Small Nodules Detected on Chest Radiography*

Does Size Predict Calcification?

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**Study objectives:** To determine whether the likelihood of lung nodule calcification can be predicted from nodule size as measured on a chest radiograph (CXR).

**Design:** Retrospective review of CXRs of patients with lung nodules ≤ 1 cm in size detected on CT scanning. CT images were used to identify calcifications and to provide spatial localization for readers to visualize nodules on a CXR and to measure their size. A subset of these nodules then was reexamined by different readers who did not view the CT scans.

**Setting:** Two university hospitals (Albuquerque, NM; Dallas, TX) and a US Air Force/Veterans Administration medical center (Albuquerque, NM).

**Patients:** Two hundred thirty-six nodules in 185 patients

**Results:** One half of the nodules (118) seen on CT scans could not be located on CXR, of which 8 (7%) were calcified. The prevalence of calcifications in the other 118 nodules visualized on CXRs was much higher (71 of 118 nodules [60%]; p < 0.005). Among the nodules visualized on CXRs, those < 7 mm in diameter (44 of 57 nodules [77%]) were more likely to be calcified than those ≥ 7 mm in diameter (27 of 61 nodules [44%]; p < 0.005). Radiographs of 42 of the smallest nodules visualized on CXRs by the initial readers later were examined prospectively by different readers who did not have access to the CT images. Thirty of 33 of the calcified nodules (91%) but only 3 of 9 of the noncalcified nodules (33%) were detected (p < 0.005). These readers also recorded 40 additional small nodules that were not seen on CT scans, which were considered to be false-positives.

**Conclusions:** Nodules detected on CXRs that measure < 7 mm in size are likely to be calcified or to represent a false-positive finding.

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**Key words:** calcinosis; coin lesion; CT; lung neoplasm; pulmonary; radiography; Tung radiology

**Abbreviations:** CXR = chest radiograph; ELCAP = Early Lung Cancer Action Project

Most primary or secondary lung neoplasms < 1 cm in diameter cannot be seen on chest radiographs (CXR). Nevertheless, many small nodules of that size are detected on CXRs, because they are made more conspicuous by the increased opacity resulting from intralesional calcification. At least one prominent text states that nodules < 9 mm in diameter are “virtually” never visible on CXRs unless calcified. Although this or similar beliefs are widely held and seem intuitive, they have not been directly studied in the literature. We sought to determine the relationships among small nodule size, calcification, and perception on plain radiographs. We hypothesized that the likelihood of nodule calcification would increase markedly as the size of nodules perceived on CXRs decreased. We further hypothesized that, below a certain size threshold, nearly all nodules that are visible on CXRs would prove to be calcified.

**Materials and Methods**

All chest CT scans performed from January 1996 to December 1997 at the University of New Mexico Health Sciences Center and the Albuquerque Federal Medical Center were examined for nodules ≤ 1 cm in size. Patients who had undergone frontal and lateral projection CXRs within a month of the CT scan were included for further study. Subsequently, a board-certified radiologist (either L.K. or the attending physician in the general reading rooms) examined the CXRs to determine whether the nodule was visible on that study. Cases in which multiple nodules were visible were included only if the observer could be sure that...
at least one nodule seen on the CXR could be correlated with a specific nodule on the CT scan. No more than three nodules were selected from any one patient. Additional data collected included the reason for performing the scan, the slice thickness, the location of the nodule with respect to the diaphragm and hilum, and the presence of definite calcification as seen on mediastinal windows. Because of the retrospective nature of the data collection, the CT techniques used were not consistent throughout the study. Slice thickness varied from 1 to 10 mm, and only 40 nodules were evaluated with thin (≤3 mm) sections. Some CT studies were performed using a spiral technique, others were performed using contiguous axial sections.

