Projected lung areas using dynamic X-ray (DXR)

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ABSTRACT

\textbf{Background:} Dynamic X-ray (DXR) provides images of multiple phases of breath with less radiation exposure than CT. The exact images at end-inspiratory or end-expiratory phases can be chosen accurately.

\textbf{Purpose:} To investigate the correlation of the projected lung area (PLA) by dynamic chest X-ray with pulmonary functions.

\textbf{Material and Methods:} One hundred sixty-two healthy volunteers who received medical check-ups for health screening were included in this study. All subjects underwent DXR in both posteroanterior (PA) and lateral views and pulmonary function tests on the same day. All the volunteers took several tidal breaths before one forced breath as instructed. The outlines of lungs were contoured manually on the workstation with reference to the motion of diaphragm and the graph of pixel values. The PLAs were calculated automatically, and correlations with pulmonary functions and demographic data were analyzed statistically.

\textbf{Results:} The PLAs have correlation with physical characteristics, including height, weight and BMI, and pulmonary functions such as vital capacity (VC) and forced expiratory volume in one second (FEV\textsubscript{1}). VC and FEV\textsubscript{1} revealed moderate correlation with the PLAs of PA view in forced inspiratory phase (VC: right, $r = 0.65$; left, $r = 0.69$; FEV\textsubscript{1}: right, $r = 0.54$; left, $r = 0.59$). Multivariate analysis showed that body mass index (BMI), sex and VC were considered independent correlation factors, respectively.

\textbf{Conclusion:} PLA showed statistically significant correlation with pulmonary functions. Our results indicate DXR has a possibility to serve as an alternate method for pulmonary function tests in subjects requiring contact inhibition including patients with suspected or confirmed covid-19.

1. Introduction

Pulmonary function tests (PFTs) provide the useful information about detection as well as characteristics or severity of lung disease. For many years, Forced vital capacity (FVC) have played an important role for the diagnosis of idiopathic pulmonary fibrosis (IPF) for many years. Patients can be diagnosed as interstitial lung disease if percent vital capacity (VC) is lower than 80%. It also correlates with a poor outcome in patients with IPF [1,2]. Forced expiratory volume in one second (FEV\textsubscript{1}) is also an important predictor in PFTs, especially for screening of chronic obstructive pulmonary disease (COPD). Forced expiratory volume percent in one second divided by FVC (FEV\textsubscript{1}/FVC, FEV\textsubscript{1}%) is used for the...
diagnosis of COPD. The severity of COPD is classified with percent predicted FEV₁ (%FEV₁) [3,4]. Previous studies have reported that total lung capacity (TLC) had a good correlation with projected lung area (PLA) by chest radiograph [5–13]. Harris et al. [8] reported the simple way of predicting TLC with chest radiograph image of both posterior-anterior (PA) and lateral views. However, the correlation between PLA and pulmonary function has not been studied.

Recently, dynamic X-ray (DXR) with flat-panel detector (FPD) enabled to evaluate pulmonary functions such as blood flow and diaphragm motion [14–19]. CT also has the potential; however, chest radiograph is simpler and less expensive. DXR can provide images of multiple phases of breath with less radiation exposure than CT. Therefore, the exact images at end-inspiratory or end-expiratory phases can be chosen accurately.

The aim of this study is to investigate the correlation between PLA measured by DXR and pulmonary functions. If good correlations between PLA and PFTs are observed, it may provide the possibility of using DXR as an alternative method for assessing pulmonary functions in patients with contact inhibition such as suspected or confirmed covid-19 or other infectious lung diseases instead of PFTs.

2. Material and methods

2.1. Study population

This prospective study was approved by the ethics committee. One hundred and ninety-three volunteers who received medical checkups for health screening from May 2013 to February 2014 were enrolled in this study. The criteria for including this study were as follows: (a) 20 years of age or more; (b) no status of pregnancy, potential pregnancy, or lactating; (c) scheduled for conventional chest radiography; (d) undergoing PFTs. Thirty-one volunteers were excluded for the reasons as follows; incomplete dataset of chest radiography such as prominent image noise (n = 14), lack of examination in deep expiratory phase (n = 12), and lack of pulmonary function test or personal data (n = 5). Finally, a total of 162 volunteers were analyzed in this study.

