



Role of chest radiographs in early lung cancer detection

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Background: Lung cancer is the second most common and the most fatal form of cancer. Although annual low-dose computed tomography is used as the primary method of cancer screening, it presents challenges regarding resources as well as potential health risks from radiation exposure. Chest radiography (CXR), though less effective, is used frequently and commonly. Moreover, often in clinical settings, CXR is the first imaging modality used; computed tomography is subsequently performed if abnormalities are detected on CXRs. This study examined whether controlling for distractors and time constraints, as well as side-by-side comparison of multiple CXRs in clinical settings can aid earlier detection of radiological abnormalities indicative of lung cancer lesions.

Methods: Thirty-two attending physicians in the Republic of Korea examined 1,750 radiographs of 50 lung cancer cases. Using “hot spot” technology, participants indicated the possible locations of cancer lesions on each radiograph. Subsequently, the same radiographs, cropped to focus the anatomical regions where lung cancers were diagnosed, were shown side-by-side to the participants. The participants were asked to identify the radiograph which first enabled the diagnosis of lung cancer and which first showed a possible lesion.

Results: Removal of systemic constraints alone significantly improved lesion identification by 221.72 ± 9.69 days. Presenting radiographs side-by-side, cropped to relevant areas, had an additional significant and positive impact on cancer detection in both hidden and open areas on CXRs. Also, lesions were detected at smaller sizes and earlier than when actually diagnosed.

Conclusions: CXR with improved methods and settings provides an easily accessible and low-risk imaging method for earlier detection of lung cancer compared to current clinical imaging settings. Further, this study demonstrates the potential effectiveness of programs that allow side-by-side comparisons of cropped areas of multiple radiographs to detect radiological abnormalities.

Keywords: Chest; lung cancer; radiography

Submitted Oct 31, 2019. Accepted for publication Mar 13, 2020.

doi: 10.21037/tlcr.2020.04.02

View this article at: <http://dx.doi.org/10.21037/tlcr.2020.04.02>

Introduction

In 2018, Siegel *et al.* predicted that the number of newly diagnosed lung cancers that year would be approximately 234,030, making it the second most common cancer.

Moreover, they estimated the number of deaths from this condition in 2018 would be approximately 154,050 (25.3% of total cancer deaths), making it the most fatal form of cancer (1).

Despite the risk of overdiagnosis, false positives, radiation exposure, and unnecessary studies, low-dose

computer tomography (LDCT) screening of at-risk patients has offered positive outcomes for lung cancer mortality. The United States preventive services task force recommends annual LDCT screening for people aged 55 to 80 years with a 30 pack-year smoking history and a history of smoking within the last 15 years (2,3).

However, this does not mean all lung cancers can be detected with LDCT (4). Additionally, although the amount of radiation exposure in LDCT is 1/6 of that in regular CT (5), the potential health risk from this exposure is still significant (6). Furthermore, abundant resources and manpower are also needed to operate this screening system.

Conversely, chest radiographs (CXR) are one of the most commonly utilized diagnostic tools for chest diseases in clinical practice. The technology is easy to operate and the procedure has a relatively low level of radiation exposure; thus, it is the standard diagnostic tool for respiratory illnesses. Also, it imposes less of a burden on radiologists than other, more sophisticated diagnostic imaging tools.

However, CXRs are not without their shortcomings. CXRs are often performed by personnel that do not specialize in radiology. Therefore, they are more prone to misinterpretation. Of all misdiagnosed lung cancer cases, 90% utilized CXRs and 10% used CTs and other diagnostic tools (7). Misinterpreting images can result in delayed diagnosis and more negative clinical outcomes. Identifying lesions early while maintaining accuracy is the key to improving lung cancer survival (8,9).

Multiple studies have suggested that using CXRs in lung cancer screening may improve survival. For instance, Strauss *et al.* reported findings from randomized controlled trials that show CXR screening can improve lung cancer survival as cancers are diagnosed at earlier stages (8,9). Another large population-based cohort study showed an 18% reduction in lung cancer mortality with CXR screening in at-risk populations (10). Furthermore, a case-control study found that lung cancer mortality was reduced by more than 20% with CXR screening (11). These studies suggest that CXRs can be significantly beneficial for the screening of lung cancer.

