

## Increased accumulation of iodine-123-IMP in the pulmonary inflammatory lesion surrounding a lung cancer

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In a patient with primary lung cancer, increased accumulation of I-123-IMP was observed in a pulmonary inflammatory lesion surrounding a lung cancer which was delineated as a photon deficient area. Ga-67-citrate uptake was observed in both the inflammatory and cancerous areas. These findings suggest that I-123-IMP may have the potential to accumulate differently in a variety of pathological conditions of the lung and thus may be a clinically useful lung imaging agent.

**Key words:** I-123-IMP, Lung imaging, Pulmonary inflammation, Lung cancer

### INTRODUCTION

N-ISOPROPYL-P-[I-123]IODOAMPHETAMINE (I-123-IMP) was developed as a brain perfusion imaging agent.<sup>1</sup> The utility of this agent in brain studies has been shown in the assessment of pathological states related to cerebral blood flow.<sup>2-6</sup> With whole-body imaging of humans, IMP uptake was seen not only in the brain, but also in the lungs and liver.<sup>2</sup> An incidental finding was that a focal uptake of IMP was related to a patient's bronchogenic carcinoma.<sup>2</sup> This suggests that IMP might also be a useful agent in the assessment of the pathological conditions of the lungs.

We report here a case of increased uptake of IMP in the pulmonary inflammatory lesion surrounding a lung cancer which itself showed diminished accumulation of IMP.

### CASE REPORT

A 48-year-old man was admitted to our hospital on June 30, 1986, with a one-month history of productive cough and a two-week history of high fever. His past history included bronchiectasis diagnosed at the

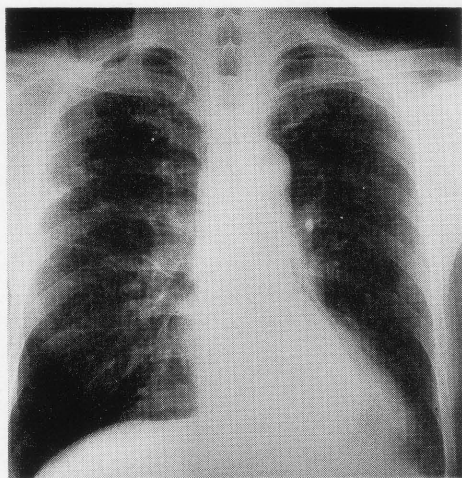
age of 38 and lung abscess located at the right upper lobe at the age of 46. A remittent fever was observed during several days following admission. Chest roentgenograms showed an ill-demarcated homogeneous shadow in the left posterior lower lung field. Chest X-ray tomograms revealed some small radiolucent areas scattered in the homogeneous shadow.

Relevant laboratory findings included white cell count of  $16,000/\text{mm}^3$  (normal range:  $4,000-8,000$ ) with 55% segments, 9% bands, 33% lymphocytes, 1% monocytes and 2% eosinophils; red cell count  $408 \times 10^4/\text{mm}^3$  (normal range:  $450 \times 10^4-510 \times 10^4$ ); hematocrit 32.6% (normal range: 38-54); hemoglobin 10.1 g/dl (normal range: 12.4-17.2); C-reactive protein (CRP) 4+. Sputum yielded *Enterobacter aerogenes* on culture. The provisional diagnosis was lung abscess on the basis of bronchiectasis. Immediately after admission, he was placed on intensive antibiotic therapy.

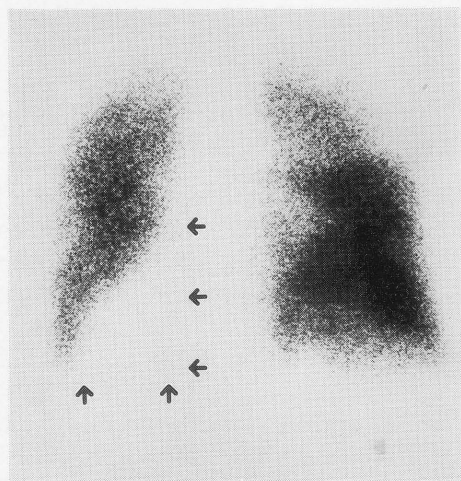
On the tenth hospital day, the chest roentgenogram (Fig. 1) showed a well-demarcated homogeneous shadow due to absorption of the marginal infiltrating shadow. On the same day, fiberoptic bronchoscopy was also performed. It revealed that the orifice of the left laterobasal bronchus was obstructed by a mass with a white surface where the biopsy was performed and the left posterobasal bronchus was stenotic probably due to an extrinsic compression pressure. The pathological diagnosis from the biopsied specimen was that it was composed of inflamed

