

## **Ventilation and perfusion scintigraphy after lung transplantation**

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**Study objective.** *Evaluation of the possibilities of ventilation and perfusion scintigraphy in detecting functional disorders and determining the severity of lung damage that may occur after organ transplantation.*

**Material and methods.** *The study included 27 patients after bilateral lung transplantation; mucoviscidosis was the main cause of terminal respiratory failure in most cases (19 patients; 77.8%). The ventilation scintigraphy was performed with <sup>99m</sup>Tc-pentatech using a nebulizer, and the perfusion scintigraphy was performed with <sup>99m</sup>Tc-albumin*

*macroaggregate. The investigations were performed on Infinia II and Discovery 670 NM/CT single-photon emission tomographs (GE, USA).*

***Results.** Changes in the quantitative parameters of ventilation and perfusion scintigraphy in patients after lung transplantation were studied. When analyzing the results of radionuclide studies, we identified a restoration of function after lung transplantation, and the appearance of disorders with the development of complications in the early (up to 4 months) and later (more than one year) periods after bilateral lung transplantation.*

***Conclusion.** The study has shown that the radionuclide method has wide possibilities for assessing the ventilation and perfusion functions in patients after lung transplantation, helping in the differential diagnosis of obliterating bronchiolitis and graft vascular sclerosis, in assessing the nature of alveolar-capillary diffusion disorders, and determining the extent of functional abnormalities in every individual patient. Monitoring the function of transplanted lungs using scintigraphy allows separate monitoring of ventilation and perfusion changes, which is important for the choice of treatment tactics.*

**Keywords:** ventilation and perfusion lung scintigraphy, lung transplantation, monitoring of transplanted lung function

99mTc, labelled technetium

ACD, alveolar-capillary (transepithelial) diffusion

LL, left lung

LT, lung transplantation

PA, pulmonary artery

PH, pulmonary hypertension

PLS, perfusion lung scintigraphy

PS, perfusion scintigraphy

RL, right lung

rPBF, regional pulmonary blood flow

RPH, radiopharmaceutical (radionuclide, radiotracer)

RV, right ventricle of the heart

SPECT/CT, single-photon emission computed tomography/computed tomography

$T_{1/2}$ PA, RPH elimination half-time from the pulmonary artery

$T_{1/2}$  RV, RPH elimination half-time from the right ventricle

VLS, ventilation lung scintigraphy

VS, ventilation scintigraphy

### **Introduction**

Lung transplantation (LT) remains the main treatment method to prolong life and improve its quality in patients with chronic pulmonary diseases in the end-stage of respiratory failure [1–4]. The patients included in the waiting list for LT have the most unfavourable prognosis [3-5], and the mortality after LT reaches 20-30% [5-8]. These are the worst figures as for the results of transplantation among vital organ transplant recipients [5–7]. They are due to a rather frequent development of various complications, both immediately after surgery, and in the long-term period.

To increase the survival rate of recipients after lung transplantation and to maintain the graft function, the complex of therapeutic and diagnostic measures has been developed, including X-ray, biochemical, and immunological diagnostic techniques [9–15]. At N.V. Sklifosovsky Research Institute for Emergency Medicine, for the first time in our country, the radionuclide method was used to monitor the function of transplanted lungs [16–18], which makes it possible to quantitatively assess both the perfusion and ventilation of the organ with minimal

patient's exposure to radiation, and to identify early the organ functional impairments.

### **Study objective**

To assess the potential of ventilation and perfusion scintigraphy in detecting functional disorders and determining the severity of lung damage that may occur after lung transplantation.

### **Material and methods**

The study included 27 patients after bilateral LT (16 men and 11 women, mean age  $33.8 \pm 8.0$  years and  $32.7 \pm 5.7$  years, respectively).

The underlying disease that led to end-stage respiratory failure in these patients was cystic fibrosis in most cases in 19 of 27 patients (70.4%), 2 patients each (7.4% each) had non-Langerhans cell histiocytosis, idiopathic pulmonary fibrosis, or obliterating bronchiolitis, and one patient each (3.7% each) had bronchiectasis, and pulmonary alveolar proteinosis.

The radionuclide investigation was performed in 9 cases (33.3%) within 4 months and in 21 (77.8%) cases after 12 months of transplantation.

The first stage was the lung ventilation scintigraphy (VL), which is based on the temporary settling of inhaled gaseous nuclides or finely dispersed aerosols of a radiopharmaceutical (RPH) on the surface of the conducting and gas-exchanging airways. 500 MBq of  $^{99m}\text{Tc}$ -pentatech in 2.0 ml of saline (effective equivalent dose 0.06 mSv) was used as an inhalation agent placed in a nebulizer chamber ("Venti-Scan" III/IV radio aerosol kit). The image acquisition in the study was started simultaneously with the inhalation. The diffusion of inhaled labelled particles through the alveolar-capillary membrane was assessed by the

rate of  $^{99m}\text{Tc}$ -pentatech entry from the pulmonary alveoli into the bloodstream. The total time for dynamic acquisition was 20 minutes.

The analysis of ventilation scintigraphy (VS) was made using qualitative and semi-quantitative criteria: at visual assessment of the image, the areas of impaired ventilation (zones of hypo- or hyperventilation) were identified and the rate of alveolar-capillary (transepithelial) diffusion (ACD) was calculated using curves plotted from the areas of upper and lower half of each lung. The normal parameters of the ventilation function and the value of the ACD rate have been described in the studies by a number of authors. Normally, the distribution of RPH in the lungs after inhalation is uniform, without focal delay in the projection of the bronchi, while the ACD is in the range from 55 to 108 minutes [16-18].