In this study, we examine whether retrospective observation of lung cancer patients confirmed by pathology can elucidate significant radiological abnormalities earlier than when diagnoses were made. We also introduce a new comparison method for CXR interpretation in lung cancer patients. We hypothesize that side-by-side comparisons of cropped CXRs will improve abnormal lesion detection.

Methods

CXRs were collected from 1,500 lung cancer patients who presented to Uijeongbu St. Mary's Hospital from 2006 to 2016 and whose diagnoses were confirmed by pathology. Excluding patients who were accurately diagnosed upon their first visit and selecting for a wide variety of lesion locations, we compiled radiographs from 50 cases. Cases were selected only from those that presented first to Uijeongbu St. Mary's Hospital without a diagnosis or suspicion of lung cancer. Cases that were transferred from other hospitals were only considered if the lung cancer was an incidental finding; overall, only patients who had initial CXRs not showing lung cancer or those for which cancer was an incidental finding were included. Patients who were diagnosed retrospectively were selected by 2 radiologists, each with 33 years of clinical experience. We also added 5 normal sets of CXRs as controls. These patients were cancer-free for at least 3 years; two were completely normal and 3 developed chronic obstructive pulmonary disease. For research participants, attending physicians who were board certified in pulmonology were recruited from 9 university hospitals in the Republic of Korea. To eliminate bias, no physicians were recruited from Uijeongbu St. Mary's Hospital. The study was approved by the Uijeongbu St. Mary's Hospital Institutional Review Board (#UC17EESI0128). Informed, written consent was obtained from each participant.

For each case, we collected the CXRs obtained until the chest CT that was used to diagnose lung cancer. We selected 6 CXRs with the earliest being a "normal" image, if possible. Subsequent radiographs were selected from those that (I) we suspected showed lesions and (II) were equally spaced chronologically. In cases that had fewer than 5 CXRs that showed lesions, additional earlier CXRs were used as supplements. In cases with more than 6 CXRs, 6 radiographs were selected between when the patient was diagnosed and the last normal CXR, with chronological spacing between the radiographs as equally as possible. Radiographs that were obtained more than 3 years before the next CXR were excluded to minimize potentially severe contrasts. Radiograph selection and confirmation of lesion location with CT were performed by 2 radiologists each with 33 years of clinical experience.

All images, after removal of patient identifiers, were converted to digital files in the jpg format at maximum quality and scaled to 100%. A computer programmer designed the examination program used to evaluate

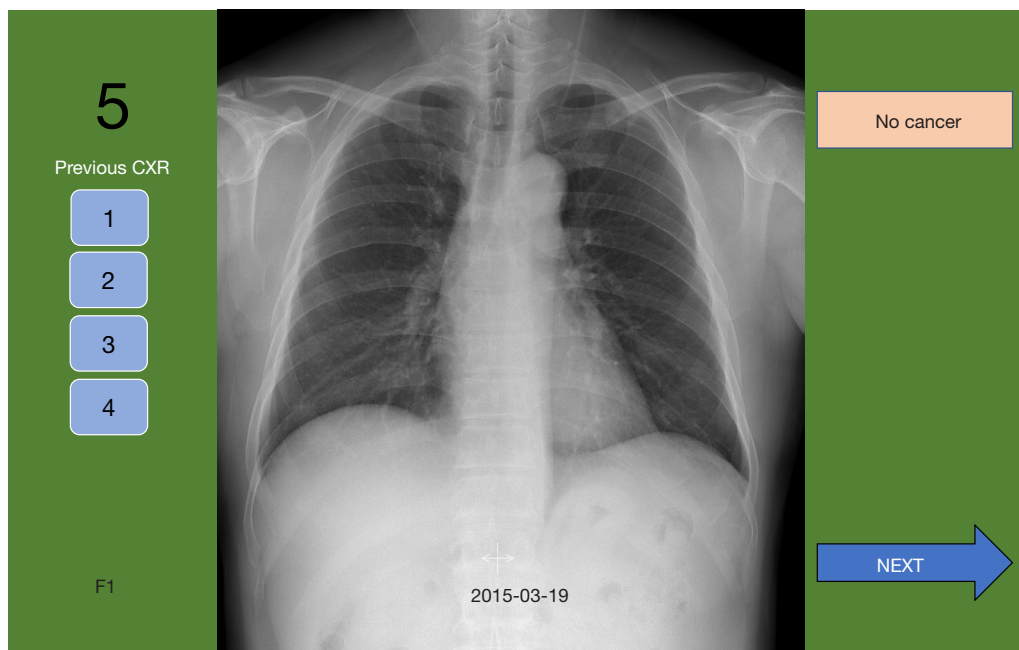


Figure 1 A sample screen of a CXR viewed by participants. CXR, chest radiography.

