Improved Detection of Subtle Lung Nodules by Use of Chest Radiographs With Bone Suppression Imaging: Receiver Operating Characteristic Analysis With and Without Localization

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OBJECTIVE. The purpose of this article is to evaluate radiologists' ability to detect subtle nodules by use of standard chest radiographs alone compared with bone suppression imaging used together with standard radiographs.

MATERIALS AND METHODS. The cases used in this observer study comprised radiographs of 72 patients with a subtle nodule and 79 patients without nodules taken from the Japanese Society of Radiological Technology nodule database. A new image-processing system was applied to the 151 radiographs to create corresponding bone suppression images. Two image reading sets were used with an independent test method. The first reading included half of the patients (a randomly selected subset A) showing only the standard image and the remaining half (subset B) showing the standard image plus bone suppression images. The second reading entailed the same subsets; however, subset A was accompanied by bone suppression images, whereas subset B was shown with only the standard image. The two image sets were read by three experienced radiologists, with an interval of more than 2 weeks between the sessions. Receiver operating characteristic (ROC) curves, with and without localization, were obtained to evaluate the observers' performance.

RESULTS. The mean value of the area under the ROC curve for the three observers was significantly improved, from 0.840 with standard radiographs alone to 0.863 with additional bone suppression images ($p = 0.01$). The area under the localization ROC curve was also improved with bone suppression imaging.

CONCLUSION. The use of bone suppression images improved radiologists' performance in the detection of subtle nodules on chest radiographs.

Keywords: bone suppression imaging, chest radiography, lung nodules, receiver operating characteristic with and without localization

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A major cause of radiologist-missed lung cancers is obscuration of a nodule by superimposed bones, such as ribs and clavicles, on standard chest radiographs [1]. Radiologists' performance for the detection of pulmonary lung nodules, including nodular lung cancers, has been shown to be improved by the use of dual-energy subtraction chest radiographs [2–4]. However, dual-energy subtraction radiographs require specialized equipment and are associated with a potential small increase in the average radiation dose. A postprocessing bone suppression imaging algorithm can suppress the conspicuity of bones on chest radiographs to create corresponding bone suppression chest images [5, 6], and radiologists' performance in the detection of small (< 20 mm) malignant nodules on chest radiographs by the use of bone suppression imaging was improved in a sequential observer study [7].

In the present study, we used a new image-processing system for bone suppression imaging. The purpose of this study was to evaluate radiologists' detection of subtle nodules by use of standard chest radiographs alone compared with standard chest radiographs plus bone suppression images in an independent observer test using receiver operating characteristic (ROC) analysis, both with and without localization.

Materials and Methods

Institutional review board approval was obtained, and the requirement for informed patient consent was waived. Our study was HIPAA compliant.

Database

The database used in this study [8, 9] included 154 standard posterior-anterior chest radiographs with a lung nodule and 93 chest radiographs without a nodule that had been created by the Japanese

Society of Radiological Technology from 14 medical centers in Japan and the United States. These chest radiographs had been digitized by a laser digitizer with 2048 × 2048 matrix size (0.175-mm pixels) and 12-bit gray scale. The presence or absence of lung nodules included in the database was confirmed by CT examination [8]. In this database, case information was provided by the database creators, including patient age, sex, diagnosis (malignant or benign), X and Y coordinates of nodule, simple diagram of nodule location, and degree of subtlety in visual detection of nodules, in addition to the raw image data (2048 × 2048 matrix size; 12-bit gray scale). The nodule subtlety was classified into five categories—1, very subtle; 2, subtle; 3, relatively subtle; 4, obvious; and 5, very obvious—according to the consensus of three chest radiologists (with 10, 16, and 26 years of experience). The size of each nodule included in the database was measured on the chest radiographs by one of the database creators according to the consensus of three radiologists, and the average size of all nodules was 17.3 mm (range, 0–60 mm). The diagnosis for malignant nodules was determined on the basis of histologic and cytologic examination, and that for benign nodules was determined on the basis of histologic examination, definitive isolation of a pathogenic organism, shrinkage and disappearance with the use of antibiotics, or no change observed during a follow-up period of 2 years. To supplement the original information provided with the database, we obtained the contours of nodules, except for a few nodules with unidentified contours, which had been drawn with the consensus of a different set of two experienced chest radiologists (both with 16 years of experience) during a previous study [10]. Note that none of the five chest radiologists mentioned in this paragraph were included in the current observer study.