The second stage was the perfusion lung scintigraphy (PLS) with the first RPH pass acquisition and recording in the "whole body" mode to identify right-to-left shunting. Perfusion scintigraphy (PS) is based on short-term embolization of the capillary bed of the pulmonary artery (PA) system with technetium ( $^{99m}\text{Tc}$ ) labelled human albumin macroaggregates or microspheres (80–120 MBq of  $^{99m}\text{Tc}$ -macrotech was injected intravenously; the effective equivalent dose was 0.88–1.1 mSv). The resulting scintigrams were assessed visually and semi-quantitatively: the zones of reduced perfusion and the rate of RPH passage were assessed with plotting the curves from the region of the right ventricle (RV) of the heart and LA. The pulmonary hypertension (PH) signs were identified by assessing the RPH disappearance half-time from the right ventricle ( $T_{1/2}$  RV) and RPH disappearance half-time from the pulmonary artery ( $T_{1/2}$  PA). Additionally, we assessed the regional pulmonary blood flow (rPBF, in per cent) in different lung fields (upper, middle, lower), the rPBF impairments being classified into 3 severity degrees: the 1st severity

degree corresponded to a 25% decrease in the blood flow from the reference values in the field or the whole lung; the 2nd and the 3rd severity degrees corresponded to 50% and 75% rPBF decreases, respectively [19–21].

In addition, we determined the RPH accumulation in the lungs in percentage of the impulse counts in the whole body (equivalent to injected radioactivity) and identified the presence of a right-to-left shunt based on the RPH accumulation (in percent) in the organs that are not normally visualized (brain, kidneys, intestine, etc.). The severity of right-to-left shunt (percentage of shunting) was calculated by the formula:

$$SH = \frac{A - (LP + LL)}{A} \times 100\%,$$

where SH is the percentage of arteriovenous shunting;

A is the impulse counts in the whole body;

LP, LL stand for RPH accumulation in the right and left lungs (impulse counts).

To determine the total perfusion deficit, each accumulation defect with an area equal to one segment was taken as a perfusion deficit of 5%, with an area equal to the lower lobe was taken as perfusion deficit of 25%; with an area equal to the right lung (RL) was taken as 55% deficit; and an area equal to the left lung (LL) as 45% deficit [21, 22].

The normal lung perfusion parameters were determined at investigating 8 healthy volunteers (7 men and one woman, mean age 33.4 ± 6.5 years) with neither clinical signs nor laboratory test results typical for diffuse lung lesions (Tables 1 and 2). The maximum values of rPBF (in percent) were obtained in the upper, middle, and lower pulmonary

fields of each lung. The signs of PH ( $T_{1/2}$  RV was  $2.5 \pm 0.7$  s;  $T_{1/2}$  PA was  $3.2 \pm 0.4$  s) and right-to-left shunts were absent.

**Table 1. Parameters of perfusion lung scintigraphy in healthy volunteers**

RPH accumulated in the lungs (% of acquired radioactivity)		The presence of right-to-left shunt	$T_{1/2}$		
			Right ventricle, s	Pulmonary artery, s	
Right lung	Left lung				
40.5±1.4	35.2±0.7	Background accumulation by the whole body tissues up to 25%	2.5±0.7	3.2±0.4	

**Table 2. Parameters of regional pulmonary blood flow according to the data of perfusion lung scintigraphy in healthy volunteers**

Regional pulmonary blood flow, %		Pulmonary fields			Total pulmonary blood flow
		Upper	Middle	Lower	
Anterior view	Right lung	10.4±0.7	27.5±0.7	17.2±0.7	56.0±0.7
	Left lung	14.6±0.6	22.0±0.7	8.3±0.8	44.9±0.7
Posterior view	Right lung	11.2±0.4	26.1±0.5	15.8±0.5	53.1±0.5
	Left lung	9.2±0.4	22.1±0.4	15.6±0.5	46.9±0.5

The data were statistically processed using the Statistica 12 software. The normality of the value distribution in parameters in the groups was tested by the Shapiro–Wilk test, the statistical significance of the differences between the mean values of the parameters in the groups was determined using the Student's test and Mann–Whitney test.

## Results and discussion

The patients examined after bilateral LT were allocated into two groups depending on the timing of surgery.

Group 1 consisted of 8 patients in whom no more than 4 months had passed after LT (from 21 to 115 days; one of the patients was investigated twice (at 38 and 115 days after transplantation). The results of 9 investigations were analyzed (Tables 3 and 4).

The ventilation lung scintigraphy (VLS) found that ACD rate was often (in 6 of 9 investigations) lower than normal (55–108 minutes): in all parts of both lungs in 3 patients, only in the upper parts on both sides in one patient, only in the lower segments in another patient, asymmetrically on both sides (in the upper segment bilaterally, and in the lower one on the left) in one more patient. The ACD rate in those cases ranged from 20 to 50 minutes. In one of the patients, the investigation performed on day 38 after transplantation revealed a local increase in ACD up to 250 minutes in the lower segments of the RL, which also persisted (making 234 minutes) at the second examination on day 115 after transplantation.

