Physiological imaging of the lung: single-photon-emission computed tomography (SPECT)

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1 Department of Anesthesiology and Intensive Care, Karolinska University Hospital Solna; 2 Section of Anaesthesiology and Intensive Care Medicine, Department of Physiology and Pharmacology, Karolinska Institutet; 3 Section of Nuclear Medicine, Department of Hospital Physics, Karolinska University Hospital Solna; and 4 Medical Radiation Physics, Department of Oncology-Pathology, Stockholm University and Karolinska Institutet, Stockholm, Sweden

Petersson J, Sánchez-Crespo A, Larsson SA, Mure M. Physiological imaging of the lung: single-photon-emission computed tomography (SPECT). J Appl Physiol 102: 468 – 476, 2007. First published September 21, 2006; doi:10.1152/japplphysiol.00732.2006.—Emission tomography provides three-dimensional, quantitative images of the distribution of radiotracers used to mark physiological, metabolic, or pathological processes. Quantitative single photon emission computed tomography (SPECT) requires correction for the image-degrading effects due to photon attenuation and scatter. Phantom experiments have shown that radioactive concentrations can be assessed within some percentage of the true value when relevant corrections are applied. SPECT is widely spread, and radiotracers are available that are easy to use and comparably inexpensive. Compared with other methods, SPECT suffers from a lower spatial resolution, and the time required for image acquisition is longer than for some alternative methods. In contrast to some other methods, SPECT allows simultaneous imaging of more than one process, e.g., both regional blood flow and ventilation, for the whole lung. SPECT has been used to explore the influence of posture and clinical interventions on the spatial distribution of lung blood flow and ventilation. Lung blood flow is typically imaged using macroaggregates of albumin. Both radioactive gases and particulate aerosols labeled with radioactivity have been used for imaging of regional ventilation. However, all radiotracers are not equally suited for quantitative measurements; all have specific advantages and limitations. With SPECT, both blood flow and ventilation can be marked with radiotracers that remain fixed in the lung tissue, which allows tracer administration during conditions different from those at image registration. All SPECT methods have specific features that result from the used radiotracer, the manner in which it is administered, and how images are registered and analyzed.

respiratory physiology; regional blood flow; pulmonary ventilation; pulmonary gas exchange; radionuclide imaging

THE NONUNIFORM DISTRIBUTIONS of regional lung blood flow and ventilation were first demonstrated utilizing radioactive tracers (radiotracers) and external scintillation detectors that registered the distribution of radioactivity within the lung (10, 14, 43, 93). Later the development of the gamma camera allowed two-dimensional imaging of the distribution of radiotracers (58). In the mid to late 1970s, both single-photon-emission computed tomography (SPECT) and positron emission tomography (PET) were developed, offering three-dimensional images of the in vivo distribution of radioactivity. These techniques can be used to study, for example, the three-dimensional distribution of regional blood flow or regional ventilation with a high spatial resolution. In this article we will first briefly explain the principles and characteristics of the SPECT method and second review studies that exemplifies how SPECT has been used to increase our understanding of lung physiology. The content is focused on the use of SPECT to image regional lung blood flow and ventilation.

SPECT IMAGING

Principles of SPECT Imaging

Emission tomography aims at noninvasive quantification and spatial localization of physiological, metabolic, or pathological processes in humans or animals through the use of a tracer that is either radioactive itself or labeled with a radioactive compound. Characteristics of some commonly used radionuclides are presented in Table 1. Photons emitted from the radiotracer are registered at various angles around the body.
Table 1. Examples of radionuclides used with radiotracers for SPECT imaging

