Pulmonary System

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Zvi Bar-Sever and Pietro Zucchetta

4.1 Clinical Indications [1–4]

- Assessment of differential perfusion to the lungs and/or regional, to lung zones (lobes) in children with congenital heart disease and associated stenosis of the pulmonary vessels, most commonly Tetralogy of Fallot, showing altered blood flow to the lungs.
- Assessment of lung perfusion following corrective surgery or cardiac catheterization with balloon dilatation of a pulmonary vessel, the most common indication for perfusion lung scintigraphy in children.
- Demonstration and quantitation of shunts between the right (pulmonary) and left (systemic) circulation, mainly in children with cyanotic heart disease.
- Evaluation of the hepato-pulmonary syndrome in patients with liver disease or after liver transplant.
- Assessment of lung function:
  - Before and after lung transplantation.
  - In congenital lung malformations (e.g. lobar emphysema, cystic adenomatoid malformation and pulmonary sequestration).
  - In structural abnormalities of the chest (e.g. congenital diaphragmatic hernia, pectus excavatum and spinal scoliosis).
  - In airway diseases (e.g. cystic fibrosis, foreign body aspiration and bronchopulmonary dysplasia).
- Diagnosis of pulmonary embolism (PE).

4.2 Pre-Exam Information

- Child's age and degree of cooperation, to determine the likelihood of obtaining a ventilation study when required and the type of ventilation scan when options are available.
- Exact anatomy of congenital cardiac malformations before or after corrective surgery.
- Presence of right-to-left shunt, of pulmonary hypertension or of solitary lung.

Study Protocol for Perfusion Lung Scan [2, 5, 6]

Radiopharmaceuticals, Activity and Mode of Delivery.

Radiopharmaceutical:

- [^{99m}Tc]macroaggregated albumin (MAA), typically 10–40 microns in size.

Z. Bar-Sever (✉)
Institute of Nuclear Medicine, Schneider Children's Medical Center, Tel Aviv University, Petah Tiqva, Israel

P. Zucchetta
Nuclear Medicine Unit, Department of Medicine, Padova University Hospital, Padova, Italy

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Activity:

- Should take into account whether a ventilation study is preceding or immediately following the perfusion scan (the order of exams depending on clinical indications and local preferences).
  - If no ventilation scan is performed: 1.11 MBq/kg (0.03 mCi/kg), minimum activity: 14.8 MBq (0.4 mCi).
  - If perfusion scan is performed immediately after ventilation scan: 2.6 MBq/kg (0.07 mCi/kg).
  - The typical number of MAA particles should not exceed 50,000 in newborns and 165,000 in 1-year-old infants. In cases of right-to-left shunt, of pulmonary hypertension or of a single functioning lung, the number of particles should be 10,000.

    Refer to the EANM paediatric dosage card and to the North American consensus guidelines on radiopharmaceutical administration in children in the respective EANM and SNMMI and image gently web sites. Reference to national regulation guidelines, if available, should be considered.

Mode of delivery:

- The tracer should be injected with the patient supine.

Acquisition protocol

- Collimator: low energy, high or ultra-high resolution.
- Planar images: anterior, posterior, 4 obliques and occasionally 2 lateral views, 300,000–500,000 counts/view, 256 × 256 matrix.
- SPECT and SPECT/CT when available are recommended in selected clinical scenarios.

Study Protocol for Ventilation Lung Scan [2, 4, 7]

Radiopharmaceuticals, Activity and Mode of Delivery.

Radiopharmaceutical

- *^{99m}Tc-labelled aerosols:* [^{99m}Tc] diethylene-triamine-pentaacetate (DTPA) is the most common agent. The aerosol is created by a jet or ultrasonic nebulizer and introduced through a face mask.
- *^{99m}Tc-labelled carbon nanoparticles*: *Technegas®,* an aerosol which consists of the ^{99m}Tc molecule cocooned by layers of graphite thus creating small particles (5–30 nm wide) that are suspended in Argon gas [8].

