Section A-Review paper

Computed Tomography Features of Pulmonary Nodules

Al Shaimaa Fathi Elshetry[1], Hadeer Khaled Safwat[1], Hazem M. El Shahat Mousa[1], Ramadan Nafea[2], Rania M. Almolla[1]

1 Radiodiagnosis Department, Faculty of Medicine - Zagazig University, Egypt
2 Chest Diseases Department, Faculty of Medicine - Zagazig University, Egypt
Email: Hadeerkhsafwat@gmail.com. h.khaled22@medicine.zu.edu.eg

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Abstract

Background: Pulmonary nodules are a common finding on chest computed tomography (CT) scans. Characterization of these nodules presents a pivotal challenge for radiologists in daily practice. However, accurate characterization is crucial for determining appropriate management strategies. This article provides a general review on CT features of pulmonary nodules. By examining these features, radiologists can differentiate benign from malignant nodules and guide clinicians for subsequent patient management.

Keywords: Pulmonary Nodules; Computed Tomography; Features

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Introduction

Pulmonary nodules are frequently encountered in chest imaging studies, particularly computed tomography (CT) **(1)**. It has been demonstrated that pulmonary nodules are encountered in up to 30% of chest CT scans **(2)**. Accurate characterization of these nodules presents a pivotal challenge for radiologists in their daily practice. While a significant number of these nodules eventually prove to be benign, others may indicate early-stage lung cancer **(3)**.

Since lung cancer is the leading cause of cancer-related deaths worldwide **(4)**, accurate diagnosis and management of potentially malignant nodules hold paramount importance. Furthermore, with the advent of lung cancer screening programs, accurate management of pulmonary nodules has become increasingly important. The National Lung Screening Trial (NLST) and the NELSON trial have demonstrated the efficacy of low-dose CT screening in high-risk individuals, leading to reduction in lung cancer mortality through the early detection of malignant nodules **(5,6)**.

To guide clinicians in the management of pulmonary nodules, various guidelines and recommendations have been established **(7-10)**. These guidelines emphasize the importance of CT features in determining the malignant likelihood of pulmonary nodules and guide subsequent management decisions.

Given the clinical significance of accurate characterization of pulmonary nodules and the role of CT features in guiding management decisions, this review aims to provide a general overview of CT features for pulmonary nodules. By elucidating the key imaging features associated with these nodules, this review aims to assist radiologists in accurately diagnosing pulmonary nodules in clinical practice.

CT features

There is considerable overlap in CT features of benign and malignant pulmonary nodules **(11)**. However, various imaging features, including nodule number, size, growth rate, density, margin, calcification pattern, location, and contrast enhancement are helpful for nodules characterization **(11-14)**.

Nodule number

Pulmonary nodules can occur as solitary or multiple lesions. For a nodule to be characterized as solitary, it must be surrounded by normal lung tissue without any associated atelectasis, enlarged hilar lymph nodes, or pleural effusion **(15)**. Solitary pulmonary nodules can arise from a variety of benign and malignant conditions **(12,16)**. In asymptomatic patients with no known risk factors, such as a smoking history, a solitary nodule is more likely to be benign **(12)**. Whereas in high-risk patients or those with a confirmed primary malignancy, the presence of pulmonary nodules, whether solitary or multiple, raises concerns about malignancy **(12)**.

CT screening studies have reported incidences of lung cancer in solitary pulmonary nodules ranging from 2-13% **(6,17,18)**. In clinical practice, multiple incidental pulmonary nodules are more frequently encountered than solitary nodules. For instance, in the NELSON trial, only approximately 50% of the individuals screened had solitary pulmonary nodules **(6)**. Similarly, in other screening studies, the median baseline nodule count was found to be 5 to 7 nodules **(19)**.

Nodule size

A pulmonary nodule is a spherical pulmonary opacity that measures up to 3 cm in diameter **(20)**. Nodule size is a key feature in assessment of the malignant likelihood of a pulmonary nodule **(10)**. As the size of pulmonary nodules increases, the likelihood of malignancy also increases **(10)**. However, it should be highlighted that the malignant likelihood of nodules cannot be solely determined based on their size. Malignancy can still occur in small pulmonary nodules measuring ≤ 1 cm in diameter **(12,21)**.

