Radiol Phys Technol (2011) 4:84–90
DOI 10.1007/s12194-010-0109-7

Clinical usefulness of temporal subtraction method in screening digital chest radiography with a mobile computed radiography system

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Received: 30 September 2010 / Revised: 17 November 2010 / Accepted: 18 November 2010 / Published online: 18 December 2010

Abstract The temporal subtraction image which is obtained by subtraction of a previous image from a current image of the same patient can enhance interval changes. In this study, we applied the temporal subtraction method for lung cancer screening and evaluated the clinical usefulness by comparing the review time and the detection accuracy of lung cancers without and with subtraction images. Since 1996, we have been performing screening chest radiography for a mass survey of lung cancers in the Iwate Prefecture, Japan, by using a van equipped with a computed radiography system and a digital archive system. During the 12 years from 1997 to 2008, a total of 186,340 examinations were performed, and 121,526 (65.2%) temporal subtraction images were provided in the lung cancer screening. Twenty-four abnormal cases with lung cancer and 270 normal cases were selected from the lung cancer screening. Five radiologists participated in an observer performance study and interpreted previous and current chest radiographs without and with temporal subtraction images. In addition, radiologists interpreted previous and current images with a double-reading method. The average ROC curves demonstrated a significant improvement in the detection accuracy of lung cancers with the temporal subtraction images compared with that without the temporal subtraction images, and that with the double-reading method. Therefore, we believe strongly that the temporal subtraction method is clinically useful for radiologists in the detection of lung cancers in mass surveys.

Keywords Temporal subtraction image · Lung cancer screening · Computed radiography · Digital radiography · ROC analysis

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1 Introduction

Chest radiography has played a key role in radiologic imaging for early detection of lung lesions, particularly lesions resulting from tuberculosis or cancer.

On the other hand, computed tomography (CT) technologies have advanced at a remarkable pace in recent years. CT can now clearly reveal subtle lung cancer lesions such as ground-glass opacity nodules which are not readily imaged on chest radiographs [1]. Therefore, the role of chest radiography has begun to shift. However, chest radiography continues to offer clear advantages over other modalities because of the low radiation exposure, low cost, and the capacity to examine a wide image area at once. In addition, digital chest radiography systems such as computed radiography (CR) systems [2] have been installed in many hospitals. Digital image processing is one of the most important advantages of the digital chest radiography systems.

The temporal subtraction method based on nonlinear image warping is a successful utilization of digital image processing in digital chest radiographs. The temporal subtraction image which is obtained by subtraction of a previous image from a current image of the same patient can enhance interval changes because of the elimination of normal structures such as ribs and pulmonary vessels [3, 4]. Many investigators reported the clinical usefulness of temporal subtraction images for assisting radiologists in the detection of interval changes in digital chest radiographs [5–8]. However, to our knowledge, the application and clinical evaluation of temporal subtraction for lung cancer screening have not been studied thoroughly.

Therefore, we applied the temporal subtraction method to lung cancer screening and evaluated the clinical usefulness by comparing the reviewing time and the detection accuracy of lung cancers without and with subtraction images.

2 Materials and methods

2.1 Temporal subtraction method

The computerized scheme of the temporal subtraction method between previous and current images includes three major steps: (1) global image matching, (2) local image matching, and (3) nonlinear image warping. The technical details of the temporal subtraction method have been published previously [3, 9–11]. For global image matching, the previous image was shifted and rotated to match the current image. For local image matching, approximately 300 template regions of interests (ROIs) with a 32 × 32 matrix size and the corresponding search area ROIs with a 64 × 64 matrix size were selected on the current and the previous image, respectively. The local shift vectors, which indicate the shift in location for all pairs of selected ROIs, were determined by use of the cross-correlation technique for finding the best-matched areas in the search area ROIs. The local shift vectors for each pixel in the previous image were obtained from two-dimensional (2-D) surface fitting with a polynomial function. Then, the previous image was nonlinearly warped according to the local shift vectors. Finally, the temporal subtraction image was obtained by subtraction of the warped previous image from the current image.

