PULMONARY NODULES—NEW SOLUTIONS TO AN OLD PROBLEM

Factors leading to decreased CAD sensitivity include: respiratory motion, the presence of ground glass opacities, peripheral volume effect, slice thickness, and adjacent pleural or parenchymal anatomy or pathology. Other more specific factors include image noise, edge indicator due to nodule thickness, cardiac motion, image compression, and radiation dose.

Its limitations and the lack of standard gold standard prevent the use of CAD as a primary screening tool. Nevertheless, a number of studies support its utility as a second reader for primary screening.

DIRECTIONS FOR FUTURE DEVELOPMENT

The failure of CAD in thoracic imaging to appear promising several centers are developing databases of lung nodules to validate and further refine CAD techniques. The most extensive effort is the Lung Image Database Consortium (LIDC), which is supported by the National Cancer Institute. The consortium endeavors to create a standard for the development of a practical radiologic definition of nodule and a reference database for the evaluation of image processing and detection algorithms.

The combination of established and emerging techniques has the potential to optimize detection, characterization, and follow-up of pulmonary nodules.

LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

• Explain the challenges of imaging pulmonary nodules

• Describe emerging methods of nodule analysis on CT

• Review the application of pulmonary nodules of computer-aided detection methods

To view and participate in this activity, please see our website www.cmecomponent.com for post testing and Reader Evaluation.

For questions about this CME activity, please contact: onlineCME@cmecomponent.com

PULMONARY NODULES—NEW SOLUTIONS TO AN OLD PROBLEM

Pulmonary Nodules—New Solutions to an Old Problem

By Stephen Waite MD, Jeany M.D., and Charles S. White, M.D.

One copy of the article provided by CME LLC may be printed by the individual participant in connection with acquiring CME credit. No other reproduction or distribution of the article without the written consent of CME LLC.

Pulmonary Nodules

Pulmonary nodules are defined as round, nearly spherical, homogeneous, radiopaque masses found on chest CT. Size remains an important factor for lung nodule detection on CT, but with a lower threshold. A retrospective study of annual lung cancer screening examinations demonstrated that nodules were missed in 26% of cases. Sixty-two percent of the retrospectively identified nodules were smaller than 4 mm and 37% were between 4 and 7 mm. Difficulty in detection may be related to the relative lack of sensitivity and specificity of the chest radiograph for mobile nodule detection, which has led to widespread utilization of CT. Size remains an important factor for lung nodule detection on CT.

Definition

A pulmonary nodule is defined as a round, nearly round, or oval density that is relatively sharply marginated. It is at least partially surrounded by lung, which means it can be characterized as a parenchymal nodule. By definition, nodules are findings of 3 cm or less. Larger spherical, well-defined opacities are referred to as “masses” and are far more likely to be malignant.

Nodules are caused by a variety of disorders, including neoplastic, infectious, inflammatory, vascular, and congenital abnormalities. Features on CT that aid in differentiating benign and malignant nodules include size, morphology, and internal composition.

Nodule size. The size of a nodule is directly related to its malignant potential. The smaller the nodule, the more likely it is to be benign. Most pulmonary nodules less than 1 cm in diameter are not visible on chest X-rays. 15 Virtually no isolated nodules less than 5 mm in size are detectable on chest CT. Diagnosis of a nodule as calcified on chest radiography is subjective and unreliable. 15 The relative lack of sensitivity and specificity of the chest radiograph for mobile nodule detection has led to widespread utilization of CT. Size remains an important factor for lung nodule detection on CT.
**PULMONARY NODULES—NEW SOLUTIONS TO AN OLD PROBLEM**

**FREE CATEGORY 1 CME CREDIT • TEST CODE #710/ PULMONARY NODULES**

A pulmonary nodule that doubles in volume more slowly than 400 days is typically benign, although a doubling time of 60 days or less is considered malignant. Thus, the volume of a nodule is the most important feature to consider when evaluating its likelihood of malignancy. Volume measurements can be calculated by summing the orthogonal diameters of the nodule. Using these measurements, the volume is calculated using the formula:

\[
\text{Volume} = \frac{4}{3} \pi r^3
\]

where \(r\) is the radius of the nodule.

**Indeterminate nodule:** A significant percentage of nodules remain indeterminate even after initial radiologic characterization. In these cases, enhancement of nodules with contrast and assessment of growth rate are considerations.