A radiologist (with 18 years of clinical experience and 16 years of research experience) who was blinded to the images included in the database decided the exclusion criteria that were used to choose the chest radiographs for the current observer study on the basis of the nodule subtlety ratings provided by the original database creators. This radiologist, as well as two other experienced (25 and 10 years of experience) radiologists, participated in this observer study.

The exclusion criteria for selection of chest radiographs in our observer study included unknown ages or ages younger than 16 years; nodule diameter greater than 30 mm; absence of contour information; nodules that had been rated as either very subtle, obvious, or very obvious (categories 1, 4, or 5); and the existence of potential false-positive results, such as confusing scars, very small (< 3 mm) or calcified nodules, and unilateral nipple shadows in images without a lung nodule, as judged by two or more radiologists who were also observers in this study.

Seventy-two patients (35 men and 37 women; mean age, 60 years) with a subtle nodule (including both subtlety categories 2 and 3) as well as 79 patients (39 men and 40 women; mean age, 56 years) without a lung nodule were used for an observer performance study. The 72 patients with a lung nodule included 47 patients with a malignant nodule and 25 patients with a benign nodule. There were 29 nodules located in the left lung and 43 located in the right lung. Among the 72 remaining nodules, eight nodules were obscured by the heart or diaphragm (but these were not excluded). The mean size of these nodules was 16 mm (range, 6–30 mm).

Bone Suppression Imaging System

A new bone suppression image–processing system (SoftView version 2.0, Riverain Medical) that has been approved for clinical use in the United States by the Food and Drug Administration was applied to the 151 chest radiographs to create corresponding bone suppression images. The techniques used to produce bone suppression images, which can suppress the conspicuity of bones by a software-only approach, are shown in Figure 1. SoftView is a software approach to bone suppression that uses image normalization, feature extraction, and regression networks to predict the bone image. Using the predicted bone image, a soft-tissue image is formed. Because SoftView is a proprietary system, details of the method have not been publicly disclosed. No operator controlled adjustments are available for this system.

Observer Performance Study

An independent test method was used for the observer study, using two image sets. The first image set included all 151 patients, with half (a randomly selected subset A) showing only the standard chest radiograph, and the other half (subset B) showing the standard chest radiograph plus bone suppression images. The second image set also included all 151 patients, with subset A shown with standard chest radiograph plus bone suppression images, and subset B shown with only standard chest radiograph images. The numbers of patients with and without nodules were balanced in each subset. The order of cases within each image set was randomized. At the first reading session, the three experienced radiologists read the first image set. Two weeks later, these same radiologists read the second image set.

The radiologists indicated their confidence levels regarding the presence of a lung nodule by clicking with the mouse to mark a point on a confidence bar (from 0 to 100), and they also marked the most likely position, if they thought a nodule was present, for each image or image pair. The chest radiographs and bone suppression images were displayed for interpretation on liquid crystal display monitors (1600 × 1200 resolutions). Window level and width could be controlled manually by the

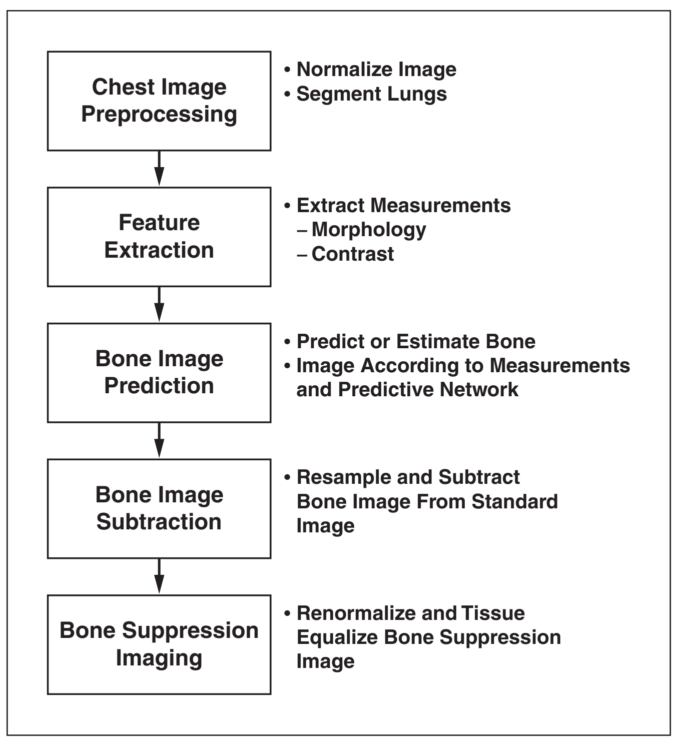


Fig. 1—Method for bone suppression imaging.