Therefore, it is important to consider that the largest nodule among multiple nodules is not always the malignant one. Findings from the Pan-Canadian Early Detection of Lung Cancer Study (PanCan) screening cohort indicate that approximately 20% of lung cancer patients had nodules that were not the largest among the multiple nodules present **(19)**. In fact, in one case, the malignant nodule was only the fifth largest in size **(19)**.

Pulmonary nodule size can be evaluated using 2D measurements of the greatest diameter in the axial CT images or by obtaining 2 or 3 perpendicular diameter measurements **(13)**. Alternatively, 3D volumetric assessment can be performed manually based on diameter measurements or using semi-automatic computer-aided detection software **(13,22-24)**.Volumetric measurements are considered the reference standard for assessing nodule size **(13)**.

Nodule growth rate

Nodule growth rate is another key feature in assessment of the malignant likelihood of a pulmonary nodule **(10)**. Assessing the potential growth of pulmonary nodules can be achieved through repeated CT scans **(25,26)**. Rapid growth is often indicative of malignancy **(Figure 1)**, whereas benign nodules tend to grow at a slower rate. Nodules that remain stable over a minimum of 2 years have a low likelihood of being malignant and are generally categorized as indolent nodules **(27,28)**.

The growth of a pulmonary nodule is often expressed as the volume doubling time (VDT), which is the duration it takes for the nodule to double in size **(23,29)**. VDT serves as a key feature in lung cancer screening **(29)**. A low VDT suggests rapid growth, and a VDT of less than 400 days has been proposed as the optimal threshold to distinguish between indolent and malignant lung nodules **(30,31)**.

However, the lack of nodule growth does not indicate benignity because lung adenocarcinomas can be slow-growing tumors **(10)**. Additionally, some benign lesions, such as perifissural nodules, may show growth rate and VDT in the range of malignant nodules **(32)**.

Nodule density

Accurate assessment of the density of pulmonary nodules plays a critical role in differentiating between benign and potentially malignant nodules **(13)**. Pulmonary nodule density reflects its internal characteristics **(12)**. The most common type is the solid nodule **(Figure 2A)**, which appears as a homogeneous soft-tissue density of approximately 40 Hounsfield units (HU) on CT images **(3,13)**. Other types include pure ground-glass nodules, part-solid nodules, nodules with internal fat density, and nodules with cavitation, pseudocavitation or air-bronchogram **(13)**.

Pure ground-glass nodules are characterized by a hazy increase in the density of lung parenchyma without obscuring the underlying bronchial and vascular structures **(Figure 2B)**. In contrast, part-solid nodules contain both solid and ground-glass density components **(3,13) (Figure 2C)**. Ground-glass and part-solid

nodules have a significantly higher likelihood of malignancy compared to solid nodules since malignant lung tumors are typically presented with these types **(33)**.

The presence of intranodal fat density, measuring -40 to -120 HU, is indicative of pulmonary hamartoma or lipoma **(12,13)**. Up to 50% of pulmonary hamartomas display internal fat density **(34)**.While cavitation can be seen in both benign and malignant (primary and metastatic) nodules, certain features can help differentiate between them **(12,13)**. Benign cavitary nodules usually have smooth and thin cavity walls of less than 4 mm. Whereas malignant cavitary nodules frequently have irregular and thick cavity walls ranging from 5 to 15 mm **(12,13) (Figure 3)**.

Pseudocavitation represents the presence of small air density within or around the periphery of the nodule and is indicative of bronchoalveolar carcinoma **(16,35) (Figure 4)**. While the presence of air bronchogram within the nodule is suggestive of pulmonary lymphoma **(16) (Figure 4)**.

Nodule margin

Nodule margin can be smooth, lobulated, irregular, or spiculated **(12) (Figure 5)**. Smooth nodule margin is suggestive of benign nodules; however, 21%-30% of malignant nodules have smooth margins **(21,36)**. Lobulated, irregular or spiculated nodule margins are associated with malignancy **(12)** and occur due to uneven growth of the nodule parts or invasiveness **(37)**. The NELSON trial has demonstrated that lobulated and spiculated nodule margins have an increased likelihood for malignacy when compared to smooth margins **(6)**. However, lobulated and spiculated margins have also been described in benign nodules, such as granulomas, hamartomas, or inflammatory pseudotumors **(37**,**10)**.

