

## Original Article



# The Value of Inverted Images for Pulmonary Nodule Detection

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## Abstract

**OBJECTIVE:** Chest X-ray (CXR) is the most commonly used initial modality for most lung diseases, including pulmonary nodules. In diseases such as lung cancer, tuberculosis, and fungal infections, detecting a single nodule in the early stages will facilitate treatment. One of the most important obstacles to searching for a single pulmonary nodule on a CXR is peripheral background contrast enhancement, and density differences. The aim of this study was to demonstrate the superiority of inverted gray scale to the standard image of CXR in the detection of a single pulmonary nodule.

**MATERIAL AND METHODS:** The design of the study included the evaluations of two radiologists unaware of each other, and past computed tomography reports. They randomly evaluated standard and inverted gray scale images of posteroanterior CXRs of both nodule-containing and non-nodule-containing patients, totaling 100 in total. Each evaluation was graded from one to three as one stood for nodule negative, two was for doubtful and three was for nodule positive ones.

**RESULTS:** The percentage of the patients who were correctly identified as having the nodule [sensitivity (inverted 68.15% - standard 57.14%)] and not having [specificity (inverted 87.56% - standard 88.71%)] showed a statistically significant difference in inverted gray scale (negative) image compared to the standard image ( $P \leq 0.001$ ).

**CONCLUSION:** Inverted chest radiogram is significantly exposing the nodule presence over the white background so that should be highlighted and considered as a part of useful scanning. So that in terms of functional benefit and additionally cost effectiveness, we advice this technique in part of routine CXR evaluation.

**KEYWORDS:** Inverted gray-scale, standard image, pulmonary nodule, chest X-ray

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## INTRODUCTION

Lung cancer, tuberculosis, fungal infections, and pneumonia are common lung diseases for public health, so that their correct diagnosis and good differentiation is important.<sup>1</sup>

Detecting a single (solitary) nodule in the early stages would certainly facilitate the treatment.<sup>2-5</sup> However, a solitary pulmonary nodule is detected in only 1/500 chest X-ray (CXR) scans, and most of these nodules, approximately 90%, exist without distinct clinical findings. The CXR alone is not sufficient imaging method as well as for diseases work-up and progress.

The literature already stated that the margin of error in diagnosis by CXR is between 20 and 50%.<sup>2,4,6,7</sup> The standard images of CXR define lung nodule as a small round or oval-shaped radiopacity that is smaller than three centimeters in diameter. While searching for a single pulmonary nodule in the CXR, one of the main obstacles is the involvement of environmental (background) contrast and density differences. Today's new digital applications advanced the image

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quality and increased the local contrast. The perception of contrast difference by the human visual system has also been studied, and it has been proven that better perception can be achieved when a dark object is presented over a light background.<sup>8</sup> The digital X-ray machine has a software program which could provide this so-called perceptual phenomenon by changing the standard (positive image) into the inverted (negative image). The main change here is that a subtle pulmonary nodule would appear as a dark spot over the white background. So we questioned in this study whether negative images would be more effective to catch an average sized solitary pulmonary nodule.

## MATERIAL AND METHODS

### Study Design

This study is a case-control study planned with a cross-over design. Computed tomography (CT) and CXR were obtained from the hospital picture archiving and communication system (PACS). This study was approved by the University of Health Sciences Türkiye Hamidiye Faculty of Medicine Ethics Committee (IRB: 20-39, date: 19.05.2020). Informed written consent was obtained for each patient who underwent CXR and CT, and the Declaration of Helsinki was fully adhered to during measurement and writing.

### Inclusion and Exclusion Criteria

A total of four hundred patients who were referred for posteroanterior (PA) CXR from the chest diseases outpatient clinic and were subsequently sent to the radiology unit were chosen in the study. Our study included patients over eighteen years. The patients were suspected to have nodules before diagnosis. We established study groups in two categories: fifty patients with a single pulmonary nodule and fifty people in the control group (without nodule). The presence of nodules in the patients had been confirmed by a previous CT reports (Figure 1). The patients were chosen from those whose nodule size was between 5 and 10 mm. Patients aged <18 years, with multiple pulmonary nodules, a history of thoracic surgery, pneumothorax, or chest trauma were excluded from the study.

