

# Scintigraphy and computed tomography findings for the diagnosis of bronchiolitis obliterans following peripheral blood stem cell transplantation

**Tsuneo Yamashiro<sup>1</sup> MD,**  
**Gyo Iida<sup>1</sup> MD, PhD,**  
**Hisashi Kamiya<sup>1</sup> MD,**  
**Akira Yogi<sup>1</sup> MD,**  
**Sadayuki Murayama<sup>1</sup> MD, PhD,**  
**Shusaku Haranaga<sup>2</sup> MD, PhD,**  
**Satomi Yara<sup>2</sup> MD, PhD**

1. Department of Radiology,  
 Graduate School of Medical  
 Science, University of the Ryukyus,  
 207 Uehara, Nishihara-cho,  
 Okinawa, Japan

2. Department of Medicine and  
 Therapeutics, Control and  
 Prevention of Infectious Diseases,  
 Faculty of Medicine, University  
 of the Ryukyus 207 Uehara,  
 Nishihara-cho, Okinawa, Japan

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## Correspondence address:

Tsuneo Yamashiro, MD  
 Department of Radiology,  
 Graduate School of Medical  
 Science, University of the  
 Ryukyus 207 Uehara, Nishihara-  
 cho, Okinawa 903-0215, Japan  
 TEL: +81-98-895-1162  
 FAX: +81-98-895-1420  
 E-mail: clatsune@yahoo.co.jp

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## Abstract

We report a case of bronchiolitis obliterans (BO) associated with allogenic peripheral blood stem cell transplantation for acute leukemia. On inspiratory and expiratory chest computed tomography (CT), characteristic findings for BO, such as air-trapping, mosaic attenuation or bronchial wall thickening were not clearly observed. However, ventilation-perfusion lung scans of the chest demonstrated multiple matched defects, which suggested severe obstructive airway disease. In the diagnosis of BO after stem cell transplantation, lung scans should be recommended when representative findings are not obvious on chest CT.

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## Introduction

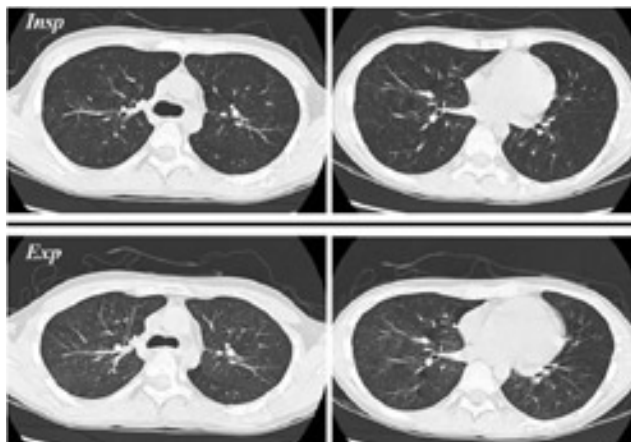
**B**ronchiolitis obliterans (BO) is an airway obstructive disease, and is associated with several conditions, particularly airway infection in childhood, connective tissue diseases, and complications after lung and heart-lung transplantation or allogenic stem cell transplantation for acute/chronic leukemia [1-18]. The utility of computed tomography (CT) for the diagnosis of BO has been reported in several articles, in which characteristic findings are considered to be air-trapping on the expiratory scan and mosaic attenuation (or mosaic perfusion) [2, 3, 5-7, 11-14, 16-18]. However, the latest studies of lung transplant recipients have suggested that the sensitivities of these findings as diagnostic criteria are relatively low, although the specificities of them are relatively high [14]. Another study has shown that the severity of the CT findings does not correlate with the clinical stages of BO [12]. In contrast, there have been many reports on the utility of the ventilation-perfusion lung scan for the diagnosis of post-infectious BO, with an emphasis on the pattern of matched defects, particularly in regard to the Swyer-James-MacLeod syndrome [2, 3, 19, 20]. However, the usefulness of the ventilation-perfusion lung scans has rarely been mentioned for other conditions causing BO and published information on the scintigraphy-based diagnosis for BO after stem cell transplantation is very limited [1, 4, 18]. It can be predicted that the sensitivity of matched defect pattern on lung scans would be very high for the diagnosis of BO: however, it is difficult to diagnose BO based on scintigraphic findings only, since other pulmonary diseases may demonstrate similar findings. Thus, it can be considered that the specificity of lung scans is not high for the diagnosis of BO.