Chest CT scans were entered into the study from the University of Texas Southwestern Medical Center during periods when K.J. served as body imaging faculty between January 1997 and February 1998. Accordingly, these scans did not represent continuous data collection during that period. Data collection at the University of Texas Southwestern Medical Center was otherwise carried out in an identical fashion to that performed at the University of New Mexico Health Sciences Center.

In the first part of our study (Fig 1), we identified all nodules that were visualized on CXRs and recorded the size of the nodule as measured on the CXR and its apparent density compared to the adjacent ribs. We then plotted nodule size as measured on the CXR vs the prevalence of calcifications seen on the CT scan. Because we realized that access to CT scan images could favor the identification of nodules that would not be detected during a routine reading of a CXR, we further studied the smallest nodules that could be visualized on CXRs in the second part of our study (Fig 2). After the completion of patient enrollment at all institutions, we identified those nodules detected on CXRs that measured <7 mm in diameter. This size was chosen based on the relationship between size and nodule calcification (see “Results” section). We were able to obtain original CXRs for 42 of the 57 nodules, which were below this size threshold and were reported to be detectable on CXR. This film set included radiographs on all but two of the noncalcified nodules. (CXRs that were not obtained for this part of the study had been lost or returned to outside institutions in the interval since their initial interpretation.)

These radiographs were prospectively examined by two board-certified general radiologists who were instructed to “identify all nodules less than or equal to 1 cm in size.” Readers were given a schematic diagram of the lungs on which to localize nodules they had detected on the CXR. Neither reader had access to CT scan images or interpretations. A nodule was scored as “detected” if it was seen and correctly located on the schematic by either reader.

In the first part of our study, the Pearson $\chi^2$ statistic with (Yates) continuity correction was used to compare the prevalence of calcifications between groups of nodules. Nodules were grouped by size (<7 mm in diameter vs ≥7 mm in diameter), by visibility on CXRs, and by density compared to an adjacent rib. The $\chi^2$ statistic also was used to compare the detection rates for small (ie, <7 mm) calcified and noncalcified nodules in the second portion of our study. The $k$ statistic was calculated for observer agreement. Statistical analysis was performed using computer software (SPSS; SPSS Inc; Chicago, IL).

**RESULTS**

We identified 240 nodules on CT scans in 185 patients. In four cases, the initial reader did not record whether the nodule was calcified, and the CT image could not be obtained for review by the investigators. These four nodules were excluded from the study. Most of the remaining 236 nodules were peripheral in location. Only 20 of 236 nodules (8%) were within 4 cm of the hilum, and only 17 of 236 nodules (7%) were located below the dome of the diaphragm.
One hundred eighteen of the 236 nodules could not be located on the CXR, even with the aid of the CT images. Only eight of these nodules (7%) were calcified. The other 118 nodules were visualized on the CXRs, and the prevalence of calcification in these nodules was much greater (71 of 128 [60%]; $p < 0.005$) (Table 1). Of the 236 nodules detected by CT scanning, CXRs were able to detect 71 of the 79 calcified nodules (sensitivity, 90%) but only 57 of the 157 noncalcified nodules (sensitivity, 36%).

When the prevalence of calcification among these nodules was plotted against nodule size, the resulting graph demonstrated a marked increase in the prevalence of calcifications among nodules $< 7\ mm$ in diameter (Fig 3). Nodules $< 7\ mm$ in diameter (44 of 57 nodules [77%]) were much more likely to be calcified than nodules $\geq 7\ mm$ in diameter (25 of 61 nodules [41%]; $p < 0.005$). Nodules $< 7\ mm$ in size that appeared to be dense or denser than a rib were more likely to be calcified (45 of 52 nodules [87%]) than nodules $\geq 7\ mm$ in size with the same apparent density (22 of 46 nodules [48%]; $p < 0.05$).

