Annals of Nuclear Medicine Vol. 16, No. 6, 423–429, 2002

Quantification of regional pulmonary flow with ^{99m}Tc-MAA SPECT and cine phase contrast MR imaging

Hisato OSADA, Kikuo MACHIDA and Norinari HONDA

Department of Radiology, Saitama Medical Center, Saitama Medical School

The purpose of this study was to evaluate the relationship between left and right pulmonary arterial flow measured by cine phase contrast magnetic resonance imaging (cine PCMRI) and the distribution of perfusion on ^{99m}Tc-MAA SPECT and to determine whether the regional pulmonary flow quantification was feasible with the combined use of these techniques. Twenty patients with different pulmonary diseases were evaluated. Left and right lung counts on ^{99m}Tc-MAA SPECT images were separately summed and the left-to-total count ratio was calculated. The left-to-total pulmonary flow ratio was calculated from the left and right main pulmonary flows measured with cine PCMRI. We evaluated the correlation and agreement between the ratio determined with ^{99m}Tc-MAA SPECT and cine PCMRI by linear regression analysis and Bland-Altman analysis. The left-to-total ratios obtained by ^{99m}Tc-MAA and cine PCMRI were 52.0 ± 22.1% and 52.2 ± 20.8%, respectively, and showed a strong correlation ($r = 0.99$, $p < 0.001$). The mean difference between the two methods in the ratio was 0.25 ± 2.3% with a 95% confidence interval from –0.84 to 1.34. The results showed that the regional pulmonary flow was calculated with both the left and right pulmonary flow measured with cine PCMRI and the ratio of regional distribution on ^{99m}Tc-MAA SPECT images.

Key words: ^{99m}Tc-MAA, SPECT, regional pulmonary flow, MRI

INTRODUCTION

CINE PHASE CONTRAST MR IMAGING (cine PCMRI) is a method of velocity measurement, based on the principle that transverse magnetization of spins moving in a magnetic field gradient develops a velocity-proportional phase shift relative to static spins.[1–3] Phase images, on which signal intensity is proportional to velocity, provide two-dimensional maps of flow velocity. This technique has been documented for its accuracy both *in vitro* and *in vivo* and clinically applied for many vessels including flow quantification of cerebral arteries,[4,5] portal veins,[6,7] stroke volume of ventricles[8,9] and valvular regurgitation.[10,11] The blood flow of the left and right pulmonary arteries can separately be quantified with cine PCMRI.

Received April 17, 2002, revision accepted July 31, 2002.

For reprint contact: Hisato Osada, M.D., Department of Radiology, Saitama Medical Center, Saitama Medical School, 1981 Kamoda, Kawagoe, Saitama 350–8550, JAPAN.

E-mail: osada@saitama-med.ac.jp

^{99m}Tc-macroaggregated albumin (MAA) pulmonary perfusion SPECT has been widely used for assessment of pulmonary flow distribution.[12–18] Regional distribution of MAA is proportional to the regional arterial blood flow, because the particles (10–60 μm) are micro-embolized in the pulmonary vascular beds.

There have been a few reports on the good correlation between left and right pulmonary flow determined with cine PCMRI and distribution on planar ^{99m}Tc-MAA scintigrams.[19,20] The authors hit upon the hypothesis that regional pulmonary flow can be quantified by means of the left and right pulmonary flow measured with cine PCMRI and the regional-to-total count ratio on ^{99m}Tc-MAA SPECT images.

The purpose of this study was to examine the relationship between left and right pulmonary arterial flow measured with cine PCMRI and distribution on ^{99m}Tc-MAA SPECT, and to quantify the regional pulmonary flow with the combined use of those techniques. We prospectively evaluated the correlation and agreement between the left-to-total ratios determined with ^{99m}Tc-MAA SPECT and

those with cine PCMRI.

MATERIALS AND METHODS

Subjects

Twenty patients were entered in this study (16 males and 4 females; age range 24 to 85 y; mean age 63.0 ± 14.3). Their diseases were lung cancer (n = 8, one was complicated by acute radiation pneumonitis), thymoma (n = 1), esophageal cancer (n = 3), metastatic lung tumor (n = 1), pulmonary artery sarcoma (n = 1), Swyer-James syndrome (n = 2), emphysema (n = 1), acute interstitial pneumonitis (n = 1) and pulmonary thromboembolism (n = 2). They had no congenital heart disease, malformation of pulmonary vessels or liver cirrhosis causing a right-to-left shunt. Table 1 shows their characteristics. ^{99m}Tc-MAA perfusion SPECT and cine PCMRI were performed within 24 hours before or after the other study.