2.2. Image protocol of dynamic X-ray

PA and lateral DXR was performed in the standing position using a prototype X-ray system (Konica Minolta Inc., Tokyo, Japan) composed of an FPD (PaxScan 4030CB, Varian Medical Systems Inc., Salt Lake City, UT, USA) and a pulsed X-ray generator (DHF-155HH) with Cineradiography option, Hitachi Medical Corporation, Tokyo, Japan). During the examination, all the participants took several tidal breaths before one forced breath. Conditions for DXR were the same as the previous reports [16–19]: tube voltage, 100 kV; tube current, 50 mA; pulse duration of pulsed X-ray, 1.6 ms; source-to-image distance, 2 m; additional filter, 0.5 mm Al + 0.1 mm Cu. The additional filter was used to filter out soft X-rays. The exposure time was approximately 10–15 s. The pixel size was 388 × 388 μm, the matrix size was 1024 × 768, and the overall image area was 40 × 30 cm. The dynamic image data, captured at 15 frames/s, were synchronized with the pulsed X-ray, which prevented excessive radiation exposure to the subjects. The entrance surface dose was approximately 0.3–1.0 mGy.

2.3. Image analysis

The data of DXR were assessed using prototype software (Konica Minolta Inc., Tokyo, Japan) installed in an independent workstation (Operating system: Windows 7 Professional 64-bit Service Pack 1; Microsoft, Redmond WA; CPU: Intel® CoreTM i5-6500, 3.20 GHz; random access memory, 16 GB). With reference to the motion of diaphragm and the graph of pixel value, the outline of the lung of both posteroanterior and lateral view was contoured manually by radiologist with seven-year experience (T.H.). The slope of pixel value frequently inversed in the transition between inspiration and expiration due to the change of lung volume as had been reported in the previous study [20]. PLA was calculated automatically by the software. PLA in both forced inspiratory and expiratory phase was measured in 162 volunteers. PLAs in both tidal inspiratory and expiratory phase was also measured with the same method in 90 volunteers. Several phases of images were gathered in tidal breathing, so the average of PLA was calculated. When the borders of lungs were ambiguous, the outer border was defined as right one in accordance with the magnification effect of lateral image. Representative cases are shown on Figs. 1–5, which include PLA curve during respiration. Note the resemblance of PLA curve over frame with those from spirometry. There was an impression that older subjects had larger tidal volume. In this study, several cases with decreased pulmonary function confirmed by PFTs were also shown in Figs. 6 and 7.
2.4. Pulmonary function tests (PFTs)

All volunteers underwent PFTs on the same day of DXR. Parameters of PFTs were decided according to the guideline of American Thoracic Society [21] using a pulmonary function instrument with computer processing (DISCOM-21 FX, Chest MI Co, Tokyo, Japan). The information of pulmonary functions was obtained as follows: tidal volume (TV), vital capacity (VC), vital capacity as percent of predicted (%VC), forced expiratory volume in 1 s (FEV₁), forced expiratory volume % in 1 s (FEV₁%), percent predicted forced expiratory volume in one second (%FEV₁), and the maximum flow rate at 25 % of forced VC divided by body height (V₂₅/Ht).

2.5. Statistical analysis

Measured numeric value was described as follows: mean value ± standard deviation. The PLAs of both PA and lateral views in forced inspiratory phase (PLA-INS-PA, PLA-INS-LAT), that in forced expiratory phase (PLA-EX-PA, PLA-EX-LAT), that in tidal inspiratory phase (PLA-ins-PA, PLA-ins-LAT) and that in tidal expiratory phase (PLA-ex-PA,
PLA-ex-LAT) was measured. The difference of PLA between the right and left lung was evaluated with paired t-test. The correlation between PLA and each demographic data including pulmonary functions, height, weight, body mass index (BMI), sex, pack-year was assessed with Spearman’s rank correlation coefficient. Several items with statistical significance in univariate analysis were assessed with multiple linear regression analysis.

