Estimation of Pulmonary Blood Flow by ^{131}I -MAA Pulmogram with Special Reference to Pulmonary Carcinoma before and after Radiotherapy

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The scintigram obtained on the lung with iodine-131 tagged macroaggregated albumin (^{131}I -MAA) demonstrates the distribution of pulmonary blood flow. Therefore, this technique is often utilized to estimate the relative amount of bilateral pulmonary blood flow on the basis of density appearing on the scintigram. As is well known, however, the scintigram is usually affected by the factors of the scanner used.

In the method to be reported here, which is also applied to estimate the relative amount of bilateral pulmonary blood flow, a specially designed slit-type collimator is used to obviate the above-mentioned disadvantages. According to this technique, the amount of blood flow is shown as a curve having two peaks corresponding to each lung. This method is not affected by the factors of the scanner and is very easy to perform. The authors applied this on cases of pulmonary carcinoma to investigate changes in pulmonary blood flow in connection with radiotherapy. In 5 out of 9 cases of hilar type there was a marked improvement in the pulmonary blood supply. In peripheral type, however, no improvement was detected in all 4 cases.

Since Taplin¹ developed macroaggregated albumin (MAA) in 1963, the visualization of the lung by scintiscanning technique has drawn many workers' attention, and MAA tagged with iodine-131 is now widely accepted for use in many laboratories. Because of the relatively unstable nature of MAA particles, there are several modifications^{2,3} in the preparation of ^{131}I -MAA suspension. In Japan, Ogawa *et al*³ succeeded after much effort in obtaining stable ^{131}I -MAA suspension of relatively constant particle size. This radiopharmaceutical is now being supplied by Daiichi Pure Chemical Co. Ltd. This lung scintiscanning technique is based on the trapping mechanism of microemboli of ^{131}I -MAA particles in the pulmonary capillaries. Therefore, the picture of lung appearing on the scan shows the distribution of blood flow through the pulmonary artery. For this reason, the lung scanning is regarded as one of the best methods for the detection of pulmonary infarction, and it is also used to estimate the relative amount of pulmonary blood

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supply.^{4,5} As is well known, however, the patterns of the scintigram (contrast, size and shape of distribution *etc.*) are always influenced by the type of collimator, rate down settings and erasing level *etc.* Therefore, the methods utilizing the scintigram as a parameter for estimation of the amount of pulmonary blood supply may lead to erroneous judgment.

The method to be reported here is devised to obviate the above-mentioned disadvantages, and it is called ^{131}I -MAA pulmogram by the authors. This technique was presented at the 25th annual meeting of Japan Radiological Society in 1966.

METHOD

1) *Equipments.* Shimazu Scientiscanner SCC-30 (crystal of 3×2 inches) (Fig. 1), specially designed slit-type collimator with two wedge-shaped adaptors (Figs. 2 and 3) and Yokokawa one-pen recorder.

Fig. 1. The picture shows actual performance. The collimator is attached to the probe which moves over the patient's chest from right to left. The ^{131}I -MAA pulmogram is obtained synchronously on the recorder which is shown on the right of the scanner.

2) *Technical details.* Fifty μCi of ^{131}I -MAA is administered intravenously to a patient lying in a supine position. The slit-type collimator is then attached to the scintillation probe so that the longer dimension of the slit parallels the longitudinal axis of the body. While the scintillation probe moves over the patient's chest from right to left at a speed of 30 cm/min, the radioactivity detected is synchronously recorded.

First, the entire lung field is examined with the above-mentioned slit-type collimator in a continuous movement. Two wedge-shaped adaptors are next inserted to narrow the collimator field. The upper and lower fields of the lungs

Fig. 2. A: Specially designed slit-type collimator for the total lung field. Slit measures 3×160 mm on the side facing to the patient, 25×75 mm at the probe side and 80 mm in depth.

B: Two wedge-shaped adaptors. They are inserted into the slit for examining upper and lower lung fields separately, making the slit size of 3×50 mm on the patient side and 25×65 mm on the probe side.

Fig. 3. The collimator field obtained by Tsuyat scan technique. The probe moves to the direction as indicated by the arrow.

are then examined separately. During this procedure, the geometrical relation between the collimator and the patient must be kept constant. In the examination of the entire lung field, therefore, the mid point of the longer dimension of the slit is set on the mid point between the sternal notch and the xyphoid. For the examina-

tion of the upper lung field, the cranial end of the slit narrowed by the inserted adaptors is set on the sternal notch; and for the lower lung field, the cranial end is set at the mid point between the sternal notch and the xyphoid.

RESULTS

1) *Normal subjects.* ^{131}I -MAA pulmograms have been obtained from 5 normal subjects. The mean value of the right to left ratio in the amount of pulmonary blood flow was 53.7: 46.3, as shown in Fig. 4.

