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V/Q SPECT—Normal Values for Lobar Function and Comparison With CT Volumes

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Ventilation and perfusion lung imaging with SPECT/CT permits accurate delineation of the individual lobes of the lungs using the CT images for use in ascribing the relative functional contribution to overall lung function of the lobes of both ventilation and perfusion. Moreover, an advantage of using Technegas as the ventilation agent and radiolabelled macroaggregated albumin microspheres as the perfusion agent is that the deposition pattern is fixed upon administration and thus different patient postures can be studied and the effect of gravity and position determined, even though the scans must be acquired with the subject supine using conventional gamma camera SPECT/CT systems.

In this paper we report on normal ranges for functional contribution of the individual lobes of the lung to overall function studied in the supine and erect positions in a small cohort of normal subjects. Differences are seen between the anatomical volumes as determined by segmentation of the CT scans and the ventilation and perfusion contributions in the different positions. As pulmonary function testing in the respiratory laboratory is usually performed in the upright position we perform all of our clinical imaging lung function studies in this position (for radiotracer administration) also. The methodology for measuring lobar function is minimally invasive, readily available, and would be hard to imagine being acquired as readily with any other technique.

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Introduction

SPECT V/Q is routinely used for detection of pulmonary embolus but is also uniquely placed for non-invasive lobar measurement using CT for anatomical identification of lobes. Measurements of lobar contribution to pulmonary function are essential to predict the impact on function from surgical procedures and assess the effectiveness of new localised treatments techniques, for example radio-ablation of airways.

Spirometry is the gold standard of lung function, but it is a global measure and fails to distinguish lobar contribution. The modern respiratory function laboratory routinely conducts a variety of tests to assess an individual's respiratory status. Spirometry, diffusion limiting capacity for oxygen, nitrogen washout, exercise capacity and the 6 minute Walk Test are also used to assess suitability for undergoing treatment which could adversely impact on respiratory function. These tests are generally non-invasive but are effort-dependent and often rely on the compliance of the individual being tested. Other more sophisticated tests, such as the multiple inert gas elimination technique to determine V:Q (ventilation:perfusion) ratio, provide greater insight into specialised function (in this case gas exchange via ventilation–perfusion matching) but are still only able to produce a single, global estimate for the lungs.

In the diseased lung, the functional contribution of different lobes and segments to overall ventilation (V) and perfusion (Q) may be heterogeneous, but this cannot be determined by standard respiratory testing and must be either inferred from anatomical imaging, such as X-ray CT, or measured with functional imaging techniques such as SPECT or PET. Functional lung scanning complements global respiratory function measurements by adding regional spatial information regarding the contribution from different anatomical segments of the lungs.

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When considering the contribution from individual lung lobes to overall function, anatomical imaging-derived volumes alone cannot be relied upon, as the contribution may be affected by regional heterogeneity due to disease, as well as being known to be gravity-dependent. Measurements to determine lobar or segmental lung function, such as using bronchoscopy-directed installation of short-lived radioactive gases (*eg*, ^{81m}Kr) or sampling for mass spectrometry directly into individual lobes, are invasive and likely to invoke a compensatory response from the unaffected lung. Hence these values cannot be considered to be able to measure the "normal" contribution to pulmonary function of one compartment of the lung.

Recently we investigated the potential effects of posture and pulmonary arterial hypertension (PAH) on pulmonary ventilation and perfusion using SPECT V/Q imaging.[1] This study found that patients with PAH or chronic thrombo-embolic pulmonary hypertension did not redistribute under the influence of gravity between upright and supine orientations.[1] In the course of undertaking this study we studied a small group of individuals with normal lung function to provide a control dataset. However, to date we have not presented the lobar analysis for these normal individuals' lung function and it is these data that are contained in this current work.

