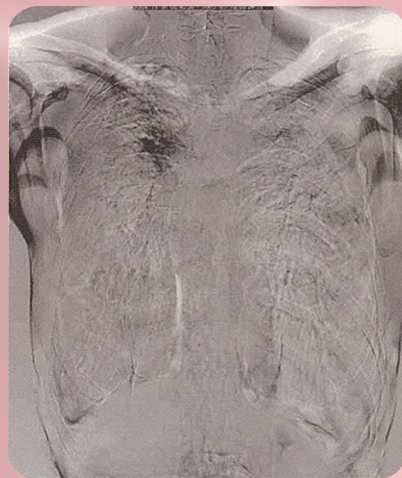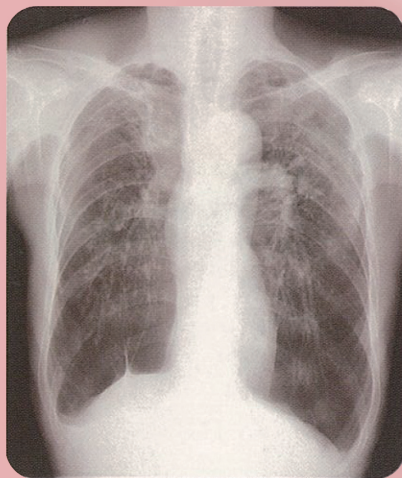Rosai Hospital Group Research and Development, and
Dissemination Projects for the 13 Fields
Field name "Respiratory Diseases Due to Dust Inhalation"

New Imaging Diagnostic Method
Temporal Subtraction Method

April 1, 2008

The Japan Labour, Health and Welfare Organization

Investigative committee on a procedural model for diagnosing
pneumoconiosis complicated by lung cancer

Preface

When we view two different radiographs taken of the same patient at different times, we arrange and interpret them in chronological order. In particular, in the early detection of lung cancer in order to find the changes in the radiographs we need to invest much time and effort into interpretation. The temporal subtraction method is a scheme that was invented with these types of cases in mind. This method gives us the verification we have been waiting for regarding the ability to diagnose abnormal opacities from new emerging malignant growths in the lung based on comparison of the current image to a previous image. In this case, before questioning the quality of the opacity, first it is essential to grasp the presence of the opacity.

Because the clinical illness of pneumoconiosis presents various sized opacities diffused throughout the lung already at the initial medical examination, we must efficiently identify the emergence of a new abnormal opacity from among them, and it is common to face difficulty that is specific to this process when using only chest radiographs. Therefore, if we can verify the usefulness of this method for cases of pneumoconiosis, we would be able to overcome the severest evaluation conditions for this method of examination.

From 2003, The Japan Labour Health and Welfare Organization has been promoting a research project with the theme of "Research, development, and dissemination of a model diagnosis method for lung cancer complicated by pneumoconiosis," and over some time the achievements of the fundamental steps of the project have been collected into the "anthology of pneumoconiosis radiographs based on occupation." This time, we gained valuable experience through the use of the new radiograph technique mentioned above and by bringing together actual cases from five of our facilities to investigate the practicality and usefulness of the technique. Although the period was limited, those who were new to the process and pneumoconiosis specialists alike significantly increased the ability to detect the abnormal opacities. However, since the initial objective of shortening the time to diagnosis was for the most part achieved, we draw this research to a close.

In the future, while considering the responsibility of the interpreting physician, radiation exposure of the test subjects, and cost effectiveness, we hope that this method will be of practical use to those in the health care profession in the various hospitals and clinics.

April 2008

Former person in charge of general research "Research, development, and dissemination of a model diagnosis method for lung cancer complicated by pneumoconiosis."

Dr. Hiroshi Kaji
President emeritus, Hokkaido Chuo Rosai Hospital

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I. Temporal Subtraction Method

Akira Oosawa
Dr. Kazuo Shimura
FUJIFILM Corporation

1. Introduction

Computer Aided Detection (CAD), a computer technology that supports physicians in their interpretation of images, is a technology that is expected to have a significant impact in terms of improving the accuracy of diagnosis and shortening the time needed for interpretation.

As a chest area diagnostic support technology we developed "the temporal subtraction method using the spring binding scheme" that aids in interpretation using a "second image," and the same technology is equipped in the image processing unit CR-IR38CL-T, which has already been commercialized.

Below, we introduce the temporal subtraction method based on a FUJIFILM Corporation proprietary method.

2. Temporal Subtraction Method

The temporal subtraction method is a technology that highlights changes over time by performing subtraction processing on chest radiograph images taken of the same patient at different times. It was reported that the accuracy of the interpretation is improved by referring to a temporal subtraction image and the original image during the interpretation process.[1]

Although subtraction processing may sound simple, there may be a change in the posture of the patient or a difference in the radiographing equipment between the images taken at different times and since the position of the subject, the bones, and the blood vessels of each internal organ in the image do not match, there are many cases in which it is difficult to detect fundamental changes over time and artifacts caused by position misalignment are generated. So that the positional relationships of the structure in both images match, we propose the temporal subtraction method (Fig.1 reference) in which subtraction processing is performed after transformation processing (warping) on every section of one image. [2,3]

3. Temporal Subtraction Method Using Spring Binding Scheme

In order to describe clearly the pathological changes etc. over time based on the temporal subtraction method, it is important to match precisely the position of the images. We achieved accurate position alignment based on a "stepwise section- position alignment method employing the spring binding scheme" in the temporal subtraction process based on the FUJIFILM proprietary scheme. In addition, after stepwise aligning the section positions and calculating the shift vector in the position of each part, we plan to shorten the processing time by warping the image once. Figure 2 shows a flow of the entire process and we introduce the details below.

(1) Global position matching considering back of rib cage

Before aligning the positions locally, first we detect for overall misalignment and then roughly align the two images. In order to improve the accuracy of the position alignment, we calculate the amount of position shift in the overall image using the image with the highlighted back of the rib cage and then shift or rotate the previous overall image.

(2) Stepwise calculation of the amount of positional shift using the spring binding scheme

This section describes the detection of the amount of positional shift between the two images. First, we set the rectangle of the "search ROI" in the chest of the current image to an equal interval, and set the small "template ROI" so that the center position of the "template ROI" matches the center of the "search ROI" (Fig. 3). While we shift each "template ROI" inside the "search ROI" we detect for the position with the highest correlation (position with highest normalized cross-correlation) and determine the amount of shiftfor each ROI position.
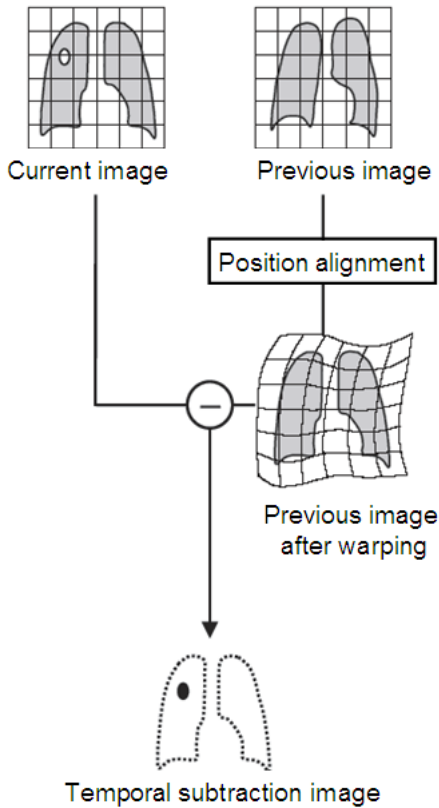

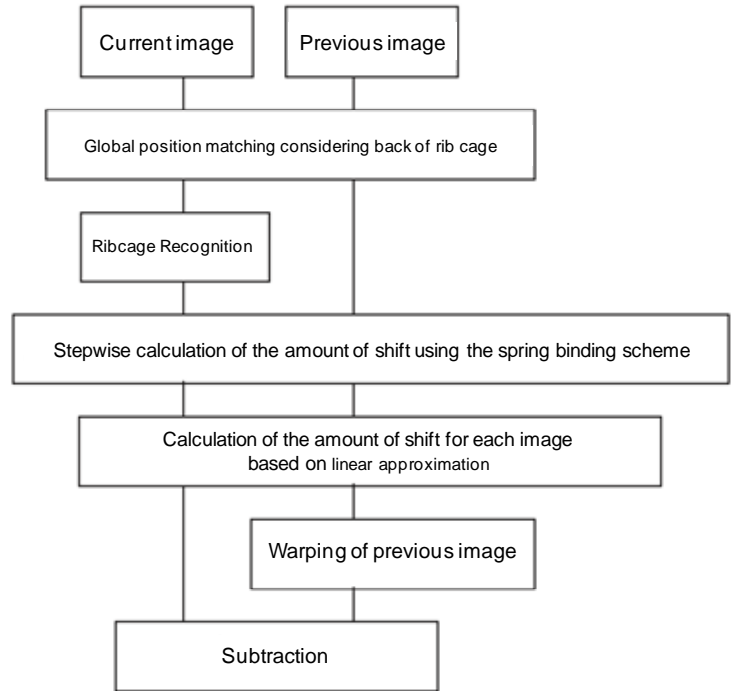Fig. 1. Temporal subtraction method employing automatic position matching technique

Fig. 2. Flow of temporal subtraction process employing spring binding scheme

Current image   Previous image

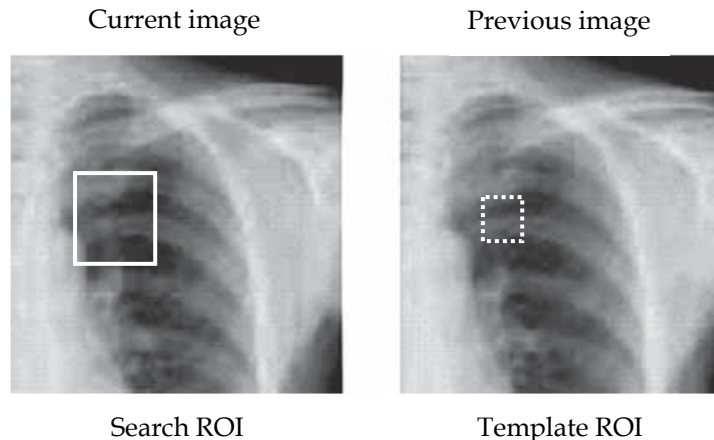Search ROI   Template ROI

Fig. 3. ROI for current and previous images

Next, as shown in Fig. 4 a shift vector is bound to a virtual spring between each ROI. Each ROI has a directional component to the positional shift and at the balance point "smoothing based on spring binding" is performed. For the final degree of positional shift, we calculate the degree of positional shift for each ROI and implement smoothing based on spring binding in three steps.
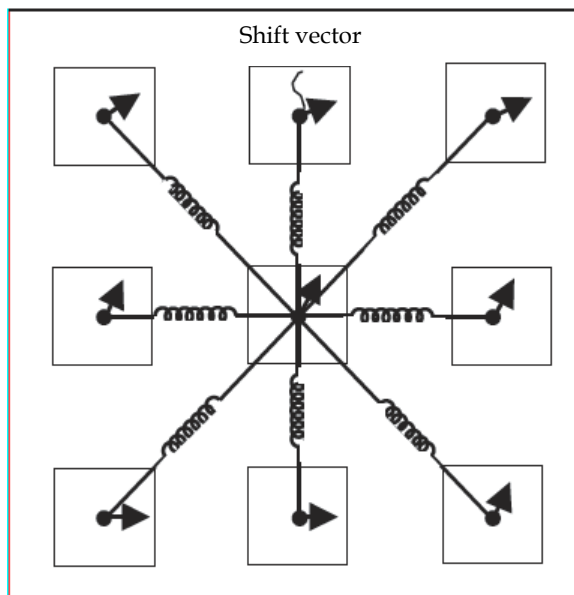

Fig. 4. Example of spring-based connections to eight neighboring shift vectors.

(3) Warping and subtraction

In order to transform the images, we must calculate the amount of positional shift in each image. In order to accomplish this, the measured amount of positional shift at each ROI is considered as the value for the center of the image of the "template ROI," and we calculate the amount of shift for the other positions in each image by the linear approximation from the amount of position shift from the four neighboring points. In this way, by applying the warping process (non-linear transformation) to the obtained amount of positional shift in the original image, we can approximately match the relative positions of the anatomical construction in the previous image and current image. Subsequently, we apply subtraction processing to the current image and the previous image that underwent the warping process, and generate the temporal subtraction image.

Figure 5 shows the current image, previous image, previous image after warping, and the temporal subtraction image with and without warping. In the subtraction image in which the positions were not aligned, artifacts from positional shift emerge and the pathological changes are difficult to see. On the other hand, in the temporal subtraction image employing warping based on the amount of positional shift for each section, there were few artifacts and the pathological changes were clearly rendered.

In addition, when a subtraction image is generated by this method, the possibility of generation of artifacts that could be mistaken for lesions tended to decrease, although such artifacts can also result from shift direction concentration or discontinuity.

4. Effectiveness of Temporal Subtraction Images

Figure 6 shows 3 chronological chest images for the same patient and the subtraction image. In the current image (Fig.6a), even if the subtraction image (Fig.6d) is not used we can easily identify the abnormality in the left lung; however, in the image taken one month earlier (Fig.6b) the abnormality is exceedingly difficult to identify.

If we further consider an image taken one year earlier(c), in the corresponding subtraction image (Fig.6e), we see that a opacity has emerged over some time. By using the temporal subtraction image this type of subtle pathological change can be detected early.

Figure 7a shows a case of pneumonia in the back of the heart. Since it is easy to overlook the pathological change overlapping the heart, using the temporal subtraction image(Fig.6c) in this type of case is useful.

(a)

(b)

(c)

(d)

(e)

Fig. 5.   Time series images and temporal subtraction images

(a) Current image
(b) Previous image
(c) Previous image after warping
(d) Temporal subtraction image with no warping
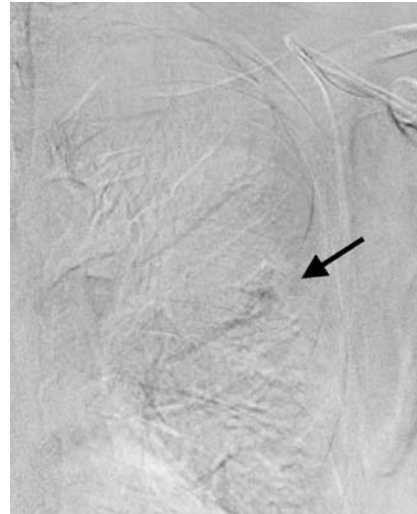(e) Temporal subtraction image with warping

(a)

(b)

(c)

(d)

(e)
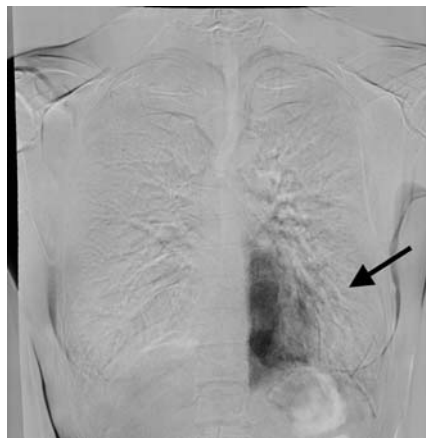
Fig. 6. **Effectiveness of Temporal Subtraction Images** (1)

(a) Current image
(b) Image from 1 month prior
(c) Image from 1 year prior
(d) Temporal subtraction image between a and b
(e) Temporal subtraction image between b and c

(a)

(b)

(c)

Fig. 7. **Effectiveness of Temporal Subtraction Images** (2)
(a) Current image
(b) Previous image
(c) Temporal subtraction image between a and b

5. Conclusion

Temporal subtraction is a technology that clearly identifies the chronological changes in the patient, and can be applied widely to detect not only isolated pathological changes in tumors etc., but also pathological changes of diffuse disease.

This technology has been introduced widely in actual clinical scene, and we hope that it will contribute to improving the accuracy of various image-based diagnoses such as in the early detection of lung cancer and identifying pathological changes in follow up examinations.

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1. M. C. Difazio, *et al.*, "Digital Chest Radiography: Effect of Temporal Subtraction Images on Detection Accuracy," Radiology, vol. 202, pp. 447-452, 1997.11.

2. J. H. Kinsey, *et al.*, "Application of Digital Image Change Detection to Diagnosis and Follow-up of Cancer Involving the Lungs," Proc. SPIE, vol. 70, pp. 99-112, 1975.