### Main Points

- The aim of this study was to demonstrate the superiority of inverted gray scale compared to the standard chest X-ray image in the detection of a single pulmonary nodule.
- The design of study included the evaluations of two radiologists unaware of each other and past computed tomography reports.
- The percentage of the patients who were correctly identified as having the nodule (sensitivity) and not having (specificity) was showing statistically meaningful difference in inverted gray scale (negative) image comparing to the standard image ( $P \leq 0.001$ ).
- An inverted chest radiogram significantly exposes the presence of nodules over the white background, which should be highlighted and considered as a part of the diagnostic process.

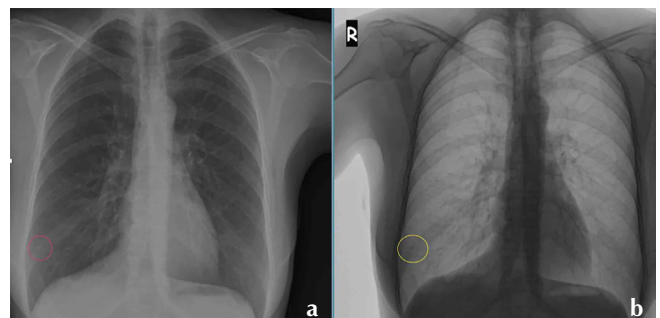
### Imaging Evaluate and Data Collection

The CXRs of these two groups were taken from the system and stored in a random order. All CXRs of the patients and the control group were evaluated at different times by two different radiologists, independently of the physician who created the data collection. These two radiologists had at least 4 years of experience in thoracic radiology. The radiologists were not informed about each other's participation, and the images were shown separately in a random sequence. The images were screened on the monitor that is 1280x1024 pixels of resolution. The CXR of patients and the control group with their standard and the gray scale (negative) images (Figure 2a, 2b) made a total of 100 images and took 4 days of radiologists' who viewed each image 15 minutes duration long. The statistical work up based on the total of 400 evaluation. The study randomization was supplied by director of the study. During the evaluation of the images zooming like operations were not interfered with. However, the use of contrast and coloring processes has been restricted.

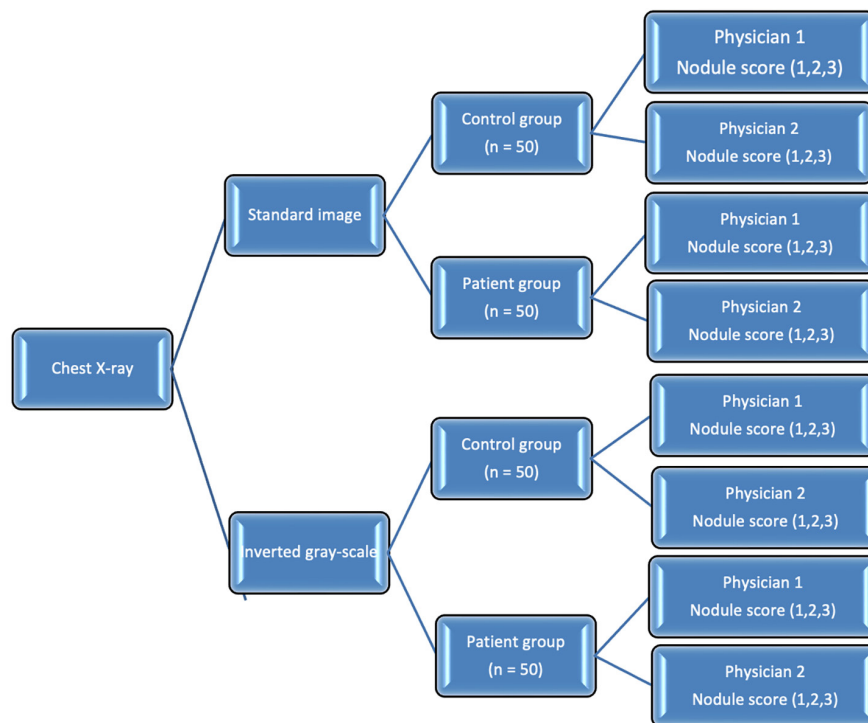
Each radiologist gave a score between one and three for each image. The score one meant there was no nodule, two was standing for undetermined or suspicious cases and three indicated a nodule (Figure 3).