Radioactive gases:

- [^{133}Xe] Xenon (^{133}Xe), is at present unavailable in some countries and more expensive than aerosols.
- [^{81m}Kr] Krypton (^{81m}Kr) is an inert gas eluted with humidified air through a ^{81}Rubidium/^{81m}Kr generator. Availability and high cost are limiting factors.

Activity:

- DTPA: scaled down according to the child's weight from DTPA aerosol adult dose of 900–1300 MBq (25–35 mCi) in the nebulizer, from which the lungs receive approximately 20–40 MBq (0.5–1.0 mCi).
- Technegas®: minimum dose 100 MBq.
- ^{133}Xe: 10–12 MBq/kg (0.3 mCi/kg), minimum 100–120 MBq (3 mCi).
- ^{81m}Kr: in adults, the dose is 40–400 MBq (1.1–10.1 mCi) which would result in an estimated effective dosage of 0.004–0.01 mSv in children.

Refer to the EANM paediatric dosage card and to the North American consensus guidelines on radiopharmaceutical administration in children in the respective EANM and SNMMI and image gently web sites.

Reference to national regulation guidelines, if available, should be considered.

Note that ^{133}Xe and ^{81m}Kr do not appear on the EANM dosage card.

Mode of delivery:

- DTPA: the child should take deep breaths for several minutes. Cooperation is important and prevents application of the study in infants and young uncooperative children.
- Technegas®*: r*equires a special apparatus, generator, for preparation of the inhaled aerosol.
- ^{133}Xe: requires a dedicated administration and trapping systems to trap and exhaust the exhaled gas.
- ^{81m}Kr: is inhaled via a face mask.

Acquisition protocol

- The ventilation scan is usually done first followed by the perfusion study.
- [^{133}Xe] scans: in supine position, posterior view dynamic imaging, 5 sec/frame. The dynamic nature of the ^{133}Xe study precludes multiple views acquisition.
- [^{99m}Tc] agents: static images at equilibrium, similar views as for the perfusion study, up to 100,000 counts/view.
- SPECT is recommended, allowing better comparison with perfusion scan.
- SPECT/CT, if available, may be also indicated, if not performed already as part of the perfusion scan.

4.3 Perfusion and Ventilation Study Interpretation

Visual patterns of perfusion and ventilation lung scans should be interpreted according to the requested clinical indication:

Congenital heart disease: [9, 10]
- Any tracer localization in the brain or kidneys should be reported as evidence of right-to-left shunt.
- In classic Glenn shunt (end-to-end pulmonary artery/superior vena cava anastomosis) upper extremity injection will result in tracer travelling through the superior vena cava into the right lung only. Tracers injected in the lower extremity will result in localization in the left lung only. In cases of a bidirectional Glenn shunt (end-to-side anastomosis), upper extremity injection will result in tracer accumulation in both lungs. Tracer injected into the lower extremity will travel from the inferior vena cava and enter the systemic circulation bypassing the lungs.

Hepato-pulmonary syndrome [11]:
- The shunt is intrapulmonary leading to the visualization of activity in the systemic circulation.

Congenital and acquired airway disease [4]:
- Global and regional distribution of pulmonary ventilation and perfusion are reported.

Pulmonary embolism [12, 13]:
- The hallmark of PE remains demonstrating a mismatch between absent or reduced perfusion in lung segments and preserved ventilation.

Specifically, dynamic [^{133}Xe] studies should be interpreted as follows:

- Initial images after a single breath reflect regional lung ventilation.

- Equilibrium phase images, after multiple breaths through a rebreathing inhalation system, reflect the distribution of aerated air space volume.
- Subsequent images after gas administration ceases reflect washout from the airspaces. Air trapping when present is typically evident during this phase.