3. A. Kano, *et al.*, "Digital Image Subtraction of Temporally Sequential Chest Images for Detection Of Interval Change," Med. Phys. 21, pp. 453-461,1994.3.

II. Research Related to the Usefulness of Temporal Subtraction

INTRODUCTION

We hope that the subtraction diagnosis method based on digital chest radiograph (CR) will improve the diagnostic accuracy of isolated and disseminated opacities in cases that do not have fundamental disease of the lung. However, the effectiveness in diagnosing lung cancer cases accompanied by the pervasiveness of pneumoconiosis has not been investigated yet.

Until now, in chest X-ray examinations including CR, there have been cases where abnormal opacities were hidden by the opacities of bones and the heart making interpretation difficult, and CT examination by far was thought to be the best way for early detection of lung cancer. However, we anticipate that the energy subtraction method, which is to be investigated this time, will facilitate the interpretation of the lung area because bone opacities are eliminated. Furthermore, in this trial by computer processing the differences between two CR images taken at different times, new emerging abnormal opacities, which are automatically highlighted, will facilitate interpretation. The temporal subtraction method will become a useful diagnosis method in the early detection of lung cancer complicated by pneumoconiosis.

Lung cancer accompanied with pneumoconiosis is a newly recognized important complication and patients with pneumoconiosis very often have impaired pulmonary function. Even if lung cancer is diagnosed in an early stage, it is a well-known fact that curative treatment through surgery is difficult. Therefore, it is necessary to diagnose these illnesses as soon as possible. On the other hand, from the view of early diagnosis, helical CT introduced in 2003 was employed to accomplish this, but as a screening technique it is not only inconvenient but also requires considerable time for interpretation, and the larger amount of exposure to X-rays cannot be ignored.

OBJECTIVE

When we verify the usefulness of the subtraction method based diagnosis of lung cancer in a pneumoconiosis case, we can confirm that technical problems with the subtraction method such as blurring due to breathing and posture are resolved, as a result, it is very likely that the improvement in this diagnosing method will reduce in the disparity in interpretation accuracy between by physicians with long years of experience diagnosing pneumoconiosis and by those without them.

For argument's sake, let us consider that the usefulness of the diagnosis of lung cancer complicated by pneumoconiosis is confirmed, by substituting the use of the CR based temporal subtraction method for the present helical CT, we can reduce the amount of radiation to which a patient must be exposed and possibly improve the cost effectiveness of medical examinations. Furthermore, from the special characteristics of the temporal subtraction image, the required time for diagnosis during the medical examination can be shortened considerably. For not only pneumoconiosis, it is considered that this method significantly contributes to lessening the burden of the successive lung cancer examinations for cases in the high-risk group of general lung cancer or pervasive lung disease.

Based on preliminary examination, we expect that the energy subtraction method will be effective in discerning new opacities from the collarbone and the first rib. The expected area of effect is extremely restricted and since the temporal subtraction method is a diagnostic technology that includes the effectiveness of the energy subtraction method, we concentrated on the effectiveness of the temporal subtraction method in this study.

METHOD

We selected 25 cases in which no change was indicated by CT and 25 cases in which new changes were observed by CT (18 cases were definitively diagnosed with lung cancer and the remaining 7 cases were negative for lung cancer) for a total of 50 cases as the target images in the interpretation experiment. The 50 cases ranged uniformly from PR1 to 4C, namely minor pneumoconiosis to very advanced cases.
There were three groups comprising 10 physicians each for interpretation: residents (from 1 to 3 yrs after graduation), pulmonologists (experienced as a specialist at least for 7 years), and pneumoconiosis special-

ists (experienced as a specialist at least for 5 years). The interpretation methods in the experiment were divided into two groups for the target 50 cases: the CR image group (compared the previous and current CR images to obtain a diagnosis, hereafter CR group) and the subtraction image group (used the current CR image and subtraction image to obtain a diagnosis, hereafter TS group). We divided each group of physicians into two, one group used the CR method on cases 1 -25 and the TS method on cases 26-50, and the second group used the CR method on cases 26-50 and the TS method on cases 1-25. After a period exceeding three weeks the two groups switched methods, and finally the physicians interpreted all the CR and TS images. In the interpretation process, the presence of new abnormal opacity was judged. If it was judged that an abnormal opacity was present then a response sheet was completed. The sites were also matched regarding the presence of a new opacity. The correctness of the response was judged and the sensitivity and specificity were investigated. Furthermore, if the response indicated that a new opacity was present judgment regarding the possibility of lung cancer was also required. In other words, the physician selected from any of five stages: 1) No lung cancer, 2) the probability of lung cancer was negative, 3) the possibility of lung cancer cannot be denied, 4) the probability of lung cancer is high, and 5) lung cancer. From a clinical view in the case that 3 – 5 was selected, generally a further examination is in order if lung cancer is suspected, but in the experiments by selecting this response it was judged that the diagnosis was lung cancer and the sensitivity and specificity of the lung cancer were investigated.

RESULTS

The results are given in the tables (Tables 1-4).

Table 1. Sensitivity and Specificity of New Opacity based on CR

	Sensitivity		Specificity	
	Average	Standard Deviation	Average	Standard Deviation
Pulmonologists	0.652 ∗	0.144	0.564	0.271
Residents	0.476 ∗	0.151	0.632	0.164
Pneumoconiosis Specialists	0.576	0.144	0.676	0.253

* p<0.05

Table 2. Sensitivity and Specificity of New Opacity based on TS

	Sensitivity		Specificity	
	Average	Standard Deviation	Average	Standard Deviation
Pulmonologists	0.784	0.132	0.632	0.278
Residents	0.708	0.164	0.604	0.264
Pneumoconiosis Specialists	0.724	0.149	0.744	0.230

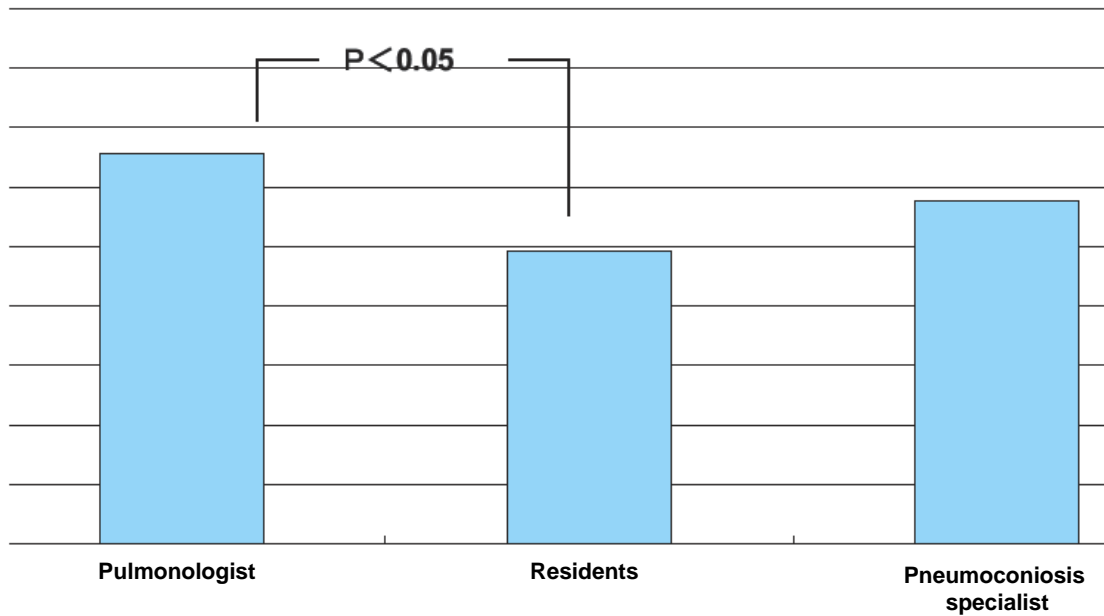Table 3. Sensitivity and Specificity of Lung Cancer based on CR

	Sensitivity		Specificity	
	Average	Standard Deviation	Average	Standard Deviation
Pulmonologists	0.583	0.168	0.791	0.136
Residents	0.428	0.180	0.772	0.161
Pneumoconiosis Specialists	0.528	0.215	0.822	0.161

Table 4. Sensitivity and Specificity of Lung Cancer based on TS

	Sensitivity		Specificity	
	Average	Standard Deviation	Average	Standard Deviation
Pulmonologists	0.606	0.199	0.715	0.182
Residents	0.467	0.208	0.731	0.201
Pneumoconiosis Specialists	0.556	0.227	0.841	0.103

Result 1: For the three groups of pulmonologists, residents, and pneumoconiosis specialists, based on the results of the investigation on the presence of new s opacity using only comparison of the previous and current CR images, pulmonologists exhibited a significantly high level of diagnosis sensitivity compared to that for residents ($p < 0.05$). However, there was no difference in sensitivity for the pneumoconiosis specialists and the other two groups (Fig. 1).

Fig. 1. Sensitivity to new opacity based solely on CR

Result 2: For the three groups of pulmonologists, residents, and pneumoconiosis specialists, the specificity related to new opacity for the CR group (Table 1) and the sensitivity and specificity related to lung cancer (Table 3) for the CR group showed no difference. For the TS group there was no difference in the sensitivity and specificity related to new opacity (Table 2), and no difference in the sensitivity and specificity related to lung cancer (Table 4) for the pulmonologists, residents, and pneumoconiosis specialists.
Result 3: On the other hand, we compared the sensitivity and specificity related to new opacities and to the lung cancer for the CR group and TS group of the three groups of physicians. When comparing the CR group and TS group based on the presence of new shadows, for all the physician groups the TS group exhibited a significantly higher level of sensitivity (Fig. 2).

Fig. 2. Sensitivity (New Opacities)
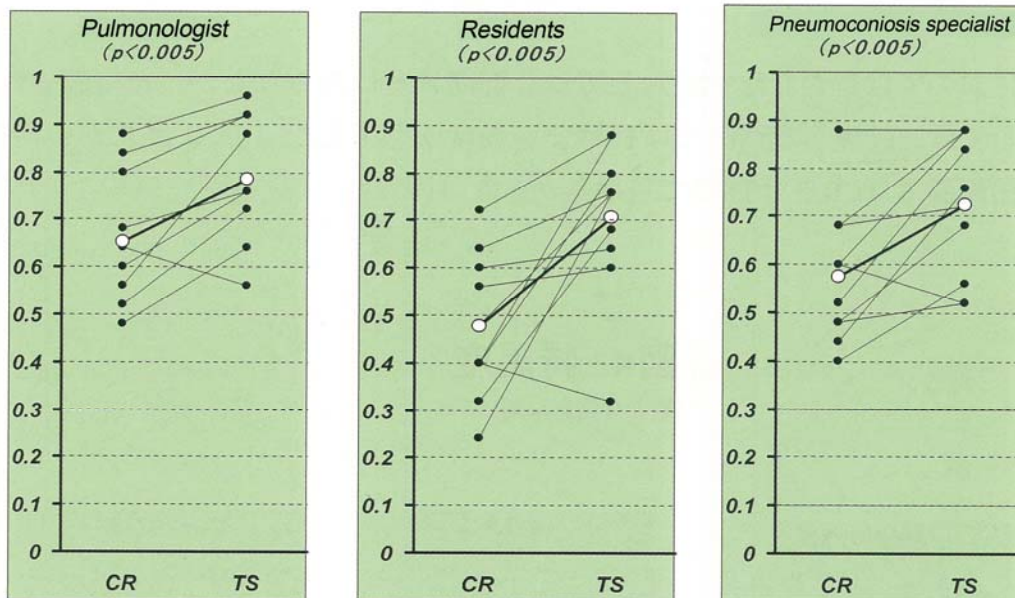
However, among the groups of pulmonologists, residents, and pneumoconiosis specialists, the CR group and TS group showed no difference in terms of sensitivity for lung cancer (Fig. 3)

Fig. 3. Sensitivity (Lung Cancer)
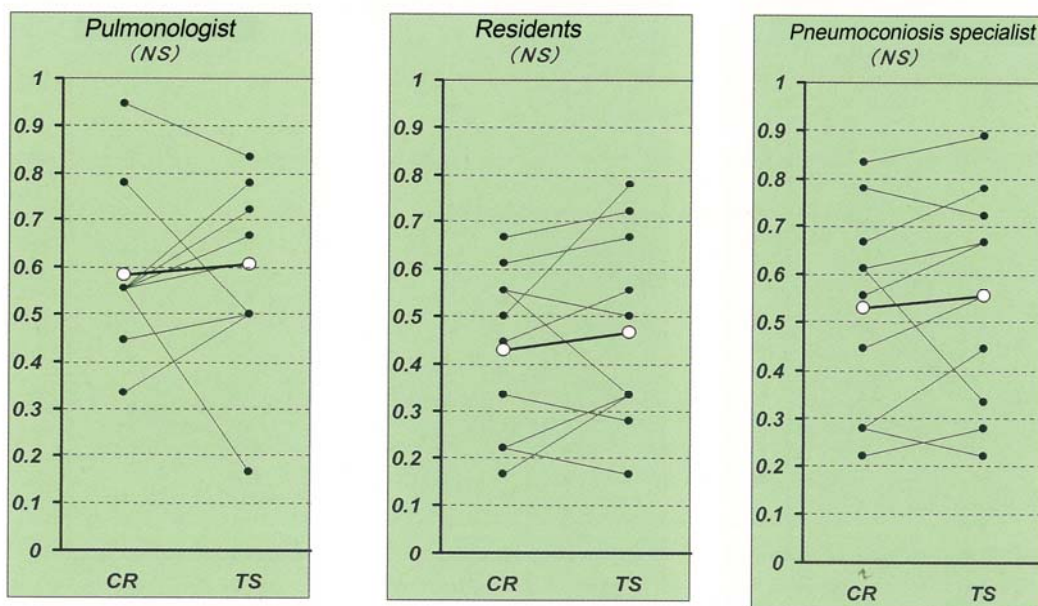
For new opacities the three groups exhibited no difference in terms of specificity (Fig. 4). On the other hand, for lung cancer the pulmonologist TS group exhibited a lower specificity (P<0.05), but the CR group for the residents and pneumoconiosis specialists exhibited no difference (Fig. 5).
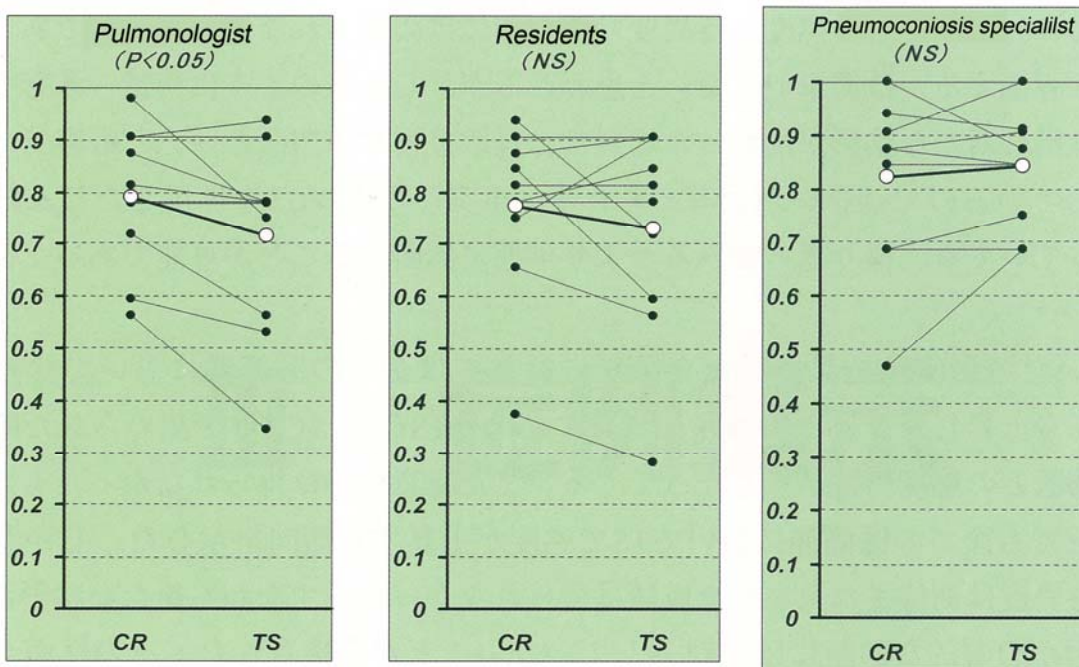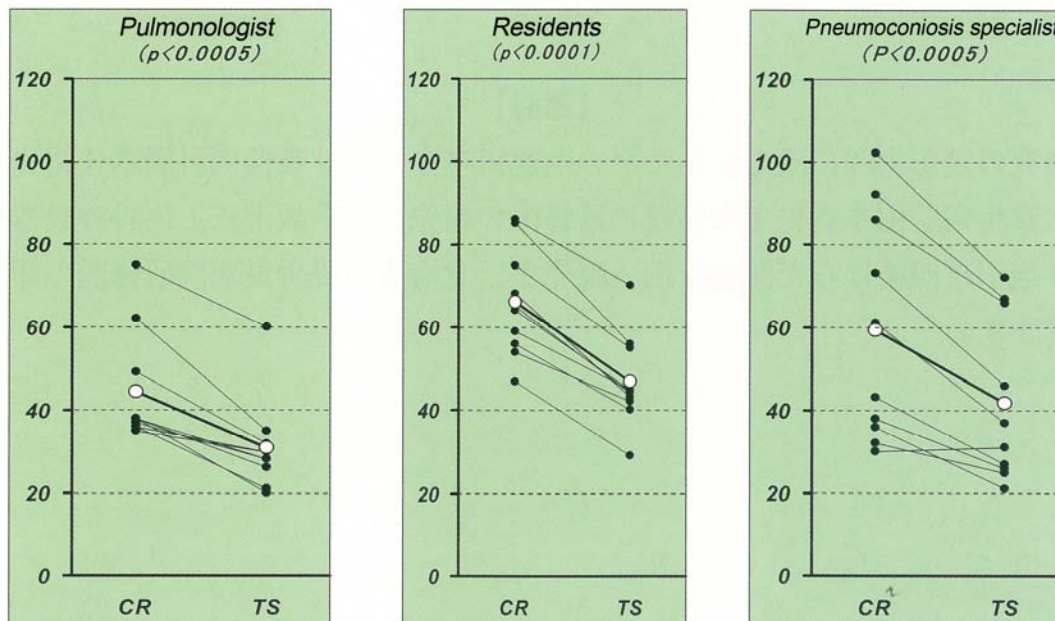
Fig. 4. Specificity (New Opacities)
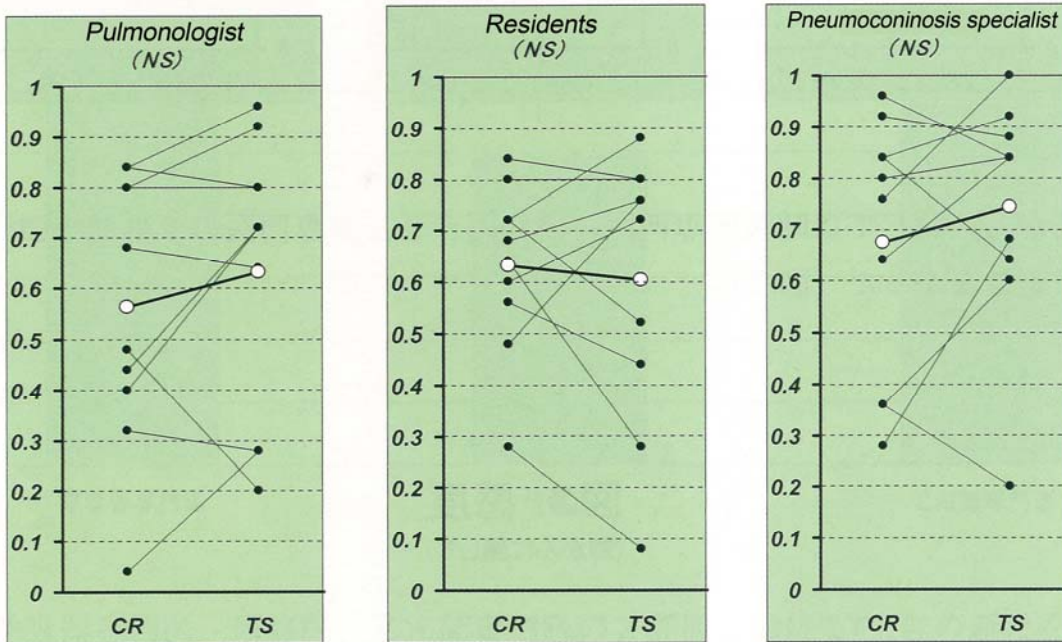
Fig. 5. Specificity (Lung cancer)