observers, and a magnification tool was available. No clinical parameters were provided to the observers. Observers were informed that images might or might not contain a nodule but were not informed regarding the proportion of patients with nodules. We provided a training session before the test with three patients who were not used in the study and instructed the observers how to use the confidence rating scales appropriately.

Data Analysis

The confidence level ratings from each observer for 151 patients were analyzed by use of the ROC method, and a quasi–maximum likelihood estimation of the binormal distribution was fitted to the radiologists' confidence ratings [11]. The statistical significance of the difference in the values of the area under the ROC curve (AUC) between observer readings with chest radiographs versus chest radiographs plus bone suppression images were tested by use of the Dorfman-Berbaum-Metz method [12, 13], which included both reader variation and case sample variation by means of an analysis-of-variance approach. Localization ROC curves [14] for observers without and with the computer-aided detection scheme were also determined for each reading condition. A "proper" binormal model [15] was used for the ROC and localization ROC curves. In this study, localization was considered correct if the indicated point was located within the contour of the nodule. The sensitivity in this study was defined according to the number of nodule lesions that were correctly located by an observer, regardless of the confidence level ratings. However, the confidence level ratings for corresponding positions (nodules or false-positives) located by all three observers were all over 0.50 in this study.

TABLE 1: Area Under the Receiver Operating Characteristic Curve Values for Three Radiologists in Detecting Subtle Lung Nodules on 151 Chest Radiographs Without and With Bone Suppression Imaging

Observer	Without Bone Suppression Imaging	With Bone Suppression Imaging
A	0.899	0.924
B	0.795	0.824
C	0.826	0.840
Mean	0.840	0.863

Note—The difference in the area under the curve values without and with the bone suppression imaging was statistically significant ($p = 0.01$ for three radiologists combined).

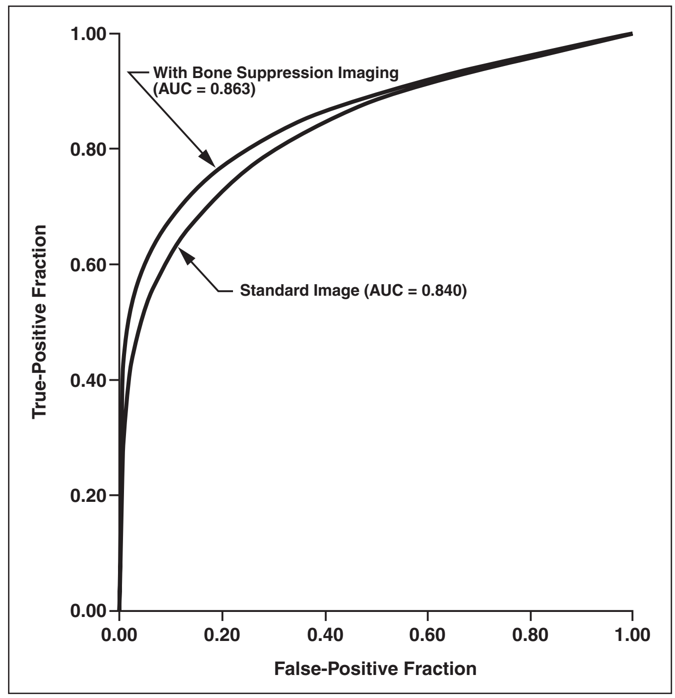


Fig. 2—Receiver operating characteristic (ROC) curves for detection of subtle nodules on chest radiographs. Difference in area under ROC curves (AUC) without and with bone suppression images was statistically significant ($p = 0.01$ for three radiologists combined).

