The 2nd Dynamic Digital Radiography Seminar

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KONICA MINOLTA JAPAN, INC.

Evaluation of pulmonary circulation by Dynamic Digital Radiography: Comparison with pulmonary perfusion scintigraphy

Munehisa Takata, MD Department of Thoracic Surgery, Kanazawa University

We have been examining the evaluation of pulmonary circulation using a Dynamic Digital Radiography (DDR). In this presentation, I will mainly report the comparison with pulmonary perfusion scintigraphy.

Evaluation of pulmonary circulation : Comparison with pulmonary perfusion scintigraphy

We compared the relative perfusion contribution by DDR and that by the pulmonary perfusion scintigraphy. The subjects were 26 patients (7 before surgery and 19 after surgery) who underwent Dynamic Digital Radiography and pulmonary perfusion scintigraphy during the same period, and 23 patients of them had lung cancer. The lung field was divided into six zones, and the relative perfusion contribution of each zone was measured by the improved PH-MODE (Cross-correlation calculation) of the DDR and pulmonary perfusion scintigraphy. Then, the relative perfusion contribution of each zone by pulmonary perfusion scintigraphy was plotted on the X-axis, and that of DDR was plotted on the Y-axis, and the correlation between those was analyzed. If the correlation coefficient was <0.2, it is regarded as no correlation, if that was 0.2-0.4, regarded as weak correlation, if that was >0.4, regarded as correlation, and P value <0.05 was regarded as significant difference.

There was a significant correlation between the relative perfusion contribution by DDR and that of pulmonary scintigraphy in the right upper lung field, right middle lung field, and right lower lung field. On the other hand, as for the left lung, the left upper lung field and left middle lung field showed correlation, but the left lower lung field did not show significant correlation. This seems to be due to the cardiac shadows. From these results, it can be said that the DDR would be an alternative examination for lung perfusion evaluation.

Based on this, we will present a case. This patient was 78-year-old man who underwent resection of the right upper lobe lung cancer. Three months after the operation, his dyspnea worsened, and he was

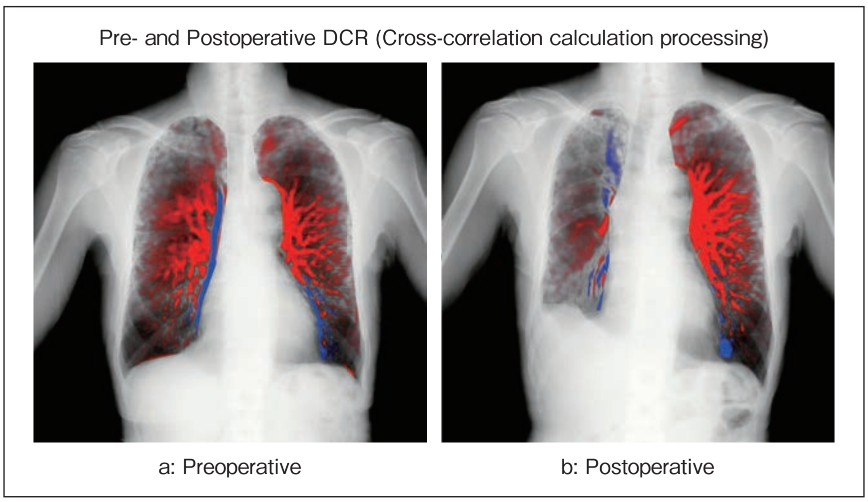
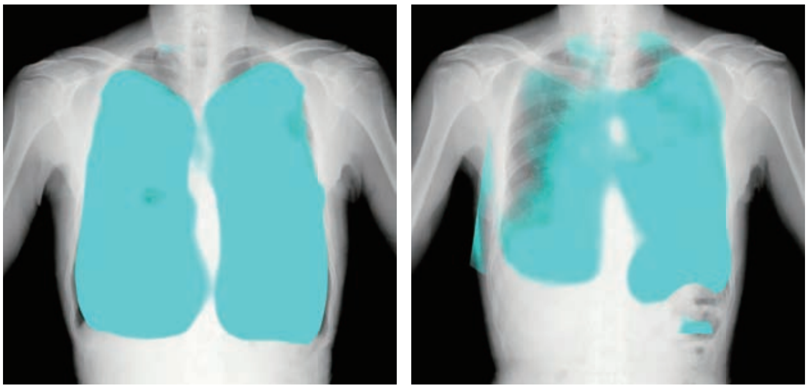


Fig. 1 Improved PH-MODE for resection of right upper lobe lung cancer

Pre- and Postoperative DCR (Reference frame ratio processing)



a: Preoperative b: Postoperative

Fig. 2 PL-MODE of the same patient as Fig. 1

re-examined. Lung ventilation and perfusion scintigraphy showed that both ventilation and perfusion of the right lung were significantly lower than those of left lung. DDR was also captured for this patient and analysis was performed. In comparing the preoperative and postoperative images of the DDR, postoperatively the movement of the vascular shadow in the right lung field reduced(PH-MODE) and the movement of the diaphragm was abnormal. Abnormalities in the mediastinum movement were also observed by PL-MODE (Reference frame ratio processing) **(Figs. 1 and 2).** As described above, the DDR can capture dynamic function information that cannot be obtained by other modalities.

Detection of pleural adhesion

We have been studying the application of the DDR to thoracic surgery. In order to examine the indications for preoperative pleural adhesion diagnosis, preoperative DDR of 151 patients who underwent thoracic surgery were captured. Abnormal factors suggesting adhesion were extracted from DDR , and the presence or absence of adhesion and its degree were also evaluated based on the video captured during the surgery as the reference, in order to check if pleural adhesion could be detect by DDR image before surgery. The abnormal factors, which is DDR image feature of pleural adhesion based on our expertise, included the following three signs such as “Gradation sign (G-sign)” with abnormal pulmonary vascular/bronchial movement, “Fixed sign (F-sign)” with fixed pulmonary vascular/bronchi with no movement, and “Tension sign (T-sign)”, which moves as if the funicular shadow were pulled.

The sum of those three findings (0/1/2/3) was used as the pleural adhesion prediction score (PAPS), and the grade of the adhesion was classified into following 5 categories; Grade 0: no adhesion, Grade 1: localized adhesion, Grade 2: adhesion in thorax 1/3 or less, Grade 3: adhesion in thorax 1/3 to 2/3, and Grade 4: total adhesion. In addition, we examined whether adhesion of moderate (Grade 2) or higher could be detected using PAPS of 2 or more as a cutoff line.

As a result, pleural adhesion was hardly observed in the low-risk groups with PAPS of 0 or 1, and pleural adhesion was more observed in the high-risk groups with PAPS of 2 or 3 with a sensitivity of 95% and a specificity of 96%. From this, it can be said that the use of PAPS obtained by the DDR would be able to predict moderate or more pleural adhesions.

Conclusion

The DDR is inexpensive, easy to operate, has high versatility, and lower dose compared to pulmonary blood flow scintigraphy, and useful for predicting postoperative pulmonary function and for searching the cause of pulmonary function decline after lung resection. Furthermore, it is possible to detect dynamic abnormal findings during thorax movement with the DDR, which was difficult to evaluate in the past. Based on these findings, DDR may be a potential alternative to pulmonary perfusion scintigraphy, and it can predict moderate or more pleural adhesions, and can also be used to evaluate adjacent organ invasion in some cases.

Prediction of postoperative pulmonary function using Dynamic Digital Radiography

Jun Hanaoka, MD, PhD Division of General Thoracic Surgery, Department of Surgery, Shiga University of Medical Science

The number of lung cancer patients with poor pulmonary function has been increasing, and it is important to evaluate strictly indications and risk factors for radical surgery for lung cancer. In this presentation, we report the validation of prediction of postoperative pulmonary function using the relative perfusion contribution by Dynamic Digital Radiography (DDR).

Validation of prediction of postoperative pulmonary function using DDR

Perioperative risks of lung resection are related to predicted postoperative pulmonary function such as FEV1 and FEV1 expressed as % predicted. Postoperative pulmonary function has been evaluated based on preoperative spirometry and the number of segments to be resected. However, it is necessary to improve its accuracy in cases near the threshold value. There are several published paper demonstrated that the accuracy can be improved by taking the relative perfusion contribution by perfusion scintigraphy into consideration, but there are problems such as labor, cost, exposure, and lack of urgency. Therefore, we conducted the study on the patients who underwent radical surgery for primary lung cancer to validate a prediction method of postoperative pulmonary function which is taking the perfusion information by DDR account.

1. Subjects and methods

The 34 patients who underwent radical surgery for primary lung cancer in our department were included. Preoperative DDR was captured for all patients and, the left and right perfusion contribution ratios were calculated from pixel values change corresponding to the pulsation of pulmonary artery during the cardiac cycle. Spirometry was measured before surgery and at 1, 3, and 6 months after surgery to evaluate the FEV1. The correlation between FEV1 measured value and the predict postoperative FEV1 three different methods; 1)the conventional method based on the number of segments to be resected, 2)the method taking perfusion contribution ratio calculated from perfusion scintigraphy and 3)the method taking perfusion contribution ratio calculated from DDR were evaluated with the Pearson's correlation coefficient (R).