Result 4: Finally, we compared the time required for interpretation in the CR group and TS group for the 50 cases (100 images for each group). As shown in Fig. 6, the interpretation time for all the pulmonologists, residents, and pneumoconiosis specialists became roughly 30% shorter.

Fig. 6. Time required to interpret opacities in CR

DISCUSSION AND SUMMARY

Examining the results this time, between the pulmonologists and residents in regard to new opacities the pulmonologists using the CR method had a 17% higher sensitivity level. For the three groups, the specificity for new shadows and the sensitivity and specificity for diagnosing lung cancer showed no difference, which was most surprising. Evaluating these results is not easy, but for cases in which new opacities further compound pneumoconiosis, which has complex and varied opacities, we believe that the results show that even for experienced specialist interpretation is not easy. In reality, even though we employed helical CT at the same time in the medical examination of pneumoconiosis and lung cancer, we experienced some cases where it should have been possible to reach a diagnosis at an earlier stage, retrospectively.

It is noteworthy that the interpretation experiment results showed that by using TS all the groups of physicians exhibited improved sensitivity in the diagnosis of new opacities by 21% - 45%. In this case, the pulmonologists and residents in the TS group exhibited no difference in sensitivity compared to those in the CR group. Furthermore, although there was no significant difference, all physicians showed a tendency for improvement in TS sensitivity for lung cancer. However, we did not obtain the expected results for the specificity for lung cancer. In other words, the results indicated that TS is not appropriate for qualitative diagnosis in determining if new opacities were lung cancer or not. On the other hand, as far as we can see from the results this time, based on the use of TS, it was possible for even physicians with almost no experience to perform lung cancer screening on patients (lung cancer) that have complex shadows such as that from pneumoconiosis.

The fact that the interpretation time for all the physician groups was more than 30% shorter is consistent with the results of other reports up to now and the current results suggest that the burden on physicians in terms of medical examinations may reduce significantly.

Finally, the physicians that participated in the interpretation experiment this time had not dealt with TS images up until now, and they only received instruction on the TS images just a mere short 15 min. prior to interpretation. When taking this into account, in the future the physicians will become more skilled in TS and will exceed the levels achieved in this experiment. Therefore, we can expect to see more effective TS diagnosis.

ACKNOWLEDGEMENT
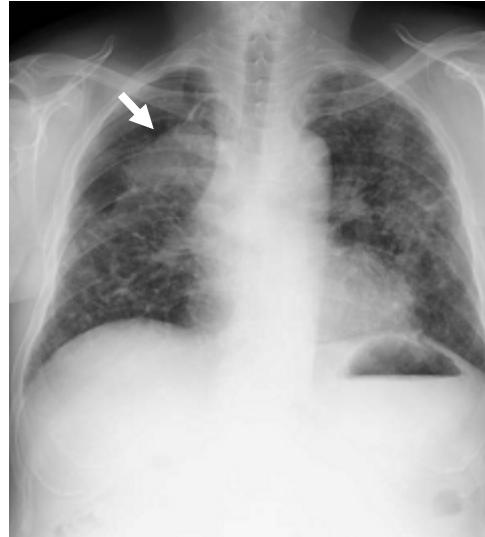
III. Presentation of Cases

Case 1
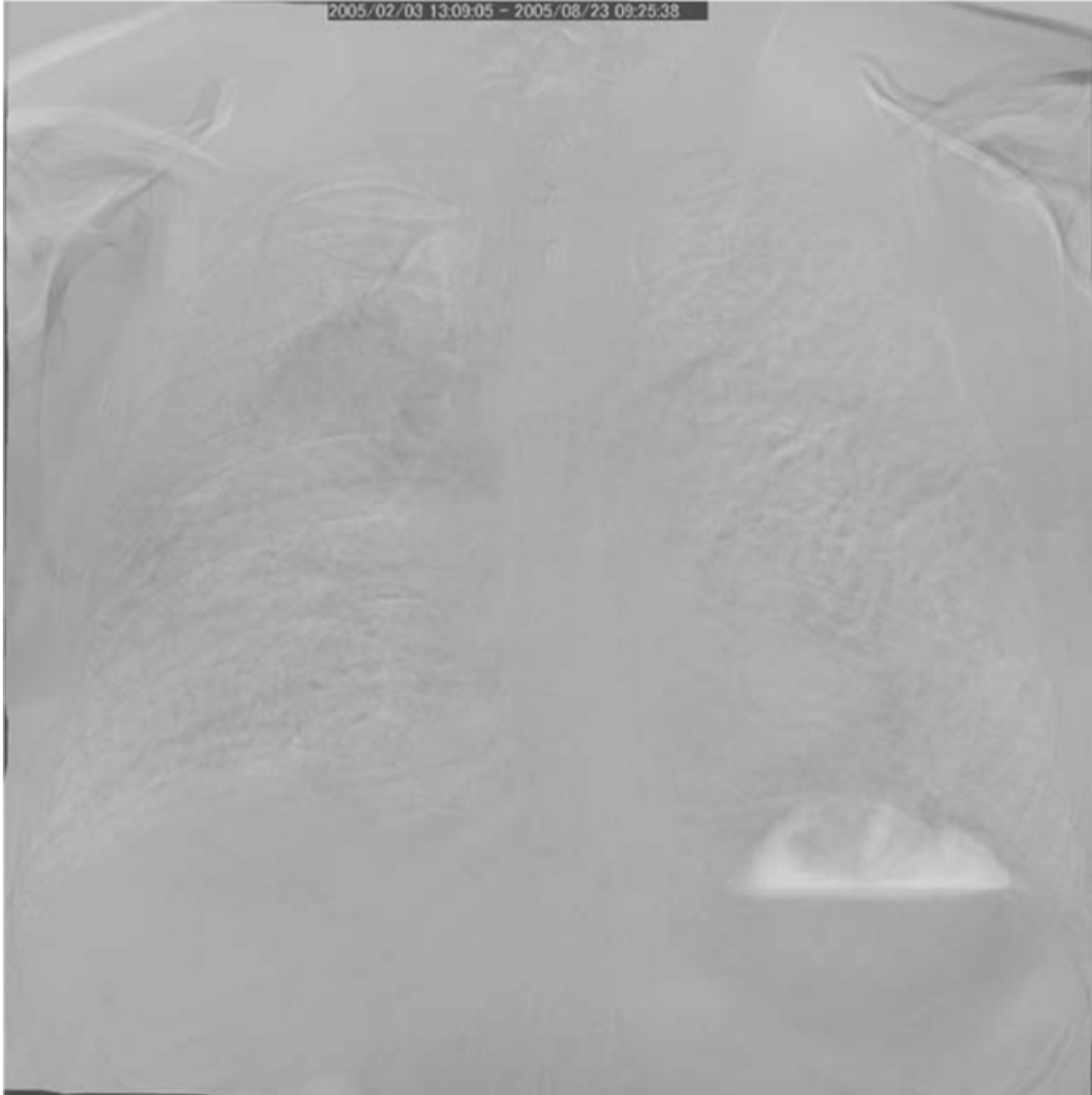
Case 1. 66 year old male: Coal miner (excavation, coal mining) 41 yrs., PR4B
TS image

Previous image: Feb. 2005


Current image: Aug. 2005

As indicated by the arrows in the TS image, there is a clear positive result. If we compare the current CR image to the past image, the outline of the large opacity of the pneumoconiosis in the upper right lung becomes clear and the opacity becomes denser as well. Among the total 30 doctors in the interpretation group 14 doctors in the CR group provided correct identification (6 pulmonologists, 6 pneumoconiosis specialists, and 2 residents: total 47%), and 23 doctors in the TS group representing 77% provided correct identification. Results from additional workup showed that there was large cell carcinoma of the right S6 of the lung.
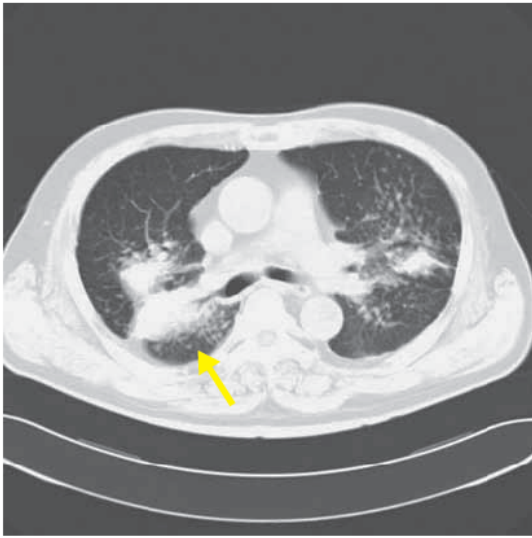
Feb. 2005 Chest CT
(pulmonary condition)
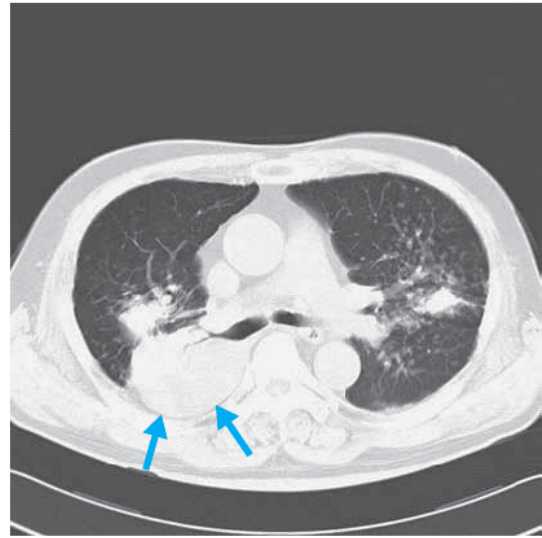
Aug. 2005 Chest CT (pulmonary condition)
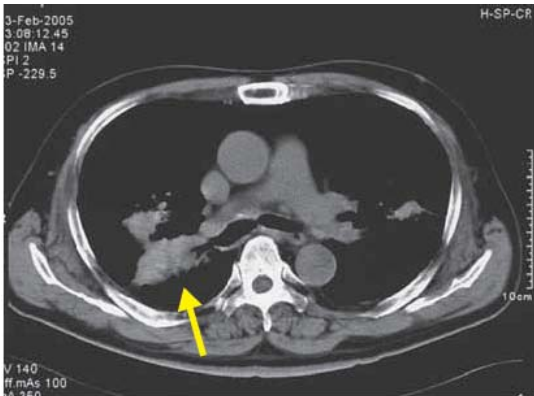
Feb. 2005 Chest CT
(mediastinal window)
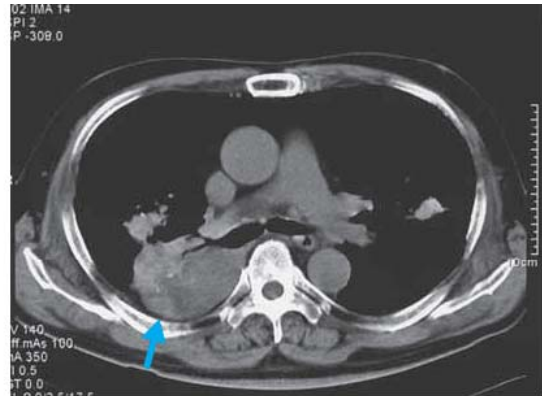
Aug. 2005 Chest CT
(mediastinal window)

CT showed consecutive tumors (blue arrows: right CT images) along the dorsum with the existing large opacity (yellow arrows: left CT image), which is accompanied by calcification.

