

QIBA Profile:

Lung Nodule Volume Assessment and Monitoring in Low Dose CT Screening

Stage: Publicly Reviewed (draft)

When referencing this document, please use the following format:

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# 1. Executive Summary

The goal of a QIBA Profile is to help achieve a useful level of performance for a given biomarker.

The **Claim** (Section 2) describes the biomarker performance.  
The **Profile Activities** (Section 3) contribute to generating the biomarker. Requirements are placed on the   
**Actors** that participate in those activities as necessary to achieve the Claim.   
**Assessment Procedures** (Section 4) defines the technical methods to be used for evaluating compliance with profile requirements. This includes the steps needed for clinical sites and equipment vendors to be compliant with the profile.

This QIBA Profile (Lung Nodule Volume Assessment and Monitoring in Low Dose CT Screening) addresses the accuracy and precision of quantitative CT volumetry as applied to solid lung nodules of 6-12 mm diameter. It places requirements on Acquisition Devices, Technologists, Radiologists and Image Analysis Tools involved in activities including Periodic Equipment Quality Assurance, Subject Selection, Subject Handling, Image Data Acquisition, Image Data Reconstruction, Image Quality Assurance, and Image Analysis.

The requirements are focused on achieving sufficient accuracy and avoiding unnecessary variability of the lung nodule volume measurement.

Two sets of claims are provided within this profile. The first claim establishes 95% confidence intervals for volumetric measurement of solid lung nodules that fall within four different diameter and volume size ranges. The second claim provides guidance on the amount of volumetric change percentage needed for a nodule to start to exhibit true change with 95% confidence. In addition, the second claim also provides guidance on the 95% confidence interval for a volumetric size change measurement, again based on the size of the nodule at two time points.

This document is intended to help clinicians basing decisions on this biomarker, imaging staff generating this biomarker, vendor staff developing related products, purchasers of such products and investigators designing trials with imaging endpoints.

Note that this Profile document only states requirements to achieve the claim, not “requirements on standard of care.” Further, meeting the goals of this Profile is secondary to properly caring for the patient.

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

# 2. Clinical Context and Claims

**Clinical Context**

The clinical context of this profile is the quantification of volumes and volume changes over time of solid lung nodules with a longest diameter between 6 mm and 12 mm. Nodules with diameter ≥ 12 mm (volume ≥ 905 mm3) are the subject of the document “QIBA Profile: CT Tumor Volume Change (CTV-1)”.

**Compliance with this Profile by all relevant staff and equipment supports the following claims**

**Claim 1: Nodule Volume**

**For a measured nodule volume of Y, and a CV as specified in table 1, the 95% confidence interval for the true nodule volume is Y ± (1.96 × Y × CV).**

**Claim 2: Nodule Volume Change**

1. **A measured nodule volume percentage change of X indicates that a true change in nodule volume has occurred if X > (2.77 x CV1 x 100), with 95% confidence.**
2. **If Y1 and Y2 are the volume measurements at the two time points, and CV1 and CV2 are the corresponding values from Table 1, then the 95% confidence interval for the nodule volume change Z = (Y2-Y1) ± 1.96 × √([Y1 × CV1]2 + [Y2 × CV2]2).**

**These Claims hold when:**

* **the nodule is completely solid**
* **the nodule longest dimension in the transverse (axial) plane is between 6 mm (volume 113 mm3) and 12 mm (volume 905 mm3) at the first time point**
* **the nodule’s shortest diameter in any dimension is at least 60% of the nodule’s longest diameter in any dimension (i.e., the nodule shape does not deviate excessively from spherical)**
* **the nodule is measurable at both time points (i.e., margins are distinct from surrounding structures of similar attenuation and geometrically simple enough to be segmented using automated software without manual editing)**

**Table 1. Coefficients of Variation (CV)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Nodule**  **Diameter (mm)** | **Nodule**  **Volume (mm3)** | **Coefficient of Variation (CV)** | **True Volume**  **95% CI Limits (**%**)** |
| 6 mm | 113 | 0.29 | ± 57% |
| 7 mm | 154 | 0.23 | ± 45% |
| 8 mm | 268 | 0.19 | ± 37% |
| 9 mm | 382 | 0.16 | ± 31% |
| 10 mm | 524 | 0.14 | ± 27% |
| 11 mm | 697 | 0.12 | ± 24% |
| 12 mm | 905 | 0.11 | ± 22% |

Discussion

Low dose CT provides an effective means of detecting and monitoring pulmonary nodules, and can lead to increased survival (1) and reduced mortality (2) in individuals at high risk for lung cancer. Size quantification on serial imaging is helpful in evaluating whether a pulmonary nodule is benign or malignant. Currently, pulmonary nodule measurements most commonly are obtained as the average of two perpendicular dimensions on axial slices. Investigators have suggested that automated quantification of whole nodule volume could solve some of the limitations of manual diameter measurements (3-9), and many studies have explored the accuracy in phantoms (10-18) and the in vivo precision (19-25) of volumetric CT methods. This document proposes standardized methods for performing repeatable volume measurements on CT images of solid pulmonary nodules obtained using a reduced radiation dose in the setting of lung cancer screening and nodule follow-up in the interval between scans (52).

Lung cancer CT screening presents the challenge of developing a protocol that balances the benefit of detecting and accurately characterizing lung nodules against the potential risk of radiation exposure in this asymptomatic population of persons who may undergo annual screening for more than two decades. Our understanding of the extent to which performing scans at the lowest dose possible with the associated increase in noise impacts our ability to accurately measure these small nodules is still evolving. Therefore, any protocol will involve a compromise between these competing needs.

This QIBA Profile makes Claims about the confidence with which lung nodule volume and changes in lung nodule volume can be measured under a set of defined image acquisition, processing, and analysis conditions, and provides specifications that may be adopted by users and equipment developers to meet targeted levels of clinical performance in identified settings. The intended audiences of this document include healthcare professionals and all other stakeholders invested in lung cancer screening, including but not limited to:

* Radiologists, technologists, and physicists designing protocols for CT screening
* Radiologists, technologists, physicists, and administrators at healthcare institutions considering specifications for procuring new CT equipment
* Technical staff of software and device manufacturers who create products for this purpose
* Biopharmaceutical companies
* Clinicians engaged in screening process
* Clinical trialists
* Radiologists and other health care providers making quantitative measurements on CT images
* Oncologists, regulators, professional societies, and others making decisions based on quantitative image measurements
* Radiologists, health care providers, administrators and government officials developing and implementing policies for lung cancer screening

Note that specifications stated as “requirements” in this document are only requirements to achieve the Claim, not “requirements on standard of care.” Specifically, meeting the goals of this Profile is secondary to properly caring for the patient.

This Profile is relevant to asymptomatic persons participating in a CT screening and surveillance program for lung cancer. In theory, the activities covered in this Profile also pertain to patients with known or incidentally-detected solid pulmonary nodules in the 6-12 mm diameter range, though surveillance in this or other settings is not specifically addressed by this Profile.

**Clinical Interpretation For Claim 1 (nodule volume)**

The true size of a nodule is defined by the measured volume and the 95% confidence intervals. The confidence intervals can be thought of as “error bars” or “uncertainty” or “noise” around the measurement, and the true volume of the nodule is somewhere within the confidence intervals. Application of these Claims to clinical practice is illustrated by the following examples:

Example 1: A nodule is measured as having a volume of 150 mm3 (6.6 mm diameter). There is a 95% probability that the true volume of the nodule is between 65 mm3 [150 – (150 x 1.96 x 0.29)] (5.0 mm diameter) and 235 mm3 [150 + (150 x 1.96 x 0.29)] (7.7 mm diameter).

