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CHEST

Visual assessment of calcification in solitary pulmonary nodules on chest radiography: correlation with volumetric quantification of calcification

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Abstract

Purpose To assess the ability of digital chest radiography (CXR) to reveal calcification in solitary pulmonary nodules (SPNs), and to examine the correlation between a visual assessment and volumetric quantification of the calcification.

Materials and methods This study was a retrospective review of 220 SPNs identified by both CXR and chest CT. Eleven observers did blind review of the CXR images and scored nodule calcification on a confidence scale of 1 to 5. The area under the receiver operating characteristics (ROC) curve (AUC) was obtained to analyze the diagnostic performance. The intraclass correlation coefficient (ICC) for interrater reliability was calculated. The AUC and ICC were calculated according to the following nodule diameter groups: group 1 (< 10 mm), group 2 (≥ 10 mm and < 20 mm), and group 3 (≥ 20 mm).

Results Of the 220 SPNs, 145 SPNs (65.6%) were identified as non-calcified and 75 (34.4%) as calcified. The average percentage of calcification volume in SPN > 160 HU (Vol160HU) among the 75 calcified nodules was 47.5%. The mean Vol160HU of the 68 SPNs classified as having definite calcification was 51.1%. The overall AUC was 0.71. The AUCs for groups 1, 2, and 3 was 0.835, 0.639, and 0.620, respectively. The ICCs for groups 1, 2, 3 was 0.65, 0.48, and 0.33, respectively.

Conclusion The overall diagnostic performance of digital CXR to predict calcification in SPNs was moderately accurate and the diagnostic performance for predicting calcification in SPNs was significantly higher, and interobserver reproducibility was good when SPN < 10 mm compared with ≥ 10 mm in diameter.

Key Points

- *The misdiagnosis of a non-calcified nodule as a calcified one by CXR could lead to poor management choices for the SPN.*
- *The diagnostic performance of CXR in predicting calcification was best for nodules < 10 mm in diameter. SPNs with calcification of approximately 50% of their volume tend to be considered calcified.*
- *The diagnostic performance of CXR in identifying calcification was low for nodules ≥ 10 mm in diameter; therefore, we should carefully evaluate calcification carefully for nodules ≥ 10 mm.*

Keywords Solitary pulmonary nodule · Radiography, thoracic · Tomography, X-ray computed

Abbreviations

AEC	Automatic exposure control
AUC	Area under the ROC curve
CI	Confidence interval
CT	Computed tomography
CXR	Chest radiography
FP	False positive
ICC	Intraclass correlation coefficient
MDCT	Multidetector CT
NPV	Negative predictive value
PPV	Positive predictive value
ROC	Receiver operating characteristic
SPNs	Solitary pulmonary nodules

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Introduction

Chest radiography (CXR) is the most widely used modality for the initial assessment of pulmonary disease, and approximately 90% of solitary pulmonary nodules (SPNs) are detected by

CXR performing for unrelated diagnostic workups [1, 2]. The prevalence of malignancy in SPN ranges widely from 5 to 69% [3–5]. In non-selected populations, there is a 20–40% of likelihood of the presence of malignancy in a newly detected SPN on CXR [6–8]. The ultimate goal of radiological evaluation of an identified SPN is not only to diagnose malignant tumors with high survival rates, but also to spare patients with benign SPNs from undergoing unnecessary procedures.

Although CT is considered as superior to plain radiography for identifying both the presence and pattern of calcification [4, 9, 10], CXR is usually the first step in the assessment of an SPN in practice, and it is crucial for deciding whether to stop further evaluation or continue the evaluation with CT scan.

The presence of benign calcification patterns is the single most valuable sign used to determine whether an SPN is benign or indeterminate [4, 11, 12]. Therefore, the prediction of calcification in an SPN could play an important role in avoiding the unnecessary radiation exposure involved with computed tomography (CT) or the risks associated with a biopsy. Specific calcification patterns (central, laminated, diffuse, or popcorn) in an SPN indicate that it is benign, and these patterns can be seen on CXR or computed tomography (CT) [13–16]. Even experienced radiologists misidentify up to 7% of non-calcified SPNs as calcified on plain radiographs [17], because the visual interpretation of a CXR regarding the presence of calcification in an SPN is very subjective.