Results

The mean AUC value of the ROC curves for the three observers was significantly ($p = 0.01$) improved, from 0.840 with chest radiographs alone to 0.863 with chest radiographs plus bone suppression images, in the detection of subtle lung nodules on 151 chest radiographs without and with bone suppression imaging (Table 1; Fig. 2). The mean detection rate of the 72 subtle nodules (correct localizations) was improved, from 60% with chest radiographs alone to 64% with chest radiographs plus bone suppression images, for the three observers. However, the mean number of false-positive results (i.e., incorrect localizations) on 151 images was increased from 18 by use of chest radiographs alone to 25 by use of chest radiographs plus bone suppression images (Table 2). The area under the localization ROC curve also improved (Fig. 3).

For the 25 nodules with a subtlety rating of 2 ("subtle"), the mean AUC value of the ROC for the three observers was slightly improved (from 0.722 with chest radiographs alone to 0.758 with chest radiographs plus bone suppression images), but this improvement fell short of statistical significance ($p = 0.15$) (Table 3; Fig. 4). Many of the subtle lung nodules were very difficult to detect on the standard chest radiographs but were relatively easy to detect on the bone suppression images (Figs. 5 and 6).

Discussion

The observers' performance for the detection and characterization of noncalcified and calcified lung nodules can be improved by using dual-energy subtraction chest radiographs, including soft-tissue images that eliminate bone shadows and bone images that enhance calcified structures [2]. Generally, the soft-tissue image is more important than the bone image for the detection of nodular lung cancers because a major cause of failure to detect these cancers is obscuration by superimposed bones, such as ribs and clavicles. Shah et al. [1] reported that, in a case series with 40 missed cancers, 95% were partly obscured by overlying ribs, including 65% that were obscured by two or three bones and 22% that were also obscured by a clavicle. In a previous observer study [3], we showed that observers' ability to detect cancers previously missed by radiologists was significantly improved by use of dual-energy subtraction chest radiographs. However, dual-energy subtraction radiographs require specialized equipment and also are associated with a small potential increase in average radiation dose.

TABLE 2: Three Radiologists' Performance for Detecting Subtle Lung Nodules on 151 Chest Radiographs Without and With Bone Suppression Imaging

Observer	Without Bone Suppression Imaging	With Bone Suppression Imaging
Detection rate of 72 nodules (%)		
A	75	79
B	49	56
C	54	57
Mean	60	64
No. of false-positive results		
A	41	51
B	4	12
C	9	11
Mean	18	25

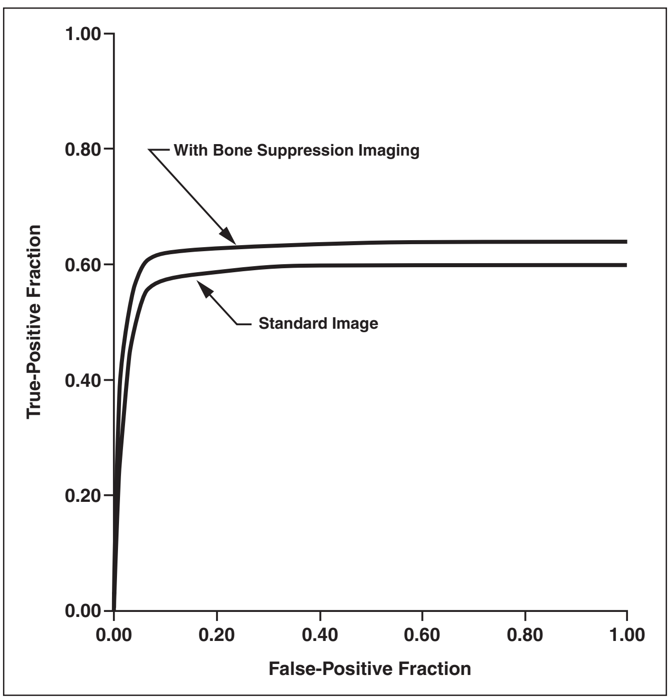


Fig. 3—Localization receiver operating characteristic (ROC) curves for detection of subtle nodules on chest radiographs with three observers. Area under localization ROC curve was improved with use of standard chest radiographs with bone suppression imaging.

TABLE 3: Area Under the Receiver Operating Characteristic Curve Values for Three Radiologists in Detecting Lung Nodules With Subtlety Category 2 ("Subtle") on 104 Chest Radiographs Without and With Bone Suppression Imaging

Observer	Without Bone Suppression Imaging	With Bone Suppression Imaging
A	0.861	0.863
B	0.655	0.703
C	0.652	0.708
Mean	0.722	0.758

Note—The difference in area under the curve values without and with the bone suppression imaging was not statistically significant ($p = 0.15$ for three radiologists).

