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Quantitative study of the difference in pulmonary perfusion in different respiratory phases in healthy volunteers

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Objective: The purpose of this study is to investigate the physiological pulmonary perfusion pattern in different respiratory phases by calculating the normalized volume center of perfusion intensity. ***Methods:*** Four nonsmoking volunteers underwent single photon emission computed tomography (SPECT) of maximum inspiration and expiration after the injection of Tc-99m-MAA in each respiratory phase at a week's interval. Quantitative analysis by calculating the normalized volume center of perfusion intensity was performed. ***Results:*** Quantitative measurement of the normalized volume center of perfusion intensity showed that the percentage averages of ventrodorsal (Y) shift in maximum respiration were 16% (left) and 15% (right) in the upper part, 15% (left) and 14% (right) in the middle part, 17% (left) and 18% (right) in the lower part, 18% (left) and 16% (right) in each total lung. These readings indicated that the normalized center of pulmonary perfusion activity at maximum expiration moved in the ventral direction in contrast to that at maximum inspiration. In horizontal (X) and craniocaudal (Z) directions, the shift in the normalized center of pulmonary perfusion activity at maximum expiration indicated no agreement in movement direction. ***Conclusion:*** The normalized center of the pulmonary perfusion activity in maximum expiration moved in the ventral direction compared to that in maximum inspiration. This phenomenon might be caused by the increase in physiological intrathoracic pressure and by a definite reserve of pulmonary perfusion.

Key words: pulmonary perfusion, Tc-99m-MAA SPECT, quantitative measurement, respiratory phase

INTRODUCTION

Pulmonary perfusion scintigraphy with Tc-99m-MAA can demonstrate the regional pulmonary perfusion difference in different positions of the patient at the time of injection. It is influenced by many correlated factors. One of them is gravity.[1–4] In the case of the upright or sitting position with resting respiration, pulmonary Tc-99m MAA distribution increases in the lower part of the lung lobe.

In the case of the supine position with resting respiration, it increases in the posterior part of each lobe. Other factors also play important roles in the distribution of pulmonary perfusion.[5–8]

To understand the exact distribution of lung perfusion in different respiratory phases, Tc-99m MAA has to be injected during the maximum inspiration and expiration phase followed by breath holding for about 20 seconds in the supine position, therefore Tc-99m MAA can reach the capillary bed in each respiratory phase.

Transaxial SPECT images in different respiratory phases were obtained with the collaboration of 4 volunteers. The center of perfusion intensity was calculated by using the static perfusion SPECT images according to the originally designed formulae. The transaxial SPECT images were analyzed not only qualitatively but also quantitatively by calculating the normalized center of perfusion intensity. The respiratory dependent distribution pattern of pulmonary perfusion in healthy volunteers was clearly

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observed and we discussed its physiological significance. A previous study[8] on the differences in the respiratory phase dependent on the distribution of pulmonary perfusion reported the use of 2 slices of SPECT data and a profile curve. In our study, the use of a normalized center of pulmonary perfusion intensity makes it unnecessary to consider volume differences.

MATERIALS AND METHODS

Subjects: Four young males gave their informed consent to participate in the experiment as volunteers. None of the subjects, ranging in age from 19 to 25 years (mean: 21), had neither any pulmonary disease nor history of smoking.

Methods: The four volunteers underwent single photon emission computed tomography (SPECT) after the injection of 185 MBq Tc-99m MAA in each respiratory phase, namely maximum inspiration and expiration at a week's interval. With the subjects in the supine position, Tc-99m MAA was injected intravenously into the arm followed by a bolus flush with 10 m*l* physiological saline during breath holding for 20 seconds at each maximum respiration. Perfusion static SPECT images were obtained at 10 min after injection of Tc-99m MAA. We used two opposite SPECT detectors (GCA-7100 R/DI; Toshiba, Tokyo, Japan) equipped with LEHR parallel collimator. Each detector was rotated at a 5 deg. step angle (20 second step intervals). Projection data (128 × 128 matrices) from the two detectors were then prefiltered with a Butterworth filter, and the converted data were then backprojected with a Ramp filter to reconstruct transaxial SPECT images with a 10.3 mm slice thickness. Digital SPECT volume data are composed of data for the horizontal axis (x), ventrodorsal axis (y) and craniocaudal axis (z).