In the second part of our study, CXRs on which nodules $< 7\ mm$ in size had been reported to be visualized in the retrospective portion of the study were reviewed prospectively by different readers. Studies were available for 45 of the 57 nodules that were $< 7\ mm$ in size, including all but two noncalcified nodules. When these radiographs were examined by readers who were searching for nodules but did not have access to a chest CT scan, only 5 of 13 of the noncalcified nodules were detected (sensitivity, 38%). In contrast, 26 of 32 calcified nodules (81%) were detected by the same readers ($p < 0.005$). The $\kappa$ statistic for reader agreement in detection of these nodules was moderately high (0.67).

The observers identified 44 additional opacities in 24 patients, which they thought were nodules $< 1\ cm$ in diameter but were not seen on CT scan. If these opacities are considered to be false-positive results, the reader’s specificity for nodule detection was 56%.

Table 1—Nodule Calcifications Stratified by Nodule Size and Visibility on CXR

<table>
<thead>
<tr>
<th>Nodule Diameter, mm*</th>
<th>Visualized on CR</th>
<th>Not Visualized on CR</th>
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<tbody>
<tr>
<td></td>
<td>Calcified</td>
<td>Noncalcified</td>
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<tr>
<td>10 12</td>
<td>1 12</td>
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<td>4 6</td>
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<td>7 10</td>
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<td>19 5</td>
<td>0 5</td>
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<td>5 15</td>
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<td>≤4 10</td>
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*Diameter of nodules not visualized on CXR that were measured on CT images.
Discussion

The detection of bronchogenic carcinoma at an early stage is a universal goal and has historically relied on the detection of lung nodules on CXRs.\textsuperscript{4,5} Lung carcinomas, however, usually are not detectable on chest radiography when they are < 1 cm in size. Most early carcinomas that are detected during screening programs using CXRs are > 1 cm in diameter.\textsuperscript{1} Similarly, cases of lung carcinomas “missed” on CXRs usually represent opacities that are > 1 cm in diameter but are not perceived due to overlying structures or to the location within the chest.\textsuperscript{6}

Nodules < 1 cm in size are seen frequently on CT scans. The results of some studies suggest that a significant number of these small nodules that are detected by CT scanning prove to be carcinomas.\textsuperscript{7} Carcinomas of this size very rarely contain calcification and are very rarely visible on CXRs.\textsuperscript{1,8} Prior data suggest that approximately 50% of noncalcified nodules that are 8 to 10 mm in diameter and virtually none of the noncalcified nodules that are < 5 mm in size are detectable on CXRs.\textsuperscript{9} Recent data from the Early Lung Cancer Action Project (ELCAP) study show similar results. In that study, only 2 of the 99 noncalcified nodules (2%) that were seen on CT scans also were detected on CXRs. CXRs detected a slightly greater proportion (14%) of nodules that were 6 to 10 mm in diameter.\textsuperscript{10}

Because the ELCAP study excluded all calcified nodules from further evaluation, the data from that study do not address the impact of nodule calcification on CXR visualization. The ELCAP data and prior work, however, indicate that noncalcified nodules that are < 1 cm in size are not commonly visualized on CXRs. Nodules of this size, we hypothesized, are most likely perceived because they contain calcifications. The smaller the nodule, the more likely that it must contain calcium in order to be visualized on a CXR.

Observations dating back to the 1950s have recognized that the rate of malignancy is low in nodules that are < 1 cm in size that are seen on a CXR.\textsuperscript{11} This probably reflects the fact that many of the small nodules that are detectable on routine chest radiography are calcified. However, data quantifying the relationships among small nodule size, perception, and calcification are lacking in the literature.

Our work suggests that nodules < 7 mm in diameter that are seen on a CXR have a high (77%) likelihood of being calcified. The actual likelihood of calcification within these nodules is probably considerably higher than in those observed in our work since the CT scan protocols used may have missed calcifications in the smallest nodules. Because the CT scans in this study were performed for a variety of indications, slice thickness was not held constant. While the optimal slice thickness for detecting central calcification in a nodule is approximately half of the nodule diameter or less, many scans in this series were performed with 8 to 10-mm collimation.\textsuperscript{12} Accordingly, some of the smallest nodules may have had calcifications within them that were missed on CT scanning. This probably accounts for the apparent fall in the prevalence of calcification among nodules that were 3 mm in diameter.