Example 2: A nodule is measured as having a volume of 500 mm3 (9.8 mm diameter). There is a 95% probability that the true volume of the nodule is between 343 mm3 [500 - (500 x 1.96 x 0.16)] (8.7 mm diameter) and 657 mm3 [500 + (500 x 1.96 x 0.16)] (10.8 mm diameter).

Example 3: A nodule is measured as having a volume of 800 mm3 (11.5 mm diameter). There is a 95% probability that the true volume of the nodule is between 612 mm3 [800 - (800 x 1.96 x 0.12)] (10.5 mm diameter) and 988 mm3 [800 + (800 x 1.96 x 0.12)] (12.4 mm diameter).

If the activities specified in this Profile are followed, the measured volume of nodules in each of the given size ranges can be considered accurate to within the given 95% confidence limits. The different coefficients of variation of the different nodule size ranges in Claim 1 reflect the increasing variability introduced as the resolution limits of the measuring device are approached, and the likely impact of variations permitted by the Specifications of this Profile.

The guidance provided here represents an estimate of minimum measurement error when conforming to the Profile over a wide range of scanner models. However, these estimates can be reduced substantially when using more advanced scanning equipment with improved performance characteristics.

These Claims have been informed by clinical trial data, theoretical analysis, simulations, review of the literature, and expert consensus. They have not yet been fully substantiated by studies that strictly conform to the specifications given here. The expectation is that during implementation in the clinical setting, data on the actual performance will be collected and any appropriate changes made to the Claim or the details of the Profile. At that point, this caveat may be removed or re-stated.

**Clinical Interpretation For Claim 2 (nodule volume change)**

The precision value in the Claim statement is the change necessary to be 95% certain that there has really been a change. If a tumor changes size beyond these limits, you can be 95% confident there has been a true change in the size of the tumor, 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.

Application of these Claims to clinical practice is illustrated by the following examples:

**Example 1:** A nodule measuring 524 mm3 at baseline (10.0 mm diameter) measures 917 mm3 (12.0 mm diameter) at follow-up, for a measured volume change of +393 mm3 (or a 75% increase in volume) [i.e. (917-524)/524 x 100 = 75%]. For this 10 mm nodule at baseline, we apply the CV from the fifth row of Table 1: since 75% > 39% [i.e. 75% > 2.77 x 0.14 x 100], we are 95% confident that the measured change represents a real change in nodule volume. To quantify the magnitude of the change, we construct the 95% confidence for the true change. The 95% confidence interval for the true change is (917-524) + 1.96 x **√** ([0.14 x 524]2 + [0.11 x 917]2), which equals 393 ± 244. The 95% CI for the change in volume is thus [149 mm3 – 637 mm3]. This means that the nodule at time point 2 is between 149 and 637 mm3 larger than at baseline.

**Example 2:** A nodule measuring 180 mm3 at baseline (7.0 mm diameter) measures 270 mm3 (8.0 mm diameter) at follow-up, for a measured volume change of 90 mm3, or +50% [i.e. (270-180)/180 x 100 = 50%]. Since this was a 7 mm nodule at baseline, we apply the CV from the first row of the table: since 50% < 80% [i.e. 50% < 2.77 x 0.23 x 100]; we cannot be confident that this measured change represents a real change in the tumor volume.

If the activities specified in this Profile are followed, the measured change in volume of nodules in each of the given size ranges can be considered accurate to within the given 95% confidence limits. The different coefficients of variation of the different nodule size ranges in Claim 1 reflect the increasing variability introduced as the resolution limits of the measuring device are approached, and the likely impact of variations permitted by the Specifications of this Profile.

These Claims represent the repeatability coefficient (RC = 1.96 × for nodules in each size range. The Claims have been informed by clinical trial data, theoretical analysis, simulations, review of the literature, and expert consensus. They have not yet been fully substantiated by studies that strictly conform to the specifications given here. The expectation is that during implementation in the clinical setting, data on the actual performance will be collected and any appropriate changes made to the Claim or the details of the Profile. At that point, this caveat may be removed or re-stated.

Claim 2 assumes the same compliant actors (acquisition device, radiologist, image analysis tool, etc.) at the two time points. If one or more of the actors are different, it is expected that the measurement performance will be reduced.

A web based calculator for computing the equations in the Claims is available at <http://www.accumetra.com/NoduleCalculator.html>.

# 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 demonstrating conformance to all Requirements in the referenced Section.

Table 3-1: Actors and Required Activities

|  |  |  |
| --- | --- | --- |
| **Actor** | **Activity** | **Section** |
| Acquisition Device | Product Validation | 3.1 |
| Image Analysis Tool | Product Validation | 3.1 |
| Technologist | Staff Qualification | 3.2 |
| Subject Handling | 3.6 |
| Image Data Acquisition | 3.7 |
| Image Data Reconstruction | 3.8 |
| Image Quality Assurance | 3.9 |
| Radiologist | Staff Qualification | 3.2 |
| Protocol Design | 3.4 |
| Subject Selection | 3.5 |
| Subject Handling | 3.6 |
| Physicist | Equipment Quality Assurance | 3.3 |
| Protocol Design | 3.4 |
| Referring Clinician | Subject Selection | 3.5 |
| Image Analyst | Staff Qualification | 3.2 |
| Image Quality Assurance | 3.9 |
| Image Analysis | 3.10 |

The requirements in this Profile do not codify a Standard of Care; they only provide guidance intended to achieve the stated Claims. Failing to comply with a “shall” in this Profile is a protocol deviation. Although deviations invalidate the Profile Claims, such deviations may be reasonable and unavoidable and the radiologist or supervising physician is expected to do so when required by the best interest of the patient or research subject. How study sponsors and others decide to handle deviations for their own purposes is entirely up to them.

For the Acquisition Device and Image Analysis Tool actors, while it will typically be the manufacturer who claims the actor is conformant, it is certainly possible for a site to run the necessary tests/checks to confirm compliance and make a corresponding claim. This might happen if a manufacturer is no longer promoting an older model device but a site needs a conformance statement to participate in a clinical trial.

The Physicist actor is the preferred person at the site responsible for managing the equipment performance related specifications. At some sites this will be a staff physicist, and at other sites it may be a person who manages a contractor or a service provided by a vendor.

The sequencing of the Activities specified in this Profile is shown in Figure 1:

Acquire

Subtract

volumes

Patient

Prep

Recon

and Post

-

process

Directly process

images to

analyze change



*Obtain images at 2 time points*

images

*Assess change per target lesion*

-

OR

-

*Assess change in target lesion volume*

Volume

change per

target

lesion

%

∆

v

t

Lesion

volume at

time

point

(

v

t

)

Calculate

volume

Calculate

volume

volume

changes

volumes

Figure 1: CT Tumor Volumetry - Activity Sequence

The method for measuring change in tumor volume may be described as a multistage process. Subjects are prepared for scanning, raw image data is acquired, images are reconstructed and possibly post-processed. Such images are obtained at one or more time points. Image analysis assesses the degree of change between two time points for each evaluable target nodule by calculating absolute volume at each time point and subtracting. When expressed as a percentage, volume change is the difference in volume between the two time points divided by the volume at time point 1. Although this introduces some asymmetry (volume measurements of 50cm3 and 100cm3 represent either a 100% increase or a 50% decrease depending on which was measured first), it is more familiar to clinicians than using the average of the two timepoints as the denominator.