There is doubt regarding the radiologist's ability to predict benign calcification in an SPN with CXR, and a few studies have investigated the diagnostic performance of CXR for predicting calcification in an SPN in comparison with CT as the gold standard [17, 18]. Although selenium-based detector systems are more sensitive than conventional film-screen techniques for nodules < 10 mm in diameter [19], it has not been determined whether digital radiography is superior to conventional CXR for the detection of calcification in SPNs. Therefore, the purpose of this study was to determine the ability of digital CXR to predict calcification in SPN. Furthermore, we aimed to determine how much calcification must be present in an SPN for it to be considered a benign calcified SPN by CXR evaluation. To do this, we quantified the amount of calcification within SPNs by using a volumetric measurement from multidetector CT (MDCT) data. Therefore, this study examined the ability of digital CXR to predict calcification in SPN, and the correlation between visual assessment and volumetric quantification of calcification by MDCT volumetric measurement.

Materials and methods

The Institutional Review Board of Ajou Medical Center approved this study and waived the requirement for informed consent because of its retrospective nature.

Study population

We retrospectively reviewed the radiology records and CXR and CT images taken at out institution between April 2014 and April 2015. The inclusion criteria for selecting eligible cases were as follows: (1) patients ($n = 9143$) who underwent both CXR and chest CT scan, (2) in whom a solitary pulmonary nodule (5 mm to 30 mm diameter on CT measurement) was identified by CXR and confirmed its existence by CT ($n = 647$), (3) with no additional parenchymal abnormalities including pneumonia or post-infection scars. Finally, 220 cases were included in the study.

Image collection and preparation

All CXR images were acquired using a digital radiographic system (Discovery XR 650, GE Healthcare). Posteroanterior views of chest radiographs were obtained in the erect position. Routine chest posteroanterior view was obtained at a tube voltage of 120 kVp, 500 mA with automatic exposure control (AEC) speed of 125, and a source-to-image distance of 180 cm. The detector had a 41 × 41 cm field of view. All CT examinations were performed using 64-row MDCT (Brilliance 64, Philips Medical Systems). The pre-contrast chest CT was only performed in 62 patients, the post-contrast chest CT was only performed in 89 patients, and both pre- and post-contrast chest CT were performed in 69 patients. The range of chest CT scans was from the lung apices to the bases. The post-contrast examination was obtained after intravenous injection of non-ionic contrast media (2.5 mL/s, 100 mL Iomeprol—Iomeron 300; Bracco) using a power injector with a fixed delay time of 45 s. The scanning parameters were as follows: 16 × 0.75 mm collimation, 0.5-s tube rotation time, 0.938 pitch, 200 mAs with automatic tube current modulation, and 120 kVp tube voltage. All images were reconstructed with 3-mm thickness and 3-mm interval using iterative reconstruction technique (iDose level 5) for observer assessment. Two radiologists who were not involved in the image evaluation process marked the SPN on each CXR image using a circular electric marker to facilitate assessment of the presence of calcification by the observers. The observers were instructed to evaluate the marked SPNs.

Reference standard for calcification on CT

Two thoracic radiologists (board-certified radiologist, 30- and 17-year experience of thoracic CT) who were not involved in assessing the CXR images performed a visual assessment of a thin-section chest MDCT image (1-mm thickness and 1-mm interval) to determine the presence of calcification and then established a reference standard for the presence of calcification. They classified the calcified nodules as either benign nodules (diffuse, central, laminated, and popcorn calcification) that do

not require further workup or indeterminate nodules (eccentric, stippled calcification) that should be evaluated or followed up.

Volumetric quantification of calcification in SPN

For semi-automated volumetric quantification of SPN calcification, 1-mm thin-section chest CT image data reconstructed using a soft kernel were transferred to an image-processing workstation (Aquarius, TeraRecon). Based on several references, we used a threshold of > 160 HU to indicate calcification [4, 20, 21]. To calculate the percentage of calcification volume in the SPN, the volume percentage of the area > 160 HU in the SPN was obtained; this was defined as Vol160HU. All semi-automated volumetric quantifications of SPN calcification were performed by one radiologist. When the vessels and tissues connected to the target nodule during semi-automated SPN segmentation, careful manual editing was done.