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half-Life</th>
<th>Energy</th>
<th>Use and Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technetium-99m</td>
<td>6 h</td>
<td>140 keV</td>
<td>Used to label albumin macroaggregates for imaging of regional blood flow. Used as $^{99m}$Tc-DTPA aerosol or Technegas for imaging of regional ventilation.</td>
</tr>
<tr>
<td>Xenon-133</td>
<td>5.3 days</td>
<td>81 keV</td>
<td>Steady-state inhalation for regional alveolar volume. Dynamic SPECT during washout for imaging of regional ventilation.</td>
</tr>
<tr>
<td>Krypton-81m</td>
<td>13 s</td>
<td>190 keV</td>
<td>Steady-state intravenous infusion for imaging of regional blood flow. Comparably expensive. The $^{81m}$Kr generator (half-life 4.5 h) is produced by a cyclotron and has to be used within 15–20 h.</td>
</tr>
<tr>
<td>Indium-113m</td>
<td>100 min</td>
<td>392 keV</td>
<td>Alternative radionuclide for labeling of albumin macroaggregates.</td>
</tr>
</tbody>
</table>

SPECT, single-photon-emission computed tomography; DTPA, diethylene-triamine pentaacetate.

by a gamma camera. These data are then used for a computational reconstruction of a three-dimensional image of the radioactivity distribution. Thus SPECT compares with planar gamma camera imaging as X-ray computed tomography (CT) with the standard chest X-ray. Typically a registration is done for 10–60 s at 64–90 consecutive angles over an interval of 360°, i.e., at 4–5.6° per angle. Nowadays, most SPECT systems use a multiheaded camera to speed up image acquisition, which normally requires 10–30 min.

Quantitative Imaging: Correction for Scatter and Attenuation

Physical interaction with tissues causes scatter and attenuation of photons emitted from the radiotracer, which results in an underestimation of the true concentration of radioactivity within the body. Scattering changes the original direction of photons emitted from the radiotracer, which contributes to image blurring. When photons interact with tissues they lose some of their energy; most scattered photons can therefore be excluded by rejecting photons with a reduced energy. However, the finite energy resolution of the gamma camera means that some scattered (secondary) photons cannot be discriminated from primary photons. When the lung is imaged, the fraction of scattered photons is typically 10–15% of all detected photons (71). The amount of attenuation and scatter depends on the photon energy and also on the length and physical properties of the pathway between the emitting radiotracer and the gamma camera. For example, half of the photons from technetium-99m ($^{99m}$Tc) are lost after passing through 4.5 cm of soft tissue (87). Scatter and attenuation are therefore not uniform throughout the body, causing distortion of the image.

Quantitative SPECT requires that measurements are corrected for these image-degrading factors (Fig. 1) (5, 62, 71, 88). One approach to this problem is the use of transmission imaging, which uses the SPECT system and an external radiation source to obtain an attenuation map of the imaged object (5, 9, 71). These data can then be applied to correction algorithms that reduce the influence of attenuation and scattered photons and retrieve the true concentration of radioactivity per unit volume. Phantom studies have demonstrated that these methods provide measurements of regional radiotracer concentrations that differ from the true concentrations within only a few percent (Fig. 1) (71).

Spatial Resolution

The spatial resolution of the SPECT method depends on the energy of the radionuclide, the specific SPECT system (especially the type of collimators), and the distance between the emitting source and the gamma camera. The resolution may be assessed by the full-width half-maximum (FWHM); two point sources can be resolved if the distance between them is at least one FWHM. For a typical SPECT system, this distance is 10–20 mm for 140 keV photons ($^{99m}$Tc). Corresponding values for PET systems are 4–6 mm and for CT or magnetic resonance imaging (MRI) systems down to 0.5 mm. With SPECT imaging of the chest, the time required for image acquisition and the constant movements of the lungs and the heart results in a further loss of resolution. The lower resolution of the SPECT method, compared with the other methods, results in a greater impact of the partial volume effect. In short, the partial volume effect means that the measured radiotracer concentration at the center of a volume with uniform concentration is influenced by the surrounding concentration if the volume is smaller than two to three times the FWHM in any direction. Thus measurements of radiotracer concentration in volume elements (voxels) below the spatial resolution will not be independent of the concentration in surrounding voxels. Rather the measurements represent an average for a cluster of juxtapositioned voxels but weighted for the voxel at interest. The partial volume effect also causes a gradual attenuation of the concentration measured at the edge of the volume of radiotracer distribution (edge effect). The finite spatial resolution means that SPECT tends to underestimate the heterogeneity of the imaged process. For example, if both regional lung ventilation and perfusion are imaged, SPECT tends to underestimate the heterogeneity of the ventilation-to-perfusion ratios (66). These principles apply also to other imaging methods, but their impact depends on the spatial resolution of the method.