The change may be interpreted according to a variety of different response criteria. These response criteria are beyond the scope of this document. Detection and classification of nodules are also beyond the scope of this document.

The Profile does not intend to discourage innovation, although it strives to ensure that methods permitted by the profile requirements will result in performance that meets the Profile Claim. The above pipeline provides a reference model. Algorithms which achieve the same result as the reference model but use different methods may be permitted, for example by directly measuring the change between two image sets rather than measuring the absolute volumes separately. Developers of such algorithms are encouraged to work with the appropriate QIBA committee to conduct any groundwork and assessment procedure revisions needed to demonstrate the requisite performance.

The requirements included herein are intended to establish a baseline level of capabilities. Providing higher performance or advanced capabilities is both allowed and encouraged. The Profile does not intend to limit how equipment suppliers meet these requirements.

## 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 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. |
| 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. |
| Image Analysts | Site | Shall confirm all participating image analysts conform to this Profile. |

## 3.1. Product Validation

This activity involves evaluating the product Actors (Acquisition Device 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.

### 3.1.1 Discussion

Performance measurements of specific protocols are not addressed here. Those are included in section 3.4.2.

The **Number of Detector Rows** can influence the scan duration, z-axis resolution, and radiation dose. A primary consideration leading to the requirement that CT scanners have a minimum of 16 detector rows is the desire for the Scan Duration to be no greater than the time for imaging the entire length of the lungs in a single breath-hold, to minimize motion artifacts, at a pitch that provides adequate z-axis resolution. 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 (52). Published investigations have demonstrated the accuracy of CT nodule volumetry meeting the Claims of this Profile using 16-detector scanners.

**Acquisition Protocol Variation** is evaluated using a **Design of Experiments (DOE)** approach. A 24 full factorial DOE for the protocol is defined and performed with variation on mAs, field of view, pitch, and iterative recon setting (if appropriate, table height if not). For example, a protocol with the following settings:

mAs 40

kVp 100

Rotation Time (s) 0.50

Filed of View (cm) 35.0

Pitch 1.50

Slice Thickness (mm) 1.00

Slice Spacing (mm) 0.75

Reconstruction Kernel I40-4

Table Height Centered

will have a DOE with the following 19 experiments consisting of 3 repeat CT scans (A,B,C) using the protocol and 16 CT scans that systematically vary mAs, FOV, Pitch, and an iterative reconstruction setting:

Experiment # mAs FOV Pitch Iterative Recon Setting Notes

A 40 30.0 1.50 I40-4 Repetition 1

01 30 30.0 1.25 I40-3 [ -, -. -, - ]

02 30 30.0 1.25 I40-5 [ -. -, -, + ]

03 30 30.0 1.75 I40-3 [ -. -, +, - ]

04 30 30.0 1.75 I40-5 [ -, -, +, + ]

05 30 40.0 1.25 I40-3 [ -, +, -, - ]

06 30 40.0 1.25 I40-5 [ -, +, -, + ]

07 30 40.0 1.75 I40-3 [ -, +, +, - ]

08 30 40.0 1.75 I40-5 [ -, +, +, + ]

B 40 35.0 1.50 I40-4 Repetition 2

09 50 30.0 1.25 I40-3 [ +, -. -, - ]

10 50 30.0 1.25 I40-5 [ +. -, -, + ]

11 50 30.0 1.75 I40-3 [ +. -, +, - ]

12 50 30.0 1.75 I40-5 [ +, -, +, + ]

13 50 40.0 1.25 I40-3 [ +, +, -, - ]

14 50 40.0 1.25 I40-5 [ +, +, -, + ]

15 50 40.0 1.75 I40-3 [ +, +, +, - ]

16 50 40.0 1.75 I40-5 [ +, +, +, + ]

C 40 35.0 1.50 I40-4 Repetition 3

The variation tested in the DOE defines an operating envelope that the acquisition device has been shown to support. Vendors may wish to repeat DOE experiments with a wider operating envelope and additional DOE variables.

### 3.1.2 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 3.4.2 "Protocol Design Specification". |
| Acquisition Device | Shall prepare a protocol conformant with section 3.4.2 "Protocol Design Specification" and validate that protocol as described in section 3.4.2. |
| Acquisition Protocol Variation | Acquisition Device | Shall also validate the protocol under varying conditions from each preferred protocol setting using a Design of Experiments (DOE) approach. |
| Acquisition Consistency | Technologist | Shall use the same compliant scanner and acquisition protocol for acquisition of all time points. |
| Reading Consistency | Image Analyst | Shall analyze all time points and shall use the same conformant image analysis tool at all analysis time points. |
| Number of Detector Rows | Acquisition Device | Shall have 16 or more detector rows. |
| Image Header | Acquisition Device | Shall record in the DICOM image header the actual values for the tags listed in the DICOM Tag column in section 3.4.2 "Protocol Design Specification"*.* |
| 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 volume at the earlier time point. |
| Scientific Validation | Image Analysis Tool | Shall provide documentation of scientific validation, including the properties of measurement linearity, coefficient of variation, and zero bias. |

## 3.2. 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.

### 3.2.1 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.

In clinical practice, it is expected that the **Radiologist** interpreting the examination often will be the **Image Analyst**. In some clinical practice situations, and in the clinical research setting, the image analyst may be a non-radiologist professional.

**Analyst Training** should be at a level appropriate for the setting and the purpose of the measurements, and may include instruction in topics such as the 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; and image artifacts.

### 3.2.2 Specification

| **Parameter** | **Actor** | **Specification** |
| --- | --- | --- |
| ACR Accreditation | Radiologist | Shall fulfill the qualifications required by the American College of Radiology CT Accreditation Program. These include certification by the American Board of Radiology or analogous non-U.S. certifying organization; appropriate licensing; documented oversight, interpretation, and reporting of the required ABR minimum number of CT examinations; and compliance with ABR and licensing board continuing education requirements.  See:http://www.acr.org/~/media/ACR/Documents/Accreditation/CT/Requirements |
| Technologist | Shall fulfill the qualifications required by the American College of Radiology CT Accreditation Program. These include certification by the American Registry of Radiologic Technologists or analogous non-U.S. certifying organization, appropriate licensing, documented training and experience in performing CT, and compliance with certifying and licensing organization continuing education requirements.  See:http://www.acr.org/~/media/ACR/Documents/Accreditation/CT/Requirements |
| Analyst Training | 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. |

## 3.3. Equipment Quality Assurance

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

### 3.3.1 Discussion

This activity is focused on ensuring that the acquisition device is aligned/calibrated/functioning normally. Performance measurements of specific protocols are not addressed here. Those are included in section 3.4.

Conformance with this Profile requires adherence of CT equipment to U.S. federal regulations (21CFR1020.33) or analogous regulations outside of the U.S., CT equipment performance evaluation procedures of the American College of Radiology CT Accreditation Program (<http://www.acr.org/~/media/ACR/Documents/Accreditation/CT/Requirements>), and quality control procedures of the scanner manufacturer. These assessment procedures include a technical performance evaluation of the CT scanner by a qualified medical physicist at least annually. Parameters evaluated include those critical for quantitative volumetric assessment of small nodules, such as spatial resolution, section thickness, and table travel accuracy, as well as dosimetry. Daily quality control must include monitoring of water CT number and standard deviation and artifacts. In addition, preventive maintenance at appropriate regular intervals must be conducted and documented by a qualified service engineer.