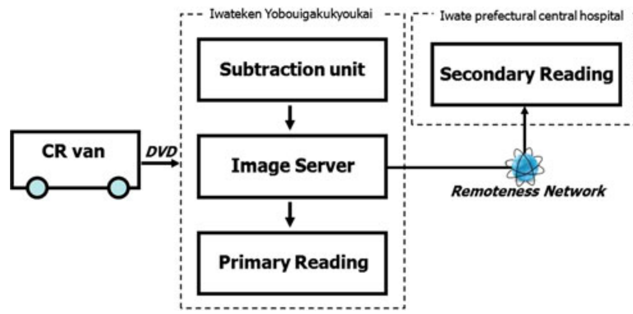


Fig. 1 Lung cancer screening with a CR system

2.2 Application of temporal subtraction method for lung cancer screening

Since 1996, we have been performing screening chest radiography for a mass survey of lung cancers in the Iwate Prefecture, Japan, by using a van equipped with a CR system (FCR 9501: FUJIFILM Medical, Tokyo) and a digital archive system [12, 13]. The application of the temporal subtraction method to lung cancer screening started in 1997. In addition, we incorporated a remote network system (SYNAPSE: FUJIFILM Medical, Tokyo) and a screening image-reading system (MC-R: FUJIFILM Medical) to enable remote reading, as shown in Fig. 1. Chest images captured by the mobile CR van in communities in the Iwate Prefecture were recorded in a storage medium and then saved to an image server. A temporal subtraction image for each patient was provided from current and previous images in the image server. Three images, of previous, current, and subtraction images, were displayed on two monitors by use of the remote network and the screening image-reading system, as shown in Fig. 2. Double reading along with the primary and secondary readings for the diagnosis of lung cancers was employed in the lung cancer screening (Fig. 1).

2.3 Observer performance study

In order to evaluate the usefulness of the temporal subtraction images in radiologists' diagnosis of lung cancers in screening chest radiography, we performed an observer performance study.

An image database used in the observer performance study included 24 abnormal cases with lung cancer and 270 normal cases which were selected from the lung cancer screening conducted in the Iwate Prefecture from 1997 to 2010. All abnormal cases were judged to be suspicious for lung cancers in the screening and were finally diagnosed as having lung cancer in further examinations and biopsies. The histologic classification of the 24 cases was as follows: adenocarcinoma ($n = 10$),

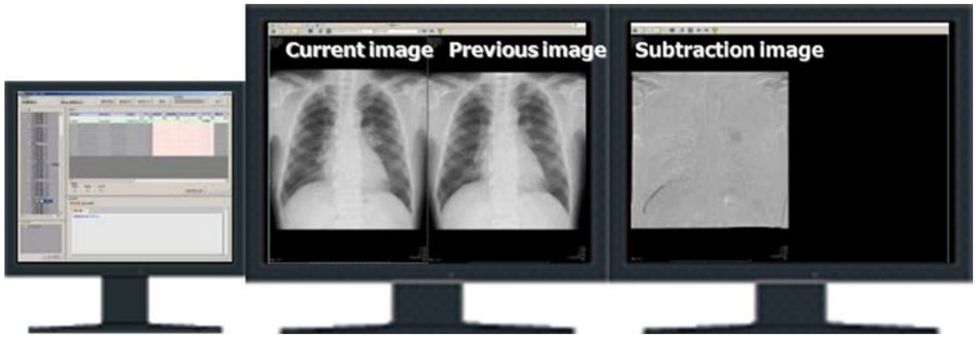


Fig. 2 Viewing and reporting system in lung cancer screening

squamous cell carcinoma ($n = 9$), small cell carcinoma ($n = 3$), non-small cell carcinoma ($n = 1$), and large cell carcinoma ($n = 1$). The physical type of the 24 cases was as follows: nodule ($n = 18$), tumor ($n = 2$), and infiltrative or amorphous ($n = 4$). The mean size of the abnormal lesions was 2.3 cm (range 1.0–5.0 cm). All 270 normal cases for which the previous images were available were selected from the screening in 2008.