In this report, we describe one patient who was clinically diagnosed with BO following peripheral blood stem cell transplantation (PST). He underwent both thin-section CT and ventilation-perfusion scans. Characteristic findings were not obvious on chest CT and findings of lung scans were definitive for the diagnosis of BO.

## Case report

A 23 years old man presented with cough and breathlessness. He had been diagnosed with acute lymphocytic leukemia at the age of 21, and had been treated with chemotherapy, followed by allogenic PST. Complete remission was achieved and had been maintained. He had also suffered from acute and chronic graft-versus-host disease (GVHD) and had been treated intermittently with corticosteroids and cyclosporine. He did not have a history of smoking. Upon admission to the department of respiratory medicine, his room air arterial blood gas samples showed a PaO<sub>2</sub> of 68mmHg with 93% oxygen saturation, and a PaCO<sub>2</sub> of 40mmHg. Pulmonary function tests revealed a marked decrease in vital capacity (VC)

of 56% predicted, and in forced expiratory volume in 1 sec (FEV<sub>1,0</sub>) of 37% predicted. Initial chest radiographs appeared almost normal except for slight hyperinflation. Inspiratory thin-section CT demonstrated minimal mosaic attenuation in the left lower lobe and slightly decreased lung attenuation bilaterally in the lower lobes. Diminution of pulmonary vascularity, bronchiectasis, deviation of the fissures, and bronchial wall thickening were not observed. Additional expiratory thin-section CT did not demonstrate obvious air-trapping in the both lungs (Fig. 1).

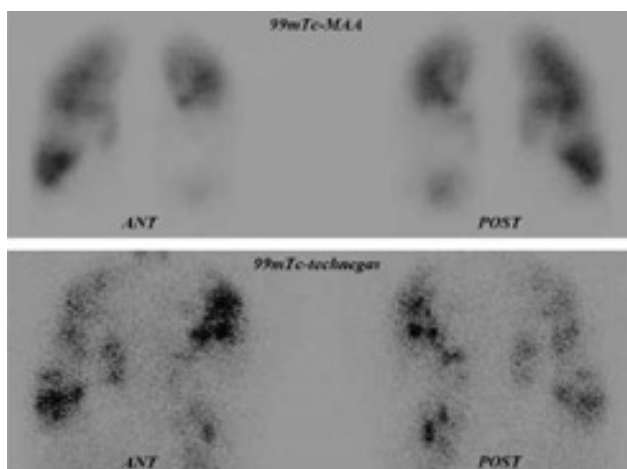


**Figure 1.** Thin-section CT (2.5mm thickness). Inspiratory scan (above) demonstrates minimal hyperlucency, particularly on the lower level. Expiratory scan on the same levels (below) shows the decrease of lung volume and the slight elevation of attenuation, however, does not clarify obvious air-trapping. INSP=inspiratory CT, EXP=expiratory CT

