Reproducibility of a semi-quantitative lobar pulmonary ventilation and perfusion technique using SPET and CT

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Abstract

Objective: Evaluation of regional lung function is valuable prior to lung surgery in patients with chronic lung disease. Our aim was to evaluate the reproducibility of a locally developed single photon emission tomography/computed tomography (SPET/CT) programme between and within three observers in assessing lobar pulmonary volumes, perfusion and ventilation. **Subjects and Methods:** Twelve lung transplantation candidates had VQ SPET and diagnostic CT to determine lobar pulmonary function and plan surgery. Their data were used retrospectively in an in-house developed programme which delineates the lung fissures on the diagnostic CT as an anatomical template used to estimate the volume of each of 5 lung lobes. These anatomical volumes were then applied to the corresponding ventilation (^{99m}Tc technegas) and perfusion (^{99m} Tc MAA) SPET studies. The data were anonymised, duplicated and then processed in random order blindly by 3 readers several weeks apart. Nine studies could be adequately processed. The programme failed in delineating lung volumes in 2 subjects and there was data corruption in the third. The results were evaluated for inter- and intra-observer variability using an intra-class Correlation Coefficient (ICC). An ICC score was calculated for each lobe for volume, ventilation and perfusion. **Results:** Inter- and intra-observer ICC scores for ventilation, and perfusion scans were all very high. Similar very strong ICC concordance scores were noted for volume except intra-observer ICC scores for left upper lobe (0.76) and right mid lobe (0.66) where scores showed strong concordance by standard statistical descriptors. The method was sensitive enough to demonstrate the expected gradient of ventilation/perfusion even in these patients with substantial pathology. **Conclusion:** Our method of lobar VQ SPET with CT quantitation has high inter- and intra- observer concordance and in this preliminary data set seems to be a reliable and reproducible test for semi-quantitation of differential volume, ventilation and perfusion of the lobes of the lungs.

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Introduction

Chronic lung disease (CLD) is a major cause or mortality and morbidity world-wide. Pre-operative evaluation of regional lung function is valuable in patients with CLD as the ability to predict loss of pulmonary function prior to lobectomy or pneumonectomy can influence the choice of therapy [1, 2].

Whilst traditionally used for the diagnosis of pulmonary thromboembolic disease (PTE), VQ SPET plays an important role in the semi-quantification of lobar lung function [1-4]. A current widely used method of semi-quantitating regional ventilation and perfusion by stratifying the lungs into rectangular zones is suboptimal because it does not reflect lung lobar anatomy [5-6].

Using an in-house customised software we have the capacity to perform lobar semi-quantitation of ventilation and perfusion of the lung using VQ SPET and transmission CT as an anatomical map. The aim of this study was to evaluate the reproducibility of this locally developed SPET/CT programme between and within three observers.

Patients and Methods

There were 12 patients who were being assessed for lung transplantation. Perfusion scanning was performed using 200-250MBq technetium-99m labeled macro-aggregated albumin (^{99m}Tc-MAA). Ventilation scanning was achieved with 40-50MBq ^{99m}Tc technegas. The studies were acquired on a hybrid dual head gamma camera / CT (GE

Discovery NM/CT 670, GE Healthcare). A standard planar acquisition was performed in the anterior and posterior projections (3 minutes acquisition, 256x256 matrix) Geometric mean semi-quantitation was then performed and reported with or routine rectangular zonal differential semi-quantitation as part of our routine protocol at the time.

As part of our departmental protocol a SPET acquisition for both ventilation and perfusion scans were subsequently performed. The SPET parameters are as follows: Matrix 128X 128; rotation: 6 0, zoom 1; ventilation 22 seconds/step, perfusion 18 seconds/step; 60 views; Butterworth filter threshold 0.3, power 10 and OSEM 2 iterations10 subsets.

The CT used for the purpose of the study was diagnostic quality non-contrast CT performed as part of the lung transplant assessment in the departments of radiology using standard protocols. The CT dicom datasets were imported for our purpose.

The VQ SPET and diagnostic CT examinations were completed between October 2013 and November 2014. The time difference between both modalities was less than 50 days, but usually within a week. The study was approved by the Royal Adelaide Hospital Human research ethics committee and access to the data approved by the managing clinicians. Ventilation and perfusion images were co-registered to the CT images by a 12 parameter affine transformation using SPM8 software (http://www.fil.ion.ucl.ac.uk/spm/; Welcome Trust Centre for Neuroimaging, UCL Institute of Neurology, London, UK).