the participants. Images for each case were arranged in chronological order. As in a previously published study, the lesion areas on each image were outlined by freeform outlining using the Adobe Captivate 9 ‘hot spot’ technique (Adobe systems Inc., San Jose, CA, USA) (12). Outlines were made 100% transparent to prevent participants from noticing them. The last image in each case was designated as ‘0’ while other images were designated with numbers that represented the number of days between when those images were taken and when image 0 was taken. If the participant placed the mouse pointer correctly within the outline and clicked, the image’s designated number was noted. If the participant clicked in an incorrect area, an ‘X’ was noted but was not visible to the participant. If the participant thought there were no noticeable lesions on the image, he or she could click a button labeled ‘N’. Participants were allowed to click on each image only once.

Participants were allowed to navigate between the slides using arrows on the screen but could not see chronologically later radiographs until they clicked to indicate their designation on the most recent image (Figure 1). This design emulated the conditions used in actual clinical settings, wherein physicians were able to compare recent CXRs with previous ones, but which eliminated the systemic limitations, such as time constraints and other distractors (A). After the reviewing the last image of a case, a slide showed a

compilation of the cropped regions of the reviewed images with the lesion. Participants were then asked to identify the image which made them primarily diagnose cancer (DX) and first suspect a lesion (E) (Figure 2). The dates of all cases of early detection were measured as that furthest away from the day of actual diagnosis. After recording DX and E, all finalized answers were presented in a portable document format (PDF) file (Figure 3).

Lesion diameters, as shown on the CXRs, and the number of days preceding the date of actual diagnosis (F) were recorded. The variables (A, DX, E, F) were compared at each TNM classification of malignant tumors stage using the Wilcoxon rank sum test. Continuous data were reported as mean \pm standard deviation, and categorical data as numbers and percentages. Missing data were treated using the Last Observation Carried Forward (LOCF) method.

Further performance comparisons between CXRs showing lesions in ‘hidden’ areas (paraaortic area, paratracheal region, retrocardiac region, subdiaphragmatic region, apices, and hilum area) and in ‘open’ areas (right upper lobe, right middle lobe, right lower lobe, left upper lobe, and left lower lobe) were performed. Also, we examined whether differences in the amount of clinical experience, measured by the number of months the physician was a medical doctor *vs.* a specialized pulmonologist, had an impact on performance. All