2. Result (Fig. 1)

There was a strong correlation between the perfusion contribution ratio of perfusion scintigraph and

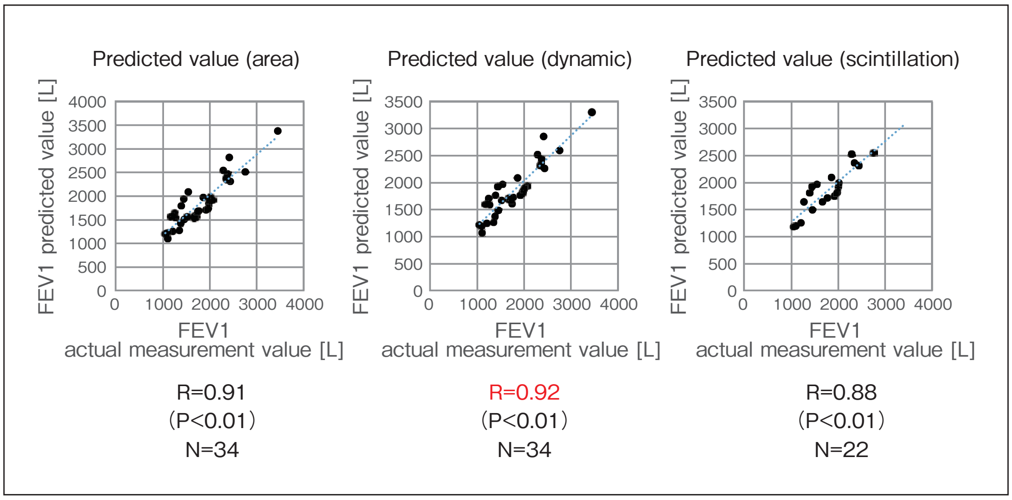


Fig. 1 Measured and predicted FEV (one month after surgery).

that of DDR (R=0.90, p<0.01, n=22). The correlation between the FEV1 measured value one month after surgery and predicted postoperative FEV1 by three different method were strong as 1) R=0.91, 2) R=0.92 and 3) R=0.88 (all p<0.01). Similar tendency was observed at three months after surgery; 1) R=0.94, 2) R=0.94 and 3) R=0.94 (all p<0.01), and at six months after surgery; 1) R=0.94, 2) R=0.94 and 3) R=0.91 (all p<0.01)

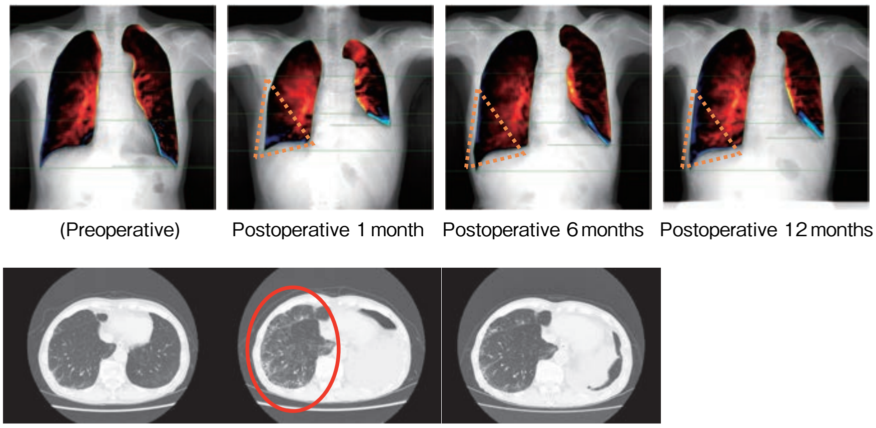


Fig. 2 Evaluation of postoperative pneumonia

3. Discussion

The postoperative prediction FEV1 using the perfusion contribution ratio obtained from DDR showed a high correlation with the measured FEV1 values. However, there was no significant difference in the prediction accuracy between the three methods, which was presumed to be due to the small variation in perfusion contribution among the patients. Compared to scintigraphy, DDR have the advantage of being able to obtain functional information at the same time as static chest radiography, and have the advantage of being a simple, short-time and lower radiation dose exam. As future tasks, it is considered necessary to increase the number of cases, examine the prediction accuracy of the surgical side and by the resected lung, evaluate cases with uneven perfusion contribution, and evaluate with other pulmonary function indices.

Cases for which blood flow evaluation is expected to be useful

1. Evaluation of postoperative pneumonia (Fig. 2)

The patient had chronic obstructive pulmonary disease (COPD), and underwent resection for left upper lobe lung cancer. Preoperative CT showed ground-glass opacities in the right lung. One month after the operation, the patient complained of malaise and breathlessness. A static chest radiography was taken, but no findings were found. CT scan revealed a magnified glassy shadow, suggesting exacerbation of pneumonia. In DDR taken at the same time, a decrease in blood flow was suggested in accordance with the shadow area of the CT. Improvement was seen at six months after the operation, and almost one year later the patient recovered. Postoperative pneumonia that were not apparent on static chest radiography could be evaluated by DDR.

2. Confirmation of the effect of hyperinflation of the remaining lung on the operation side

The patient had COPD and underwent resection of the left upper lobe lung cancer. Preoperatively, the blood flow on the left side slightly reduced, and postoperatively, the blood flow in the lower left lobe continued to significantly reduce. When the volume of each of whole lung lobe was measured from the CT data at the workstation, preoperatively the remaining lower lobe on the operation side was 896 mL whereas at 6 months postoperatively it was 1,255 mL, which is hyperinflation of about 1.5 times. It was considered that the blood volume relatively decreased due to hyperinflation.

Conclusion

According to this study, the perfusion contribution ratio calculated by DDR was similar to that of perfusion scintigraphy. In addition, it was suggested that more accurate predictions could be made by adding the perfusion contribution ratio of DDR to the conventional postoperative pulmonary function prediction method. DDR can be more easily taken to evaluate blood flow, and are considered to be useful methods that can be expected in the future.

Evaluation of pulmonary function by Dynamic Digital Radiography: basic study in cynomolgus monkeys

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We report the evaluation of pulmonary blood flow and detection of pulmonary embolism using cynomolgus monkeys by Dynamic Digital Radiography (DDR).

Purpose of this study

In recent years, pulmonary embolism following a large-scale natural disaster has become a topic in cardiovascular care. Contrast-enhanced CT is the gold standard for diagnosing pulmonary embolism, but there are risks such as radiation, allergy, and renal dysfunction, and it can be performed only in facilities equipped with CT and other equipment. On the other hand, DDR can evaluate the motion of the lungs, blood flow, and the motion of the heart with a minimally invasive motion image. Therefore, we examined whether it is possible to evaluate pulmonary blood flow in the supine and standing positions and detect pulmonary embolism(PE) using the cynomolgus monkey by DDR.

Methods&Results

1. Experiments with cynomolgus monkeys

In this study, five cynomolgus monkeys were intubated and fixed on a table, and a pulmonary blood flow obstruction model was created by inserting a Swan-Ganz catheter. Then, the pixel values of DDR images in both lung field of the normal model and the PE model were compared.

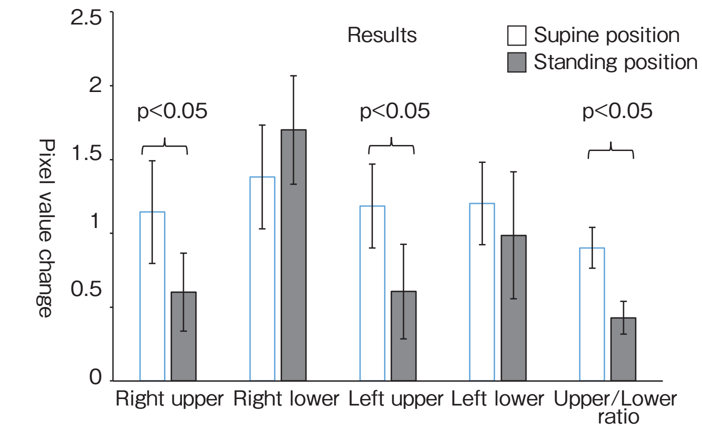
In this study, we developed a bed that could be rotated 90° vertically and captured DDR image in supine and standing positions. DDR image for eight seconds was taken under stop breathing. As an analysis method, Region of Interest (ROI) were set at the top, bottom, left, and right of the lung field of the taken images, and the average and maximum change of the pixel values in each ROI during one cardiac cycle was measured. In addition, the difference in pixel values between the left and right lungs of the normal model and those of the PE model was analyzed using SPSS, and a color-coded image of the pixel value change of DDR was also created.

A periodicity was observed in the waveform of the pixel values change in the normal model. The waveform that change in similar cycle as ECG was extracted with removing low frequency component, which is corresponding to respiratory cycle. There was no significant difference between the pixel value change at upper lung field and that at lower lung field in supine position. On the other hand, in the standing position, there was a significant difference in the range of the pixel value change in the upper lung field and that in the width of change in the lower lung field. Statistical analysis revealed that in the normal model, the pixel value change rate was lower in the standing position than in the supine position, and in both the left and right upper lung fields, the pixel value in standing positions was significantly lower. This result suggested that in the standing position, blood flow amount in the lower lung field would be less than that in the upper lung (**Fig. 1**).

On the other hand, in PE model, the range of the pixel value change in left lung, where the pulmonary artery was occluded, decreased, and that in right lung where occlusion wasn't there, increased significantly. In addition, on the color-coded image, the lower left lung field was less red-colored and much black-colored than the lower right lung field. Statistical analysis showed that there was no difference between the range of pixel value change in left and that in right in normal cases, but in PE model, the range of the pixel value change on the occluded side was significantly less than that on the un-occluded side **(Fig. 2)**.

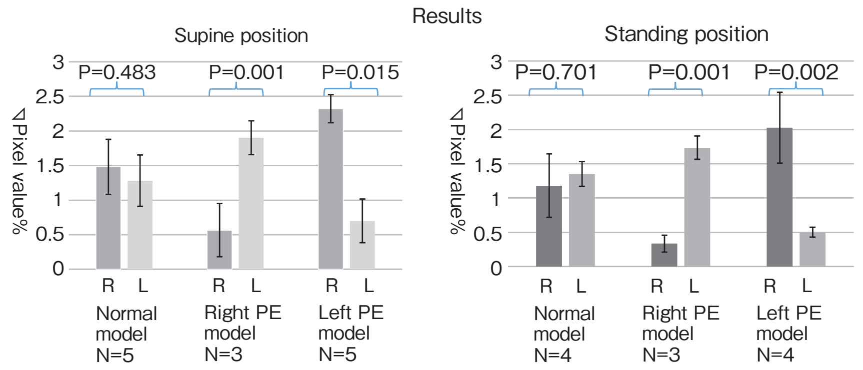
From those results, it can be said that (1) the pixel value change in lung field has similar cycle as ECG, which is Pulsation, after removing low frequency component. (2) the amount of the pixel value change in the upper lung field is less than that in the lower lung field at the standing position when compared with in the supine position, and (3) the amount of the pixel value change at occlusion site is less than that in the non-occlusion site.

