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Recommendations for Measuring Pulmonary Nodules at CT: A Statement from the Fleischner Society[1]

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These recommendations for measuring pulmonary nodules at computed tomography (CT) are a statement from the Fleischner Society and, as such, incorporate the opinions of a multidisciplinary international group of thoracic radiologists, pulmonologists, surgeons, pathologists, and other specialists. The recommendations address nodule size measurements at CT, which is a topic of importance, given that all available guidelines for nodule management are essentially based on nodule size or changes thereof. The recommendations are organized according to practical questions that commonly arise when nodules are measured in routine clinical practice and are, together with their answers, summarized in a table. The recommendations include technical requirements for accurate nodule measurement, directions on how to accurately measure the size of nodules at the workstation, and directions on how to report nodule size and changes in size. The recommendations are designed to provide practical advice based on the available evidence from the literature; however, areas of uncertainty are also discussed, and topics needing future research are highlighted.

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The likelihood of malignancy in a pulmonary nodule correlates strongly with both its size and its growth rate, allowing for additional factors, such as a history of prior lung cancer or extrathoracic malignancy (1). Thus, accurate measurement of nodule size is crucial for three reasons: *(a)* to determine the risk for malignancy at baseline computed tomography (CT), *(b)* to correctly allocate patients with nodules to available management algorithms, and *(c)* to detect any change in size on follow-up CT images, which might have bearing on the likelihood of malignancy or might influence treatment in patients who are being monitored during therapy. Although nodule size is a key criterion in current recommendations for nodule management (2–4), there is relatively little information about how best to approach lung nodule measurement in clinical practice, which is the main motivation for these recommendations.

Size and growth of pulmonary nodules can be determined by measuring their diameter or volume. Measurement of the nodule diameter with electronic calipers is convenient to perform and is currently the most widely used routine clinical approach. Nodule volumes can be measured either manually by delineating nodule boundaries or semiautomatically by using software that detects CT attenuation thresholds. Semiautomatic volume determination typically requires either remote workstations or dedicated software applications; hence, it is currently not widely used in routine clinical practice (5). Automated segmentation is also the initial step underlying approaches that measure nodule mass rather than size (6); this approach has been proposed for subsolid nodules and is still under investigation.

Independent of which nodule component is measured (solid component, ground-glass component, or both) and regardless of which technical approach is used, the resulting measurement will be affected by a number of technical and observer-related factors. Moreover, serial follow-up examinations of nodules are often performed with different CT units and are assessed by different radiologists using different technical acquisition and reconstruction parameters.

In the first part of this article, we will present our recommendations for measurement of the size of pulmonary nodules. These recommendations are organized around specific questions that are often raised in clinical practice and are presented together with corresponding answers. In the second part, we will describe the technical factors, such as section thickness, reconstruction algorithms, and display window settings, that affect these measurements. There is increasing evidence that the technical aspects of these factors are closely interrelated, with cross-influences that are not yet fully understood (7,8). Although discussing them one by one might appear overly simplistic, we hope that this incremental approach will provide the reader with practically useful information to perform and interpret lung nodule measurements. In the third and final part of this article, we will highlight areas of uncertainty and ongoing investigation, focusing on questions that will need to be addressed in future research, to make lung nodule measurements more accurate and clinically meaningful.

The current recommendations can be used to measure pulmonary nodules on any given CT image. However, their use should also be determined by the clinical circumstances. For example, the recommendations are not intended to replace other measurement approaches, such as use of Lung CT Screening Reporting and Data System or Response Evaluation Criteria in Solid Tumors, which are recommended for lung cancer screening and assessment of treatment response in oncologic imaging, respectively. Furthermore, if a different approach to nodule measurement was initially chosen at serial CT, this approach should be retained for the sake of consistency.

Given the frequency with which the size of pulmonary nodules is measured in clinical practice and given the variability of these measurements between different observers (3,5,9), we believe that the need for guidelines such as these is evident. In developing these recommendations, the Fleischner Society, as a multidisciplinary group of thoracic specialists, has weighed available scientific evidence and expert consensus regarding current practice and future developments. The following recommendations will mainly focus on manual diameter measurements, which are the most widely used technique, at present. However, given the rapid technical advances in recent years, especially with respect to the role of automated image-based disease quantification, we anticipate that refinements and modifications to these recommendations will be forthcoming, as information continues to emerge from ongoing research.

Part 1: Recommendations

The recommendations are summarized in Figure 1 and Table E1 (online), organized by practical questions and the corresponding answers. The evidence grades for the individual recommendations shown are based on those developed by the American College of Chest Physicians (10).

Part 2: Technical and Observer-related Factors

Dimensions of a Pulmonary Nodule

The dimensions of a pulmonary nodule are measured differently by pathologists and radiologists. Whereas pathologists record only the maximum diameter of a nodule (11), radiologists

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Conflicts of interest are listed at the end of this article.

Figure 1

How should the dimension of a solid pulmonary nodule be expressed?
For purposes of risk estimation, the dimension of small pulmonary nodules (<10 mm) should be expressed as the average of maximal long-axis and perpendicular maximal short-axis measurements in the same plane. For larger nodules and masses, both long- and short-axis measurements should be recorded (grade 2B evidence).
How should part-solid nodules be measured?
As with solid nodules, the average of the long and short dimensions of the nodule, including ground-glass and any cystic components, should be measured and recorded for smaller nodules (<10 mm). For larger nodules, both long and short dimensions should be recorded. For all part-solid nodules, the maximum diameter of the solid component should be measured if this component is >3 mm, understanding that measurements may be unreliable for small solid components. Dimensions of both solid and nonsolid components should be recorded to document change in the future (grade 2B evidence).
Which measurement unit should be used?
Measurements and averages should be expressed to the nearest whole millimeter (grade 1B evidence).
Should the dimension of every pulmonary nodule be measured?
No, small nodules <3 mm should not be measured due to accuracy limitations. Descriptors such as "micronodule" are preferable. Also, when multiple nodules are present, only the largest or morphologically most suspicious nodules need be measured. The location of each measured nodule should be explicitly referenced in the report (grade 1C evidence).
What CT section thickness should be used for measuring lung nodules?
Critical measurements for small (<10 mm) lung nodules and small solid components should be obtained by using contiguously reconstructed sections with a thickness ≤1.5 mm. Larger nodules and masses can usually be measured adequately on thicker sections (grade 1B evidence).
What should the section orientation be?
Measurements should be performed on transverse (axial) sections, unless the maximal dimensions lie in a coronal or sagittal plane, in which case the measurements should be made in those planes and this should be documented in the radiologic report. Measurement on off-axis oblique reformations are difficult to reproduce and thus are not recommended (grade 2B evidence).
Which reconstruction algorithm should be used?
A high-spatial-frequency (sharp) filter should be used when measuring nodules <10 mm. For nodules ≥10 mm, the reconstruction algorithm has no substantial effect on measurement accuracy (grade 1C evidence).
Which display window settings should be used?
Although a soft-tissue window can be useful when evaluating changes in nodule density over time, lung nodules, including the solid portion of part-solid nodules, should be measured on lung windows by using a high-spatial-frequency (sharp) filter (grade 2B evidence).
Which dose settings and image noise reduction algorithms can be used?
Dose reduction techniques are appropriate up to a point at which significant loss of image quality occurs. Evidence suggests that excessive radiation dose reduction and image noise reduction algorithms can have a significant effect on the accuracy of pulmonary nodule measurements. The clinical implications of this effect are under investigation (grade 2B evidence).
At which lung volume should CT examinations for the measurement of lung nodules be acquired?
CT examinations to measure lung nodules should be acquired at full inspiration (grade 2B evidence).
When can a pulmonary nodule be stated to have changed in size?
A pulmonary nodule can be determined to have changed in size when its average diameter has increased or decreased by at least 2 mm (rounded to the nearest millimeter). Smaller changes in measured diameter can be spurious, especially for ill-defined nodules (grade 2A evidence) and do not reliably indicate change.
Which previous CT examination should be used for comparison when evaluating for potential growth?
Although the last available examination should be used as a reference to determine interval growth, comparisons with earlier prior examinations will increase reader confidence and accuracy when evaluating the longitudinal evolution of a given nodule (grade 1 evidence).

Figure 1: Recommendations for measurement of the size of pulmonary nodules.