Image-processing techniques for suppressing skeletal structures on standard chest radiographs have been reported recently [5, 6]. Postprocessing bone suppression imaging algorithms can suppress the conspicuity of bones, thereby creating an appearance similar to that of a dual-energy soft-tissue image. On bone suppression images, the conspicuity of both normal soft-tissue structures and abnormal lesions, such as noncalcified lung nodules, can be enhanced.

Oda et al. [7] reported that rib suppression with processed chest images by using a massive training artificial neural network technique developed by Suzuki et al. [6] significantly improved the detection of lung nodules (AUC values improved from 0.816 to 0.843). In our observer study, we applied a new bone suppression image–processing system to the chest radiographs to create corresponding bone suppression images. Our results showed that the radiologists' performance for the detection of subtle nodules was also significantly improved (AUC values improved from 0.840 to 0.863) by using chest radiographs together with bone suppression images compared with using standard chest radiographs alone.

The same published lung nodule database [8, 9] was used by Oda et al. [7] and in the present study. The differences between the two studies include the larger number of cases used, the criteria for selection of cases from the database, and the independent observer test method used. Specifically, the number of cases (72 patients with a nodule and 79 patients without a nodule) in our study was substantially larger than that in the study by Oda et al. [7], which used a total of 60 patients (randomly selected) with or without a nodule. The case selection criteria differed in that we excluded obvious nodules and very subtle nodules from our observer study. The reason for the exclusion of very subtle nodules was that these cases were usually not considered actionable on the basis of the chest radiograph [16]. The independent test method used in our study is a well established experimental design, although it requires more time than the sequential test method. Another difference in our study was the use of ROC analysis with localization. Finally, the techniques to create bone suppression images were different in the two studies.

Many factors, including the imaging technique and location and subtlety of lung nodules, might influence radiologists' decisions in detecting lung nodules in observer tests

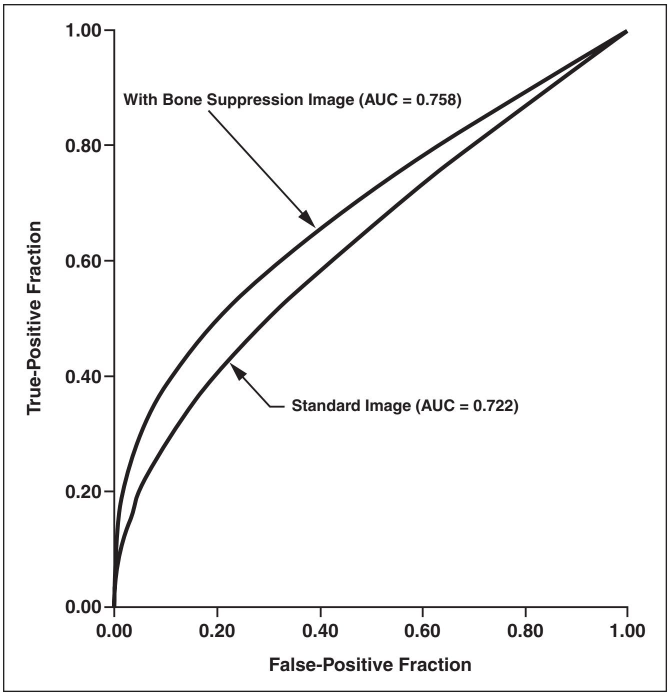
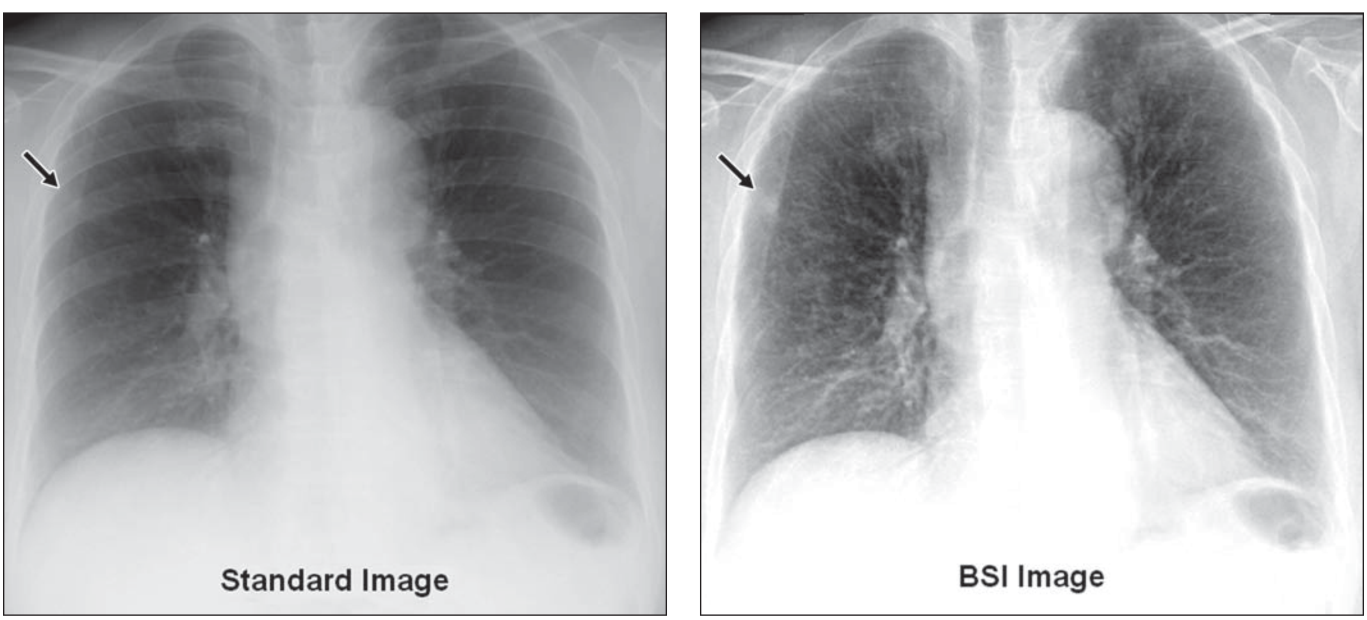