The amount of pixel value change would be corresponding to the blood flow amount, and it would be thought that either the change in pulmonary artery pressure or diameter is cause of the pixel value change in this case.



In the upper lung field, the pixel values on both the left and right sides decreased significantly in the standing position.

Fig. 1 Pixel value change difference between supine and standing positions



Compared with the normal model, in the pulmonary embolism model, the pixel value change decreased on the embolism side and increased on the non-embolism side.

Fig. 2 Comparison of the pixel value change rate between normal model and PE model

2. Experiment with vessel phantom

As an additional experiment, DDR image of two types of vessel phantom was captured. A pressure sensor was connected to an artificial blood vessel and a pressure-resistant tube (both were filled with physiological saline) and pressure was manually applied to both. The pixel change of DDR image was observed. As a result, in the artificial blood vessel, the correlation between the pixel value and the pressure was observed, but not for the pressure-resistant tube. This suggests that the pixel values change of DDR image would reflects dilation of artery rather than pressure.

Conclusion

From this study, it was suggested that the amount of change in the pixel value of the lung is correlated with the pulmonary artery blood flow. Compared with conventional contrast-enhanced CT and pulmonary perfusion scintigraphy, DDR may be able to diagnose PE earlier, less invasively, at lower cost, and at various places outside the hospital. It is thought to be useful diagnostic tool for disaster medical care.

There were several limitations in this study. The cynomolgus monkeys used in this experiment generally do have arteriosclerosis. On the other hand, human do have that and also there would be a variety of factors affecting the pixel value change, so future investigation is required.

DDR is a simpler and less invasive method for evaluating pulmonary blood flow compared to existing imaging modality, and is useful for detecting diseases that cause decreased blood supply such as PE.

Based on this study, we are currently making an application to the Ministry of Health, Labour and Welfare for a prospective study DDR for heart failure and PE in humans.

Study on new pulmonary function evaluation method using Dynamic Digital Radiography

Noriyuki Ohkura, MD Department of Respiratory Medicine, Kanazawa University

We have been studying the clinical application of Dynamic Digital Radiography (DDR). In this presentation, we report the study results on the change rate of lung area due to respiratory variability.

Introduction

Chest DDR can evaluate the pulmonary function in a minimally invasive and simple manner, and visualize and observe the pulmonary function. We examined the change rate of lung area due to respiratory variability using chest DDR in patients with obstructive ventilatory defect and interstitial lung disease.

Study in obstructive ventilatory defect

In this study, of the 233 patients who underwent chest DDR, 118 patients with preoperative lung cancer with FEV1% < 70%, chronic obstructive pulmonary disease (COPD), bronchial asthma, and asthma and COPD overlapping syndrome (ACO) were included. Of these, 87 were males, the average age was 71.4 years, and they were a mild COPD population. FEV1% = 59% on average, % FEV1 = 95.9% on average, which was considered as mild airflow limitation, and % maximum expiratory medium flow (% MMF) = 28% on average, Residual Capacity (RV) was elevated and Lung Diffusion Capacity (DL_{CO}) was decreased. As for the relationship between the change rate of lung area and Body plethysmography results(lung volumes) and Spirometry results, the results showed that the lung volumes such as RV had a higher correlation value than Spirometry results such as FEV1 (**Table 1**). The highest is RV, which is considered as hyperinflation. Furthermore, when the patients were stratified based on FEV1 (FEV1 ≧ 80%: mild case, 80%>FEV1 ≧ 50% : moderate case, FEV1< 50%: severe case), mild cases are not much different from normal cases, but the change rate of lung area decreased as the disease progressed from moderate to severe, indicating that the change rate of lung area decreased as the airflow restriction progressed.

In addition, in comparison of each parameter with that of the MostGraph, which can visualize pulmonary function under ventilation at rest, the values of airway resistance and respiratory reactance were all significantly correlated, and it was considered to be related to airflow restriction and imbalanced ventilation.

The patient was 53-year-old man, who had obstructive ventilatory defect during preoperative pulmonary function test (**Fig. 1**).

Table 1 Relationship between the change rate of lung are and lung volumes in obstructive ventilatory defect .

Relationship of lung area change rate (Rs) with lung volume fraction and forced exhalation curve in patients with obstructive ventilatory defect (n=118)

	Rs	
	r	p
VC (% pred.)	-0.29	<0.01
FVC (% pred.)	-0.28	<0.01
FEV_1 (% pred.)	-0.33	<0.01
FEV_1/FVC	-0.19	0.04
MMF (% pred.)	-0.26	<0.01
FRC (% pred.)	-0.14	0.12
RV (% pred.)	0.31	<0.01
TLC (% pred.)	-0.01	0.93
RV/TLC ratio	0.48	<0.01
DL_{CO} (% pred.)	-0.12	0.18

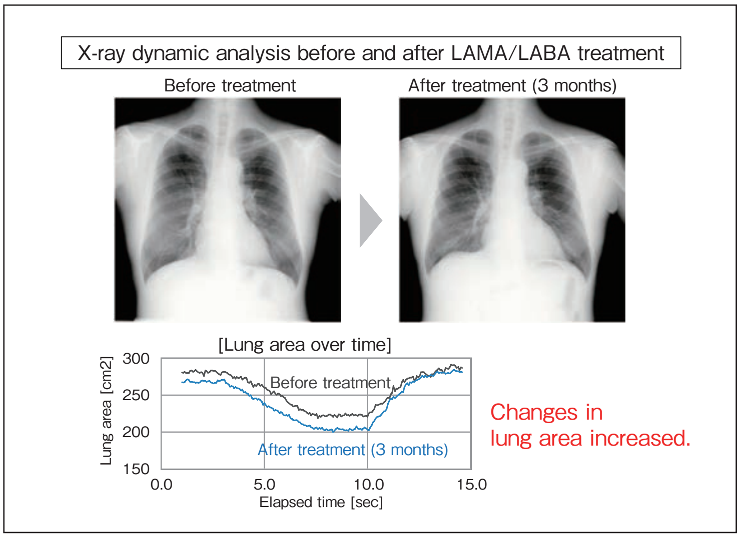


Fig. 1 Case: 53-year-old male patient with COPD

Table 2 Relationship between the change rate of lung are and lung volumes in interstitial lung disease

Relationship of lung area change rate (Rs) with lung volume fraction, and forced exhalation curve in patients with interstitial lung disease (n = 40)

	Rs	
	r	p
VC (% pred.)	-0.43	<0.01
FVC (% pred.)	-0.43	<0.01
FEV_1 (% pred.)	-0.32	0.04
FEV_1/FVC	0.09	0.56
MMF (% pred.)	-0.06	0.70
FRC (% pred.)	-0.16	0.32
RV (% pred.)	0.01	0.94
TLC (% pred.)	-0.19	0.23
RV/TLC ratio	-0.39	0.01
DL_{CO} (% pred.)	-0.27	0.11

The patient had no complications or a history of bronchial asthma or rhinitis, but was the current smoker with a CAT score of 15. %FEV1 was 49.7%, RV increased, DL_{CO} decreased, and COPD was suspected from symptoms and function. When anticholinergic inhalant (LAMA) and β2-agonists (LABA) were administered, the change rate of lung area increased after certain period.

Study in interstitial lung disease

In this study, of 40 patients with interstitial lung disease were studied among 233 patients who underwent DDR. The patients were composed of mainly idiopathic pulmonary fibrosis (IPF), scleroderma, and interstitial lung disease with progressive fibrosis with decreased vital capacity (VC), restricted dysfunction, DL_{CO} as low as 38.3% on average. As for the relationship between the change rate of the lung area, lung volumes, and Spirometry, in the case of obstructive ventilatory defect, they were significantly correlated, and correlation with the residual volume rate (RV/TLC) was also found **(Table 2).** When the patients were stratified based on %VC (mild : 80% ≧ %VC, moderate: 80%> %VC ≧ 65%, severe : %VC ≦ 65%), the change rate of lung area becomes lower in moderate and severe cases as in the case of obstructive ventilatory defect, and the change rate of lung area also decreased with a decrease in %VC. The relationship between the change rate of lung area and the 6-minute walking distance was examined in 20 patients with interstitial lung disease. The results showed that the lower the change rate, the shorter the walking distance, which indicated a correlation with physical activity. This indicated that it would be possible to evaluate exercise tolerability by DDR.

Conclusion

The change rate of lung area in obstructive ventilatory defect reflects airflow restriction and a hyperinflation. The lower change rate of lung area in interstitial lung disease reflects lower %VC and less exercise tolerance. Based on those results, it was confirmed that DDR would be an imaging modality that was clinically useful as a new method for evaluating pulmonary function. In the future, it is necessary to study more detailed analysis such as the type and stage classification on various disease, and the application of artificial intelligence (AI) for that purpose would be expected.

Study on clinical usefulness of tracheal diameter evaluation using Dynamic Digital Radiography

Akinaga Sonoda, MD, PhD Department of Radiology, Shiga University of Medical Science

Since Dynamic Digital Radiography(DDR) enables direct observation of tracheal movement, it may be a convenient tool for screening patients with ventilatory disorders such as tracheomalacia and Excessive Dynamic Airway Collapse where the trachea moves during inspiration and expiration. In this presentation, we will introduce a study on tracheal diameter evaluation using DDR.

Method

Of the patients scheduled to undergo thoracic surgery at our hospital, 52 patients with written consent participated in the study. DDR image was captured in the supine position. The patient was forced to breathe according to the voice guidance, and DDR imaging was taken for 15 seconds from maximum inspiration to expiration and inspiration at frame of 15 fps.

Results

Result 1: Difference in the degree of tracheal narrowing depending on the type of ventilation disorder

Of 52 patients, 7 patients who underwent Spirometry at another hospital and 1 patient with mixed ventilation disorder were excluded, and 28 normal subjects, 12 patients with obstructive ventilatory defect and 4 patients with restricted ventilation disorder were included. The diameter of the trachea at the start of expiration (the most dilated) and the trachea at the end of expiration (the narrowest) were measured. The measurement location was between the caudal side of the sternoclavicular joint and one vertebral head side of the tracheal bifurcation.