Image analysis

Non-thoracic radiologists and radiology residents participated as readers in this study to obtain results potentially more indicative of general radiology practice. Eleven observers (four board-certified radiologists and seven radiology residents) who were blinded to the clinical and thin-section CT data evaluated all of the CXR images. The observers were instructed to evaluate the pulmonary nodules as follows: (1) to score the confidence level for the presence of calcification in the SPN on a scale from 1 to 5, where a score of 5 represents the greatest degree of confidence (definite calcification), and a score of 1 represents the lowest degree of confidence (definite non-calcification), and (2) to record the largest diameter of the SPN. All CT data were directly displayed on the picture archiving and communication systems (Infinitt PACS; INFINITT Healthcare) workstation monitors [5.2-megapixel TFT LCD medical-grade, gray scale monitor (IF2105A;Wide corporation)], and the full functionality of the PACS software was available to the participating radiologists (e.g., window and level settings and zoom function)

Statistics

Analysis of diagnostic performance

Receiver operating characteristic (ROC) analysis was performed and the area under the ROC curve (AUC) was calculated to evaluate the radiologists' overall diagnostic performance in predicting SPN calcification on CXR. The AUC for the overall diagnostic performance was compared with the values according to the nodule diameter (group 1, < 10 mm; group 2, ≥ 10 mm and < 20 mm; group 3, ≥ 20 mm). The AUCs were compared by using the method developed by DeLong et al [22]. The positive predictive value (PPV) and negative predictive value (NPV) were calculated based on the SPNs with confidence score of 5 (definite calcification) or 1 (definite non-calcification), respectively. Furthermore, the PPV and NPV were also calculated according to the nodule size.

Interreader agreement

The interreader agreement among observers 1–11 was assessed by calculating the intraclass correlation coefficient (ICC) with the 95% confidence interval (CI) and by applying a one-way ICC with a random rater assumption. The ICC was calculated for all 2420 observations (220 nodules × 11 observers) and according to nodule size (groups 1–3) and nodule calcification. The ICCs ranged from 0 to 1.00, with values closer to 1.00 representing better reproducibility. The ICCs were interpreted as follows: 0.00–0.20, slight reproducibility; 0.21–0.40, mild reproducibility; 0.41–0.60, moderated reproducibility; 0.61–0.80, good reproducibility; and 0.81–1.00, excellent reproducibility [23].

The calculated p values were two-sided, and a value less than 0.05 was considered as statistically significant. All statistical analyses were performed using MedCalc Statistical Software version 15.0 (MedCalc Software bvba).

Result

Demographics

The average time interval between performing CXR and MDCT was 21 days (0~83 days). Of the 220 SPNs, 58 pulmonary nodules were in the right upper lobe, 18 nodules in the right middle lobe, 46 nodules in the right lower lobe, 66 nodules in the left upper lobe, and 32 nodules in the left lower lobe. The largest diameter of the nodules (measured by CT image) ranged from 6.4 to 27.1 mm, with an average of 13.9 mm. Based on the diameter of the nodules, 56 SPNs were categorized into group 1 (< 10 mm), 127 into group 2 (≥ 10 mm and < 20 mm), and 37 into group 3 (≥ 20 mm).

A total of 145 SPNs (65.6%) were identified as non-calcified and 75 SPNs (34.4%) were classified as calcified after the CT evaluation and a consensus reading by the two radiologists. CT identified 68 SPNs with a benign pattern of calcification (61 diffuse, 6 central, and 1 punctate) and 7 SPNs with an indeterminate focal eccentric pattern of calcification (Table 1). The 145 non-calcified nodules comprised of 31 unidentified benign nodules (based on a 2–3-year follow-up), pathologically proven 55 benign nodules (19 granulomas, 16 tuberculomas, 13 hamartomas, 4 pneumocytomas, and 3

Table 1 Volumetric quantification of calcification in 220 SPNs according to the diameter