These specifications reflect the clinical and clinical trial settings which produced the data used to support the Claims of this Profile. Data were obtained from a broad range of CT scanner models having a range of performance capabilities that is reflected in the size of the confidence bounds of the Claims. Ongoing research is identifying the key technical parameters determining performance in the lung cancer screening setting, and establishing metrics that may allow Claims with narrower confidence bounds than are found in this Profile to be met for certain CT scanners through more specific technical specifications and associated assessment procedures. Such metrics and assessment procedures more specific to CT volumetry in lung cancer screening will be addressed in subsequent versions of this Profile.

### 3.3.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Quality Control | Physicist | Shall perform quality control procedures consistent with those generally accepted for routine clinical imaging. |
| Quality Control | Physicist | Shall adhere to installation and periodic quality control procedures specified by the scanner manufacturer and the American College of Radiology CT Accreditation Program.  See http://www.acr.org/~/media/ACR/Documents/Accreditation/CT/Requirements |
| Maintenance | Physicist | Shall ensure that preventive maintenance is conducted and documented by a qualified service engineer as recommended by the scanner manufacturer. |

## 3.4. 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.

### 3.4.1 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 (such as increasing acquisition mAs and reconstruction DFOV for larger patients), while reaching the performance targets. Again, the technique parameter sets provided by vendors in their Conformance Statements may be helpful for those looking for more guidance.

**Automatic Exposure Control** aims to achieve consistent noise levels throughout the lungs by varying the tube current during scan acquisition. Use of automatic exposure control is expected to have little effect on Profile Claims and is considered optional, though as with other acquisition parameters its use should be consistent with baseline. This scanner feature may be a useful tool for reducing unnecessary radiation exposure in certain patients, but it also can increase radiation exposure depending on the target noise level, patient size and anatomy, and the method employed by the vendor. These factors should be kept in mind when deciding whether to use automatic exposure control in an individual patient.

**Rotation Time** may vary as needed to achieve other settings. Generally it will be less than or equal to 0.5 seconds.

In CT screening for lung cancer, the choice of scan acquisition parameters is strongly influenced by the desire to minimize radiation dose. The radiation dose delivered by volumetric CT scanning is indicated by the volume CT Dose Index (CTDIvol). The CTDIvol should be chosen to provide the lowest radiation dose that maintains acceptable image quality for detecting pulmonary nodules. Variability in CT nodule volumetry using low dose techniques is comparable to that of standard dose techniques (14, 16-18, 29). As a general guideline, CTDIvol ≤3 mGy should provide sufficient image quality for a person of standard size, defined by the International Commission on Radiation Protection (ICRP) as 5’7”/170 cm and 154 lbs/70 kg. The CTDIvol should be reduced for smaller individuals and may need to be increased for larger individuals, but should be kept constant for the same person at all time points. CTDIvol is determined by the interaction of multiple parameters, including the Tube Potential (kV), Tube Current (mA), tube Rotation Time, and Pitch. Settings for kV, mA, rotation time, and pitch may be varied as needed to achieve the desired CTDIvol. Pitch is chosen so as to allow completion of the scan in a single breath hold with adequate spatial resolution along the subject z-axis.

**Nominal Tomographic Section Thickness** (T), the term preferred by the International Electrotechnical Commission (IEC), is sometimes also called the Single Collimation Width. Choices depend on the detector geometry inherent in the particular scanner model. The Nominal Tomographic Section Thickness affects the spatial resolution along the subject z-axis and the available options for reconstructed section thickness. Thinner sections that allow reconstruction of smaller voxels are preferable, to reduce partial volume effects and provide higher accuracy due to greater spatial resolution.

**Reconstruction Kernel** is recommended to be a medium smooth to medium sharp kernel that provides the highest resolution available without edge enhancement.

X-ray CT uses ionizing radiation. Exposure to radiation can pose risks; however as the radiation dose is reduced, image quality can be degraded. It is expected that health care professionals will balance the need for good image quality with the risks of radiation exposure on a case-by-case basis. It is not within the scope of this document to describe how these trade-offs should be resolved.

### 3.4.2 Specification

**Note:** The Radiologist is responsible for the protocol parameter requirements, although they may choose to use a protocol provided by the vendor of the acquisition device. The Radiologist is also responsible for ensuring that protocol validation has taken place (e.g. when it is created or modified), although the Physicist actor or the Technologist actor may also perform the validation. 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.

| **Parameter** | **Actor** | **Specification** | **DICOM Tag** |
| --- | --- | --- | --- |
| Acquisition Protocol | Radiologist | Shall prepare a protocol to meet the specifications in this table.  Shall ensure technologists have been trained on the requirements of this profile. |  |
| IEC Pitch | Radiologist | Shall set IEC Pitch to less than or equal to 2.0 for single source scanners, or the equivalent for dual source scanners. | Spiral Pitch Factor  (0018,9311) |
| Nominal Tomographic Section Thickness (T) | Radiologist | Shall set the nominal tomographic section thickness to achieve reconstructed slice thickness less than or equal to 1.25mm. | Single Collimation Width  (0018,9306) |
| Reconstruction Protocol | Radiologist | Shall prepare a protocol to meet the specifications in this table.  Shall ensure technologists have been trained on the requirements of this profile. |  |
| Reconstructed Image Thickness | Radiologist | Shall set reconstructed image thickness to less than or equal 1.25mm. | Slice Thickness (0018,0050) |
| Reconstructed Image Interval | Radiologist | Shall set reconstructed image interval to less than or equal to the Reconstructed Image Thickness (i.e. no gap, may have overlap). | Spacing Between Slices (0018,0088) |
| Resolution | Radiologist | Shall validate that when using settings for an average-size patient the protocol achieves:   * An in-plane PSF with a standard deviation of less than or equal to 1.5mm3, and * A Z-axis PSF with a standard deviation of less than twice the in-plane PSF.   See section 4.1. Assessment Procedure: Image Quality |  |
| Edge Enhancement | Radiologist | Shall validate that when using settings for an average-size patient the protocol achieves edge enhancement less than or equal to 5%.  See section 4.1 Assessment Procedure: Image Quality |  |
| Voxel Bias | Radiologist | Shall validate that when using settings for an average-size patient the protocol achieves voxel bias of less than 35 HU for each of Air, Acrylic, Delrin, and Teflon.  See section 4.1 Assessment Procedure: Image Quality |  |
| Voxel Noise | Radiologist | Shall validate that when using settings for an average-size patient the protocol achieves  a voxel noise standard deviation of <= 50 HU in each of Air, Acrylic, Delrin, and Teflon.  See section 4.1 Assessment Procedure: Image Quality |  |
| Spatial Warping | Radiologist | Shall validate that when using settings for an average-size patient the protocol achieves in spatial warping of less than Z MSE.  See section 4.1 Assessment Procedure: Image Quality |  |
|  |  |  |  |

## 3.5. 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.

### 3.5.1 Discussion

**Pulmonary Symptoms** may signify acute or subacute abnormalities in the lungs that could interfere with or alter pulmonary nodule volume measurements, or prevent full cooperation with breath-holding instructions for scanning. Therefore, subjects should be asymptomatic, or at baseline if symptomatic, with respect to cardiac and pulmonary symptoms. If scanning is necessary to avoid an excessive delay in follow-up of a known nodule or to evaluate new symptoms, and these clinical status conditions cannot be met then measurements may not be of sufficient quality to fulfill the Profile Claims. Chronic abnormalities such as pulmonary fibrosis also may invalidate Profile Claims if they affect nodule volume measurement accuracy.

Recent diagnostic or therapeutic **Medical Procedures** may result in parenchymal lung abnormalities that increase lung attenuation around a nodule and invalidate the Claims of this Profile. Examples include bronchoscopy, thoracic surgery, and radiation therapy.