Fig. 4—Receiver operating characteristic (ROC) curves for detection of nodules with subtlety category 2 ("subtle") on chest radiographs. Difference in area under ROC curve (AUC) values without and with bone suppression imaging was improved but not statistically significant ($p = 0.15$ for three radiologists combined).

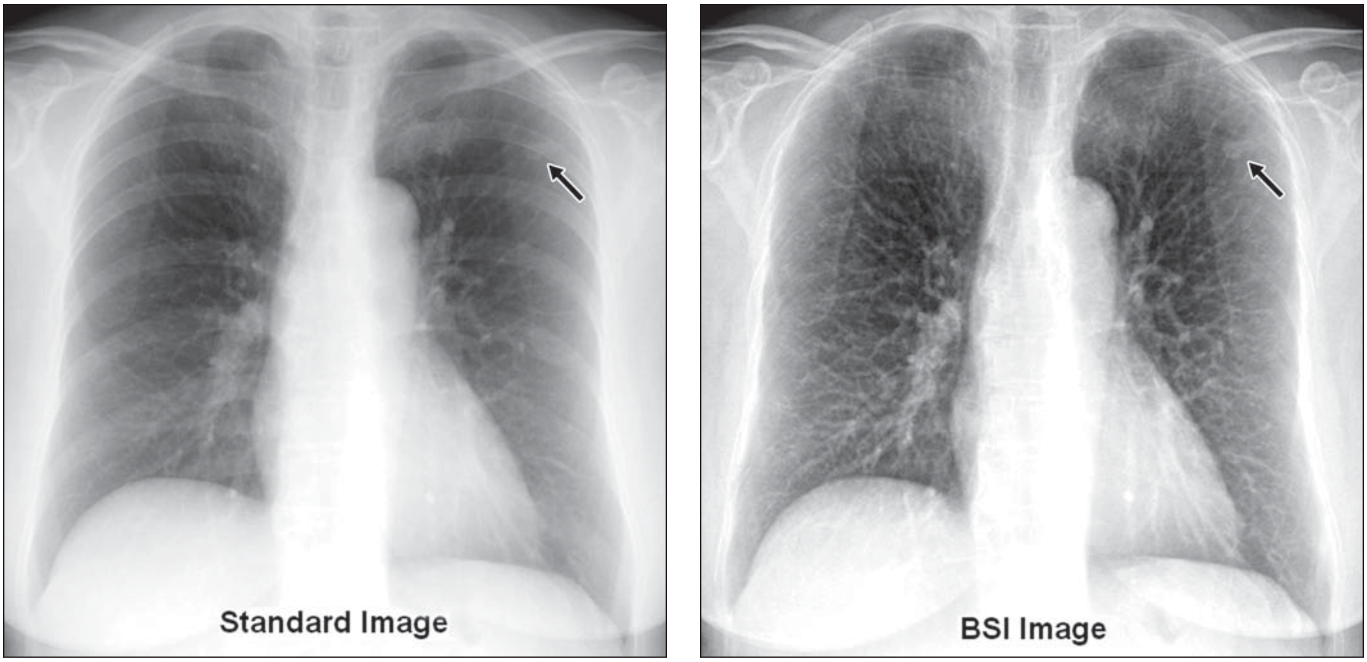
[17–20]. The number of false-positive results can increase when observers use image-processing or computer-aided detection systems [19, 20]. Our results showed that the mean sensitivities by three radiologists were relatively low when using both chest radiographs alone (60%) and chest radiographs plus bone suppression images (64%), probably because we only included subtle nodules. Although the mean numbers of false-positive results were slightly increased by use of chest radiographs plus bone suppression images, the more important result showed that ROC curves with localization were improved by use of chest radiographs plus bone suppression images compared with use of chest radiographs alone, in a manner similar to the general ROC curves.