4.4 Perfusion and Ventilation Differential Lung Function Analysis

- In addition to visual inspection of images, studies can be processed to provide a quantitative analysis.
- Quantification of lung perfusion is usually assessed on anterior and posterior planar projections, and more recently using quantitative SPECT or SPECT/CT segmentation methods.
  - Differential lung perfusion and/or ventilation is calculated by comparing left and right lung counts obtained from whole lung regions-of-interest (ROIs) and is expressed in percentages.
  - ROIs can be placed on the posterior view only or both the posterior and anterior view to obtain conjugate counts for calculating the geometric mean.
  - ROIs can be split into upper middle and lower zones for each lung for a crude assessment of regional lung perfusion and ventilation. Modern processing software allows determination of these values according to lung lobes and segments and should be preferred when available.
- In patients with shunting between the pulmonary and systemic circulations, MAA particles embolize pre-capillary arterioles in the systemic circulation. The brain and kidneys that receive a large portion of the cardiac output, are visualized.
- Right-to-left (R-L) shunt magnitude calculation can be obtained by drawing whole body and lung ROIs and using the following formula:

  R-L shunt (%) = [(total body counts−lung counts)/total body counts] × 100 [1].

- Alternatively, it is possible to calculate the shunt index by obtaining the ratio between brain counts from a brain ROI and lung counts from a ROI placed on both lungs on the posterior view, corrected by background:

  Background corrected brain counts/background corrected lung counts x 100 (Normal value 0.42 ± 0.30) [14].

4.5 Correlative Imaging

- Chest radiograph correlation is required when PE is suspected.
- CT pulmonary angiography (CTPA) correlation may increase the specificity of ventilation/perfusion (V/Q) scans.

Red Flags

- For perfusion studies, injection should be given in supine position to reduce the effect of gravity on the particle distribution between the upper and lower lung zones.
- In complex situations (e.g. cavo-pulmonary anastomosis, aka Glenn shunt and Fontan circulation) it is required to split the bolus administration to upper and lower limbs.
- Blood should not be drawn into the injection syringe since this may result in blood clots containing MAA particles that can affect the radiotracer distribution in the pulmonary circulation.
- Images may appear inhomogeneous when using a small number of MAA particles but they can be sufficient for visual assessment and semi-quantitation of whole lung and regional perfusion. The number of MAA particles:
  - Should not exceed 50,000 in newborns and 165,000 in 1-year-old infants.
  - Should be around 10,000 cases of right-to-left shunt, of pulmonary hypertension or of a single functioning lung.
- Tracer localization in the thyroid gland, seen on the chest views, requires additional scans of the head to distinguish between free Pertechnetate due to improper MAA labelling and right-to-left shunt. Pertechnetate can be

seen in the thyroid, the gastric mucosa and renal collecting systems. In case of shunts the tracer will be seen in the brain.
- Inadequate ventilation can result in low radiolabelled aerosol concentration in the periphery of the lungs and accumulation in the trachea, large airways, oropharynx, oesophagus and stomach, limiting the diagnostic accuracy. These effects are accentuated in cases with an abundance of airway secretions.
- The ^{81}Rubidium/^{81m}Kr generator is expensive and not widely available [3, 15, 16].
- The original PIOPED and revised PIOPED criteria as well as the new European guidelines for lung scintigraphy in adults with suspected PE have not been validated in children [13].