The segmentation software was written by BC in IDL version 6.3, making use of its object graphics capabilities. The CT serves as an anatomical map on which the positions of the fissures are determined by the observer. Initially the user is prompted to select a seed region which is automatically grown to fill the whole lungs. A three dimensional rendered image of the lungs is then produced. The user can threshold the image to enhance blood vessels. Major fissures are identifiable by the absence of blood vessels crossing them. The user rotates the image to the desired angle, specifies the target region using a check box and draws a closed curve around the target region which is projected through the whole image (Figure 1). The end result is a differential semi-quantitation of activity in the 5 lung lobes expressed as percentages of the total.

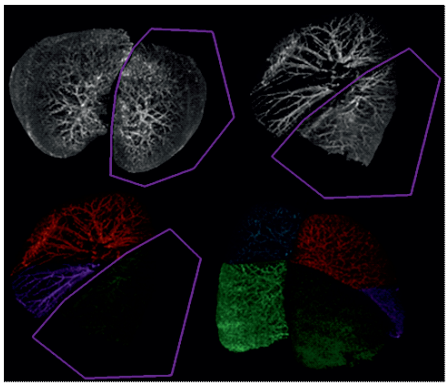

Figure 1. The user rotates the image to the desired angle, specifies the target region using a check box and draws a closed curve around the target region which is projected through the whole image

The three observers included a radiologist-nuclear medicine registrar (EB) and two physicians in nuclear medicine (GC and BC). The combined datasets of the 12 subjects were de identified and assigned random codes. Each observer then processed the blinded studies in random order using the programme. Each subject's study was processed twice by each observer.

The inter and intra observer reproducibility of the technique was assessed. An intra-class correlation coefficient (ICC) was generated. This coefficient allows the measurement of the degree of agreement between the three readers and gives a score of how much homogeneity or consensus there is in the ratings. ICC also allows the measurement of the degree of agreement of one or more outcome scores performed by a single reader. An ICC score was calculated for each lobe for volume, ventilation and perfusion.

Results

Of the 12 subjects, 9 studies could be adequately processed. The programme failed in delineating lung volumes in 2 subjects and there was data corruption in the third. Table 1 outlines the results. Inter- and intra- observer ICC scores for ventilation, and perfusion scans were all very high. Similar very strong ICC concordance scores were noted for differential lung volume estimation. The intra-observer ICC scores were lower for left upper lobe (0.76) and right mid lobe (0.66) but the scores still represent a strong concordance by standard statistical descriptors.

In addition, Pearson correlation coefficient was also applied to measure inter- and intra-observer variability. Figures 2, 3 and 4 show a very highly correlated first vs second reading (Mean r of 0.919) for all 3 observers. Figure 5 shows strong inter-observer agreement between the 3 observers. Table 2 illustrates the mean relative volumes of lobes for all observers.

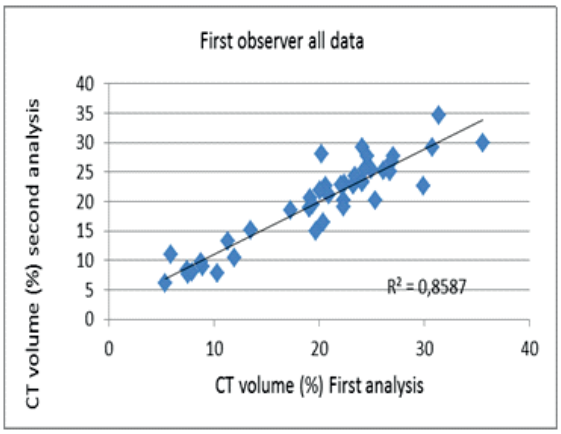

Figure 2. (see desctiption on Figure 4)

Figures 6, 7 and 8 show only moderate correlation of volumes with global ventilation and perfusion as one might expect naturally. Figure 9 illustrates the expected physiological relative increase in perfusion in the lower lobes after separating out the lower lobes from the other lobes. Physiologically,

Table 1. *Intra class correlation coefficients (ICCs)*

	Inter-observer			Intra-observer		
	Volume	Ventilation	Perfusion	Volume	Ventilation	Perfusion
L lower lobe	0.96	0.99	0.99	0.90	0.98	0.97
L upper lobe	0.91	0.98	0.99	0.76	0.95	0.96
R lower lobe	0.82	0.93	0.95	0.87	0.95	0.97
Middle lobe	0.84	0.95	0.93	0.66	0.92	0.93
R upper lobe	0.85	0.98	0.97	0.90	0.98	0.97

Correlation strengths: 0.8-1.0 – very strong 0.6-0.8 – strong 0.4-0.6 – moderate 0.2-0.4 –weak 0.0-0.2 - very weak to negligible. L=left, R=right.