The perfusion lung scintigraphy (PLS) revealed the RPH accumulation (in per cent of the administered radioactivity) RL being from 27.0 to 50.0% (mean  $40.6 \pm 2.5\%$ ), meanwhile, the accumulation lower 40% (the conditional norm, as determined by the study in healthy volunteers, see Table 1) was noted in 3 out of 8 the investigated patients. The RPH accumulation in LL ranged from 18.0 to 43.5% (mean  $35.2 \pm 2.9\%$ ) only in 2 out of 8 patients. The percentage of shunting in patients of the 1st group ranged from 17.0 to 34.0, exceeding 30% only in 2 patients (mean,  $24.2 \pm 2.3\%$ ).

$T_{1/2}$  RV exceeded the value of healthy volunteers ( $2.5 \pm 0.7$  s) in 3 patients (3.5; 3.7, and 8.0 s), and PA  $T_{1/2}$  was higher than normal ( $3.2 \pm 0.4$  s) in 4 of 9 patients (2.6, 4.0, 4.8, 4.2 s).

The rPBF parameters in different lung fields (Table 4) corresponded to the normal values obtained in healthy volunteers, with the exception of  $T_{1/2}$  PA.

Thus, the results of PLS in the 1st group showed a satisfactory status of pulmonary perfusion and contractile function of the heart RV, however, rather frequent increases in the  $T_{1/2}$  PA values raised concern. An increase in this parameter indicated an increased peripheral arterial vascular resistance in the transplanted lungs, with a normal  $T_{1/2}$  RV and no signs of PH at echocardiography (systolic pressure in the PA was  $27.3 \pm 0.9$  mm Hg).

The comprehensive assessment of the VLS and PLS results in the 1st group of patients (investigated within up to 4 months after LT) can be important for an early detection of impaired pulmonary functions to predict the rejection crisis development (with decreased perfusion) and to correct ventilation disorders. We believe that the signs of increased peripheral arterial vascular resistance at early stages after LT may be associated with the past ischemic and reperfusion injury of the graft.

**Table 3. Parameters of alveolar-capillary diffusion and perfusion scintigraphy in the first group of patients after bilateral lung transplantation (up to 4 months, n = 9)**

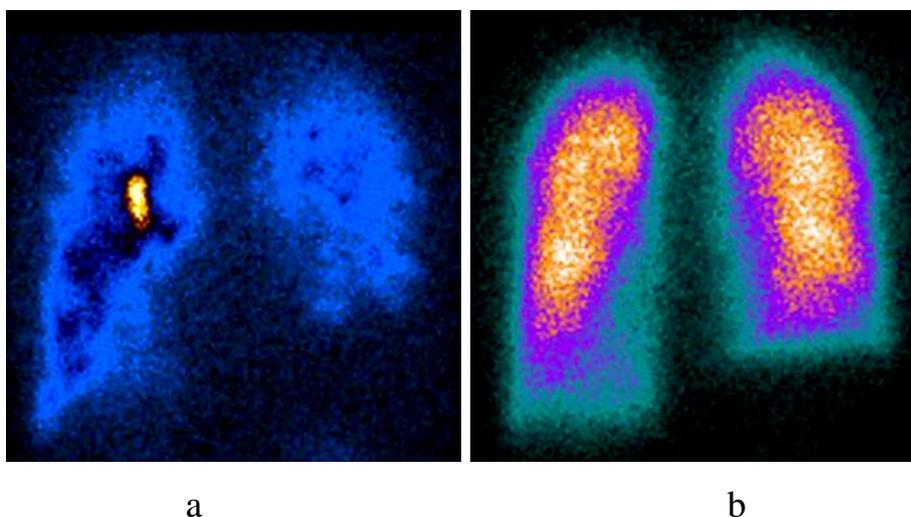
Patients (Initials)	Gender	Age (years)	Number of days after transplantation	Alveolar-capillary diffusion parameters (min)*				RPH accumulated in lungs (% of acquired radioactivity) (%)		Right-to-left shunt (%)	T <sub>1/2</sub>	
				Right lung		Left lung		Right lung	Left lung		Right ventricle, s	Pulmonary artery, s
				Apical segments	Basal segments	Apical segments	Basal segments					
AVP	m	24	21	41	82	39	40	39.5	43.5	17.0	8.0	26.0
BDA	m	21	23	29	34	44	44	44.0	27.0	29.0	3.5	4.0
EEA	m	49	96	42	62	50	45	50.0	18.0	32.0	1.6	1.8
ZGA	m	41	38	40	250	65	55	27.0	39.0	34.0	1.7	2.8
ZGA	m	41	115	59	234	60	58	35.0	41.0	24.0	2.3	3.0
LDD	m	27	49	49	20	36	49	45.0	37.0	18.0	3.7	4.8
PEL	f	29	25	70	38	58	50	43.0	37.0	20.0	2.6	4.2
PEV	m	27	26	140	83	100	98	–	–	–	1.1	1.2
SRV	m	37	85	26	42	31	24	41.0	39.0	20.0	1.5	3.0
M ± m		32.9 ± 3.2	53.1 ± 12.0	55.1±11.6	93.9±28.9	53.7±6.9	51.4±6.7	40.6±2.5	35.2±2.9	24.2±2.3	2.9±0.7	5.6±2.6

\* The normal range of alveolar-capillary diffusion: 55-108 min

**Table 4. Parameters of regional pulmonary blood flow in the first group of patients after bilateral lung transplantation (up to 4 months, n = 9)**