Figure 2

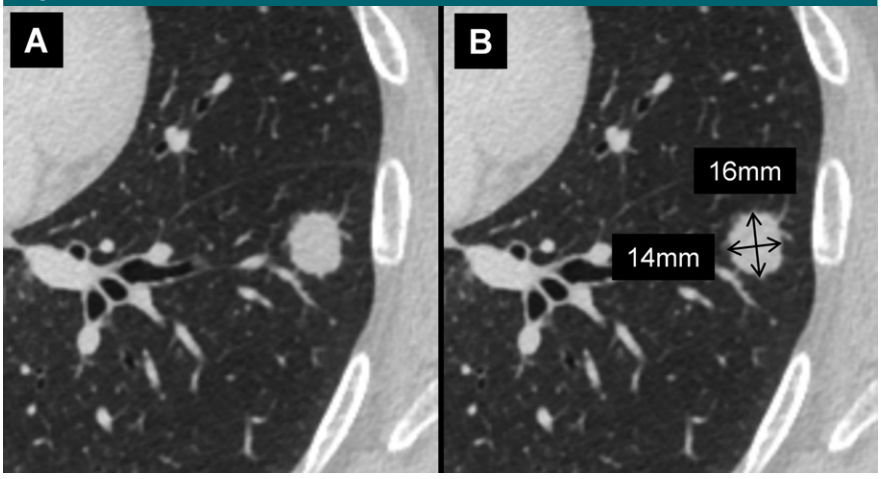

Figure 2: Transverse CT sections of a solid nodule in the left lower lobe. *A,* The nodule is anatomically well defined. *B,* First, the maximal long-axis diameter is measured (16 mm, vertical arrow). Then, perpendicular to the long-axis measurement, the maximum short-axis diameter is measured (14 mm, horizontal arrow). The average diameter of the nodule is 15 mm. As detailed in the first recommendation, for purposes of risk estimation, the dimension of small pulmonary nodules (<10 mm) should be expressed as the average of maximal long-axis and perpendicular maximal short-axis measurements in the same plane. For larger nodules and masses (≥10 mm), long- and short-axis measurements should be recorded. Because the average diameter of this nodule is larger than 10 mm, both long- and short-axis measurements are given.

Figure 3

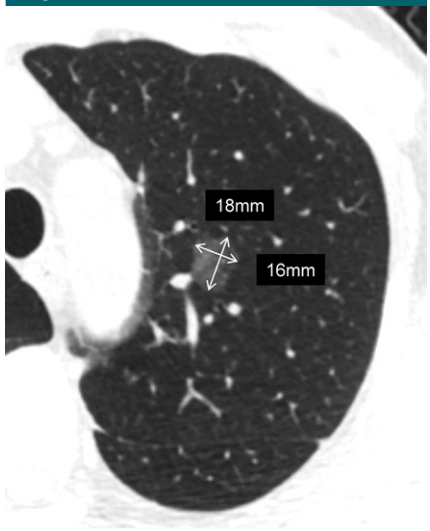

Figure 3: Transverse CT section of a pure ground-glass nodule in the left upper lobe. The same approach to nodule measurement described in Figure 2 applies in this image. The average diameter of the nodule is 17 mm.

have been expressing the dimensions of small (<10 mm) nodules as the average of the long- and short-axis measurements, notably when they are used for risk assessment (2,12). For larger nodules, particularly for staging, bidimensional measurements reporting both long- and short-axis diameter are the most commonly used (Figs 2, 3). Given the importance of nodule dimensions for management recommendations and oncologic staging and the increasingly collaborative approach to pulmonary nodules in the fields of pathology and radiology (11,13,14), more research is needed to establish which CT parameter most closely correlates with final stage and outcome.

Historically, the transition in radiology from using the maximum diameter to using the average of long- and short-axis diameters of small nodules for risk assessment occurred in the late 1990s, when the latter approach was adopted by the Early Lung Cancer Action Program (15). The same approach was described in the first management guidelines for pulmonary nodules published by the Fleischner Society (2). Finally, the American College of Radiology recommends use of the average dimension in its current CT lung cancer screening guidelines (16). Although the National Lung Cancer Screening Trial used the maximum dimension rather than the average dimension (17,18), it has been suggested that this could have resulted in the misclassification of nodules as positive findings, most notably when the nodules were small (12,19). This is supported by the findings of three recent studies that retrospectively applied American College of Radiology Lung CT Screening Reporting and Data System criteria to large lung cancer screening cohorts; this reduced the false-positive rate in all three studies (20–22). We continue to use the average dimensions in the upcoming revision of the Fleischner Society management guidelines for pulmonary nodules (23) because we assume that the average dimension likely correlates better with tumor volume than one measurement, particularly in elongated nodules and in nodules where the short dimension is better defined (5). In practical terms, we recommend that the long-axis diameter of a nodule be determined first and that thereafter, on the same CT section, the short axis be measured perpendicular to the long axis. Recommendations for measuring spiculated and morphologically heterogeneous nodules are detailed in the next sections.

Measurement Unit

All measurements and their derivatives should be expressed to the nearest millimeter, which is the basic dimensional unit used in current nodule management guidelines (2,3,23). Although picture archiving and communication system consoles display measurements to the nearest 0.1 mm, we believe that this level of apparent precision is deceptive in the context of pulmonary nodules and given the multiple technical factors that influence their measurements. Consequently, a nodule with a long-axis diameter of 4.5 mm should be rounded to 5 mm. Likewise, a nodule with a short-axis diameter of 3.4 mm should be rounded to 3 mm. Thus, the average diameter of the nodule would be as follows: (5 + 3)/2 = 4 mm. If the mathematic average of the

Figure 4

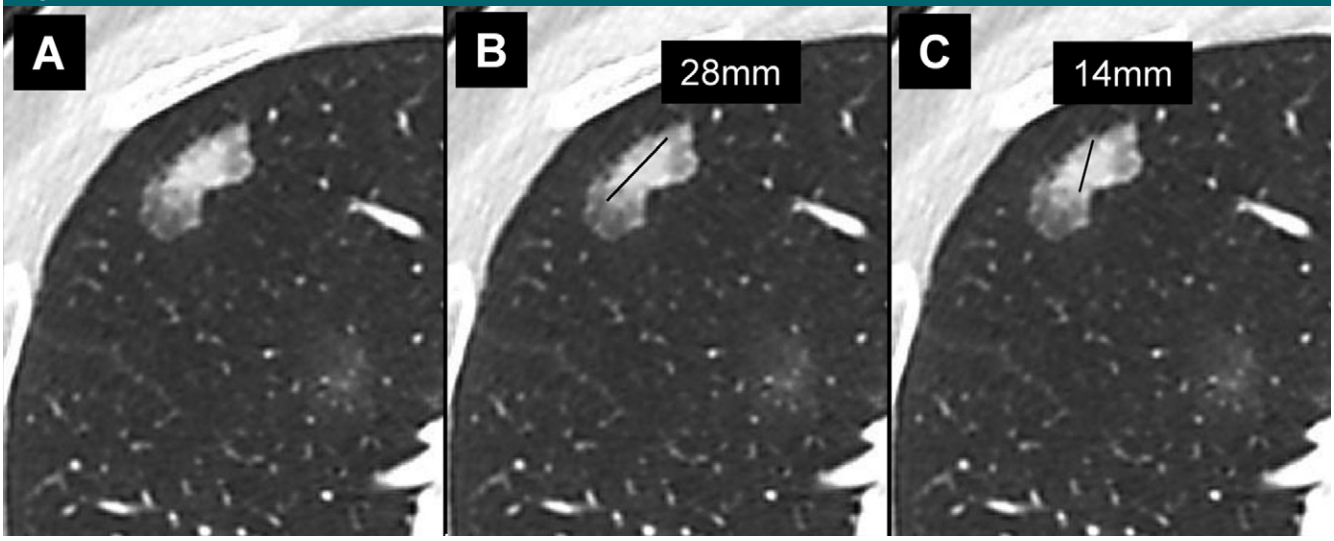

Figure 4: Transverse CT sections of a part-solid nodule in the right upper lobe. *A,* The solid component of the nodule is ill defined, resulting in variability of measurements, as performed by two radiologists. The two long-axis diameters of the solid component were, *B,* 28 mm and, *C,* 14 mm. On the basis of the clinical implications, we recommend use of the larger long-axis diameter. Only solid component measurements are shown in this figure; however, in clinical practice, nonsolid and solid components must be measured.

long- and short-axis diameters results in a number with a decimal fraction, it should similarly be rounded to the nearest whole millimeter. Recorded long- and short-axis diameters should also be rounded to the nearest millimeter. To estimate average diameter based on manual measurements or obtained with automated measurement tools, fractional measurements may be considered, but the result should still be recorded as a whole number.

Observer and Measurement Variability

Measurement of nodule diameter with electronic calipers is subject to substantial inter- and intrareader variability (24–26) (Fig 4). Studies also suggest that variability increases with increasing complexity of nodule morphology, notably in part-solid nodules in which both the overall size and the size of the solid component are measured (3,5,9). One study showed that when observers measured nodules 20 mm in diameter or smaller, the limits of inter- and intrareader variability were 1.73 mm and 1.32 mm, respectively (26). This would mean that a nodule could confidently be determined to have grown only if its diameter had increased beyond these limits. For example, because a 26% increase in diameter of a spherical nodule corresponds to one volume doubling (27), it could be falsely concluded that a nodule measuring 5.0 mm at baseline and then 6.3 mm at follow-up had doubled in volume, while this apparent growth could be an artifact of measurement variability. In the same way, measurement variability may result in growing nodules being falsely determined to be stable.