**Figure 1.** Coronal computed tomography image right inferosuperior segment 4 mm peripherally located non-calcifying nodule



**Figure 2.** (a) Postero-anterior chest X-ray of right inferosuperior nodule. b) Negative (gray-scale inverted) image of right inferosuperior nodule



**Figure 3.** Evaluation of pulmonary nodules on chest X-ray

### Statistical Analysis

All analyses of the data were made using Statistical Package for the Social Sciences version 22, (IBM, Armonk, NY, USA). All numerical variables were defined as median, minimum, maximum, and categorical variables were defined as frequency and percentages. Spearman's Rho, Pearson chi-square, and Fisher's exact test were used to evaluate interpersonal correlation. According to Spearman's coefficient values ( $P$ ),  $<0.3$  represents a weak relationship,  $0.3-0.7$  represents a moderate relationship, and  $>0.7$  represents a strong relationship. Statistical significance was obtained at  $P < 0.01$  level. Since the data did not show a normal distribution, all analyses were performed with non-parametric methods.

### RESULTS

The study included 56 female and 44 male patients over the age of 18 (minimum 21-maximum 93), and median age was 39.50. The twenty nodule positive (+) patients were female and thirty nodule positive (+) patients were male; the minimum age of nodule positive patients was 22, maximum 93, and the median age was 53. The thirty-six nodule negative (-) patients were male, and fourteen nodule negative (-) patients were female; the minimum age of nodule negative patients was 21 years, maximum 50 years; the median age was 29.

Two radiology physicians evaluated the images, and their assessments were compared using Spearman's correlation. All of the radiology physicians' X-ray image assessments were positively correlated with each other; the lowest positive correlation was  $P < 0.04$  ( $P = 0.29$ ), and the highest was  $P < 0.0001$  ( $P = 0.62$ ). All of the radiology physicians' inverted image assessments were positively correlated with each other. The lowest positive correlation within the physicians was  $P < 0.0001$ , ( $P = 0.42$ ), and the highest was  $P < 0.0001$ , ( $P = 0.66$ ).

Fifty X-ray control (nodule negative) lung images and fifty inverted control lung images were evaluated by the radiologists. The results of their evaluations were categorized as 1: I did not diagnose any nodules, 2: I am not sure, 3: I did diagnose nodules. Fifty X-ray positive (nodule positive) lung images and fifty inverted positive lung images were also evaluated by the same radiologists. The results of their evaluations were categorized as described above.

In the 100 X-ray control lung image evaluations (50 images, 2 radiology physicians, 100 evaluations), 82 evaluations were 1 (right answer); 11 evaluations were 3 (wrong-positive answer); and 7 evaluations were 2 (not sure). Seven evaluations in category 2 were included in category 3, because the radiology physicians reported those as "Nodule". Therefore, there were 18 false-positive evaluations in the X-ray control lung images.

In the 100 inverted control lung image evaluations (50 images, 2 radiology physicians, 100 evaluations), 84 evaluations were rated as 1 (right answer), 12 evaluations were rated as 3 (wrong-positive answer) and 4 evaluations were rated as 2 (not sure). Four evaluations in category 2 were included in category 3, because the radiology physicians reported those as "Nodule (?)". Therefore, there were 16 false-positive evaluations in the inverted control lung images.

According to the evaluations of the control lung images, inverted images provided more accurate evaluations than X-ray images. The higher number of the true-negative evaluations of the inverted control lung images was statistically significant ( $P = 0.0001$ ), and the lower number of the wrong-positive evaluations was statistically significant ( $P = 0.002$ ) as shown in Table 1.

In the 100 X-ray positive lung images evaluations, (50 images, 2 radiology physicians, 100 evaluations), 48 evaluations were 3 (correct-positive response), 36 evaluations were 1 (incorrect-negative response), and 16 evaluations were 2 (uncertain). Sixteen evaluations in category 2 were included in category 3 because the radiology physicians reported them as “Nodule (?)”. Therefore, there were 64 true positive evaluations and 36 false negative evaluations in the X-ray positive lung images.