Study Design

The original PAH study examined the effect on ventilation and perfusion of the lungs of supine vs upright (erect) administration of [^{99m}Tc]Technegas (Cyclomedica Pty Ltd, Sydney, AUS) and [^{99m}Tc] macro-aggregated albumin (Jubilant Draximage, Québec, CAN) using SPECT V/Q imaging. The study order was randomised. Subjects were imaged on two separate occasions separated by more than 48 hours. In one examination the ventilation and perfusion agents were administered with the patient in an upright posture and then imaged on the gamma camera conventionally in the supine position. On the other occasion, the subjects were administered the ventilation and perfusion agents in the supine position on the scanning bed and scanned supine (Fig. 1). SPECT/CT was performed on all study visits as well as basic measurements of respiratory function to confirm that lung status was within normal limits. The details of the image acquisition and reconstruction parameters are documented in the aforementioned publication of Lau et al.[1] As the ventilation image always preceded the perfusion scan, with the ratio of the administered activities at approximately 1:4 (V:Q), the small ventilation component present during the perfusion scan was subtracted prior to reconstruction, after allowing for differences due to different acquisitions times between the ventilation and perfusion scans, and for a small amount of radioactive decay of the [^{99m}Tc]Technegas before the perfusion scan was acquired. Both scatter and attenuation corrections were applied to the SPECT data during reconstruction. It should be noted that a limitation of the study is that all SPECT and CT data were acquired without breath-hold, during tidal breathing.

Data Analysis

The CT data were segmented into the five lung lobes using in-house developed software (IDL/Harris Geospatial, Reston VA). Briefly, after extracting the lungs from the thoracic CT by thresholding on Hounsfield numbers (−950 to −250), the user was asked to define the oblique and horizontal fissures slice-by-slice using the computer mouse. The software then separates the lobes and indexes them with unique integer values to identify the individual lobes. They are then able to be used as regions of interest. An example of a segmented lung data set is shown in Figure 2.

As the voxel dimensions for the CT scan are known, the anatomical volume of each lobe during tidal breathing can be determined. The lobar regions were applied to the reconstructed SPECT ventilation and perfusion images and the total number of events in each lobe determined. The total number of events in the two lungs combined was taken to represent 100% of the administered dose reaching the lungs and from this and the total events per lobe the fractional contribution of each lobe could be determined. This was repeated for both the upright and supine administrations of the radiopharmaceuticals, although of course the CT volumes are always determined in the supine position as required by the scan acquisition.

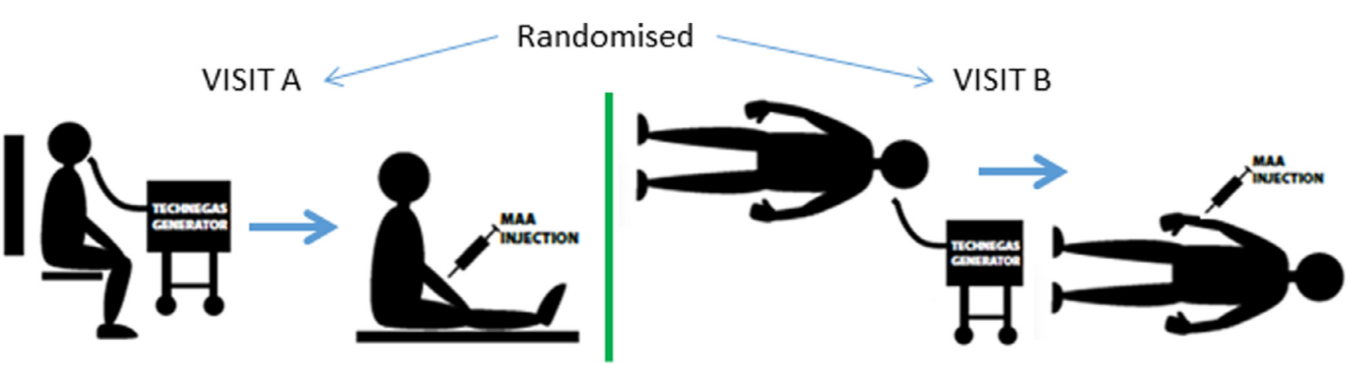

Figure 1 Diagrammatic representation of how the administration of the ventilation and perfusion imaging agents was randomized between upright and supine orientation on the two separate study days.

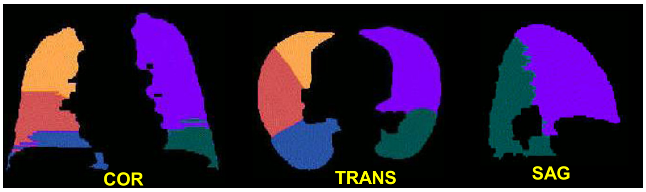

Figure 2 An example of the segmented lung output for three representative orthogonal views (coronal [COR], transverse [TRANS] and sagittal [SAG]) following the procedure described in the text. Each lobe is specified by a unique integer identifier and can be used as a region of interest.