Preprocessing was first performed to minimize the influence of artifacts in the original digital SPECT data. For this purpose, we transfer a set of the original data $f(x, y, z)$ into another set of data $g(x, y, z)$, which will contribute to calculation of the center of perfusion intensity. If value $f(x, y, z)$ is smaller than threshold 125, we treat it as an artifact and delete it. We obtained threshold $T = 125$ through testing.

To study the exact pattern of pulmonary perfusion in different parts of the lung, we divided each lung image from top to base into 3 portions, upper, middle and lower.

The normalized center of perfusion intensity for each part was calculated separately according to the following procedure.

To calculate the normalized center of perfusion intensity, the $x_{\min}$, $x_{\max}$, $y_{\min}$, $y_{\max}$, $z_{\min}$ and $z_{\max}$ should be decided on to confine the contributing region to the volume data. The contributing region should then be divided into two parts in the x direction in position $x_{\text{mid}} = (x_{\min} + x_{\max})/2$ that represents the left and right lung separately. Centers of left and right lung are defined as follows:

$$X_{CL} = M_{XL}/M_L \quad (1)$$
$$Y_{CL} = M_{YL}/M_L \quad (2)$$
$$Z_{CL} = M_{ZL}/M_L \quad (3)$$
$$X_{CR} = M_{XR}/M_R \quad (4)$$
$$Y_{CR} = M_{YR}/M_R \quad (5)$$
$$Z_{CR} = M_{ZR}/M_R \quad (6)$$

Where M_{XL}, M_{YL}, M_{ZL}, M_{XR}, M_{YR} and M_{ZR} are static moments of perfusion intensity of the two parts of the lung about ox, oy and oz. M_L and M_R are the total perfusion intensities of the two parts. They are defined as follows:

$$M_{XL} = \sum_{k=Z_{\min}}^{Z_{\max}} \sum_{j=Y_{\min}}^{Y_{\max}} \sum_{i=X_{\min}}^{X_{\text{mid}}} ig(i,j,k) \quad (7)$$

$$M_{YL} = \sum_{k=Z_{\min}}^{Z_{\max}} \sum_{j=Y_{\min}}^{Y_{\max}} \sum_{i=X_{\min}}^{X_{\text{mid}}} jg(i,j,k) \quad (8)$$

$$M_{ZL} = \sum_{k=Z_{\min}}^{Z_{\max}} \sum_{j=Y_{\min}}^{Y_{\max}} \sum_{i=X_{\min}}^{X_{\text{mid}}} kg(i,j,k) \quad (9)$$

$$M_{XR} = \sum_{k=Z_{\min}}^{Z_{\max}} \sum_{j=Y_{\min}}^{Y_{\max}} \sum_{i=X_{\text{mid}}}^{X_{\max}} ig(i,j,k) \quad (10)$$

$$M_{YR} = \sum_{k=Z_{\min}}^{Z_{\max}} \sum_{j=Y_{\min}}^{Y_{\max}} \sum_{i=X_{\text{mid}}}^{X_{\max}} jg(i,j,k) \quad (11)$$

$$M_{ZR} = \sum_{k=Z_{\min}}^{Z_{\max}} \sum_{j=Y_{\min}}^{Y_{\max}} \sum_{i=X_{\text{mid}}}^{X_{\max}} kg(i,j,k) \quad (12)$$

Then, the normalized center of perfusion intensity can be obtained by using the following equations:

$$X_{NCL} = (X_{CL} - x_{\min})/(x_{\text{mid}} - x_{\min}) \quad (13)$$
$$Y_{NCL} = (Y_{CL} - y_{\min})/(y_{\max} - y_{\min}) \quad (14)$$
$$Z_{NCL} = (Z_{CL} - z_{\min})/(z_{\max} - z_{\min}) \quad (15)$$
$$X_{NCR} = (x_{\max} - X_{CR})/(x_{\max} - x_{\text{mid}}) \quad (16)$$
$$Y_{NCR} = (Y_{CR} - y_{\min})/(y_{\max} - y_{\min}) \quad (17)$$
$$Z_{NCR} = (Z_{CR} - z_{\min})/(z_{\max} - z_{\min}) \quad (18)$$

The influence induced by shifting of the subject's position and differences in the lung size of different subjects can be eliminated with this kind of normalization.