As a result, the tracheal diameter was significantly narrowed in the obstructive ventilatory disorder group compared to the normal group and the restrictive ventilation disorder group (**Fig. 1**). In the obstructive ventilatory disorder group, the trachea was considered likely to be narrowed during expiration.

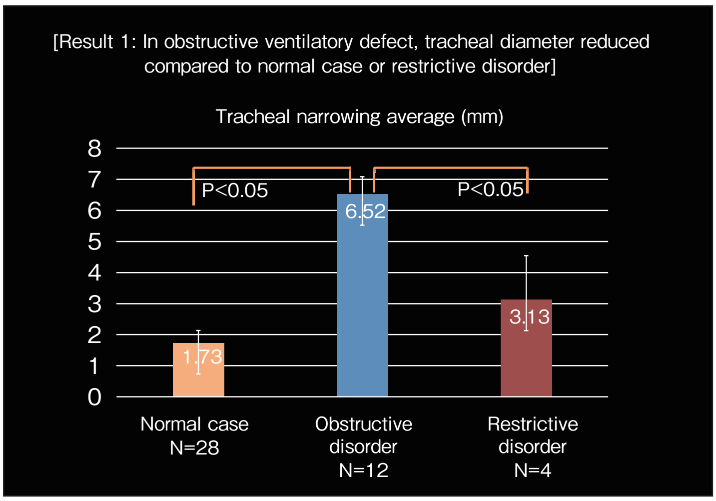


Fig. 1 Result 1: Degree of tracheal narrowing by type of ventilation disorder

Result 2: Inter-observer differences

Three observers, who did not know the results of Spirometry, measured manually the diameter of the trachea at the start of expiration (most dilated) and the trachea at the end of expiration (most narrowed) in 28 normal subjects and 12 patients with obstructive ventilatory disorder.

As a result, there was no large difference in the results between the measurers, and the trachea tended to be narrowed in the obstructive ventilatory disorder group at the time of expiration as in result 1. Therefore, it is considered that obstructive ventilatory defect may be detectable by DDR.

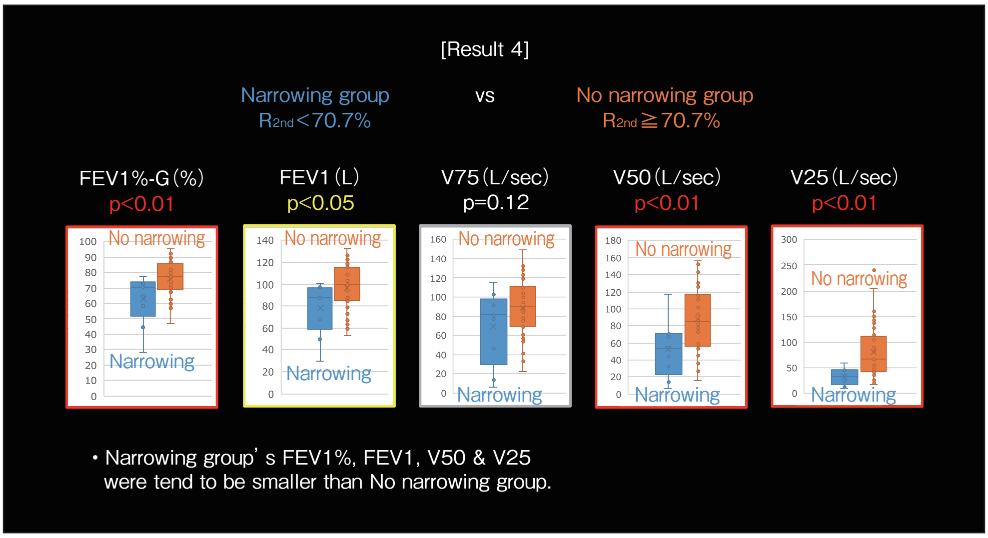


Fig. 2 Result 4: Relationship between tracheal narrowing and pulmonary function test

Result 3: Reduction of measurement errors

In order to reduce the impact of tiny fluctuation during breathing on the measurement accuracy, the average value of trachea diameter during certain period was used for the evaluation. The measurement location was the midpoint between Th2 and the bronchial bifurcation. Four patients with obstructive ventilatory disorder and four normal subjects were randomly selected, and the tracheal diameter was manually measured for 15 seconds (225 frames per person). From the obtained data, the change rate of the tracheal diameter was calculated from the average diameter at the start of expiration and at the end of expiration. The diameter for 1 sec, which is a total 15 diameter values, were used for averaging. As a result, it was confirmed that the change rate in tracheal diameter tended to be small due to obstructive ventilatory disorder.

The question like, the same result can be obtained by static chest radiography at the maximum inspiration and expiration, may be arisen. However, the movement of the diaphragm does not always match the movement of the trachea, and it has been reported that a hard breathing leads to more severe tracheal narrowing. Therefore, it was suggested that DDR would be better tool for evaluating tracheal narrowing .

Result 4: Relationship between changes in tracheal diameter and pulmonary function test

We verified whether there was a relationship between the change rate of tracheal diameter and pulmonary function in 28 normal subjects and 12 patients with obstructive ventilatory disorder. The change rate of tracheal diameter at the time of starting and ending of the was measured. In this study, subjects were divided into a group; tracheal diameter narrowing (diameter change ≦70.7%) and a group with non-narrowing.

As a result, among the pulmonary function test results, the values of 1 second rate (FEV1%), V50, and V25 were significantly correlated to the change in tracheal diameter **(Fig. 2)**. Those results suggested that patients with abnormal pulmonary function could be detected by tracheal diameter narrowing evaluation.

Conclusion

The number of patients in this study was very small and there is also several limitations such as measurement accuracy and measurement labor because the all measurement should be performed manually. The relationship between the degree of tracheal diameter narrowing and the severity of obstructive ventilatory defect will also need to be examined.

DDR can dynamically observe the narrowing of the tracheal diameter that occurs during expiration, and it would be possible to identify and evaluate the severity of patients with obstructive ventilatory defect by observing and measuring tracheal narrowing. The development of software that can measure and evaluate the tracheal diameter more objectively and efficiently is our current task.

Dynamic Digital Radiography : Method on chest application

Ryotaro Yuji Radiological Technology Department, Clinical Technology Division, Tokai University Hachioji Hospital

In January 2018, our hospital introduced the first Dynamic Digital Radiography (DDR) system in the world and started clinical research. In this presentation, we will report the outline of the system and the actual flow and points of DDR for chest application.

Evolution from static x-ray image to dynamic x-ray image

In the DDR, it becomes possible to create an motion x-ray image having a time resolution in addition to a spatial resolution by adding a time axis to a conventional x-ray.

The work of medical X-ray technicians is also changing from "taking pictures" to "taking videos". Compared with conventional x-ray, DDR requires more appropriate positioning and understanding/cooperation of patients for examination in order to capture the patient's disease condition. In addition, the examination may be performed a plurality of times because it can be a functional inspection, and the reproducibility is also important.

Overview of DDR and examination

The DDR system is composed of Konica Minolta's x-ray dynamic image analysis workstation "KINOSIS", portable digital x-ray imaging device "AeroDRfine", and Shimadzu Corporation's general imaging device "RADspeedPro". As a supplementary function of a conventional radiography system, a dynamic x-ray image (a sequential radiography) can be captured with pulsed x-rays exposure at 15 frames per second, and the obtained images are displayed as a movie. This movie has a spatial resolution of 400 µm and a gray scale image density resolution is 16 bits.

The normal procedure of conventional radiography is to check the patient condition and explain how the exam is going to be, set the exposure conditions, conduct positioning and exposure, check whether the image has been properly captured and processed, and deliver to physicians. In addition, DDR requires a more detailed explanation before the examination, attention to patient positioning, and practice of breathing to obtain maximum inspiration and expiration **(Fig. 1).** Prior explanation is particularly important for obtaining patient cooperation. In our hospital, a leaflet for the examination guide were prepared and the all patient is asked to read carefully before the examination.

In positioning, in order to reduce unnecessary tension of muscle used for breathing, the handle shall be grasped in a comfortable position, and the height of the forearm and