Five radiologists with more than 11 years experience in diagnostic radiology participated as observers. Before the test, five training cases which were not included in the database were presented for the observers to be familiar with the observer performance study. Then, the observers were informed about the total number of cases in the study and the fraction of lung cancers.

An independent test method was employed for the 24 abnormal and 270 normal cases included in the image database. After random intermixing of abnormal cases with normal cases, one case was shown at a time, and the reading time was not limited. The observer performance study consisted of three reading sessions. In the first session, observers viewed current and previous images only. In the second session, observers viewed current and previous images as well as temporal subtraction images. In the third session, observers viewed current and previous images, taking into account the diagnostic result of a specific observer. The third session simulated the conventional double-reading method in lung cancer screening [14]. Three weeks elapsed between reading sessions so that learning effects were reduced.

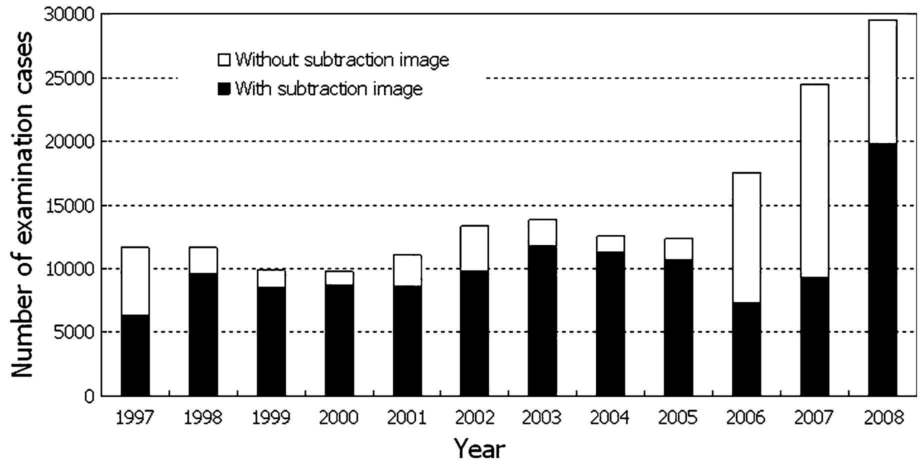
For the observer performance study, current and previous images were displayed on a monochromatic liquid-crystal display (LCD) monitor (RadiForce GS320-CL-P: Nanao, Hakusan) with 1,536 × 2,048 pixels, and a temporal subtraction image was displayed on another LCD monitor of the same model, as shown in Fig. 2. The observers were permitted to change the brightness and contrast of the LCD monitors. Each observer's confidence rating regarding the presence or absence of a lung cancer was recorded on a 5-point rating scale defined as follows: 1, definitely absent; 2, probably absent; 3, uncertain; 4, probably present; 5, definitely present. The reviewing time was measured from the moment that the first image was displayed on the monitor to the moment that the observer recorded his or her confidence rating for a final case used in each reading session.

An ROC analysis was employed for comparison of observer performance for detection of lung cancers in the three reading sessions. The area under the ROC curve (AUC) was obtained by use of the computer software ROCKIT provided by Metz [15]. The statistical significance of the difference in AUC values among the three reading sessions was estimated by use of one-tailed paired Student's t test. In addition, we determined the difference between the observers' confidence ratings without and with temporal subtraction images in order to estimate the beneficial and detrimental effects of temporal subtraction images on the detection of lung cancers. It should be noted that the confidence rating without the temporal subtraction image was obtained when an observer viewed current and previous images alone at the first reading session, and not at the third reading session.