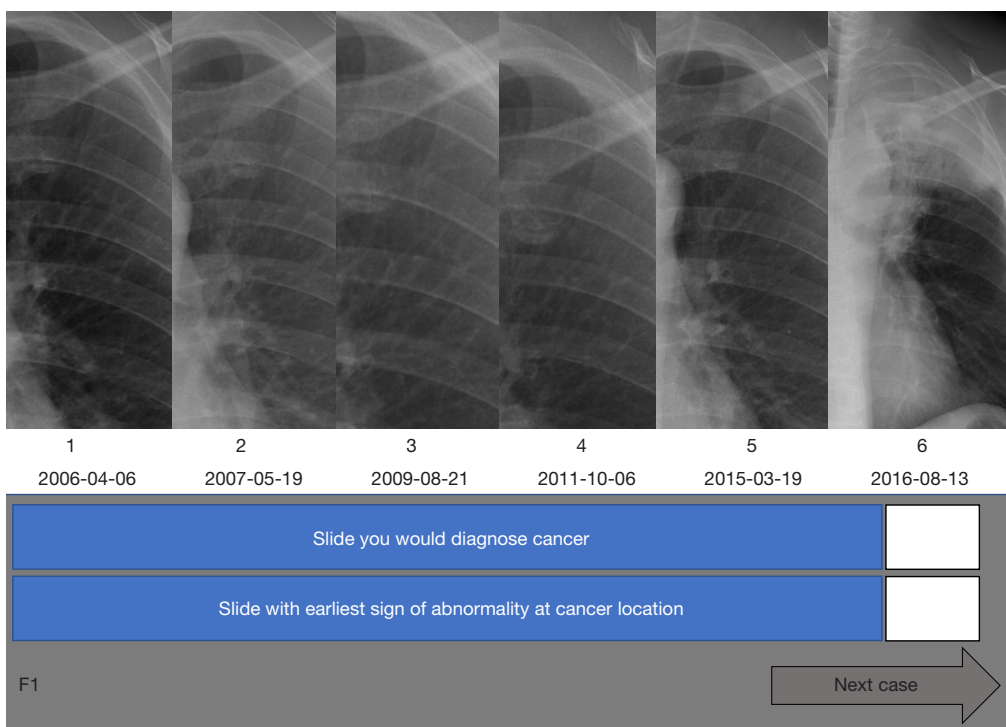


Figure 2 A sample screen of cropped side-by-side images of CXRs viewed by participants. CXR, chest radiography.

ID		Career (mons)	MD		Pul		Phone				
Earlier diagnosis days than actual diagnosis date of lung cancer											
By usual diagnosis method in clinical practice											
No	Case ID	1	2	3	4	5	6	7	8	By side by side comparison	
										DX	EX
1	A1	\$\$A11\$\$	\$\$A12\$\$	\$\$A13\$\$	\$\$A14\$\$	\$\$A15\$\$	\$\$A16\$\$			\$\$A1D\$\$	\$\$A1T\$\$
2	I1	\$\$I11\$\$	\$\$I12\$\$	\$\$I13\$\$	\$\$I14\$\$	\$\$I15\$\$	\$\$I16\$\$			\$\$I1D\$\$	\$\$I1T\$\$
3	F1	\$\$F11\$\$	\$\$F12\$\$	\$\$F13\$\$	\$\$F14\$\$	\$\$F15\$\$	\$\$F16\$\$			\$\$F1D\$\$	\$\$F1T\$\$
4	I2	\$\$I21\$\$	\$\$I22\$\$	\$\$I23\$\$	\$\$I24\$\$	\$\$I25\$\$	\$\$I26\$\$			\$\$I2D\$\$	\$\$I2T\$\$
5	J1	\$\$J11\$\$	\$\$J12\$\$	\$\$J13\$\$	\$\$J14\$\$	\$\$J15\$\$	\$\$J16\$\$			\$\$J1D\$\$	\$\$J1T\$\$
6	J2	\$\$J21\$\$	\$\$J22\$\$	\$\$J23\$\$	\$\$J24\$\$	\$\$J25\$\$				\$\$J2D\$\$	\$\$J2T\$\$
7	H3	\$\$H31\$\$	\$\$H32\$\$	\$\$H33\$\$	\$\$H34\$\$	\$\$H35\$\$	\$\$H36\$\$			\$\$H3D\$\$	\$\$H3T\$\$
8	B1	\$\$B11\$\$	\$\$B12\$\$	\$\$B13\$\$						\$\$B1D\$\$	\$\$B1T\$\$
9	F2	\$\$F21\$\$	\$\$F22\$\$	\$\$F23\$\$	\$\$F24\$\$					\$\$F2D\$\$	\$\$F2T\$\$
10	C1	\$\$C11\$\$	\$\$C12\$\$	\$\$C13\$\$	\$\$C14\$\$					\$\$C1D\$\$	\$\$C1T\$\$
11	C2	\$\$C21\$\$	\$\$C22\$\$	\$\$C23\$\$	\$\$C24\$\$	\$\$C25\$\$	\$\$C26\$\$			\$\$C2D\$\$	\$\$C2T\$\$
12	D1	\$\$D11\$\$	\$\$D12\$\$	\$\$D13\$\$	\$\$D14\$\$	\$\$D15\$\$				\$\$D1D\$\$	\$\$D1T\$\$
13	G1	\$\$G11\$\$	\$\$G12\$\$	\$\$G13\$\$	\$\$G14\$\$	\$\$G15\$\$				\$\$G1D\$\$	\$\$G1T\$\$
14	E3	\$\$E31\$\$	\$\$E32\$\$	\$\$E33\$\$	\$\$E34\$\$					\$\$E3D\$\$	\$\$E3T\$\$
15	H1	\$\$H11\$\$	\$\$H12\$\$	\$\$H13\$\$	\$\$H14\$\$	\$\$H15\$\$	\$\$H16\$\$			\$\$H1D\$\$	\$\$H1T\$\$
16	I4	\$\$I41\$\$	\$\$I42\$\$	\$\$I43\$\$	\$\$I44\$\$					\$\$I4D\$\$	\$\$I4T\$\$
17	E4	\$\$E41\$\$	\$\$E42\$\$	\$\$E43\$\$	\$\$E44\$\$	\$\$E45\$\$	\$\$E46\$\$			\$\$E4D\$\$	\$\$E4T\$\$
18	E5	\$\$E51\$\$	\$\$E52\$\$	\$\$E53\$\$	\$\$E54\$\$	\$\$E55\$\$	\$\$E56\$\$			\$\$E5D\$\$	\$\$E5T\$\$
19	E6	\$\$E61\$\$	\$\$E62\$\$	\$\$E63\$\$	\$\$E64\$\$	\$\$E65\$\$				\$\$E6D\$\$	\$\$E6T\$\$
20	J3	\$\$J31\$\$	\$\$J32\$\$	\$\$J33\$\$	\$\$J34\$\$					\$\$J3D\$\$	\$\$J3T\$\$