Nodule calcification

Nodule calcifications on non-contrast CT scans have an attenuation value greater than 200 HU **(38)**. Calcifications in pulmonary nodules are typically associated with benignity, while primary lung cancer rarely exhibits calcifications, found in only 13% of cases **(39)**. Calcification in metastatic nodules is also rare and often indicates the presence of specific types of primary tumors, including osteogenic sarcoma, chondrosarcoma, or synovial sarcoma **(40)**. While in carcinoid tumors, calcifications range from 8% to 35% **(41)**.

The pattern of nodule calcifications is crucial in determining the benign and malignant nature of the pulmonary nodule **(12)**. Benign calcification patterns include diffuse, laminated, or central calcifications **(Figure 6)**, which are often associated with previous infections like tuberculosis and histoplasmosis, as well as, popcorn-like calcifications, which are characteristic of hamartomas **(12)**. In contrast, malignant nodules tend to exhibit dystrophic calcifications that are more amorphous or punctate **(Figure 6)**, occurring in smaller numbers and frequently located eccentrically **(42,43)**.

Nodule location

There is substantial evidence indicating that certain nodules can be confidently classified as benign based on their location and morphological features **(13)**. Specifically, well-defined, elongated nodules with smooth margins that are found within 1.5 cm of a fissure (perifissural nodules) or connected to the pleural surface by a fine linear opacity are indicative of intrapulmonary lymph nodes (juxtapleural nodules) **(13) (Figure 7)**. Numerous prospective screening trials and retrospective studies have consistently shown that the perifissural nodules do not develop into cancers **(19,31,44)**.

Additionally, the anatomic location of a non-perifissural nodule holds theoretical value in its evaluation. In high-risk populations undergoing screening CT, there is a general tendency for malignancy to be more common in the upper lobes, particularly the right upper lobe nodules. Studies, such as the NLST and PanCan have demonstrated increased odds ratios for malignancy in upper lobe nodules compared to middle and lower lobe nodules **(5,19)**. However, it is important to note that location alone is not a sufficient feature for nodule characterization. Nodule size and density remain more reliable features in determining the potential malignancy of a nodule **(14)**.

Nodule contrast enhancement

Evaluation of contrast enhancement of pulmonary nodules on CT images, following the administration of a contrast agent is valuable in assessing the likelihood of malignancy. One of the key differences between benign and malignant pulmonary nodules is vascularity **(13)**. Malignant pulmonary nodules, characterized by

neovascularization, exhibit greater enhancement on contrast-enhanced CT scans (CECT) compared to benign nodules. In fact, lack of significant contrast nodular enhancement or enhancement of less than 15 HU is suggestive of benign nodule. Whereas nodular enhancement of more than 20 HU is suggestive of malignant nodule **(45)**. Furthermore, malignant nodules demonstrate greater washout of contrast material compared to benign nodules **(46).**

Numerous studies have investigated the potential of dynamic CECT to differentiate between benign and malignant pulmonary nodules **(47-52)**. By analyzing the different enhancement patterns observed, these studies have shown high sensitivity rates ranging from 95% to 100%, specificity rates ranging from 58% to 93%, and overall accuracies exceeding 77% with cut-off values of 15 and 20 HU **(47-52)**. These findings suggest that dynamic CECT could be a useful tool for distinguishing between benign and malignant nodules. However, despite its potential benefits, the clinical utility of dynamic CECT remains limited **(13)**. This is primarily due to its high radiation dose and the availability of alternative imaging methods such as fluorodeoxyglucose positron emission tomography/CT with comparable capabilities **(13)**.

CT features and diagnostic algorithms

The development of clear diagnostic algorithms is essential for the management of pulmonary nodules, with the goal of effectively diagnosing and treating early-stage lung cancer while minimizing patient morbidity, distress, and overall costs **(3)**. Current established guidelines offer diagnostic algorithms for managing pulmonary nodules based on evaluating nodules CT features and patients' risk factors **(3)**. These algorithms assist clinicians in determining the most appropriate management strategy, which may involve follow-up CT scans, additional imaging tests, biopsies, or surgical intervention.