Nodule volumetry may be less sensitive to variability depending on the method used. While the majority of volumetric measurements showed a variability of less than 10%, a maximum deviation up to approximately 27% has been reported in nodules with irregular margins and nonspherical morphology, causing more variable segmentation (28,29). When the mass of part-solid nodules is measured, inter- and intraobserver variability ranges from −17.5% to 11.8% and from −8.4% to 9.4% (9,30). It must be stressed that all of these reported results strongly depend on the software used and the characteristics of the study lesions; this is a caveat that can be applied to any computerized quantification tool. Despite these generally encouraging results for semiautomated nodule volume and mass measurements, it should be kept in mind that different software implementations can yield substantially different results (30,31) (Fig 5). Thus, from a practical perspective, it is desirable to perform sequential nodule evaluations with the identical software type and version.

From a clinical perspective, several practical recommendations should be added. First, not every nodule needs to be measured, notably nodules of up to 3 mm in size. Such small nodules are impossible to measure accurately, and observer variability is prone to produce erroneous and potentially misleading results, both at initial assessment and at follow-up (Fig 6). For such nodules, it is preferable to omit any caliper measurements and instead use the term *micronodule* to describe such a finding (32). Second, when performing sequential follow-up examinations of nodules, reference should always be made to the examination that first revealed the nodule, not just the last available examination. In this regard, it is important to take into account changes in nodule appearance that may occur due to variations

Figure 5

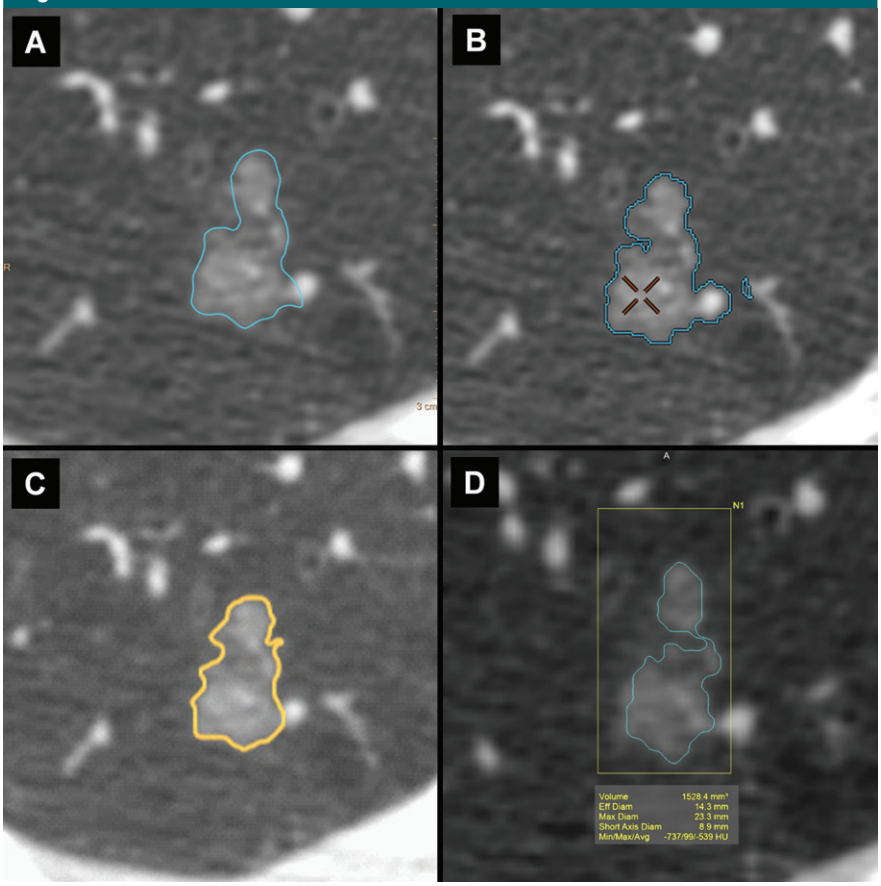

Figure 5: Segmentation and volumetry of a ground-glass nodule with four different software packages. The nodule volumes calculated were, *A,* 2019, *B,* 2059, *C,* 1949, and, *D,* 1528 mm^3, resulting in a maximum difference of 531 mm^3 between measurements.

in inspiratory effort or the appearance of adjacent parenchymal abnormalities. Although the last available examination will be used as the reference to determine interval growth, comparisons with earlier prior examinations will increase confidence for long-term growth or stability when evaluating the evolution of a given nodule over time (Figs 7, 8). Third, when performing simple attenuation measurements by placing a region of interest over a nodule or when calculating an attenuation profile along a line through a nodule—for example, to verify the presence of calcium or fat—this should be done on images reconstructed without edge enhancement, typically the mediastinal soft-tissue series. This is because such attenuation measurements are prone to substantial inaccuracy in smaller nodules on sharpened (edge-enhanced) images. Finally, measurements at follow-up CT, which were acquired with techniques that were as similar as possible to the original technique, should be made through the centroid of the nodule, which may not be at the same anatomic level on sequential images, and by using the same orientation and location of caliper anchor points.

Definition of Growth

Growth of a pulmonary nodule refers to an increase in size between two given CT examinations. In the context of bidimensional measurements, this will translate into an increase in diameter. Because this is a three-dimensional structure, however, the increase in diameter should reflect an increase in nodule volume. If we assume a perfectly spherical geometry, a 26% increase in diameter will correspond to a doubling in the volume of a nodule (27). For example, a nodule that has increased in diameter by 2 mm (from 7 mm to 9 mm) between two CT examinations has approximately doubled its volume. Given that diameter measurements vary by 1.73 mm across observers for nodules smaller than 2 cm (26), it appears reasonable to report growth when a change in measured diameter of at least 2 mm is detected (actually at least 1.5 mm due to rounding). Use of this 2-mm threshold would reduce the likelihood of an incorrect diagnosis of growth when the apparent difference in size is in fact within an expected range of uncertainty owing to observer-related imprecision. Moreover, several relatively recent studies have used a 2-mm threshold to define growth in both solid and part-solid nodules (33–35). A 2-mm threshold for growth was also adopted by The British Thoracic Society in a recent management recommendation (4). Furthermore, a threshold in millimeters is consistent with the principle of this recommendation to express nodule dimensions to the nearest millimeter and to avoid any fractions of this unit (16). The 2-mm threshold for defining growth should be applied to both overall nodule size in both solid and part-solid nodules, as well as to the solid component of a part-solid nodule. Although nodule growth is important, it is just one of several criteria used to estimate cancer risk. Thus, it must be reemphasized that any change in nodule size, including growth as defined previously, must always be interpreted together with other morphologic nodule characteristics, such as shape, borders, and internal texture (Fig 9). Finally, potential growth must be related to the interval between two CT examinations. A recent recommendation has emphasized that accuracy of growth assessment increases with increasing intervals between examinations (4).

Attenuation Measurements

There has been recent interest in using CT attenuation to assess the mass

(which reflects the product of size and attenuation) rather than the size of pulmonary nodules (6). CT attenuation has also been used to assess growth of part-solid and nonsolid pulmonary nodules (36,37). Both overall attenuation and characteristics of the attenuation distribution within nodules have been used to differentiate adenocarcinoma subtypes, evaluate progression, and predict prognosis, notably in part-solid nodules (38–42). These studies provide promising preliminary insights into the potential of attenuation measurement as a tool to assess pulmonary nodules more accurately. However, the published series are small, and no study derived a generalizable attenuation threshold or a metric that could be seamlessly translated into clinical practice, and the proposed attenuation thresholds differ between studies (42–44). Thus, more evidence, notably with regard to measurement standardization and the pathologic implications of attenuation changes over time, is required before use of these techniques can be recommended for clinical lung nodule management.

Figure 6

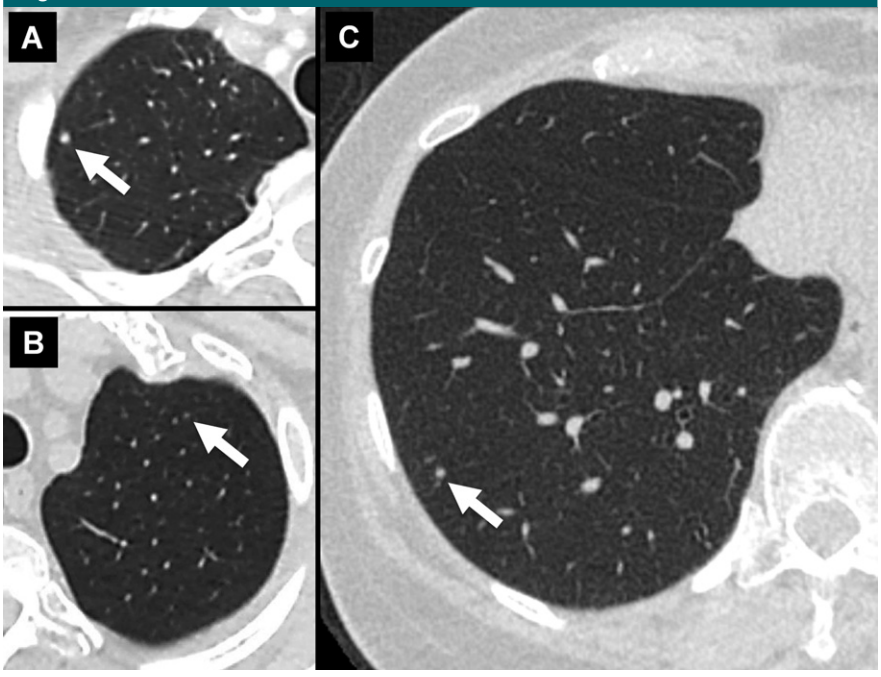

Figure 6: Transverse CT sections through nodules 3 mm or smaller (arrow) in the, *A,* right upper lobe, *B,* left upper lobe, and, *C,* right lower lobe. Such small nodules should not be measured, given inherent accuracy limitations and variability in determining whether the lesion is a solid, part-solid, or ground-glass nodule.