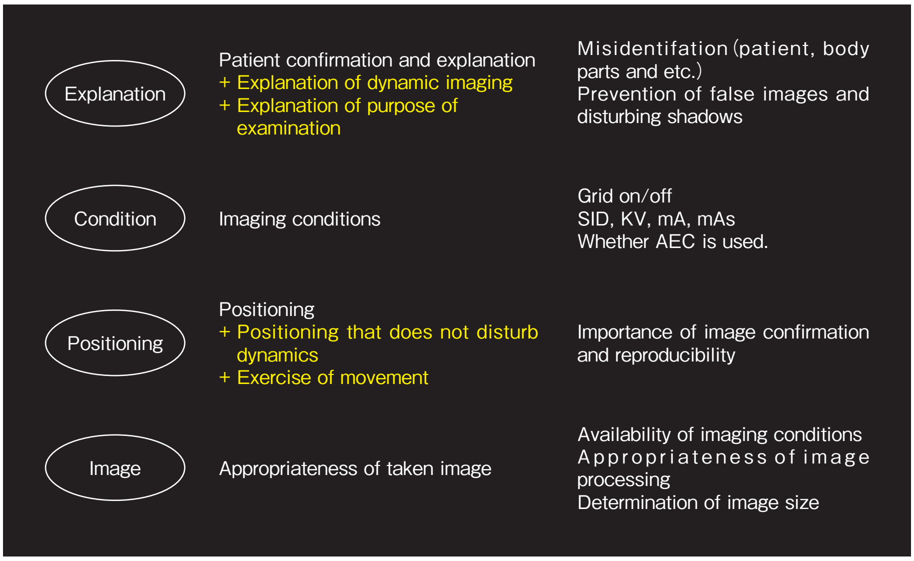


Fig. 1 Procedure Flow of DDR

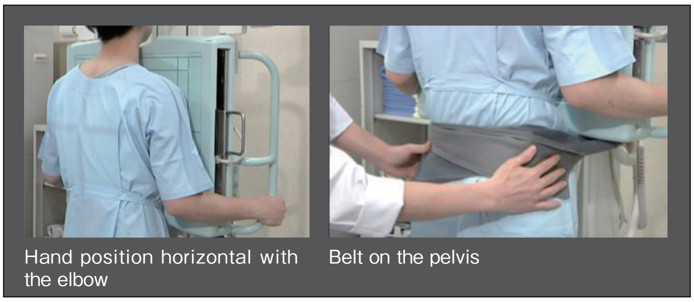


Fig. 2 Key Points of Positioning

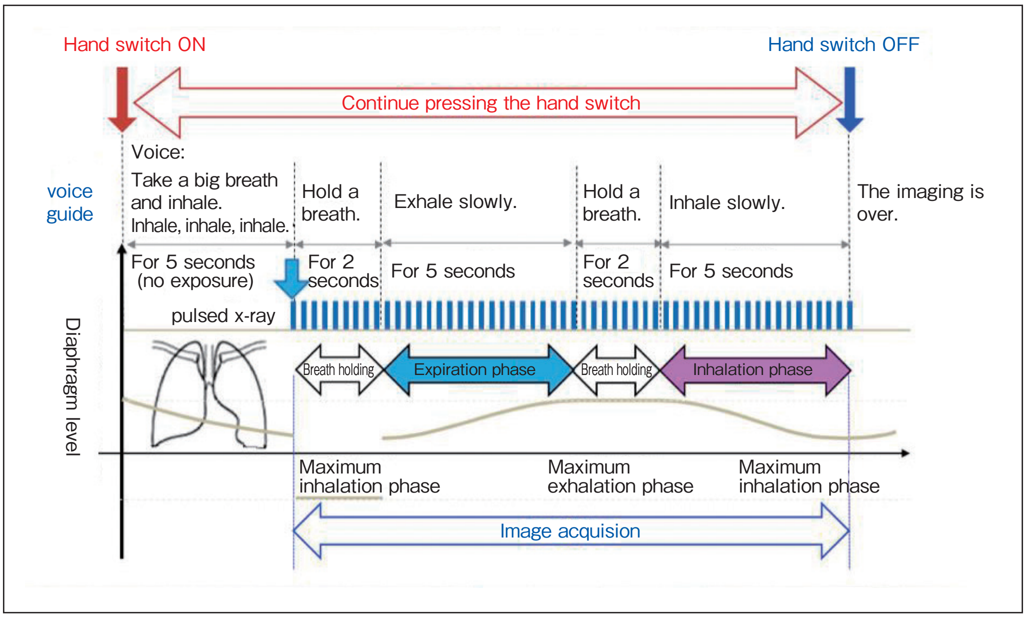


Fig. 3 An example of breathing pattern (Deep breathing) with voice guide

wrist shall be horizontal so that the upper arm muscles won't have unnecessary tension. The pelvis shall be fixed with a belt to prevent body movement (**Fig. 2**).

To improve the reproducibility of the examination, automated voice guide is used for breathing instructions (**Fig. 3**). In addition, the voice guide can be operated for breathing practice in the radiographing room, so that the medical X-ray technicians can confirm how the voice is heard and how the body of the patient moves near the patient. By unifying the timing of the start of radiography among the operator in the radiology department, there is almost no difference among medical X-ray technicians at present.

The exposure dose (entrance surface dose) is calculated as 1 pulse dose × 15 fps × imaging time (seconds). In our hospital, the average scan time was 16.6 seconds, and the average exposure dose was 1.82 mGy, which is lower than the International Atomic Energy Agency (IAEA) guidance level of 1.9 mGy for the front and side of the chest. In addition, it is possible to perform examinations at a much lower exposure dose than our low-dose lung CT screening.

Regarding the procedure of DDR, a manual was prepared by our hospital and Konica Minolta to ensure consistency of the examination. As a result, the average examination time from the patient's calling to leaving the room at our hospital is 4.9 minutes.

Conclusion

With a leaflets for the patient and procedure manuals for medical X-ray technicians, high reproducible examinations are possible, and our hospital has realized a system that can immediately respond to exam order of DDR. In addition, it is expected that the DDR would be useful tool for the orthopedic application as well as the chest application in the future.

Medical X-ray technicians are also required to have a new role, including understanding of respiratory physiology, and we believe that DDR is one of the challenging modalities for medical X-ray technicians.

Focusing on patients with COPD, and Ventilation defect

Fumio Sakamaki, MD Department of Respiratory Medicine, Tokai University Hachioji Hospital/Respiratory Division, Department of Internal Medicine, Tokai University School of Medicine

In our hospital, about 100 cases of Dynamic Digital Radiography (DDR) have been captured by October 2019 using Konica Minolta's DDR system. In this presentation, we report the results of thoracic cage movement in patients with chronic obstructive pulmonary disease (COPD), and report the usefulness and potential of this system in COPD and alveolar hypoventilation syndrome.

Study on thoracic cage movement in COPD patients

1. Background and purpose

In COPD, it is known that the diaphragm becomes flat due to hyperinflation of the lungs, and paradoxical movements of the diaphragm and deterioration of movement have been reported. On the other hand, in severe COPD, abnormal movement of the ribs in the lower rib cage (Hoover's sign) has been known for a long time, but there are few quantitative studies on this movement. We analyzed the coordination of the posterior ribs and the movement of the diaphragm from DDR in 31 patients with suspected COPD and compared mainly with the pulmonary function test [1)].

2. Method

At the time of expiration and inspiration, a fixed point was set immediately below the pleura of the posterior rib, and the change in the moving angle of the fixed point was automatically tracked by special software to calculate the direction of movement. The angle of the movement of the posterior rib between the upper-middle lung field, the middle-lower lung field, and the upper-lower lung field was calculated, and the similarity of the movement between the ribs was compared.

3. Results

As for the similarity of the movements of the posterior ribs in the mild group and the severe group, the lower rib moved in a different direction from the upper and middle ribs in the mild group, whereas it moved in the same direction in the severe group. On the other hand, there was no difference in diaphragm movement due to airflow limitation. In addition, a correlation was found between the airflow limitation (% FEV1) and similarity. We conclude that there is a possibility that the severity of COPD can be evaluated visually and objectively using DDR.

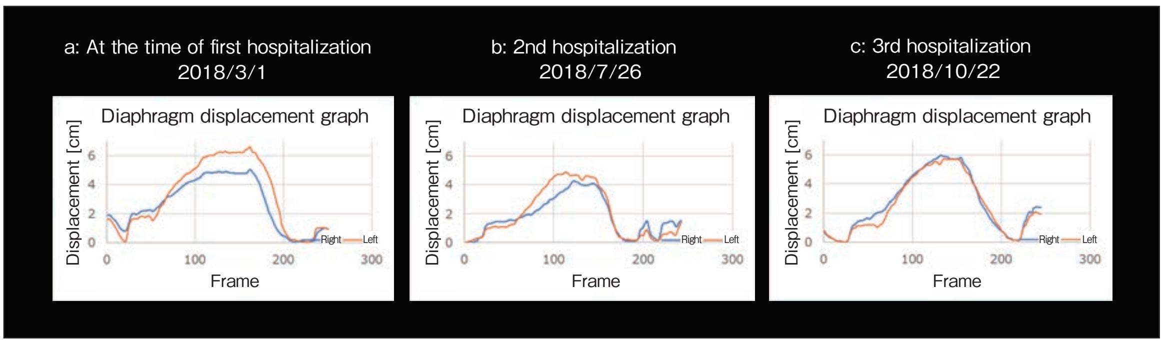


Fig. 1 Case 1: Diaphragm Excursion

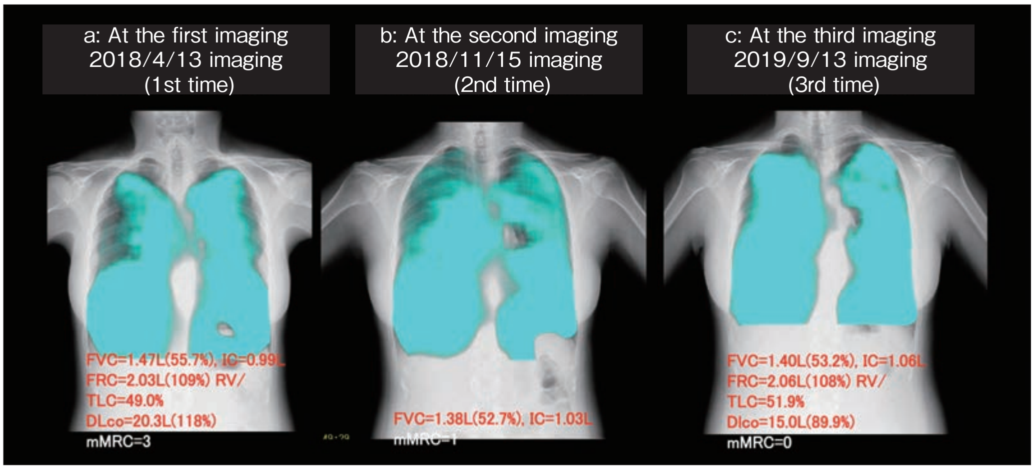


Fig. 2 Case 3: PL-MODE on alveolar hypoventilation syndrome patient

Case presentation

Case 1: Severe case of COPD (follow-up case)

This patient was hospitalized 3 times in 2018 due to worsening symptoms. Dyspnea and airflow limitation were severe, and the severity classification of COPD (ABCD classification) was as severe as D. Treatment was conducted focusing on LABA/LAMA combination drugs and inhaled steroids (ICS), and the stable trend of patient condition began in 2019.

On DDR, the lung was slightly hyperinflated and the heart looked like "drop heart", but FEV1 recovered slightly over time. There is no change over time in the movement of the posterior ribs, but the displacement graph of the diaphragm (**Fig. 1**) shows a smooth up and down movement without any imbalance between the left and right and COPD-specific shaking at the third hospitalization. It is expected that the improving effect of pulmonary function could be confirmed from the displacement of the diaphragm.