^{99m}Tc-MAA Pulmonary Perfusion SPECT

After intravenous injection of ^{99m}Tc-MAA 185 MBq in the supine position, SPECT was performed with a 3-head gamma camera equipped with parallel-hole low-energy collimators (Prism3000, Picker, Cincinnati, OH), and the zoom factor was 1.0. The data were collected in 72 directions in 5° steps over 360° for 15–20 seconds in each direction, and the matrix size was 64 × 64. The projection datasets were prefiltered with a Butterworth filter, and reconstructed with a Ramp filter without attenuation correction. A section thickness of 14.24 mm and pixel size of 7.12 mm were generated in the transverse planes. The data processing was done on a computer (Odyssey, Titan 750).

The left and right lung contours were separately determined by an iso-count method with a threshold value of 20% of the maximum pixel counts for the individual lungs. The left and right lung counts for each transverse image were separately summed and the left-to-total count ratio was calculated.

Pulmonary Flow Measurement with Cine PCMRI

All MR studies were obtained with a 1.5-T superconducting MR imaging unit (Signa Horizon LX 1.5, GE Medical Systems, Milwaukee, WI) equipped with a torso phased array coil. The cine phase contrast sequence was preceded by a gradient echo sequence to determine the planes for measuring the left and right pulmonary flow. As previously described,[21] the double oblique planes for flow measurement were positioned perpendicular to the left and right pulmonary arteries and proximal to any branch vessels, which were prescribed from oblique planes determined on transverse images. Cine phase contrast MR data were collected with a 256 × 128 matrix and two signals were averaged. Flow compensation in the readout was used. The velocity encoding value was 150 cm/sec in 18 patients, and 240 cm/sec in 2 patients. Other imaging parameters were set as follows: TR/TE, 30–40/minimum; flip angle, 20°; field of view, 24 cm; section thickness, 5 mm. The data were retrospectively segregated into 16 images per cardiac cycle with plethysmographic signals as time marks. A complex reconstruction of these data produced two kinds of images; a magnitude image and a phase image.

Regions of interest (ROIs) were set on the left and right pulmonary arteries on a magnitude image, and then applied to the corresponding phase image. The signal intensity in the ROI of each frame on the phase image revealed

Table 1 Clinical characteristics in 20 patients

Patient no.	Age	Sex	Diagnosis	Treatment	Dominant site of pathology
1	78	M	Lung carcinoma	Post radiation	Left lung
2	65	M	Lung carcinoma	(–)	Left lung
3	78	M	Lung carcinoma	Post radiation	Right lung
4	63	M	Lung carcinoma	Post radiation	Left lung
5	78	M	Lung carcinoma	Post radiation	Right lung
6	76	M	Lung carcinoma	(–)	Left lung
7	64	M	Lung carcinoma	(–)	Left lung
8	85	M	Lung carcinoma, radiation pneumonitis	Post radiation	Right lung
9	72	F	Thymoma	Post radiation	Mediastinum
10	65	M	Esophageal carcinoma	Post radiation	Mediastinum
11	64	M	Esophageal carcinoma	Post radiation	Mediastinum
12	54	M	Esophageal cardinoma	Post operation & radiation	Mediastinum
13	47	F	Metastatic tumors	(–)	Right lung
14	48	M	Pulmonary artery sarcoma	(–)	Right lung
15	24	M	Swyer James syndrome	(–)	Left lung
16	44	F	Swyer James syndrome	(–)	Left lung
17	59	M	Emphysema	(–)	Bilateral lung
18	62	M	Acute interstitial pneumonitis	(–)	Bilateral lung
19	66	M	Pulmonary thromboembolism	Post anticoagulant therapy	Bilateral lung
20	67	F	Pulmonary thromboembolism	Post anticoagulant therapy	Bilateral lung

Table 2 Data obtained with ^{99m}Tc-MAA SPECT and cine PCMRI

Patient no.	Left/Total count radio of ^{99m}Tc-MAA %	Left/Total flow ratio with cine PCMRI %	Flow measurement with cine PCMRI		
			Left ml/min	Right ml/min	Total ml/min
1	32	38	1100	1810	2910
2	47	45	2070	2530	4600
3	85	80	2580	640	3220
4	27	30	970	2250	3220
5	90	88	2570	360	2930
6	39	40	2310	1570	3880
7	43	43	1810	2390	4200
8	90	87	2040	300	2340
9	40	40	1670	2470	4140
10	50	51	1420	1380	2800
11	42	42	1480	2040	3520
12	34	32	1510	3190	4700
13	73	73	2990	1100	4090
14	98	97	4280	120	4400
15	43	41	2280	3280	5560
16	36	35	1450	2680	4130
17	49	50	1750	1750	3500
18	31	33	1100	2200	3300
19	52	52	2350	2170	4520
20	43	42	2140	2370	4510
Mean ± SD	52.2 ± 22.1	52.0 ± 20.8	1830 ± 930	1990 ± 770	3830 ± 800