Fig. 4 A

Fig. 4 B

Fig. 4. Normal subject.

A: ^{131}I -MAA pulmogram. B: Lung scintigram.

2) *Benign mediastinal tumor.* Three cases of benign mediastinal tumor have been examined by using ^{131}I -MAA. The pattern of the scintigram shows a simple defect on its mediastinal side and the lung field close to it is uniformly well visualized on the scan usually. This is different from the usual patterns of pulmonary carcinoma which often show a cold area having indistinct boundaries on the scan. ^{131}I -MAA pulmogram reveals nearly normal ratio of the right to the left lung (Fig. 5).

Fig. 5 A

Fig. 5 B

Fig. 5. Y.S. a 52-year-old female. Benign mediastinal tumor. A: ^{131}I -MAA pulmogram shows almost normal distribution of pulmonary blood flow to bilateral lungs. B: Lung scintigram. The arrow indicates the defect caused by the tumor. The lung field neighboring the defect shows almost normal blood flow.

3) *Pulmonary carcinoma in connection with radiotherapy.* We have obtained ^{131}I -MAA pulmograms on 13 cases of pulmonary carcinoma. There were 9 cases of hilar type (5 anaplastic cell carcinomas, 3 squamous cell carcinomas, and 1 adenocarcinoma) and 4 cases of peripheral type (2 squamous cell carcinomas and 2 adenocarcinomas). As a rule, the total radiation dose ranged between 3,800 and 10,000 rads with 6 MeV Linac x-ray. In this series, all the cases were determined on the type of histology by Tsuboi's Transbronchial Biopsy⁶ before the initiation of radiotherapy. Out of 9 cases of hilar type, 5 cases (3 anaplastic cell carcinomas, 1 squamous cell carcinoma and 1 adenocarcinoma) showed a definite improvement in

Fig. 6 A

Fig. 6 B

Fig. 6 C

Fig. 6 D

Fig. 6. S.H. a 57-year-old male. Left pulmonary carcinoma (adenocarcinoma), hilar type.

A: ^{131}I -MAA pulmogram obtained before radiotherapy. The upper and lower fields of the left lung show a marked decrease in pulmonary blood flow.

B: ^{131}I -MAA pulmogram obtained after radiotherapy (6,000 rads of Linac x-ray).

The pulmonary blood flow is markedly increased in the upper and lower fields of the left lung.

C: Lung scintigram obtained before radiotherapy. A cold area is seen in the left upper field. The left lower field shows a less remarkable accumulation of radioactivity in comparison with the other side.

D: Lung scintigram obtained after radiotherapy. The upper field of the left lung is well visualized on the scintigram.

the pulmonary blood supply on ^{131}I -MAA pulmogram after the radiotherapy (Fig. 6). In the above-mentioned 5 cases, 3 (1 anaplastic cell carcinoma, 1 squamous cell carcinoma and 1 adenocarcinoma) showed almost a complete return of the pulmonary blood supply to a normal level (Fig. 7). The remaining 4 cases (2 anaplastic cell carcinomas, and 2 squamous cell carcinomas) did not show any improvement on the ^{131}I -MAA pulmogram. In those 4, one of the cases of anaplastic cell carcinoma had a huge roentgenologically demonstrable lesion in the right hilar area, and one of the cases of squamous cell carcinoma developed pyothorax and the patient died several weeks later.

In all the 4 cases of peripheral type, no improvement in the pulmonary blood supply was recognized on the ^{131}I -MAA pulmogram upon completion of radiotherapy. Especially, one case of adenocarcinoma and one case of squamous cell carcinoma showed a marked decrease in pulmonary blood flow even though x-ray findings revealed a good response to the radiotherapy (Fig. 8).

Fig. 7 A

Fig. 7 B

Fig. 7. K.N. a 65-year-old female. Right pulmonary carcinoma (anaplastic cell carcinoma), hilar type.

A: ^{131}I -MAA pulmogram obtained before radiotherapy. There is a marked decrease in the right pulmonary blood flow, especially in the lower field.

B: ^{131}I -MAA pulmogram obtained after radiotherapy (6,150 rads of Linac x-ray). The pulmonary blood flow on the affected side returned almost completely to a normal level.

Fig. 8 A

Fig. 8 B

Fig. 8 C

Fig. 8 D

Fig. 8 E

Fig. 8 F

Fig. 8. T.S. a 77 year-old male. Right pulmonary carcinoma (squamous cell carcinoma), peripheral type.

A: ^{131}I -MAA pulmogram obtained before radiotherapy. The right to left ratio of the pulmonary blood flow is 57.4: 42.6 in the total lung field.

B: ^{131}I -MAA pulmogram obtained after radiotherapy (3,800 rads of Linac x-ray). The right to left ratio became 46.2: 53.8, indicating a marked decrease of the pulmonary blood flow on the irradiated side.