4.6 Take Home Messages

- Plan the study carefully, keeping in mind that ventilation scans may be difficult to obtain in young children.
- When both ventilation and perfusion studies are performed sequentially, the activities of the administered doses should be adjusted so the count rate from the second study is 3 times higher than that from the first study.
- When both perfusion and ventilation SPECT studies are obtained, they should be aligned and displayed side by side [13].
- Comparison to previous studies, when present, is essential to determine temporal changes and to assess the effectiveness of therapeutic interventions. This requires meticulous standardization of the study, including patient positioning and ROI drawing.
- When a right-to-left shunt is suspected the field-of-view of the perfusion study should be extended to visualize the presence or absence of tracer in the brain or renal parenchyma.
- A meticulous technique is important during the inhalation phase of the ventilation studies to achieve good tracer penetrance into peripheral airways and to prevent environmental contamination.
- Semi-quantitation of differential and regional lung perfusion and ventilation can be easily calculated and is important for planning and monitoring therapeutic decisions, and for long-term follow-up.
- The diagnosis of PE in adults as well as, although less common, in children, shifted in recent years from scintigraphic techniques to CT angiography (CTA). There are a number of risk factors for PE in children, the most common being the presence of a central line catheter. There has been some resurgence of ventilation/perfusion scintigraphy not only as a solution for PE evaluation when CTA is contraindicated (contrast allergy, chronic renal failure), but also to reduce the radiation burden compared with CTA.
- Perfusion and ventilation SPECT and/or SPECT/CT processed with iterative reconstruction methods because of the low count rates have improved the diagnostic accuracy for diagnosis of PE.
- For certain indications such as PE, a normal perfusion study performed first may eliminate the need for a ventilation study if it is normal.
- The most common congenital cardiac malformation with associated pulmonary stenosis is Tetralogy of Fallot. Baseline perfusion studies assess the severity of the condition and follow-up studies can determine the impact of therapeutic measures (balloon dilatation, stent placement etc.).
- When interpreting perfusion lung scans, in cases of congenital heart disease, it is essential to know:
  - The anatomy of the malformations and the corrective surgery that was performed.
  - If tracer was injected in the upper or lower extremity veins.
- Technegas® behaves as a ‘pseudo-gas’ with good penetration into the peripheral airspaces. Inhalation of Technegas® requires less patient cooperation and produces high-quality ventilation images.
- ^{133}Xe ventilation can be applied successfully to children with limited cooperation. It is a dynamic study, allowing only one view, typically posterior. The study should be performed prior to the perfusion acquisition.
- ^{81m}Kr enters the alveolar spaces and pulmonary circulation by diffusing into the alveolar capil-

laries. It returns from the peripheral circulation to the lungs and is exhaled. Equilibrium is reached rapidly with a constant concentration in the lungs allowing static images.

- ^{81m}Kr ventilation requires little cooperation, has a very low radiation burden due to the short half-life of ^{81m}Kr of 13 seconds and can be applied in studies of infants and young children.

4.7 Representative Case Examples

Case 4.1. Assessment of Pulmonary Artery Stenosis (Fig. 4.1)