Regional pulmonary blood flow, %		Pulmonary fields			Total pulmonary blood flow
		Upper	Middle	Lower	
Anterior view	Right lung	12.2±1.6	24.7±2.3	13.6±2.1	50.5±4.7
	Left lung	15.3±1.9	22.2±2.1	12.0±1.0	49.5±4.7
Posterior view	Right lung	12.3±1.6	22.6±2.3	14.5±2.7	49.4±5.0
	Left lung	13.6±1.8	21.6±1.9	15.4±1.8	50.6±5.0

Ventilation disorders at the level of the main bronchi in the 1st group were revealed in 4 patients, manifesting themselves in the form of aerosol hyperfixation in the sites of bronchial obstruction or in the zones of local aerosol retention in the pulmonary parenchyma. In two of those cases, the VS demonstrated the RPH accumulation over the area of accumulated purulent secretions with preserved perfusion, according to PS data, which was confirmed by fiberoptic bronchoscopy (Fig. 1).



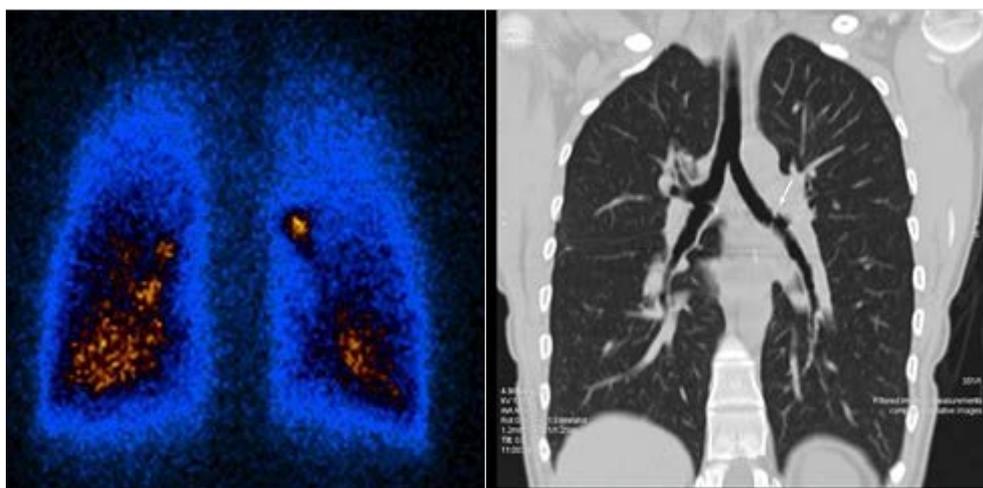
**Fig. 1. Ventilation (a) and perfusion (b) scintigrams (posterior view) of patient SRV, 37 years old, on day 85 after bilateral lung transplantation demonstrated a focal delayed transit of the inhaled radiopharmaceutical at the level of the left main bronchus and pronounced hypoventilation of the right lung lower segments; a moderate decreased diffused perfusion in the inferio-posterior segments of both lungs**

In two other cases, an additional hybrid study - single-photon emission computed tomography / computed tomography (SPECT/CT) was required to clarify the location and cause of the identified ventilation disorders. In the first of those two cases, at overlaying the images, the areas of impaired bronchial patency and ventilation coincided with scar stenosis of the main bronchus. In the second case, the impaired ventilation in the anastomotic area was caused by the disparity between the diameters of the donor and recipient bronchi according to SPECT/CT imaging.

Group 2 included 21 patients investigated after a year or more (from 13 to 72 months, median 35.3 months, mean  $36.7 \pm 14.0$  months) after bilateral LT.

Primary attention was drawn to the identified signs of chronic organ rejection, its main mechanisms being the obliterating bronchiolitis and vascular sclerosis of the transplanted lung. Post-transplant obliterating bronchiolitis develops (as reported in literature) in 20-50% of patients [23]. The difficulty in establishing the diagnosis is associated with the variability of the abnormalities encountered, since one and the same patient may simultaneously experience constrictive and proliferative changes in the bronchioles, thickening and fibrosis of the arterial intima and hyaline sclerosis of the veins.

To confirm the diagnosis in such cases, a set of data is required: thoracic computed tomography scans, functional tests (for blood gas composition, external respiratory function, and nitric oxide assessment in expired air), as well as the bronchoalveolar lavage cytogram and lung tissue histology assessments. It seems promising to use the radionuclide method, as well, which is able to simultaneously characterize both structural and functional changes in the lungs (Fig. 2).



a

b

**Fig. 2. Ventilation scintigram (a) and single-photon emission computed tomography/computed tomography scan (b) (posterior view) of patient G., 26 years old; Condition after bilateral lung transplantation: a focal delayed transit of inhaled radiopharmaceutical at the level of the left main bronchus and the signs of bronchial mucosa prolapse at computed tomography**

In patients of the 2nd group (according to VLS data), the alterations in the ACD rate of varying severity and duration were detected in 19 of 21 patients (90.5%, 95% CI 77.2–100.0%) (Table 5). Meantime, in 9 patients (42.9%) there was a decrease in the rate (from 112 to 1155 minutes), including 3 patients showing that in all pulmonary fields. In one more patient, the ACD slow-down was observed in the lower segments of both lungs (165 minutes on the right and 245 minutes on the left) with a slight ACD acceleration in the upper part of the LL (50 minutes). In 9 patients (42.9%), the rate increase (from 23 to 53 minutes) was revealed, including 4 patients showing that in all pulmonary fields.