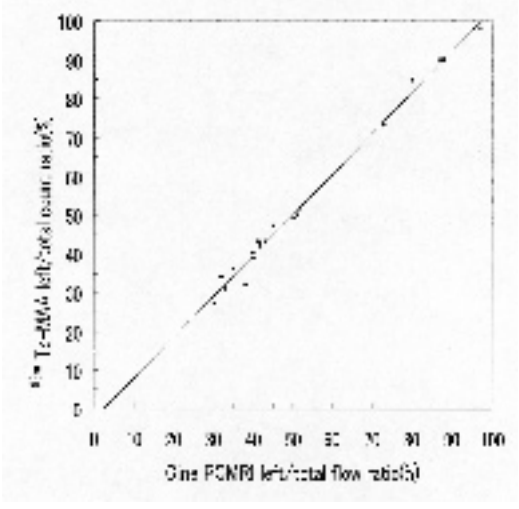


Fig. 1 Linear regression of left-to-total ratio of pulmonary flow determined by ^{99m}Tc-MAA SPECT versus by cine PCMRI.

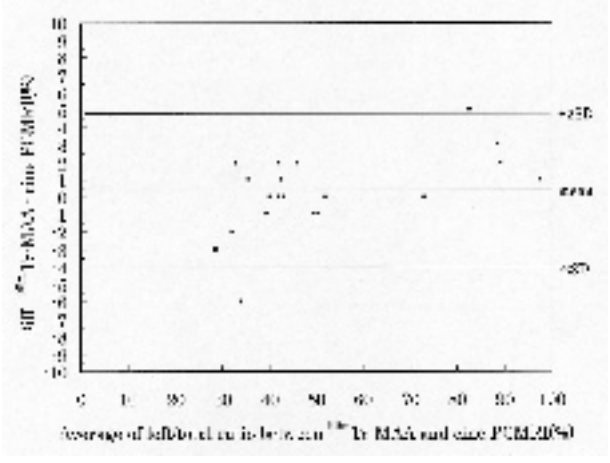


Fig. 2 The plot of difference versus mean for left-to-total ratio of pulmonary ratio by ^{99m}Tc-MAA SPECT and by cine PCMRI.

the mean velocity. The flow volume (ml/min) was calculated by integrating the products of mean velocity and area of ROI on 16 frames, and heart rate (/min). The left-to-total pulmonary flow ratio was calculated from the left and right pulmonary flow values.

^{99m}Tc-MAA SPECT and MR data were processed by independent operators who were blind to the data obtained by the other method.

Quantification of Regional Pulmonary Flow

We proposed the method of regional pulmonary flow quantification with ^{99m}Tc-MAA SPECT and cine PCMRI. The rationale of regional pulmonary flow quantification is simple: The regional flow can be quantified by the concomitant use of the ratio of regional-to-unilateral total count on ^{99m}Tc-MAA SPECT and the ipsilateral pulmonary flow measured with cine PCMRI. We, therefore, developed a computer program for quantifying regional