Conclusion

CT imaging plays a pivotal role in the evaluation of pulmonary nodules. By analyzing the various CT features, radiologists can gain valuable insights into the likelihood of malignancy and guide clinicians regarding appropriate management strategies. While certain features favor benignity or malignancy, a comprehensive evaluation considering all imaging findings and the clinical context through clear diagnostic algorithms is crucial for accurate diagnosis and optimal patient care.

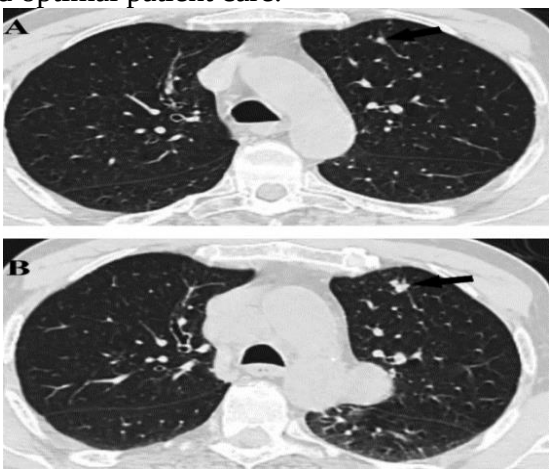

Figure 1: Example case of rapid growth rate of a malignant pulmonary nodule (arrows). **A,** baseline CT scan; **B,** follow-up CT scan at a 6-month interval.

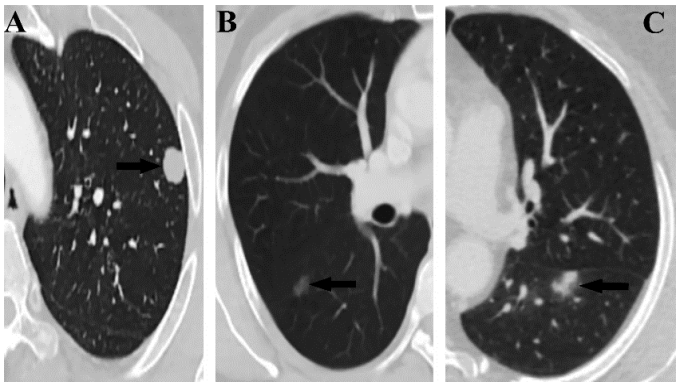

Figure 2: Axial CT images lung window showing different types of pulmonary nodules: **A**, solid; **B**, pure ground-glass; and **C**, part-solid pulmonary nodules (arrows).

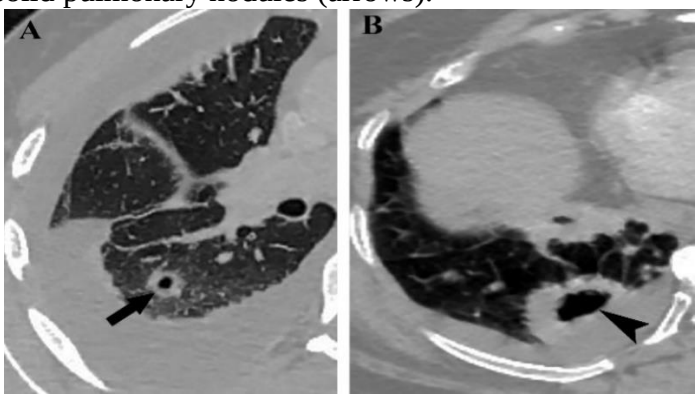

Figure 3: Axial CT images lung window showing **A**, a benign cavitary nodule (arrow) and **B**, a malignant cavitary nodule (arrowhead).