Table 2. *Mean relative volumes of lobes: All observers*

LUL	LLL	RUL	RML	RLL	Left Lung	Right Lung
24.3%	22.4%	21.1%	8.4%	23.4%	47%	53%

LUL: left upper lobe LLL: left lower lobe RUL: right upper lobe RLL: right left lobe

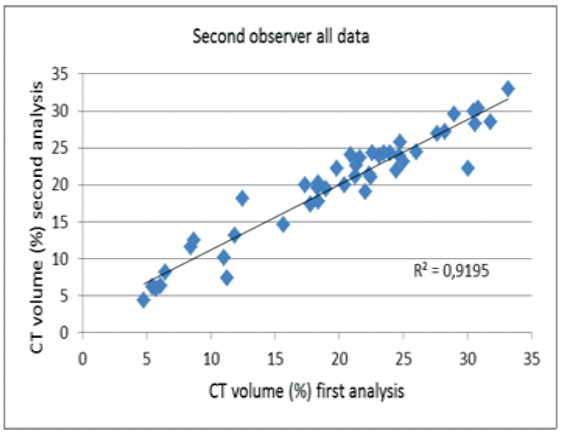

Figure 3. (see description on Figure 4).

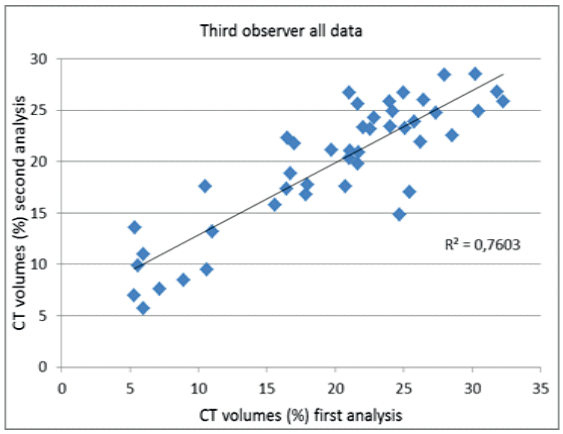

Figure 4. Figures 2, 3 and 4 show a very highly correlated first vs second reading (Mean r of 0.919) for all 3 observers.

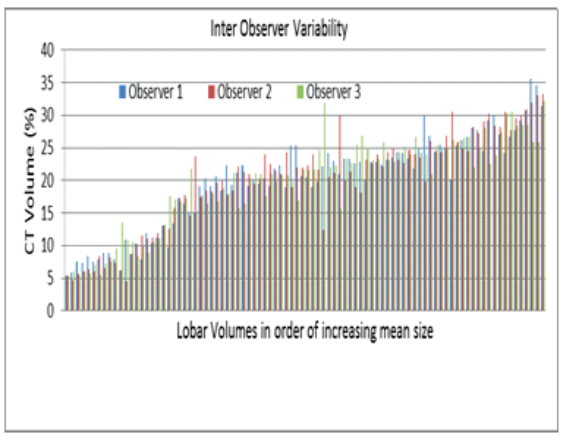

Figure 5. Shows strong inter-observer agreement between the 3 observers.

the more dependent part of the lung receives relatively more perfusion than ventilation [4, 5].

Discussion

Chronic lung disease is a leading cause of mortality and morbidity worldwide. During the past decades the number of patients with CLD has been increasing worldwide. This increase is influenced by a number of factors including increased rates of smoking, air pollution, occupational exposures, genetics growing and ageing population [1-6].

VQ SPET has been increasingly relied upon as an accurate and non-invasive imaging technique in the pre-transplant evaluation in patients with CLD along with established methods such as diagnostic CT [1-7].

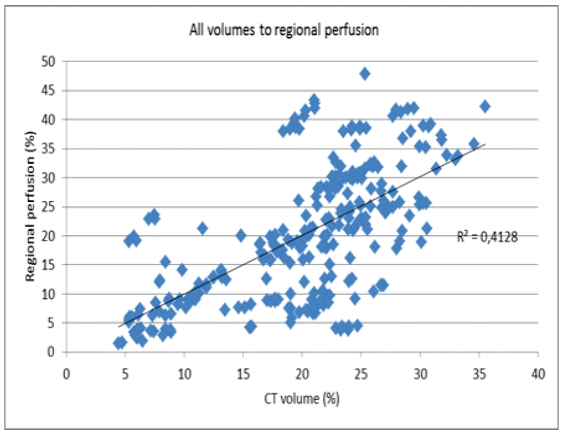

Figure 6. (see description on Figure 8).