Oral contrast administered for unrelated gastrointestinal imaging studies or abdominal CT that remains in the esophagus, stomach, or bowel may cause artifacts in certain areas of the lungs that interfere with quantitative nodule assessment. If artifacts due to oral contrast are present in the same transverse planes as a quantifiable lung nodule, the Profile Claims may not be valid.

### 3.5.2 Specification

| **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 |
| 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 |

## 3.6. Subject Handling

This activity involves handling each imaging subject at each time point. It includes subject handling details that are necessary to reliably meet the Profile Claim.

### 3.6.1 Discussion

This Profile will refer primarily to “subjects”, keeping in mind that the requirements and recommendations apply to patients in general, and subjects are often patients too.

Subject handling guidelines are intended to reduce the likelihood that lung nodules will be obscured by surrounding disease or image artifacts, which could alter quantitative measurements, and to promote consistency of image quality on serial scans.

**Intravenous Contrast** is not used for CT lung cancer screening (26). Because of the inherently high contrast between lung nodules and the surrounding parenchyma, contrast is unnecessary for nodule detection and quantification. Its use incurs additional cost, the potential for renal toxicity and adverse reactions, and may affect volume quantification (21, 27, 28). If contrast must be used for a specific clinical indication (e.g. for characterization of the nodule, hilar nodes, or another abnormality) the Profile Claims are invalidated.

After obtaining the localizer (scout) image, the technologist should evaluate the image for **Artifact Sources** such as external metallic objects that may produce artifacts that may alter the attenuation of lung nodules, and work with the subject to remove these devices. Internal metallic objects, such as pacemakers and spinal instrumentation, also may produce artifacts.

Bismuth breast shields (used by some to reduce radiation exposure in the diagnostic CT setting) increase image noise. The impact of this imaging artifact on lung nodule volume quantification is unknown, but is likely to be magnified in the lung cancer screening setting due to the lower radiation dose used for screening. The effects of breast shields on image quality may vary depending on the types of shields and their positioning on the chest. The American Association of Physicists in Medicine currently does not endorse the use of breast shields, recommending the use of other dose reduction methods instead (<https://www.aapm.org/publicgeneral/BismuthShielding.pdf>). Thus, the use of breast shields is not compatible with the Profile Claims and is not recommended for lung cancer screening. However, organ dose modulation techniques that reduce dose in the anterior thorax may be used if implemented on all studies being compared.

Consistent **Subject Positioning** is important, to reduce variation in x-ray beam hardening and scatter and in nodule orientation and position within the gantry. Positioning the chest (excluding the breasts) in the center of the gantry improves the consistency of relative attenuation values in different regions of the lung, and should reduce scan-to-scan variation in the behavior of dose modulation algorithms. The subject should be made comfortable, to reduce the potential for motion artifacts and to facilitate compliance with breath holding instructions.

To achieve these goals, subjects should be positioned supine with arms overhead, in keeping with standard clinical practice. The sternum should be positioned over the midline of the table. The **Table Height and Centering** should be adjusted so that the midaxillary line is at the widest part of the gantry. The use of positioning wedges under the knees and/or head may be needed for patient comfort, or may help to better align the spine and shoulders on the table, and is optional. It is expected that local clinical practice and patient physical capabilities and limitations will influence patient positioning; an approach that promotes scan-to-scan consistency is essential.

Scans should be performed during Breath Holding at maximal inspiration, to reduce motion artifacts and improve segmentation. Efforts should be made to obtain consistent, reproducible, maximal inspiratory lung volume on all scans. The use of live breathing instructions given at a pace easily tolerated by the patient is strongly recommended. However, depending on local practice preference and expertise, the use of prerecorded breathing instructions may provide acceptable results. Compliance with breathing instructions should be monitored by carefully observing the movement of the chest wall and abdomen to insure that the breathing cycle stays in phase with the verbal instructions. The scan should not be initiated until maximal inspiratory volume is reached and all movement has ceased.

To promote patient compliance, performing a practice round of the breathing instructions prior to moving the patient into the scanner also is strongly recommended. This will make the subject familiar with the procedure, make the technologist familiar with the subject’s breathing rate, and allow the technologist to address any subject difficulties in following the instructions.

Sample breathing instructions:

1. “Take in a deep breath” (watch anterior chest rise)
2. “Breathe all the way out” (watch anterior chest fall)
3. “Now take a deep breath in…..in……in…..in all the way as far as you can”
4. When chest and abdomen stop rising, say “Now hold your breath”.
5. Initiate the scan when the chest and abdomen stop moving, allowing for the moment it takes for the diaphragm to relax after the glottis is closed.
6. When scan is completed, say “You can breathe normally”

### 3.6.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Intravenous contrast | Image Analyst | Shall not use images in which intravenous contrast was administered for quantitative nodule volumetry in lung cancer screening or follow-up of screen-detected nodules. |
| Radiologist |
| Artifact sources | Technologist | Shall remove or position potential sources of artifacts (specifically including breast shields, metal-containing clothing, EKG leads and other metal equipment) such that they will not degrade the reconstructed CT volumes. |
| Subject Positioning | Technologist | Shall position the subject consistent with baseline. |
| Table Height & Centering | Technologist | Shall adjust the table height for the mid-axillary plane to pass through the isocenter of the gantry.  Shall be consistent with baseline. |
| Breath holding | Technologist | Shall instruct the subject in proper breath-hold and start image acquisition shortly after full inspiration, taking into account the lag time between full inspiration and diaphragmatic relaxation.  Shall ensure that for each tumor the breath hold state is consistent with baseline |

## 3.7. Image Data Acquisition

This activity involves the acquisition of image data for a subject at either time point. It includes details of data acquisition that are necessary to reliably meet the Profile Claim.

### 3.7.1 Discussion

CT scans for nodule volumetric analysis can be performed on equipment that complies with the Specifications set out in this Profile. However, performing all CT scans for an individual subject must be done on the same platform (manufacturer, model and version) to reduce variation.

Note that the requirement to "select a protocol that has been prepared and validated for this purpose" is not asking the tech to scan phantoms before every patient. Sites are required in section 3.4.2 to have validated the protocols that the tech will be using and conformance with the protocol depends on the tech selecting those protocols.

Many scan parameters can have direct or indirect effects on identifying, segmenting and measuring tumors. To reduce this potential source of variance, all efforts should be made to have as many of the scan parameters as possible consistent with the baseline.

**Consistency with the baseline** implies a need for a method to record and communicate the baseline settings and make that information available at the time and place that subsequent scans are performed. Although it is conceivable that the scanner could retrieve prior/baseline images and extract acquisition parameters to encourage consistency, such interoperability mechanisms are not defined or mandated here beyond requiring that certain fields be populated in the image header. Similarly, managing and forwarding the data files when multiple sites are involved may exceed the practical capabilities of the participating sites. Sites should be prepared to use manual methods instead.

**Image Header** recordings of the key parameter values facilitate meeting and confirming the requirements to be consistent with the baseline scan.

The goal of **parameter consistency** is to achieve consistent performance. Parameter consistency when using the same scanner make/model generally means using the same values. Parameter consistency when the baseline was acquired on a different make/model may require some “interpretation” to achieve consistent performance since the same values may produce different behavior on different models. See Section 3.4 "Protocol Design".

**Anatomic Coverage** For screening purposes a baseline scan should include the entire volume of the lungs (apex through base), minimizing the volume scanned above and below the lungs to avoid unnecessary radiation exposure. For nodule measurement, the scan should include the full nodule and typically 5 to 10 mm of lung region above and below the nodule.