Group by diameter of SPN		
Group 1, < 10 mm ($n = 56$)		
Calcification	Pattern of calcification	Mean Vol160HU
Calcified ($n = 31$)		
Benign	Diffuse ($n = 30$)	56.85% (31.2~90.03%) (30.18~90.03%)
Indeterminate	Focal eccentric ($n = 1$)	19.4%
Non-calcified ($n = 25$)		0.32% (0~0.7%)
Group 2, ≥ 10 mm and < 20 mm ($n = 127$)		
Calcification	Pattern of calcification	Mean Vol160HU
Calcified ($n = 40$)		
Benign	Diffuse ($n = 31$), Central ($n = 3$)	48.74% (25.5~81.65%)
Indeterminate	Focal eccentric ($n = 6$)	10.69% (6.54~18.05%)
Non-calcified ($n = 87$)	87	0.59% (0~0.83%)
Group 3, ≥ 20 mm ($n = 37$)		
Calcification	Pattern of calcification	Mean Vol160HU
Calcified ($n = 4$)		
Benign	Punctate ($n = 1$), Central ($n = 3$)	28.53% (20.05~35.1%)
Indeterminate	$n = 0$	
Non-calcified ($n = 33$)		0.2% (0~2.96%)

cryptococcal infections), pathologically proven 57 malignant nodules (50 primary lung cancers and 7 metastases) (Fig. 2), and clinically proven 2 round pneumonias. All 75 calcified nodules, comprising 69 unidentified granulomas and pathologically proven 6 nodules (3 tuberculomas and 3 hamartomas), were confirmed as benign. Of the 220 nodules, 163 were ultimately diagnosed as benign (88 non-calcified nodules and all 75 calcified nodules) and 57 as malignant (all of which were non-calcified nodules).

Diagnostic performance

The AUC values of all observers for predicting SPN calcification ranged from 0.658 to 0.790 (Table 2). To evaluate the overall diagnostic performance of the observers, ROC analysis was performed to calculate the AUC for a total of 2420 observations (220 SPNs × 11 observers); the AUC was 0.71 (95% confidence interval [CI] 0.694 to 0.731). ROC analyses were performed according to the nodule diameter (groups 1 to 3), yielding an AUC of 0.835 (95% CI 0.803–0.863) for group 1, 0.639 (95% CI 0.613–0.664) for group 2, and 0.620 (95% CI 0.567–0.664) for group 3 (Fig. 1). The independent ROC curves were compared, and the AUC for group 1 was significantly higher than those for groups 2 and 3 ($p < 0.0001$).

The overall sensitivity and specificity were also calculated for the 2420 SPNs. For this analysis, the confidence score of 4 and 5 were considered as positive test results and the confidence scores of 1–3 as negative test results. The overall sensitivity was 58.8%, and the overall specificity was 76%. The overall PPV was 55.94% and the NPV was 78.1%. To focus on the SPNs predicted with a confidence score of 5 (definite calcification) or 1 (definite non-calcification), the PPV based on SPNs with confidence score of 5 and the NPV based on SPNs with confidence score of 1 were calculated. Of the 2420 observations (220 SPNs × 11 observers), 291 were given a confidence score of 5, and 232 were deemed to be true calcified nodules; 193 were given a confidence score 1, and 159 were deemed to be true non-calcified nodules. Therefore, the PPV was 79.7% (232/291) and the NPV was 82.4% (159/193). For the same SPNs scored as 5 or 1, the PPV and NPV were calculated according to the nodule diameter group as follows: group 1 (< 10 mm), PPV = 95% (134/141) and NPV = 95.2% (40/42); group 2 ((≤ 10 mm and < 20 mm), PPV = 75% (93/124) and NPV = 74.8% (89/119); group 3 (≥ 20 mm), PPV = 19.2% (5/26) and NPV = 93.8% (30/32) (Table 3). The PPV for SPNs of group 1 was significantly higher than those for groups 2 and 3 ($p < 0.0001$). The NPV for SPNs of group 1 was significantly higher than that for group 2 only.