We can suppose that the ACD slow-down was associated with the alterations in the alveolar membrane due to the past primary graft dysfunction, as well as the development of pneumopathy of drug origin.

PLS in the patients of the 2nd group revealed the RPH accumulation was from 23.0 to 61.0% (mean  $38.3 \pm 2.0\%$ ) for the RL, being lower 40% (the conditional norm, see Table 1) in 12 of 20 investigated patients (60.0%, 95% CI

37.2-82.9%), including that below 35% in 4 patients only (20.0%, 95% CI 1.3–38.7%). The RPH accumulation in the left lung ranged from 16.0 to 51.0% (mean  $32.7 \pm 1.7\%$ ) in 15 of 20 patients (75.0%, 95% CI 54.8-95.2%), including that below 30% in 4 patients (20.0%, 95% CI 1.3–38.7%).

The percentage of shunting in patients of the 2nd group ranged from 16.0 to 49.0 (mean  $29.7 \pm 2.1\%$ ), making 30% or higher in 9 of the 19 investigated (47.4%, 95% CI 23.4–71.3%), incl. 40% or higher in 3 (15.8%, 95% CI 0.0–33.3%).

The  $T_{1/2}$  RV (mean  $2.1 \pm 1.0$  s) in patients of the 2nd group practically did not exceed that of the healthy volunteers ( $2.5 \pm 0.7$  s), the maximum value of 3.0 was in one patient. The  $T_{1/2}$  PA exceeded the normal range ( $3.2 \pm 0.4$ ) in only one patient making 4.8 s.

The rPBF parameters in different lung fields (Table 6) corresponded to the normal values obtained in the healthy volunteers.

**Table 5. Parameters of alveolar-capillary diffusion and perfusion scintigraphy in the second group of patients after bilateral lung transplantation (over 12 months, n = 21)**

Patients (Initials)	Gender	Age (years)	Number of days after transplantation	Alveolar-capillary diffusion parameters (min)*				RPH accumulated in lungs (% of acquired radioactivity) (%)		Right-to-left shunt (%)	T <sub>1/2</sub>	
				Right lung		Left lung		Right lung	Left lung		Right ventricle, s	Pulmonary artery, s
				Apical segments	Basal segments	Apical segments	Basal segments					
AVP	m	26	618	307	127	1155	1150	39.0	43.0	18.0	–	–
AAA	f	30	2168	157	175	150	172	40.0	31.0	19.0	2.7	2.9
AEN	f	31	1060	118	85	148	91	38.0	32.0	30.0	2.3	2.7
BAB	m	32	450	144	600	150	441	35.0	33.0	32.0	2.5	3.5
BMV	f	38	2040	31	40	21	43	39.0	32.0	29.0	1.5	3.3
BON	f	35	1675	120	97	219	160	49.0	28.0	23.0	2.3	3
DDV	m	39	1142	169	107	112	95	40.0	37.0	23.0	–	–
DEA	m	28	849	51	54	42	68	23.0	51.0	26.0	2.5	3.4
EEA	m	50	394	73	165	50	245	54.0	24.0	22.0	–	–
ESV	m	39	665	53	63	70	72	23.0	30.0	47.0	1.1	1.7
ZhAL	f	26	1435	75	29	75	48	37.0	34.0	29.0	–	–
ILA	f	34	1644	139	63	166	80	41.0	43.0	16.0	2.3	2.2
LDD	m	28	399	35	29	54	35	30.0	30.0	40.0	3	3.7
KIV	m	46	1057	101	32	73	65	36.0	31.0	33.0	1.8	2.6
OAS	m	28	707	42	29	40	40	38.0	34.0	28.0	1.5	4.8
POV	f	33	981	115	68	89	77	29.0	35.0	36.0	2.1	2.9
PGV	m	31	1238	66	46	0	0	61.0	–	–	2.3	3.1
PES	m	39	1804	190	25	146	108	41.0	25.0	34.0	2	3.9
SNA	f	32	1124	23	42	26	42	37.0	33.0	30.0	2	3.1
TOL	f	46	1175	108	81	61	36	35.0	16.0	49.0	2.4	2.3
FRA	m	33	549	40	25	62	31	–	–	–	2.1	2.4
M ± m		34.5 ± 1.5	1103.5 ± 116.1	102.7 ± 14.8	94.4 ± 27.1	138.5 ± 52.3	147.6 ± 54.4	38.3 ± 2.0	32.7 ± 1.7	29.7 ± 2.1	2.1 ± 0.1	3.0 ± 0.2