In our study, observer bias (from reviewing CT images) also increased the detection of small noncalcified nodules, lowering the apparent proportion of nodule calcification. The review of CXRs in the second portion of our study demonstrates that most of the nodules, when reviewed on CT, are typically calcified. This suggests that the majority of the small nodules in our study that were not visible on CXR were actually calcified, but were not perceived because the slice thicknesses were not adequate to detect the calcification.
small noncalcified nodules that were visualized on CXRs by readers with the aid of a CT scan would not have been seen during routine CXR readings. The sensitivity of CXRs for noncalcified nodules < 7 mm in diameter was poor (38%) in the second portion of our study, even though reader vigilance for lung nodules was artificially high. The latter resulted in a high false-positive rate (56%). This result is similar to that in the ELCAP study, in which chest radiography had a false-positive detection rate of 50% for noncalcified nodules that were < 1 cm in diameter.

A subjective assessment of nodule density on CXRs added little to the measurement of nodule size in determining whether calcifications were present. Many of the nodules that were ≥ 7 mm in size appeared to be as dense as or denser than an adjacent rib, despite the absence of calcification seen on CT scanning. In some cases, this may represent the underdetection of calcification by CT scanning due to volume averaging, as described above. Additionally, sufficiently large noncalcified nodules could appear as dense as a rib if the nodule diameter exceeds the thickness of a rib. Our findings are in agreement with other work that has shown the subjective assessment of nodule density on CXR to be of limited sensitivity and specificity in detecting calcifications within the lung.

In summary, our study shows that nodules < 7 mm in diameter that are visualized on CXRs are likely to be either calcified nodules or false-positive findings. For example, the likelihood that a 6-mm nodule that is seen on a routine CXR is calcified, and therefore benign, is probably > 77%, and possibly > 90% if it appears as dense or denser than an adjacent rib. Nevertheless, the data from this study do not justify a disregard for nodules of this size that are seen on CXRs. More accurate data would need to be derived from a prospective study in which all nodules < 7 mm in diameter were evaluated with thin-section CT scanning. Even these data might be influenced by factors such as patient demographics, smoking prevalence, and regional variations in endemic fungal infections.

It is important to note that all the CXRs in our study were obtained with film-screen techniques rather than digital systems. It remains uncertain whether digital imaging will offer any advantages in small-nodule detection. A small series has suggested that a selenium-based detector system may be more sensitive than conventional radiography for nodules < 1 cm in size, but data comparing the sensitivity of the system for calcified and noncalcified nodules are not available. Digital radiography also offers the opportunity to create dual-energy subtraction images, in which simultaneous images are made using different beam energies. This method allows calcified tissue to be "subtracted" from soft tissues. To our knowledge, this method has not yet been applied specifically to the characterization of small pulmonary nodules.

Our study suggests that, within our study population, nodules < 7 mm in size might be evaluated either by comparison with prior radiographs or with radiographic follow-up. Thin-section CT scanning might be reserved for patients in whom there is a high clinical suspicion for primary or secondary pulmonary malignancy. Further study is necessary before these findings can be applied to populations with a different prevalence of granulomatous infections and tobacco exposure.

References
2 Davis S. CT evaluation for pulmonary malignancy. Radiology 1991; 180:1–12
10 Henschke CI, McCanley DI, Yankelevitz EF. Early lung cancer action project: overall design and findings from baseline screening. Lancet 1999; 354:99–105
11 Vivas JR, Crabtree SF. The significance of the size and radiographic density of solitary lesions in the lungs. Am Practitioner Dig Treatment 1953; 4:857–861