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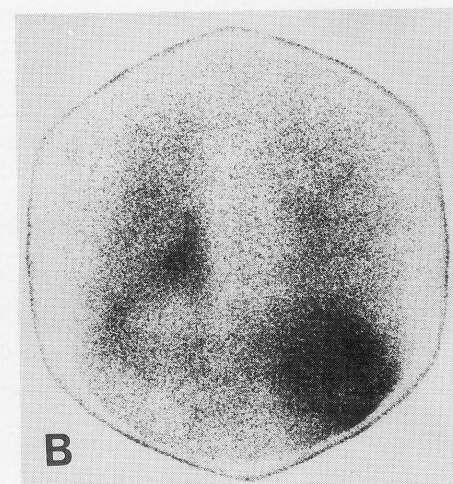
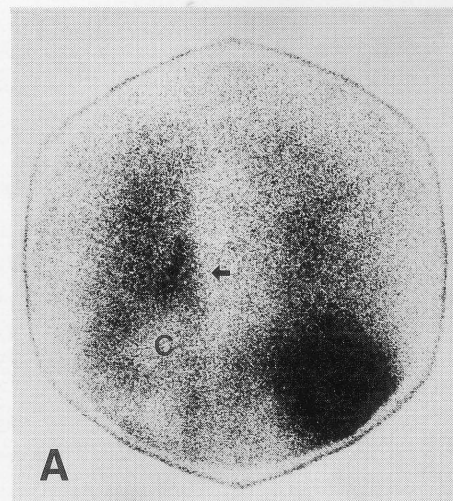
**Fig. 1** A well-demarcated mass shadow overlapping the heart is observed in the left lower lung field in this chest radiograph taken on the same day as I-123-IMP lung imaging was performed.



**Fig. 2** Posterior Tc-99m-MAA lung perfusion image shows a perfusion defect (arrows) in the left lower lung field.

granulation tissue and inflammatory exudate, and there was evidence of neither malignant tissue nor of specific inflammation.

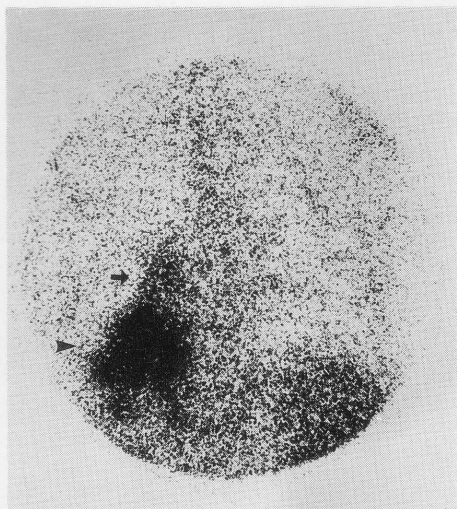
**Radionuclide imaging studies:** On day 8 in hospital, a Tc-99m-MAA lung perfusion scan was performed. It disclosed a perfusion defect in the left posterior lower lung field corresponding to the location of the lesion (Fig. 2). On day 10 in hospital, I-123-IMP lung imaging was performed to examine the imaging findings of the lesion: Thyroidal uptake of I-123 was blocked by oral administration of potassium iodide 300 mg a day beginning on the day before i.v. injection of I-123-IMP and continuing for 3 days afterwards. 1.5 mCi of I-123-IMP containing 0.15 mg/m<sup>l</sup> of IMP in a volume of 1.5 ml was i.v. injected in the supine position. Static chest images



**Fig. 3** Posterior lung I-123-IMP images taken at 30 min (A) and 4 hr (B). In the 30 min image, a triangular shaped accumulation (arrow) is noted in the left S<sub>6</sub> where an inflammatory process was pathologically observed. The cancerous portion (C) is delineated as a photon deficient area. The triangular shaped accumulation and the activity surrounding the cancerous portion became clearer in the 4 hr image.

including anterior, posterior and both lateral views were obtained at 30 min and 4 hrs after i.v. injection of I-123-IMP, by using a gamma camera with a medium energy multi-parallel hole collimator. The energy window was centered on the 159 keV energy emission of I-123 with a 20% width. 500,000 counts were acquired for each view. Data of anterior and posterior static images were recorded in 64 × 64 matrices of a nuclear minicomputer at 30 min and 4 hrs.