Case 2

Case 2. 68 year old male: Coal miner (excavation, coal mining) 31 yrs., PR4C
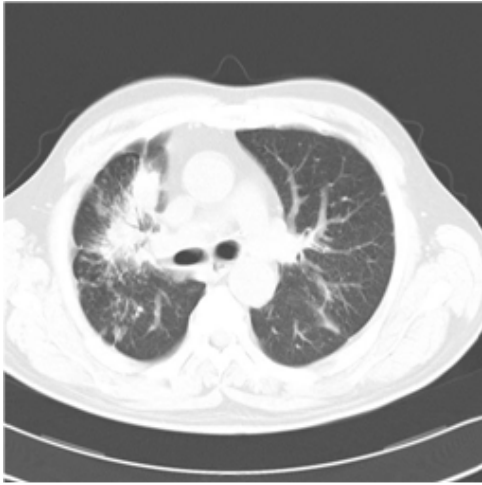TS image

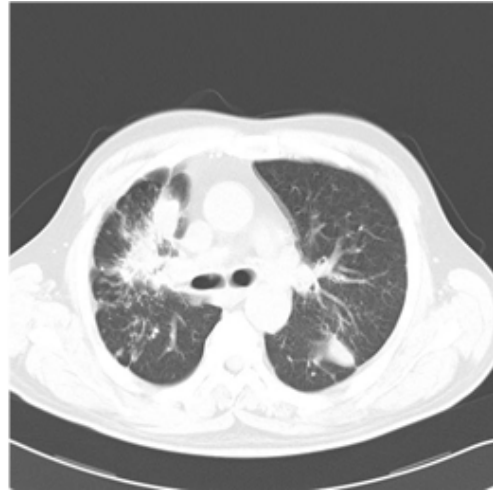Previous image: May 2005   Current image: Dec. 2005

      Although the TS image indicates light positive findings in the left upper lung, it is difficult to identify clearly the difference in the same area even when comparing the previous image to the current CR image.

May 2005 Chest CT
(pulmonary condition)

Dec. 2005 Chest CT
(pulmonary condition)

In the CT image of a slice from approximately the same site, the interlobar fissures match and the opacity indicates a homogeneous rise in density. This is interlobular pleural effusion. For this example, only 10 of the 30 doctors in the CR group who interpreted the CR were able to identify this abnormality. On the other hand, 27 doctors in the TS group were able to identify correctly the abnormality. This case showed the largest difference between the diagnosis rates of the CR group and TS group. Because the mediastinal condition showed a hardly detectable increase in the density of the shadow, it was very difficult to conclude a correct diagnosis using CR. However, in this type of case TS facilitates a diagnosis.

Case 3

Case 3. 67 year old male: Construction worker (earthen work) 13 yrs., PR4B
TS image

Previous image: Nov. 2004   Current image: May 2005


The TS image, which was generated based on the difference in the May 2005 compared to the November 2004 image, indicates a clear positive in the top right part of the mediastinum. Although an increase in the density of the large opacity in the same part can be identified, a change in the size of the opacity is not apparent, and it is not easy to identify the abnormality from these findings.
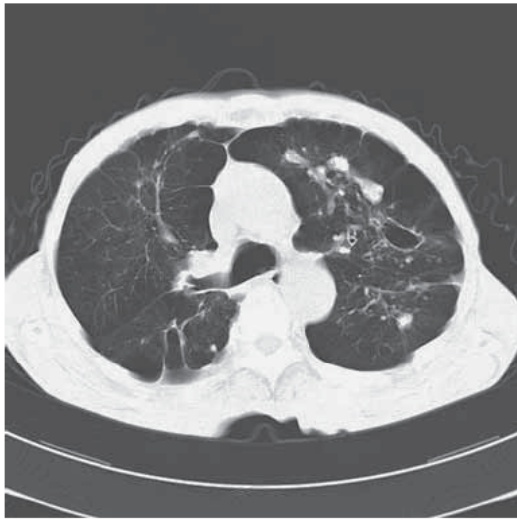
Nov. 2004 Chest CT
(pulmonary condition)
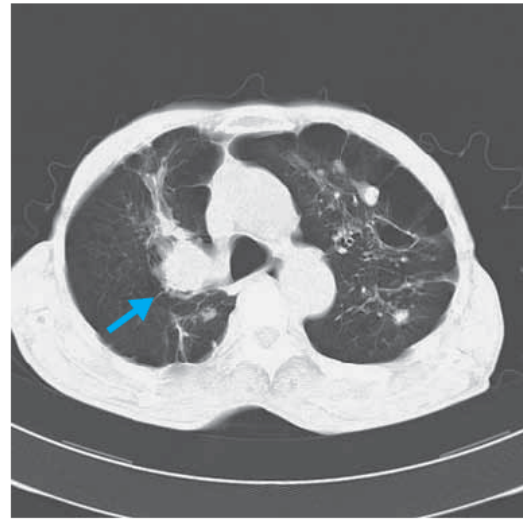
May 2005 Chest CT
(pulmonary condition)

Nov. 2004 Chest CT
(mediastinal window)

May 2005 Chest CT
(mediastinal window)

Based on a CT comparison, slightly cephalad of the tracheal bifurcation it is clear that there is a tumor running along the right main bronchus (small cell carcinoma of the right S1). However, identifying the presence of the tumor with certainty based on the CR image was difficult in this case due to the existing pneumoconiosis lesion. Although in this case only 18 doctors (60%) were able to identify with certainty the abnormality based on the CR, 28 doctors (93%) were able to identify the abnormality with certainty based on the TS image.

Case 4

Case 4. 62 year old male: Coal miner 28 yrs., PR3•2q
TS image

Previous image: Feb. 2006   Current image: July 2006
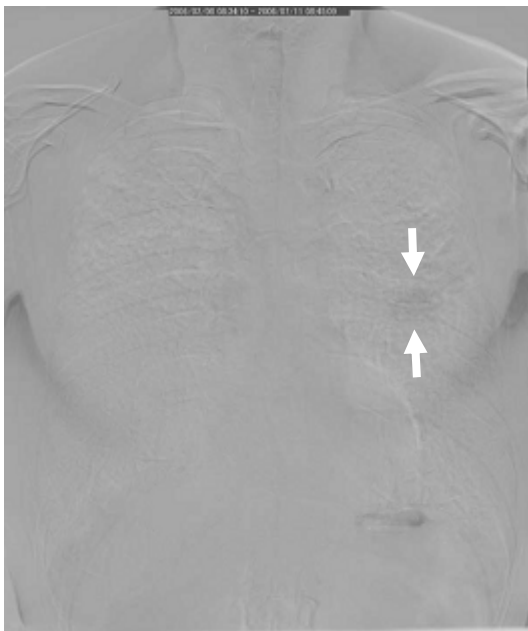
The TS image indicates slight positive findings in the outer portion of the middle of the left lung. If we compare the CR images using the TS image as a reference, the change in the nodular opacity in the part indicated by the TS image is uncertain, and for the other parts because there are multiple pneumoconiosis opacities throughout the lung, it is difficult to grasp the change without using the TS as a guide in the CR image comparison. Although there were 10 doctors (33%) who pointed out this change in the CR images in the interpretation experiment, 25 doctors (83%) diagnosed new opacities based on the TS image.
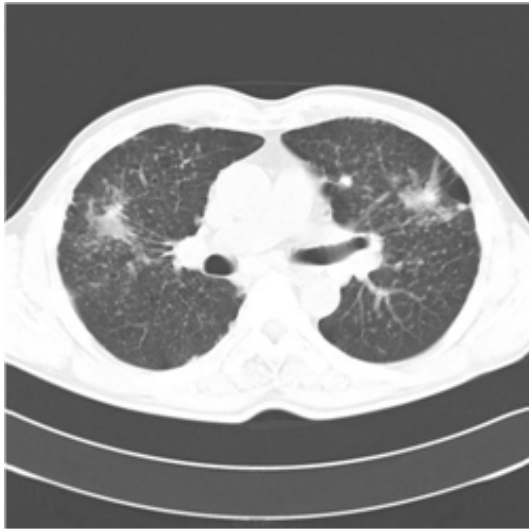
Feb. 2006 Chest CT
(pulmonary condition)
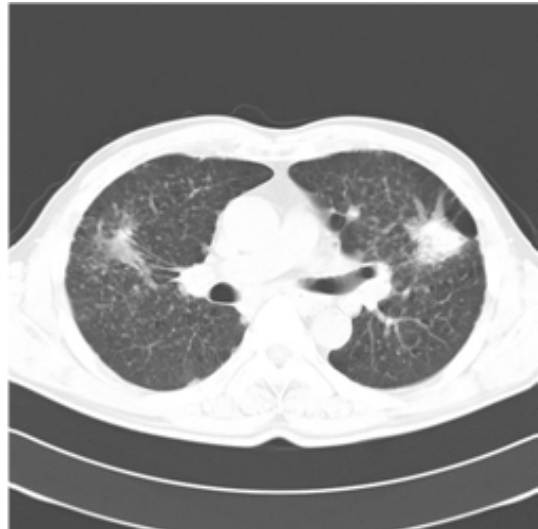
July 2006 Chest CT
(pulmonary condition)
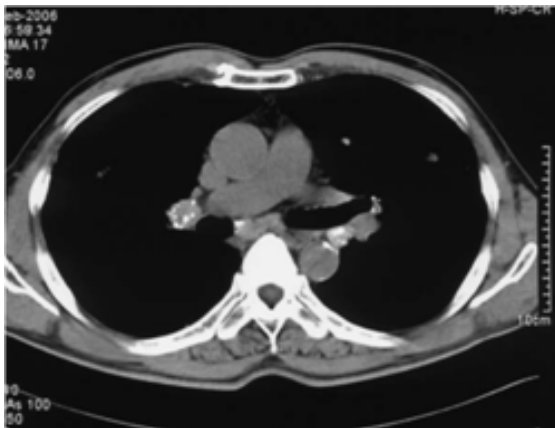
Feb. 2006 Chest CT
(mediastinal window)
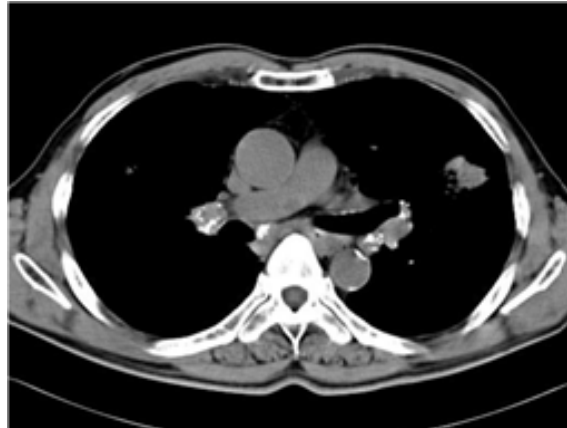
July 2006 Chest CT
(mediastinal window)

If we view this CT we can confirm the onset of a new opacity at the left S4 (subsequently this opacity disappeared completely, and inflammatory changes were diagnosed).

Case 5

Case 5. 77 year old male: Coal miner (excavation, coal mining) 37 yrs., PR4B
TS image

Previous image: Nov. 2004   Current image: Nov. 2006

The arrow in the TS image from the November 2006 image and the November 2004 image indicates accumulation of a slight opacity.

Based on the previous and current CR images at the top of the page, there is nothing that leads us to suspect the presence of a new opacity. In the TS image, however, we are able to perceive positive findings.
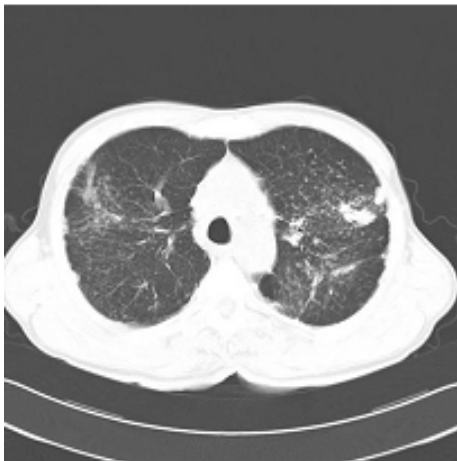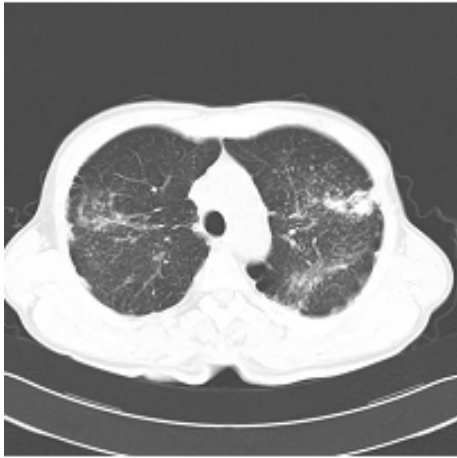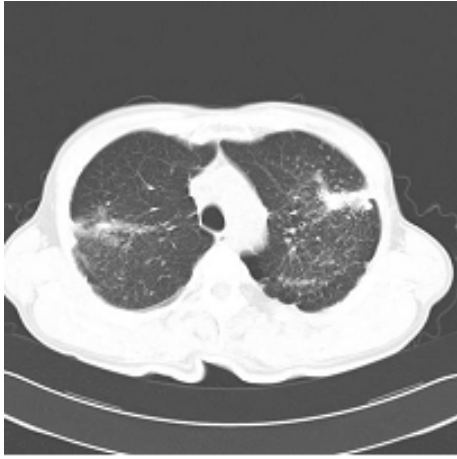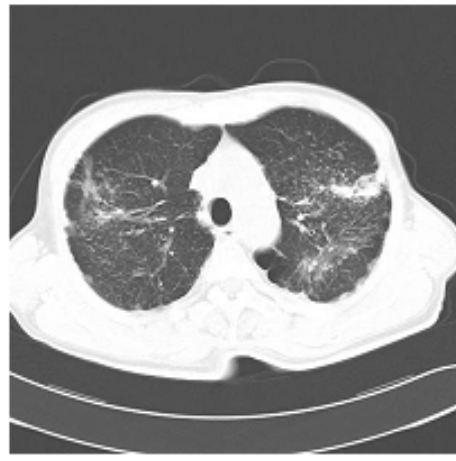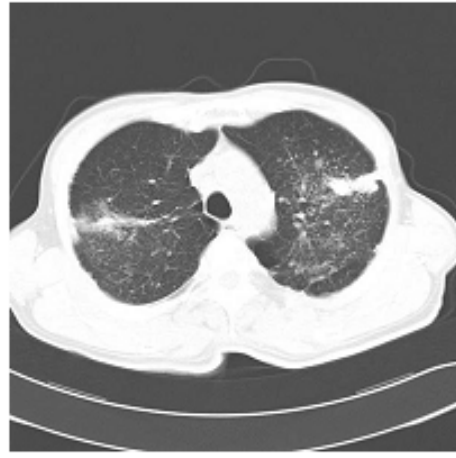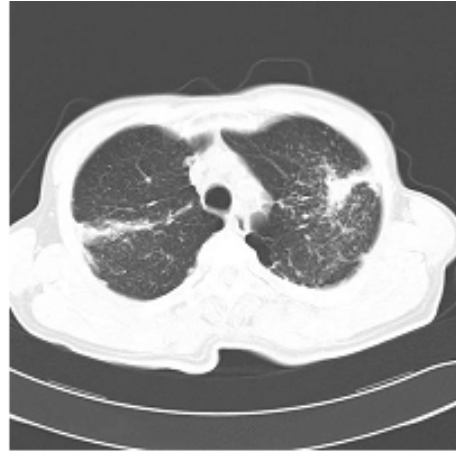
Nov. 2004 CT image   Nov. 2006 CT image

In this case, 16 doctors (53%) participating in the interpretation of the CR images diagnosed a new opacity in the same part as 21 doctors (70%) who used the TS image. Although there was a subtle difference in the slice site for the CT image, we could not confirm the presence of a new opacity even using CT. At present, we believe that this represents false positive findings using TS imaging.

