

QIBA Profile:

Lung Nodule Volume Assessment and Monitoring in Low Dose CT Screening

Version 1.0

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Note to users – when referencing this QIBA Profile document, please use the following format:

CT Volumetry Technical Committee. Lung Nodule Assessment in CT Screening Profile, Quantitative Imaging Biomarkers Alliance. Version 1.0. Reviewed draft. QIBA.

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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 **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) for evaluating specific requirements are defined as needed.

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, Reconstruction Software and Image Analysis Tools involved in activities 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 measurements in order to meet the Claims of the Profile.

This document is intended to help clinicians who make clinical management decisions, imaging staff generating this biomarker, vendor staff developing related products, purchasers of such products, and investigators designing trials with imaging endpoints. Note that this document only states 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.

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

# 2. Clinical Context and Claims

X-ray computed tomography 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 pulmonary nodules obtained using a reduced radiation dose in the setting of lung cancer screening and post-screening surveillance.

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 pulmonary nodules in the 6-12 mm diameter range, though surveillance in this or other settings is not specifically addressed by this Profile.

# Clinical Context

Quantifying the volumes and volume changes over time of lung nodules smaller than 12 mm. Nodules with diameter ≥12 mm (volume ≥905 mm3) are the subject of the document “QIBA Profile: CT Tumor Volume Change (CTV-1)”. Conformance to this Profile by all relevant staff and equipment supports the following Claim(s):

## Claim 1: Nodule volume

## For nodule diameter ≥6 mm and <12 mm (volume ≥113 mm3 and < 905 mm3) with a measurement CV (coefficient of variation) as specified in the table below, the following holds:

## Claim: For a measured nodule volume of Y, the 95% confidence interval for the true nodule volume is Y ± (1.96 × Y × CV).

**These Claims hold when:**

* the nodule diameter is the longest dimension in the transverse plane (use of longest dimension in any plane may result in a lower coefficient of variation)
* the nodule shape does not deviate excessively from spherical (the nodule’s shortest diameter in any dimension is at least 60% of the nodule’s longest diameter in any dimension)
* the nodule is measurable (i.e., tumor margins are distinct from surrounding structures of similar attenuation and geometrically simple enough to be segmented using automated software without manual editing)
* lung nodule volume measurement bias and covariance are zero
* the CT scanner meets the conformance requirements of Section 4 in this Profile
* the following table is used to lookup Coefficients of Variation (CV):

**Table 1. Coefficients of variation**

|  |  |  |
| --- | --- | --- |
| **Nodule**  **Diameter (mm)** | **Nodule**  **Volume (mm3)** | **Coefficient of Variation (CV)** |
| ≥ 6 and < 8 mm | ≥ 113 and < 268 | 0.29 |
| ≥ 8 and < 10 mm | ≥ 268 and < 524 | 0.19 |
| ≥ 10 and < 12 mm | ≥ 524 and < 905 | 0.14 |
| ≥ 12 mm | ≥ 905 | 0.11 |

A web based reference calculator for computing Claim 1 equations is available at <http://www.accumetra.com/NoduleCalculator.html>.

Clinical Interpretation

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 314 mm3 [500 - (500 x 1.96 x 0.19)] (8.4 mm diameter) and 686 mm3 [500 + (500 x 1.96 x 0.19)] (10.9 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 580 mm3 [800 - (800 x 1.96 x 0.14)] (10.3 mm diameter) and 1020 mm3 [800 + (800 x 1.96 x 0.14)] (12.4 mm diameter).

Discussion

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.

## Claim 2: Nodule volume change between two time points

## For a nodule at time point 1 with diameter ≥6 mm and <12 mm (volume ≥ 113 mm3 and < 905 mm3) with measurement coefficients of variation CV1 and CV2 corresponding to the volumes at time point 1 and time point 2, as specified in the table above, the following holds:

## Claim: A measured change in nodule volume of X% indicates that a true change in nodule volume has occurred if X > (2.77 x CV1 x 100), with 95% confidence. To quantify the amount of change, if Y1 and Y2 are the volume measurements at the two time points, then the 95% confidence interval for the true change is (Y2-Y1) ± 1.96 × √([Y1 × CV1]2 + [Y2 × CV2]2).