Limitations of the SPECT Method

An obvious limitation of SPECT is the radiation exposure, which depends on the chosen radionuclide and the process studied. A typical combined ventilation and perfusion lung study using $^{99m}$Tc exposes the subject to an effective dose of 2–3 mSv. For comparison, in Scandinavia, the annual exposure to background radiation amounts to 2–5 mSv. A chest CT done for diagnosing pulmonary embolism exposes the patient to 5–10 mSv. The effective dose approved for studies of healthy volunteers varies between countries. In Sweden, an effective dose of 5 mSv is approved if the study is considered of significant value, which allows up to four measurements in each subject (65). A further limitation of SPECT is the time required for image acquisition; if the protocol includes transmission imaging, the time required might be 45 min. During
this time, the imaged object needs to remain in a fixed position in relation to the camera. In general, the time required for image acquisitions is longer for SPECT than for CT- and PET-based methods. The importance of scatter and attenuation corrections and the finite spatial resolution are limitations that have been discussed above. It is essential to understand that, although sharing the same imaging modality, all SPECT methods have unique features that result from the used radiotracer, the manner in which it is administered, and how images are registered and analyzed. We will exemplify and discuss this further below.

Comparison with Other Methods Imaging Regional Blood Flow and Ventilation

During recent years, SPECT, PET, CT, and MRI techniques have all been employed in new methods that image regional lung blood flow and ventilation (4, 36, 39, 55, 71, 76, 89, 91, 92). These methods differ in their advantages and limitations and should therefore be considered as complementary. Compared with other methods, SPECT is widely spread, and radiotracers are available that are easy to use and comparably inexpensive. Compared with other methods, SPECT suffers from a lower spatial resolution, and the time required for image acquisition is longer than for some alternative methods. However, in contrast with several other methods, SPECT allows simultaneous studies of both regional blood flow and ventilation for the whole lung (45, 66, 71). Both regional blood flow and ventilation can be marked during normal tidal breathing; no breathing maneuver is required. A unique feature of SPECT is that both blood flow and ventilation can be marked using radiotracers that remain fixed in the lung tissue after administration. Even if imaged later, the distributions of the radiotracers correspond to the distribution at the time of administration. This can be taken advantage of to explore the distribution of blood flow and ventilation during conditions that are not otherwise amenable to modern imaging methods. For example, we recently administered macroaggregates to healthy volunteers in a human centrifuge to explore the effect of hypergravity on the distribution of lung blood flow (65).

Of note is that imaging methods provide estimates of, e.g., regional lung blood flow or ventilation, expressed in units with different denominators, such as unit lung volume, unit lung tissue, or unit alveolar gas volume. Measurements obtained with different methods might be poorly comparable since the amount of lung tissue or the alveolar gas volume per unit lung volume varies between lung regions and with changes in body.
posture, lung volume, mode of ventilation, etc. SPECT measurements are generally expressed per unit lung volume, which complicates the comparison of images of blood flow or ventilation obtained during different conditions if the distribution of lung tissue varies with the condition (67). A further use of radiotracers that remain fixed in the lung after administration is that regional blood flow and ventilation can be marked repeatedly (at different occasions) during different conditions, e.g., postures or ventilator settings, while the conditions can be identical for all image acquisitions (67). With this study design, image comparison is simplified since tissue distribution can be assumed to be identical in all images. Another advantage, when all images are obtained with identical tissue distribution, is that the image-degrading effects of scatter, attenuation, and the finite resolution do not contribute to differences between images.