CT Section Thickness

Several authors have studied the relationship between the accuracy of nodule measurement and CT section thickness (31,45–47). They consistently found that variability decreased with decreasing section thickness (31,45,46) and that the thinnest sections (usually 1 mm) provided the most consistent results (47). The studies also found that the effect of section thickness on variability was particularly pronounced for nodules smaller than 10 mm and for spiculated rather than smooth nodules (31). This can be explained by the increased partial volume averaging effect for small nodules when thicker sections are used, whereas the same effect is less severe with larger nodules. From a practical perspective, these findings support the use of contiguous thin (≤1.5 mm) sections for the purpose

Figure 7

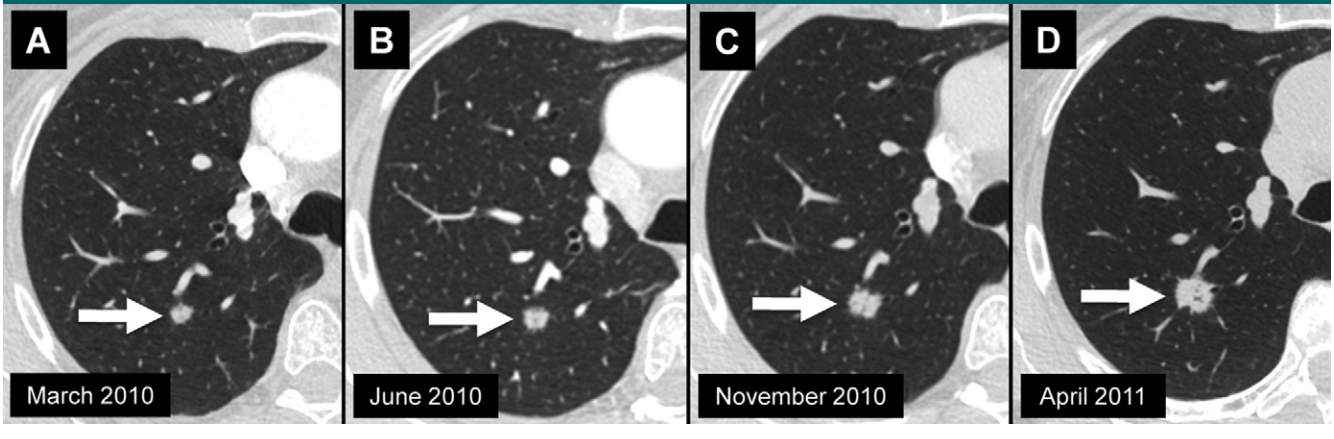

Figure 7: Sequential transverse CT sections through a solid nodule (arrow) in the right upper lobe. Average diameters of the nodule were, *A,* 8, *B,* 9, *C,* 11, and, *D,* 13 mm. Nodule growth is most obvious when we compare the earliest image with the most recent image. Surgery confirmed adenocarcinoma.

Figure 8

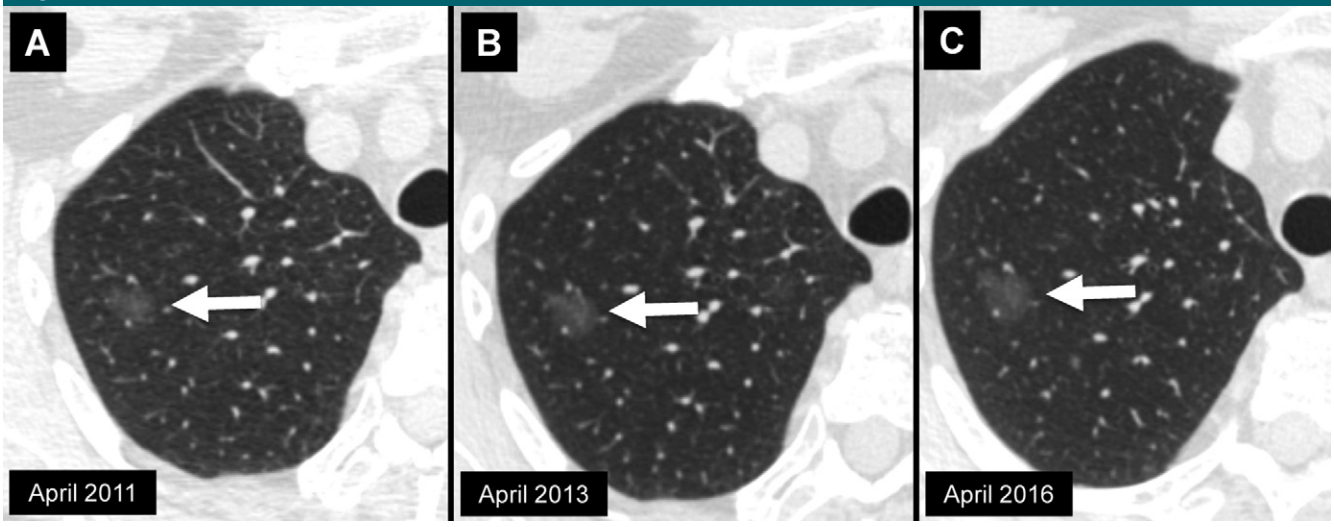

Figure 8: Sequential transverse CT sections through a ground-glass nodule (arrow) in the right upper lobe. Average diameters of the nodule are *A,* 13, *B,* 14, and, *C,* 18 mm. Nodule growth is most obvious when we compare the earliest image with the most recent image.

of small lung nodule measurements, as recommended by current clinical guidelines (23). For spiculated nodules, only the nodule core should be measured, and the spiculations should not be part of the measured diameter (Fig 10). Thin sections also provide the advantage of sufficient spatial resolution to allow for the visual assessment of morphologic nodule characteristics, such as shape and spiculations, that might refine the assessment of risk and subtle changes over time (5) (Fig 11).

Orientation of the CT Section

Transverse reconstructions of the CT data set constitute the traditional basis for clinical reporting of thoracic CT examinations, and most nodule measurements can be performed through a transverse plane, with the maximal long axis and maximal perpendicular short axis measured on the same image. A given nodule, however, may be oriented in the lung parenchyma such that its biggest or smallest diameter is aligned along a craniocaudal axis, making its true extent difficult to assess on transverse images alone. In such cases, multiplanar reconstructions in the coronal and sagittal planes should be used to obtain a more accurate assessment of nodule size, with long and short axes again measured on the same image (Fig 12). In part-solid nodules, the CT sections should be chosen for measurements that display the largest portion of the overall nodule and the solid component, respectively. Often, these will not be displayed on the same section. In such cases, measurements should be performed on the sections that display the largest overall nodule diameter and the largest diameter of the solid component, respectively, and these sections should be identified in the radiologic report (Fig 13). While

Figure 9

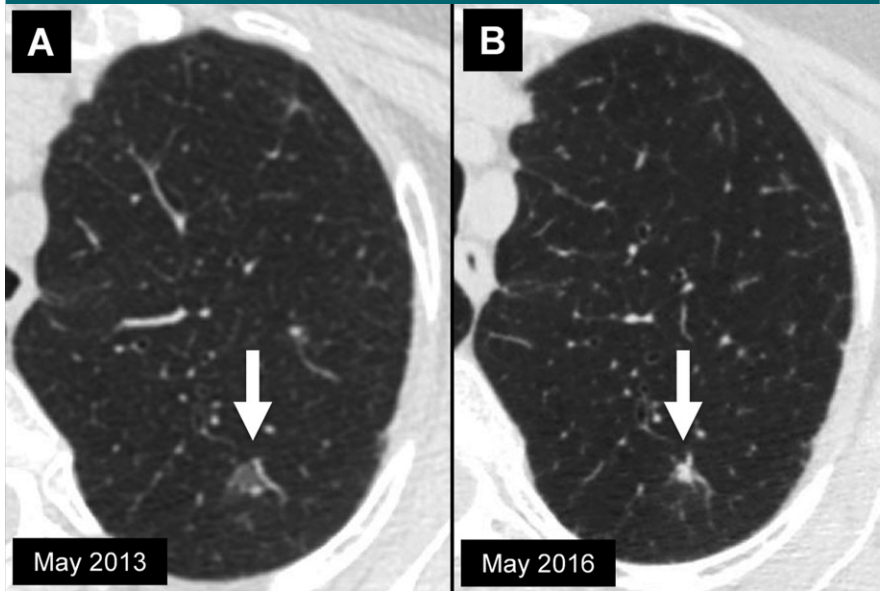

Figure 9: Sequential transverse CT sections of a nodule (arrow) in the left upper lobe. Although the average diameter of the nodule has decreased from, *A,* 13 to, *B,* 8 mm, solid transformation and irregular margins make it suspicious. Later resection confirmed invasive adenocarcinoma.