Figure 3 A sample PDF of answers recorded by participants. The “\$” signs instruct the Adobe Captivate program to retrieve data from the attached variable. ID, identification number; PDF, portable document format.

Table 1 Baseline characteristics of variables

Characteristics of participants	Data
Number of doctors	35
Career	
As pulmonologist (months)	146.13±112.71, 97 [50–240]
As medical doctor (months)	219.06±112.41, 188 [128–311]
Characteristics of radiographs*	
Tumor size at time of final diagnosis (mm)	42.27±19.30
Characteristics of early diagnosed CXRs*	
Number of radiographs evaluated	1,750
T stage, number of radiographs evaluated (%)*	
T1b	245 (14.0)
T1c	350 (20.0)
T2a	315 (18.0)
T2b	280 (16.0)
T3	385 (22.0)
T4	175 (10.0)

Data are expressed as mean ± standard deviation or median and interquartile range. *, categories of variables regarding radiographs evaluated. CXR, chest radiography.

statistical analyses were conducted by SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and a P value below 0.05 was considered statistically significant. Data for these comparisons were expressed as means ± standard deviations or as medians with interquartile ranges.

Results

Thirty-five physicians participated in this study. Participants had 146.13±112.71 months of clinical experience as pulmonologists. CXRs compiled from 50 cases yielded 1,750 lesion evaluations at various stages of lung cancer (Table 1). Data analysis showed participants performed significantly better without systemic constraints, making diagnoses on average 221.72±9.69 days earlier. Furthermore, cropping of relevant areas on the CXRs had a significant, positive impact on cancer detection. Cropping of images to focus on the same area on multiple CXRs further expedited diagnosis by 161.83±10.66 days, with a reduction of the lesion size by 2.36±0.33 mm at the time of diagnosis (P<0.05). This

benefit was evident regardless of the lesion location or the physician's length of clinical experience (Table 2). Thus, cropping allowed participants to detect lesions at significantly smaller diameters and significantly earlier than when a cancer diagnosis would have been made (P<0.001). Comparisons between 'hidden' and 'open' areas showed significantly better performance with 'open' areas at all stages (P<0.001) (Tables 2,3). Comparisons between different lengths of clinical experience showed no significant difference between the two subgroups at all stages (Tables 2,4).

Discussion

This study demonstrated that CXRs can be used to diagnose lung cancer earlier and that a side-by-side comparison of cropped images can enhance lung cancer detection. On average, participants were able to identify lesions 221.72 days before actual diagnoses were made using this approach. All radiographs presented were subject to the same independent analysis as would be expected in real-life situations, with no second opinion from radiologists or patients present to provide additional information. As improved performance was observed with less systemic constraints, it is plausible that better CXR reading can be achieved with improvements to the health care system. Such improvements would allow physicians to evaluate these images with fewer distractions and less time pressure. Additionally, assessing cropped CXRs displayed side-by-side offered further significant improvements, with participants detecting lesions 629.32 days earlier on average. These benefits seemed to exist across different anatomical regions and different lengths of clinical experience. This suggests that the development of software that can display all relevant CXRs side-by-side while allowing physicians to crop them all simultaneously would have significant potential advantages. These benefits will likely improve lung cancer detection at all levels of clinical practice.