3 Results

The number of examinations and the use of temporal subtraction images in the lung cancer screening in the Iwate Prefecture for each year are shown in Fig. 3. During the 12 years from 1997 to 2008, a total of 186,340 examinations were performed, and then 121,526 (65.2%) temporal subtraction images were provided for lung cancer screening. About one quarter of the total subtraction images were selected randomly for subjective evaluation of the image quality. A radiologist judged the image quality as being acceptable for the diagnosis in the lung cancer screening when the subtraction image had a relatively small amount of misregistration artifacts, as shown in Fig. 4. As a result, 26,504 (88.4%) of 29,987 temporal subtraction images were considered acceptable. The results obtained over the years indicate that the temporal subtraction method could be applied for more than 60% of

Fig. 3 Number of examinations in lung cancer screening in the Iwate Prefecture for each year



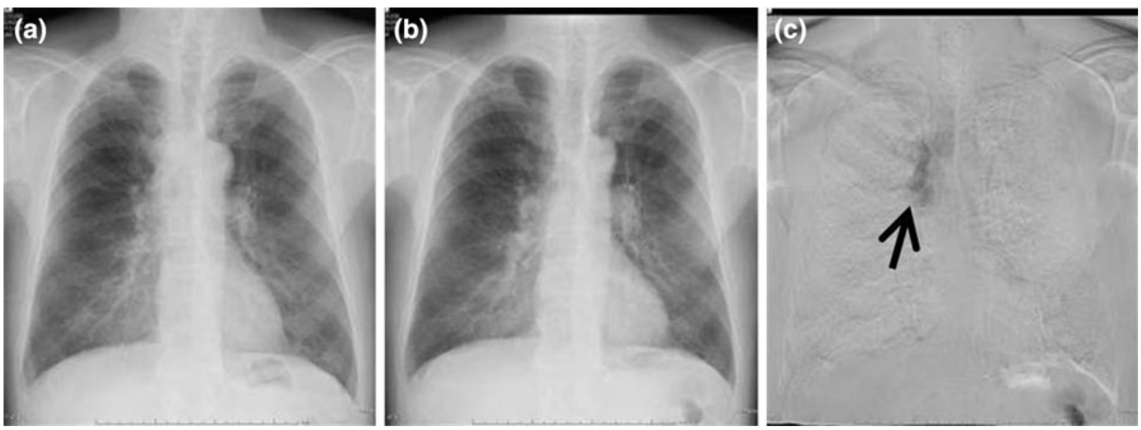


Fig. 4 Demonstration of a temporal subtraction image: **a** current image with a lung cancer, **b** previous image, and **c** temporal subtraction image. The temporal subtraction image clearly enhanced an abnormal lesion due to lung cancer as shown by an *arrow*. The subtraction image had a relatively small amount of misregistration artifacts

cases examined in the lung cancer screening in the Iwate Prefecture, for which previous images were available, and the image quality of most subtraction images was acceptable for the detection of lung cancers.

The average ROC curves demonstrated a significant improvement in the detection accuracy of lung cancers when temporal subtraction images were used, in comparison with that without the temporal subtraction images and that with the double-reading method, as shown in Fig. 5. The average AUC value increased significantly from 0.951 without the temporal subtraction image and 0.890 with the double-reading method to 0.990 with the temporal subtraction image ($P = 0.028$ and $P = 0.002$). However, there was no statistical significance ($P = 0.199$) between the average AUC values without the temporal subtraction image and with the double-reading method.

The beneficial and detrimental effects of the temporal subtraction images in lung cancer cases and normal cases for each observer are shown in Figs. 6 and 7, respectively.