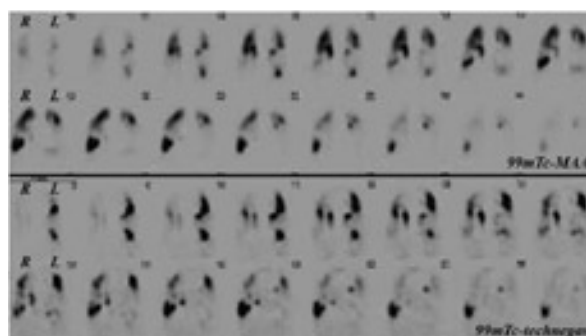
Since the CT findings were not sufficient for the diagnosis of BO, lung scintigraphy was recommended. A technetium-99m-labeled macroaggregated human albumin (<sup>99m</sup>Tc-MAA) perfusion scan was performed after the injection of 406MBq of <sup>99m</sup>Tc-MAA into an antero-cubital vein. The ventilation scan using technegas, technetium-99m-labeled carbon aerosol (<sup>99m</sup>Tc-technegas), was performed after inhalation of technegas with tidal breathing in upright position. Planar images and single photon emission tomography (SPET) images of each scan were obtained by a double headed gamma camera. Obtained images demonstrated severe, essentially matched defects in both lung fields (Fig. 2 and 3). On ventilation scan, some hot spots were observed mainly in the left lung. These hot spots were considered to be partial impactions of aerosol in the relatively severe lesions of BO. The results of these studies led to the diagnosis of BO without lung biopsy. His symptom was improved after he was treated with corticosteroids and cyclosporine.

### Discussion

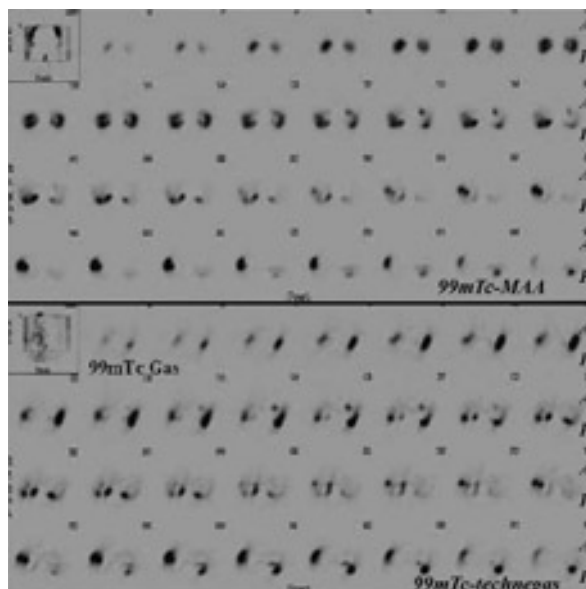
Although BO is considered to be a relatively rare, it has recently become the focus of renewed interest because of the increasing number of patients receiving allografts, including hematopoietic stem cell and heart-lung transplants. One of the most important posttransplantation respiratory complications is BO leading to late morbidity and decreased survival after transplantation. The incidence of BO is reported to be 1.7% to 26% after allogenic stem cell transplantation [8, 9], and approximately 60% after lung transplantation [12,



**Figure 2.** Planar images of lung scans. <sup>99m</sup>Tc-MAA perfusion scan (above) and <sup>99m</sup>Tc-technegas ventilation scan (below) reveal multiple matched defects. On ventilation scan, some hot spots are demonstrated mainly in the left lung. ANT=anterior view. POST=posterior view.



3a



3b

**Figure 3.** SPET images of coronal (3a) and axial views (3b) also demonstrate essentially matched defects. Compared with perfusion scan, ventilation scan reveals relatively high uptakes mainly in the left lung, which are consistent with hot spots on the planar images.

14]. After stem cell transplantation, it has been reported that a mortality rate of BO is very high and overall 5-year survival of patients with BO is significantly less than that of patients without BO [21, 22]. Thus, an accurate diagnosis for early BO is important for subsequent treatment.