The 30-min posterior chest image showed a triangular shaped area of increased uptake of IMP in the superior segment (S<sub>6</sub>) with a photon deficient area just below it in the left lower lung field (Fig. 3A). The intensity of the activity in the triangular and

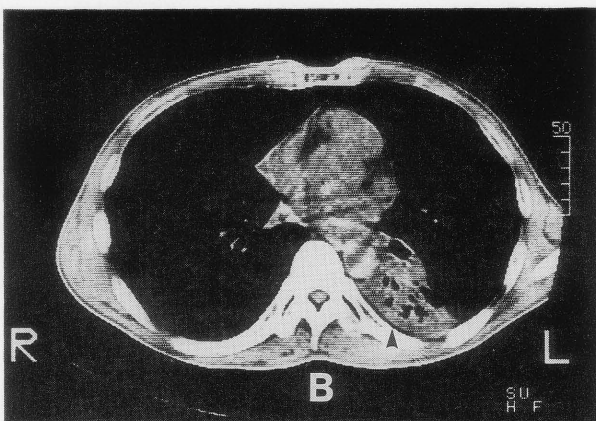
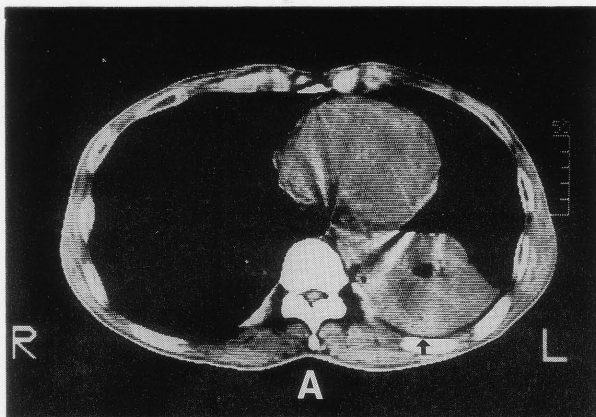


**Fig. 4** Posterior lung Ga-67-citrate image. The tracer accumulated in both the inflammatory (arrow) and cancerous (arrowhead) portions where increased and decreased uptakes of I-123-IMP were respectively observed.

marginal areas of the lesion increased in the 4-hr posterior image (Fig. 3B).

Rectangular regions of interest (ROIs) were set over the triangular shaped area, the photon deficient area and the left upper normal lung field, respectively, to assess the change in activity from 30 min to 4 hr. The size of the ROI was 16 pixels in each region. The counts in each ROI were as follows; 4,945 at 30 min and 5,146 at 4 hr in the triangular shaped area, 2,661 at 30 min and 2,785 at 4 hr in the photon deficient area, and 3,496 at 30 min and 3,017 at 4 hr in the left normal lung field. The acquisition time was 224 sec at 30 min and 215 sec at 4 hr respectively. The radioactivity in each ROI was normalized for acquisition time (180 sec) and radioactive decay (the 4-hr activity was 83% of the 30-min activity). The corrected activity at 4 hr increased to 130% in the triangular shaped area, 131% in the photon deficient area and 108% in the left upper normal lung field, when compared to the activity in each area at 30 min. Between 30 min and 4 hr, the count ratios of the triangular shaped and photon deficient areas to the left upper normal lung field changed from 1.41 to 1.71 and 0.76 to 0.92, respectively. These data indicate that the amount of accumulated activity was larger in the triangular shaped and photon deficient regions than in the upper normal lung field during this period.