Statistical analyses were conducted with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R 2.13.0 (R Foundation for Statistical Computing, Vienna, Austria) [22,23]. More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics. A two-sided P values of less than 0.05 were considered statistically significant.

3. Results

3.1. Demographic data and the PLA

Demographic characteristics and pulmonary function are shown in Table 1. In this study, %VC was lower than 80 % in three subjects and FEV1% was lower than 70 % in six subjects. No significant change is observed between the dataset of all the volunteers and that of ninety volunteers with PLA of both forced and rest breathing. The right PLA

Fig. 4. Projected Lung Area (PLA) of right and left lungs in PA projection.
93-year-old man with smoking history: 40 pack-years. PLA in PA projection in the tidal end-inspiratory phase. The graph on the right represents averaged signal value of the image. Measurement was performed manually with reference to the graph and diaphragm motion.

Fig. 5. Projected Lung Area (PLA) of right and left lungs in PA projection.
79-year-old woman with no smoking history. PLA in PA projection in the forced end-inspiratory phase. The graph on the right represents averaged signal value of the image. Measurement was performed manually with reference to the graph and diaphragm motion.
was larger than that of the left lung in both PA and lateral view images of each phase with statistical significance (Table 2).

3.2. Association between the PLA and demographic data or pulmonary function

Table 3 showed the result of univariate analysis between the PLA of PA image and each parameter including pulmonary function and personal data. The PLA of PA image presented moderate correlation with height, sex, VC and FEV₁, BMI and V₂₅/Ht. There was a tendency that the numeric values of correlation coefficient were higher in forced breathing. The mild correlation between PLA and tidal volume (TV) was observed only in forced inspiratory phase. The mild correlation between PLA and pack/year was observed only in forced breathing. No significant correlation between PLA and FEV₁% or %FEV₁ was observed.

The PLA in lateral image demonstrated the different results as shown.
Table 1: Age, Sex, Height, Weight, BMI, Smoking History, and pulmonary functions.

| Variables          | All volunteers (n = 162) | Volunteers with PLA in both forced and tidal phase (n = 90) |
|--------------------|--------------------------|------------------------------------------------------------|
| Age (years)        | 56.8 ± 10.3 [36–93]      | 57.0 ± 11.0 [36–90]                                       |
| Sex                |                          |                                                            |
| Female             | 69 ± 42.60% [22.2–23.0]  | 43 ± 47.80% [21.2–23.0]                                    |
| Male               | 93 ± 57.40% [22.1–6.9]   | 47 ± 52.20% [22.1–6.9]                                    |
| Height (cm)        | 163.4 ± 9.0 [137.9–184.2]| 162.6 ± 9.2 [137.9–183.7]                               |
| Weight (kg)        | 60.2 ± 10.8 [35.0–98.4]  | 59.7 ± 10.7 [37.0–98.4]                                   |
| BMI (kg/m²)        | 22.4 ± 2.8 [15.1–34.2]   | 22.5 ± 2.9 [15.1–34.2]                                   |
| Smoking History    |                          |                                                            |
| Never              | 91 ± 56.20% [0–76]       | 61 ± 67.80% [0–76]                                       |
| Current or former  | 71 ± 43.80% [0–76]       | 29 ± 32.20% [0–76]                                       |
| Pack/year          | 10.8 ± 16.9 [0–76]       | 7.9 ± 15.5 [0–76]                                       |

BMI, body mass index; FEV1, forced expiratory volume in one second; FEV1%, forced expiratory volume percent in one second divided by forced vital capacity; %FEV1, percent predicted FEV1; %VC, percent vital capacity; PLA, projected lung area; SD, standard deviation; TV, tidal volume; V25/Ht, the maximum flow rate at 25% of forced VC divided by body height; VC, vital capacity.