To measure the shift in the normalized center of perfusion intensity in three directions, six other parameters were calculated according to following equations:

$$DX_{NCL} = (X_{NCL}(\text{Insp}) - X_{NCL}(\text{Exp}))/X_{NCL}(\text{Insp}) \quad (19)$$
$$DX_{NCR} = (X_{NCR}(\text{Insp}) - X_{NCR}(\text{Exp}))/X_{NCR}(\text{Insp}) \quad (20)$$
$$DY_{NCL} = (Y_{NCL}(\text{Insp}) - Y_{NCL}(\text{Exp}))/Y_{NCL}(\text{Insp}) \quad (21)$$
$$DY_{NCR} = (Y_{NCR}(\text{Insp}) - Y_{NCR}(\text{Exp}))/Y_{NCR}(\text{Insp}) \quad (22)$$
$$DZ_{NCL} = (Z_{NCL}(\text{Insp}) - Z_{NCL}(\text{Exp}))/Z_{NCL}(\text{Insp}) \quad (23)$$
$$DZ_{NCR} = (Z_{NCR}(\text{Insp}) - Z_{NCR}(\text{Exp}))/Z_{NCR}(\text{Insp}) \quad (24)$$

RESULTS

Tc-99m MAA perfusion SPECT images on maximum inspiration and maximum expiration of one case (case 1) are shown in Figures 1 and 2. Shift of pulmonary perfusion that moves forward in the ventral direction in the expiration phase compared to in the inspiration phase was observed in all parts of the lung.

The normalized centers of perfusion intensity in both lungs were divided into three tables according to three components of *X* (horizontal component), *Y* (ventrodorsal component), *Z* (craniocaudal component) and total lung listed in Table 1, Table 2 and Table 3.

Within each table, each component was then subdivided into three groups, upper, middle and lower parts.

Table 1 shows that the percentage average horizontal *X* shifts of the normalized center of perfusion intensity were −2% (left) and −6% (right) in the upper part, −4% (left) and −7% (right) in the middle part, 1% (left) and −6% (right) in the lower part of the lung and 0% (left) and −4% (right) in the total lung. In the horizontal *X* direction, the normalized center of pulmonary perfusion activity

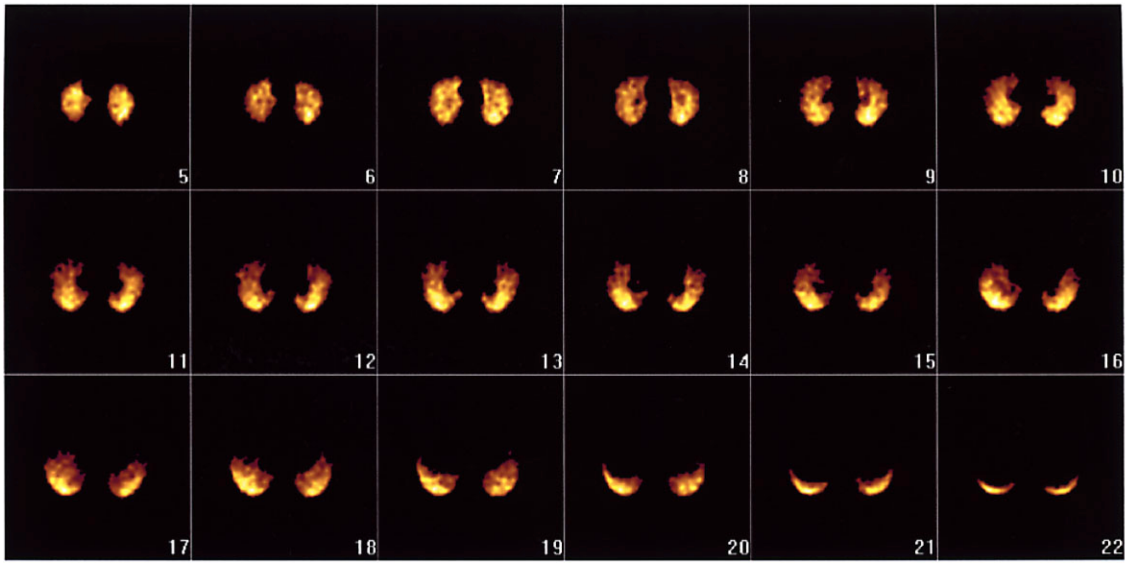

Fig. 1 Tc-99m MAA perfusion SPECT images of case 1 at maximum inspiration. Increased dorsal pulmonary perfusion in all parts of the lung is identified at maximum inspiration.