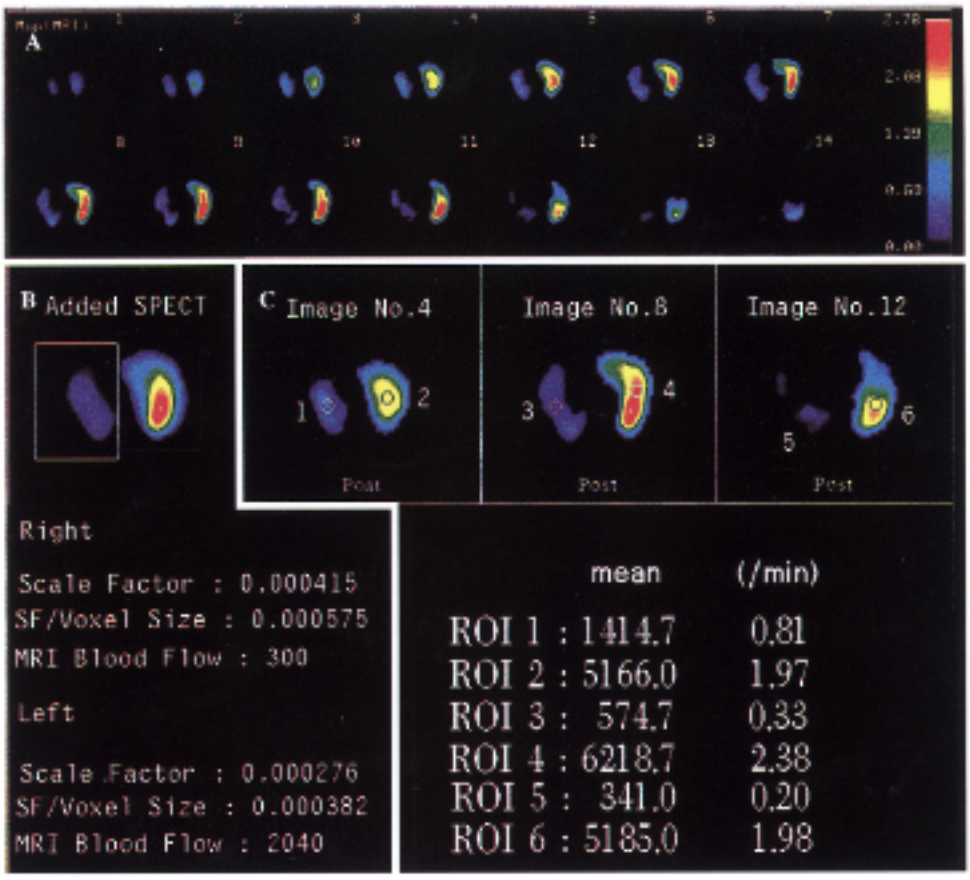


Fig. 3 (A) ^{99m}Tc-MAA SPECT images. (B) Scale factor per voxel volume of each lung is calculated from SPECT and MRI data. (C) ROIs are placed on selected SPECT images. Regional pulmonary flow in each ROI is calculated from the scale factor per voxel volume and the mean count per voxel.

pulmonary flow in any region. At first the ratio of the unilateral pulmonary flow to the total count for the ipsilateral lung was taken as the scale factor (m*l*/min/count), and the scale factor per voxel volume (/min/count) was also calculated (the scale factor divided by voxel volume). Secondly, a ROI was placed on a ^{99m}Tc-MAA SPECT image and the mean count per voxel volume in the ROI was determined. Finally, the regional pulmonary flow (m*l*/m*l* lung/min) was determined by multiplying the scale factor per voxel volume by the mean count per voxel in the ROI.

Statistical Analysis

Data are shown as mean ± SD. Linear regression analysis and Bland-Altman analysis[22] were used to compare the data obtained from ^{99m}Tc-MAA SPECT and cine PCMRI. A paired Student's t-test was used to determine significance of difference, defined as $p < 0.05$.

RESULTS

The data acquisition of both ^{99m}Tc-MAA SPECT and cine PCMRI was successful in all patients. A summary of the data obtained with ^{99m}Tc-MAA SPECT and cine PCMRI is shown in Table 2. The left-to-total ratios obtained with ^{99m}Tc-MAA SPECT and cine PCMRI were 52.0 ± 22.1% and 52.2 ± 20.8%, respectively, showing no significant difference ($p = 0.64$). Four patients had total pulmonary blood flows of 3000 m*l*/min or less, but the patients were physically small individuals, and all had a cardiac index greater than 2000 m*l*/min/m^2. Figure 1 shows the linear regression analysis of the left-to-total ratio obtained with ^{99m}Tc-MAA SPECT vs. cine PCMRI. The ratio of ^{99m}Tc-MAA distribution (y) and the ratio measured with cine PCMRI (x) showed an excellent correlation ($y = 1.06x - 2.66$, $r = 0.99$, $n = 20$, $p < 0.001$). Figure 2 shows the agreement between the two methods according to the Bland-Altman plot. The mean difference was 0.25 ± 2.3% with 95% confidence interval −0.84 to 1.34.

A case of regional pulmonary quantification in a patient (patient 8) with acute radiation pneumonitis is shown in Figure 3.

DISCUSSION

In the present study we evaluated the relationship between

left and right pulmonary arterial flow measured with cine PCMRI and the distribution in each lung on ^{99m}Tc-MAA SPECT, and demonstrated good agreement between the two methods. The results indicate that regional pulmonary flow can be quantified by combined use of ^{99m}Tc-MAA SPECT and cine PCMRI.