- **Contrast enhancement:** CT measurement of nodule enhancement with iotinated contrast media is an example of dynamic or functional imaging. Lung malignancies tend to enhance more than benign lung nodules, possibly secondary to increased expression of vascular endothelial growth factor.1

- **Growth rate:** CT measurement of nodule enhancement with iotinated contrast media is an example of dynamic or functional imaging. Lung malignancies tend to enhance more than benign lung nodules, possibly secondary to increased expression of vascular endothelial growth factor.2

Several disadvantages are evident with these established methods. The most important shortcoming among these is that the growth rate is not always a reliable indicator of malignancy. Using these techniques, 62% of 45 hamartomas were diagnosed on CT. None of 355 cases of lung cancer had these characteristics.1

- **Calcification:** Four patterns of calcification have been described: (1) round (bulla), (2) ring-enhancing, (3) popcorn-like. The first three types of calcification are characteristic of a chondroid matrix, whereas calcification in the fourth pattern is most commonly found in metastatic disease. Calcification in a nodule can reflect adjacent hemorrhage or necrosis. Air bronchograms may occur in bronchovascular lesions.

The presence of a small fat sign signifies a benign hamartoma or a lipid lesion and is indicated by a signal intensity of -10 to -120 HU. Features diagnostic of a hamartoma include diameter less than 2.5 cm; sharp, smooth, well defined, and fat or calcification and fat. Using these criteria, 62% of 45 hamartomas were diagnosed on CT. None of 355 cases of lung cancer had these characteristics.

- **Calcification:** Four patterns of calcification have been described: (1) round (bulla), (2) ring-enhancing, (3) popcorn-like. The first three types of calcification are characteristic of a chondroid matrix, whereas calcification in the fourth pattern is most commonly found in metastatic disease. Calcification in a nodule can reflect adjacent hemorrhage or necrosis. Air bronchograms may occur in bronchovascular lesions.

**PITFALLS**

- **false-positive:** The false-positive rate with automated detection software can be high. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-positive identifications per CT quadrant or false-positive detections range from one to 5.48 false-positives per detection.48

- **malignant:** The number of CAD-detected nodules is the objective product of computer-aided detection. However, the presence of ground truth malignancy is a major limitation in assessing the utility of CAD with chest CT. As a result, various statistical approaches, including receiver operating characteristics (ROC) analysis and area under the curve (AUC), have been developed to empirically evaluate the performance of a CAD system.

**COmputational ADvanceMents**

- **Determination of the ability to distinguish a malignant from a benign nodule:** The most common use of computer-aided detection is to reduce the number of false-positive findings on CT. For example, in the study by Novak et al, a computer-aided detection system reduced the number of false-positive detections by 92% (from 2.8 to 0.21 per CT slice).**

- **true-positive:** The true-positive rate with automated detection software can be low. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative rates range from one to 5.48 false-negatives per detection.48

**false-negative:** The false-negative rate with automated detection software can be high. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative identifications per CT quadrant or false-negative detections range from one to 5.48 false-positives per detection.48

**false-positives:** The false-positive rate with automated detection software can be high. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-positive identifications per CT quadrant or false-positive detections range from one to 5.48 false-positives per detection.48

**true-positives:** The true-positive rate with automated detection software can be low. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative rates range from one to 5.48 false-negatives per detection.48

**false-negatives:** The false-negative rate with automated detection software can be high. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative identifications per CT quadrant or false-negative detections range from one to 5.48 false-positives per detection.48

**true-negatives:** The true-negative rate with automated detection software can be low. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative rates range from one to 5.48 false-negatives per detection.48

**false-positives:** The false-positive rate with automated detection software can be high. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-positive identifications per CT quadrant or false-positive detections range from one to 5.48 false-positives per detection.48

**true-negatives:** The true-negative rate with automated detection software can be low. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative rates range from one to 5.48 false-negatives per detection.48

**false-negatives:** The false-negative rate with automated detection software can be high. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative identifications per CT quadrant or false-negative detections range from one to 5.48 false-positives per detection.48

**true-positives:** The true-positive rate with automated detection software can be low. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative rates range from one to 5.48 false-negatives per detection.48

**false-positives:** The false-positive rate with automated detection software can be high. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-positive identifications per CT quadrant or false-positive detections range from one to 5.48 false-positives per detection.48

**true-negatives:** The true-negative rate with automated detection software can be low. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative rates range from one to 5.48 false-negatives per detection.48

**false-negatives:** The false-negative rate with automated detection software can be high. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative identifications per CT quadrant or false-negative detections range from one to 5.48 false-positives per detection.48

**true-positives:** The true-positive rate with automated detection software can be low. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-negative rates range from one to 5.48 false-negatives per detection.48

**false-positives:** The false-positive rate with automated detection software can be high. Several studies have evaluated the performance of CAD systems with lung nodules on CT. In one study, false-positive identifications per CT quadrant or false-positive detections range from one to 5.48 false-positives per detection.48
benign lesion; however, 21% of malignant nodules have well-defined margins. A lobulated contour containing an irregular or spiculated border often indicates unear growth, and spread of the tumor into adjacent parenchyma. These findings are often, but not exclusively, found in malignant tumors. A nodule with surrounding ground glass is typically benign, although thin, slowly growing, low-density nodules have been reported. Doubting of nodules in less than 30 days is often due to an autocrine phenomenon.