**These Claims hold when:**

* the nodule diameter is the longest dimension in the transverse plane (use of longest dimension in any plane may result in a lower coefficient of variation)
* the nodule shape does not deviate excessively from spherical (the nodule’s shortest diameter in any dimension is at least 60% of the nodule’s longest diameter in any dimension)
* the tumor is measurable at both time points (i.e., tumor margins are distinct from surrounding structures of similar attenuation and geometrically simple enough to be segmented using automated software without manual editing)
* the nodule diameter at the first of the two time points is within one of the given size ranges
* change is calculated as the difference in volume between two time points relative to the volume at the earlier time point
* the measurement system (scanner model, software, and operator) is the same at the two time points
* the Claim for the smaller of the two nodule size time points is applied
* the CT scanner meets the conformance requirements of Section 4 in this Profile

Clinical Interpretation

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 75%) [i.e. (917-524)/524 x 100 = 75%]. For this 10 mm nodule at baseline, we apply the CV from the third 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 0.29 x 100]; we cannot be confident that this measured change represents a real change in the tumor volume.

Discussion

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 Claim 2 equations 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 meeting all Requirements in the referenced Section.

Table 2: Actors and Required Activities

|  |  |  |
| --- | --- | --- |
| **Actor** | **Activity** | **Section** |
| Acquisition Device | Periodic Quality Assurance | 3.3 |
| Image Data Acquisition | 3.6 |
| Image Data Reconstruction | 3.7 |
| Technologist | Periodic Quality Assurance | 3.3 |
| Subject Selection | 3.4 |
| Subject Handling | 3.5 |
| Image Data Acquisition | 3.6 |
| Image Data Reconstruction | 3.7 |
| Image Quality Assurance | 3.8 |
| Radiologist | Subject Selection | 3.4 |
| Subject Handling | 3.5 |
| Image Data Acquisition | 3.6 |
| Image Data Reconstruction | 3.7 |
| Referring Clinician | Subject Selection | 3.4 |
| Image Analyst | Image Quality Assurance | 3.8 |
| Image Analysis | 3.10 |
| Image Analysis Software | Image Analysis | 3.10 |

This Profile is “nodule-oriented” rather than “patient-oriented”. 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.

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 : 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. The Profile requires that images of a given nodule be acquired and processed the same way each time, and all efforts should be made to achieve this goal. Volume change is the volume difference between the two time points divided by the volume at the earlier time point, expressed as a percentage. 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.

This initial Profile is expected to be revised as further innovation and validation data emerge. The above pipeline provides a reference model. Algorithms which achieve the same or a better result compared to the reference model but use different methods are expected. The Profile Specifications 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.

Since much of this Profile emphasizes performing subsequent scans with the same technical parameters that were used for the baseline scan of the subject, the parameter values chosen for the baseline scan are particularly important. In some scenarios, the “baseline” might be defined as a reference point that is not necessarily the first scan of the patient.

## 3.1. Pre-delivery

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

### 3.1.1 Discussion

No specific pre-delivery activities are required by this Profile.

## 3.2. Installation

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

### 3.2.1 Discussion

Equipment vendor guidelines shall be followed. No other specific installation activities are required by this Profile.

## 3.3. Periodic Equipment Quality Assurance

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

### 3.3.1 Discussion

Quality control procedures shall be consistent with those generally accepted for routine clinical imaging. Adherence to procedures specified by the scanner manufacturer and the American College of Radiology CT Accreditation Program (<http://www.acr.org/~/media/ACR/Documents/Accreditation/CT/Requirements>) and scanner manufacturer are recommended. Daily quality control must include monitoring of water CT number and standard deviation and artifacts. Preventive maintenance at appropriate regular intervals shall be conducted and documented by a qualified service engineer as recommended by the scanner manufacturer.

## 3.4. 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.3.4.1 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 these clinical status conditions cannot be met, such as due to the time-dependent nature of follow-up, the Profile Claims regarding quantitative volumetry may not be valid. 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. To meet Profile Claims, scans should be performed prior to or at an appropriate time following such procedures.

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.