Cine PCMRI can provide noninvasive measurement of blood flow velocity and volume. Cardiovascular applications have also been reviewed.[23,24] Cine PCMRI of the main pulmonary artery has been used for shunt volume quantification in congenital heart disease[25] and flow profile analysis in pulmonary hypertension.[26,27] With regard to proximal left and right pulmonary arteries, cine PCMRI is applicable to left and right main pulmonary arterial flow quantification.[19,21] Nevertheless, peripheral pulmonary arterial flow measurements by cine PCMRI are limited and nonrealistic due to several factors: a) artifacts due to cardiac and respiratory motion and susceptibility effects arising from air may result in erroneous measurement; b) difficulty in determination of anatomically complex vessels; and c) considerable time consumption due to the increasing number of vessels.

Doppler echocardiography and right heart catheterization (RHC) with a thermodilution catheter also enable measurement of pulmonary arterial blood flow. Echocardiography has the advantages of noninvasiveness and simplicity, but the accuracy of flow measurement is dependent on the operator's skill and availability of an acoustic window. With echocardiography, it is also difficult to quantify blood flow in the left and right pulmonary arteries separately. RHC has some limitations for the assessment of low cardiac output,[28] and is so invasive that it is not suitable for routine and repeated patient assessment.

^{99m}Tc-MAA pulmonary SPECT allows for the noninvasive and quantitative study of the three-dimensional distribution of pulmonary circulation and has been widely used for pulmonary perfusion assessment.[12–18] Recently, MRI of pulmonary perfusion has become feasible and is a promising technique for detecting lung perfusion defects,[29] but this technique cannot provide quantitative assessment of pulmonary perfusion.

The threshold value of 20% was used to exclude scatter on ^{99m}Tc-MAA SPECT images in this study. Although we preliminarily compared the left-to-total count ratio obtained with five different threshold values (0, 10, 20, 30, 40%) with the flow ratio determined with cine PCMRI, there were no significant differences among the threshold values (unpublished data). Determination of lung contours on ^{99m}Tc-MAA SPECT is especially necessary for comparison with other methods such as CT or ventilation SPECT.

It is necessary to determine each lung contour separately on SPECT, because when the perfusion of a unilateral lung is remarkably reduced such as in patients 3, 5, 8 and 14, the size of the affected lung is underestimated if the same threshold value is applied. This separate determination of each lung outline allowed us to obtain excellent agreement for the left-to-total ratio obtained with ^{99m}Tc-MAA SPECT and cine PCMRI despite various perfusion abnormalities of the affected lungs among patients.

A right-to-left cardiac or pulmonary shunt causes abnormal extrapulmonary accumulation of ^{99m}Tc-MAA[30] and results in overestimation in quantification of the regional pulmonary flow. Our study population did not contain any patients with right-to-left shunt, including congenital heart disease, pulmonary arteriovenous fistula and liver cirrhosis. In such patients, the quantification of the regional pulmonary flow should be preceded by evaluation of the shunt ratio for the whole body ^{99m}Tc-MAA scans.

Serizawa et al.[31] and Schuster et al.[32] reported methods for measuring regional pulmonary flow *in vivo* with $H_2{}^{15}O$ and PET, based on a one compartment model. In comparison with their methods, the theory of our method is simple, based on the determination of flow volume at the level of the main left and right pulmonary arteries with MRI and regional flow ratio with ^{99m}Tc-MAA SPECT, and avoids complicated procedures and the limitations of PET.

The disadvantage of our method of regional pulmonary quantification is that it requires two imaging methods, but MRI provides morphological information on the mediastinum, heart and pulmonary hilar regions, and ^{99m}Tc-MAA SPECT enables assessment of pulmonary flow distribution. Recently, combinations of two or more imaging techniques are more frequently used in the assessment of lesions such as fusion of PET and CT.

Abnormalities in the distribution of pulmonary perfusion are seen in a wide variety of pathological pulmonary vessels, including pulmonary embolism, pulmonary stenosis, primary pulmonary hypertension, Takayasu's arteritis and other types of vasculitis. Moreover, many airway diseases or other causes can result in abnormal perfusion, including asthma, chronic obstructive pulmonary disease (COPD), infection, radiation therapy and chemotherapy, etc. Quantification of regional pulmonary flow is useful in analyzing the physiology and pathology of the lung, and could be applied to assess response to therapy and make a prognosis. Another potential clinical application is to predict pulmonary function after lung or lobe resection, but further studies are required to estimate the clinical significance of measuring regional pulmonary flow.