Table 2: Projected areas of the right and left lungs on PA and RL projections during forced breathing and tidal breathing.

| PLA               | Right lung Mean ± SD [range] | Left lung Mean ± SD [range] | p value |
|-------------------|------------------------------|-----------------------------|---------|
| Forced breathing   |                              |                             |         |
| (n = 162)          |                              |                             |         |
| PLA-INS-PA (cm²)   | 241.3 ± 95.5 [129.0–325.9]  | 200.6 ± 31.5 [86.6–277.8]  | <0.001  |
| PLA-EX-PA (cm²)    | 173.1 ± 30.0 [91.3–246.7]   | 141.3 ± 26.7 [61.3–216.7]  | <0.001  |
| PLA-INS-LAT (cm²)  | 434.5 ± 60.3 [253.3–591.1]  | 398.2 ± 54.7 [266.2–534.4] | <0.001  |
| PLA-EX-LAT (cm²)   | 286.4 ± 51.6 [162.4–431.3]  | 269.7 ± 43.8 [173.8–401.8] | <0.001  |
| Tidal breathing    |                              |                             |         |
| (n = 90)           |                              |                             |         |
| PLA-ins-PA (cm²)   | 211.6 ± 31.4 [111.9–281.2]  | 172.0 ± 30.7 [77.6–253.9]  | <0.001  |
| PLA-ex-PA (cm²)    | 197.4 ± 31.4 [108.7–268.8]  | 160.3 ± 28.9 [73.8–229.1]  | <0.001  |
| PLA-ins-LAT (cm²)  | 365.9 ± 55.1 [217.5–488.9]  | 329.3 ± 48.4 [231.4–454.1]| <0.001  |
| PLA-ex-LAT (cm²)   | 332.9 ± 55.2 [191.6–461.2]  | 300.1 ± 48.2 [204.2–433.5] | <0.001  |

TLC, total lung capacity; VC, vital capacity; PLA, projected lung area; PA, posterior-anterior projection; RL, right-left projection; FEV1, forced expiratory volume in one second; PFT, pulmonary function test; %FEV1, percent predicted FEV1; %VC, percent vital capacity; PLA, projected lung area; SD, standard deviation; TV, tidal volume; V25/Ht, the maximum flow rate at 25% of forced VC divided by body height; VC, vital capacity.

Discussion

Several studies have shown that PLAs measured by chest radiograph had good correlation with TLC. Barnhard et al. divided lung images into ellipsoidal components and estimated the lung volume with multiple diameters obtained by chest radiograph [3]. This method was modified by Loyd [6], in which multiple of PLAs by both PA and lateral views had good correlation with TLC [3,4]. These studies have been re-examined and improved for many years [5–9]. Some studies reported that CT image was also useful for the measurement of TLC in infants or children [11,13]. VC is calculated by TLC minus residual volume, thus VC and TLC correlate with each other. If VC and PLA have correlation with each other, there is a possibility that pulmonary functions have correlations with PLA measured by DXR. These findings indicate the possibility of using DXR instead of spirometry in subjects with whom close contact or use of mouth-piece is prohibited.

The PLAs of the left lung were smaller than those of the right lung. In PA view, the left PLA exclude the area overlapping cardiac shadow in accordance with the prior studies of planimetry [6,13,25]. Previous study reported that about 30% of lung volume overlaps with shadows of diaphragm, heart and mediastinum by comparison with chest CT [24]. This fact might affect the PLAs measured in this study. In lateral views, flat panel detector was located along left side chest. It is also the reason why the left lung is smaller in volume compared to the right lung, when measured by DXR.