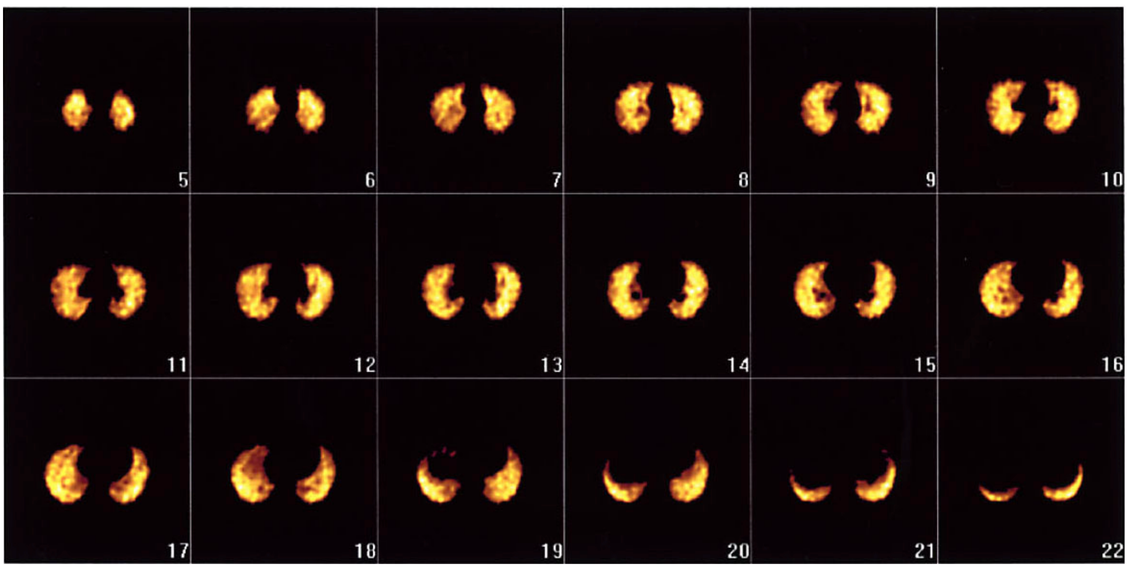

Fig. 2 Tc-99m MAA perfusion SPECT images of case 1 at maximum expiration. Increased ventral pulmonary perfusion in all parts of the lung is identified at maximum expiration compared to maximum inspiration. We noticed more uniform distribution of the tracer at maximum expiration.

Table 1 Horizontal (X) component of normalized center of perfusion intensity of left and right lung and corresponding percentage of shift due to expiration along X axis

Lung		Position X axis				Shift due to expiration along X axis*	
		Left		Right			
		Inspiration	Expiration	Inspiration	Expiration	Left	Right
Zone	case#						
Upper	1	44	61	44	68	–0.39	–0.55
	2	35	41	48	48	–0.17	0.00
	3	41	14	46	28	0.66	0.39
	4	34	35	35	38	–0.03	–0.09
Mean		38	38	43	46	–0.02	–0.06
Middle	1	36	52	39	60	–0.44	–0.54
	2	30	36	41	41	–0.20	0.00
	3	34	14	35	25	0.59	0.29
	4	27	30	34	34	–0.11	–0.03
Mean		31	33	37	40	–0.04	–0.07
Lower	1	34	46	39	60	–0.35	–0.54
	2	34	34	39	32	–0.10	0.08
	3	32	11	38	30	0.66	0.21
	4	30	35	27	27	–0.17	0.00
Mean		33	32	36	37	0.01	–0.06
Total lung (average)	1	38	53	41	63	–0.39	–0.54
	2	33	37	43	40	–0.16	0.12
	3	36	13	40	30	0.64	0.29
	4	30	33	32	33	–0.10	–0.04
Mean		34	34	39	42	0.00	–0.04