In terms of interobserver reproducibility, the overall ICC for radiologists predicting of calcification by CXR was 0.516 (moderate reproducibility). According to the nodule diameter regardless of calcification, ICCs for predicting of calcification by CXR for groups 1–3 were 0.65 (good reproducibility), 0.48 (moderate reproducibility), and 0.33 (mild reproducibility), respectively. According to the diameter of the calcified nodules, ICCs for predicting of calcification by CXR for groups 1–3 were 0.58 (moderate reproducibility), 0.47 (moderate reproducibility), and 0.17 (slight reproducibility), respectively. According to the diameter of the non-calcified nodules, ICCs

Table 2 AUC value in ROCs for all observers for prediction of pulmonary nodule calcification on chest radiographic images

Observers (experience year)	AUC values (95% CI)
1 (Resident, first year)	0.658 (0.591–0.720)
2 (Resident, third year)	0.667 (0.660–0.729)
3 (Resident, first year)	0.661 (0.595–0.723)
4 (Resident, second year)	0.748 (0.686–0.804)
5 (Radiologist, 1 year)	0.709 (0.644–0.768)
6 (Radiologist, 2 years)	0.703 (0.638–0.762)
7 (Radiologist, 4 years)	0.689 (0.623–0.749)
8 (Resident, third year)	0.790 (0.730–0.841)
9 (Resident, second year)	0.725 (0.661–0.783)
10 (Resident, fourth year)	0.727 (0.664–0.785)
11 (Radiologist, 7 years)	0.790 (0.730–0.841)
Overall	0.710 (0.694–0.731)

AUC area under the ROC curve, *ROC* receiver operating characteristics

for predicting of calcification by CXR for groups 1–3 were 0.28 (mild reproducibility), 0.23 (mild reproducibility), and 0.13 (slight reproducibility), respectively.

Volumetric quantification of calcification in pulmonary nodules

For the 75 calcified SPNs analyzed, the mean Vol160HU was 47.5. The mean Vol160HU of the 68 SPNs classified as having definite benign calcification was 51.1%, while the Vol160HU of the one SPN of seven with indeterminate calcification was 11.9%. The Vol160HU of the SPNs were determined according to all observers' confidence score, ranging from 1 to 5. Of the 2420 observations (220 nodules × 11 observers), the mean Vol160HU of the SPNs given confidence score of 5 ($n = 291$), 4 ($n = 576$), 3 ($n = 579$), 2 ($n = 781$), and 1 ($n = 193$) were 50.3%, 27.9%, 18.3%, 13.92%, and 12.02%, respectively. For the 825 calcified observations (75 nodules × 11 observers), the meanVol160HU values of the calcified SPNs given confidence scores 5 ($n = 232$), 4 ($n = 253$), 3 ($n = 151$), 2 ($n = 155$), and 1 ($n = 34$) were 61.2%, 49.1%, 41.5%, 33.8%, and 30.6%, respectively. Figure 2 shows some of the typical cases.

Discussion

In routine clinical practice, radiologists need to determine whether an SPN is calcified when evaluating CXR images. SPNs are usually considered as a benign when their size on CXR remains stable for over 2 years or they exhibit specific radiological characteristics initially. Although the presence of calcification in an SPN does not guarantee benignity absolutely, it does indicate a high probability of benignity. Nevertheless, the reported incidence of visible calcifications within lung cancer is approximately 1% on CXR [17, 24, 25]. Furthermore, an inaccurate interpretation can occur when assessing an SPN by CXR, and approximately 19% of non-small cell lung cancers were identified retrospectively on CXR images that had been interpreted previously as being normal [26]. Therefore, it is difficult to judge whether an SPN is a benign by CXR. When an SPN is classified as indeterminate after assessing its

