation (attached surface area $\leq 1/3$ of total nodule surface area).
Nodule Size	Image Analyst	Shall confirm nodule longest in-plane bi-dimensional diameter is between 6 mm and 10 mm.
Overall Nodule Measurability	Image Analyst	Shall disqualify any nodules and images with features that might reasonably be expected to degrade measurement reliability.

4.10. Image Analysis

This activity involves measuring the volume change for subjects over one or more timepoints, including criteria and procedures necessary to reliably meet the Profile Claim.

4.10.1 Discussion

- Image analysis should be performed using scientifically validated tools.
- The same software program (manufacturer, model, and version) must be used for all time points of a nodule being evaluated for change.
- Segmentation Analysis should be conducted to inspect concordance with visually-assessed nodule margins.
- Reading Paradigm involves direct side-by-side comparison of current and previous image data.
- Nodule characteristics affecting measurement quality: isolation, smooth borders, and separation from adjacent structures [40-45].

4.10.2 Specification

Table 12: Image Analysis - Actors and Requirements

Parameter	Actor	Requirement
Image Analysis Tool	Image Analyst	Shall use the same tool (manufacturer, model, version) for measurements at all time points. Shall verify tool achieves specified performance metrics

		(see Section 5.1 Technical Evaluation Methods).
Segmentation Analysis	Image Analyst	Shall disqualify nodules with inadequate or non-comparable segmentations at both time points.
Image Display Settings	Image Analyst	Shall set display settings (window and level) to the same lung-appropriate settings for all time points.
Claim Calculations	Image Analyst	Shall use linear interpolation for calculating intermediate values between those provided in the CV table (Table 1).

5. Conformance

To conform to this Profile, participating staff and equipment ("Actors") shall support each activity assigned to them in Table 2, meeting the requirements listed in the specifications table of each activity subsection in Section 4.

Overview

- Many critical performance-oriented requirements require assessment procedures outlined in Section 4.
- This section covers:
 - Technical Evaluation Methods (Section 5.1)

5.1. Technical Evaluation Methods

Two types of equipment evaluations:

- CT scanner and acquisition protocol (Section 5.1.1)
- Analysis software (Section 5.1.2)

Note: Alternative, technically equivalent approaches may be submitted to the SLN Biomarker Committee for consideration as acceptable conformance methods.

5.1.1 CT Image Quality Characteristics

Six metrics assess image quality:

1. Resolution: Estimated response to a point source (PSF - point spread function), characterized as a Gaussian with standard deviation (sigma) in mm [46].
2. Resolution Aspect Ratio: Ratio of PSF sigma along Z-axis to X-axis.
3. HU Bias: HU difference between mean and expected value for uniform density material.
4. Voxel Noise: Standard deviation of pixel HU values in uniform density material.
5. Edge Enhancement: Maximum percent increase in HU contrast above expected along outer edge of ideal cylinder.
6. Spatial Warping: Mean squared error of outer cylindrical surface compared to ideal reference.

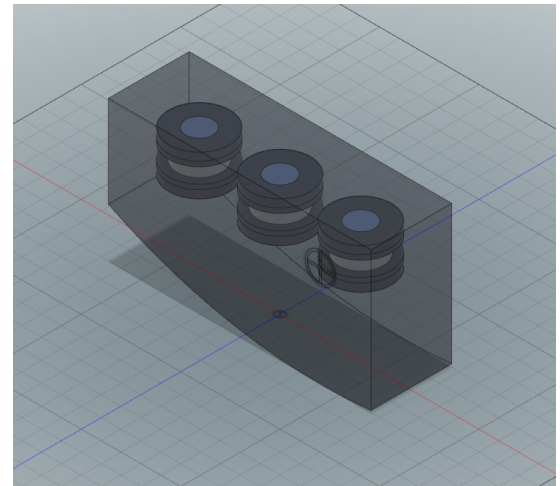


Figure 1: An illustration with translucency showing an SLN Profile CT Lung Nodule Phantom.

Assessment process:

- Scan the SLN Profile accepted Quantitative CT reference object (example in Fig. 2)
- Calculate metrics at two locations closest to iso-center and at 160.0 mm
- Use linear interpolation for 160.0 mm measurements
- Follow specific calculation methods for each metric

Note: Alternative protocols may be needed for small Field of View (FOV) scans.