The **localizer (scout) image** should be restricted as closely as possible to the anatomic limits of the thorax, using the minimum kV and mA needed to identify relevant anatomic landmarks. Inspecting the image also provides the opportunity to remove any external objects that may have been missed prior to positioning the subject on the table.

In CT screening for lung cancer, the choice of scan acquisition parameters is strongly influenced by the desire to minimize radiation dose. The radiation dose delivered by volumetric CT scanning is indicated by the volume CT Dose Index (**CTDIvol**). The CTDIvol should be chosen to provide the lowest radiation dose that maintains acceptable image quality for detecting pulmonary nodules. Variability in CT nodule volumetry using low dose techniques is comparable to that of standard dose techniques (14, 16-18, 29). As a general guideline, CTDIvol ≤3 mGy should provide sufficient image quality for a person of standard size, defined by the International Commission on Radiation Protection (ICRP) as 5’7”/170 cm and 154 lbs/70 kg. The CTDIvol should be reduced for smaller individuals and may need to be increased for larger individuals, but should be kept constant for the same person at all time points. CTDIvol is determined by the interaction of multiple parameters, including the **Tube Potential** (kV), **Tube Current** (mA), tube **Rotation Time**, and **Pitch**. Settings for kV, mA, rotation time, and pitch may be varied as needed to achieve the desired CTDIvol. Pitch is chosen so as to allow completion of the scan in a single breath hold with adequate spatial resolution along the subject z-axis. It is recommended that pitch does not exceed 2.0 for CT acquisitions obtained with a single x-ray tube, or the equivalent for acquisitions with dual-source technology.

### 3.7.2 Specification

The Acquisition Device shall be capable of performing scans with all the parameters set as described in the following table. The Technologist shall set the scan acquisition parameters to achieve the requirements in the following table.

| **Parameter** | **Actor** | **Requirement** | **DICOM Tag** |
| --- | --- | --- | --- |
| Acquisition Protocol | Technologist/Radiologist | Shall select a protocol that has been previously prepared and validated for this Profile (See section 3.4.2 "Protocol Design Specification").  Shall report if any parameters are modified beyond those specifications. |  |
| Scan Duration | Technologist | Shall perform the scan in a single breath hold. |  |
| Consistency | Technologist | Shall ensure that follow-up scans use the same CT scanner model and acquisition protocol settings. |  |

## 3.8. Image Data Reconstruction

This activity involves the reconstruction of image data for a subject at either time point. It includes criteria and procedures related to producing images from the acquired data that are necessary to reliably meet the Profile Claim.

### 3.8.1 Discussion

Many reconstruction parameters can have direct or indirect effects on identifying, segmenting, and measuring nodules. To reduce this source of variance, all efforts should be made to have as many of the parameters as possible on follow-up scans consistent with the baseline scan.

**Reconstruction Field of View** interacts with image matrix size (512x512 for most reconstruction algorithms) to determine the reconstructed pixel size. Pixel size directly affects voxel size in the x-y plane. Smaller voxels are preferable to reduce partial volume effects that can blur the edges of nodules and reduce measurement accuracy and precision. Pixel size in each dimension is not the same as spatial resolution in each dimension, which depends on a number of additional factors including the section thickness and reconstruction kernel. Targeted reconstructions with a small field of view minimize partial volume effects, but have limited effect on the accuracy of nodule volumetry compared to a standard field of view that encompasses all of the lungs (11, 12). A reconstructed field of view set to the widest diameter of the lungs, and consistent with baseline, is sufficient to meet the Claims of this Profile.

The **Reconstructed Slice Thickness** should be small relative to the size of the smallest nodules detected and followed by CT screening (11-13, 31).

The **Reconstruction Interval** should be either contiguous or overlapping (i.e. with an interval that is less than the reconstructed slice thickness). Either method will be consistent with the Profile Claims, though overlap of 50% may provide better accuracy and precision compared to contiguous slice reconstruction (32). Reconstructing datasets with overlap will increase the number of images and may slow down throughput, increase reading time, and increase storage requirements, but has NO effect on radiation exposure. A reconstruction interval that results in gaps between slices is unacceptable as it may “truncate” the spatial extent of the nodule, degrade the identification of nodule boundaries, and confound the precision of measurement for total nodule volumes.

The **Reconstruction Algorithm Type** most commonly used for CT has been filtered back projection. More recently introduced methods of iterative reconstruction can provide reduced image noise and/or radiation exposure (33). Studies have indicated that iterative methods are at least comparable to filtered back projection for CT volumetry (16-18, 29, 34). Both algorithm types are acceptable for this Profile.

The **Reconstruction Kernel** influences the texture and the appearance of nodules in the reconstructed images, including the sharpness of the nodule edges. In general, a softer, smoother kernel reduces noise at the expense of spatial resolution, while a sharper, higher-frequency kernel gives the appearance of improved resolution at the expense of increased noise. Kernel types may interact differently with different software segmentation algorithms. Theoretically, the ideal kernel choice for any particular scanner is one that provides the highest resolution without edge enhancement, which generally will be a kernel in the medium-smooth to medium-sharp range of those available on clinical scanners. With increasing kernel smoothness, underestimation of nodule volume becomes a potential concern, while with increasing kernel sharpness, image noise and segmentation errors become potential concerns. Use of a reconstruction kernel on follow-up scans consistent with baseline therefore is particularly important for relying on the Profile Claims.

### 3.8.2 Specification

| **Parameter** | **Actor** | **Specification** | **DICOM Tag** |
| --- | --- | --- | --- |
| Reconstruction Protocol | Technologist | Shall select a protocol that has been previously prepared and validated for this purpose (See section 3.4.2 "Protocol Design Specification").  Shall report if any parameters are modified beyond those specifications. |  |
| Reconstruction Field of View | Technologist | Shall ensure the Field of View spans at least the full extent of the thoracic and abdominal cavity, but not substantially greater than that, and is consistent with baseline. | Reconstruction Field of View (0018,9317) |
| Reconstructed Image Thickness | Technologist | Shall set reconstructed image thickness to less than or equal to 1.25 mm and consistent (i.e. within 0.5mm) with baseline. | Slice Thickness (0018,0050) |
| Reconstruction Interval | Technologist | Shall set to less than or equal to the Reconstructed Image Thickness (i.e. no gap, may have overlap) and consistent with baseline. | Spacing Between Slices (0018,0088) |
| Reconstruction Kernel | Technologist | Shall set the reconstruction kernel and parameters consistent with baseline (i.e. the same kernel and parameters if available, otherwise the kernel most closely matching the kernel response of the baseline). | Convolution Kernel (0018,1210), Convolution Kernel Group (0018,9316) |

## 3.9. Image Quality Assurance

This activity involves evaluating the reconstructed images prior to image analysis. It includes image criteria that are necessary to reliably meet the Profile Claim.

### 3.9.1 Discussion

This Image QA activity represents the portion of QA performed between image generation and analysis where characteristics of the content of the image are checked for compliance with the profile. The Image QA details listed here are the ones QIBA has chosen to highlight in relation to achieving the Profile claim. It is expected that sites will perform many other QA procedures as part of good imaging practices.