Case 2: Patient with moderate to severe COPD

This patient had %FEV1≃53%, which means this patient was moderate to severe COPD, and was hospitalized once due to exacerbation and had shortness of breath. FE-MODE (Frequency enhancement processing) of DDR image can confirm trachea narrowing during expiration, which is frequently observed in severe cases.

Case 3: Alveolar hypoventilation syndrome (follow-up case)

The patient was diagnosed with idiopathic pulmonary arterial hypertension at another hospital, but it was considered to be type II respiratory failure according to the results of pulmonary function test. The decreased mobility of the diaphragm detected on DDR images cannot be ruled out as a cause of hypercapnia, and noninvasive positive pressure ventilation (NPPV) was conducted during sleep, which improved subjective symptoms.

There was no change over time in forced vital capacity (FVC), but the maximum inspiratory volume (IC) increased from 0.99 L to 1.06 L. Furthermore, the improvement of ventilation was confirmed in the PL-MODE (Reference frame ratio calculation processing) image (**Fig. 2**), and the shortness of breath index (mMRC) was also improved. Pulmonary circulation improvement was observed in PH-MODE (Cross-correlation calculation processing). We believe that DDR could be an index of ventilation evaluation.

Conclusion

In COPD and alveolar hypoventilation syndrome, quantitative evaluation of posterior rib and diaphragm movements on DDR images can be an index for severity evaluation and time-course observation. We also believe that it would be possible to visually evaluate the rib cage movement, abnormality on the central airway, ventilation imbalance and pulmonary circulation defect.

●References

1) Genki Takahashi et al., *Annals of the Japanese Respiratory Society*, 8 (Suppl.): 262, 2019.

Study on application to chronic respiratory disease

Takefumi Nikaido, MD, PhD Department of Pulmonary Medicine, Fukushima Medical University

We introduced Dynamic Digital Radiography (DDR) to evaluate pulmonary circulation for chronic pulmonary thromboembolism. Furthermore, recently, we tried to apply DDR to chronic respiratory diseases. In this presentation, we present a case of interstitial pneumonia and emphysema with giant bullae as an initial study.

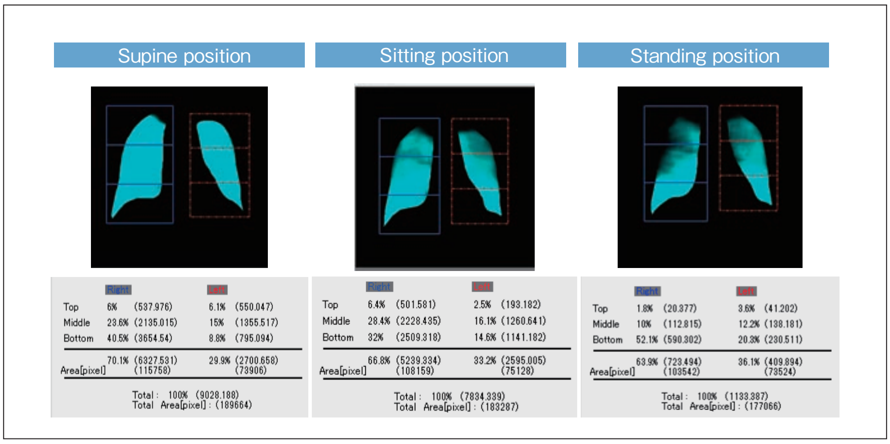


Fig. 1 Case 1: Interstitial Pneumonia. Ventilation evaluation image

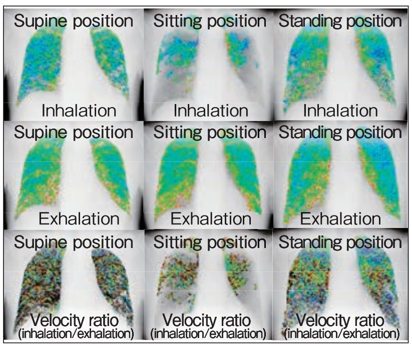


Fig. 2 Case 1: Interstitial Pneumonia. Airflow velocity analysis image during tidal breathing

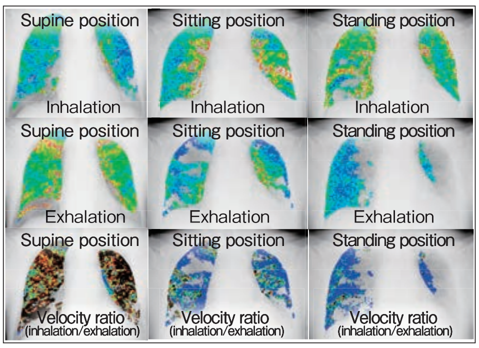


Fig. 3 Case 1: Interstitial Pneumonia. Airflow velocity analysis image during deep breathing

Interstitial Pneumonia

Case 1 was a 77-year-old male with idiopathic interstitial pneumonia (IIP). Pulmonary function such as vital capacity (VC) are within normal ranges, and there is a slight decrease in lung diffusion capacity (DL_{CO}), but overall pulmonary function was considered as normal. Although there is no hypoxemia, serum markers for interstitial pneumonia are high.

Static chest radiography showed diffuse reticular shadows, ground-glass opacity, and slight ventilation defect in the left lung. CT showed diffuse reticular shadows on the pleura side with emphysema and many ground-glass opacities. It was considered to be the case classified to Alternative Diagnosis (A shadow that could also be taken as a predominant cyst/ground-glass shadow) of ATS/ERS/JRS/ALAT International Diagnosis Guideline [1] rather than IIP.

Ventilation evaluation by DDR showed that the ventilation of the left lung reduced, but the lesion in the lower lobe was not so severe, and there was almost no differences between patient's posture **(Fig. 1)**.

Next, in the airflow velocity analysis image by DDR, the expiration velocity, the inspiration velocity, and the velocity ratio (inhalation/

exhalation) were color-coded and displayed superimposed on the image. Red (high velocity) to blue (low velocity) was set according to the velocity, and the velocity ratio was set to red/black (high velocity) to blue (low velocity). Data missing parts were blank. In this case, the velocity ratio during tidal breathing was higher in the supine position than in the standing position **(Fig. 2),** and even higher during deep breathing **(Fig. 3)**.

Emphysema

Case 2 was a 64-year-old male with emphysema developing giant bullae. He had a history of repeated pneumothorax, and resection and suturing of bullae was performed on the left side in 2001 and on the right side in 2008. After that, he became aware of the worsening of dyspnea around 2017, and in 2019, his exacerbation of dyspnea and emphysematous change became prominent, and he was referred to our department. For evaluation, DDR was performed.

Static chest radiography showed giant bullae and hyperpermeability, especially in the bilateral middle lung. The pulmonary function test showed obstructive ventilatory defect, and the flow volume curve showed a typical obstructive disorder pattern. CT showed marked emphysematous change in the upper lobe, giant bullae on both sides in the middle and lower lobes, and emphysematous change in the lower lobe.

Ventilation evaluation based on DDR showed that the ventilation volume decreased, especially according to the mid-lung bullae **(Fig. 4).** Airflow velocity analysis images did not show an increase in velocity ratio due to patient posture during tidal breathing **(Fig. 5)**, but showed a decrease in velocity during deep breathing **(Fig. 6)**, which appeared to be different from interstitial pneumonia.

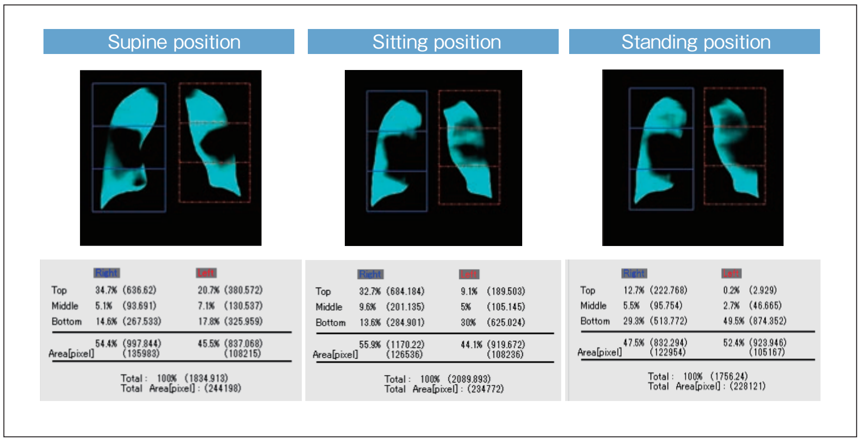


Fig. 4 Case 2 : Emphysema. Ventilation evaluation image

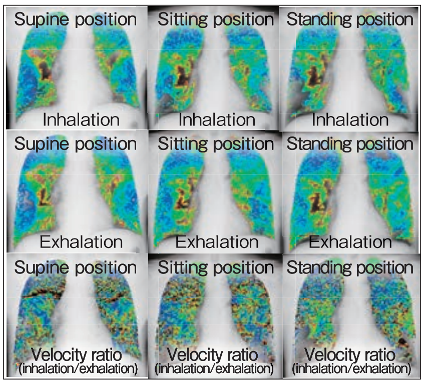


Fig. 5 Case 2: Emphysema. Airflow velocity analysis image during tidal breathing

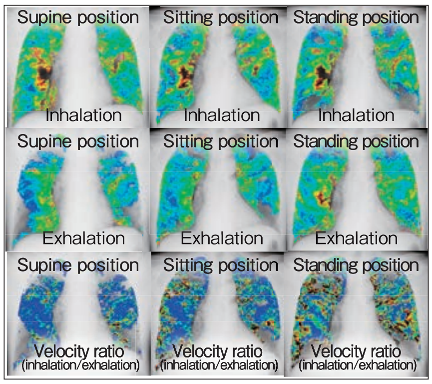


Fig. 6 Case 2: Emphysema. Airflow velocity analysis image during deep breathing

Conclusion

At our institution, DDR has been used to evaluate a regional ventilation/perfusion in chronic respiratory diseases, especially chronic obstructive pulmonary disease (COPD) and interstitial pneumonia. With the expectation that various parameters, that are useful for evaluating disease states and progression, would be obtained, we have begun accumulating various cases. In the future, we would like to evaluate the relationship of these data with various information and test results at the time of admission to hospital, or new biomarkers, as well as the relationship with disease progression.