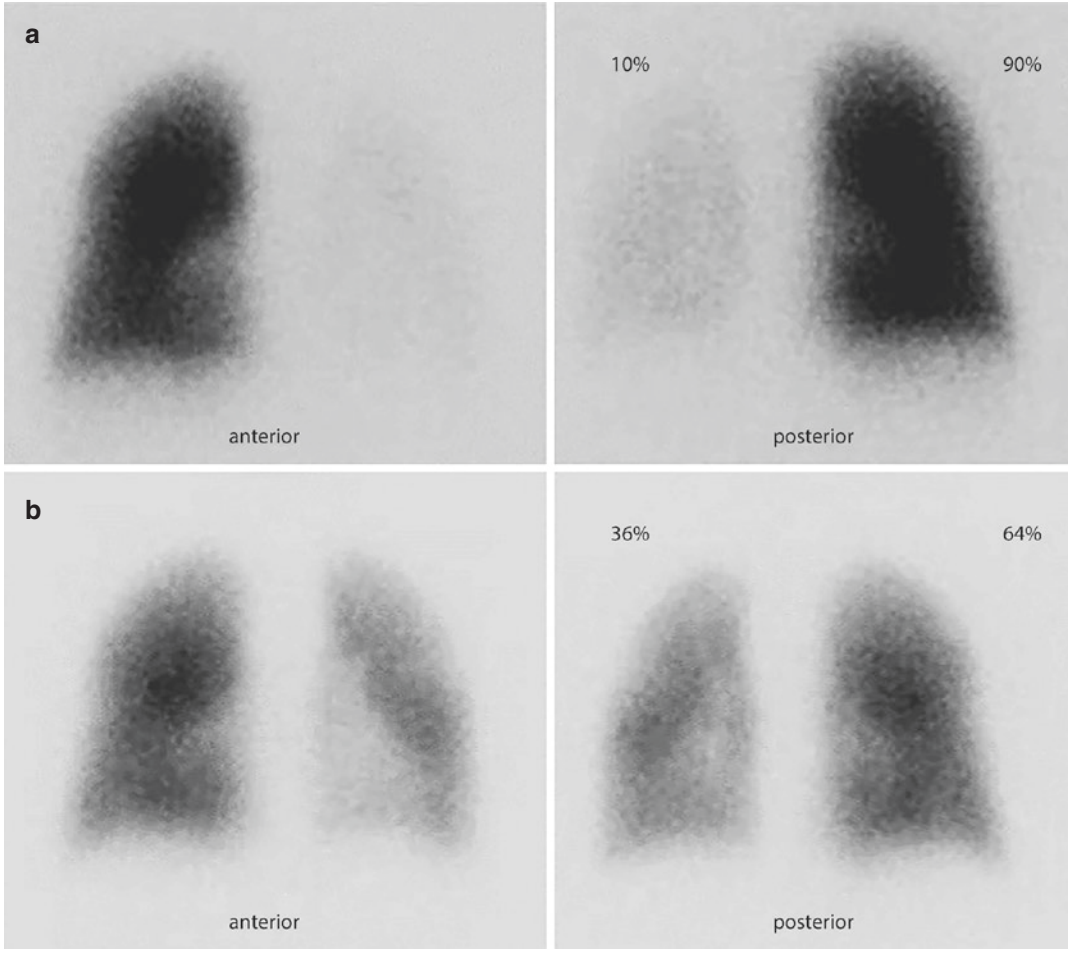

Fig. 4.1 History: A 4-year-old boy underwent perfusion lung scintigraphy to assess the impact of an isolated left pulmonary artery stenosis on the differential pulmonary perfusion. Anterior and posterior images (**a**) show a marked global reduction of the perfusion of the left lung. The differential perfusion was 90% and 10% to the right and left lungs, respectively. Based on these results he underwent cardiac catheterization with balloon dilatation of the left main pulmonary artery. A follow-up lung scan performed 6 months later (**b**) demonstrates improved perfusion to the left lung. The differential perfusion to the left lung increased from 10% to 36%. Impression: Marked improvement in left lung perfusion due to the successful intervention. NB: This case demonstrates how a perfusion lung scan guides decisions on the need for therapeutic interventions and evaluates their success

Case 4.2. Right-to-Left Shunt (Fig. 4.2)