Numerous factors can affect image quality and result in erroneous nodule volume measurements. **Motion artifacts** and **Dense Object Artifacts** can alter the apparent size, shape, and borders of nodules. Certain **Thoracic Disease** processes may alter the attenuation of the lung surrounding a nodule and interfere with identification of its true borders. Contact between a nodule and anatomic structures such as pulmonary vessels or the chest wall, mediastinum, or diaphragm also may affect **Nodule Margin Conspicuity** and obscure the true borders. Although screening may still be performed on them, the Claims of this Profile do not apply to nodules affected by image quality deficiencies that impair **Overall Nodule Measurability** and the sensitivity for nodule detection may be reduced.

### 3.9.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Motion Artifacts | Technologist | Shall confirm the Images to be analyzed are free from motion artifacts. |
| Image Analyst |
| Dense Object Artifacts | Technologist | Shall confirm the Images to be analyzed are free from artifacts due to dense objects or anatomic positioning. |
| Image Analyst |
| Thoracic disease | Image Analyst | Shall confirm the Images to be analyzed are free from disease processes affecting the measurability of the nodule. |
| Nodule Margin Conspicuity | Image Analyst | Shall confirm the Nodules to be analyzed are sufficiently distinct from and unattached to other structures of similar attenuation. |
| Nodule Size | Image Analyst | Shall confirm (now or during measurement) that tumor longest in-plane diameter is between 6 mm and 12 mm.  (For a spherical tumor this would roughly correspond to a volume between 113 mm3 and 905 mm3.) |
| Overall Nodule Measurability | Image Analyst | Shall disqualify any Nodules and images with features that might reasonably be expected to degrade measurement reliability. |

## 3.10. Image Analysis

This activity involves measuring the volume change for subjects over one or more timepoints. It includes criteria and procedures related to producing quantitative measurements from the images that are necessary to reliably meet the Profile Claim.

### 3.10.1 Discussion

Image analysis should be performed using **Image Analysis Tool** programs that have received appropriate scientific validation. Because different programs use different segmentation algorithms that may result in different volumetric measurements even for ideal nodules, and different versions of the same program or its components may change its performance, a nodule being evaluated for change must be analyzed at both time points with the same software program (manufacturer, model, and version).

The volume of a lung nodule is typically determined by defining the nodule boundary (referred to as segmentation) and computing the volume within the boundary. Segmentation typically is performed by an automated algorithm after the user designates the location of the nodule to be measured with a starting seed point, cursor stroke, or region of interest. A subjective **Segmentation Analysis** should be conducted to closely inspect segmentation volumes in three dimensions for concordance with the visually-assessed nodule margins. Assessment of this concordance can be affected by the **Image Display Settings**, so a window and level appropriate for viewing the lung should be used and kept the same for all time points being compared.

Nodules for which the segmentation tracks the margins most accurately, without manual editing, will most closely meet the Claims of this Profile. If in the radiologist’s opinion the segmentation is unacceptable, quantitative volumetry shall not be used and nodule size change should be assessed using standard clinical methods. Nodule location and margin characteristics impact segmentation quality and variance in nodule measurement, which are more favorable for nodules that are isolated, well-separated from adjacent structures, and have smooth borders compared to nodules abutting pulmonary vessels or parietal pleura, and also for smooth nodules compared to spiculated or irregularly shaped nodules (35-40).

When deriving the nodule volume difference between two time points, the **Reading Paradigm** involves direct side-by-side comparison of the current and previous image data at the same time, to reduce interobserver and intraobserver variation. Storing segmentations and measurement results for review at a later date is certainly a useful practice as it can save time and cost. However, segmentation results at both time points shall be inspected visually in three dimensions to make sure that they are of sufficient and comparable accuracy in order to meet the Claims of the Profile. If a previous segmentation is unavailable for viewing, or the previous segmentation is not of comparable accuracy to the current segmentation, segmentation at the comparison time point should be repeated.

Methods that calculate volume changes directly without calculating volumes at individual time points are acceptable so long as the results are compliant with the specifications set out by this Profile. Regardless of method, the ability of software to calculate and record volume change relative to baseline for each nodule is recommended.

These Image Analysis specifications are intended to apply to a typical user working in the clinical setting (i.e. without extraordinary training or ability). This should be kept in mind by vendors measuring the performance of their tools and sites validating the performance of their installation. Although the performance of some methods may depend on the judgment and skill of the user, it is beyond this Profile to specify the qualifications or experience of the operator.

Image Analysis Tools may calculate and make available to the operator the 95% confidence interval for tumor volume change based on the equation:

Where

*Y1* and *Y2* is the volume measurement at timepoint 1 and 2,

*wCV1* and *wCV2* is the within-nodule coefficient of variation for *Y1*   
 and *Y2* as taken from Table 1 in Section 2.

Refer to <http://www.accumetra.com/NoduleCalculator.html> for a reference implementation of these calculations.

### 3.10.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Image Analysis Tool | Image Analyst | Shall use the same Image Analysis Tool (manufacturer, model, version) for measurements at all time points. |
| Segmentation Analysis | Image Analyst | Shall disqualify nodules with inadequate automated segmentations or nodules with non-comparable segmentations at both time points. |
| Image Display Settings | Image Analyst | Shall set the Image display setting (window and level) for the segmentation initiation to the same lung appropriate settings for all time points. |
| Equipment | Technologist | Shall use the same measurement system (scanner model, software, and operator) at the two time points. |

# 4. Assessment Procedures

Most of the requirements described in Section 3 can be assessed for conformance by direct observation, however some of the performance-oriented requirements are assessed using a procedure. When a specific assessment procedure is required or to provide clarity, those procedures are defined in subsections here in Section 4 and the subsection is referenced from the corresponding requirement in Section 3.

## 4.1. Assessment Procedure: Image Quality

This procedure can be used by a manufacturer or an imaging site to assess five quality characteristics of reconstructed images:

* Resolution is assessed in terms of the standard deviation (in mm) of the PSF or Point Spread Function (which is the estimated response of the imaging system to a point source). The standard deviation of the PSF is measured both in-plane and along the Z-axis. Note: decreasing values indicate improving resolution.
* Voxel Bias is assessed in terms of the difference (in HU) of the mean pixel value from the expected value for a material with uniform density.
* Voxel Noise is assessed in terms of the standard deviation (in HU) of pixel values when imaging a material with uniform density.
* Edge Enhancement is assessed in terms of the maximum percent increase in HU contrast above expected along the outer edge of an ideal hollow cylinder surrounded by air.
* Spatial Warping is assessed in terms of the mean squared error of the outer cylindrical surface compared to an ideal cylindrical reference object surface.

The assessor shall obtain a phantom (See **Figure 1)** with an isocentering and alignment target mark on the outer surface and three modules centered at three distances (0mm, 102mm, 204mm) from the target mark. Within each module is:



**Figure 1**: An illustration with translucency showing the {QIBA Quantitative CT Phantom}.

* A hollow cylinder made of Delrin plastic with an inner radius of 17.0 mm +- 0.02mm, an outer radius of 28.0 mm +- 0.02mm and a height of 19.0mm +- 0.02mm, and an expected density of ??? HU.
* A homogeneous Air cylinder (inside the hollow Delrin cylinder) with a height of 19.0mm +- 0.02mm and a diameter of 17.0 mm +- 0.02mm, and an expected density of ??? HU.
* A homogeneous Acrylic cylinder (approximately 6.0 mm above the hollow cylinder) with a height of 10.0mm +- 0.1mm and a diameter of 34mm +- 0.1mm, and an expected density of ??? HU.
* A homogeneous Teflon cylinder (6.0 mm below the hollow cylinder) with the same dimensions as the Acrylic cylinder, and an expected density of ??? HU.