● References

1) Raghu, G., et al., *Am. J. Respir. Crit. Care Med*., 198(5): e44-e68, 2018.

Interstitial disease movement

Masakuni Ueyama, MD Department of Respiratory Medicine, Tenri Hospital

In this presentation, we report the usefulness of Dynamic Digital Radiography (DDR) in interstitial pneumonia (IP) by presenting cases.

Case 1: IP predominantly in the lower lung field

Case 1 is a 68-year-old female with IP predominantly in the lower lung field. A cough developed in September 2018. An IP was pointed out by a another physician nearby on December, and she visited our department on January 2019. Currently, being followed-up without any treatment. A former smoker (20 pieces/day × 30 years) with a history of renal disease, appendicitis, uterine adnexitis, and phlebangioma. The results of the blood test were antinuclear antibody (ANA): 640-fold, anticentromere antibody: positive, KL-6: 1,082 U/mL, SP-D: 362.1 ng/mL. According to the results of the pulmonary function test, the vital capacity (VC) was 2.19L(88.2% as percent predicted), and the lung diffusion capacity (% DL_{CO}) was 71.9% as percent predicted.

Static chest radiography showed reticular shadows and ground-glass opacities predominantly in the lower lung field. On CT image **(Fig. 1),** in the lower lung field, reticular and ground-glass shadows were observed from around the bronchial vessels to the subpleura, though there was not as much shadow as the upper lung field, suggesting a collagen disease lung. The DDR image **(Fig. 2)** showed that the movement of the lower lung field and the width of the rib cage was worse than in the normal case. In

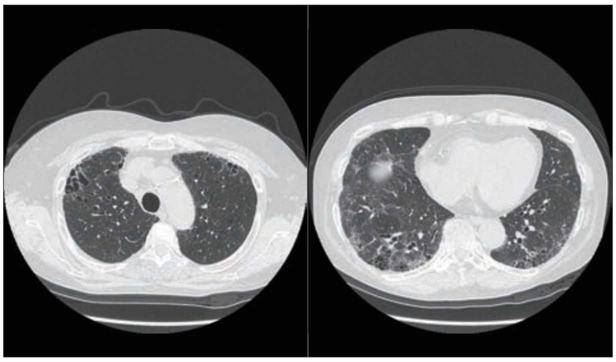


Fig. 1 Case 1: CT image

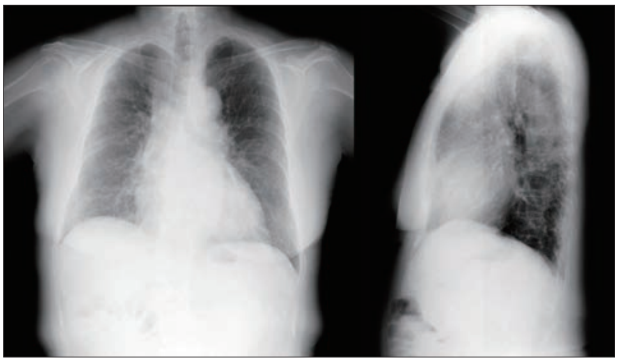


Fig. 2 Case 1: DDR image (PA and Lateral)

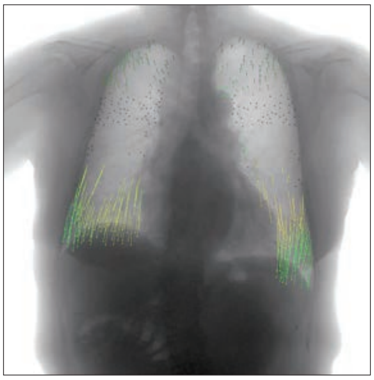


Fig. 3 Case 1: Motion vector-map

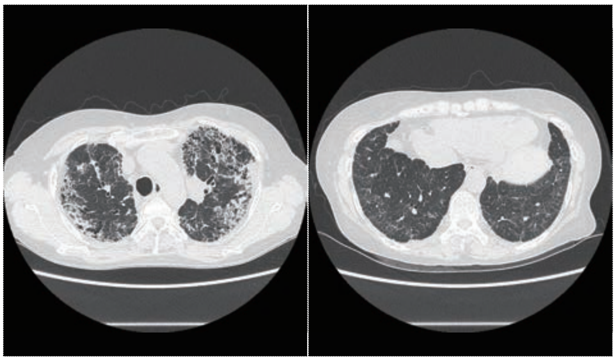


Fig. 4 Case 2: CT image

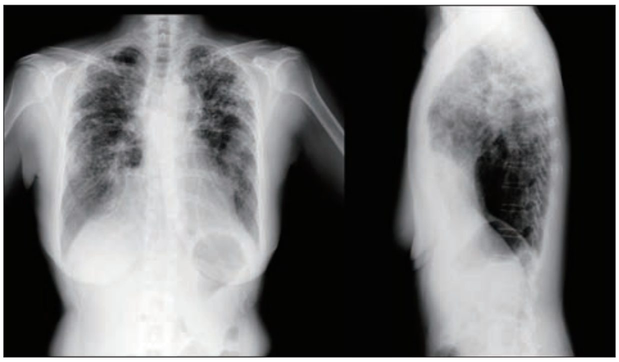


Fig. 5 Case 2: DDR image (PA and Lateral)

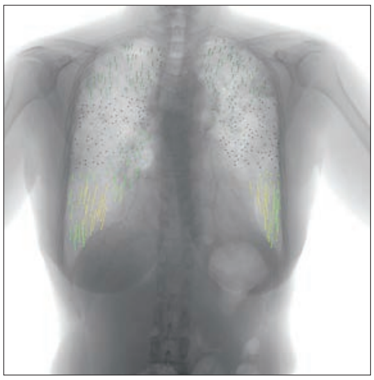


Fig. 6 Case 2: Motion vector-map

addition, it seemed that the movement of lower lung field is worse than normal control case based on a motion vector-map **(Fig. 3)** created from DDR image.

Case 2: IP predominantly in the upper lung field

Case 2 was a 65-year-old female with IP predominantly in the upper lung field. The main complaint was paroxysmal dyspnea on exercise (DOE). An abnormal finding was pointed out on static chest radiography in a annual health check-up for the first time in 2001, and an abnormal condition was pointed out again in a 2012 health check-up, thus the patient visited the previous doctor. The DOE appeared around July 2017, and she visited our department in February 2018 and underwent cryobiopsy. She was a nonsmoker with a history of childhood asthma, appendicitis, and fibroids. No serologically predominant positive findings were found, with KL-6: 739 U/mL and SP-D: 829.5 ng/mL. The results of the pulmonary function test were VC (%VC): 1.91 L (74%) and $\%DL_{CO}$: 63.1%.

Static chest radiography showed reticular shadows and infiltration shadows predominantly in the upper lung field. CT image **(Fig. 4)** showed strong reticular shadows and consolidation in the upper lung field. DDR image **(Fig. 5)** showed that the movement was generally poor and the movement of the diaphragm is abnormal, and lateral DDR image showed the impression that the lower lobe of the lung mainly contributed to breathing. Even in the vector-map **(Fig. 6)**, the movement of the entire lung field seemed to be poor.

DDR for IP : Current status and future issues

In our hospital, IP-focused DDR has been performed, and data on 30 to 40 cases have been obtained so far. In all cases, PA and a Lateral DDR image were taken, and when the estimated lung volume obtained from those images was compared with the results of pulmonary function test, a good correlation was obtained. At present, there was only one stable case followed-up, and similar results were obtained in comparison of the past and present image. The follow-up of deteriorated cases, correlation with prognosis, and detection accuracy will be examined in the future.

In addition, as a feature of movement in IP, there is an impression that lower lung field movement and thorax cage movement are poor in patients with IP predominantly in the lower lung field, and that overall movement is poor in patients with IP predominantly in the upper lung field. In all patients, the movement of the thorax cage is better in the upper part than in the lower part. Although we have not yet performed a quantitative analysis of these, we would like to examine the differences in movement between IP subtypes in the future.

Evaluation of pulmonary circulation by Dynamic Digital Radiography

Yuzo Yamasaki, MD, PhD Department of Clinical Radiology, Graduate School of Medical Sciences, Kyushu University

In this presentation, I present pulmonary circulation imaging by Dynamic Digital Radiography (DDR) on two patients.

Case 1: Chronic thromboembolic pulmonary hypertension (CTEPH)

Case 1 was a 69-year-old female. Around January 2019, she visited another hospital with a complaint of shortness of breath during exercise, and was diagnosed with pulmonary embolism (PE). Anticoagulant therapy was performed, but the symptoms remained and chronicity was suspected. Therefore, DDR was performed at our hospital.

Static chest radiography **(Fig. 1a)** showed no obvious abnormalities, but x-ray pulmonary circulation image by DDR **(Fig. 1b)** revealed multiple segmental defects in both lung fields. ^{99m}Tc-MAA pulmonary perfusion scintigraphy **(Fig. 1c)** showed frequent segmental defects, which is a characteristic of CTEPH, and this finding was consistent with pulmonary circulation image by DDR. Similar findings were found in iodine map of the contrast CT **(Fig. 1d)**. As a result of right heart catheterization, the mean pulmonary artery pressure was 43 mmHg, and the patient was diagnosed with CTEPH. Pulmonary hypertension (PH) is classified into five types such as (1) Pulmonary arterial hypertension (PAH), (2) PH due to left heart disease, (3) PH due to lung disease and/or hypoxemia, (4) CTEPH, and (5) PH due to unknown cause and/or complex factors, and these are differentiated in diagnosis.

CTEPH is defined as the state having an organized thrombus in the pulmonary artery that does not dissolve with anticoagulant therapy for 6 months or more, and the mean pulmonary artery pressure is ≥25 mmHg (normal value <20 mmHg). It has two aspects, PH and PE, and may be found triggered by PH without any apparent history of PE.