**Imaging More Than One Process**

The same radionuclide can be used to image two processes sequentially or to repeat imaging of the same process, if either the physical decay or the clearance of the radiotracer is very rapid (63). In this case the number of studies is limited by the radiation dose. Other radiotracers can be used for repeated imaging within a short time span using image subtraction (54, 60, 65). With this approach, the radioactivity that remains from the first radiotracer administration is subtracted from the images obtained after the second experiment, which allows the distribution of the radiotracer at the second administration. This requires that images are obtained both before and after the second administration and that the imaged object remain in a fixed position in relation to the camera throughout the procedure. The second dose of the radiotracer should be adjusted so that the majority of the imaged radioactivity originates from the second administration. A further alternative is to use two radiotracers labeled with different energies (dual-isotope imaging), which allows two processes to be marked and imaged simultaneously (45, 66, 71, 72).

**SPECT Imaging of Regional Lung Perfusion**

**Radiotracers for Imaging of Regional Blood Flow**

Regional lung blood flow is typically imaged using intravenous administration of macroaggregates of albumin (MAA) labeled with $^{99m}$Tc. The size of these particles (10–150 μm) causes them to become trapped in the pulmonary microcirculation in proportion to regional blood flow, which has been confirmed with other measurement methods (52). A maximum dose of MAA corresponds to ~700,000 particles, which occupies <1 × 10^{-4} % of the pulmonary capillaries (Mallinckrodt Medical, Petten, The Netherlands), according to one manufacturer the particles have a biological half-life of 11 h (Mallinckrodt Medical). With planar gamma camera imaging, regional blood flow has also been studied using intravenous bolus injection of radioactive gases that is allowed to evolve into the alveoli during breathhold (58). The time required for image registration excludes the use of this technique for regional delivery, i.e., blood flow. However, it has been demonstrated that regional measurements of blood flow obtained with this technique are influenced by regional ventilation abnormalities (18).

**Posture and the Distribution of Lung Blood Flow**

Maeda et al. (50) pioneered the use of SPECT to explore the effect of body posture on the distribution of pulmonary blood flow in healthy volunteers. When administering the macroaggregates with subjects in the upright posture and imaging the distribution with subjects in supine position, they observed a gravitational gradient with increasing blood flow from apex to the base of the lung. In the prone and supine posture, the cranial-to-caudal blood flow distribution was uniform. Similar results have been reported by other SPECT studies (5). These results are consistent with the zonal model (94), which explains a greater blood flow to dependent lung regions with the influence of gravity. SPECT studies of healthy volunteers have demonstrated greater blood flow to dependent (dorsal) regions also in the supine posture (5, 44, 50, 54, 60, 63). In the prone posture the results have been more divergent, with studies showing either a uniform vertical blood flow (60) or greater blood flow to either dependent (50, 63) or nondependent regions (54). Including very few subjects (50, 63), image acquisition in different postures (54, 60), analyzing distributions within the whole lung or only within a section of the lung, and comparing blood flow between regions of equal or non-equal size (54, 60) are all differences between studies that might contribute to varying results.

**Blood Flow Variation Within Isogravitational Planes**

In a series of studies, Hakim and coworkers used SPECT to demonstrate a heterogeneous distribution of lung blood flow within isogravitational planes in both animals and humans (31, 33, 34, 48). A gradient with decreasing flow from central to peripheral regions was demonstrated both in humans and in excised dogs lungs; in the latter case the gradient was also observed when a section of the lung was studied using planar imaging (32, 48). This is of importance since it showed that the phenomenon was not solely due to SPECT underestimating flow to peripheral regions (edge effect). Hakim et al. (31, 32) concluded that other factors besides gravity, possibly regional vascular conductance, must be of importance for the regional distribution of pulmonary blood flow.

**Active Regulation of Lung Blood Flow**

In a recent study, Rimeika et al. (70) used SPECT to demonstrate that local production of nitric oxide (NO) influences the distribution of lung blood flow in normal subjects. In the supine posture inhibition of NO synthase caused a redistribution of blood flow from dorsal to ventral regions. On the other hand, inhibition of NO production in the prone posture caused no change in the distribution of regional blood flow.

