A New Perspective and Old Problems

In this issue of The Journal of Nuclear Medicine Maeda and his colleagues describe a single-photon tomographic approach to the determination of the pleural edge (1). They have joined a growing number of investigators who have demonstrated potentially important clinical applications for this diagnostic mode. The authors suggest that their combined emission-transmission images will help characterize the nature and extent of peripheral dysfunction in perfusion lung scans. It is clear that their technique will differentiate perfusion defects due to pulmonary vascular occlusion, pneumothorax, obstructive, and early fibrotic disease from defects caused by solid masses, consolidation, or pleural effusions. Beyond these applications, however, it is natural to consider the impact of single-photon emission tomography on the primary application of lung scanning—that of assessing the likelihood of pulmonary embolization (PE). To this end, regional ventilation and perfusion must be characterized to differentiate other causes of pulmonary dysfunction from the parenchymal compromise associated with embolization. Since the sensitivity to macroscopic dysfunction is strongly dependent on spatial separation of normal and abnormal lung regions, tomographic images provide an attractive alternative to conventional scans. Unfortunately, two-dimensional studies are largely topographical representations where image values represent averages of pulmonary function within a poorly defined cylinder standing perpendicular to the collimator face. Moreover, the functional characteristics of lung tissue within this cylinder are represented by a weighted average, with activity in regions closest to the camera detected more efficiently than activity in more distant regions. For example, the 80 keV gamma rays of Xe-133 undergo a 45% attenuation through 10 cm of inflated lung (2). The circumferential data collection of a tomographic device not only reduces errors due to limited angular sampling, but also provides transaxial images that are relatively independent of background and the functional effects that would otherwise be superimposed. Thus, there are significant advantages to tomographic images of the lung. The problems common to standard pulmonary scintigraphy—attenuation, background error, and functional averaging—are greatly reduced.

It is clear that improved descriptions of the distribution of regional perfusion will aid in the detection of parenchymal disease, but perfusion imaging by itself may not suffice to demonstrate embolization with high probability (3). Although normal four to six view perfusion scans have been shown to exclude embolic disease (4,5) reliably, abnormal perfusion scans are nonspecific since nearly all pulmonary diseases can cause perfusion abnormalities. To increase scintigraphic specificity, an assessment of regional ventilation has been required. The addition of Xe-133 ventilation imaging, for example, provides significant improvement in the specificity and accuracy of perfusion lung scanning for diagnosing PE (6). Unfortunately, because of the time required for multiaxial tomographic data collection, only equilibrium xenon distributions can be assessed, and these represent regional lung volume, not ventilation. Clearly, a tracer with a "static" distribution that is proportional to air flow is necessary. Although krypton-81m could be used (7), it is relatively expensive and may be unavailable on short notice. Technetium radioaerosols (8,9) are the most likely alternative for ventilation studies. The settling-reservoir technique developed by Taplin has been demonstrated to produce high-quality images reflecting regional ventilation (10). In addition to its alveolar stability, the use of a technetium aerosol would make attenuation corrections unnecessary in quantitative evaluations of regional ventilation/perfusion (V/Q) ratios.

The flood of image information contained in multiple transaxial views of the distribution of ventilation, perfusion, and V/Q ratio will present special challenges to those interpreting these scans. In addition to the necessity of integrating the images spatially, the complexities of pulmonary pathophysiology need to be superimposed on a three-dimensional model of segmental anatomy. More than ever, therefore, it will be important to have a clear understanding of the pathophysio-
logic states of pulmonary function.

Unfortunately, physiologic ventilation and perfusion are not uniformly distributed. Regional perfusion increases toward the bottom of the lung, its gradient of change determined by the relationships between alveolar, capillary arterial, and capillary venous pressures (11–13). Alveolar pressure acts on the capillary bed as a microscopic sphygmomanometer. At the top of the lung, often referred to as zone one, there is very little blood flow because the alveolar pressure exceeds both capillary arterial and venous pressures. In zone two, toward the base of the lung, the capillary arterial pressure becomes increasingly greater than the alveolar pressure, and blood flow increases in proportion to their difference. Lower still, in zone three, both capillary arterial and venous pressures are greater than the alveolar, causing a full distention of the capillary. Here flow is dependent on the difference between the arterial and venous pressures alone. At the very bottom of the lung, in zone four, flow may be reduced by compression of the lung from abdominal viscera. As gravitational effects are equal at all horizontal levels, it is reasonable to expect that normal lung perfusion is homogeneous horizontally. Although this simple rule is generally correct within a given segment, two segments at the same horizontal level may not demonstrate the same capillary flow, because perfusion pressure in a segment is in part determined by the height of the orifice of its pulmonary artery. In the upright position, for example, alveoli of the superior segment will receive a larger flow than alveoli of the anterior segment at the same horizontal level, because the artery feeding the superior segment leaves the arterial tree at a lower point.

Regional ventilation normally increases gradually toward the bottom of the lung, following the influence of the intrapleural pressure gradient (13,15). This gradient is formed by three factors: (a) the outward pull of the chest wall; (b) the opposing inward pull of the lung; and (c) the weight of the lung. Intrapleural pressure is most negative at the top of the lung and least negative at the bottom, where the weight of the lung is the greatest. Because alveoli at the top of the lung experience a greater distending pressure, they are larger at end expiration than those at the bottom of the lung. Therefore, the alveoli at the top of the lung fill to a lesser extent during inspiration than those at the bottom. This causes the ventilatory flow to decrease down the lung in a smooth pattern that is horizontally homogeneous. Where alveolar morphology is changed by alveolar disease, however, ventilatory flow will no longer be homogeneous. There are two main changes in alveolar morphology that cause ventilatory dysfunction—either abnormal airway resistance or abnormal alveolar compliance (16). Increasing either or both will decrease regional ventilation. Thus, a local reduction of ventilation may be associated with increased resistance due to excessive airway secretions or with increased alveolar compliance due to alveolar wall damage. On the other hand, where alveolar wall fibrosis decreases alveolar compliance, regional ventilation will increase.