The recently proposed algorithm for the diagnosis of PH[1] emphasized that early screening of CTEPH by pulmonary ventilation/perfusion scintigraphy was important. However, we consider the possibility that pulmonary perfusion image by DDR can be used as the screening test

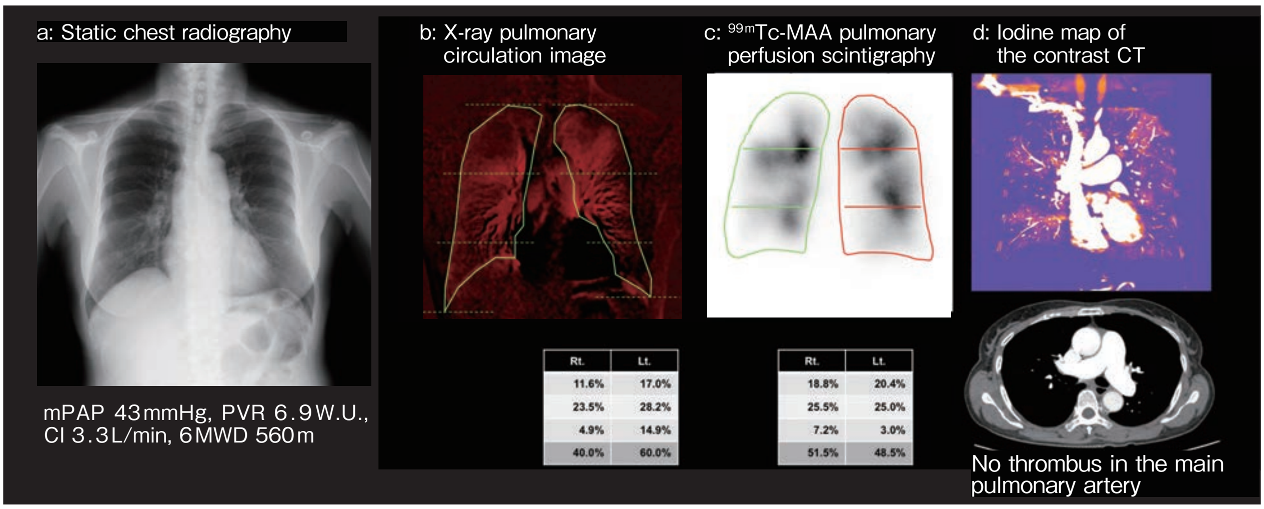


Fig. 1 Case 1: Chronic thromboembolic pulmonary hypertension (CTEPH)

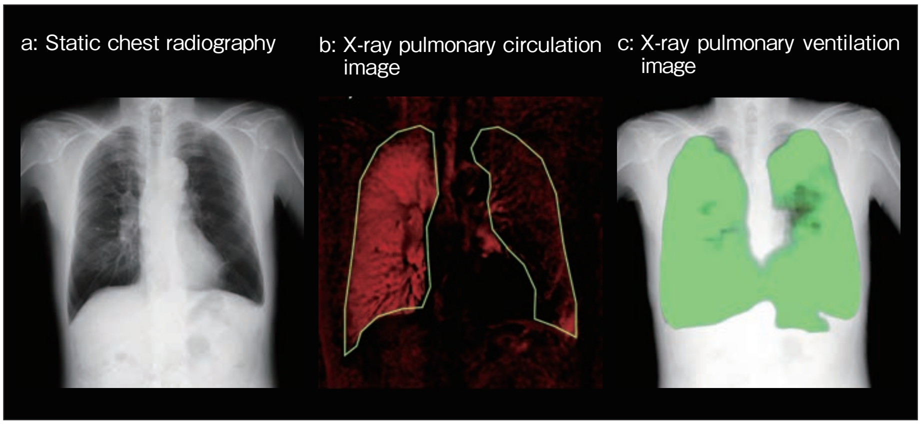


Fig. 2 Case 2: Giant cell arteritis, severe left pulmonary artery stenosis

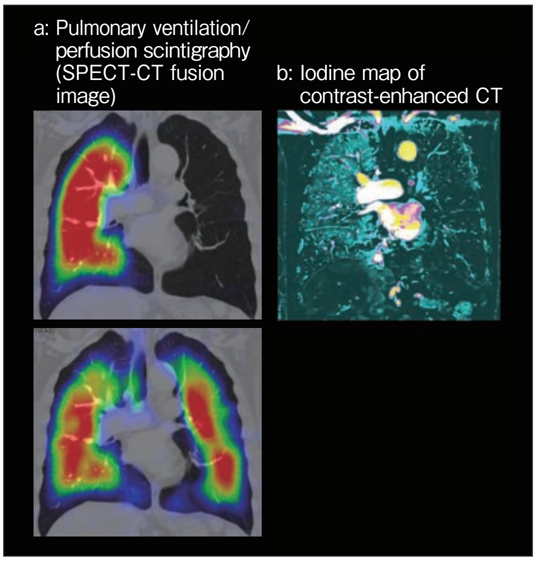


Fig. 3 Ventilation/perfusion scintigraphy and Iodine map of contrast-enhanced CT in Case 2

before pulmonary ventilation/perfusion scintigraph in the future.

Comparison of pre- and postoperative pulmonary artery angiography with circulation image by DDR in another patient with CTEPH also showed that pulmonary circulation was restored after surgery. Thus, x-ray pulmonary circulation image by DDR was also expected to be used for evaluation of pulmonary circulation before/after treatment.

Case 2: Giant cell arteritis, severe left pulmonary artery stenosis

Case 2 was a 74-year-old male. He visited a previous physician complaining of dyspnea and cough, and diagnosed as having pneumonia. The symptoms remained even after antibiotic treatment, so DDR was performed at our hospital. On static chest radiography **(Fig. 2a),** the right pulmonary vasculature was dilated while the left pulmonary vasculature was less visible. The x-ray pulmonary circulation image by DDR **(Fig. 2b)** shows that the circulation in the left lung is extremely poor. On the other hand, x-ray pulmonary ventilation image by DDR **(Fig. 2c)** showed that both lungs were uniformly ventilated. Similar findings were obtained on pulmonary ventilation/perfusion scintigraphy and iodine map of contrast-enhanced CT **(Fig. 3)**. Contrast-enhanced CT showed that the main trunk of the left pulmonary artery was highly narrowed and soft shadows were widespread around it. Depiction of left pulmonary vessels was poor in 3D pulmonary artery images. FDG-PET/CT showed a high accumulation of SUVmax = 7.6, which was consistent with the soft shadow of contrast-enhanced CT. Based on these results, we diagnosed severe left pulmonary artery stenosis due to giant cell arteritis.

By performing DDR, pulmonary ventilation/perfusion information can be easily obtained, and it is considered to be useful even in situations where contrast-enhanced CT and scintigraphy cannot be used easily.

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1) Frost, A., et al.: Diagnosis of pulmonary hypertension. *Eur. Respir. J.*, 53 (1): 1801904, 2019.

Executive Remark

Shoji Kudoh, MD, PhD Chairman, Board of Directors, Japan Anti-Tuberculosis Association / Professor Emeritus, Nippon Medical School Foundation

I was amazed that there was a great progress in the research for just one year since the first Dynamic Digital Radiography Seminar in 2018. I would like to express my sincere respect to the researchers who have conducted research throughout Japan.

I would like to mention three things that were particularly impressive through today's presentation and discussion. First, I felt that the possibility of realizing visualization of ventilation and perfusion by separating ventilation related signal and perfusion related signal, which was beginning of the development of Dynamic Digital Radiography (DDR), and detection of pulmonary thromboembolism has increased. Compared with ventilation and perfusion scintigraphy, although each modality has its own characteristics, there may be a possibility that DDR image would be equivalent to those, or could be used instead. Above all, it could be widely used in clinical practice because the examination cost is lower and it could be performed in small - medium hospitals. Although there are some issues, there are some reports that they are on par with ventilation and perfusion scintigraphy, and further research is expected.

Second, I felt the spread of applications. At the beginning of the development of DDR, target diseases which came to mind, were a few such as chronic obstructive pulmonary disease (COPD) and interstitial pneumonia. However, this time, there were clinical case presentations of application to various diseases such as alveolar hypoventilation syndrome and chronic thromboembolic pulmonary hypertension, and studies on the relationship with diaphragm pacing were also reported. I felt that the spread of applications was very fresh and important.

Third, new points of interest have been raised, such as the change rate in lung area, tracheal diameter, and posterior ribs. In the "Atlas Concept of Movement" introduced in the manufacturer's report, we received an important message that "dynamic images have a large number of landmarks in the lung thorax". As for what we should pay attention to, I think that the researchers who are interested will work on each of them, but it is important that there are so many landmarks. I recall the textbook "Felson's Principles of Chest Roentgenology", by which I first studied static chest radiography. The first edition was issued in 1965, and 70 years have passed since the discovery of x-rays in 1895, and finally a "silhouette sign" was raised. With that in mind, I feel that having many landmarks was like having a treasure mountain in front of you, and that there might be a possibility of new discoveries over time.

Currently, DDR has been introduced to 17 facilities nationwide. We believe that a DDR, that has the advantage of being able to conduct examination in small and medium hospitals, should ultimately aim for insurance coverage in Japan, but it is also expected to be deployed in developing countries such as the Asian region. DDR could be used in developing countries where scintigraphy is not readily available. In terms of easy-to-perform, even in recent frequently occurring disasters such as earthquakes and floods, there is a possibility that economy-class syndrome can be easily screened in the evacuation centers, and its use is expected to expand in the future. I can't imagine what presentation will be coming in the next seminar or later, but I'm really looking forward to them.

The 2nd Dynamic Digital Radiography Seminar

Date: November 2, 2019 (Sat)

Venue: Fukuracia Yaesu Conference Room A

Part 1 and 3 Chair:
Atsuko Kurosaki, MD, PhD
(Fukujuji Hospital, Japan Anti-Tuberculosis Association)

Part 2 Chair:
Kazuo Kasahara, MD, PhD
(Kanazawa University)

Part 3 Chair:
Terumitsu Hasebe, MD, PhD
(Tokai University)