Role of CXRs

CXRs are used as screening tests for chest diseases as well as other disorders. They have a low cost, can be used conveniently at bedside, have low radiation exposure, and provide an abundance of information that is useful in follow-up studies. Although survival benefits are much higher with LDCT and the advantages of screening with CXRs are still being investigated (8,9,13-16), the possible

Table 2 Comparison of different types of diagnoses

Characteristics of lesions	F	A	DX	E	Difference 1	Difference 2	Difference 3	P value 1	P value 2	P value 3
Total group										
Diameter (mm)	42.27±0.46	33.69±0.57	31.92±0.51	26.84±0.48	2.36±0.33	3.48±0.30	6.14±0.36	<0.001	<0.001	<0.001
Duration (days)	39 [24-54]	29 [19-48]	26 [16-48]	21 [14-37]	0 [0-3]	0 [0-3]	0 [0-10]	<0.001	<0.001	<0.001
	0±0	221.72±9.69	447.91±14.54	629.32±15.35	161.83±10.66	157.44±8.19	319.28±12.64	<0.001	<0.001	<0.001
	0 [0-0]	5 [1-268]	206 [13-753]	459 [160-933]	0 [0-83]	0 [0-187]	64 [0-479]	<0.001	<0.001	<0.001
Subgroup (hidden, 1,155 radiographs)										
Diameter (mm)	46.15±0.55	40.30±0.74	35.08±0.61	30.36±0.60	4.97±0.35	3.06±0.31	8.03±0.44	<0.001	<0.001	<0.001
Duration (days)	44 [31-56]	37 [24-53]	19 [13-32]	29 [16-41]	0 [0-0]	0 [0-3]	0 [0-13]	<0.001	<0.001	<0.001
	0±0	178.67±11.49	474.45±19.61	667.84±20.84	212.57±14.86	162.29±10.66	374.86±17.31	<0.001	<0.001	<0.001
	0 [0-0]	1 [1-162]	201 [23-755]	480 [160-953]	0 [0-159]	0 [0-195]	63 [0-547]	<0.001	<0.001	<0.001
Subgroup (open, 595 radiographs)										
Diameter (mm)	34.75±0.76	24.62±0.73	26.56±0.86	20.67±0.70	1.82±0.62	4.28±0.63	2.46±0.59	0.613	<0.001	<0.001
Duration (days)	29 [21-48]	19 [14-27]	19 [14-29]	17 [13-22]	0 [0-0]	0 [0-2]	0 [0-6]	<0.001	<0.001	<0.001
	0±0	305.29±17.27	401.62±20.39	561.92±20.96	63.35±11.22	148.04±12.34	211.38±14.93	<0.001	<0.001	<0.001
	0 [0-0]	91 [1-506]	238 [13-637]	418 [155-829]	0 [0-1]	0 [0-187]	64 [0-310]	<0.001	<0.001	<0.001
Subgroup (pulmonologist duration <97 months, 900 radiographs)										
Diameter (mm)	42.27±0.64	33.60±0.83	31.06±0.71	26.21±0.66	3.43±0.49	3.20±0.41	6.62±0.53	<0.001	<0.001	<0.001
Duration (days)	39 [24-54]	27 [19-48]	24 [16-45]	20 [14-34]	0 [0-5]	0 [0-3]	0 [0-11]	<0.001	<0.001	<0.001
	0±0	215.79±13.46	471.74±20.73	665.21±21.89	193.18±15.89	171.36±10.84	364.54±18.65	<0.001	<0.001	<0.001
	0 [0-0]	1 [1-196]	0 [0-157]	506 [186-953]	0 [0-157]	0 [0-240]	116 [0-536]	<0.001	<0.001	<0.001
Subgroup (pulmonologist duration ≥97 months, 850 radiographs)										
Diameter (mm)	42.27±0.66	33.77±0.79	32.84±0.74	27.49±0.69	1.85±0.41	3.77±0.43	5.62±0.49	<0.001	<0.001	<0.001
Duration (days)	39 [24-54]	29 [19-48]	29 [16-48]	22 [14-37]	0 [0-0]	0 [0-3]	0 [0-8]	<0.001	<0.001	<0.001
	0±0	227.99±13.98	422.02±20.28	590.13±21.36	128.64±14.00	142.70±12.34	271.35±16.79	<0.001	<0.001	<0.001
	0 [0-0]	13 [1-268]	188 [9-637]	431 [137-844]	0 [0-9]	0 [0-170]	1 [0-393]	<0.001	<0.001	<0.001

Difference 1 and P value 1, A vs. DX; Difference 2 and P value 2, DX vs. E; Difference 3 and P value 3, A vs. E. Missing data were treated using the Last Observation Carried Forward (LOCF) method. Data are expressed as mean ± standard deviation or median and interquartile range; P values were calculated using the Wilcoxon rank sum test. A, earliest image with which cancer was diagnosed when the radiographs were viewed without time constraints, distractors, and side-by-side cropped images; DX, earliest image suggestive of cancer when viewing side-by-side cropped radiographs; E, earliest image suggestive of a lesion when viewing side-by-side cropped radiographs; F, image at the time of actual diagnosis. MD, medical doctor.