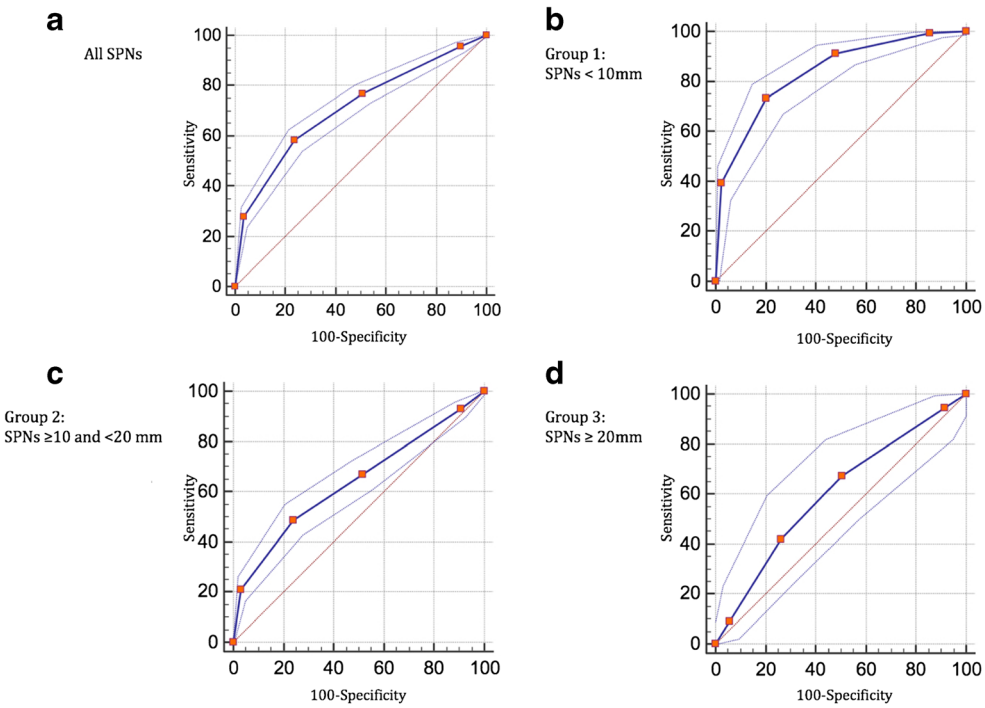

Fig. 1 The AUC for all SPNs (**a**), SPNs < 10 mm (**b**), SPNs ≥ 10 mm and < 20 mm (**c**), and SPNs ≥ 20 mm (**d**) ROC curves for predicting calcification in SPNs according to the diameter of the SPN. **a** All SPNs, AUC = 0.710; **b** group 1 (< 10 mm), AUC = 0.835; **c** group 2 (≥ 10 mm and < 20 mm), AUC = 0.639; **d** group 3 (≥ 20 mm), AUC = 0.620. The AUC for group 1 was significantly higher than those for groups 2 and 3 ($p < 0.0001$)

Table 3 Positive predictive values, negative predictive values, and false positive results for SPNs rated with confidence score of 5 (definite calcification) or 1 (definite non-calcification) among 2420 SPNs

Overall SPNs		
	Confidence score	
Presence of calcification	5 (definite calcification)	1 (definite non-calcification)
(+)	232	34
(−)	59	159
PPV	79.7%	
NPV	82.4%	
FP	20.3%	
Group 1 (< 10 mm)		
	Confidence score	
Presence of calcification	5 (definite calcification)	1 (definite non-calcification)
(+)	134	2
(−)	7	40
PPV	95%	
NPV	95.2%	
FP	4.96%	
Group 2 (≥ 10 and < 20 mm)		
	Confidence score	
Presence of calcification	5 (definite calcification)	1 (definite non-calcification)
(+)	93	30
(−)	31	89
PPV	75%	
NPV	74.8%	
FP	25%	
Group 3 (≥ 20 mm)		
	Confidence score	
Presence of calcification	5 (definite calcification)	1 (definite non-calcification)
(+)	5	2
(−)	21	30
PPV	19.2%	
NPV	93.8%	
FP	80.8%	

PPV positive predictive value, *NPV* negative predictive value, *FP* false positive result

radiological characteristics, patient risk factors can lead to a diagnostic dilemma.

One study investigated whether the likelihood of SPN calcification can be predicted based on nodule size, and reported that SPNs < 7 mm in diameter detected by CXR have a 77% likelihood of being calcified or to suggest false-positives [18]. Although our study design differed, our series included 25 SPNs < 7 mm, of which 16 were calcified (64%). This implies that pre-selected SPNs < 7 mm in our retrospective surveillances of CXR images have a 64% likelihood of being calcified, which was similar to the previously reported value of 77%.