### 3.4.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Pulmonary Symptoms | Referring clinician | If pulmonary symptoms are present, scanning shall be delayed for a time period that allows resolution of potential reversible CT abnormalities. If scanning is necessary to avoid an excessive delay in follow-up of a known nodule or to evaluate new symptoms, measurements may not be of sufficient quality to fulfill the Profile Claims. |
| Technologist |
| Radiologist |
| Medical Procedures | Referring clinician | Scanning shall be performed prior to or at an appropriate time following procedures that could alter the attenuation of the lung nodule or surrounding lung tissue. If this specification is not met, and the attenuation of the lung or nodule is altered, Profile Claims will not be valid. |
| Radiologist |

## 3.5. Subject Handling

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.

### 3.5.1 Discussion

**Intravenous Contrast** is not used for CT 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 is administered, nodule measurements will not be subject to the Profile Claims.

After obtaining the topogram, the technologist should evaluate the topogram 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. To meet Profile Claims, the images of nodules shall be free from streak and other metal artifacts. If such artifacts occur, screening may still be performed, but the Claims of this Profile will not be met for nodules affected by metal artifacts, and the sensitivity for nodule detection may be reduced.

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.

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. In some cases, motion from cardiac pulsation or inability to maintain breath-hold may produce motion artifacts. To meet Profile Claims, the images from which volumetric calculations are made shall be free from artifact due to patient motion, with no perceptible motion blurring or ‘double exposure’ appearance of the nodule borders. 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”

### 3.5.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Intravenous contrast | Technologist | Intravenous contrast shall not be used for lung cancer screening or follow-up of screen-detected nodules. If contrast is administered, quantitative nodule measurements will not be subject to the Profile Claims. |
| Radiologist |
| Artifact sources | Technologist | Metallic objects on or underneath the chest and abdomen should be removed prior to scanning, and breast shields shall not be used. |
| Subject Positioning | Technologist | The Technologist should position the subject supine with arms overhead, and the sternum positioned over the midline of the table. Positioning shall be consistent with baseline. |
| Table Height & Centering | Technologist | The Technologist should adjust the table height for the mid-axillary plane to pass through the isocenter of the gantry. Table position shall be consistent with baseline. |
| Breath holding | Technologist | The Technologist should instruct the subject in proper breath-hold procedures to achieve maximal inspiration. Providing live voice breath-holding instructions is preferred, and close visual monitoring for compliance with instructions is strongly recommended. |

### 

## 3.6. Image Data Acquisition

3.6.1 Discussion

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

Many scan parameters can have direct or indirect effects on identifying, segmenting and measuring nodules. To reduce variance, all efforts should be made to have as many of the follow-up scan parameters as possible consistent with the baseline scan parameters. Parameter consistency when using the same scanner brand/model generally means using the same values. Parameter consistency when the baseline was acquired on a different brand/model may require some “interpretation” to achieve consistent performance since the same values may produce different behavior on different models. The parameter sets in Appendix C may be helpful in this task (to be obtained where possible).

**Anatomic Coverage** should include the entire volume of the lungs, minimizing the volume scanned above and below the lungs to avoid unnecessary radiation exposure.

The **Number of Detectors** can influence the scan duration, z-axis resolution, and radiation dose. The use of CT scanners with a minimum of 16 detectors is required to allow the Claims of this Profile to be met. A primary consideration leading to this requirement 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. Published investigations have demonstrated the accuracy of CT nodule volumetry meeting the Claims of this Profile using 16-detector scanners. However, some 16-detector scanners may not meet the conformance requirements (Section 4) of this Profile (Rick Avila, Accumetrix, unpublished data). Z-axis resolution may be inadequate for nodule volumetry in some patients using scanners with fewer than 16 detectors and pitch high enough to allow the entire lung to be scanned in a single breath hold (Rick Avila, Accumetrix, unpublished data), and shall not be used.

The **Topogram** 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 topogram 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, 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.

**Automatic Exposure Control** aims to achieve consistent noise levels throughout the lungs by varying the tube current during scan acquisition (30). 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.

**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. The Nominal Tomographic Section Thickness should allow a reconstructed slice thickness of 1.25 mm or less (see below).

Exposure to ionizing radiation from CT 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.