Additional notes: A Modulation Transfer Function at a 50% cutoff frequency (MTF 50) value can be translated to an **In-plane Point Spread Function** sigma using the following equation [46]:

$$\sigma_{xy} = \frac{\sqrt{-2 \ln m_0}}{2\pi\mu_0}$$

where m_0 is the MTF value and μ_0 is the frequency. Thus, a conversion from gaussian PSF to MTF is:

$$m_0 = e^{-\frac{(2\pi\mu_0\sigma_{xy})^2}{2}}$$

More specifically, the conversion from PSF to MTF50 is:

$$m_0 = e^{-\frac{(\pi\sigma_{xy})^2}{2}}$$

5.1.2 Nodule Analysis Software Characteristics

Two metrics assess measurement quality:

1. Measurement Bias: Deviation of mean value from true value for volumetric measurements
2. Coefficient of Variation (CV): Ratio of standard deviation to mean for repeated measurements

Assessment methods:

- Measure volumes of geometric objects with known volumes
- Measure volumes of short-time interval repeat scans of nodules with varying characteristics

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Appendices

Appendix A: Discussion on Clinical Context

1. Low-dose CT benefits:
 - Effective for detecting and monitoring pulmonary nodules
 - Can increase survival [1] and reduce mortality [2] in high-risk individuals
2. Nodule measurement:
 - Automated quantification of whole nodule volume, addressing limitations of manual measurements [3-9]
 - Accuracy explored in phantoms [10-18] and in vivo precision studies [19-25]
3. Challenges in lung cancer CT screening:
 - Balancing accurate nodule detection and characterization with radiation exposure risks
 - Optimizing protocols for long-term screening (potentially over two decades)
4. Profile aims:
 - Establish confidence levels for measuring nodule volume and changes
 - Quantifies nodule volume and volume doubling time to support standardized nodule management per European Society of Thoracic Imaging recommendations [62]
 - Provide specifications for users and equipment developers
 - Target various stakeholders involved in lung cancer screening
5. Intended audience:
 - Healthcare professionals (radiologists, technologists, physicists)

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- Equipment manufacturers and software developers
 - Biopharmaceutical companies and clinical trialists
 - Policy makers and administrators

6. Relevance:

- Primarily for asymptomatic persons in CT screening programs

May also apply to patients with known or incidentally-detected solid pulmonary nodules (6-10 mm diameter range)

Appendix B: Clinical Interpretation Examples

Claim 1: Nodule Volume

The true size of a nodule is defined by the measured volume and the 95% confidence intervals. These intervals represent the range within which the true volume likely falls.

Example 1:

- Measured volume: 150 mm³ (6.6 mm diameter)
- 95% confidence interval: 65 mm³ to 235 mm³ (5.0 mm to 7.7 mm diameter)

Example 2:

- Measured volume: 500 mm³ (9.8 mm diameter)
- 95% confidence interval: 343 mm³ to 657 mm³ (8.7 mm to 10.8 mm diameter)

Example 3:

- Measured volume: 800 mm³ (11.5 mm diameter)
- 95% confidence interval: 612 mm³ to 988 mm³ (10.5 mm to 12.4 mm diameter)

Claim 2: Nodule Volume Change

This claim helps determine if a change in nodule size is real or due to measurement variability.

Example 1:

- Baseline: 524 mm³ (10.0 mm diameter)
- Follow-up: 917 mm³ (12.0 mm diameter)
- Measured change: +75%
- Interpretation: Since 75% > 39%, we are 95% confident this is a real change.
- 95% confidence interval for true change: 149 mm³ to 637 mm³ increase

Example 2:

- Baseline: 180 mm³ (7.0 mm diameter)
- Follow-up: 270 mm³ (8.0 mm diameter)
- Measured change: +50%
- Interpretation: Since 50% < 80%, we cannot be confident this is a real change.

Note: These claims have been informed by clinical trial data, theoretical analysis, simulations, review of the literature, and expert consensus. They assume compliance with the Profile specifications and may be subject to refinement based on clinical implementation data. The claims have not yet been fully substantiated by studies that strictly conform to the specifications given here. It is expected that during implementation in the clinical setting, data on the actual performance will be collected and any appropriate changes made to the claims or the details of the Profile.

Appendix C: Acknowledgements and Attributions

This document is proffered by the Small Lung Nodule (SLN) Biomarker Committee. The group is composed of scientists representing academia, the imaging device manufacturers, image analysis tool software developers, image analysis laboratories, biopharmaceutical industry, government research organizations, professional societies, and regulatory agencies, among others. All work is classified as pre-competitive.

A description of the former QIBA SLN Biomarker Committee and its work can be found at the following web link: [QIBA Small Lung Nodule Biomarker Committee Wiki page](#). Since the cessation of QIBA, the activities of the SLN Biomarker Committee moved to sponsorship of the American Lung Association (ALA). This is the largest lung disease advocacy organization in the United States with long standing and extensive support of lung imaging research both alone and in collaboration with the National Heart, Lung and Blood Institute of the National Institutes of Health. The SLN Biomarker Committee will continue its work on optimizing quantitative imaging processes for chest CT screening with the recently formed Quantitative Medical Imaging Coalition (QMIC), the European consortium, Strengthening the Screening of Lung Cancer in Europe (SOLACE) project and other relevant parties to inclusively make progress in the critical area.

Appendix D: CT Image Quality Conformance

See the separate Appendix D document

Appendix E: Work In Progress (WIP) Information

See the separate Appendix E document