Case 6

Case 6. 77 year old male: Coal miner (excavation, coal mining) 40 yrs., PR4C
TS image

Previous image: May 2006   Current image: May 2007
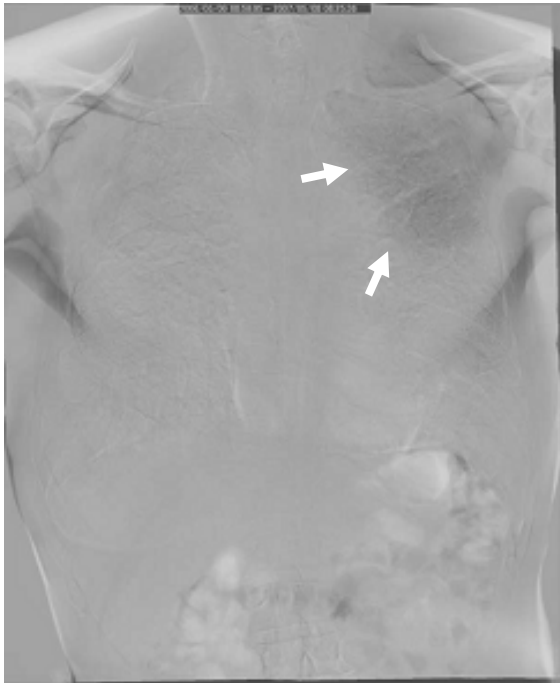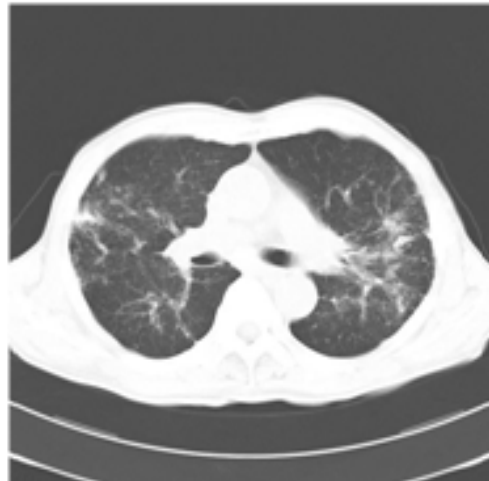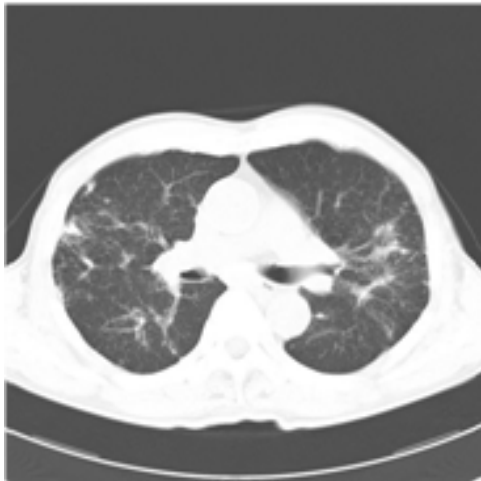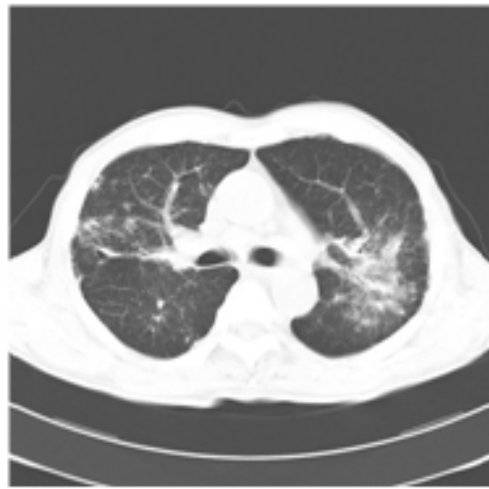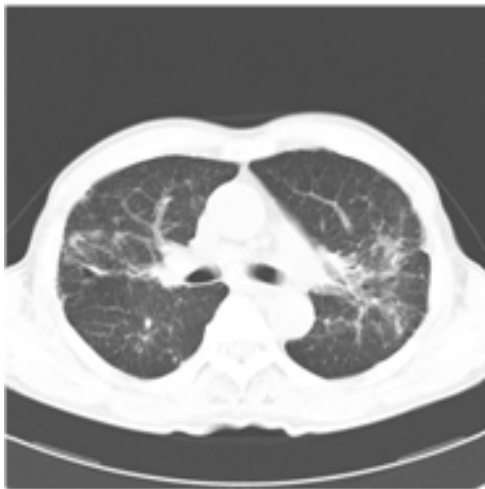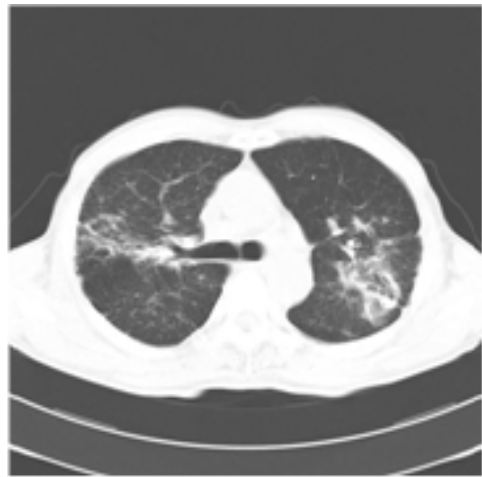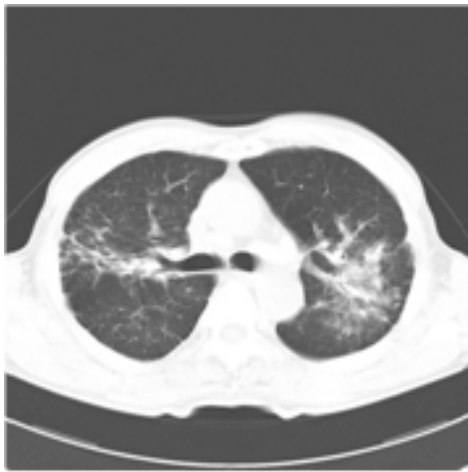
May 2006 Chest CT
(pulmonary condition)

May 2007 Chest CT
(pulmonary condition)

In this case, 29 doctors (97%) interpreting the TS image agreed on identification of positive findings in the upper left lobe. Of course accurate identification is difficult because of the subtle difference in the CT slice sites; however, the suspected entire upper left lobe in the TS image cannot be extended to include the presence of the opacity of a new abnormality. Therefore, in this study we judged that there was no new opacity in this case. However, the site of the upper left lobe matches in the TS image, and the indicated findings show no artifacts in the other parts, so the problem of easily judging the artifacts remains. This is a very interesting case because there is the possibility that only pneumatic decrease is being exhibited and not extreme atelectasis.

Case 7
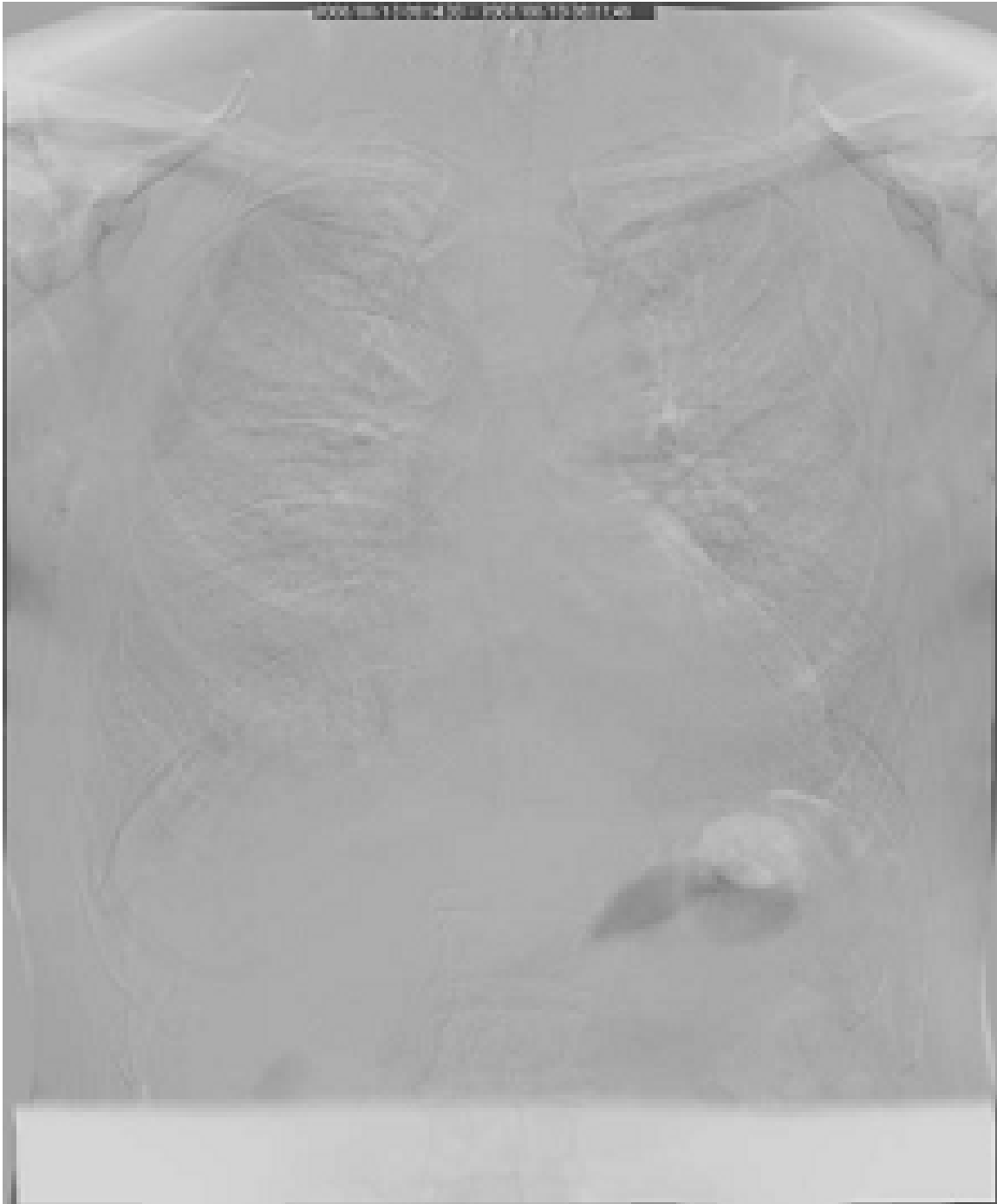
Case 7. 68 year old male: Grinder, coal mining 24 yrs., PR1/0p
TS image

Previous image: June 2006   Current image: June 2007


There are several places where positive findings are suspected in the TS image. However, all the parts indicated by an arrow are opacities overlapping ribs and in particular the opacity located at the first rib is expressed darkly, so these may be diagnosed as false opacities.
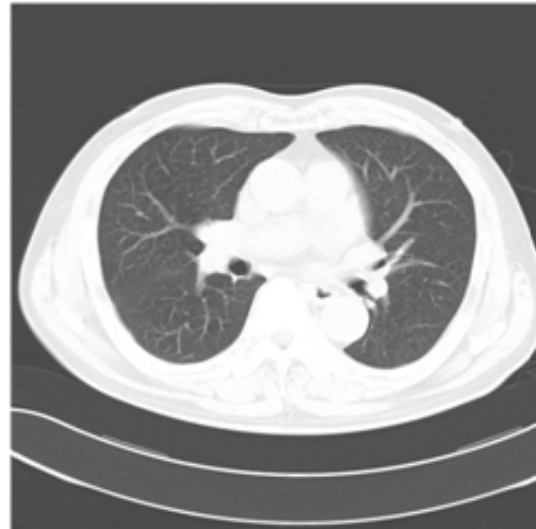
June 2006 Chest CT   June 2007 Chest CT
(pulmonary condition)   (pulmonary condition)

Although the CT shows slices of two sections, no new opacity was found. In the interpretation experiment, 5 doctors (17%) using the CR images and 10 doctors (33%) using the TS image diagnosed a false positive for this case. However, we believe that once the usage of the TS image is mastered the number of diagnosed false positives will significantly decrease.

We presented cases 1-4 where the TS image had a significant influence and cases 5 -7 where there were more false positives based on the TS image. Finally, from the cases that we were not included in this interpretation experiment, we present one very interesting case.

Case 8

Case 8. 68 year old male: Demolition work 54 yrs., PR0/1
TS image

Previous image: Dec. 2006   Current image: Dec. 2007
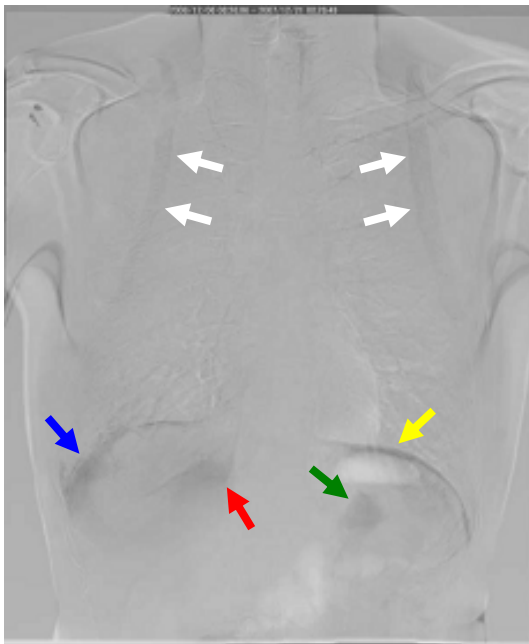
In the TS image, we can easily see the false opacities due to blurring of the diaphragm indicated by the yellow arrow and scapula indicated by the white arrow. In addition, the green arrow indicates a false positive opacity, which was from the image of gas in the digestive tract in the last image. We can regard the other blue and the red arrows as indicating positive findings based on the TS image.
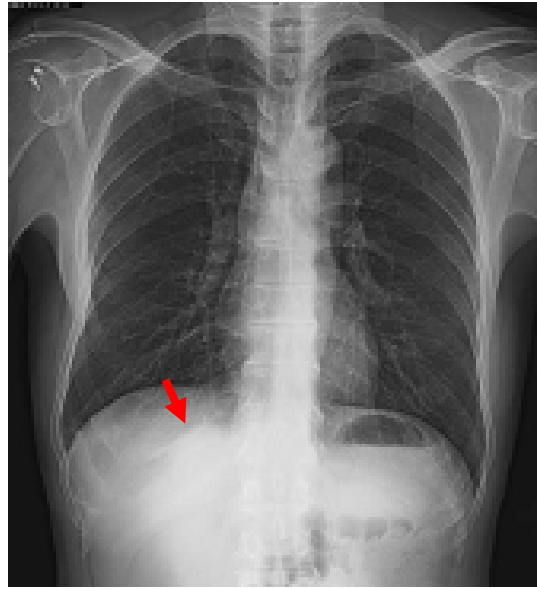
Therefore, by generating the highlighted image which disregards the lung condition and comparing previous and current images, we can see based on the TS image the emergence of a previously unobserved opacity as indicated by the red arrow.
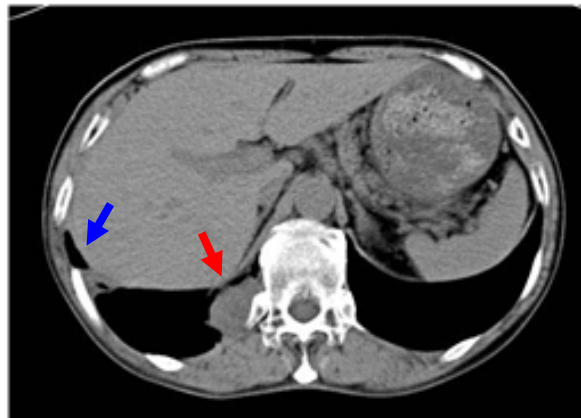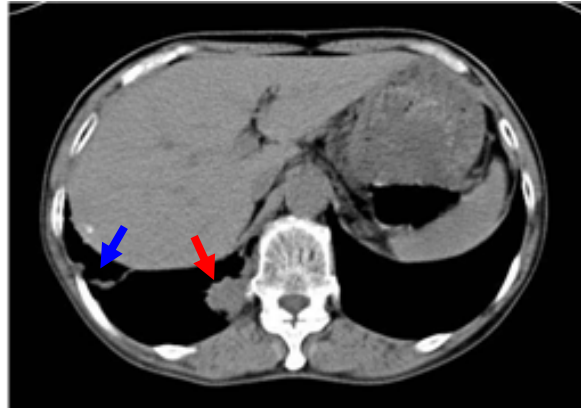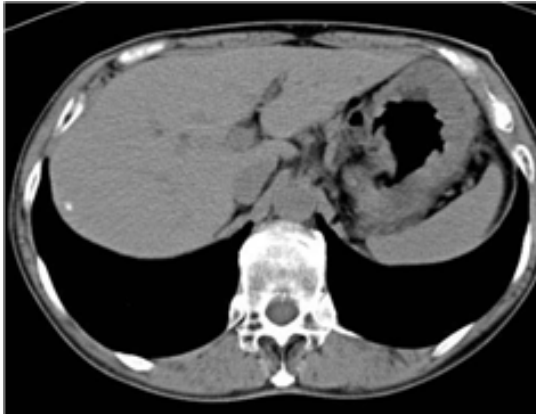
Dec. 2006 Chest CT
(mediastinal window)

Dec. 2007 Chest CT
(mediastinal window)

Based on the CT, if we compare the previous and current images the emergence of a tumor opacity becomes clear as indicated by the red arrow, and we verified that it matches the opacity indicated by the red arrow in the TS image. In addition, the CT indicates the emergence of a new shadow in the part indicated by the blue arrow in the TS image (the shadow indicated by this blue arrow can also be diagnosed using the CR images).