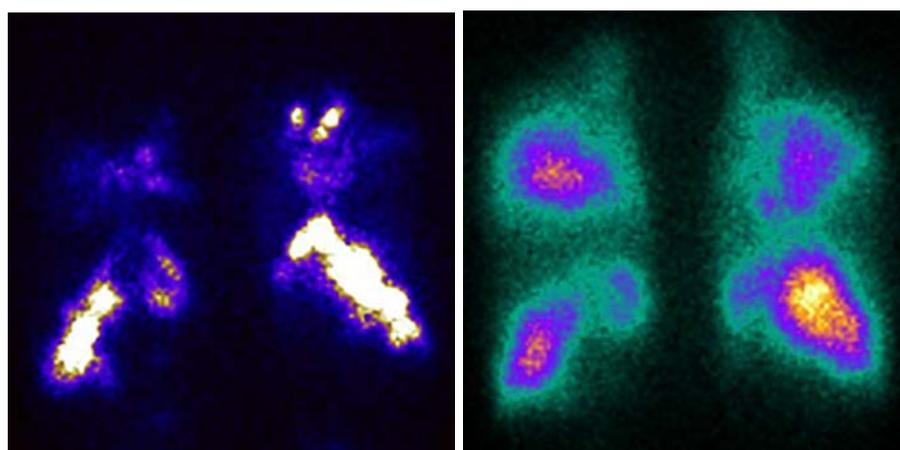
\* The normal range of ACD: 55-108 min

**Table 6. Parameters of regional pulmonary blood flow in the second group of patients after bilateral lung transplantation (over 12 months, n = 21)**

Regional pulmonary blood flow, %		Pulmonary fields			Total pulmonary blood flow
		Upper	Middle	Lower	
Anterior view	Right lung	12.2±0.8	24.8±1.0	17.0±1.1	54.0±1.8
	Left lung	12.0±0.5	20.0±0.8	13.9±0.9	46.0±1.8
Posterior view	Right lung	11.5±0.7	23.7±0.8	18.2±1.0	53.4±1.5
	Left lung	10.2±0.4	19.3±0.6	17.1±1.1	46.6±1.5

As in the 1st group, the most informative was the comparison of the VLS and PLS data in each patient to determine the predominant alterations in ventilation or perfusion for optimal correction of disorders.

The most illustrative was the clinical case of a female patient with the chronic rejection of transplanted lungs (Fig. 3) confirmed by histological examination of a lung biopsy specimen (proliferative-sclerotic abnormalities were found). The VLS and PLS parameters in this patient, indicating a pronounced ACD acceleration in both lungs and the presence of a moderate right-to-left shunt (shunting up to 30%), led to the conclusion in favour of obliterating bronchiolitis, rather than a sclerosing process in the PA system.



a

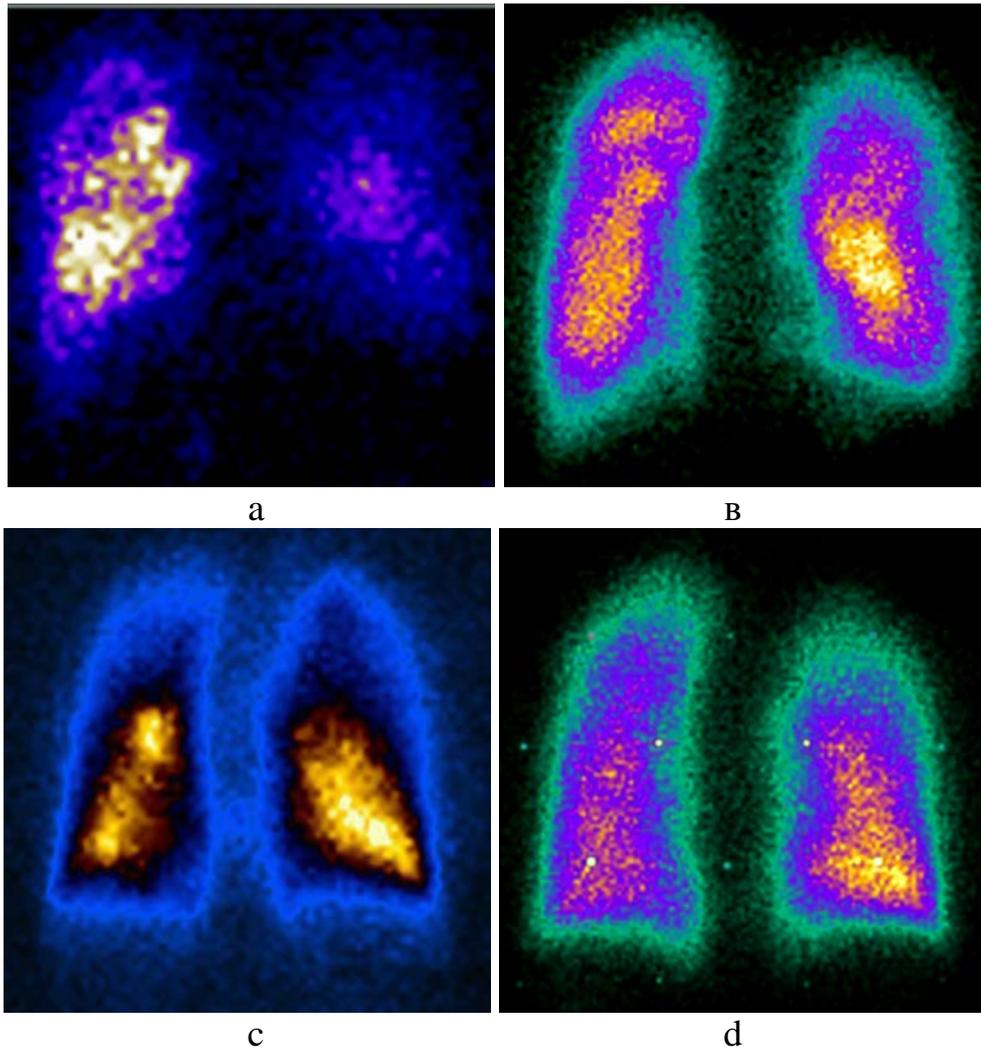
b

Alveolar-capillary diffusion				RPH accumulated in lungs (% of acquired radioactivity) (%)		Right-to-left shunt (%)	T <sub>1/2</sub>	
Right lung		Left lung					Right ventricle, s	Pulmonary artery, s
Apical segments	Basal segments	Apical segments	Basal segments	Right lung	Left lung			
31	40	21	43	39	32	30	1.5	3.3