This analysis allowed the following variables to be examined:

- CT lobar volumes and contribution to overall lung volume;
- SPECT lobar contribution to ventilation in upright orientation;
- SPECT lobar contribution to perfusion in upright orientation;
- SPECT lobar contribution to ventilation in supine orientation;
- SPECT lobar contribution to perfusion in supine orientation.

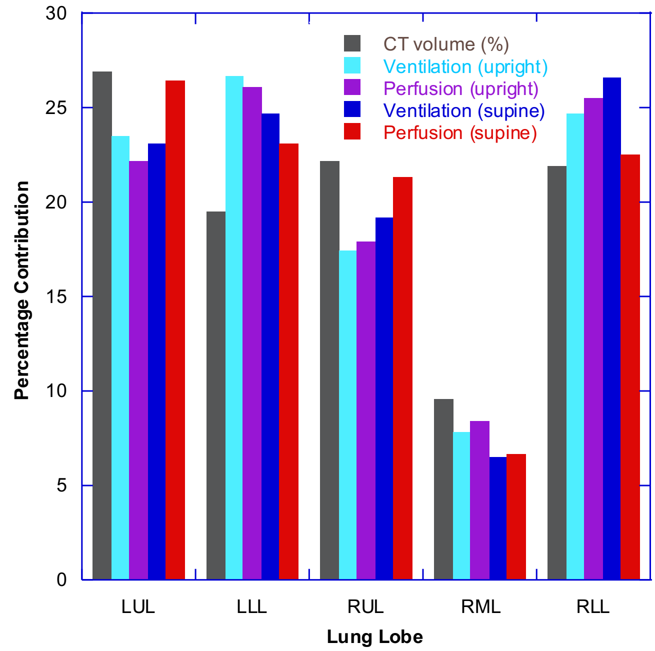

Figure 3 CT volume and SPECT functional lung contributions per lobe during tidal breathing in 11 normal subjects. In general, the CT volume overestimates the contribution in the upper lobes, especially compared with the upright orientation for ventilation and perfusion and underestimates the lower lobes contribution to overall function.

Results

Four females and seven males were included in the normal dataset (N = 11). Their mean age was 51 ± 21 years. The normal subjects' mean BMI was 26 ± 7 kg/m^2. Table 1 shows the contribution of left and right lungs for the three scanning situations: CT, SPECT (upright), and SPECT (supine) for both ventilation and perfusion.

The results for all lobes are shown in Figure 3, where anatomical volumes measured by CT are compared with the functional contribution of the lobes using the same regions of interest, and in Table 2 which includes the 95% confidence intervals from the volumetric and functional estimates.

Discussion

The measurement of individual lobar lung function is receiving increasing attention today. Assessment of the potential impact of procedures such as surgical pneumonectomy or lobectomy, or installation of a one-way valve to permanently deflate a diseased lobe or lung in an attempt to re-establish a normoxic physiological state, is increasing. Pulmonary function tests only provide global measures and, whilst essential in the work-up prior to an intervention that is likely to have a negative impact on overall pulmonary function, cannot predict the impact on function that the removal of a particular lung or lobe is likely to have. The paper by Wechalekar et al in this issue of *Seminars* discusses the clinical applications further.

Measurement of individual lung lobar contribution to pulmonary function has historically presented a significant challenge. For example, anatomical measurements using X-ray CT have been tested against spirometry measures of global function.[2] However, as most awake activity in humans is conducted in the upright orientation, as opposed to the supine position required for X-ray CT scanning, it is likely that the volumetric estimates of fractional lobar contribution from CT scans are likely to be non-representative of the actual lobar contribution during daily life. Complicating this approach even further is the heterogeneity of disease throughout the lungs, such that the fractional volume of a lung compartment (ie, segment, lobe, lung) alone does not necessarily reflect the fractional contribution to overall function. In many cases, the diseased compartment may already be contributing very little in the way of overall lung function, and hence its removal may have minimal impact on post-procedural lung function. Such an assessment would not be possible using anatomical volumes alone. *Post-mortem* examination of inflated lungs to determine lobar volumes[3] are likewise unlikely to accurately reflect the contribution in the living individual.