The 72-hr Ga-67-citrate imaging was performed 5 days after the I-123-IMP lung scan. The posterior chest Ga-67-citrate image showed an intense Ga-67 accumulation in the massive lesion delineated as a photon deficient area by the I-123-IMP lung scan



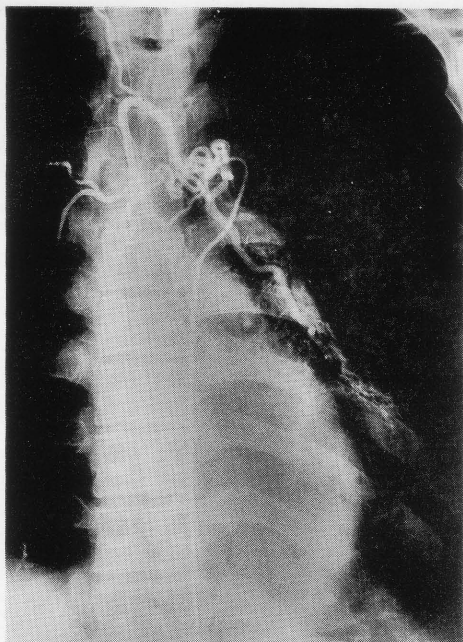
**Fig. 5** TCT image at the level of the cancerous portion (A) in the left S<sub>9</sub> and S<sub>10</sub> shows a well-demarcated homogeneous mass with a few small cavities (arrow). TCT image at the level of the inflammatory portion (B) in the left S<sub>6</sub> shows a well-demarcated inhomogeneous lesion with multiple small cavities due mainly to bronchiectasis (arrowhead).

with a lesser degree of Ga-67 activity in the I-123-IMP hot triangular lesion (Fig. 4).

On day 11 in hospital, TCT (transaxial computed tomography) was performed. It (Fig. 5) showed a well-demarcated soft tissue mass with a small number of air density areas at the level of the main lesion located in the left laterobasal segment (S<sub>9</sub>) and posterobasal segment (S<sub>10</sub>) and a well-demarcated inhomogeneous density lesion with multiple air-containing areas due mainly to bronchiectasis at the level of the triangular region (S<sub>6</sub>). The bronchiectasis was confirmed by bronchography performed on day 36 after admission.

The patient became afebrile on day 26 in hospital, although leukocytosis continued and the mass shadow on the chest roentgenogram was unchanged. He was permitted to go home for 4 days on day 45 in hospital. However, he returned to hospital with recurrent high fever. It was decided to operate on the lesion because of the ineffectiveness of the antibiotic therapy.





**Fig. 6** Bronchial arteriogram shows that the arterial branches were richly distributed in the region where the intense uptake of I-123-IMP was observed, while scanty branches were distributed in the main lesion where the uptake of I-123-IMP was slight.

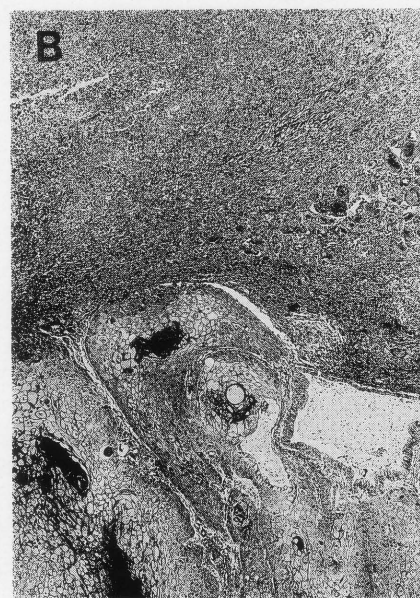
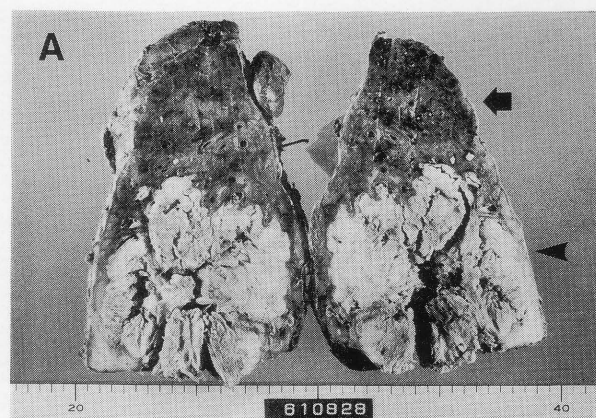
Before operation, on day 52 after admission, he underwent bronchial arterial embolization to reduce the amount of bleeding during operation. The bronchial arteriogram at that time showed a dilated main bronchial artery with hypervascularity in the triangular shaped portion and scanty vascularization in the main lesion which had showed diminished accumulation of I-123-IMP (Fig. 6).