Assessment of ventilation/perfusion (V_A/Q) ratios is significant because V_A/Q unevenness is a prominent cause of hypoxemia. Radionuclide study is the only method to assess V_A/Q unevenness among imaging methods. Recently, several attempts have been made to image ventilation and perfusion distributions by means of dual radionuclide SPECT, which is a useful method for evaluating the regional V_A/Q ratio,[33–38] but the absolute values

of regional V_A/Q ratios have not yet been determined in radionuclide examinations. Almquist et al.[39] reported a method to obtain regional V_A/Q ratios with ^{133}Xe and SPECT, but this is not ideal because of underestimation as the authors mentioned. In this study, absolute values of the regional pulmonary flow were measured by our method. Therefore, if a technique to quantify regional alveolar ventilation volume is developed, the absolute regional V_A/Q ratios can be determined.

CONCLUSION

We demonstrated excellent correlation and agreement between the left-to-total ratio of ^{99m}Tc-MAA distribution and that of pulmonary arterial flow measured with cine PCMRI. The results indicate that regional pulmonary perfusion is quantified with the combined use of left and right pulmonary flows measured with cine PCMRI and the regional distribution on ^{99m}Tc-MAA SPECT images. This is a simple, accurate and practical method for quantification of regional pulmonary flow. Further studies are required to estimate the clinical significance of this measurement in various pathological entities.

ACKNOWLEDGMENTS

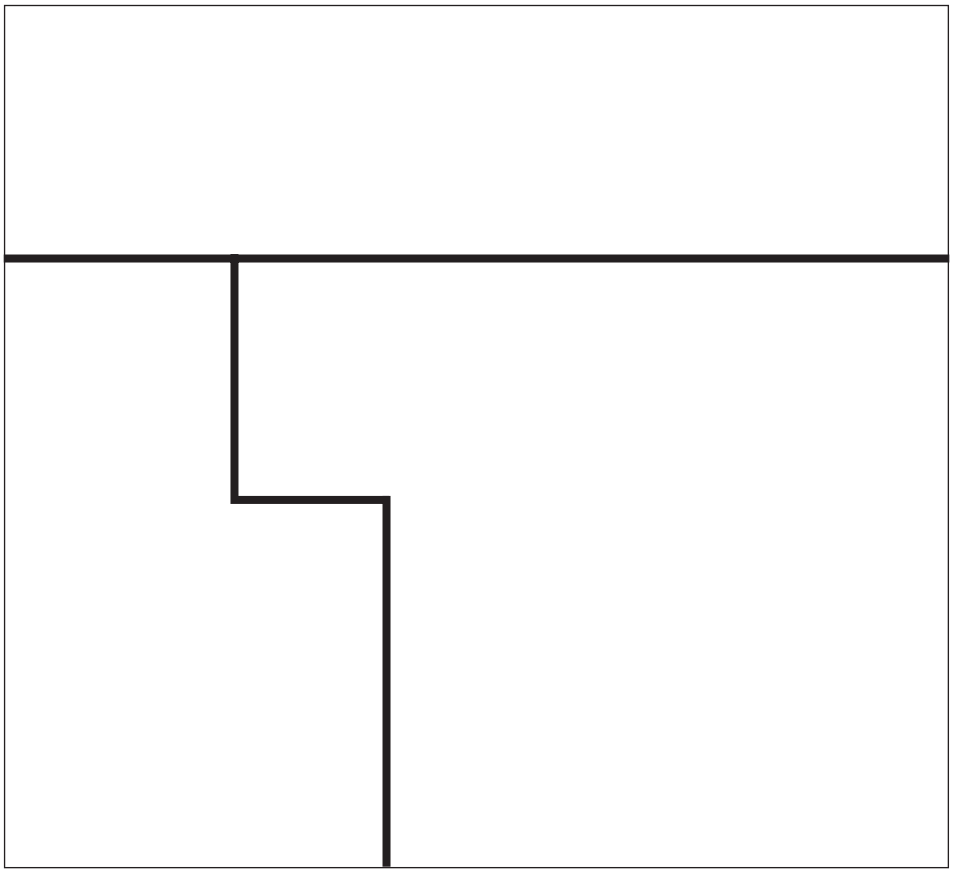
The authors are grateful to Makoto Hosono M.D., Takeo Takahashi M.D. and Akio Kashimada M.D. for valuable advice.

This work was supported by a grant from the Japanese Ministry of Education (No. 10670869).