Nodules can be measured by a variety of methods on CT. Three-dimensional volume measurements are commonly used to assess the likelihood of malignancy. Volumetric measurements are calculated by summing the errors of inter- and intraobserver variability contribute to the percentage of missing nodules on both chest radiography and on CT. Another approach to detecting and characterizing nodules is the addition of an independent second reader to interpret a study.10

Innovations in computer-aided detection technology have led to the development of software algorithms capable of analyzing radiographic images with the aim of improving nodule detection (computer-aided detection). The addition of computational analysis to develop a differential diagnostic pathway based on preprogrammed criteria is called computer-aided diagnosis. The acronym "CAD" is used interchangeably for both strategies. Much of the current research, however, focuses on nodule detection.

CAD is capable not only of processing a large number of images, but also of reducing detection, recognition, and misinterpretation errors made by radiologists.23 The detection process can also be tailored here includes image digitization and processing, image segmentation, feature extraction, and classification.

CAD requires data to be in digital form and thus is an appropriate technique for screening processes to emphasize or de-emphasize certain aspects of the image. Adjustments may include selecting a window level and level width, and choosing the type of image segmentation, feature extraction, and classification. Performance of CAD systems with lung nodules on chest CT remains a major limitation in assessing the utility of CAD with chest CT. As a result, various statistical approaches, including receiver operating characteristics (ROC) analysis and area under the curve (AUC), have been developed to empirically evaluate the performance of a CAD system.

Recent studies evaluating the performance of CAD systems with lung nodules on chest CT have reported sensitivities between 29% and 49%, depending on the method. The rates of false-positive detections range from one to 5.48 false-positives per independent CAD system.42 The detection process can also be tailored where CAD requires data to be in digital form and thus is an appropriate technique for screening processes to emphasize or de-emphasize certain aspects of the image. Adjustments may include selecting a window level and level width, and choosing the type of image segmentation, feature extraction, and classification. Performance of CAD systems with lung nodules on chest CT remains a major limitation in assessing the utility of CAD with chest CT. As a result, various statistical approaches, including receiver operating characteristics (ROC) analysis and area under the curve (AUC), have been developed to empirically evaluate the performance of a CAD system.

Recent studies evaluating the performance of CAD systems with lung nodules on chest CT have reported sensitivities between 29% and 49%, depending on the method. The rates of false-positive detections range from one to 5.48 false-positives per independent CAD system.42 The detection process can also be tailored where CAD requires data to be in digital form and thus is an appropriate technique for screening processes to emphasize or de-emphasize certain aspects of the image. Adjustments may include selecting a window level and level width, and choosing the type of image segmentation, feature extraction, and classification. Performance of CAD systems with lung nodules on chest CT remains a major limitation in assessing the utility of CAD with chest CT. As a result, various statistical approaches, including receiver operating characteristics (ROC) analysis and area under the curve (AUC), have been developed to empirically evaluate the performance of a CAD system.

Because the lack of "ground truth" (historical proof of malignancy for a detected abnormality) for nodules detected by multislice CT, focus has shifted toward identification of nodules that by their inherent characteristics require further evaluation or monitoring. This increased invasiveness involved with lung biopsy makes the magnomorphic approach inferior for lung segregation.

The number of CAD-detected nodules is the objective product of computer-aided detection. But the absence of ground truth remains a major limitation in assessing the utility of CAD with chest CT. As a result, various statistical approaches, including receiver operating characteristics (ROC) analysis and area under the curve (AUC), have been developed to empirically evaluate the performance of a CAD system.