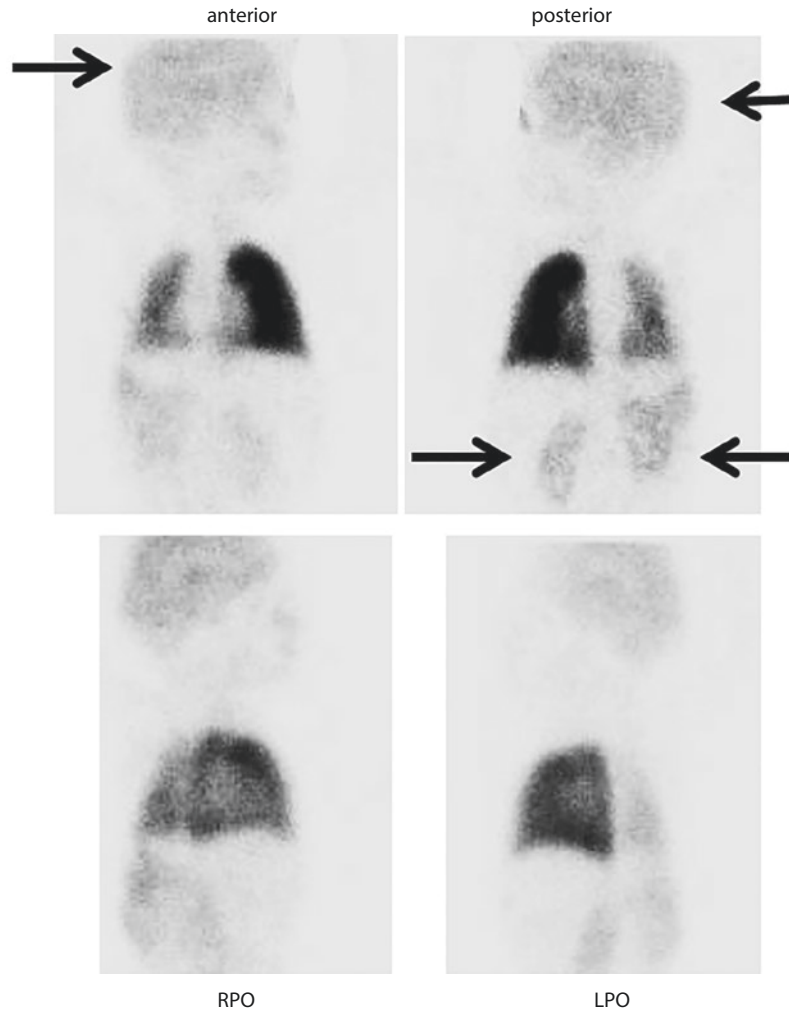

Fig. 4.2 History: A 10-month-old boy with complex congenital cardiac anomalies including situs inversus, corrected transposition of the great arteries and pulmonary atresia, underwent a left-sided modified Blalock Taussig shunt at the age of 1 month. Perfusion lung scan was performed to assess a stenosis of the right pulmonary artery. Study report: There is a reduction in the pulmonary perfusion of the right lung. In addition, there is diffuse tracer activity in the brain, in the parenchyma of both kidneys and in the spleen located in the right upper quadrant due to situs inversus (arrows). Impression: The findings suggest the presence of a shunt from the pulmonary to the systemic circulation, a right-to-left shunt

Case 4.3. Congenital Cystic Adenomatoid Malformation (Fig. 4.3)