3.6.2 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** |
| --- | --- | --- | --- |
| Anatomic Coverage | Technologist | Apex through base of lungs |  |
| Number of detectors | Technologist | Shall be 16 or greater |  |
| Scan Duration | Technologist | Scanning shall be performed in a single breath hold.  If the patient is unable to suspend breathing for the entire scan, multiple overlapping single breath hold scans may be obtained in a manner insuring that the entire volume of each nodule lies within the images from a single breath hold. |  |
| Topogram | Technologist | Restrict to the anatomic limits of the thorax.  Use the minimum kV and mA needed to identify anatomic landmarks.  Absence of metallic or other artifact sources should be confirmed and remaining external objects should be removed. Scanning may be performed if metallic objects are present, but resulting artifacts may invalidate Profile measurement Claims. |  |
| CTDIvol | Radiologist | Shall be ≤3 mGy for a person of standard size (5’7”/170 cm and 154 lbs/70 kg), and reduced for smaller persons and increased for larger persons as appropriate to maintain image quality for detection of pulmonary nodules. | CTDIvol (0018,9345) |
| Tube Potential (kVp) | Radiologist | Shall be adjusted to achieve appropriate CTDIvol. | KVP  (0018,0060) |
| Technologist |
| Tube Current-Time Product (mAs) | Radiologist | Shall be adjusted to achieve appropriate CTDIvol. | Exposure Time (0018,1150), X-ray Tube Current (0018,1151), Exposure (0018,1152) |
| Technologist |
| Rotation time | Radiologist | May vary as needed to achieve other settings. Generally ≤0.5 sec. |  |
| Technologist |
| Pitch | Radiologist | Shall be no greater than 2.0 for single source scanners, or the equivalent for dual source scanners. | Spiral Pitch Factor  (0018,9311) |
| Technologist |
| Automatic exposure control | Radiologist | Optional. |  |
| Technologist |
| Nominal Tomographic Section Thickness (T) | Radiologist | Shall adjust to achieve reconstructed slice thickness ≤1.25 mm | Single Collimation Width  (0018,9306) |
| Technologist |

## 3.7. Image Data Reconstruction

3.7.1 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). A thickness of 1.25 mm or less is required to meet the Profile Claims.

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, which meets the Claims of this Profile. 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), and are also acceptable.

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 improves 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, overestimation 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.

3.7.2 Specification

The Reconstruction Software shall be capable of producing images that meet the following specifications. The Technologist shall set the image reconstruction parameters to achieve the requirements in the following table:

| **Parameter** | **Actor** | **Specification** | **DICOM Tag** |
| --- | --- | --- | --- |
| Reconstruction Field of View | Technologist | Should be set to the widest diameter of the lungs. | Reconstruction Diameter(0018,1100), Reconstruction Field of View (0018,9317) |
| Reconstructed Slice Thickness | Radiologist | Shall be less than or equal to 1.25 mm and consistent with baseline. | Slice Thickness (0018,0050) |
| Technologist |
| Reconstruction Interval | Radiologist | Shall be less than or equal to slice thickness and consistent with baseline. | Spacing Between Slices (0018,0088) |
| Technologist |
| Reconstruction Algorithm Type | Radiologist | Shall use filtered back-projection or iterative methods. | Reconstruction Type (0018,9315) |
| Technologist |
| Reconstruction Kernel | Radiologist | Shall be consistent with baseline (i.e. the same kernel if available, otherwise the kernel most closely matching the kernel response of the baseline).  Recommend a medium smooth to medium sharp kernel that provides the highest resolution available without edge enhancement. | Convolution Kernel (0018,1210), Convolution Kernel Group (0018,9316) |
| Technologist |

## 

## 3.8. Image Quality Assurance

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

### 3.8.1 Discussion

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. The Claims of this Profile do not apply to nodules affected by image quality deficiencies that impair **Overall Nodule Measurability**.

### 3.8.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Motion Artifacts | Technologist | Images to be analyzed shall be free from motion artifacts. |
| Image Analyst |
| Dense Object Artifacts | Technologist | Images to be analyzed shall be free from artifacts due to dense objects or anatomic positioning. |
| Image Analyst |
| Thoracic disease | Image Analyst | Images to be analyzed shall be free from disease processes affecting the measurability of the nodule. |
| Nodule Margin Conspicuity | Image Analyst | Nodules to be analyzed shall be sufficiently distinct from and unattached to other structures of similar attenuation. |
| Overall Nodule Measurability | Image Analyst | Nodules and images with any features that might reasonably be expected to degrade measurement reliability shall be disqualified from quantitative volumetric assessment. |

## 3.9. Image Distribution

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

### 3.9.1 Discussion

No specific image distribution activities are required by this Profile.