Conclusion:

For Cases 1 – 4, after we found that there were new opacities based on the CT and other images, we took another look back and examined the CR images in detail. We suspect that there may be new findings. However, practically at a clinic based on physical examination of cases with the presence of various opacities of pneumoconiosis shown this time, it is clear that there are cases in which making a diagnosis based only on a comparison of CR images is difficult. On the other hand, we showed that in the medical examination of pneumoconiosis the use of the TS images is effective in quickly diagnosing new opacities. In addition, under normal conditions Case 8 would be considered impossible to diagnose using the CR images, and we believe this is a valuable case because the use of the TS images led us to suspect the presence of the opacity.

IV. Symposium on Temporal Subtraction

Chairman

Hisahiko Sekihara
(General Research Director, The Japan Labour Health and Welfare Organization)

Attendants

Kiyonobu Kimura
(President, Hokkaido Chuo Rosai Hospital, The Japan Labour Health and Welfare Organization)

Atsuko Kurosaki
(Former Director, Toranomon Hospital, Federation of National Public Service Personnel Aid Association)

Kazuo Shimura
(Executive Chief Engineer, Image Technology Department, Software Development Center, R&D General Headquarters, FUJIFILM Corporation)

Masahisa Takagi
(Chief Radiological Technologist, Department of Radiology, Kanto Rosai Hospital, The Japan Labour Health and Welfare Organization)

Katsumi Nakamura
(Director, Department of Radiology, Tobata Kyouritsu Hospital, Kyoaikai Medical Corporation)

Chariman Mr.Hisahiko Sekihara

Sekihara

Let us begin. From 2004, already 4 years have passed since we at the Japan Labour Health and Welfare Organization began clinical medicine research on the 13 fields of occupational injuries and illnesses. We have produced various results, and most recently we have been focusing on one result in particular, the endeavor by Dr. Kimura from the Hokkaido Chuo Rosai Hospital who is the principal researcher on the project "Respiratory diseases due to dust inhalation." From this project has come results in the form of the temporal subtraction method which is useful in the diagnosis of pneumoconiosis patients. Today, we have gathered together specialists in this field to discuss the temporal subtraction method.

The attendants are Dr. Kimura the President of the Hokkaido Chuo Rosai Hospital, his associate Dr. Masahisa Takagi, the Chief Radiological Technologist at the Kanto Rosai Hospital, Dr. Nakamura of the Tobata Kyouritsu Hospital, Dr. Kurosaki previously of the Toranomon Hospital, and the developer of the temporal subtraction method, Dr. Shimura of the FUJIFILM Corporation. I hope that our distinguished guests will share their experience and discuss what exactly the temporal subtraction method is and in what way it should be used clinically to be effective.

We hope to hear first from Dr. Kimura. In the suuroundings of Iwamizawa, the coalmines are now gone, but previously it was a coal mining area, and physicians were extremely troubled because of the exceptionally large number of pneumoconiosis patients. After the coalmines were closed, pneumoconiosis was often thought to be the past disease, but Dr. Kimura and his colleagues have treated many pneumoconiosis patients.

As time progressed, these pneumoconiosis patients had further complications with lung cancer, and we were faced with how to deal with this in regular examination. Because pneumoconiosis cases have basically various complex opacities, it is extremely troublesome to find the lung cancer at an early stage from among those opacities. It is from this point of view that we hope that the specialists will speak based on their experience regarding the usefulness of the temporal subtraction method.

Dr. Kiyonobu Kimura

Kimura

One reason why we think that the temporal subtraction method can be used in the diagnosis of lung cancer complicated pneumoconiosis is that in 2003 it was legally established that lung cancer was a complication of pneumoconiosis. As such, how do we appropriately diagnosis lung cancer that is a complication of pneumoconiosis? As Dr. Sekihara pointed out, pneumoconiosis, as we all know, has various opacities in the background. Moreover, there is often impaired pulmonary function, so even if we find it, radical operation is sometimes difficult in cases where it has progressed.

Since we are faced with such a background, I wondered if we could not somehow find an effective diagnosis method. In 2003 when it was established that lung cancer was a complication, physicians when required were allowed to use tentatively the sputum cytological examination and helical CTs. Because there are various opacities in the background and as physicians we hate to overlook things, the always use of sputum cytological examination and helical CTs is now the status quo.

As we are all aware however, putting cytological diagnosis of sputum aside for the moment, is it permissible to perform helical CT once a year? Is subjecting a young person during his or her active working years to this procedure the right thing to do? Actually, in the clinic even if we perform a CT we can still overlook quite a bit.

The reason why I draw attention to the temporal subtraction method is that probably this method was not yet developed by the time of the lung cancer meeting in 2003. In 2004 when the research began on the 13 fields, I very much wanted to verify the effectiveness of this subtraction method on pneumoconiosis. The first thought I had was whether or not the subtraction could be well done despite the varied background as found with pneumoconiosis. This is what I am most interested in.

If subtraction can be done effectively in the case of pneumoconiosis and new opacities can be reliably detected, then it is clear that it will be effective in other general examinations. At the Hokkaido Chuo Rosai Hospital, there are about 400 pneumoconiosis patients who have been compensated by workers' accident compensation insurance and about another 700 cases who have not yet received compensation.

Fig. 1. Sensitivity to new opacities based solely on CR
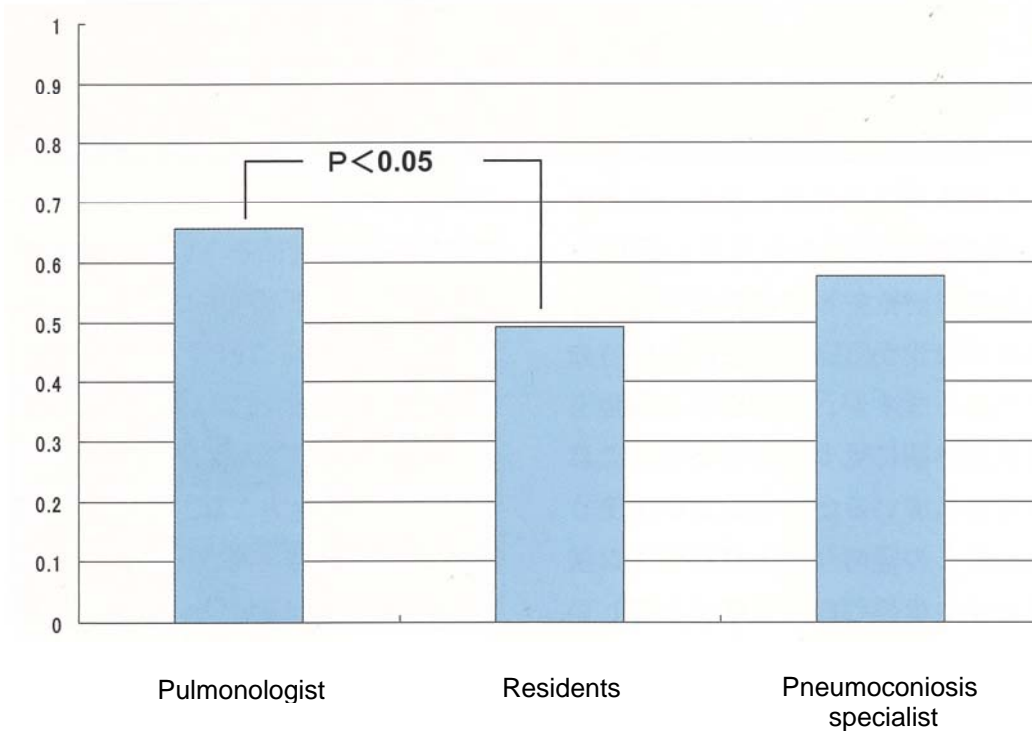
Fig. 2. Sensitivity (New Opacities)
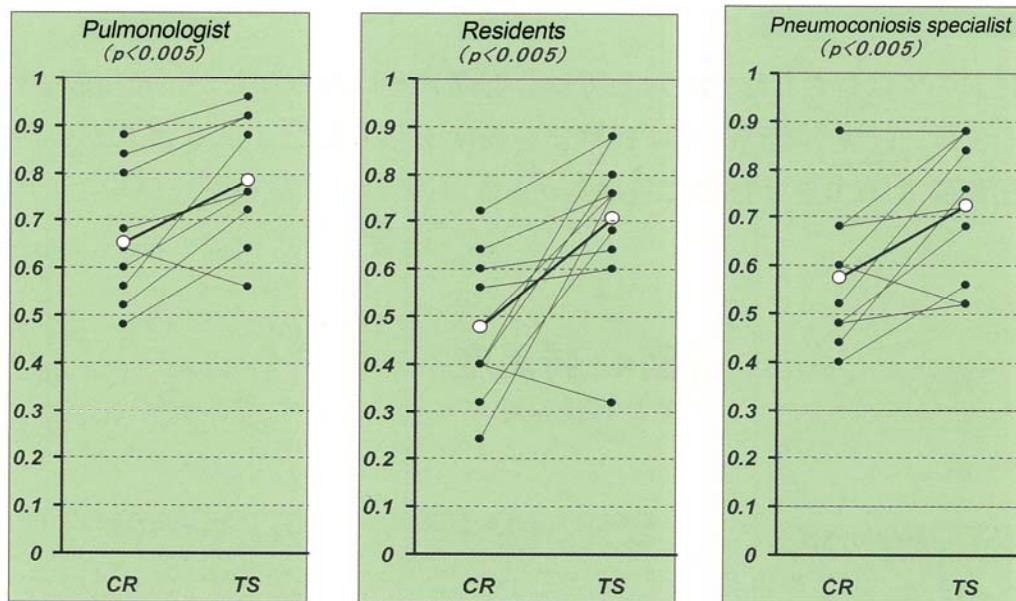
(TS: Temporal Subtraction Method)

Since we are very accustomed to examining these types of cases, we believe that this method is certainly effective for pneumoconiosis, for general cases this method of examination will be applied ubiquitously. This was our way of thinking, so we selected it as a research theme.

First of all, I would like to present the results of our research. I believe that each of you have a copy of the document "Research related to the usefulness of temporal subtraction". I would like to simply explain the results.

For this experiment we gathered together 10 pulmonologists, 10 residents, and 10 pneumoconiosis specialists to interpret images. We had them interpret the images of 50 pneumoconiosis cases that were taken at random varying in degrees of progress from unusually slight to extremely advanced. The images for the 50 cases comprised 25 cases in which based on CT were judged to exhibit no new changes and the remaining 25 cases were judged to exhibit new changes based on CT. Among these last 25 cases, 18 cases were confirmed to have lung cancer and remaining 7 cases were confirmed not to have lung cancer.

I'll omit the details, but if we look at the sensitivity to new opacities based on CR as indicated in Fig. 1, there is some difference in the sensitivity for the pulmonologists and residents. However, the results show that there was no difference between the pneumoconiosis specialists and either of the other two groups. If you would, please direct your attention next to Fig. 2.

We can see in the figure the t test results show that the pulmonologists, residents, and pneumoconiosis specialists all exhibited increased sensitivity to new opacities which included lung cancer cases and cases without lung cancer.

Although there was a significant difference in the sensitivity to new opacity for the residents and pulmonologists based on CR, this difference disappeared when subtraction was used, and the sensitivity increased uniformly. However, for the sensitivity and specificity in determining the presence of lung cancer, as we can see in the following figure there is no difference. As far as our experiment is considered, in terms of specificity, subtraction may not have been very effective.

Figure 3 shows the interpretation time, and all the groups showed a reduction of more than 30%. Certainly because we are dealing with pneumoconiosis it has complex opacities, and these results indicate a large difference, but given that they were pulmonologists and pneumoconiosis specialists, seeing this big a difference has extraordinary meaning.

Based on this, if the sensitivity to new opacity is improved, then it should be used as the primary screening test. If we have the patients who test positive in the screening take a CT, we can avoid unnecessary radiation exposure, we can reduce the chance of overlooking something, and combine effective CT in the examination. I believe that the research results supports this type of thinking. Briefly, those were the results.

Fig. 3. Time required to interpret opacities in CR
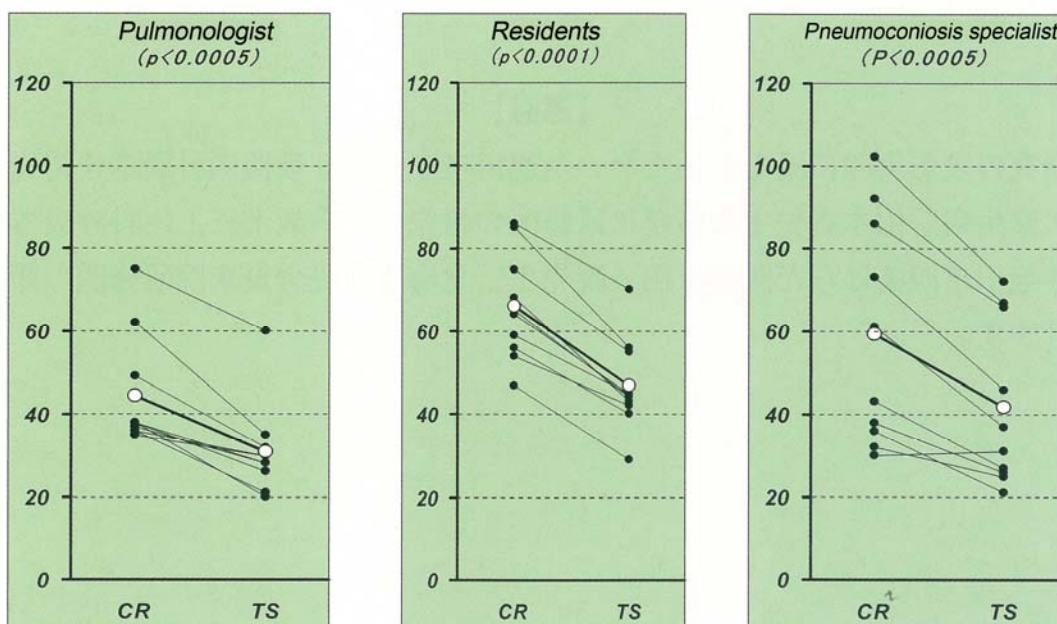
Sekihara

Thank you very much. Then can we take this to mean that even if new opacity emerges from lung cancer in an area that already has complex opacities, although it was very difficult to compare two chest radiographs and conclude a diagnosis, by using this new technique we can in a comparatively simple way and in a shorter time, yet with high probability, detect the emergence of new opacity.

Kimura

I think that can be said. However, one problem is knowing to what degree radical surgery can be performed on the tumor found using the new method. I am sure that there is a next step.

Sekihara

Since we have the Chief Radiological Technologist Dr. Takagi here with us, I would like to ask his opinion. We have heard that this new method seems to be quite promising, but hasn't the amount of work for radiologists increased?

Although we'd like to hear from Dr. Shimura later on regarding the theory and other topics, in regard to the practical day-to-day examination routine was there any trouble or was it difficult to generate images using the temporal subtraction method?

Dr. Masahisa Takagi

Takagi

We didn't experience any trouble in particular when using the TS method. Since we started to use the subtraction method for research, conversely we had to fundamentally come back to taking chest X-rays, and so we reaffirmed it.

Actually, after we started using TS and ran into the problem of the artifacts, we investigated to what degree we could suppress generating false positives. For that purpose, new types of software for example for the warping process or the spring binding scheme were developed; however, to our regret if the basic CR image was poor, as we suspected the corrections using the software were not altogether effective.

Therefore, returning to basics we pulled the scapula, and corrected using axial shift. Then, with caution we need to have the patient breathe steadily and then hold his or her breath tightly. Recently I've started to recall such things.

Sekihara

Then, since we subtract the two pictures, it's important that we don't let artifacts or blurring occur. That sounds like very difficult work, but "returning to the basics" is important.

In short, the basics are for example the position when taking a chest radiograph, as you mentioned about the scapula, so if we closely adhere to the basics, then we can trust that the software developed by Dr. Shimura can clearly process most images.

Takagi

Yes. In my experience up to now, that has been the case. Misalignment of the scapula and the difference in the breathing phase of the diaphragm are related to artifacts. Close to the heart, due to the misalignment of the mediastinum part there is a difference in the density that causes artifacts no matter what we do. These are the causes of wrong diagnosis that we discussed with Dr. Kimura. If I could say one more thing, the method really does negate the various opacities caused by pneumoconiosis.