Figure 10

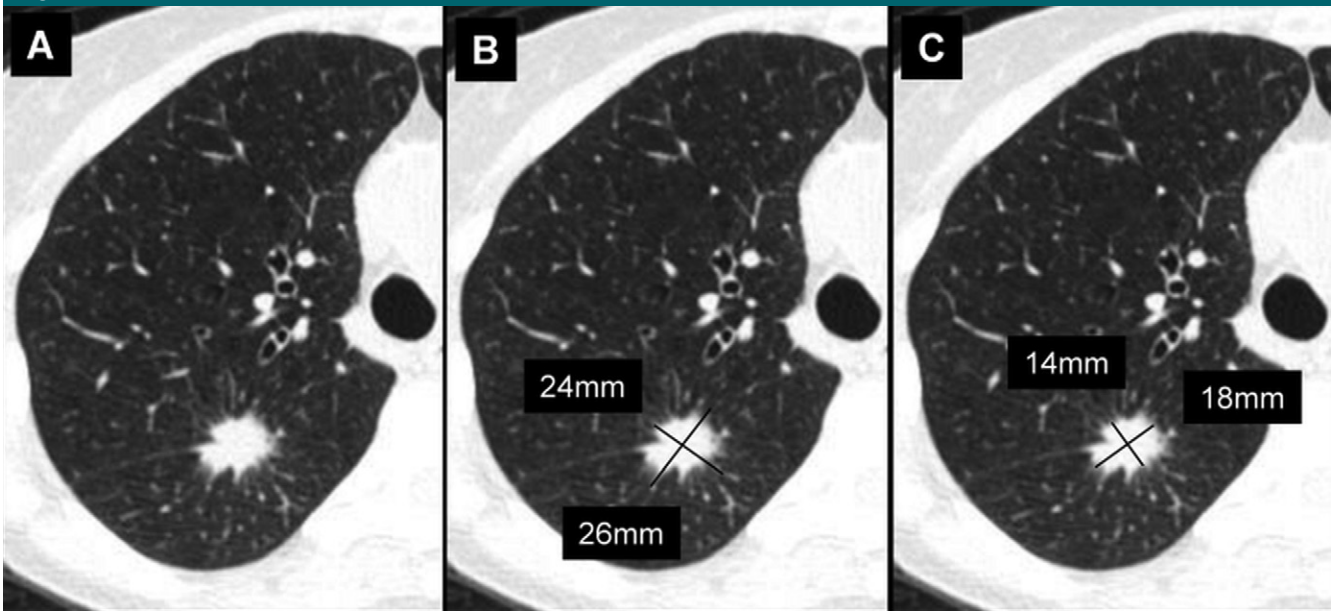

Figure 10: *A,* Transverse CT section through a spiculated right lung nodule. *B,* Inclusion of spiculations into the measurement causes substantial overestimation of nodule size. *C*, The recommended approach is to measure only the solid core.

oblique reformations might allow longer long axis or shorter short axis measurements than do the traditional anatomic planes, the challenge of reproducing the same degree of obliquity for serial examinations hinders the generalizability of this method; thus, off-axis oblique reformations are not recommended.

Reconstruction Algorithm and Field of View

The effect of reconstruction algorithm and field of view on the accuracy of lung nodule measurements is controversial. Several published studies failed to show a significant effect of either one on the accuracy of lung nodule measurements (45–47,48), while other studies that did report significant effects provided conflicting results, suggesting that either high-spatial-frequency algorithms (49) or low-spatial-frequency algorithms (47) yield the most repeatable results. However, the weight of evidence suggests that for nodules smaller than 10 mm, the reconstruction algorithm does effect measurement accuracy (23,46,48) and that a high-frequency (sharp) algorithm is likely to yield the most accurate measurement results, whereas for nodules larger than 10 mm, the choice of reconstruction algorithm has no significant effect on measurement accuracy.

Display Window Settings

The effect of display window setting on the apparent size of pulmonary nodules is well established, particularly in the case of subsolid nodules. Most previous studies investigating the accuracy and variability of lung nodule measurements have been performed by using wide (lung) window settings (window level range, −700 to −500 HU; window width range, 1500–2000 HU). This is because the overall size of subsolid lesions in particular appears artificially smaller when soft-tissue (mediastinal) window settings (window level range, 30–70 HU; window width range, 350–400 HU) are used because of low-attenuation (ground-glass) components falling below the narrower range of displayed attenuation values (3,13) (Fig 14). In the past, however, soft-tissue windows have been systematically applied in combination with lung windows to determine the so-called tumor disappearance rate of part-solid nodules (ie, the ratio between the nodule portion seen on soft-tissue windows and the nodule portion seen on lung windows) (49). Although the tumor disappearance rate has shown promise in optimizing the surgical approach of invasive nodule components (49), the terminology can be misleading when referring to the assessment of nodule size by suggesting that a part of the nodule resolves, while in reality it is merely rendered invisible by a technical maneuver. Note that although the window setting does not affect attenuation measurements, a sharp lung filter can substantially affect attenuation measurements in unpredictable ways. Thus, only unsharpened images should be used to measure attenuation.

The current literature on nodule measurement with lung and mediastinal display window settings reflects considerable controversy. In a study of 43 patients, the authors (50) found that tumor size measured on images obtained with lung windows correlated better with histologic measurements. The same authors also noted that tumor size was a better predictor of

advanced disease when measured on mediastinal rather than lung windows. However, separate measurements of the solid component on images obtained with lung windows were not performed. In a study including 52 patients, the authors found no significant differences between the invasive tumor component and the solid portions, as measured on images obtained with lung and mediastinal windows, respectively (51). In another study including 58 patients, the authors (52) also found that interobserver agreement was slightly better with mediastinal window settings than with lung window settings. Finally, this same study found that measuring the solid component of nodules with lung windows yielded a stronger correlation with histologic evidence of tumor invasion than when the measurements were performed with mediastinal windows.

Although it has been suggested that mediastinal window settings may perform better than lung window settings when used to assess the size of the solid component (3), there is little data on the comparison of these two approaches. Data for minimally invasive adenocarcinomas and small lung adenocarcinomas suggest that lung window measurements may yield results that are closer to pathologic measurements (41,51,52) and that use of mediastinal window settings may result in underestimation of invasive size (51). When interobserver agreement and accuracy were compared with histology in subsolid nodules with a solid component smaller than 8 mm, lung window settings had comparable reproducibility but higher accuracy than did mediastinal window settings (53). At the present time, expert opinion tends to favor use of lung window settings to detect and measure solid components in subsolid nodules. Thus, we recommend use of a lung window setting with a high-spatial-frequency (sharp) algorithm for solid component nodule measurements, while we recognize that this deviates from previous recommendations (3) (Fig 15). What appears solid on images obtained with lung window settings and high-spatial-frequency reconstructions should be considered as such (54) (Fig 16).