* Positive and negative values mean outward and inward shift of the center, respectively

Table 2 Ventrodorsal (Y) component of normalized center of perfusion intensity of left and right lung and corresponding percentage of shift due to expiration along Y axis

Lung		Position Y axis				Shift due to expiration along Y axis*	
		Left		Right			
		Inspiration	Expiration	Inspiration	Expiration	Left	Right
Zone	case#						
Upper	1	51	39	55	40	0.24	0.27
	2	52	47	55	51	0.10	0.07
	3	48	39	51	43	0.19	0.16
	4	58	51	61	55	0.12	0.10
Mean		52	44	56	47	0.16	0.15
Middle	1	55	38	60	39	0.31	0.35
	2	58	52	60	57	0.10	0.05
	3	54	49	62	58	0.09	0.06
	4	61	55	62	56	0.10	0.10
Mean		57	49	61	53	0.15	0.14
Lower	1	62	42	64	42	0.32	0.34
	2	73	67	72	71	0.08	0.01
	3	64	47	69	54	0.27	0.22
	4	62	61	72	62	0.02	0.16
Mean		65	54	69	57	0.17	0.18
Total lung (average)	1	56	40	60	40	0.29	0.32
	2	61	55	62	60	0.09	0.04
	3	55	45	61	52	0.18	0.15
	4	60	56	65	58	0.14	0.12
Mean		58	49	62	52	0.18	0.16

* Positive and negative values mean ventral and dorsal shift of the center, respectively

Table 3 Craniocaudal (*Z*) component of normalized center of perfusion intensity of left and right lung and corresponding percentage of shift due to expiration along *Z* axis

Lung		Position *Z* axis				Shift due to expiration along *Z* axis*	
		Left		Right			
		Inspiration	Expiration	Inspiration	Expiration	Left	Right
Zone	case#						
Upper	1	54	56	53	56	−0.04	−0.06
	2	56	56	55	53	0.00	−0.06
	3	62	58	50	53	0.06	0.00
	4	50	51	54	56	−0.02	−0.04
Mean		56	55	53	55	0.00	−0.04
Middle	1	50	51	47	49	−0.02	−0.04
	2	45	48	43	44	−0.07	−0.02
	3	47	50	46	47	−0.06	−0.02
	4	42	49	35	41	−0.17	−0.17
Mean		46	50	43	45	−0.08	−0.06
Lower	1	35	31	39	43	0.11	−0.10
	2	38	31	31	33	0.18	−0.06
	3	37	32	40	42	0.14	−0.05
	4	27	22	53	46	0.19	0.13
Mean		34	29	41	41	0.16	−0.02
Total lung	1	46	46	45	49	0.02	−0.07
(average)	2	46	45	43	43	0.04	−0.05
	3	49	47	45	47	0.05	−0.02
	4	40	41	47	48	0.00	−0.03
Mean		45	45	45	47	0.03	−0.04

* Positive and negative values mean cranial and caudal shift of the center, respectively

indicated no agreement in movement direction.

Table 2 shows that the average percentages of ventrodorsal *Y* shift of the normalized center of perfusion intensity were 16% (left) and 15% (right) in the upper part, 15% (left) and 14% (right) in the middle part, 17% (left) and 18% (right) in the lower part of the lung and 18% (left) and 16% (right) in the total lung.

These indicated that the normalized center of pulmonary perfusion activity in the maximum expiration moved in the ventral direction compared to that in maximum inspiration.

Table 3 shows that the average percentages of craniocaudal *Z* shift of the normalized center of perfusion intensity were 0% (left) and −4% (right) in the upper part, −8% (left) and −6% (right) in the middle part, 16% (left) and −2% (right) in the lower part of the lung and 3% (left) and −4% (right) in the total lung. In the *Z* direction, the normalized center of the pulmonary perfusion activity also indicated no agreement in the direction of movement.