On day 60 after admission, a left lower lobectomy was performed. The specimen was composed of two distinct lesions; the main lesion showed a light gray appearance with many projections from its margin and the surrounding lung tissue showed a dark brownish appearance with bleeding (Fig. 7A). The pathological diagnosis of the main lesion was well differentiated squamous cell carcinoma with hyperkeratinization. Chronic granulomatous inflammation with superimposed acute inflammation was observed in the surrounding lung tissue (Fig. 7B).

Comparison of the findings in the IMP image (Fig. 3) with those in the removed specimen (Fig. 7A) confirmed that I-123-IMP accumulated intensely in the inflammatory lesion and only slightly in the cancerous portion.

## DISCUSSION

I-123-IMP has been proposed as a potentially useful agent for nonparticulate lung perfusion scans as



**Fig. 7** A) Cross section of the removed left lower lobe. The cancerous portion (white color, arrowhead) was surrounded by the inflammatory lung tissue (dark color, arrow). B) Microscopic findings: Dense inflammatory cell infiltration, mainly composed of neutrophils, lymphocytes and multinucleated giant cells, was noted above the cancer nest composed of well differentiated squamous cell carcinoma with conspicuous keratinization (H.E.  $\times 10$ ).

well as for metabolic lung scans.<sup>7</sup> However, the clinical utility of this agent for a variety of pulmonary pathological conditions has not been established. The present case showed that I-123-IMP accumulated intensely in the inflammatory lesion and little in the cancerous portion of the lung.

The mechanism of I-123-IMP uptake in the normal lung has not been fully elucidated, although endothelial amine receptors have been suggested as its binding sites.<sup>8</sup> It has been reported that a turpentine oil-induced abscess in the mouse was visualized with I-123-IMP imaging.<sup>9</sup> However, the mechanism of I-123-IMP accumulation in inflammatory lesions is not known. In the present case, the inflow of I-123-

IMP into the pulmonary inflammatory lesion may be via the pulmonary artery. However, the increased accumulation of I-123-IMP in the inflammatory lesion may not have been due to increased pulmonary arterial blood flow, because the Tc-99m-MAA lung perfusion scan showed a perfusion defect in the region including both the inflammatory and cancerous portions (Fig. 2). Another possible inflow route of I-123-IMP into the lesion is that of the bronchial artery, because the vascular distribution of the lesion in the bronchial arteriogram (Fig. 6) is analogous to the radioactive distribution in the IMP image (Fig. 3). It is not clear which the main inflow route was, because I-123-IMP is a nonparticulate agent and Tc-99m-MAA lung perfusion scans show only the relative distribution of pulmonary arterial blood flow.<sup>10</sup>

The approximately 130% increase in decay corrected activity that was observed in the inflammatory and cancerous portions during the 3.5 hrs from 30 min to 4 hr after i.v. injection of the tracer contrasts with the slight increase or equilibrated state noted in the "normal" lung field during this period. The increase in the cancerous portion may not have been due to accumulation of activity in the cancer itself, but may be due to its accumulation into the inflammatory lesion surrounding the centrally located cancer (Fig. 7A). Quantification of activity by using the SPECT imaging would have clearly answered this hypothesis. These data suggest that during this period, I-123-IMP and/or its undetermined metabolite, if present, was continuously circulating and was trapped by both inflammatory and "normal" lung tissue. Washout of the tracer may be slower from the inflammatory lesion than the "normal" lung tissue, suggesting that there may be different mechanism(s) of storage and/or release of the tracer in the inflammatory lesion and "normal" lung tissue.

The cancer showed diminished accumulation of the tracer. This finding is analogous to that of brain tumors in I-123-IMP brain perfusion imaging;<sup>11</sup> reduced blood flow and/or lack of binding sites may be the mechanisms of the diminished activity in the lung cancer as well as in brain tumors.

Concentration of Ga-67-citrate in a wide variety of malignant and benign lung diseases is well known and specificity is low.<sup>12</sup> Increased accumulation of Ga-67-citrate was observed in both the pulmonary inflammatory and cancerous portions, while I-123-IMP accumulated intensely in the inflammatory lesion and only slightly in the cancerous portion in the present case. These findings suggest that I-123-IMP may have the potential to accumulate differently in

a variety of pathological conditions of the lung and thus may be a clinically useful lung imaging agent.

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