In univariate analysis, height, weight and sex showed significant correlation with PLA in each view. VC presented significant correlation with the PLAs as TLC did. These results indicate that the size of physique is associated with them. As for FEV1, we have to keep in mind that it had significant correlation with VC (r = 0.94, p < 0.001). BMI, which is calculated by weight divided by square of height, showed no significance in some views. This was probably due to the cancellation by division. The same theory may be true of relative values such as %VC, %FEV1, and V25/Ht. The fact is equally important that the PLAs correlated with each other, there is a possibility that pulmonary functions have correlations with PLA.
P values and rank correlation coefficients were calculated using Spearman’s rank correlation. * indicates P < 0.05; ** indicates P < 0.01; BMI, body mass index; FEV1, forced expiratory volume in one second; FEV1%, forced expiratory volume percent in one second divided by forced vital capacity; %FEV1, percent predicted FEV1; %VC, percent vital capacity; PLA, projected lung area; PLA-INS-PA, PLA of PA view in forced inspiratory phase; PLA-EX-PA, PLA of PA view in forced expiratory phase; PLA-ins-PA, PLA of PA view in tidal inspiratory phase; PLA-ex-PA, PLA of PA view in tidal expiratory phase; TV, tidal volume; V25/ht, the maximum flow rate at 25 % of forced VC divided by body height; VC, vital capacity.

| Variables | PLA-INS-PA | PLA-EX-PA | PLA-ins-PA | PLA-ex-PA |
|-----------|------------|-----------|------------|-----------|
| Age       | -0.13 [-0.29, 0.02] | -0.15 [-0.30, 0.01] | 0.08 [-0.14, 0.02] | 0.06 [-0.12, 0.00] |
| Height    | 0.70 [0.60, 0.77] | 0.49 [0.30, 0.60] | -0.01 [-0.02, -0.00] | 0.22 [-0.03, 0.00] |
| Weight    | 0.33 [0.19, 0.47] | 0.12 [-0.04, 0.02] | 0.66 [0.56, 0.74] | 0.63 [0.52, 0.75] |
| BMI       | -0.01 [-0.02, -0.00] | -0.02 [-0.03, -0.01] | 0.01 [-0.01, 0.00] | 0.05 [-0.05, 0.01] |
| Sex       | 0.54 [0.42, 0.65] | 0.16 [0.04, 0.31] | 0.52 [0.39, 0.62] | 0.51 [0.38, 0.63] |

Table 3
Association of PLA of PA image with each parameter by Spearman’s rank correlation.
fibrosis of diaphragm muscles [25].

The result of multivariate analysis suggests that BMI, VC and sex can be independent correlation factor. The coefficient of sex in multivariate analysis was higher in lateral views. The PLAs in lateral view is possibly obscure due to the artifact of bone and soft tissue.

In conclusion, PLA showed statistically significant correlation with VC; percent vital capacity; PLA-INS-LAT, PLA of lateral view in forced inspiratory phase; PLA-EX-LAT, PLA of lateral view in forced expiratory phase; TV, vital capacity; PLA-EX-LAT, PLA of lateral view in forced expiratory phase; PLA-INS-LAT, PLA of lateral view in forced inspiratory phase; TV, vital capacity; V25/HT, the maximum flow rate at 25 % of forced VC divided by body height; VC, vital capacity.

Table 4

| Variables | Right | Left | Right | Left |
|-----------|-------|------|-------|------|
| Sex       | 0.20  | 0.02 | 0.24  | 0.001*|
| BMI       | 0.30  | 0.04 | 0.23  | 0.001**|
| Age       | 0.18  | 0.03 | 0.17  | 0.001**|
| Height    | 0.54  | 0.02 | 0.29  | 0.005**|
| Weight    | 0.54  | 0.02 | 0.29  | 0.005**|
| VC        | 0.54  | 0.02 | 0.29  | 0.005**|
| FEV<sub>1</sub> | 0.23  | 0.01 | 0.01  | 0.001**|
| 0.05 - 0.09 | 0.23  | 0.01 | 0.01  | 0.001**|
| %VC       | 0.54  | 0.02 | 0.29  | 0.005**|
| %FVC<sub>1</sub> | 0.23  | 0.01 | 0.01  | 0.001**|
| V25/HT    | 0.08  | 0.02 | 0.07  | 0.001**|
| V25/HT    | 0.08  | 0.02 | 0.07  | 0.001**|