## 3.10. Image Analysis

3.10.1 Discussion

Image analysis should be performed using **Image Analysis Software** 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 should 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** shall 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 nodules compared to nodules abutting pulmonary vessels or parietal pleura, and also for smooth compared to spiculated or irregularly shaped nodules (35-40).

When deriving the nodule volume difference between two time points, the **Reading Paradigm** shall involve 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.

3.10.2 Specification

| **Parameter** | **Actor** | **Requirement** |
| --- | --- | --- |
| Image Analysis Software | Image Analyst | The Image Analysis Software shall have appropriate scientific validation, including the properties of measurement linearity and zero bias.  The same Image Analysis Software (manufacturer, model, version) shall be used for measurements at all time points. |
| Segmentation Analysis | Image Analyst | Nodules with inadequate automated segmentations or nodules with noncomparable segmentations at both time points from quantitative volumetric assessment shall be disqualified from quantitative volumetric assessment. |
| Image Display Settings | Image Analyst | Image display setting (window and level) during the segmentation initiation and review process shall be appropriate for viewing the lung and shall be the same at all time points. |
| Reading Paradigm | Image Analysis Tool | Images from both time points shall be presented side-by-side for comparison. |

## 3.11. Image Interpretation

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

### 3.11.1 Discussion

Image interpretation is discussed in Section 2 (Claims) under the heading Clinical Interpretation following Claim 1 and Claim 2. Guidance on clinical management decisions related to measurements of nodule volume and its change over time is beyond the scope of this Profile.

# 4. Assessment Procedures

To conform to this Profile, participating staff and equipment (“Actors”) shall support each activity assigned to them in Table 2.

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

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

Formal claims of conformance by the organization responsible for an Actor shall be in the form of a published QIBA Conformance Statement. Vendors publishing a QIBA Conformance Statement shall provide a set of “Model-specific Parameters” (as shown in Appendix C to be obtained where possible) describing how their product was configured to achieve conformance. Vendors shall also provide access to or describe the characteristics of the test set used for conformance testing.

## 4.1. Assessment Procedure: CT Equipment Specifications and Performance

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 procedures reflect the clinical and clinical trial settings which produced the data used to support the Claims of this Profile. These 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 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.

## 4.2. Assessment Procedure: Technologist

Radiologic technologists shall fulfill the qualifications required by the American College of Radiology CT Accreditation Program (<http://www.acr.org/~/media/ACR/Documents/Accreditation/CT/Requirements>). 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.

## 4.3. Assessment Procedure: Radiologists

Radiologists shall fulfill the qualifications required by the American College of Radiology CT Accreditation Program (<http://www.acr.org/~/media/ACR/Documents/Accreditation/CT/Requirements>). 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.

## 4.4. Assessment Procedure: Image Analyst

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. While there are currently no certification guidelines for image analysts, a non-radiologist performing CT image volumetric analysis of lung nodules in lung cancer screening shall undergo documented training by a radiologist having qualifications conforming to the requirements of this profile. The level of training should be 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.

## 4.5. Assessment Procedure: Image Analysis Software

To be determined

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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 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>.

The Lung Nodule Volume Assessment and Monitoring in Low Dose CT Screening Working Group (in alphabetical order):

Denise Aberle, MD University of California, Los Angeles (UCLA)

Samuel G. Armato III, PhD University of Chicago

Rick Avila, MS Accumetra

Roshni Bhagalia, PhD GE Global Research

Matthew Blum, MD, FACS University of Colorado Health

Kirsten L. Boedeker, PhD Toshiba Medical Research Institute-USA, Inc.

Andrew J. Buckler, MS Elucid Bioimaging Inc.

Paul L. Carson, PhD University of Michigan Medical Center

Dominic Crotty, PhD GE Healthcare

Harry de Koning, MD, PhD Erasmus University Medical Center

Ekta N. Dharaiya, MS Philips Healthcare

Les Folio, DO, MPH National Institutes of Health (NIH)

Matthew Fuld, PhD Siemens AG Healthcare

Kavita Garg, MD University of Colorado, Denver

David S. Gierada, MD Washington University, Mallinckrodt Institute of Radiology

Fergus Gleeson, MBBS Churchill Hospital--Headington, (Oxford, UK) / British Society of Thoracic Imaging

Gregory V. Goldmacher, MD, PhD, MBA Merck

Jin Mo Goo, MD, PhD Seoul National University Hospital (South Korea)

Tomasz Grodzki, MD, FETCS Regional Hospital for Lung Diseases/European Society of Thoracic Surgeons (Poland)

Bernice E. Hoppel, PhD Toshiba Medical Research Institute USA, Inc.