**Fig. 3. Ventilation (a) and perfusion (b) scintigrams in the posterior view of patient BMV, 38 years old, with chronic graft rejection at 68 months after bilateral lung transplantation: a pronounced decrease in ventilation of both lungs with the foci of an increased radiopharmaceutical accumulation in the projection of the first and second order bronchi; polysegmental disorder of perfusion**

Statistical analysis of the VLS and PLS data in the 1st and 2nd groups revealed a tendency towards an ACD slow-down, lung perfusion decrease without signs of an increased pulmonary resistance (pulmonary hypertension).

Three patients were investigated twice: in the early and again in the later period after lung transplantation. The post-transplant positive changes of the lung status over time can be illustrated by the clinical case of a patient investigated using the radionuclide method three times (Fig. 4).



Date of investigation	Alveolar-capillary diffusion				RPH accumulated in lungs (% of acquired radioactivity) (%)		Right-to-left shunt (%)	$T_{1/2}$	
	Right lung		Left lung		Right lung	Left lung		Right ventricle, s	Pulmonary artery, s
	Apical segments	Basal segments	Apical segments	Basal segments					
11.04.17	41	82	39	40	39,5	43,5	17	6	26
29.11.18	307	127	1155	1150	39,0	43,0	18	-	-
15.11.19	60	56	73	67	42,3	42,0	15,7	3,7	5,2

**Fig. 4. Patient AVP, 24 years old, on day 21 and at 21 months after bilateral lung transplantation. Ventilation (a, c) and perfusion (b, d) scintigrams of the lungs in the posterior view demonstrate an abrupt decrease in the right lung ventilation combined with a moderately decreased perfusion of its apical segments. Repeated ventilation-perfusion scintigraphy performed at 21 months confirmed the recovery of the right lung ventilatory function (c, d)**

The ventilation function status in the patient in Fig. 4 is consistent with literature data on incomplete recovery of the forced vital capacity of the lungs in the early period, which can be observed during the first year after transplantation [15]. The principal condition for the ventilation function recovery is known to be the preserved blood flow in the organ, which was confirmed by a repeated investigation. When comparing the ACD parameters in this patient, the attention was drawn to the transient slow-down in the ACD parameters at the second study, which was most likely related to the change in the dose of immunosuppressive therapy, because no abnormal findings were seen either on the X-ray examination or computed tomography scans in the patient in that period of time. According to the dynamics of changes in the RPH first pass parameters ( $T_{1/2}$  RV and  $T_{1/2}$  PA), a gradual regression of LH can be noted due to the decrease in pulmonary vascular resistance.

### **Conclusion**

This study made it possible to identify ventilation and perfusion impairments in the early post-transplantation period (within up to 4 months), which could have been associated with reperfusion injury, graft rejection, infection and destruction of the anastomosis, as well as the selection of the immunosuppressive therapy dose. In the late postoperative period (over 12 months), the functional status of the transplanted lungs was seen to being stabilized in most cases. Delayed ventilation and perfusion scintigraphy investigations were also appropriate since they enabled us to identify the most common alterations in ventilation or perfusion for undertaking an optimal correction of functional impairments in transplanted lungs in every individual patient.

The present study has shown that the radionuclide method has ample opportunities in assessing ventilation and perfusion functions in patients after lung transplantation. We should emphasize that the ventilation-perfusion scintigraphy is unique in determining the alveolar-capillary diffusion rate by means of a direct semi-quantitative method (the RPH penetration through the alveolar-capillary membrane), and in a detailed assessment of the transplanted lung microvasculature with minimal patient exposure to radiation and the absence of adverse reactions.

The implementation of this method into clinical practice will help in the differentiated diagnosis of obliterating bronchiolitis and graft vascular sclerosis, in assessing the nature of alveolar-capillary diffusion disorders and determining the extent of functional impairments in every patient individually.

### References

1. Nathan SD, Shlobin OA, Weir N, Ahmad S, Kaldjob JM, Battle E, et al. Long-term course and prognosis of idiopathic pulmonary fibrosis in the new millennium. *Chest*. 2011;140(1):221–229. PMID: 21729893 <https://doi.org/10.1378/chest.10-2572>
2. Jo HE, Glaspole I, Grainge C, Goh N, Hopkins PM, Moodley Y, et al. Baseline characteristics of idiopathic pulmonary fibrosis: analysis from the Australian idiopathic pulmonary fibrosis registry. *Eur Respir J*. 2017;49(2).pii:1601592. PMID: 28232409 <https://doi.org/10.1183/13993003.01592-2016>
3. Mahajan AK, Folch E, Khandhar SJ, Channick CL, Santacruz JF, Mehta AC, et al. The diagnosis and management of airway complications following lung transplantation. *Chest*. 2017;152(3):627–638. PMID: 28274791 <https://doi.org/10.1016/j.chest.2017.02.021>