**SPECT Imaging of Regional Ventilation**

**Radiotracers for Imaging of Regional Ventilation**

Both radioactive gases, mostly krypton-81m ($^{81m}$Kr) and xenon-133 ($^{133}$Xe), and particulate aerosols labeled with radiotracer have been used for SPECT imaging of regional ven-
tilation. Each of these carries specific advantages and limitations; radiotracers useful for diagnostic imaging are not always equally suited for quantitative measurements. Regional radiotracer concentration after aerosol administration is a result of regional delivery and retention of aerosol particles, which does not necessarily equal regional ventilation.

Radioactive gases. The use of a radioactive gas diminishes concerns that the distribution of the radiotracer might be different from the distribution of regional ventilation; however, it also creates limitations. The rapid decay of $^{81m}$Kr (half-life = 13 s) means that regional concentration of radioactivity during steady-state inhalation is proportional to regional ventilation (7, 8, 26). However, at increased minute ventilation and in children, regional concentration of the radiotracer is influenced not only by regional ventilation but also by regional alveolar volume (8, 19). The methodology requires that imaging is done during continuous administration of the radiotracer. The cost and the short half-life of the $^{81m}$Kr generator (4.5 h) limit the use of this radiotracer. $^{133}$Xe has a much longer half-life (5.3 days), regional concentration during steady-state inhalation is therefore a reflection of regional gas volume. However, dynamic SPECT, e.g., repetitive 30-s image acquisitions of the whole lung, during the washout phase after steady-state inhalation can be used to study regional ventilation (80). This technique has mostly been used to study abnormalities in regional ventilation in patients with obstructive lung disease (73, 78–81). The low energy of $^{133}$Xe (80 keV) results in a spatial resolution lower than that for $^{99m}$Tc and $^{81m}$Kr.

$^{99m}$Tc-diethylenetriamine pentaacetate aerosol. Clinically the most common ventilation radiotracer is $^{99m}$Tc-diethyleneetriamine pentaacetate (DTPA) aerosol. The aerosol is comparably inexpensive, easy to use, and available at most nuclear medicine departments. Modern nebulizers produce an aerosol with an aerodynamic mass median diameter close to 1.0 μm, which is consistent with a predominating alveolar deposition (13, 47). However, impaction of the aerosol particles in central airways (20). Several studies using planar imaging have found that the deposition of the radioaerosol differs from the distribution of regional ventilation measured with $^{81m}$Kr (1, 16, 20). We are not aware of studies that used SPECT to compare the distribution of $^{81m}$Kr and DTPA aerosol. A further problem with the $^{99m}$Tc-DTPA aerosol is that the activity is cleared from the lung by absorption through the alveolar-capillary membrane at a rate that might cause distortion of the images. In fact, the clearance of $^{99m}$Tc-DTPA has been used to quantify lung injury (61). In normal nonsmoking subjects, Monaghan et al. (53) found a mean half-clearance time of 52 min (range 20–132 min); in diseased lung this was reduced to 5 min (range 2–26 min). In contrast, animal studies of irradiation and amiodaron-induced lung injury have shown a retarded clearance (2, 24, 77, 90). Clinical studies after radiotherapy against the thorax and of amiodaron-induced pulmonary toxicity have, however, found increased DTPA clearance (23, 83, 84, 99). DTPA aerosols with larger particle sizes have been used to study the distribution of inhaled aerosols within the airways (25, 59).