One study reported that among 72 malignant SPNs, calcification was visible on 10 specimen radiographs, but only one SPN was identified as calcified SPN by standard CXR. In the same study, 67 of 135 benign SPNs were found to contain calcifications on specimen radiographs, and in 46 (68.6%, 46/67) of these SPNs, the calcifications were also visible on standard CXR images [27]. The overall sensitivity for the 2420 SPNs was lower (58.5%) in our study than the prior study [27].

William et al analyzed the overall diagnostic performance for detecting calcification in SPNs using ROC analysis and reported an AUC of 0.751; there was no correlation between SPN size and accuracy [17]. Our overall AUC of 0.71 was similar. However, the diameter of the SPN affected the detectability of calcification in the SPNs, and the AUC was significantly greater for group 1 (< 10 mm, AUC = 0.835) than for group 2 (≥ 10 mm and < 20 mm, AUC = 0.639) and group 3 (≥ 20 mm, AUC = 0.60). Additionally, for the 485 SPNs rated as "definite calcification" ($n = 291$) or "definite non-calcification" ($n = 193$), the smaller the size of SPN is, the

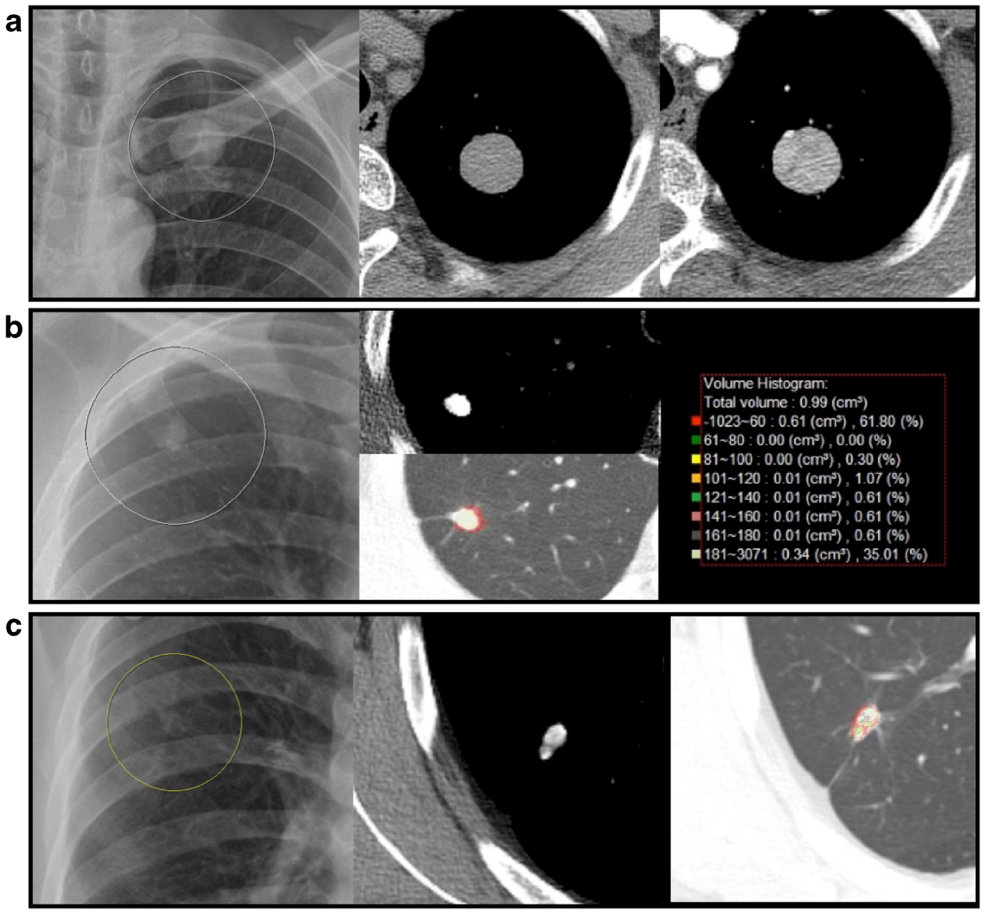

Fig. 2 **a** A 53-year-old man with hepatocellular carcinoma (HCC). A 22-mm round SPN was noted in the left upper lung. Five observers (5/11, 45.5%) assessed this nodule as calcified (confidence scores of 4 and 5). On CT, this nodule was confirmed as having no calcification. This nodule showed strong contrast enhancement of approximately 70 HU. This nodule was ultimately diagnosed as metastatic HCC. **b** A 47-year-old woman with calcified granuloma. An approximately 11 mm, ovoid SPN was seen in the right upper lung. This SPN completely overlapped with the right second rib anterior arc. Nine readers (9/11, 82%) identified this nodule as calcified. Volumetric quantification of the calcification in the SPN yielded a Vol160HU value of 36.62% (Vol160HU indicates the volume % of area > 160 HU in the SPN). **c** A 54-year-old man with calcified granuloma. A 10.6 mm, ovoid SPN was seen in the right upper lung. Eight readers (8/11, 72.7%) identified this nodule as non-calcified. Volumetric quantification of the calcification in the SPN yielded a Vol160HU value of 26.1% (Vol160HU indicates the volume % of area > 160 HU in the SPN)

greater the diagnostic performance in detecting calcification in the SPN. The PPV (95%) for group 1 SPNs was significantly superior to those for groups 2 and 3 (75% and 19.2%, respectively). In comparison, the NPVs for groups 1 and 3 SPNs were similar (95.2% and 93.8%, respectively), while that for group 2 SPNs was the lowest (74.8%).

False positive predictions of calcification in an SPN are also important when managing an SPN; if a non-calcified SPN is interpreted as calcified, and no further evaluation is performed, the consequences could be frightening. Even if the SPN is not calcified, SPNs ≥ 7 mm in diameter may appear to be as dense as or denser than an adjacent rib [18]. In line with this flaw in visual subjective assessments, the 291 SPNs rated as having "definite calcification" (confidence score of 5) included 59 