4. Hoechter DJ, von Dossow V. Lung transplantation: from the procedure to managing patients with lung transplantation. *Curr Opin Anaesthesiol.* 2016;29(1):8–13. PMID: 26545145 <https://doi.org/10.1097/ACO.0000000000000268>
5. Sulania A, Sachdeva S, Jha D, Kaur G, Sachdeva R. Organ donation and transplantation: An updated overview. *MAMC J Med Sci.* 2016;2(1):18–27. <https://doi.org/10.4103/2394-7438.174832>
6. Fine NM, Kushwaha SS. Recent advances in mammalian target of rapamycin inhibitor use in heart and lung transplantation. *Transplantation.* 2016;100(12):2558–2568. PMID: 27495747 <https://doi.org/10.1097/TP.0000000000001432>
7. Jakubec P, Žurková M, Hajdová L, Křenková A, Kolek V. The complications after lung transplantation. *Vnitř Lek.* 2018;63(11):848-859. PMID: 29303288
8. Boytsova EV, Ovsyannikov DYu. Postinfectious obliterans bronchiolitis in children. *Children infections.* 2014;13(2):24–28. (In Russ.). <https://doi.org/10.22627/2072-8107-2014-13-2-24-28>
9. Potestio C, Jordan D, Kachulis B. Acute postoperative management after lung transplantation. *Best Pract Res Clin Anaesthesiol.* 2017;31(2):273–284. PMID: 29110799 <https://doi.org/10.1016/j.bpa.2017.07.004>
10. Costa J, Benvenuto LJ, Sonett JR. Long-term outcomes and management of lung transplant recipients. *Best Pract Res Clin Anaesthesiol.* 2017;31(2):285–297. PMID: 29110800 <https://doi.org/10.1016/j.bpa.2017.05.006>
11. Leal S, Sacanell J, Riera J, Masclans JR, Rello J. Early postoperative management of lung transplantation. *Minerva Anesthesiol.* 2014;80(11):1234–1245. PMID: 24518214

12. Porhownik NR. Airway complications post lung transplantation. *Curr Opin Pulm Med.* 2013;19(2):174–180. PMID: 23287284 <https://doi.org/10.1097/MCP.0b013e32835d2ef9>
13. Gillespie M, Rizzolo D. A systems-based approach to patient care after liver transplantation. *JAAPA.* 2018;31(1):14–19. PMID: 29227319 <https://doi.org/10.1097/01.JAA.0000527694.68417.0a>
14. Kao CC, Parulekar AD. Postoperative management of lung transplant recipients. *J Thorac Dis.* 2019;11(Suppl 14):S1782–S1788. PMID: 31632755 <https://doi.org/10.21037/jtd.2019.05.60>
15. Gautier SV, Golovinskiy SB, Poptsov VN, Tsiroulnikova OM, Nechaev NB, Spirina EA, et al. First pediatric bilateral lobar lung transplantation for cystic fibrosis in Russian Federation. *Russian Journal of Transplantology and Artificial Organs.* 2017;19(4):11–15. (In Russ.). <https://doi.org/10.15825/1995-1191-2017-4-11-15>
16. Gottschalk A, Sostman HD, Coleman RE, Juni JE, Thrall J, McKusick KA, et al. Ventilation-perfusion scintigraphy in the PIOPED study. Part II. Evaluation of the scintigraphic criteria and interpretations. *J Nucl Med.* 1993;34(7):1119–1126. PMID: 8315488
17. Rubin MP, Kuleshova OD, Chechurin RE. Radionuklidnaya ventilyatsionnaya aerazol'naya stsintigrafiya legkikh: metodika issledovaniya i interpretatsiya rezul'tatov. *Radiology – Practice.* 2002;(1):19–24. (In Russ.).
18. Lishmanov YuB, Krivonogov NG, Ageyeva TS, Dubodelova AV, Mishuchstina EL. Basic parameters of pulmonary ventilation-perfusion scintigraphy in healthy individuals. *Journal of radiology and nuclear medicine.* 2007;(6):34–39. (In Russ.)
19. Migunova EV, Kudryashova NE, Nikitina OV, Beresneva EA, Goldina IM, Zabavskaya OA, et al. Assessment of the effectiveness of

thrombolytic therapy of pulmonary tromboembolism by lung perfusion scanning. *Molecular medicine*. 2013;(4):46–50. (In Russ.).

20. *Tromboemboliya legochnoy arterii. Metody diagnostiki: ucheb.-metod. posobiye*. Moscow: N.V. Sklifosovsky Research Institute for Emergency Medicine Publ., 2014. (In Russ.).

21. Savelyev VS, Yablokov EG, Kiriyeiko AI. *Massivnaya emboliya legochnoy arterii*. Moscow: Meditsina Publ., 1990. (In Russ.).

22. Pistolesi M, Lavorini F, Allesscia G., Miniati M. Diagnostic strategies for suspected pulmonary embolism. In: Bankier AA. *Imaging. European respiratory monograph*. 2004. Monograph 30. Ch. 6. p. 89–105. <https://doi.org/10.1183/1025448x.00030006>

23. Avdeyev SN. Novyye vozmozhnosti v terapii bronkhiolitov. *The Journal of Practical Pulmonology (Atmosphere. Pulmonology and Allergology)*. 2009;(4):12–18. (In Russ.).

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