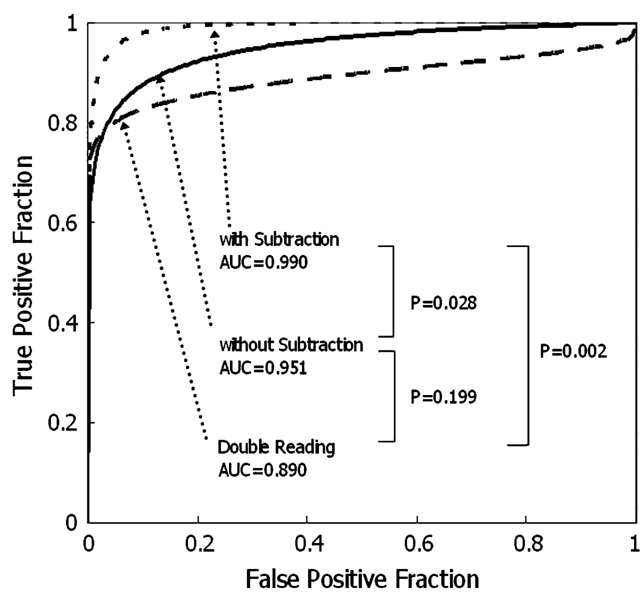


Fig. 5 Average ROC curves for detection of lung cancers

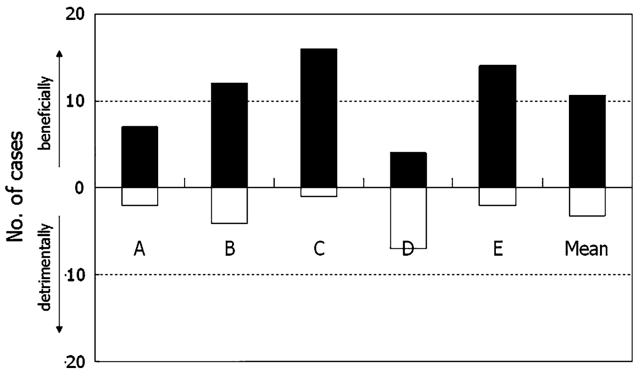


Fig. 6 Number of cases affected by temporal subtraction images in lung cancer cases (*A*–*E* represent the five observers)

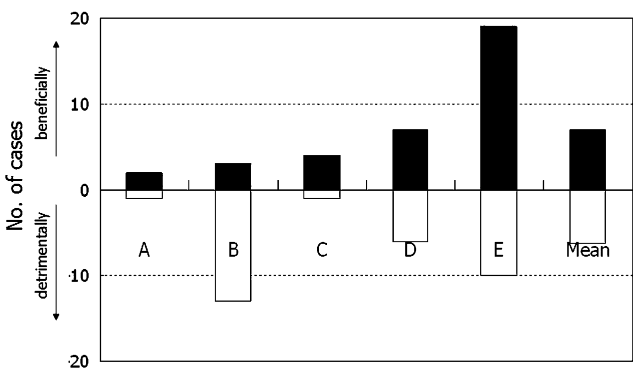


Fig. 7 Number of cases affected by temporal subtraction images in normal cases (*A*–*E* represent the five observers)

Table 1 Average reviewing time per case for each observer

	Average reviewing time per case (s)					
	A	B	C	D	E	Mean
Without subtraction	14.3	10.8	14.5	13.1	18.4	14.2
With subtraction	11.2	13.3	14.1	13.9	14.3	13.3
Double reading	10.6	9.8	19.4	14.3	17.3	14.3

A–E represent the five observers

The effect of the subtraction images was beneficial for all but one observer in improving the performance in lung cancer cases, but was less effective in normal cases. The average numbers of cases beneficially affected and detrimentally affected by use of subtraction images in lung cancer cases were 10.6 and 3.2 ($P = 0.038$), respectively, whereas the average numbers of cases beneficially affected and detrimentally affected by use of subtraction images in normal cases were 7.0 and 6.2 ($P = 0.404$), respectively.

The average reviewing times per case without and with subtraction images for all five observers are shown in Table 1. When subtraction images were available, the mean reviewing time per case was reduced slightly by 0.9 s (6.3%), from 14.2 to 13.3 s. However, the difference in the mean reviewing time per case without and with subtraction images was not statistically significant ($P = 0.236$).

4 Discussion

The results of our observer performance study indicate that the temporal subtraction method can significantly improve the observers' performance for the detection of lung cancers in screening. These results for cases selected from the mass survey of lung cancers were very similar to other previous results for cases selected from the examinations in various hospitals [5–8].

In the analyses for beneficial and detrimental effects, the effect of the temporal subtraction image was beneficial for all but one observer in improving the detection accuracy in lung cancer cases, but was less effective in normal cases. One possible cause for the lesser effectiveness in normal cases might be misregistration artifacts remaining in the normal lung. It is necessary to reduce the artifacts on subtraction images for further improving observers' detection performance.