In the evaluations of 100 inverted positive lung images (50 images, 2 radiology physicians, 100 evaluations), 61 evaluations were 3 (right answer), 28 evaluations were 1 (wrong-negative answer), and 11 evaluations were 2 (not sure). Eleven evaluations in category 2 were included in category 3 because the radiologists reported them as “Nodule (?)”. Therefore, there were 72 right-positive and 28 wrong-negative evaluations in the inverted positive lung images.

According to the evaluations of the nodule positive lung images, inverted images were evaluated more accurately than X-ray images. The higher number of the true-positive evaluations of the inverted positive lung images was statistically significant ( $P = 0.0001$ ), and the fewer number of the wrong-negative evaluations of the inverted positive lung images was statistically significant ( $P = 0.0001$ ) as shown in Table 2. For routine CXR images, sensitivity was calculated as 57.14% and specificity as 88.71%. In inverted roentgenogram, sensitivity was found to be 68.15% and specificity 87.56%.

## DISCUSSION

In our study we aimed to see is there any advantage of the inverted image so that the common sized and shaped nodules

are better visible in the most frequently used method? For this, we set out from physiological studies on vision which indicated the dark-coloured images on a bright background were more easily discernible than bright images on a dark background.<sup>8</sup> In the literature, first, MacMahon et al.<sup>9</sup> studied 60 PA and anteroposterior chest radiograms diagnosed as hemithoraces with non-calcified pulmonary nodules, pneumothorax, interstitial infiltrate, and bone lesion, which were evaluated by twelve radiologists. There were no significant differences between positive and negative images in nonlinear and true gray scale inversion.<sup>9</sup> However they mentioned in case if negative mode was chosen for image presentation, true gray scale reversal was necessary for adequate contrast resolution. Differently, our aim was to address one specific diagnosis, and based on the physiological study, the finding that black density was clear on white was observed. In their study, there were four diagnoses and four different densities which were not all black and white. Lungren et al.<sup>10</sup> later reported that gray scale inversion and choice display sessions resulted in significantly higher nodule detection specificity and decreased sensitivity, thereby reducing false positivity. They interpreted 144 chest radiograms (72 normal and 72 with pulmonary nodules) with a 6-segment distribution. Three radiologists evaluated a different number of nodules, reporting them as three, two, or one.<sup>10</sup> In our study there was only one nodule which should be diagnosed, and we limited the contrast arrangements on machine. Sheline et al.<sup>11</sup> compared standard and inverse-intensity images to determine their ability to identify pathologically confirmed malignant pulmonary nodules and suggested that inverted images may have some advantages in the detection of pulmonary nodules. Instead of malignant lesions, in our study, we focused on the function of inverted images for ordinary sized and shaped

**Table 1.** Assessment of the evaluations according to the control (nodule-negative) lung images

| Categorized control lung image evaluations<br>(Total n = 100) | The imaging technique |          | Diagnosis evaluations | P          |
|---------------------------------------------------------------|-----------------------|----------|-----------------------|------------|
|                                                               | X-ray                 | Inverted |                       |            |
| 1. Did not diagnose nodules (n)                               | 82 (%)                | 84 (%)   | True-negative         | 0.0001***c |
| 2. Not sure<br>“Nodule (?)” (n)                               | 7 (%)                 | 4 (%)    | Wrong-positive        | 0.002**c   |
| 3. Did diagnose nodules (n)                                   | 11 (%)                | 12 (%)   |                       |            |
| Wrong-positive (n)                                            | 18 (%)                | 16 (%)   |                       |            |

n: number of evaluations.  
c: chi-square-Fisher’s exact test, \*:  $P < 0.05$ , \*\*:  $P < 0.01$ , \*\*\*:  $P < 0.0001$