Technegas. Another alternative for SPECT imaging of regional ventilation is Technegas, a dispersion of ultrafine graphite particles labeled with $^{99m}$Tc (15). The aerosol is produced by a Technegas generator, which heats a graphite crucible with pertechnetate to 2,500°C in an atmosphere of 100% argon. Although there is some disagreement regarding the particle size, most authors agree that the diameter is <200 nm (15, 37, 46, 49, 75); some suggest much smaller. The smaller particle size compared with other aerosols results in a greater alveolar deposition and less impaction in central airways. Several studies, using planar gamma camera imaging, have found $^{81m}$Kr and Technegas images of regional ventilation to be highly equivalent (6, 20, 22), even during conditions when $^{99m}$Tc-DTPA aerosol suffered from significant deposition in central airways (20). However, pharmacologically induced bronchostenosis increases the deposition in central airways, resulting in different distributions of Technegas and $^{81m}$Kr (64). Technegas deposition in central airways in patients with chronic obstructive pulmonary disease has also been reported in some clinical studies (21, 38). Hinz et al. (35) found a good correlation between SPECT measurements of regional ventilation obtained with Technegas and $^{81m}$Kr in an animal model of acute lung injury. A special concern with the use of Technegas is that presence of oxygen at the time of combustion leads to contamination with Pertechnegas (74, 98). These particles permeate the alveolar-capillary barrier and are cleared very rapidly from the lung (half-life = 10 min), which will cause a distortion of images acquired during this phase. In contrast, after administration of Technegas the reduction of radioactivity in the lung is almost entirely explained by physical decay (15). Contamination with Pertechnegas is easily detected if the change in radioactivity in the lung is followed during the first 20–30 min after Technegas administration. Pertechnegas has been used for measurement of the permeability of the alveolar-capillary membrane (53). Recent work has shown that modification of the Technegas generation process eliminates Pertechnegas contamination, minimizes leach of radioactivity from the particles, and reduces the growth of the particles through aggregation and absorption of water (56). Human studies have found that the retention of these particles within the lung during the first 24–70 h after administration is nearly complete (95, 96). Technegas is not approved by the US Food and Drug Administration.

Posture and Regional Ventilation

Several SPECT studies of spontaneously breathing healthy volunteers have demonstrated greater regional ventilation in dependent (dorsal) regions in the supine posture (54, 63). In the prone posture two previous studies have found greater ventilation in nondependent (dorsal regions) (54, 63). In a small number of subjects, Orphanidou et al. (63) also showed that the distribution of ventilation was uniform in the cranial-to-caudal direction in the supine and prone postures, which is in agreement with previous studies.

Airway Closure

Studying normal subjects, King et al. (41, 42) used SPECT to demonstrate a close correlation between the lung volume without radioactivity after inhalation of a bolus of Technegas from residual lung volume and closing capacity measured with a single-breath nitrogen test. In normal subjects, regions affected by airway closure were contiguous and mostly located in...
dependent regions, while a patchy distribution was observed in asthmatic subjects (42).

**Ventilation Heterogeneity**

Several recent SPECT studies have evaluated objective estimates of ventilation heterogeneity in normal and diseased lung (57, 97). For example, Xu et al. (97) showed that intraregional ventilation heterogeneity discriminated between normal and emphysematous lungs.

**SPECT Imaging of Regional Ventilation-to-Perfusion Ratios**

Regional ventilation-to-perfusion ratios can be calculated if both regional ventilation and perfusion are measured (45, 54, 66, 72). With this study design it is an advantage if radionuclides with similar energies are used or if the same radionuclide is used sequentially. Similar energy levels mean that attenuation and scatter affect ventilation and perfusion measurements equally, which makes the ventilation-to-perfusion ratio insensitive to these phenomena. A different approach was employed by Almquist et al. (4), who imaged regional ventilation-to-perfusion ratios using steady-state intravenous infusion of $^{133}$Xe, a method previously applied to PET imaging using nitrogen-13 as the radiotracer (68, 69). In all six subjects studied supine, they observed a gravitational gradient with decreasing ventilation-to-perfusion ratios down the lung. However, they also noted difficulties with the method with curiously low ventilation-to-perfusion ratios. Underestimation of the xenon concentration in mixed venous blood, measured as the activity in the right ventricle, was proposed as a potential explanation. In normal subjects, SPECT has been used to demonstrate a narrow frequency distribution of ventilation-to-perfusion ratios (66, 72), consistent with efficient gas exchange. Increased width of the SPECT-measured frequency distribution correlates with the alveolar-arterial oxygen difference in patients with lung diseases (72).