Edward F. Jackson, PhD University of Wisconsin, School of Medicine & Public Health

Philip F. Judy, PhD Harvard-Brigham and Women's Hospital

Ella A. Kazerooni, MD University of Michigan

David A. Lynch, MD National Jewish Health

Ashkan A. Malayeri, MD NIH/CC/DRD

Theresa C. McLoud, MD Massachusetts General Hospital/Society for Thoracic Radiology

Michael McNitt-Gray, PhD University of California, Los Angeles (UCLA)

Steve Metz, PhD Philips

James L. Mulshine, MD Rush University Medical Center

Reginald Munden, MD, DMD, MBA Houston Methodist Hospital-Physician Organization

Nancy Obuchowski, PhD Cleveland Clinic Foundation

Michael O’Connor, MBA, PhD PAREXEL International

Matthijs Oudkerk, MD, PhD University Medical Center Groningen (the Netherlands)

Eric S. Perlman, MD Perlman Advisory Group, LLC

Mathias Prokop, MD, PhD Radboud University Medical Center (Nijmegen, the Netherlands)

James G. Ravenel, MD Medical University of South Carolina

Anthony P. Reeves, PhD Cornell University

Marthony Robins, PhD Duke University

Ehsan Samei, PhD Duke University

Lawrence H. Schwartz, MD New York Presbyterian Hospital/Columbia University Medical Center

Jenifer Siegelman, MD, MPH Harvard Medical School Brigham and Women's Hospital

Mario Silva, MD University of Parma (Italy)

Gary Smith, MD Vanderbilt University

Daniel C. Sullivan, MD Duke University

Rozemarijn Vliegenthart, MD, PhD University Medical Center Groningen (the Netherlands)

David F. Yankelevitz, MD Mount Sinai Hospital

Lifeng Yu, PhD Mayo Clinic

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Fiona Miller, Director Department of Research

Joseph Koudelik, Assistant Director Scientific Affairs, Department of Research

Julie Lisiecki,  Manager Scientific Affairs, Department of Research

Susan Weinmann, Senior Administrative Assistant Department of Research

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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: Model-specific Instructions and Parameters

May transfer this to conformance section for protocols that have demonstrated conformance

For acquisition modalities, reconstruction software and software analysis tools, profile conformance requires meeting the activity specifications above in Sections 2, 3 and 4.

This Appendix provides, as an informative tool, some specific acquisition parameters, reconstruction parameters and analysis software parameters that are expected to be compatible with meeting the profile requirements. Just using these parameters without meeting the requirements specified in the profile is not sufficient to achieve conformance. Conversely, it is possible to use different compatible parameters and still achieve conformance.

Sites using models listed here are encouraged to consider using these parameters for both simplicity and consistency. Sites using models not listed here may be able to devise their own settings that result in data meeting the requirements.

**IMPORTANT: The presence of a product model/version in these tables does not imply it has demonstrated conformance with the QIBA Profile. Refer to the QIBA Conformance Statement for the product.**

Table C.1 Model-specific Parameters for Acquisition Devices

| Acquisition Device | Settings Compatible with Conformance |
| --- | --- |
| Acme Medical  CT Lights  V3.14 | *Submitted by: Gotham University Hospital* |
| |  |  | | --- | --- | | kVp | 120 | | Number of Data Channels (N) | 64 | | Width of Each Data Channel (T, in mm) | 0.625 | | Gantry Rotation Time in seconds | 1.0 | | mA | 120 | | Pitch | 0.984 | | Scan FoV | Large Body (500mm) | |

Table C.2 Model-specific Parameters for Reconstruction Software

| Reconstruction Software | Settings Compatible with Conformance |
| --- | --- |
| Acme Medical  CT WS  V3.14 | |  |  | | --- | --- | | Reconstructed Slice Width, mm | 1.25 | | Reconstruction Interval | 1.0mm | | Display FOV, mm | 350 | | Recon kernel | STD | |

## Appendix D: Metrology Methods

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