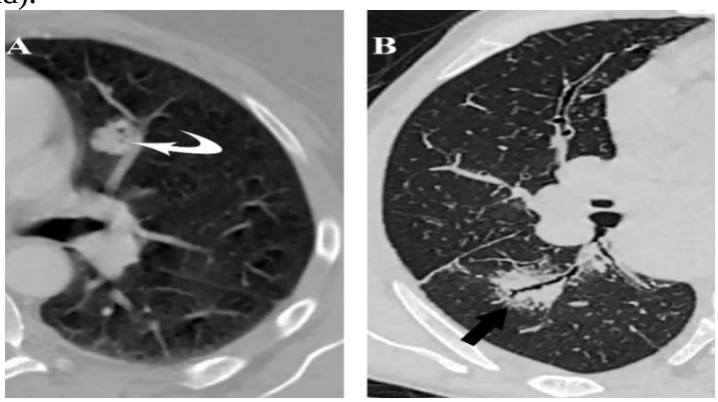

Figure 4: Axial CT images lung window showing **A**, a malignant pulmonary nodule with pseudocavitation (white curved arrow) and **B**, a malignant pulmonary nodule with air bronchogram (black arrow).

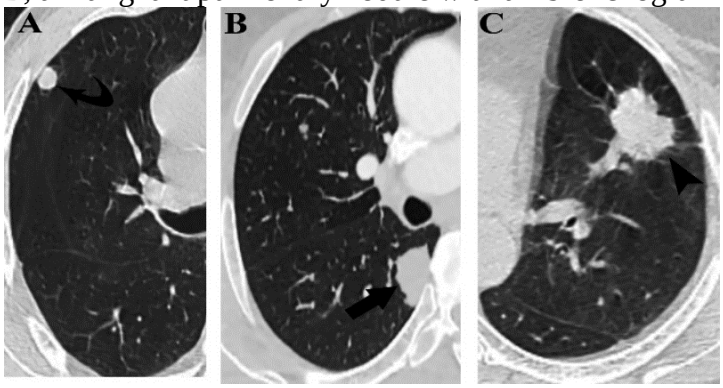

Figure 5: Axial CT images lung window showing various pulmonary nodule margins: **A**, smooth (curved arrow); **B**, lobulated (arrow); and **C**, spiculated (arrowhead) nodule margins.

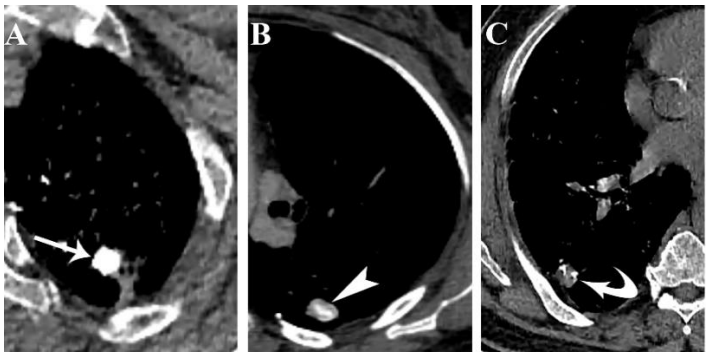

Figure 6: Axial CT images mediastinal window showing different patterns of pulmonary nodules calcifications: **A**, diffuse (thin arrow); **B**, central (arrowhead); and **C**, punctate (curved arrow) nodule calcifications.

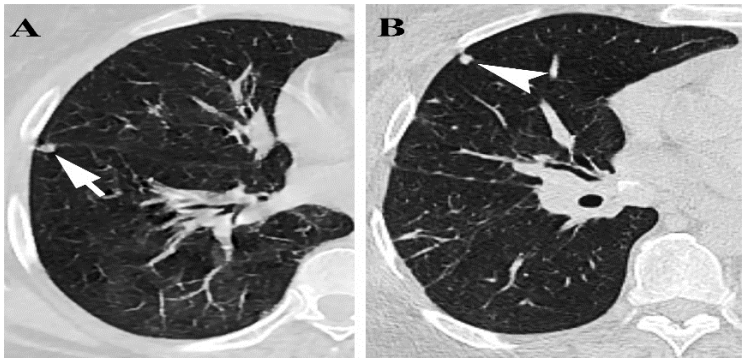

Figure 7: Axial CT images lung window showing **A**, a perifissural nodule (arrow) and **B**, a juxtapleural nodule (arrowhead).

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