Figure 11

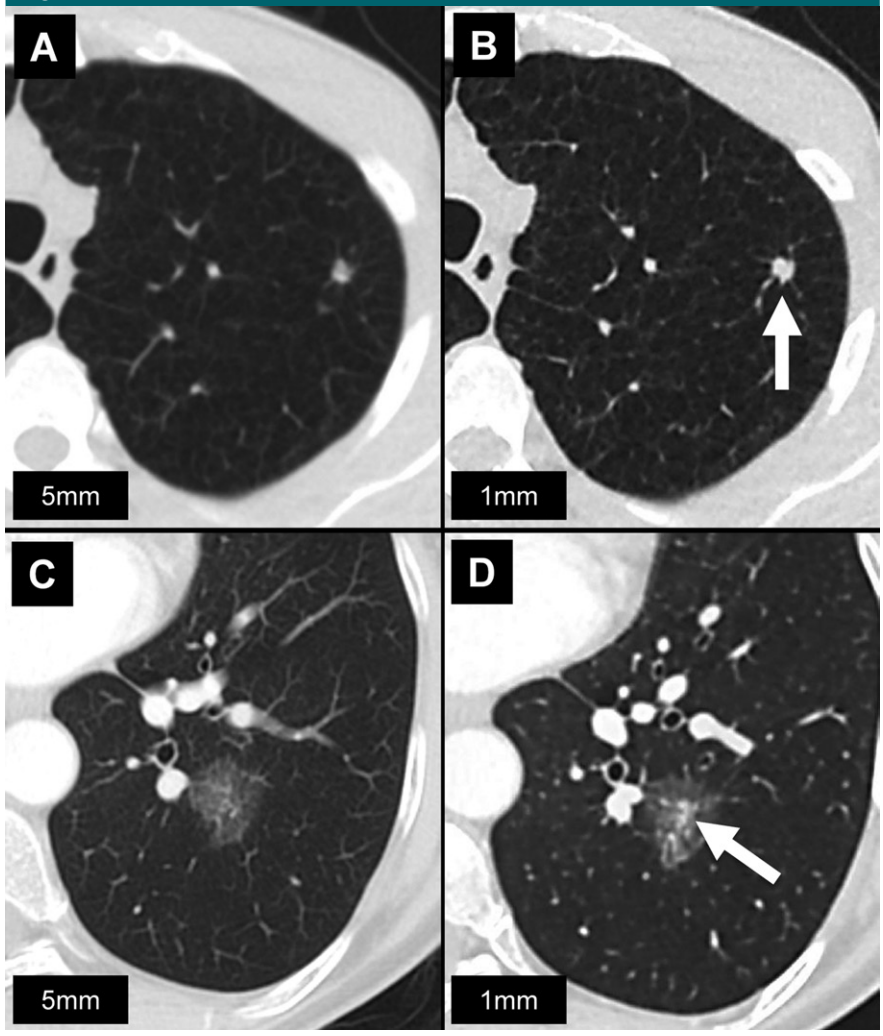

Figure 11: Transverse CT sections at the level of, *A, B,* a solid nodule (arrow) in the left upper lobe and, *C, D,* a part-solid nodule (arrow) in the left lower lobe. Solid and part-solid nodule margins are less well defined on *A* and *C* than on *B* and *D*. In addition, *D* better shows solid nodule components.

Radiation Dose and Image Noise-reduction Algorithms

Tube current settings are determined by the trade-off between a desire to minimize radiation dose and a competing desire to maintain image quality. Several studies have concluded that substantial reductions in radiation dose can be achieved without adversely affecting nodule measurement accuracy (5). However, the effect of radiation dose on volumetric measurement error has been difficult to establish, with many studies failing to demonstrate a significant difference between nodule measurements made across a spectrum of exposure levels (48,54–57). Nevertheless, excessive dose reduction affects image quality by degrading nodule boundary definition. The magnitude of these effects will vary depending on overall body habitus and on the size, morphology, and location of the nodule, thereby making generalizable recommendations regarding minimum radiation exposure levels particularly challenging; however, one general rule for achieving consistent image quality is to tailor imaging technique to patient size. The use of iterative reconstruction algorithms can also

Figure 12

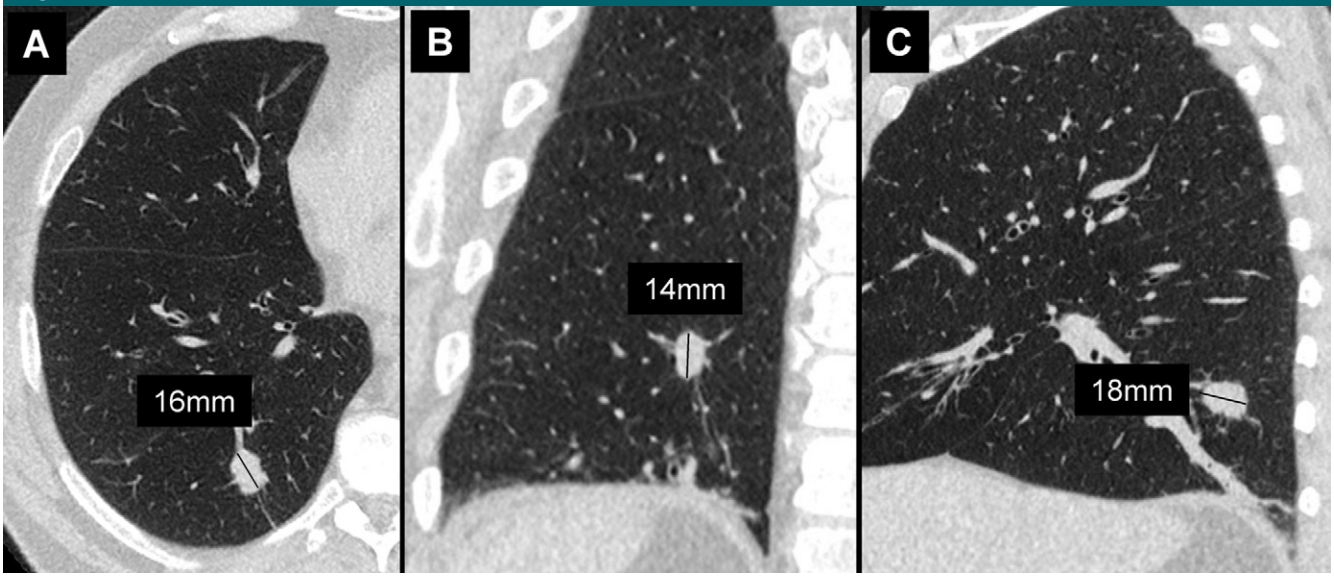

Figure 12: *A,* Transverse, *B,* coronal, and, *C,* sagittal reconstruction planes through a pulmonary nodule in the right lower lobe. The long-axis diameter of the nodule was 16, 14, and 18 mm in *A*, *B*, and *C*, respectively. Thus, long- and short-axis nodule diameters should be measured in the sagittal plane in this patient.

affect the accuracy of nodule dimension measurements (7), particularly ground-glass components; however, more data are needed to assess the effect of the many variations of iterative reconstruction algorithms currently implemented by various CT manufacturers.

Lung Volume

One study measured both the diameter and the volume of lung nodules on CT images acquired at total lung capacity and residual volume (55). The researchers found that both nodule diameter and nodule volume varied nonuniformly from total lung capacity to residual volume, with some nodules decreasing in size and other nodules increasing. There was a 16.8% mean change in absolute volume across all nodules. When stratified by size, the mean of the absolute percentage volume change for nodules larger than 5 mm and that for nodules 5 mm or smaller was not significantly different (P = .26) (55). Although not acquired at total lung capacity and functional residual capacity, other studies also observed significant, albeit small, absolute differences in nodule size when measured at different lung volumes (56,57). In practice, standardized breathing commands are likely to provide reasonably reproducible lung volumes on serial CT images (58).

Part-Solid Lesions with Several Solid Components

Part-solid lesions with several solid components can pose a particular challenge, as there currently is no consensus on how the solid components of these lesions should be measured. One possible approach is to determine the single largest focus and measure it, while reporting but not measuring the remaining foci (Fig 17). An alternative approach was recently used (59) to measure the invasive component of part-solid adenocarcinomas on pathology slides. In this study, the researchers measured all nonlepidic components and expressed their sum as a percentage of the overall tumor volume, which they multiplied by the total nodule diameter to arrive at a linear measurement. Thus, a 25% solid component in a 20-mm nodule would correspond to a 5-mm diameter. Although this approach has some merit, it has not been used or tested in the context of CT images, it would be time consuming, and it would require highly subjective estimates. Currently, the practice in pathology is to measure only the greatest dimension of the largest solid component. Thus, although additional volumetric or bidimensional measurements have merit, at a minimum, we recommend measuring the long axis of the largest solid component on images reconstructed with a high-frequency algorithm and displayed on a lung window image to enable direct comparison with pathologic measurements. If the result is greater than 5 mm, invasion may be considered more likely (54).

Part 3: Directions for Future Research

Maximum Diameter or Average of Long- and Short-Axis Measurements?

Whereas pathologists express nodule size as the maximum diameter, radiologists have transitioned to expressing the size of small pulmonary nodules as the average of long- and short-axis measurements. Currently, there is no evidence from prospective multicenter studies about the relationship between these two approaches or about which approach will yield more robust predictive information. In this context, it is important to emphasize that pathologists measure nodule size primarily

for staging (11), whereas radiologists measure nodule size primarily for allocation into risk categories (2). It also must be emphasized that pathology measurements are not well standardized. Indeed, the previous 4th edition to the TNM supplement states: "Neither in the TNM classification nor in the 1st to 3rd edition of the TNM supplement are any statements concerning the way to measure tumor size for pT classification." According to the American Joint Committee on Cancer Cancer Staging Manual 2009, pT is derived from the actual measurement of the unfixed tumor in the surgical specimen. It should be noted, however, that up to 30% of shrinkage of soft tissues may occur in the resected specimen. Thus, in cases of discrepancies of clinically and pathologically detected tumor size, the clinical measurement should also be used for pT classification (60). This statement underlines not only the lack of standardization of pathology measurement, but also the importance of close interaction between pathology and radiology with regard to assessment of nodule dimensions, given the known limitations of both methods. Although the effect of formalin fixation on the size of small lung cancers has been investigated (61), there is no evidence as to how the amount of shrinkage will affect in vivo CT measurements of a resected nodule. Correlations between CT images and resected lung tumors have been investigated (62), but the series are small and no information on prognostic implications has been provided. Finally, there is recent preliminary evidence that the degree of sphericity of small lung tumors is potentially related to outcome, with less spherical nodules showing improved prognosis (63). This would support undertaking future investigation on potential advantages of providing more than one number for the dimensions of a nodule. Inevitably, these studies will have to be focused not only on measurement precision and validation, but also on outcomes, to frame the results of technical measurements into a predictive clinical context.