**SPECT Imaging of Regional Blood Flow and Ventilation During Clinical Interventions**

**Continuous Positive Airway Pressure-Breathing**

Mure et al. (54) explored the effect of continuous positive airway pressure (CPAP) and posture on regional lung blood flow and ventilation in normal subjects. CPAP induced a ventilation-perfusion mismatch in both postures, but the effect was greater in the prone posture. In supine position, CPAP caused a redistribution of both blood flow and ventilation to dependent (dorsal) regions. In prone position, blood flow was again shifted to dependent (ventral regions) while ventilation was redistributed to nondependent (dorsal) regions.

**Mechanical Ventilation and General Anesthesia**

Tokics et al. (85, 86) employed both SPECT, CT, and the multiple inert gas elimination technique (MIGET) to increase...
our understanding of the gas-exchange impairment induced by general anesthesia and mechanical ventilation. CT demonstrated that general anesthesia causes atelectasis in the dependent lung regions. SPECT showed that these regions were not ventilated but still perfused. Moreover, estimates of shunt obtained by either SPECT or MIGET correlated with the amount of atelectasis. MIGET measurements also showed that the matching of ventilation to perfusion deteriorated during mechanical ventilation compared with when subjects were awake and breathing spontaneously. SPECT showed that during mechanical ventilation (supine) regional ventilation was preferentially distributed to nondependent regions while blood flow was greater in dependent regions.

**Effect of the Prone Position in Acute Lung Injury**

Lamm et al. (45) used a dual-isotope SPECT method to explore the mechanisms by which the prone position improves oxygenation in an animal model of acute lung injury. In the supine posture the impaired oxygenation was mostly explained by dorsal lung regions with a low ventilation-to-perfusion ratio. Turning the animals prone improved the ventilation-to-perfusion ratio in dorsal regions and reduced the overall ventilation-to-perfusion dispersion, which resulted in a great increase in arterial oxygenation. A previous study using the same animal model demonstrated a similar distribution of blood flow in the supine and prone postures (3). The authors therefore concluded that the major effect of the prone posture is an improved ventilation of dorsal lung regions.

**RECENT INNOVATIONS AND FUTURE DEVELOPMENTS**

**Multimodality Imaging**

A recent innovation is the introduction of combined SPECT-CT scanners, which provides both functional and anatomical images (Fig. 2). With these systems, CT images provide additional morphological information, e.g., regarding the localization of a disease process, that can be linked to the functional information obtained from the SPECT images. CT images can also replace transmission images used for attenuation corrections. An alternative approach to multimodality imaging is to digitally fuse images obtained with different techniques at different occasions (29, 40, 82).

**Gated SPECT**

The constant movement of the lung during image acquisition reduces the spatial resolution. Image registration gated to end-inspiration has been shown to increase the diagnostic yield of SPECT imaging (82). Although not yet demonstrated, it is likely that this technique would improve quantitative imaging of regional blood flow and ventilation.

**Micro-SPECT**

Another recent development is the construction of SPECT systems dedicated for the functional studies of small animals (11, 17, 28). Application of pin-hole collimator techniques and the proximity of the imaging field to the camera result in a spatial resolution that allows imaging of radiotracer distributions even in small objects. In the mouse, structures down to a size of 0.5 mm have been clearly visualized (11), suggesting that molecular uptakes in volumes down to 0.1 μl can be estimated (11). Together with molecular imaging techniques (12, 30), these systems open up new fields of exciting physiological imaging.

**SUMMARY**

SPECT allows accurate measurements of physiological processes within the lung when images are corrected for the degrading effects of attenuation and scatter. Although imaging techniques with a higher spatial resolution are available, SPECT also has advantages compared with other methods. SPECT systems and radiotracers suitable for lung imaging are widely available; both regional blood flow and ventilation can be imaged for the whole lung simultaneously. From the literature it is clear that SPECT imaging has contributed greatly to our present understanding of lung physiology.

**REFERENCES**


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Invited Review