Sekihara

Well I thought that we'd hear complaints such as we can't do this or give me a break. But it doesn't sound like that at all. This software seems to be exceptionally well developed and as long as we follow the basics we can expect a clear image.

Takagi

I think it is a good support system.

Sekihara

Next, we'd like to hear from Dr. Shimura regarding what kind of method the temporal subtraction method is from the viewpoint of FUJI-FILM and as an expert on the method. From some time ago the topic of discussion has been the problem of misalignment, and to correct this the software was developed. How is the misalignment corrected? Would you please let us hear your comments regarding this?

Dr. Kazuo Shimura

Shimura

First when we mention subtraction, digital subtraction angiography comes to mind because it is used in most medical treatment fields. Digital subtraction angiography, in other words contrast of the blood vessels, calculates before and after live and mask images to enable the contrast. Based on this all that remains is an image of the blood vessels.

You could say that this temporal subtraction is the same as digital subtraction angiography, but one difference is that the time period between radiographs is totally different. For example, one year earlier. Then, naturally, a person's body will change over the one year period, and the positioning will change somewhat, the heart will also move, and even if the patient holds his or her breath there is misalignment due to timing. The degree to which these can be suppressed is the technology of this subtraction processing software.

If that goes well, the misalignment artifact disappears very cleanly and only the changes remain. If it doesn't go well, the area of change and unfortunately the parts that naturally should not change both remain.

When we first took on this subject, we thought that the human body is by nature made three dimensionally, and projecting that onto a two dimensional subtraction image no matter how much we account for positional drift is fundamentally impossible. Honestly to our amazement, the blurring cleanly disappeared, and conversely as technicians we were very surprised. As a technician, I'd have to say that it's knowledge that is important, and we thought that no matter how much we compensate it is impossible to project something that is moving three dimensionally. But the misalignment artifact cleanly disappeared. I remember that the first set of results were good.

One reason why the results were good was as Dr. Takagi mentioned, I think the radiolo-

gist who took the images was skilled. In short, correcting for three dimensional distortion projected into a two dimensional image is half software technology and the remaining half is reproducing the positioning when radiographing. By combining these two, I think that for the first time we obtained a good subtraction image.

Even in the field of medical treatment, comparative diagnosis is very widely used. In the various types of examinations such as periodical health examinations or in follow up examinations of those who become ill, the more the original structure is complex the more difficult we can see the difference in just one radiograph. If at this point if we can obtain a clean subtraction image, even in a case where the original structure is extremely busy, for example a case of pneumoconiosis that has an extremely complex lung area, I think that image is expressed such that the difference is extremely easy to see.

The advantages to the subtraction technology are that it is easy to see the radiographic changes in the shape of the tumor and overall we can grasp the fluctuations in the density. As was also indicated in Dr. Kimura's report, I think that the new opacity is a key and in any case, if there is a change that change is rendered in the image. Afterwards the doctors can carefully view the images, or perform additional examinations, and obtain a correct diagnosis. I think this shows the effectiveness of the method.

Well, we are currently distributing the document for discussion of the technology. Figure 4 shows simply the theory behind the temporal subtraction processing.

Fig. 4. Temporal subtraction method employing automatic position matching technique

Current image   Previous image

Position alignment

Previous image
after warping

Temporal subtraction image
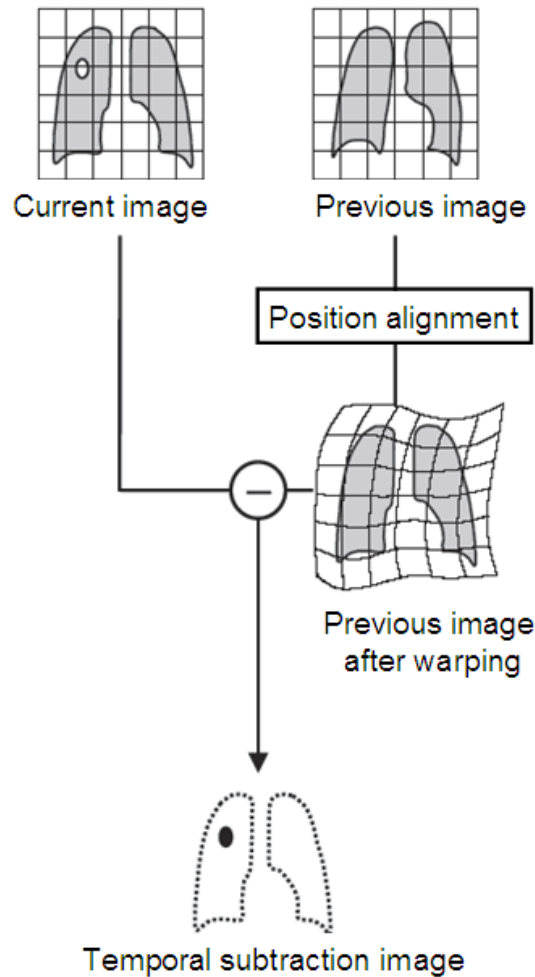
There are two images the current image and previous image, and the positions are aligned and warping is performed. Warping is a process in which the image is distorted.

For example, if we consider that this is an image taken a year earlier, we can understand that between that image and the current image, there are many changes such as to the form of the body, breathing, and heartbeat. Of course there is some misalignment in the positioning, but by distorting the image, we can generate an image that is extremely close to the current image. By performing subtraction we suppress the motion artifacts as much as possible and generate the temporal subtraction image. This is the process.

Considering this, how to implement the distortion is an important point. First of all, the structure is roughly aligned and then the fine structures are aligned. This is the kind of processing that is done. In other words, we take a large

form for example the chest, and after performing global position alignment, gradually section-by-section we correct for positional shift of each small area. By doing this, the large structure aligns perfectly. In the fine areas, we gradually align the positions.

In this case, each position does not independently and randomly move, it's as if they are bound by a spring. If there is some positional shift in the neighboring locations, we can smoothly change the amount of positional shift. Briefly, by using an arrangement in which a location and another location are bound by a spring, we can determine the direction of the distortion. By doing this, we can align two images taken at different times with minimal motion artifacts.

The important point, naturally while leaving the amount of misalignment from pathological change, we correct for the large misalignments from the structure of the body. That's the point. If

the aligning goes too well and the pathological change disappears, we lose everything, so while leaving just the pathological change, we correct the large changes. This is the key to the temporal subtraction technology.

Sekihara

I was deeply impressed by the things that Dr. Shimura just discussed, and as Dr. Kimura first said regarding temporal subtraction, if we use common sense, if the two X-rays taken at different times don't align perfectly artifacts are generated. So how do we correct for these artifacts? Can we really accomplish this? This is what we thought, so Dr. Takagi verified if this was actually possible.

As we were listening to Dr. Shimura regarding the process for the correction, if we roughly make corrections, then the fine areas will follow later, and the theory behind that correction is that, well after all, the human body is constructed so that it can easily accept changes. Isn't that the way things are?

Shimura

First regarding the positional shift, we want to align the large structures as much as possible. Actually if the time differs, we find that in the fine areas such as the blood vessels of lungs between the ribs, the direction of movement is rarely reversed. If we try to force align these areas we end up with a strange image, so it is important that we start with aligning the large structures. I also think that it is important that we don't force the fine structures so that they align.

Sekihara

If we align them roughly, then the small areas follow and align exactly, isn't that the way it is?

Shimura

It depends on the image. If the original image is quite close, then in the way as you just mentioned, we roughly align the structures and gradually one after the other we obtain an image that almost perfectly matches. In the areas without change we should get an extremely clean image. No matter what we do motion artifacts due to breathing timing or other causes will occur. However, even in these cases, we use this approach so that we can avoid large artifacts as much as possible.

Sekihara

Thank you very much. I'd like to take this opportunity to ask the other physicians if they have any questions for Dr. Shimura.

We have heard from Dr. Shimura regarding the theory behind temporal subtraction. Previously Dr. Takagi mentioned that the method functions well and that there is no misalignment. We also heard Dr. Shimura talk about the various difficulties from development stage and that we don't have to worry about the artifacts too much. I think that we talked about that the human body is created well, and I think that we all have a good understanding of the temporal subtraction method.

So we have heard from Dr. Kimura and Dr. Takagi about the usefulness of the method in regard to pneumoconiosis. Also we'd like to hear from Dr. Nakamura and Dr. Kurosaki regarding general diagnosis by pulmonologists, other applications besides pneumoconiosis, and on any good experiences with this method. Let's start with Dr. Nakamura.

Dr. Katsumi Nakamura

Nakamura

I too previously have been involved with this temporal subtraction for a comparatively long time and have tested it in various fields. I also investigated the emergence of lung cancer in pneumoconiosis for a period of time, and those results are the same as those presented by Dr. Kimura. The background opacities were very diverse and when interpreting the chest X-ray films detecting subtle change was difficult. There is also a heavy psychological burden on the interpreting physician. Considering this, the temporal subtraction is an extremely useful method.

We also conducted a similar interpretation experiment, and in that experiment as well the detection sensitivity, for those with experience and

those with little experience, achieved extremely effective levels.

Aside from this experiment, through medical examination or other means when we found nodular opacities in the lung, lung cancer, metastases to the lung or other lung nodular changes that are not related to lung cancer, this method was extremely useful.

At that time, we considered two things. The first is that because it is lung cancer there are many irregular shaped opacities that are limited to the origin of the lung cancer. For these we investigated using SCR only and CR plus the temporal subtraction, and as we thought using the temporal subtraction in the interpretation improved the detection sensitivity. For metastases to the lung also, we could see a comparatively clear outline of the tumor, even including small one, and the results were as we thought using the method improved the detection sensitivity.

Aside from that, it was naturally useful in detecting localized opacities such as in the case of pneumonia. In particular new opacities or things that may be present other than nodules, we have perhaps pneumonia or some kind of opacity. Among the cases that I investigated there was a case of interstitial pneumonia, in which a new opacity emerged. That case of interstitial pneumonia became acutely aggravated or became complicated with infection, and interstitial pneumonia in the same way as pneumoconiosis has very diverse background opacities and detecting new opacity is very difficult. In that case I think the method was quite useful.

The second thing was conversely in immuno-compromised patients that are afflicted with pneumocystis carinii pneumonia etc., extremely light opacities emerge. Using only simple X-rays to diagnosis this is difficult. In the case of light ground glass opacities, even if you take a CT, if you don't take a high resolution CT, it sometimes difficult to diagnosis, but this temporal difference method can detect this light change in density.

The temporal subtraction method is quite capable of detecting slight changes in density. For things that are hard recognize visually due to the radiographic conditions, I have experience that by using this temporal subtraction method, we are able to detect opacities comparatively well. Therefore, for nodules, localized opacities, and diffuse infiltrative opacities, etc. in the lung, I believe that this method is useful.

Sekihara

Thank you very much. Then, not only for

tumors but also for interstitial pneumonia and pneumocystis carinii pneumonia or that kind of inflammatory change we can see a difference.

Nakamura

That's right.

Sekihara

Dr. Atsuko Kurosaki

Let's hear from Dr. Kurosaki.

Kurosaki

Today I'd like to explain two topics that were presented at the Japan Radiological Society meeting held in April of last year. The first is an investigation on the fundamental use of TS on pulmonary nodules, and the other is a its' clinical evaluation.

As you are all aware, recently the number of lung cancer cases has increased tremendously. To improve the survival rate, it is important that we find lung cancer when it is small or light.

Small lung cancer is less than 2 cm in diameter and light cancer is called alveolar epithelium substitution type lung cancer and is a type of cancer where in the cancer mass natural air still remains in the alveolar spaces. We are not only trying to find this type of early stage lung cancer to increase the survival rate, there is also the corresponding reduction in medical expenses, so current health care professionals are very hard at work detecting these types of cancer.

For that method the main image is CT, but by using CT no matter what we do the number of subjects is limited. The medical expenses and the amount of radiation are both high, so we hope that TS will be the method we have been looking for to perform analysis using some form of a simple imaging.

In a basic examination, we conducted an

experiment employing a phantom and a sham mass of less than 1 cm in diameter. Sham tumors created from acrylic resin were modeled based on solid and ground glass level tumors and attached to a chest phantom. We evaluated TS by taking images while rotating and bending the phantom backward and forward. The results showed that for a 5-mm diameter solid tumor or 10-mm diameter ground glass level tumor, if the rotation or bending backward and forward was within ±2 degrees, it is possible to detect the tumors using TS.

The clinical evaluation that we are conducting includes these basic evaluation results. We received the cooperation of the physicians at the Hokkaido Chuo Hospital, and last year we examined 6 cases and collected 7 lung cancer 、 the diameter of which were less than 2 cm. By using TS we were able to improve the recognition rate of the X-ray changes and the confidence level of the diagnoses.

In front of you we have an actual case, the diameter of the tumor is small, and other anatomical structures overlap, there are multiple changes, and there is coexistence with existing pulmonary disease, with the use of TS an improved level of confidence was achieved. Therefore, by using TS before taking a CT, we concluded that the probability of finding small lung cancer is quite high.

Sekihara

Thank you very much. From Dr. Nakamura and Dr. Kurosaki as well we heard that even in cases other than pneumoconiosis TS was extremely useful and that at the clinical level the diagnostic accuracy probably improved.

If we judge two radiographs visually, in the temporal subtraction case if we look at the subtracted image, as Dr. Kimura previously mentioned, temporal subtraction is much better. So then we can consider temporal subtraction to be superior, right? When we are interpreting 2 X-rays, by quickly looking at the subtracted image, which is superior?

Nakamura

Bottom line, I believe that the temporal subtraction image is the reference image. Even from Dr. Kimura's results, in one method the current CR image and previous CR image were compared, and in another method current CR image was compared to the temporal subtraction image. When we view the temporal subtraction image and if we detect abnormal opacity, then perhaps as the remaining work we need to view the current CR image. Because no matter what we do artifacts

are inevitable, so we have to check in the current CR image if it is really there.

Therefore, temporal subtraction is the first computer-support diagnosis method, or one of the computer image processing methods, that detects abnormal or new opacities. Physicians can make their diagnosis by using this image that indicates this type of abnormal candidate opacity as the reference image and viewing the original image. This is the kind of thing that they are using.

Of course in this discussion, the shortening of the interpretation time, in terms of efficiency is extremely important, as indicated by the results.

Sekihara

Then, the important point being discussed is that viewing the subtracted image is the last reference, in other words while viewing the two original images we need to view carefully the subtracted image. Then based on careful comparison of the three images the diagnosis accuracy improves. Reaching a diagnosis becomes quicker and the accuracy improves. We shouldn't make a diagnosis only on the subtraction image.

Nakamura

Yes, a diagnosis shouldn't be made solely on the subtraction image.

Sekihara

Please, Dr. Kimura.

Kimura

Yes, I believe that what you said is correct. The subtraction image is absolutely a reference image. However, do we always really need the previous and current CR images? For the most part, at first we view the subtraction image in many cases. For more practical and simpler method, we are conducting an interpretation experiment using the current image and subtraction image.

In short, we need to determine if any of the opacities that are currently there and the new opacities that were revealed through subtraction match. Then I think we can make a proper estimation. We do not have to always go back and view the previous CRs.

Sekihara

Dr. Kimura says that, if we compare the current and subtraction images we can find out a considerable amount.

Kimura

Bottom line, from the screening viewpoint, that may be the way to do things.

Sekihara

We don't need the first image. From a practical standpoint I think that this is an important point, do you agree?

Nakamura

What I did previously was to use all three images, current image, previous image, and subtraction. Of course viewing all three takes time, and as Dr. Kimura mentioned earlier, if two images are enough to screening I think it just makes the time that much shorter.

Sekihara

How about the accuracy?

Nakamura

Although I really can't speak to that since I did not investigate it, if the accuracy is secure, I think that it is a good method to promote.

Sekihara

What are your thoughts Dr. Kurosaki? I think in order to disseminate the subtraction method from now on this is an extremely important point.

Kurosaki

I don't have experience either with the interpretation experiment, and I can't really speak to the accuracy, but now film interpretation is for the most part no longer used and viewer or monitor diagnosis is more common. Previously as Dr. Nakamura mentioned, the current image, previous image, and one other image or although the images become smaller three images, no matter what we do the number of film images increases. This is where monitor diagnosis comes in, there are no costs due to film and we can diagnose using only the monitor. I think that the timing of this in addition to the proliferation of TS is just right and is following the popular trend.