C: Lung scintigram obtained before radiotherapy. The middle field of the right lung shows the area where the pulmonary blood flow is slightly decreased.

D: Lung scintigram obtained after radiotherapy. There is a marked decrease in the pulmonary blood flow in the irradiated area of the middle to lower field

COMMENT

Before the introduction of ^{131}I -MAA into the lung scintiscanning, ceramic microspheres containing radioactive nucleides had been used in experimental animals or in patients in their terminal stage.^{7,8} However, this technique has an inevitable danger to humans, because the particles stay within the pulmonary capillaries throughout the life. Therefore, this method could not come into routine laboratory procedure. On the other hand, it is known that the patency of the capillaries is restored in a relatively short time, after ^{131}I -MAA particles have once stuck as microemboli.

Tow *et al.*⁵ reported that the effective half life of ^{131}I -MAA in the lung was 0.31 ± 0.06 days. According to the recent paper of DeLand,⁹ the decrease in the radioactivity of ^{131}I -MAA in the lung could be approximated by at least three exponential functions with biological half times of 0.25, 3.0 and 55 days. As mentioned already, this ^{131}I -MAA scintiscanning technique is one of the best methods to demonstrate pulmonary infarction. In some diseases, however, conventional methods such as roentgenologic examinations are much superior to scintiscanning technique that has inevitably a limitation in its resolution capacity. Furthermore, the lung has not only a considerable thickness, but also respiratory movement which cannot be stopped during the examination. Therefore, it cannot be expected that the scintigram yields so sharp a delineation of tumor lesions as the chest x-ray film. As far as the diagnosis of pulmonary carcinoma is concerned, we consider that it is not theoretically acceptable to use a collimator of high resolution and a large amount of ^{131}I -MAA for a good visualization. From this point of view, our main effort is made to know the change in the amount of pulmonary blood flow with ^{131}I -MAA pulmogram during radiotherapy and not to establish the diagnosis of pulmonary carcinoma. The scintigram with a rather sensitive 37 hole honey comb collimator which has rather poor resolution is effective enough to demonstrate a rough distribution of the pulmonary blood flow. The dose given to the patients is only $50 \mu\text{Ci}$.

There have been several papers in regard to the estimation of pulmonary blood flow by using ^{131}I -MAA scintiscanning technique. In Japan, Ueda *et al.*⁴ reported their own method in which the number of dots on the scintigram was used as an indicator for pulmonary blood flow. Others⁵ use the density appearing on the scan film for the same purpose. However, the shape and the contrast are always influenced by the type of the collimator used, as well as the rate down settings or the erasing level *etc.* Furthermore, the external counting such as scintigraphy is influenced by the distance between the probe and organ. This becomes especially important when thick organs are scanned. As shown in Fig. 3, the field of our slit-type collimator diverges as the collimator is farther apart from the object. There-

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of the right lung.

E: Chest x-ray film taken before radiotherapy.

F: Chest x-ray film taken after radiotherapy. The tumor is decreased roentgenologically in its size and consolidation. The fibrotic changes are observed in the irradiated area.

fore, when the probe moves toward the direction as indicated with an arrow in Fig. 3, it will take a longer time to pass over a more distant area resulting in a low count rate than to pass over a nearer area, from which a high count rate is obtained. In other words, the more distant the scanned area is, the longer time will it take for the extended collimator field to pass through the area. This fact will lessen the loss in count rate to some extent, which is caused by the distance between the probe and organ. For example, if the count rate at 7 cm from the tip of the collimator is assumed to be 100% (this means 15 cm from the probe because the collimator has a depth of 8 cm), it becomes in our experiment 86% at 10 cm, and 67% at 15 cm, when the probe moves horizontally. These results are apparently much higher than the count rate which is calculated on the stationary probe, on the basis of reciprocal proportion to the square of distance.

In our experiences in pulmonary carcinoma, 5 out of 9 cases of hilar type showed an improvement in pulmonary blood supply after radiotherapy. Especially in 2 cases, ^{131}I -MAA pulmogram revealed almost a complete recovery of blood flow to the normal level. It is thought that this improvement is due to regression of the mechanical stenosis which has once occurred in the main branches of the pulmonary artery. Therefore, ^{131}I -MAA pulmogram is considered to reflect the degree of improvement in cases of hilar type; in other words, it reveals how much radiotherapy has been effective.

In all the 4 cases of peripheral type, none showed an improvement in pulmonary blood supply after radiotherapy. Furthermore, it would be worthwhile to know that the pulmonary blood flow reflected on ^{131}I -MAA pulmogram showed a marked decrease in 2 cases, even though x-ray films revealed that the tumor shadow had decreased in its extension and consolidation. This may be due to pneumonitis or fibrosis induced by irradiation.

Our pulmogram is very easy to perform, from which a precise information about pulmonary blood flow can be obtained.

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