**Table 2.** Assessment of the evaluations according to the positive (nodule-positive) lung images

| Categorized control lung image evaluations<br>(Total n = 100) | The imaging technique |          | Diagnosis evaluations | P          |
|---------------------------------------------------------------|-----------------------|----------|-----------------------|------------|
|                                                               | X-ray                 | Inverted |                       |            |
| 1. Did not diagnose nodules (n)                               | 36 (%)                | 28 (%)   | Wrong-negative        | 0.0001***c |
| 2. Not sure<br>“Nodule (?)” (n)                               | 16 (%)                | 11 (%)   | True-positive         | 0.0001***c |
| 3. Did diagnose nodules (n)                                   | 48 (%)                | 61 (%)   |                       |            |
| Wrong-negative (n)                                            | 36 (%)                | 28 (%)   |                       |            |

n: number of evaluations.  
c: chi-square-Fisher’s exact test, \*:  $P < 0.05$ , \*\*:  $P < 0.01$ , \*\*\*:  $P < 0.0001$



single nodule detection and its contribution to the early diagnosis, that would inevitably contribute to the treatment. In some other studies pneumothorax, pulmonary nodule, rib fractures, proximal dental problems and bullous lung diseases were studied.<sup>12-14</sup>

Musalar et al.<sup>15</sup> studied pneumothorax on anterior CXR images of a total of 268 patients (106 patients with spontaneous pneumothorax and 162 patients of control groups) with ten non-radiologists. The study was carried out by nonradiologists and was aimed at searching for non-nodular pathology. In our study, we based our analysis on the physiological principles of the human visual system, which claim the density would be discreet on the white background, as is done in negative imaging. In the case of pneumothorax, the opposite was true; their study found that negative imaging was not prioritized for diagnosing pneumothorax.<sup>15</sup>

De Boo et al.<sup>16</sup> evaluated the efficacy of gray-scale using the PACS on 74 patients and 54 nodule-negative controls. There were a total of 129 solid pulmonary nodules in these patients, and the nodule diameter range was 5-30 mm (mean: 13 mm). Six radiologists with varying levels of experience evaluated the gray-scale inversion and the standard CXR images in two separate reading sessions. Five radiologists showed a slight increase in sensitivity with the use of gray-scale reversal, but on average, the difference was not significant ( $P > 0.05$ ).<sup>16</sup> Schalekamp et al.<sup>17</sup> investigated the effect of bone suppression imaging (BSI) on the performance of observers in the detection lung nodules on CXR, compared to standard gray-scale. PA and lateral digital CXR of 111 patients with a CT proven solitary nodule (median diameter: 15 mm), and 189 controls were read by 5 radiologists and 3 residents. The prominence of nodules on radiographs was classified into four groups: marked ( $n = 32$ ), moderate ( $n = 32$ ), mild ( $n = 29$ ), and very mild ( $n = 18$ ). Observers read the PA and lateral CXRs without, then with an additional PA BSI (ClearRead Bone Suppression 2.4, Riverain Technologies) within one reading session. Nodules were better detected using BSI than with standard CXR, with the increase in detection performance being greatest for moderately and mildly prominent nodules ( $P = 0.02-0.03$ ).<sup>17</sup>

This study had a few limitations. First, the relatively small number of cases ( $n = 100$ ) evaluated was compared to other studies,<sup>10,15-17</sup> which limits the generalizability of the results. Secondly, the number of physicians (two radiologists) performing CXR evaluation was lower compared to some studies.<sup>9,10,15-17</sup> The third is that only CXRs taken in the PA plane were evaluated.<sup>9</sup> The fourth limitation is that only a single pulmonary nodule is evaluated.<sup>17</sup> Another limitation is the lack of a similar study using a similar nodule scoring (1,2,3) with which we can make a comparison.<sup>10,11</sup>

## CONCLUSION

As a result, CXRs are the most common first methods for most lung pathologies, including pulmonary nodules. Predicting existing physiological facts, we wanted to see whether the diagnostic capability of the most commonly used technique would be enhanced by inverting standard images to negative images for the usual sized solitary lung nodule, which in turn

inevitably contributes to early diagnosis and better treatment choice. We have obtained positive results supporting our hypothesis, so that in terms of functional benefit and additionally cost effectiveness, we advice this technique in part of routine CXR evaluation.

## Ethics

**Ethics Committee Approval:** This study was approved by the University of Health Sciences Türkiye Hamidiye Faculty of Medicine Ethics Committee (IRB: 20-39, date: 19.05.2020).

**Informed Consent:** Informed written consent was obtained for each patient.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices - Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search - Writing: All authors contributed equally to all contribution sections.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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