Table 3 Comparisons in detection dates depending on anatomical regions

Open vs. hidden areas	F	A	DX	E
P value	N/A	<0.001	<0.001	<0.001

A, earliest image with which cancer was diagnosed when the radiographs were viewed without time constraints, distractors, and side-by-side cropped images; DX, earliest image suggestive of cancer when viewing side-by-side cropped radiographs; E, earliest image suggestive of a lesion when viewing side-by-side cropped radiographs; F, image at the time of actual diagnosis. N/A, not applicable.

Table 4 Comparison in detection dates depending on length of clinical experience as pulmonologist

Less than vs. more than 97 months career	F	A	DX	E
P value	N/A	0.665	0.165	0.485

A, earliest image with which cancer was diagnosed when the radiographs were viewed without time constraints, distractors, and side-by-side cropped images; DX, earliest image suggestive of cancer when viewing side-by-side cropped radiographs; E, earliest image suggestive of a lesion when viewing side-by-side cropped radiographs; F, image at the time of actual diagnosis. N/A, not applicable.

merit of CXRs as a screening tool cannot be ignored.

In 2015, 24,267 patients in the Republic of Korea were diagnosed with lung cancer. Among them, 13,366 (55%: 9,868 males and 3,498 females) were aged between 55 and 75 years (17). A significant portion of the patient population does not meet the indication criteria for annual LDCT screening as it focuses on at-risk and symptomatic patients. Furthermore, financial difficulties, both in developed and underdeveloped countries, as well as patient aversion to radiation exposure can inhibit LDCT utilization. Considering these factors, there is a potential for increased CXR utilization as an alternative screening method.

Notably, with the commencement of the campaign for increased lung cancer awareness, there has been an increase in the utilization of CXR and in the proportion of lung cancer cases diagnosed in the earlier stages (proportion of patients diagnosed with stages I & II lung cancer: before campaign, 26.5% *vs.* during campaign, 35.3%), as well as a reduction in the number of lung cancer cases diagnosed in the later stages (absolute number of patient diagnosed with stage III & IV lung cancer: before campaign, 1,254 *vs.* during campaign, 1,137) (18). Although the correlation between these observations has not yet been proven, it is a plausible conjecture that the increase in CXR screening contributed to this phenomenon. Our study is notable in that it demonstrates that CXRs are a potentially effective tool in lung cancer screening and confirms previous, retrospective findings in a controlled setting. Furthermore, we show that side-by-side comparisons enhanced by purposeful cropping can amplify its benefits. Hence, the addition of a simple feature to existing image viewing

software can greatly enhance the ability of physicians to diagnose lung cancer earlier.

It is important to note that, although LDCT screening remains the standard screening method, it has certain shortcomings. Despite adequate LDCT screening, some lung cancers may still be missed (19). Importantly, the total annual cost between LDCT screening and CXR screening is not significantly different (20). Thus, because CXR is performed in much larger proportion of cases than LDCT, it is important for physicians and radiologists to accurately read CXRs. Well-organized education in CXR interpretation may improve accuracy (21).

Misinterpretations in radiology

Approximately 1–4% of radiology reports are misinterpreted (22,23). This results in approximately 30% of abnormalities being missed in radiologic examinations (24). Diagnostic errors can be categorized into missed (no diagnosis made), false (incorrect diagnosis), or delayed (diagnosis delayed although sufficient information was available earlier) (24,25). Several factors are involved in diagnostic errors. ‘Hidden’ areas are locations on images where lesions are harder to see due to adjacent or overlapping structures; lesions can also be hard to find due to weak contrast or density. Furthermore, lesions can be missed due to observer fatigue, sleepiness, lack of adequate lighting, or time constraints. To help minimize errors, interpretation conditions or technical factors such as reading room light conditions, viewing distance, and monitor resolution must be improved (26).