In our observer performance study, the average reviewing time per case with subtraction images was reduced only slightly. However, Kakeda et al. [16] reported that the average reviewing time per case with subtraction images was reduced significantly for detection of newly developed abnormalities on chest radiographs. We suppose that the reviewing time per case was affected by the number of cases used in the observer performance study. Kakeda et al. used 120 cases, and we used 294 cases in the observer performance studies. Because the number of cases in our study was much larger, observers tended to view images quickly to shorten the elapsed time in the observer performance study. Therefore, the average reviewing time per case with subtraction images was comparable to that without subtraction images in our observer performance study. However, it should be noted that the reviewing time per case with subtraction images was not increased despite the addition of a subtraction image to the previous and current images.

The detection accuracy with temporal subtraction images is significantly superior to that with the double-reading method, which is the conventional reading method for screening in Japan. Therefore, this result suggests that a single-reading method with previous, current, and subtraction images might replace the double-reading method with previous and current images alone in lung cancer screening. If the single-reading method with subtraction images is actualized in lung cancer screening, the productivity of the screening will be improved because of a reduction of the human resources needed and of the reviewing time.

In order to bring the conditions of our observer performance study close to an actual lung cancer screening, we used a large number of normal cases (270 cases, 91.8%) and a small number of abnormal cases (24 cases, 8.2%) in comparison with the usual observer performance studies [5–8]. Because the incidence rates of lung cancer are approximately 0.06% for males and 0.02% for females in Japan [17], the percentage of lung cancer cases in our observer study was large. However, 24 abnormal cases in our observer study were necessary for statistical reliability in the ROC analysis. Therefore, we consider that the conditions of our observer performance study were not completely the same as, but were very similar to, the actual mass survey for the detection of lung cancers.

For application of the temporal subtraction method to lung cancer screening, some issues need to be addressed. Because a digital system such as a CR system is required to provide temporal subtraction images, the initial cost of the screening with a digital system is larger than that with an analog system such as a photofluorography system, which is employed conventionally in Japan. However, the digital system allows the performance of digital image processing for improvement of the diagnostic accuracy [18, 19], and the easy and safe management of images in a digital archive system [20]. Therefore, digital systems will be used in many lung cancer screening programs in the near future. Then the temporal subtraction method can be widely applied to many screening programs. Another issue is that temporal subtraction images cannot be provided when previous images are not available. Only 65.2% of cases in the lung cancer screening program in the Iwate Prefecture had previous images to provide temporal subtraction images. Further public relations campaign regarding lung cancer screening is necessary for increasing the application of temporal subtraction images.

5 Conclusions

We applied the temporal subtraction method to lung cancer screening. The image quality of most temporal subtraction images provided in the screening was acceptable because of a relatively small amount of misregistration artifacts. Our observer performance study demonstrated a significant improvement in the detection accuracy of lung cancers with the temporal subtraction images, in comparison with that without the temporal subtraction images and that with the double-reading method. Therefore, we believe strongly that the temporal subtraction method is clinically useful for radiologists in the detection of lung cancers in mass surveys.

Acknowledgments The authors are grateful to Keiko Mizuno, MD, PhD; Marie Takasugi, MD; Shigeo Oikawa, MD, PhD; Ryohei Takasugi, MD; and Yuko Chiba, MD, PhD, for participating as observers and/or helpful discussions. The authors thank Takao Komaki, FUJIFILM Medical, Tokyo, Japan, for his technical assistance and helpful suggestions. The authors would like to express their appreciation to editors and reviewers for their helpful advice to improve our manuscript.