Figure 13

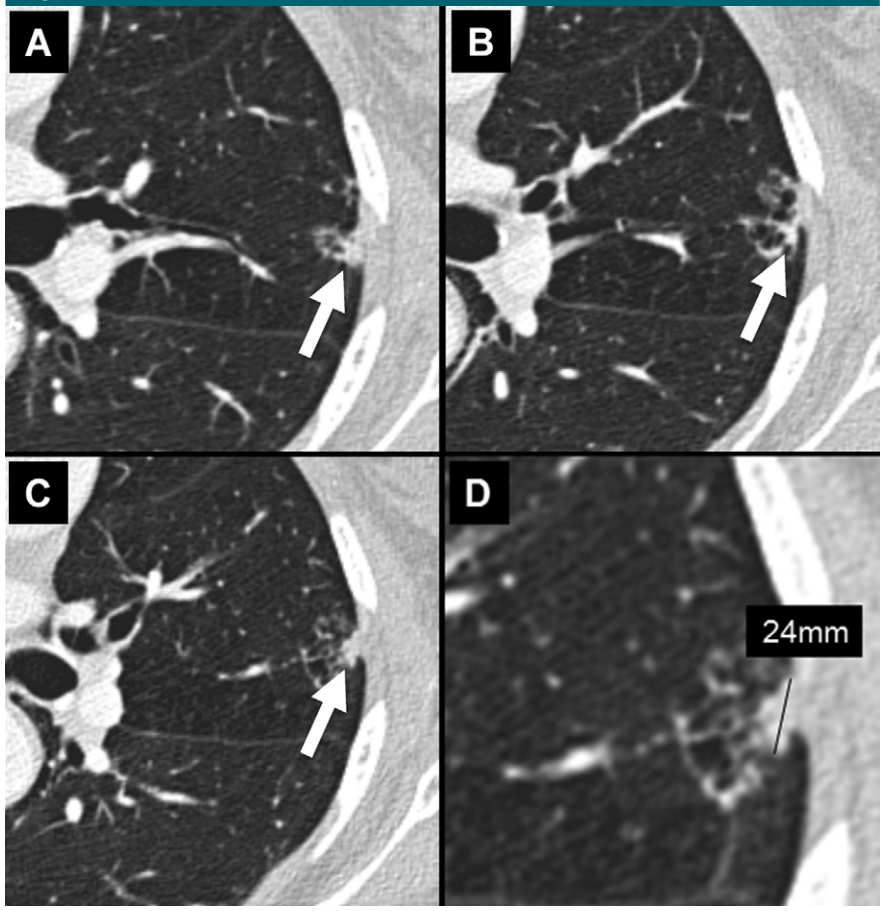

Figure 13: Transverse CT sections through a complex adenocarcinoma with cystic components in the lingula. Measurement of the solid component is challenging in such cases. *A–C*, The length of the largest substantial solid component is indicated (arrow) in each of three representative sections through the nodule. The morphologic complexity and the fact that the nodule abuts the chest wall make measurements difficult. The walls of cystic components may contain some solid elements, but accurate or consistent measurement of such components is often impossible with manual techniques. We recommend selecting the largest nodular solid component for measurement, as shown in *C. D,* Detailed view of the nodule shows placement of the measurement anchor points.

Is Automated Nodule Measurement a Remedy?

Both the advantages and the drawbacks of automated or semiautomated quantitative lung nodule assessment (64) and the uncertainties inherent to using CT as a measurement tool (65) have recently been summarized in the literature. While providing advantages in terms of measurement consistency, mostly due to less human interaction, the results generated by quantitative nodule assessment still depend on a spectrum of technical factors, including section thickness, reconstruction interval, number of detectors, x-ray beam energy, application of radiation-reducing exposure variation, and presence or absence of contrast material (64). Moreover, it has been shown that the results generated by quantitative nodule assessment yield substantially different results depending on the software package and the CT acquisition parameters used (30). Two recent studies investigated the effects of dose and reconstruction algorithms on lung nodule measurements (7,8). One of these

Figure 14

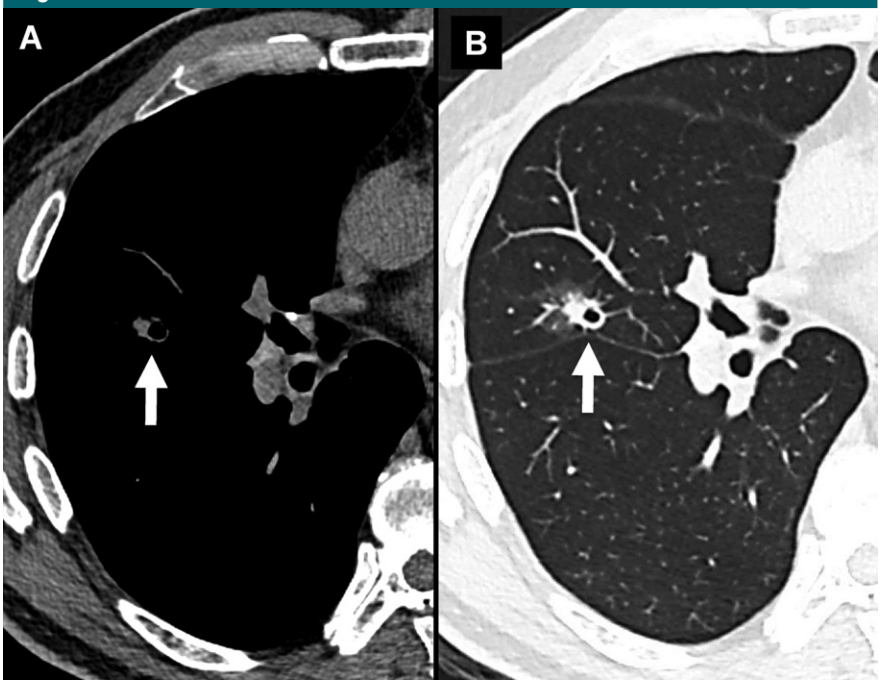

Figure 14: Transverse CT sections through a nodule (arrow) in the right upper lobe. *A,* Image obtained with the mediastinal window setting shows only the core of the solid nodule component. *B,* Image obtained with lung window settings shows the entire solid component and the cystic and ground-glass components of the nodule. Thus, all nodule measurements should be performed on images obtained with lung window settings.

Figure 15

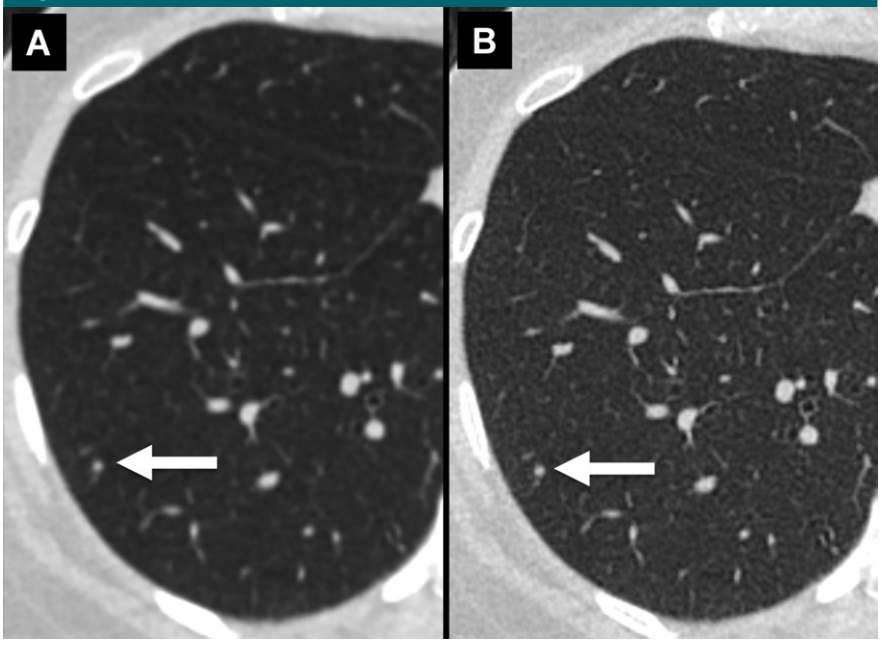

Figure 15: Transverse CT sections through a small nodule in the right lower lobe (same nodule as in 6, *C*) reconstructed, *A,* without and, *B,* with a high-spatial-frequency (sharp) filter. If all other technical parameters are kept equal, image reconstruction with this filter improves visibility of anatomic detail, notably in the pulmonary nodule (arrow).