DISCUSSION

Pulmonary perfusion scintigraphy with Tc-99m MAA is widely used in cases of pulmonary embolism[9–12] and various other pulmonary diseases,[13,14] in which perfusion distribution is impaired. Planar images were widely used but nowadays SPECT images are more often used, because they provide more detailed information about disease location.[15–17]

It is well known that the pulmonary perfusion pattern depends on the position of the subject at the time of injection of Tc-99m MAA.[1–4] When the position of the subject is standing or sitting, the predominant perfusion distribution is in the lower lung lobe, whereas in the supine or prone position, significant changes happen in the posterior and anterior directions. To achieve uniform distribution of the tracer, they receive two intravenous injection of the tracer, once while in the supine position and once while in the prone position.

This phenomenon is thought to be due to the fact that the distribution of pulmonary perfusion greatly depends on gravity.[1–4]

Hakim[5] reported from his experimental SPECT data that other factors also play an important role in the distribution of pulmonary blood flow. These factors may be related to conduction in the vascular pathways that lead to different regions of the lung.

We saw the redistribution of perfusion in a clinical case of increased pulmonary wedged pressure caused by cardiac failure. This redistribution phenomenon exists not only in cardiac failure, but also in strenuous exercise.

Votion[18] reported in an experimental study that acute treadmill exercise ($12.4 + 0.8$ msec^{-1}) caused an increase in PAP (mean pulmonary arterial pressure) and increased pulmonary distribution in the dorsocaudal region in normal horses. He concluded that this physiological phenomenon in the case of strenuous exercise is one of the causes of EIPH (exercise induced pulmonary hemorrhage) in the dorsocaudal areas of horses.

The pattern of distribution of Tc-99m MAA in the lung depends not only on the position of the subject at time of the injection but also on the respiratory phase. In a study of the healthy volunteer group, we found that the Tc-99m MAA distribution in the phase of maximum expiration shifted more in the ventral direction against gravity in the supine position. Kosuda[8] reported in his paper that subjects might receive one injection while in the supine position and holding their breath at residual volume to obtain uniform distribution of the tracer. On the basis of this phenomenon, two factors are speculated. One is high pulmonary vascular resistance during this residual volume phase. The other one is lower lung volume during this phase, which produces low weight of the lung in dependent parts of the lung.

This controversial phenomenon can mainly be explained by the changes in intrathoracic pressure. In controls, intrathoracic pressure at rest is $-2.5 \sim -7.0$ mmHg, whereas on maximum inspiration followed by breath-hold it is $-30 \sim -80$ mmHg and on maximum expiration $+50 \sim +100$ mmHg. The increase in intrathoracic pressure during maximum expiration causes decreased venous return to the right ventricle and increased pulmonary capillary resistance. This increased vascular resistance could cause the ventral shift of pulmonary perfusion in the supine position.[20–23]

Another possible factor involved in the distribution of Tc-99m MAA that shifted more in the ventral direction during expiration than that during inspiration is that more crushed alveoli due to shrinkage of the lung cause a relative decrease in perfusion in the posterior part.

On the other hand, Suga[19] reported a difference in distribution of pulmonary perfusion with Xe-133 between rest and exercise in controls and patients with slight silicosis. He supposed that the much greater increase in pulmonary perfusion in the upper part of the lung during exercise in controls in the sitting position plays an important role in satisfying the need for effectively oxygenated blood, which is supplied to the entire pulmonary capillary bed. In contrast, this phenomenon was not observed in patients with silicosis. This indicated that the control group has a larger pulmonary reserve than patients with silicosis. The difference in tracer distribution during maximum inspiration and expiration which we saw might indicate a reserve of pulmonary perfusion in healthy volunteers.

CONCLUSION

Single photon emission computed tomography (SPECT) after the injection of Tc-99m MAA was used to investigate the physiological pulmonary perfusion pattern in different respiratory phases. We found a change in the pattern of pulmonary perfusion between maximum inspiration and maximum expiration, as well as in different parts of the lung, by quantitatively measuring the normalized center of perfusion intensity, which was originally devised for this study. From this quantitative measurement, we found that the pulmonary perfusion activity in maximum expiration phase moved in the ventral direction. This might be caused by the increase in physiological intrathoracic pressure and by a definite reserve of pulmonary perfusion in healthy volunteers.

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