Recent studies evaluating the performance of CAD systems with lung nodules on chest CT have reported sensitivities between 29% and 49%, depending on the method. The rates of false-positive detections range from one to 5.48 false-positives per independent CAD system.42 The detection process can also be tailored where CAD requires data to be in digital form and thus is an appropriate technique for screening processes to emphasize or de-emphasize certain aspects of the image. Adjustments may include selecting a window level and level width, and choosing the type of image segmentation, feature extraction, and classification. Performance of CAD systems with lung nodules on chest CT remains a major limitation in assessing the utility of CAD with chest CT. As a result, various statistical approaches, including receiver operating characteristics (ROC) analysis and area under the curve (AUC), have been developed to empirically evaluate the performance of a CAD system.
PULMONARY NODES—NEW SOLUTIONS TO AN OLD PROBLEM

Factors leading to decreased CAD sensitivity include: respiratory motion, the presence of ground glass opacities, partial volume effect, slice thickness, and adjacent pleural or parenchymal anatomy or pathology. Other more specific factors include image noise, due to low thickness, cardiac motion, image compression, and radiation dose. 3

Its limitations and the lack of a gold standard prevent the use of CAD as a primary screening tool. Nevertheless, a number of studies support its utility as a second reader for detecting lesions. 4

FUTURE DIRECTIONS FOR CAD

The failure of CAD in thoracic imaging appears promising. Several centers are developing database of lung nodules to validate and further refine CAD techniques. The most extensive effort is the Lung Image Database Consortium (LIDC), which is supported by The National Cancer Institute. The consortium endeavors to create a standard for the development of a practical radiologic definition of a nodule and a reference database for the evaluation of image processing and detection algorithms. 5

The combination of established and emerging techniques has the potential to optimize detection, characterization, and follow-up of pulmonary nodules.

LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

• Explain the challenges of imaging pulmonary nodules

• Describe emerging methods of nodal analysis on CT

• Review the application of pulmonary nodules of computer-aided detection methods

Pulmonary Nodules—New Solutions to an Old Problem

By Stephen Waite M.D., Jean Jeudy M.D., and Charles S. White, M.D.

One copy of the article provided by CME LLC may be printed by the individual participant in connection with acquiring CME credit. No other reproduction or distribution of the article without the written consent of CME LLC.

Pulmonary nodules are an asymptomatic condition affecting the lung parenchyma. A pulmonary nodule is defined as a round, nearly marginated lesion, by definition, nodules are not more than 1500 micrometers in diameter. Pulmonary nodules are commonly detected on routine chest radiographs, and approximately 150,000 nodules are noted as malignancies in the United States each year. 1

The evaluation of an incidental nodule to determine whether it reflects malignant disease can lead to a determination of whether a lesion is benign or malignant. The future of CAD in thoracic imaging appears promising. Several centers are developing database of lung nodules to validate and further refine CAD techniques. The most extensive effort is the Lung Image Database Consortium (LIDC), which is supported by The National Cancer Institute. The consortium endeavors to create a standard for the development of a practical radiologic definition of a nodule and a reference database for the evaluation of image processing and detection algorithms. 5

The combination of established and emerging techniques has the potential to optimize detection, characterization, and follow-up of pulmonary nodules.

DEFINITION

A pulmonary nodule is defined as a round, nearly marginated, or oval density that is relatively sharply defined. A pulmonary nodule is defined as a round, nearly marginated lesion, by definition, nodules are not more than 1500 micrometers in diameter. Pulmonary nodules are commonly detected on routine chest radiographs, and approximately 150,000 nodules are noted as malignancies in the United States each year. 1

The evaluation of an incidental nodule to determine whether it reflects malignant disease can lead to a determination of whether a lesion is benign or malignant. The future of CAD in thoracic imaging appears promising. Several centers are developing database of lung nodules to validate and further refine CAD techniques. The most extensive effort is the Lung Image Database Consortium (LIDC), which is supported by The National Cancer Institute. The consortium endeavors to create a standard for the development of a practical radiologic definition of a nodule and a reference database for the evaluation of image processing and detection algorithms. 5

The combination of established and emerging techniques has the potential to optimize detection, characterization, and follow-up of pulmonary nodules.

DEFINITION

A pulmonary nodule is defined as a round, nearly marginated, or oval density that is relatively sharply defined. A pulmonary nodule is defined as a round, nearly marginated lesion, by definition, nodules are not more than 1500 micrometers in diameter. Pulmonary nodules are commonly detected on routine chest radiographs, and approximately 150,000 nodules are noted as malignancies in the United States each year. 1

The evaluation of an incidental nodule to determine whether it reflects malignant disease can lead to a determination of whether a lesion is benign or malignant. The future of CAD in thoracic imaging appears promising. Several centers are developing database of lung nodules to validate and further refine CAD techniques. The most extensive effort is the Lung Image Database Consortium (LIDC), which is supported by The National Cancer Institute. The consortium endeavors to create a standard for the development of a practical radiologic definition of a nodule and a reference database for the evaluation of image processing and detection algorithms. 5

The combination of established and emerging techniques has the potential to optimize detection, characterization, and follow-up of pulmonary nodules.