Sekihara

In short, previously we generated the subtraction image, so there is one more film image. However, that subtraction image is no longer on film but appears on the monitor.

Kurosaki

The current and previous images as well, now the monitor is very commonly used.

Sekihara

Since we can see all the images on the monitor, that's very convenient.

Kurosaki

Moreover, we don't have to hang the images, we can change images jut by moving the cursor a little.

Sekihara

Yes, that's right.

Kimura

However, in the case of pneumoconiosis, current regulations indicate that we must have a film image. Right now, that's the way it is.

Sekihara

Therefore, you three, and Dr. Takagi from a radiologist's standpoint conclude that from now on this method will spread widely, and that everyone will be using it.

Kimura

In relation to our subtraction experiment, there wasn't much familiarity among the participants, and as it's written here, at most there was only a 15 min. orientation. In short, this is what the subtraction method is. In this type of situation, artifacts appear in these places. This is an artifact. All we explained were things such as be careful around the heart.

In a nutshell, positive findings show up as dark areas. We only showed them a few cases and they viewed them for only about 15 min. Those are the results of the experiment that we conducted in this manner. Therefore, if we study subtraction a little more, we can reduce the required time further, and well may be saying getting better results is a bit strange but it will get better.

Sekihara

Therefore, from now on in examining general lung cancer, we should think that this method should be used widely? In regard to this, I'd like to hear a few words from each of you. Dr. Kurosaki, please let's start with you.

Kurosaki

From the conclusion that we heard, I concur that this is what will happen. This time, we didn't examine clinically the light shadows, but as was mentioned earlier, we need to find those small opacities and light opacities in diagnosing lung cancer. By using TS and then going to CT, I think

that there is a higher probability that we find such things.

Sekihara

Simply, if we take a X-ray and if it looks strange then we apply the subtraction method. So it's a good idea to apply subtraction before going to CT.

Kurosaki

Yes, it should be used as an existing diagnosis method.

Sekihara

Dr. Nakamura, what do you think?

Nakamura

In terms of screening in the chest area, now CT is becoming considerably widespread. In medical examinations, many physicians are also turning to CT.
Furthermore, in medical institutions as well, CT has become diffuse in medical examinations and treatment. I think that because it's relatively simple to take, the reality is that it is the way chest screening is done.

Considering this, what kind of position will chest X-rays have from now on? I don't think that it will disappear. Because the extreme usefulness of the method has been established, I don't think that it will disappear, but when the position of using X-rays comes into question, this temporal subtraction method is the first CAD application, and if we refer to this temporal subtraction technology in particular, I think that the probability that the ability of diagnosis by using chest x-rays will improve.

Therefore, if the area to be radiographed can be taken simply, as long as there is a previous image, then this image can be used as a reference. If we reference it, as Dr. Kimura mentioned, or as previously published several times, certainly the ability of diagnosis of simple images improves, and there is a boost in our diagnostic ability. It significantly facilitates the interpretation. I think we can say that about this.

Sekihara

Dr. Kimura, do you have any comments?

Kimura

I agree with what Dr. Nakamura said. Even if we look at this using a trained physician's eye, there are things that no matter what we do we still don't know. I think Dr. Nakamura mentioned

this a little while ago, this is not limited to tumors, and I think that really light shadows and conversely the difference in pneumatization are shown.

This time it seems that we didn't perceive the difference between before and after the CT. The dark images in the subtraction image, the dark area in the upper left lung represents positive findings, but we were going to respond that it was a false positive. I think that it's these types of things that we didn't perceive that the subtraction method can pick up.

This time I'd like to describe a very recent case that we experienced. No matter what we did with CR there was a opacity that we couldn't diagnosis. But by using subtraction we were able to find out what it was. It was a opacity behind the liver, no matter how you look at it there's no way we could know what it was using a regular CR. Even if we took a CR from the side, I don't think it would have made a difference, but we were able to get a clear image using subtraction (Case 8, Pg. 48-50).

Therefore, if there is a previous image and the circumstances allow the use of subtraction, a more than adequate screening can be performed. You may wonder where CT will fit in. Is CT the last step, after subtraction is used? I think that's an important point. In cases such as pneumoconiosis, if we move in the direction of taking CTs for all the patients, we have to wonder if is this OK as a method of medical examination. Previously, from the various points that we identified, it seems that the subtraction method has partly an ability that far exceeds that of radiologists.

I have data from a recent case that we experienced. Please take a look. I think that you all have experienced the same type of case.

Nakamura

I think that what Dr. Kimura is true. The subtraction method is particularly effective in perceiving those things that the human eye mistakes or overlooks. No matter what we do, we overlook opacities those overlap the diaphragm, the heart, the hilum, or when the ribs overlap the opacities, or opacities those overlap these types of normal structures. In my past experience, I think the subtraction method has this type of usefulness. When there was an isolated opacity in the middle of the lung area, and if I looked very carefully it was relatively easy to find, but it overlapped normal structures so it would be easy to overlook.

By using subtraction technology these normal structures disappear, and we can find the

lung cancer in those sites. When there are opacities those overlap the diaphragm or those are behind the heart, it's easy to overlook even advanced cancer. I think that the penalty for this is large, but it is possible to improve the detectability in these areas.

Sekihara

I'd like to hear from Dr. Shimura. For example just now as we heard from Dr. Kimura regarding the case with the opacity overlapping the liver, we can't discern this from one image, right? However, we can see this if we use the subtraction method. Therefore, when viewing opacity in the current image, if we look carefully, we can see the light shadow as Dr. Nakamura expressed it, and this is the type of thing that is overlooked. Then it appears in the X-ray, right?

Shimura

I think that there is also a problem with the conditions under which it is displayed. Especially in this case underneath the diaphragm, or heart or mediastinum, no matter what we do if we use normal x-ray to show it, it is extremely white and hard to see. From the displayed image it is extremely difficult to see, but after all the data is there.

Sekihara

Therefore, we must improve the sensitivity of the human eye, because it appears in the X-ray. So should we think that this is just us as the interpreters not noticing?

Shimura

I think that the equipment also has something to do with it. I think there are display conditions that make it easier to discern the opacities and we need a good way to achieve that.

Nakamura

I think that only the things that we can see will manifest themselves. The things that are difficult to see will become easier to see. Therefore, the number of instances that we overlook things will decrease. Most cases, we perform subtraction and then when we take another look and say "ah here it is." I think saying that we can see things that we couldn't see before is a bit overdoing it.

Sekihara

Indeed. It makes things that were difficult to see easier to see.

Nakamura

Yes, that's right.

Sekihara

Then, from now on this subtraction method will spread widely, and as a vision of the future, Dr. Shimura and others like him will make this a high level application. Earlier we heard from Dr. Kurosaki regarding light opacities. We are very familiar with the use of the word "light," but even in what Dr. Nakamura said just now that it makes things that were difficult to see easier to see, if it is extremely thin and with a light opacity we would still probably over look it.

However, we could intensify this light opacity 1000 times. This is possible through technology right? Then, at an extremely early stage, for those opacities that are currently too light that we can't see or that we're not sure if it is there or not, in the future by amplifying and making them more opaque, it will become possible to make a diagnosis. What do you think?

Shimura

Certainly I think that it is extremely important that we intensify the light opacities. When doing this, the biggest problem is of course artifacts. How can we suppress the artifacts? I think that from now on the development of that technology is important. For example, we limit the area and then we want to perfectly match up that area. There is a little artifact but this doesn't go well using the existing software. Subtraction technology that can align a particular spot more closely will also be important.

As mentioned earlier, diagnosis of pneumoconiosis using monitor images has not yet not been fully accepted, but monitors can display various images and they have an extreme range of freedom. Therefore, I think our task is to develop a total observation system by combining functions, viewing temporal subtraction images and simple x-rays in which we make the images of the mediastinum or underneath the diaphragm relatively easier to see and make the subtraction image so that it can be more freely displayed or depending on the original image change the display conditions.

Sekihara

Thank you very much. We have heard much discussion on subtraction. What is the current status of subtraction overseas? We now have a good idea of the current status here in Japan. I think that in the future there will be various de-

velopments, but for example what is the state of affairs in the West? Dr. Nakamura, when you were in the US, I heard that you were involved with this. Would you care to comment?

Nakamura

Temporal subtraction technology was first announced at the University of Chicago. In 1994 in the journal "Medical Physics" Dr. Kano, who is currently working at Konica Company, did the research and development while he was studying abroad at the University of Chicago.

Thereafter, at the University of Chicago they continued to work on improvements, but in the US this type of image processor doesn't readily get approved by the FDA and currently it is not sold in the US.

Shimura

I see.

Nakamura

Currently, this is not being very actively researched in the US. When I was at the University of Chicago, I had the opportunity to gain experience in using the device. When I returned to Japan, I conducted research to a certain extent using the same device as I used at the University of Chicago. What I mentioned earlier was pretty much my experiences at that time, but after that in Japan, a company called Mitsubishi Space Software commercialized a device. I think that device has made its way into a fair number of universities nationwide. After that, the system by FUJIFILM was commercialized.

Therefore, in that respect Japan is more advanced. Currently, in terms of clinical application of this temporal subtraction, I think Japan is leading the rest of the world.

Sekihara

Japan is leading the rest of the world.

Nakamura

Yes.

Sekihara

Then, in the future, I hope that by all means the doctors gathered here today will become the core, spread the temporal subtraction method throughout Japan, and assume a pioneering role.

Finally, we'd like to publish the discussion from this symposium for the benefit of young Japanese doctors. As their seniors, is there any message you would like to send to the young doctors

regarding the usefulness of this temporal subtraction method? I'd like to begin with Dr. Nakamura.

Nakamura

Currently we are in the IT era, and computer technology has forced its way into medical care as well. The temporal subtraction method is an enhancement to the established technique of chest x-ray in many years of medical examination, and will further increase the ability of diagnosis. I think that young doctors are familiar with this type of computer technology. Therefore, they will proactively take in this technology and this will contribute more and more to the development of medical examinations.

Sekihara

Next, Dr. Kurosaki.

Kurosaki

I don't know much about computers, so I let the specialists deal with the image based diagnosis. No matter what the image is, the important thing is if it's possible a comparison should be done with a previous image. In regard to that, it's a big advantage to be able to immediately view as an image the results of subtraction from the current and previous images that TS generates on the computer. Of course we can't just accept 100% the computer results, but it does aid considerably in calling attention to opacities, and it is extremely useful in image diagnosis and treatment.

One more thing that should be said, if all chest screening is done by CT, recently Multidetector-row computed tomography is being used, an enormous number of images such as several hundred are collected. Interpreting that many images is difficult, and if we have to compare them to past images, image diagnosis and treatment will become extremely stressful.

On the other hand, since we can observe diffuse changes and changes in the sections using simple chest x-ray and TS, the amount of stress is much less.

Sekihara

Dr. Kimura, your thoughts.

Kimura

As Dr. Kurosaki said, for pneumoconiosis if we regularly take a CT and make a comparison to the previous image, no matter how much time we have we won't make any progress. Furthermore, we will overlook things. Therefore, if we use subtraction in the screening process, we can pre-

vent overlooking anything that will be a surprise, and I think that we can performs diagnoses very efficiently. Therefore, in order to continue to perform examinations over many years, certainly implementing this subtraction method is realistic.

Sekihara

Dr. Takagi please say a few words regarding this method as a message to the radiologists in Japan.

Takagi

Up until now, we have been conducting retrospective verifications. This research from now on will change to a prospective method. This is what I hope will happen. I think that it is software that will reduce the diagnostic burden on doctors and this type of dramatic change in the images for medical treatment will motivate us. From the standpoint of radiologists, I'd like to be able to announce this type of thing.

Sekihara

By all means, we all hope that comes to fruition. Finally Dr. Shimura, from the standpoint of developing such a magnificent method, how do you plan to improve on the method in the future? Is that even possible? Please if you would speak about your dream to the young doctors.

Shimura

As Dr. Nakamura said earlier, chest x-ray is very basic and has been with us for a very long time, and I don't see it disappearing in the future. In order to make this even more effective, I think that as the manufacturer, we have to develop still more various types of image processing and diagnostic support technologies.

In this field, it was mentioned earlier that Japan is the center, but I think that the scope is a bit wider than just Japan, actually Asia is taking the lead in the field. Chest x-ray examinations etc. are being actively performed. From this meaning, I think that Japan can spread this field to the world. From the manufacturer standpoint, we will by all means develop new technologies in the future and hope that physicians will use these tools.

Sekihara

By all means, we hope that you succeed in your endeavors. Just now Dr. Shimura mentioned Asia. From now on I think that Japan should provide various types of information to the other Asian countries and should assume a leadership role. By all means, I think that the pamphlet should be translated into English and distributed. Dr. Shimura, we sincerely hope that you will continue your support.

Is there anything else? Please, if there is anything else you would like to discuss, let us take this opportunity to do so.

Takagi

I would like to add something if I may. Within this image diagnosis support system, there is also the energy subtraction method. We have all had experience with the easy misinterpretation of the opacities in the vicinity of the first rib. By using the energy subtraction method, if TS can cause the bones to disappear from the images, then there will be less stress in dealing with the images. I think that the artifact problem will also improve. In the future, I hope that we can investigate this further.

Also, various physicians have been asked for a second opinion, for example, but even if you were requested to perform TS, if the equipment manufacturers are different a dilemma arises in that it is extremely difficult to perform TS, so in that respect we hope that there will be more effort in development.

Sekihara

By all means, we hope that there will be more development in energy subtraction.

Shimura

Yes, I think so too.

Nakamura

I think that in regard to energy subtraction, temporal subtraction, further nodule detection using temporal subtraction images, and image processing technology, there are many component technologies that have been developed, and by combining these we can further improve the ability of diagnosis.

I have one more thing I'd like to add. Dr. Takagi said that there is a part in which we need to return to basics, for this technology recently I especially feel that this is extremely important. If chest X-ray images are taken so that they can be clearly reproduced, and for argument's sake let's say they are taken in exactly the same way, then probably the spring binding scheme image processing is totally unnecessary, and simple subtraction can be performed.

Although I think that can't be done, to the extent possible it is best to take the images under the same conditions, so that we can obtain good

subtraction results as we are beginning to understand, and as Dr. Shimura mentioned, the factors related to the radiographing system represent half the battle. Presently that's what I think, and certainly because image processing has advanced, the quality of the images that form the basis of this method must also increase or we can't achieve effective processing technology. Therefore, returning to basics is an extremely good idea. To summarize, although I think everyone understands, I think this is an extremely important point.

Sekihara

That's one of the fruits of today's symposium. Returning to basics. In what Dr. Nakamura just said, although various corrections are made using the software, I think the point is that, essentially if the basic photographing is reliable, when we subtract the 2 images we quickly obtain a new image. Essentially I think this is what the point is. Dr. Takagi what do you think?

Takagi

I think what you said is correct. That was one of the greatest tasks imposed upon us I think. I'd like to add to the earlier discussion when we were addressing the younger doctors. I think that they should take chest x-ray images that are true to the basics.

Sekihara

That's right. I think that the more various technologies such as temporal subtraction and energy subtraction progress, the more we need to go back to the basics for creating the original image.

Are there any other comments? Is that OK? Then, thank you all very much for taking the time out of your busy schedules to gather today and share with us your valuable experience regarding temporal subtraction.

I graduated from medical school in 1965 and have been internist since then. During this time, I think that the advancements in imaging in Japan are ground breaking. When I was a student, or just after I became a doctor, I came across diseases that we just couldn't diagnose, for example the pancreas or a dissecting aortic aneurysm, and at the time of autopsy for the first time I found that the cause of myocardial infarction was a dissecting aortic aneurysm from a blockage at the mouth of the coronary artery. Because of this blockage, a myocardial infarction occurred. I've had many such bitter experiences.

Then when CT arrived I thought that was a groundbreaking technology. I thought that the

world of medical care changed considerably. Hearing what you all have said, this temporal subtraction method is a technology that rivals that of CT and in the future it will continue to develop.

On this occasion, with the cooperation of Dr. Kimura, Dr. Nakamura, Dr. Kurosaki, Dr. Shimura, and Dr. Takagi, I think that the next revolution, in other words as a new diagnostic technology, this method should be spread widely. By doing so early detection will become possible for lung cancer patients, and if this leads to saving lives, I think that it is magnificent. With that in mind, I hope that we can count on your support. Thank you all for taking the time out of your busy schedules to gather here today. This concludes the symposium.

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