non-calcified SPNs. Therefore, the false positive rate was 20.3% (59/291), and eight cases were confirmed as primary lung cancers. Consequently, 2.74% of the malignant SPNs would have been missed in the primary CXR evaluation because they were identified as benign calcified SPNs. Based on the SPN diameter, the false positive rates for groups 1–3 were 4.96% (7/141), 25% (31/124), and 80.8% (21/26), respectively. Overall, there were no malignant SPNs in group 1, one malignant SPN in group 2, and seven malignant SPNs in group 3. This implies that a false positive interpretation is more common for larger than smaller SPNs. All seven false positive SPNs in group 1 overlapped with a rib or the scapula. Therefore, careful assessment is warranted when evaluating calcification in such SPNs, even when SPN is small. A high CT threshold for assessing suspicious SPNs should not be applied for these SPNs.

To classify a calcified SPN as benign, calcification should involve over 10% of the nodule in a CT image and pattern of calcification should be central, diffuse, laminated, or popcorn type [14–16, 28]. In our series, the MDCT volumetric quantification of SPNs classified as having definite benign

calcification revealed that the smaller the size of SPN, the greater the volume percentage of calcification in the SPN (56.85%, 48.74%, and 28.53% of calcification in groups 1–3, respectively) and this volumetric information of current study is greater than that of previous study. It might be explained partially by the CT data obtained using a slice thickness of 1 mm, which would minimize the partial volume averaging artifact.

This study had several limitations. First, it is subject to the inherent flaws associated with its retrospective nature. Second, the number of calcified nodules was not comparable among the three SPN diameter groups. Further studies including and even distribution of calcified SPNs according to diameter are warranted. Third, the pattern of calcified on the CT image was mostly diffuse. Other benign patterns of calcification (e.g., laminated or popcorn) could influence the volume of calcification in the SPNs. Finally, further study with larger samples could help to understand more clearly visual assessment of nodule calcification on chest radiography in relation with volume of calcification in solitary pulmonary nodule.

In conclusion, the overall ability of digital CXR to predict calcification in SPNs was moderately accurate (AUC = 0.71) and the diagnostic performance for predicting calcification in SPNs was significantly higher, and interobserver reproducibility was good when the SPN < 10 mm in diameter. Based on the MDCT measurements, the SPNs with benign calcification contain calcification of approximately 50% of their volume, and the SPNs scored as having "definite calcification" by radiologists using digital CXR also calcified in approximately 50% of their volume.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Joo Sung Sun.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- Retrospective
- Observational
- Performed at one institution

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