REFERENCES

1. Moran PR. A flow velocity zeugmatographic interlace for NMR imaging in humans. *Magn Reson Imaging* 1982; 1: 197–203.
2. Nayler GL, Firmin DN, Longmore DB. Blood flow imaging by cine magnetic resonance. *J Comput Assist Tomogr* 1986; 10: 715–722.
3. Pelc LR, Pelc NJ, Rayhill SC, Castro LJ, Glover GH, Herfkens RJ, et al. Arterial and venous blood flow: noninvasive quantitation with MR imaging. *Radiology* 1992; 185: 809–812.
4. Marks MP, Pelc NJ, Ross MR, Enzmann DR. Determination of cerebral blood flow with a phase-contrast cine MR imaging technique: evaluation of normal subjects and patients with arteriovenous malformations. *Radiology* 1992; 182: 467–476.
5. Kashimada A, Machida K, Honda N, Mamiya T, Takahashi T, Kamano T, et al. Measurement of cerebral blood with two-dimensional cine phase-contrast MR imaging: evaluation normal subjects and patients with vertigo. *Radiation Medicine* 1995; 13: 95–102.
6. Applegate GR, Thaete FL, Meyers SP, Davis PL, Talagala SL, Recht M, et al. Blood flow in the portal vein: velocity quantitation with phase-contrast MR angiography. *Radiology* 1993; 187: 253–256.
7. Burkart DJ, Johnson CD, Ehman RL, Weaver AL, Ilstrup DM. Evaluation of portal venous hypertension with cine phase-contrast MR flow measurements: high association of hyperdynamic portal flow with variceal hemorrhage. *Radiology* 1993; 188: 643–648.
8. Kondo C, Caputo GR, Semelka R, Foster E, Shimakawa A, Higgins CB. Right and left ventricular stroke volume measurements with velocity-encoded cine MR imaging: *in vitro* and *in vivo* validation. *AJR Am J Roentgenol* 1991; 157: 9–16.
9. Niezen RA, Doornbos J, van der Wall EE, de Roos A. Measurement of aortic and pulmonary flow with MRI at rest and during physical exercise. *J Comput Assist Tomogr* 1998; 22 (2): 194–201.
10. Dulce MC, Mostbeck GH, O'Sullivan M, Cheitlin M, Caputo GR, Higgins CB. Severity of aortic regurgitation: interstudy reproducibility of measurements with velocity-encoded cine MR imaging. *Radiology* 1992; 185: 235–240.
11. Honda N, Machida K, Hashimoto M, Mamiya T, Takahashi T, Kamano T, et al. Aortic regurgitation: quantitation with MR imaging velocity mapping. *Radiology* 1993; 186: 189–194.
12. Carratu L, Salvatore M, Lopez-Majano V, Sofia M, Muto P, Ariemma G. Single photon emission computed tomography study of human pulmonary perfusion: preliminary findings. *Nucl Med Commun* 1984; 5: 91–99.
13. Touya JJ, Corbus HF, Savala KM, Habibe MN. Single photon emission computed tomography in the diagnosis of pulmonary thromboembolism. *Semin Nucl Med* 1986; 16: 306–336.
14. Hirose Y, Imaeda T, Doi H, Kokubo M, Sakai S, Hirose H. Lung perfusion SPECT in predicting postoperative pulmonary function in lung cancer. *Ann Nucl Med* 1993; 7: 123–126.
15. Ogawa Y, Nishimura T, Hayashida K, Uehara T, Shimonagata T. Perfusion lung scintigraphy in primary pulmonary hypertension. *Br J Radiol* 1993; 66: 677–680.
16. Marks LB, Munley MT, Spencer DP, Sherouse GW, Bentel GC, Hoppenworth J, et al. Quantification of radiation-induced regional lung injury with perfusion imaging. *Int J Radiat Oncol Biol Phys* 1997; 38: 399–409.
17. Suga K, Nishigauchi K, Matsunaga N, Kawakami Y, Kume N, Sugi K, et al. Three-dimensional surface displays of perfusion SPET in the evaluation of patients with pulmonary emphysema for thoracoscopic lung volume reduction surgery. *Nucl Med Commun* 1997; 18: 719–727.
18. Mitomo O, Aoki S, Tsunoda T, Yamaguchi M, Kuwabara H. Quantitative analysis of nonuniform distributions in lung perfusion scintigraphy. *J Nucl Med* 1998; 39: 1630–1635.
19. Silverman JM, Julien PJ, Herfkens RJ, Pelc NJ. Quantitative differential pulmonary perfusion: MR imaging versus radionuclide lung scanning. *Radiology* 1993; 189: 699–701.
20. Gamroth AH, Schad LR, Wacker CM, Gehling U, Knopp MV, Betsch B, et al. MR blood velocity measurements in the pulmonary arteries with magnetic resonance imaging. *Radiologe* 1992; 32: 182–184. German.
21. Caputo GR, Kondo C, Masui T, Geraci SJ, Foster E, O'Sullivan MM, et al. Right and left lung perfusion: *in vitro* and *in vivo* validation with oblique-angle, velocity-encoded cine MR imaging. *Radiology* 1991; 180: 693–698.
22. Bland JM, Altman DG. Statistical methods for assessing