The assessor shall position the phantom nominally flat on the X-Z scanning plane (i.e. the patient table) with the alignment target located at the scanner isocenter…

The assessor shall scan the phantom and assess the five image quality characteristics for each of the three modules. The scan may be performed at any time in the day after the CT scanner has passed its daily ACR CT accreditation and manufacturer calibration checks.

Note: A reference implementation of the following calculations can be accessed by submitting the phantom images to x.y.org.

The assessor shall determine the 3D Gaussian PSF sigmas that best fit the partial volume voxels near the inner surface of the hollow cylinder. The 3D Gaussian PSF sigma ellipsoid volume () is the volume of an ellipsoid with semi-axis lengths of X, Y, and Z PSF sigmas, which is expressed as . The in-plane resolution and Z resolution.

An **In-plane PSF** **sigma** can be translated to a Modulation Transfer Function at a 50% cutoff frequency (MTF 50) value using the following equation [53]:

where is the MTF frequency and is the line pairs per millimeter.

For each material (Acrylic, Teflon, Delrin and Air), the assessor shall identify all voxels that are > 2\*sigma millimeters inside the surface of the material (to avoid bias from partial volume artifact).

The assessor shall subtract the expected density of the material from the mean value of the identified voxels and record the result as the **Voxel Bias** for the material.

The assessor shall calculate the standard deviation of the identified voxels and record the result as the **Voxel Noise** for the material.

The assessor shall identify an arbitrary number of 10 degree arc-shaped sampling paths with each path at varying arbitrary radial distances inside the hollow cylinder center and centered on the X axis. The assessor shall calculate the mean value of the voxels along each path and identify the maximum of those mean values. The assessor shall calculate the maximum observed contrast due to edge enhancement (EEmax) as that maximum minus the measured mean value of the Air voxels along that path. The assessor shall calculate the reference level of edge enhancement (EEref) as the mean value of the Delrin voxels along all of the paths minus the mean value of the Air voxels along all of the paths. The assessor shall calculate and record the **Edge Enhancement** percentage as .

The assessor shall determine the outer cylindrical surface of the hollow cylinder by taking an ideal geometric cylinder with the nominal dimensions and location of the hollow cylinder and using a Marching Cubes algorithm with a threshold halfway between the measured mean value of the Delrin voxels and the measured mean value of the Air voxels. The assessor shall compute the mean square error (MSE) between the center of all the voxels determined to be on the outer surface of the hollow cylinder and the surface of the ideal geometric cylinder and record the result as the **Spatial Warping** value.

*<Still need to explain whether you have to get a passing score vs the target values at each of the three module locations or whether you are supposed to average the values for the three module locations and compare that result to the target>*

## 4.2. Assessment Procedure: Nodule Volume Bias and Variation

This procedure can be used by a manufacturer or an imaging site to assess the quality of nodule volume measurements by an Image Analysis Tool. Quality is assessed in terms of bias and coefficient of variation (CV).

Measurement Bias is the deviation of the mean value from its true value for a set of volumetric measurements. This metric is assessed by measuring the volume of repeat scans of geometric objects, each with a manufactured and verified volume, where the objects have varying size and shape.

Coefficient of Variation (CV) is a measure of variation for repeated volumetric measurements of an object. It is calculated as the ratio of the standard deviation to the mean for a set of measurements. This metric is assessed by measuring the volume of short-time interval repeat scans of nodules, where the nodules have varying size, shape, and attachments as well as by measuring the volume of geometric object scans.

The assessor shall obtain two sets of CT scans from the QIBA quality assurance site x.y.org. A “phantom nodule dataset” contains 10 CT scans of a QIBA provided phantom with numerous geometric objects embedded in foam. A “clinical nodule dataset” contains 5 repeat CT scans of 14 different lung nodules of varying shape and size all acquired within a short time interval such that the amount of volumetric change must be zero.

Two spreadsheet files are also provided at the x.y.org website. An “object location file” in \*.xls format contains the RAS coordinate locations of the geometric objects in the “phantom nodule dataset”. A “measurement reporting file” in \*.xls format is also provided with a volumetric measurement data entry location for each object to be measured.

The assessor shall load each CT series in the “phantom nodule dataset” and the “clinical nodule dataset” into the nodule measurement software and obtain a volumetric measurement. The assessor shall enter each volumetric measurement into the “measurement reporting file” which will automatically verify that the values reported are compliant. This will specifically verify that the bias for each volumetric measurement of a geometric object is <= 5% of the object’s manufactured volume. The spreadsheet will also verify that the coefficient of variation for both geometric objects and repeat lung nodules does not exceed the values in **Table 1**. The assessor shall also enter the analysis software name and version number into the “measurement reporting file” and upload the file to the QIBA quality assurance site x.y.org. The specific version of the lung nodule analysis software will be considered compliant when at least two independent clinical sites have successfully performed this procedure.

Sites can follow the vendor equipment procedure to verify compliance of software that is not on the list.

.

Analysis software will be run against a set of testing datasets to assess that the volumetric measurement software performs at a minimum level of performance. Datasets will include phantom scans containing geometric objects of known volumes (i.e. phantom nodule dataset) as well as clinical zero change clinical nodule datasets (i.e. clinical nodule dataset). The phantom nodule dataset and the clinical nodule dataset will be available at x.y.org for download. In addition, a template analysis software measurement spreadsheet for measurement findings will be available at x.y.org that provides the RAS location and data placeholders for software calculated measurements.

Analysis software conformance testing is specific to the name and version number of an analysis software system available to clinical sites for the measurement of CT lung nodules.

Analysis software testing of the phantom nodule dataset will consist of the following steps:

1. Sequentially load each longitudinal CT series in the phantom nodule dataset into the analysis software and perform automated or semi-automated segmentation of the nodule(s).
2. Place each calculated volume measurement into the analysis software measurement spreadsheet. As measurements are placed into the spreadsheet the bias and coefficient of variation of each simulated nodule will be automatically calculated by the spreadsheet.
3. After all measurements have been calculated all bias and coefficient of variation values must be within acceptable limits for this profile. The phantom nodule dataset measurements must produce coefficients of variation no greater than those listed in Table 1. Volume bias may not exceed 5% of the phantom nodule manufactured volume.

Analysis software testing of the clinical nodule dataset will consist of the following steps:

1. Sequentially load each longitudinal CT series in the clinical nodule dataset into the analysis software and perform automated or semi-automated segmentation of the nodule(s).
2. Place each calculated volume measurement into the analysis software measurement spreadsheet. As measurements are placed into the spreadsheet the coefficient of variation of each clinical nodule will be automatically calculated by the spreadsheet.
3. After all measurements have been calculated all coefficient of variation values must be within acceptable limits for this profile. The clinical nodule dataset measurements must produce coefficients of variation no greater than those listed in Table 1.
4. .
5. .
6. .
7. .
9. .

# 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 Image Analysis Tool), 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 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.

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# Appendices

## Appendix A: Acknowledgements and Attributions

This document is proffered by the Radiological Society of North America (RSNA) Lung Nodule Volume Assessment and Monitoring in Low Dose CT Screening Working Group of the Volumetric Computed Tomography (v-CT) Technical 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 more detailed description of the v-CT committee and its work can be found at the following web link: <http://qibawiki.rsna.org/index.php?title=Quantitative-CT>.

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## Appendix B: Background Information

## B.1 Summary of selected references on nodule volumetry accuracy

<http://qibawiki.rsna.org/index.php/Work_Product_for_Review>

## B.2 Summary of selected references on nodule volumetry precision

<http://qibawiki.rsna.org/index.php/Work_Product_for_Review>

## Appendix C: Metrology Methods

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