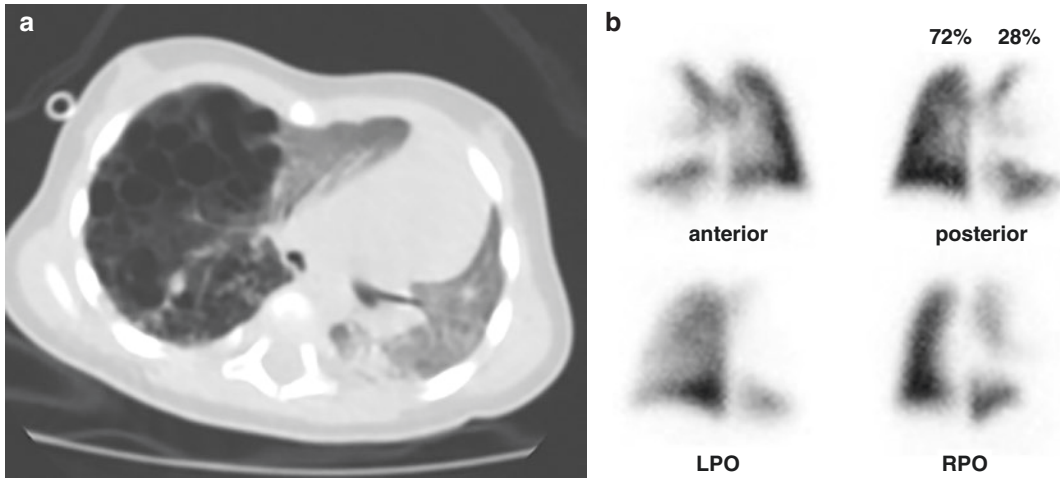

Fig. 4.3 History: A 4-month-old girl with a large congenital cystic adenomatoid malformation of the right lung as seen on chest CT (**a**). Study report: Baseline perfusion lung scintigraphy (**b**) shows a large perfusion defect in the right lung corresponding to the malformation. The differential perfusion was: right lung 28%, left lung 72%. Impression: Decreased perfusion to right lung corresponding to the structural malformation seen on CT. Subsequently, the infant underwent surgery to resect the malformation and to reconstruct the right pulmonary artery

Case 4.4. Hypoplastic Left Lung (Fig. 4.4)

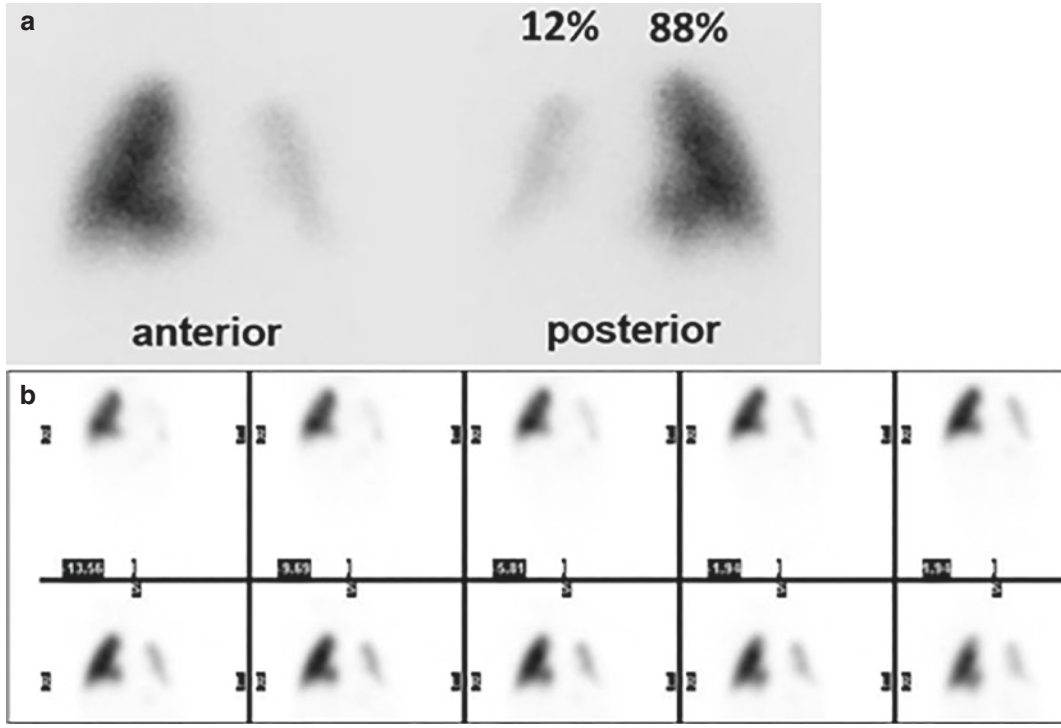

Fig. 4.4 History: A 7-month-old preterm infant with a hypoplastic left lung caused by congenital paralysis of the left hemi-diaphragm had lung perfusion scintigraphy to assess the differential pulmonary perfusion. Study report: Anterior and posterior perfusion images (**a**) and coronal SPECT slices (**b**) show a small left lung with a marked reduction in pulmonary perfusion contributing only 12% to the total pulmonary perfusion. Impression: Hypoplastic left lung with a marked decrease in relative perfusion

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