Although the presence of parenchymal disease can be detected by local abnormalities in the distribution of ventilation or perfusion, the functional state of the lung is largely determined by the relationship between these two flow rates (13,17). The optimum conditions for gas transfer occur when the rates of capillary perfusion and alveolar ventilation are nearly matched. As the flow in these two compartments departs from an ideal ratio of about one, the ability of the alveolar-capillary unit to maintain its function declines. Mismatch occurs physiologically because capillary perfusion tends to be greater than the alveolar ventilation in dependent lung zones and falls more rapidly than ventilation toward the top of the lung. In the upright lung, for example, the \( V/Q \) ratio approximates values of 0.5 to 1 in the lower lobes and increases to about 3.5 in the apical zones (17). Because the gradients of these two flow rates tend to change smoothly and are homogeneous along horizontal planes, the ventilation/perfusion ratio increases smoothly toward the top of the lung. Thus, as with ventilatory or perfusion distributions, pulmonary dysfunction is reflected by regionally inhomogeneous patterns of \( V/Q \) ratios.

Although the identification of regions of abnormal lung function depends on a general understanding of both normal physiology and segmental anatomy, a scan interpretation also requires an evaluation of the cause of dysfunction, specifically, an estimate of the likelihood of pulmonary embolization. Generally, there are four states of abnormal function that produce local distortions of ventilation and perfusion. These abnormal conditions are found in the vascular occlusive, the consolidative, the obstructive, and the restrictive diseases.

A mismatch of ventilation and perfusion is characteristic of pulmonary embolization, and, in general, any vascular occlusive lung disease. Alveoli are structurally intact although airway pneumoconstriction may be caused either by substances released from the clot or by reductions in al-
veolar levels of carbon dioxide, a potent airway dialator. This response is usually transient and is rarely observed in scintigraphic studies (18-22). In the absence of this effect, ventilation is preserved in these regions of perfusion compromise—the functional mismatch characteristic of pulmonary emboli.

The vascular occlusive pattern is not found in about 10% of emboli where pulmonary infarction causes pulmonary consolidation (23). Consolidative processes are those in which damage to the capillary bed causes loss of intravascular components into the alveolar space. Pulmonary embolism infrequently leads to infarction in normal lung because the lung is oxygenated from the bronchial circulation and to some extent directly from the alveolar air. When cardiovascular and pulmonary disease compromise these sources of oxygen, however, the loss of arterial flow may cause pulmonary infarction (23). With inadequate supplies of oxygen for alveolar metabolism, pulmonary surfactant production stops, leading to alveolar collapse and atelectasis (24). Infectious processes can cause similar alveolar damage either through bacterial or host defense mechanisms. Although the degree of ventilation compromise and perfusion compromise can vary, both are usually severely reduced (23).

In obstructive lung disease, chronic destructive loss of alveolar walls and capillary bed results in increased alveolar volumes. Airway compromise can occur, either from loss of airway support or from excessive bronchial secretions. The airway changes increase resistance to airflow, which results in decreased alveolar oxygen tensions. The precapillary sphincters respond to this alveolar hypoxia by constricting, thereby protecting the patient from large shunts of unoxygenated blood. Thus, this state is associated with increased regional lung volumes, ventilation compromise, and perfusion compromise either from loss of capillary bed or hypoxic vasoconstriction.

The morphologic features of restrictive lung disease are caused by chronic inflammation and fibrosis, which may eventually obliterates the alveolus (25). The fibrotic alveolar stiffening, however, helps to keep the airways from collapsing. Furthermore, as secretions are not excessive in this state, ventilation may be preserved, or may even be increased by the decreases in alveolar compliance (16). Perfusion is compromised, however, as the capillaries become entrapped by the thickened and inflamed alveolar wall (25).

To summarize, the normal state shows a matched pattern of horizontally homogeneous perfusion and ventilation associated with a vanishing probability of significant pulmonary embolization (5,26-29). The vascular occlusive state shows an uneven perfusion pattern and a normal ventilation. Given a normal chest radiograph, this mismatch indicates a high probability for pulmonary embolization (5,26-29). The consolidative state can present a problem because it can be caused by either infection or by pulmonary embolization complicated by infarction. In this case inhomogeneous losses of both ventilation and perfusion produce a relative match of regional function. In the obstructive state, both perfusion and ventilation are compromised, a match of regional function indicating a low probability for pulmonary embolization (5). Differentiation of obstructive and consolidative processes must depend on additional information such as is provided by the chest roentgenogram. Finally, in the restrictive state perfusion is inhomogeneously reduced, but ventilation may appear either normal or slightly inhomogeneous. As this mismatch can simulate pulmonary embolization, a pulmonary angiogram may be required to determine the significance of the scan findings.

Looking to the future, the tomographic data from combined ventilation/perfusion studies might be best analyzed through interactive image analysis, relying on the computer to provide information on the statistical certainty of V/Q ratios, the relative deviation of local V/Q values from those adjacent at the same horizontal level, and the extent of clustering of high V/Q in neighboring slices. The clinician might then evaluate the significance of the regional abnormality having to complete the more difficult task of pattern recognition relative to expected physiology and within the context of normal three-dimensional segmental anatomy. It is not difficult to envision the results of this interaction being used to update a data base for the purposes of combining a priori clinical data with the scintigraphic findings (30). Undoubtedly, future investigators will continue to improve our ability to diagnose pulmonary embolization and further our understanding of the complexities of pulmonary pathophysiology.
REFERENCES