While the clinical criteria and classification of bronchiolitis obliterans syndrome by the International Society for Heart and Lung Transplantation are based on the results of pulmonary function tests, in the latest revised guideline chest CT has also been identified as the most accurate imaging tool for diagnosing BO [13]. CT findings of BO have been discussed in several articles, in which air-trapping seen on the expiratory scan is considered to be the most important diagnostic finding [13, 14]. Other findings, including mosaic attenuation (perfusion), diminution of peripheral vascularity, decreased lung attenuation (hyperlucency), bronchiectasis, and bronchial wall thickening, have been reported to be useful for diagnosis [5, 7, 11-14]. However, there seem to be several limitations to CT diagnosis for BO, including as follows: relatively low sensitivities of CT findings as diagnostic criteria [6, 14], poor correlation of the extent of air-trapping with the severity of BO [12, 16], existence of other respiratory diseases that demonstrate similar CT findings [23], and minimal abnormalities seen on the inspiratory scan, as well as the necessity of an expiratory scan [1, 6, 23]. These limitations suggest that accurate CT diagnosis of BO is potentially difficult without sufficient clinical information, and further indicate that other modalities, especially functional imaging, can play an important role in the diagnosis of BO.

The utility of the ventilation-perfusion lung scan for the diagnosis of postinfectious BO has been recognized [2, 3, 19, 20]. The primary finding on the ventilation-perfusion scan of BO is observed in patients with Swyer-James-MacLeod syndrome, which is multiple matched defects in the affected lung fields as the result of hypoxic vasoconstriction following airway obstruction. This finding is widely observed in BO by other causes, and useful in differentiating BO from pulmonary embolism or pulmonary veno-occlusive disease, which show mismatched defects on lung scans and may also demonstrate mosaic attenuation (perfusion) on CT [1, 2, 24]. Further, it has been pointed out that unexpected lung involvement that is not visualized on CT can be revealed by the ventilation-perfusion scan [2].

For the diagnosis of BO after stem cell transplantation, scintigraphy can be a definitive imaging modality when abnormalities are minimal or absent on the CT scan [1]. However, matched defects seen on lung scan are not specific to BO, and occur with other obstructive pulmonary diseases such as bronchial asthma or chronic bronchitis [25, 26]. Similarly, matched defects can also be found in patients with pulmonary infarction [26]. Thus, the radiological diagnosis of BO also requires assessments of lung field morphology obtained by chest CT. Compared with BO by other causes, BO after stem cell transplantation usually affects both lungs, which often lead to homogeneous decrease in lung density and therefore makes chest X-ray or CT appear 'normal' [1, 4]. If multiple matched defects are observed on lung scans in these apparently normal patients, the disturbance between scintigraphic findings and CT or X-ray findings strongly suggests existence of BO, and lung scans can play a definitive role in the diagnosis of BO. Although it has not been rigorously assessed in previous studies, it can be predicted that repeated lung scans would also be useful for the management of BO in order to follow up pulmonary function or evaluate the effect of treatments, when chest CT does not reveal obvious abnormalities.

Although ventilation scan using technegas is convenient and easy to manage, it may be still controversial that technegas scintigraphy is truly accurate [27-30]. In comparison with other ventilation scans using 133-xenon or 81m-krypton, technegas scintigraphy contains some imaging disadvantages including hot spot phenomenon and peripheral deposition. Among them, focal abnormal hot spots are frequently observed in cases of obstructive lung diseases [27, 28]. These hot spots have been explained by aerosol particles impaction in obstructive airways. Interestingly, we could not find previous literature discussing about this confusing finding in the diagnosis of BO. As our case showed, patients of BO also can demonstrate hot spot phenomenon on technegas scintigraphy.

Regarding our case, characteristic CT findings for BO, including air-trapping or mosaic attenuation, were not clearly detected although his condition was very serious. However, severe matched defects were clearly demonstrated by ventilation-perfusion lung scans, which was decisive for the diagnosis of BO. *In conclusion*, if characteristic findings are not observed on chest CT, ventilation-perfusion lung scans are definitely recommended to make a correct diagnosis for BO after stem cell transplantation since hidden obstructive lesions can be demonstrated by the ventilation-perfusion lung scans.

*The authors declare that they have no conflicts of interest.*

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