Table 1 Comparison of Each Lung Contribution as Assessed by the Techniques Indicated

Lung & Orientation	Left Lung (%)	Right Lung (%)
CT Volume Supine	46.4	53.6
SPECT Ventilation Supine	47.7	52.3
SPECT Perfusion Supine	49.5	50.5
SPECT Ventilation Upright	50.1	49.9
SPECT Perfusion Upright	48.2	51.8

Table 2 Comparison of Lobar Contributions and 95% Confidence Intervals (95% CI) Averaged for All Subjects. The Upright Orientation is Not Applicable for X-Ray CT Scanning

Lobe	CT Volume		Ventilation		Perfusion	
Supine	Mean (%)	Range (95% CI)	Mean (%)	Range (95% CI)	Mean (%)	Range (95% CI)
LUL	26.9	24.7-29.1	23.1	21.3-24.9	26.4	24.0-28.9
LLL	19.5	17.0-22.0	24.7	21.9-27.5	23.1	19.2-27.0
RUL	22.2	19.5-24.8	19.2	16.9-21.4	21.3	18.2-24.4
RML	9.6	8.1-11.1	6.5	5.2-7.8	6.7	5.5-7.9
RLL	21.9	19.6-24.1	26.6	24.0-29.2	22.5	19.1-25.9
Upright						
LUL	-	-	23.5	21.8-25.2	22.2	19.3-25.1
LLL	-	-	26.7	24.0-29.3	26.1	22.7-29.5
RUL	-	-	17.4	15.6-19.2	17.9	15.1-20.6
RML	-	-	7.8	6.2-9.4	8.4	7.0-9.7
RLL	-	-	24.7	21.8-27.6	25.5	22.3-28.7

Previous attempts to measure normal lobar function have relied on invasive procedures. Denison and colleagues in the 1980s used bronchoscopy to study individual lobes sequentially with either a short-lived radioactive gas (^{81m}Kr [$t_{1/2}$ = 13.1 s] from a ^{81}Rb generator on site)[4] or mass spectroscopy analysis of single breath exhaled air.[5] Such methods are invasive and may invoke a compensatory response from the remaining lung. Compared to such attempts, SPECT V/Q scanning is simple, non-invasive and quick to perform.

In this small study (N = 11) we have examined the lobar contribution to pulmonary function during tidal breathing. Changes between the upright and supine administration of the radiopharmaceutical were observed, as expected.

In general, supine upper lobe CT-derived volumes, and hence suggested contributions, were overestimated compared to the upright orientation (LUL: 26.9% (CT) vs 23.5% (VENT) and 22.2% (PERF); RUL: 22.2% (CT) vs 17.4% (VENT) and 17.9% (PERF)) and conversely the lower lobes were underestimated (LLL: 19.5% (CT) vs 26.7% (VENT) and 26.1% (PERF); RLL: 21.9% (CT) vs 24.7% (VENT) and 25.5% (PERF)).

The limitations of this study should be borne in mind, namely, that the numbers are small and all measurements were made during tidal breathing. Nevertheless, the results establish indicative normal values for lobar function in man and serve to emphasise the difference between anatomical estimation of lobar contribution and functional contribution. Further, the effect of different orientations (upright vs supine) has been studied. It is implicit in the assumptions in these results that the individuals studied had normal patterns for ventilation and perfusion, which was likely to be fairly homogeneous. However, when studying the diseased lung these assumptions would no longer be valid and hence the value of the SPECT functional assessment at the lobar level becomes even more evident.

Using higher resolution CT techniques, with a breath-hold at a pre-determined phase in the respiratory cycle, it may be possible to extend this technique for functional assessment even further down to a segmental level by having an automated segmentation algorithm that tracks along the individual airways which will branch with successive generations until arriving at a segmental or sub-segmental level.[6]

Conclusion

In summary, the non-invasive measurement of functional contribution in the normal and diseased lung, for both ventilation and perfusion, is possible using SPECT/CT techniques. It is simple to perform and is finding an increasing role in clinical applications.

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