agreement between two methods of clinical measurement. *Lancet* 1986; 1: 307–310.
23. Rebergen SA, van der Wall EE, Doornbos J, de Roos A. Magnetic resonance measurement of velocity and flow: technique, validation, and cardiovascular applications. *Am Heart J* 1993; 126: 1439–1456.
24. Pelc NJ, Sommer FG, Li KCP, Brosnan TJ, Herfkens RJ, Enzmann DR. Quantitative magnetic resonance flow imaging. *Magn Reson Q* 1994; 10: 125–147.
25. Brenner LD, Caputo GR, Mostbeck G, Steiman D, Dulce M, Cheitlin MD, et al. Quantification of left to right atrial shunts with velocity encoded cine nuclear magnetic resonance imaging. *J Am Coll Cardiol* 1992; 20: 1246–1250.
26. Kondo C, Caputo GR, Masui T, Foster E, O'Sullivan M, Stulbarg MS, et al. Pulmonary hypertension: pulmonary flow quantification and flow profile analysis with velocity-encoded cine MR imaging. *Radiology* 1992; 183: 751–758.
27. Tardivon AA, Mousseaux E, Brenot F, Bittoun J, Jolivet O, Bourroul E, et al. Quantification of hemodynamics in primary pulmonary hypertension with magnetic resonance imaging. *Am J Respir Crit Care Med* 1994; 150: 1075–1080.
28. Hillis LD, Firth BG, Winniford MD. Analysis of factors affecting the variability of Fick versus indicator dilution measurements of cardiac output. *Am J Cardiol* 1985; 56: 764–768.
29. Berthezene Y, Croisille P, Wiart M, Howarth N, Houzard C, Faure O, et al. Prospective comparison of MR lung perfusion and lung scintigraphy. *J Magn Reson Imaging* 1999; 9: 61–68.
30. Kume N, Suga K, Uchisako H, Matsui M, Shimizu K, Matsunaga N. Abnormal extrapulmonary accumulation of ^{99m}Tc-MAA during lung perfusion scanning. *Ann Nucl Med* 1995; 9: 179–184.
31. Serizawa S, Suzuki T, Niino H, Arai T, Hara T. Using $H_2(^{15})O$ and $C^{15}O$ in noninvasive pulmonary measurements. *Chest* 1994; 106: 1145–1151.
32. Schuster DP, Kaplan JD, Gauvain K, Welch MJ, Markham J. Measurement of regional pulmonary blood flow with PET. *J Nucl Med* 1995; 36: 371–377.
33. Lavender JP, Al-Nahhas AM, Myers MJ. Ventilation perfusion ratios of the normal supine lung using emission tomography. *Br J Radiol* 1984; 57: 141–146.
34. Klumper A, Zwijnenburg A. Dual isotope ($^{81}Kr^{m}$ and $^{99}Tc^{m}$) SPECT in lung function diagnosis. *Phys Med Biol* 1986; 31: 751–761.
35. Narabayashi I, Suematsu T, Suematsu C. Assessment of SPECT ventilation-perfusion imaging in patients with lung cancer. *Eur J Nucl Med* 1986; 12: 329–332.
36. Honda N, Machida K, Mamiya T, Takahashi T, Kamano T, Kashimada A, et al. Dual-energy data acquisition for simultaneous ^{81m}Kr ventilation/^{99m}Tc-MAA perfusion SPECT: ventilation/perfusion ratio mapping in cross section. *KAKU IGAKU (Jpn J Nucl Med)* 1993; 30: 789–794. [Japanese]
37. Sando Y, Inoue T, Nagai R, Endo K. Ventilation/perfusion ratios and simultaneous dual-radionuclide single-photon emission tomography with krypton-81m and technetium-99m macroaggregated albumin. *Eur J Nucl Med* 1997; 24: 1237–1244.
38. Sasaki Y, Imai T, Shinkai T, Ohishi H, Otsuji H, Uchida H, et al. Estimation of regional lung function in interstitial pulmonary disease using ^{99m}Tc-Technegas and ^{99m}Tc-macroaggregated albumin single-photon emission tomography. *Eur J Nucl Med* 1998; 25: 1623–1629.
39. Almquist H, Jonson B, Palmer J, Valind S, Wollmer P. Regional V_A/Q ratios in man using ^{133}Xe and single photon emission computed tomography (SPECT) corrected for attenuation. *Clin Physiol* 1999; 19: 475–481.



A B C