studies showed that radiation dose had a significant effect on size, conspicuity, and intralesion pixel distribution when evaluating lung nodules (8). This same study also showed that, when compared with filtered back projection, a model-based iterative reconstruction algorithm had a significant effect on objective measurements of lung nodule size, attenuation, and texture (8). Moreover, reconstruction of simulated monochromatic energy levels with dual-energy CT resulted in the measurement of significantly different CT numbers (7). This is particularly relevant if the use of different dual-energy CT platforms for serial examinations results in changes in measured CT attenuation characteristics that are erroneously attributed to actual changes in tumor attenuation or texture. The implications of these studies are substantial. When one considers the multitude of reconstruction algorithms on the market and the proprietary nature of their technical design, it is likely that the so-called black box nature of these algorithms influences lung nodule measurement in ways that are difficult to quantify. These implications apply not only to mere size assessment of nodules, but also to measures of their volume and CT characteristics of their internal matrix. Overall, before automated or semiautomated quantitative lung nodule assessment can be generally recommended, the factors causing variability between software packages and between CT examinations need to be better understood. Ideally, this better understanding, including understanding the interaction between these factors, would result in a uniform standard for both image reconstruction and image processing, similar to the Digital Imaging and Communications in Medicine standard for the distribution and viewing of medical images. Such a standard could be developed and propagated by the Quantitative Imaging Biomarker Alliance or by other similar organizations. Eventually, outcome studies will have to prove whether automated or semiautomated quantitative nodule assessment provides advantages that are relevant to patient morbidity and prognosis in

Figure 16

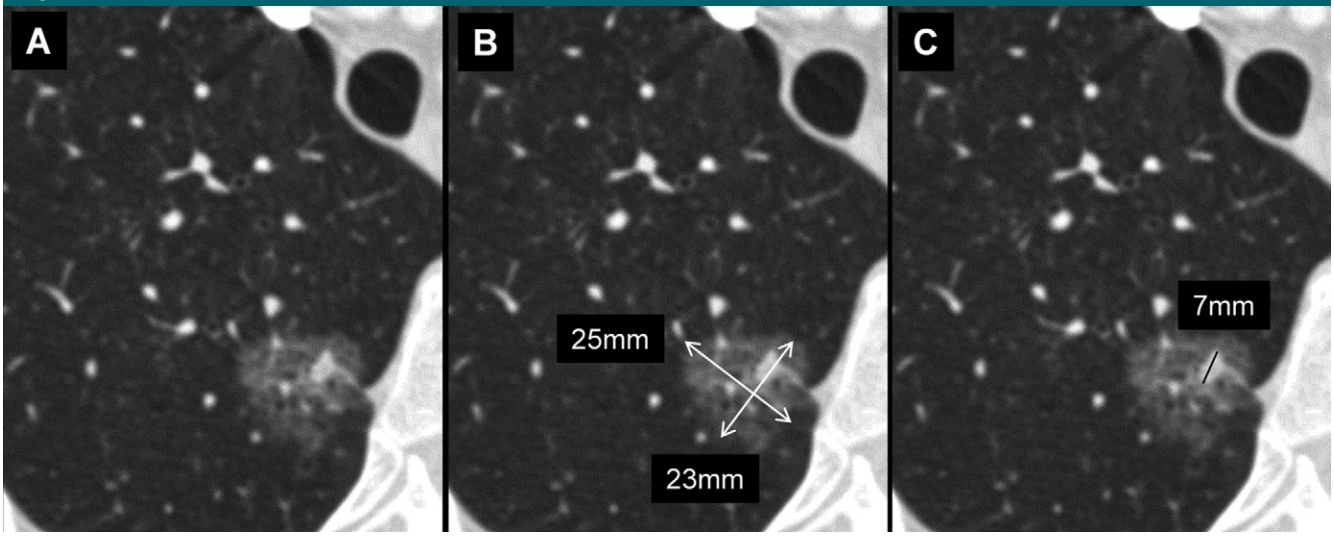

Figure 16: Transverse CT sections of a part-solid nodule in the right lower lobe. *A,* Both ground-glass and solid components are well defined. *B,* First, overall nodule dimensions are measured, resulting in an average diameter of 24 mm. *C,* Then, the long axis of the solid component is measured separately, resulting in a diameter of 7 mm.

addition to interpreter efficiency and measurement reproducibility.

Is Greater Consistency and Quality of Nodule Characterization Achievable?

Recent studies have shown that the categorization of pulmonary nodules is subject to substantial variability, even among experienced thoracic radiologists (66,67). With κ values of 0.619 and 0.670 for characterization of solid and ground-glass nodules, respectively, interobserver agreement for the categorization of nodules among six experienced thoracic radiologists was not more than "good." Moreover, with a κ value of 0.792, intraobserver agreement also was limited. Finally, correct allocation to either the solid or the subsolid category among the six radiologists was achieved for only 58% (70 of 120) of nodules (66). These findings of moderate inter- and intraobserver agreement have been corroborated subsequently, with κ values of 0.51 and 0.57, respectively, and discordant categorization in 36.4% (1630 of 4480) of nodules where two-thirds of discordant readings (1061 of 1630) would potentially have changed nodule management by using management rules relying on nodule classification and size measurements alone (67). Although both studies have potential limitations, they nonetheless address an important problem. Current management recommendations

Figure 17

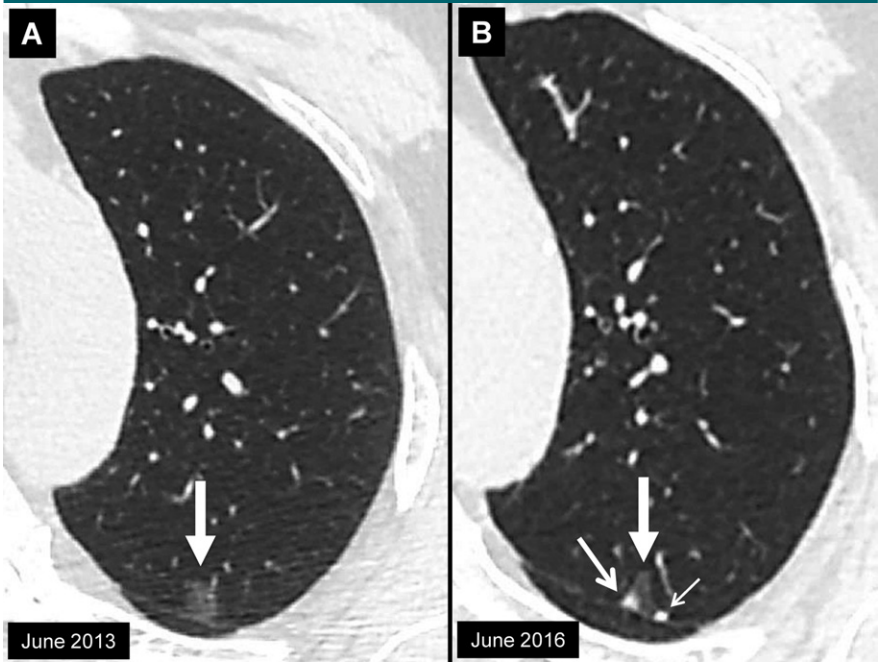

Figure 17: Transverse CT sections through a nodule (large arrow) in the left upper lobe at, *A,* baseline and, *B,* 3 years later. Over this time, the nodule has developed two solid components (small arrows). In part-solid nodules with multiple solid components, the maximum diameter of the largest solid component should be measured. In this nodule, only the larger component was measured (maximum diameter, 5 mm). The smaller solid component did not need to be measured.

for pulmonary nodules are indeed based on the inherent assumption that nodule categorization is accurate. One conclusion that could be drawn from these studies is that radiologists should be aware of the inherent subjectivity in allocating pulmonary nodules into descriptive categories, such as *solid* and *subsolid*. A second conclusion could be that a fundamental reconsideration of current descriptive categories is needed to replace them with more objective descriptors based on quantitative criteria. This would certainly require a substantially higher degree of standardization among producers of software packages and manufacturers of CT scanners, as described previously. The result, however, could be a scale or set of scales of continuous variables characterizing a pulmonary nodule, rather than a limited number of binary descriptive categories. This would potentially allow for more accurate and reproducible nodule assessments, notably better reflecting the complex and diverse morphology of nodules currently classified as subsolid.

Conclusion

Measurement of pulmonary nodules is one of the more common tasks for radiologists, and this set of recommendations is intended to guide the practical aspects of this task. It is our intention that these guidelines will help standardize the approach to nodule measurements and decrease measurement variability for nodules that may be measured by different radiologists using various CT scanners and acquisition protocols. These recommendations also emphasize the potential sources of variability and highlight areas in which further research is needed to improve measurement accuracy, consistency, and nodule characterization. A number of advanced semiautomated and automated measurement techniques are currently under investigation, including nodule attenuation, mass assessment, or both; measurements based on attenuation gradients; threshold-based methods; and advanced three-dimensional texture analysis. Further research and development in these areas will likely lead to more widespread clinical implementation in the future. As with previous guidelines, the current guidelines are subject to changes in the future, as it can be expected that the underlying body of knowledge will evolve. Thus, we recommend that these recommendations be applied with clinical judgment and common sense, and we recognize the importance of other nodule characteristics, such as shape, borders, and composition, as well as the patients' risk profile and clinical history.

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