P values and rank correlation coefficients were calculated using Spearman’s rank correlation. * indicates P < 0.05; ** indicates P < 0.01; BMI, body mass index; FEV<sub>1</sub>, forced expiratory volume in one second; FEV<sub>1</sub>/%VC, forced expiratory volume percent in one second divided by forced vital capacity; %FVC<sub>1</sub>, percent predicted FEV<sub>1</sub>; %VC, percent vital capacity; PLA, projected lung area; PLA-INS-LAT, PLA of lateral view in forced inspiratory phase; PLA-EX-LAT, PLA of lateral view in forced expiratory phase; PLA-INS-LAT, PLA of lateral view in tidal inspiratory phase; PLA-EX-LAT, PLA of lateral view in tidal expiratory phase; TV, tidal volume; V25/ht, the maximum flow rate at 25 % of forced VC divided by body height; VC, vital capacity.

Declaration of competing interest

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Disclosure

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CRediT authorship contribution statement

Takuya Hino: Conceptualization, Investigation, Formal analysis, Writing - original draft. Akinori Hata: Writing - review & editing. Tomoyuki Hida: Writing - review & editing. Yoshitake Yamada: Writing - review & editing. Masako Ueyama: Data curation, Writing - review & editing. Tetsuro Araki: Writing - review & editing. Takeshi Kamitani: Writing - review & editing. Mizuki Nishino: Writing - review & editing. Atsuko Kurosaki: Data curation, Writing - review & editing. Masahiro Jinzaki: Writing - review & editing. Kouei Ishigami: Writing - review & editing. Hiroshi Honda: Writing - review & editing. Shoji Kudoh: Resources, Writing - review & editing.
Table 5

Association of PLA with each parameter by multivariate analysis.

| Variables         | Right | Coefficient | SE    | P value | Left | Coefficient | SE    | P value |
|-------------------|-------|-------------|-------|---------|------|-------------|-------|---------|
| Intercept         | PLA-INS-PA | -0.045      | 0.338 | 0.731   | PLA-EX-LAT | 0.029 | 0.701   | 0.474 |
| Age               | PLA-INS-PA | 0.007       | 0.001 | 0.944   | PLA-EX-LAT | 0.006 | 0.001 | 0.944 |
| BMI               | PLA-INS-PA | -0.002      | 0.001 | 0.959   | PLA-EX-LAT | 0.002 | 0.001 | 0.959 |
| Sex               | PLA-INS-PA | 0.010       | 0.001 | 0.917   | PLA-EX-LAT | 0.010 | 0.001 | 0.917 |
| VC                | PLA-INS-PA | 0.001       | 0.001 | 0.978   | PLA-EX-LAT | 0.001 | 0.001 | 0.978 |

Coefficient, standard error (SE), and P values were calculated using multiple linear regression analysis. * indicates P < 0.05; ** indicates P < 0.01; BMI, body mass index; PLA, projected lung area; PLA-INS-PA, PLA of lateral view in tidal inspiratory phase; PLA-ex-PA, PLA of PA view in tidal inspiratory phase; PLA-ins-PA, PLA of PA view in forced inspiratory phase; PLA-EX-LAT, PLA of lateral view in forced expiratory phase; PLA-EX-PA, PLA of PA view in forced expiratory phase; PLA-INS-LAT, PLA of lateral view in forced inspiratory phase; PLA-INS-PA, PLA of PA view in tidal inspiratory phase; PLA-ex-PA, PLA of PA view in tidal expiratory phase; PLA-EX-LAT, PLA of lateral view in tidal inspiratory phase; PLA-EX-LAT, PLA of lateral view in tidal expiratory phase; VC, vital capacity.

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