A limitation of this pilot study includes the use of digitized chest radiographs, because digitization is not frequently used currently for film interpretation. However, the use of bone suppression imaging also improved radiologists' accuracy for the detection of small lung cancers on computed radiographs that were obtained from our medical center in another observer study [21]. In that study [21], our goal was to compare bone suppression imaging with dual-energy subtraction chest radiographs, so we used a different test method (sequential observer test). Also, the differences in the detection of small lung cancers by using chest radiograph alone, chest radiograph plus bone suppression imaging, and chest radiograph plus dual-energy subtraction were compared for two observer groups (experienced and less experienced) and two reading-time groups (time limited and unlimited). We think that the benefits of bone suppression imaging applied to computed radiography should be comparable or superior to those with digitized radiography, on the basis of our experience with image processing using these digital detectors, not least because computed radiography captures a greater gray-scale range.



A B

Fig. 5—69-year-old woman with inflammatory subtle nodule (subtlety 2 on standard radiograph) in right upper lobe.
A, Standard chest radiograph shows nodule (*arrow*) that is extensively overlapped by ribs.
B, Bone suppression image (BSI) clearly shows nodule (*arrow*). Average recorded confidence level regarding presence of nodule by three observers was 0.21 by use of standard chest radiograph alone, versus 0.68 by use of standard chest radiograph plus bone suppression imaging.



A B

Fig. 6—69-year-old woman with nodular cancer (subtlety 3 on standard radiograph) in left upper lobe.
A, Standard chest radiograph shows cancer (*arrow*) that is partly overlapped with ribs.
B, Bone suppression image (BSI) clearly shows cancer (*arrow*). Average recorded confidence level regarding presence of nodule by three observers was 0.67 by use of chest radiograph alone, versus 0.77 by use of chest radiograph plus bone suppression imaging.

Other limitations include the fact that this study was a preliminary test by a small observer group using selected images. A few "normal" cases with potentially confusing findings were excluded, which might lead to a reduction in the false-positive rate. Our case selection was based on the visual subtlety of nodules but not the lesion size per se, because obvious nodules do not require bone suppression imaging for detection. On the other hand, if the technique can improve diagnostic accuracy in the detection of subtle nodules that may be overlooked by radiologists, it has the potential to benefit patients.

Even in our small observer group, two types of radiologists were included. Observer A had much higher sensitivity but also a much higher false-positive rate compared with the other two observers. In fact, observer A had average rating scores for all 151 chest radiographs of 0.487 without and 0.598 with bone suppression imaging, whereas the other two observers had average scores of 0.380 and 0.430 and of 0.338 and 0.352, respectively, without and with bone suppression imaging. This meant that observer A was progressive and the other two observers were conservative for identifying lung nodules on chest radiographs. However, this result would not affect the ROC curve fittings because the fitting algorithm was not affected by the absolute value of the original rating score but depended on the order of rating scores for each case.

In summary, the results of this study suggest that the use of bone suppression images can significantly improve the detection of subtle lung nodules compared with standard chest radiographs alone.

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