References

1. Henschke CI, McCauley DI, Yankelevitz DF, Naidich DP, McGuinness G, Miettinen OS, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. Lancet. 1999;354:99–105.
2. Sonoda M, Takano M, Miyahara J, Kato H. Computed radiography utilizing scanning laser stimulated luminescence. Radiology. 1983;148:833–8.
3. Kano A, Doi K, MacMahon H, Hassell DD, Giger M. Digital image subtraction of temporally sequential chest images for detection of interval change. Med Phys. 1994;21:453–61.
4. Nakagawa K, Oosawa A, Tanaka H, Ohtomo K. Clinical effectiveness of improved temporal subtraction for digital chest radiographs. Proc SPIE. 2002;4686:319–30.
5. Difazio MC, MacMahon H, Xu XW, Tsai P, Shiraishi J, Armato SG, et al. Effect of time interval difference images on detection accuracy in digital chest radiography. Radiology. 1997;202:447–52.
6. Uozumi T, Nakamura K, Watanabe H, Nakata H, Katsuragawa S, Doi K. ROC analysis of detection of metastatic pulmonary nodules on digital chest radiographs with temporal subtraction. Acad Radiol. 2001;8:871–8.
7. Kakeda S, Nakamura K, Kamada K, Watanabe H, Nakata H, Katsuragawa S, Doi K. Improved detection of lung nodules by using a temporal subtraction technique. Radiology. 2002;224:145–51.
8. Okazaki H, Nakamura K, Watanabe H, Matsuki Y, Uozumi T, Kakeda S, Kameda K, Oda N, Nakata H, Katsuragawa S, Doi K. Improved detection of lung cancer arising in diffuse lung diseases on chest radiographs using temporal subtraction. Acad Radiol. 2004;11:498–505.
9. Ishida T, Ashizawa K, Engelmann R, Katsuragawa S, MacMahon H, Doi K, Application of temporal subtraction for detection of interval change in chest radiographs: Improvement of subtraction image using automated initial matching. J Digit Imaging. 1999;12:77–86.
10. Ishida T, Katsuragawa S, Nakamura K, MacMahon H, Doi K. Iterative image warping technique for temporal subtraction of sequential chest radiographs to detect interval change. Med Phys. 1999;26:1320–9.
11. Katsuragawa S, Tagashira H, Li Q, MacMahon H, Doi K. Comparison of the quality of temporal subtraction images obtained with manual and automated methods of digital chest radiography. J Digital Imaging. 1999;12:166–72.
12. Sasaki Y, Katsuragawa S, Doi K, Application of temporally subtracted images with mobile computed radiography system in screening chest radiographs. Proc CARS 1998; p. 21–4.
13. Katsuragawa S, Sasaki Y, MacMahon H, Ishida T, Doi K. Application of temporal subtraction to screening chest radiographs with a mobile computed radiography system. In: Doi K, MacMahon H, Giger ML, Hoffmann KR, editors. Computer-aided diagnosis in medical imaging. Amsterdam: Elsevier; 1999. p. 51–6.
14. Hessel SJ, Herman PG, Swensson RG. Improving performance by multiple interpretations of chest radiographs: effectiveness and cost. Radiology. 1978;127:589–94.

15. Metz CE. Some practical issues of experimental design and data analysis in radiological ROC studies. Invest Radiol. 1989;24: 234–45.
16. Kakeda S, Kameda K, Hatakeyama Y, Aoki T, Korogi Y, Katsuragawa S, Doi K. Effect of temporal subtraction technique on interpretation time and diagnostic accuracy of chest radiography. AJR. 2006;187:1253–9.
17. Marugame T, Kamo K, Katanoda K, Ajiki W, Sobue T, The Japanese Cancer Surveillance Research Group. Cancer incidence and incidence rates in Japan in 2000: Estimates based on data from 11 population-based cancer registries. Jpn J Clin Oncol. 2006;36:668–75.
18. Doi K, MacMahon H, Katsuragawa S, Nishikawa RM, Jiang Y. Computer-aided diagnosis in radiology: potential and pitfalls. Eur J Radiol. 1999;31:97–109.
19. Katsuragawa S, Doi K. Computer-aided diagnosis in chest radiography. J Comput Imaging Graph. 2007;31:212–23.
20. Morishita J, Watanabe H, Katsuragawa S, Oda N, Sukenobu Y, Okazaki H, et al. Investigation of misfiled cases in the PACS environment and a solution to prevent filing errors for chest radiographs. Acad Radiol. 2005;12:97–103.