According to Kundel *et al.*, errors in reading radiographs are caused by scanning, recognition, and decision-making

errors. Of the false negative errors they reported, 30% were by scanning, 25% were by recognition, and 45% were by decision-making (27). Kim *et al.* have categorized causes of errors as complacency, faulty reasoning, lack of knowledge, under-reading, miscommunication, technique, prior examination, history, lesion location, search satisfaction, complications, and report satisfaction (28). Improving CXR reading skills, either through education, removal of constraints, or through the development of better tools, could drastically reduce these errors. Our study was able to show that the removal of systematic constraints and utilization of better viewing tools results in significantly earlier lesion detection.

Moreover, the sensitivity and accuracy of CXR interpretation can be improved by increased knowledge and experience regarding how to read normal lines, spaces, stripes, and signs on relevant images in comparison to CTs. Errors can be minimized by improving search patterns or paying more attention to blind spot areas. New technologies, such as bone suppression software, dual-energy radiography, and computer-aided design systems are being developed to facilitate more accurate image assessments (29-32). It remains to be seen how these changes will help physicians interpret images.

Radiographs must be compared to previous images, consecutively from the least recent to the most recent. In this study, we compared the same regions in CXRs cropped and placed side-by-side, which increased participants' sensitivity to lesion changes. However, such side-by-side, focused comparisons are difficult to achieve in real clinical situations. Further research will be needed to examine the utility of this method. As new technologies such as deep convolutional neural networks that allows automatic CXR comparisons to identify abnormalities have been recently developed, more research will be able to help determine its utility (33).

Relationship between missed diagnoses and prognoses

Although it is reasonable to assume delayed lung cancer detection will result in progression to higher stages, thereby having a negative impact on prognoses, it is difficult to say with certainty that delayed detection on CXRs has a direct negative impact on outcomes, as demonstrated by related previous studies that examined different patient populations with different methods (34-37). For instance, Quekel *et al.* examined cases of non-small cell lung cancer patients with nodular lesions and found that lesions were missed in

19% of the cases. They attributed this to a smaller median diameter of the lesions. The median delay in their study was 472 days, similar to that in our study. It is difficult to examine any changes in the N or M staging because CT was not performed in cases with missed cancer diagnosis (34). Because of the limitations in their study design, we cannot comment on its impact on cancer prognoses. However, the detection of cancers at smaller sizes with CXRs suggests that CXRs have the potential to play a significant role in the earlier detection of cancers.

Education regarding CXR interpretation is often limited to several hours during medical school. Even during residency and beyond, medical professionals often do not receive specialized training in reading CXRs. This may be attributable to the CXR marginalization with the increased use of CTs. Despite this deficiency, many clinicians make medical decisions based on CXR readings without assistance from radiologists. Therefore, routine education of medical professionals in reading CXRs would be beneficial.

Limitations

This study is limited by its relatively small sample size. Also, we were not able to compare the advantages of this study's features between different medical specialties. Moreover, the potential benefits of cropped side-by-side comparisons of CXRs could have been further explored if the participant pool had been extended to include resident physicians. These variables should be further examined in subsequent studies.

Conclusions

All medical professionals must be able to interpret images accurately to maintain quality patient care. Education regarding CXR interpretation is conducted on a routine basis and can be achieved through various methods. However, education is often limited and capabilities between physicians vary, even within the field of pulmonology. All medical professionals, regardless of his or her specialty, should receive a more structured and specialized education on this subject. This study demonstrates that CXRs may have a significant role in earlier lung cancer detection. Also, comparing cropped radiographs side-by-side improves detection, highlighting a potential feature that could be implemented in image viewing programs. Future research is needed to examine whether the application of this method will help with

earlier lung cancer detection and outcome.

Acknowledgments

We would like to thank Seunghyun Kim, M. Eng. (Cornell University Department of Computer Science) for developing the exam software used by participants and for assisting in the data analysis.

Funding: None.

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tlcr.2020.04.02>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Uijeongbu Institutional Review Board (#UC17EESI0128). Written informed consent was obtained from each participant.

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Cite this article as: Kim J, Kim KH. Role of chest radiographs in early lung cancer detection. *Transl Lung Cancer Res* 2020;9(3):522-531. doi: 10.21037/tlcr.2020.04.02