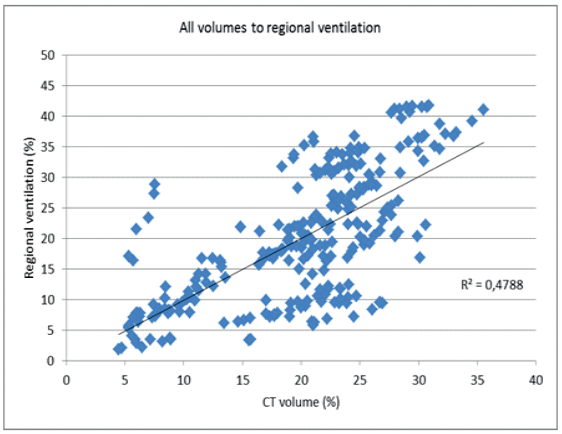

Figure 7. (see description on Figure 8).

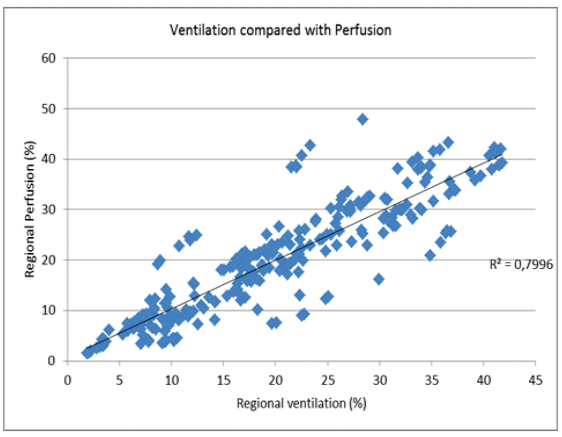

Figure 8. Figures 6, 7 and 8 show only moderate correlation of volumes with global ventilation and perfusion as one might expect naturally

A currently widely used method of regional quantitation of lung ventilation and perfusion uses planar VQ scan acquired in the anterior and posterior projections. The radioactivity in each lung is then semi-quantitated and the geometric mean of the anterior and posterior datasets is determined. The regional activity is then divided into 6 geometric zone (3 zones - upper, middle and lower in each lung). This method is suboptimal as the zones do not match lung anatomy [8].

We have developed an alternative semi-method of quantitation using VQ scan acquired as a SPET which quantitates ventilation and perfusion according to the lobes of the lungs. A separate CT is needed for this new technique. The CT can either be a diagnostic quality high energy scan or a low energy study acquired as part of the VQ scan using a hybrid gamma camera. For the purpose of our study the diagnostic CT was used as it had been already performed as part of lung transplant assessment.

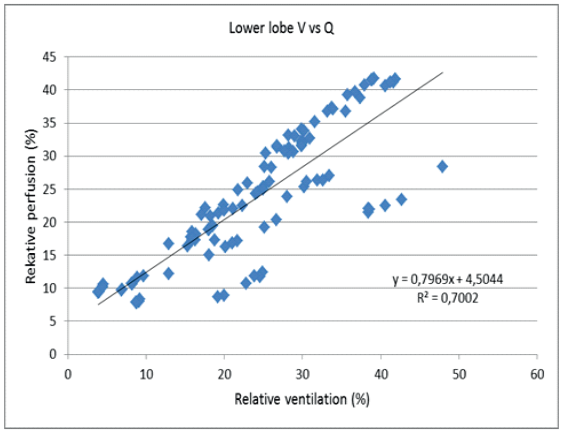

Figure 9. Illustrates the expected physiological relative increase in perfusion in the lower lobes after separating out the lower lobes from the other lobes.

Our technique of lung regional semi-quantitation is a novel approach, which is yet to be validated as far as the regional volumes are concerned. Yu et al (2015) published a supplement investigating a similar software for lobar quantification using a 3D segmentation algorithm that extracts the lobar regions from the diagnostic CT on 115 patients. However, they are yet to publish their full article so the details cannot be verified [7] Bailey et al (2009), also developed a similar software method but to our knowledge has yet to verify the reproducibility of their technique and only 5 patients were included in their study [3].

This study aimed at evaluating the reproducibility of the technique. All of the data used were acquired as part of routine lung transplant assessment and therefore there was no extra procedure or radiation exposure imposed on the subjects.

Our study is limited by the small number of only 9 patients. These patients were being considered for lung transplantation, thus have extensive CLD. Despite the poor lung quality complicating the task of delineating the fissures on the CT map, our method appears to be very reproducible. This study however does not validate the method as there is no gold standard for the true lobar differential ventilation and perfusion in this cohort of patients. We believe that our method of lobar semi-quantitation using VQ SPET and CT has the potential to be part of the pre operative work-up of lobectomy and in bronchoscopic lung volume reduction. We are currently engaged in prospective trials to evaluate the value of our technique for these two clinical indications.

In conclusion, our method of lobar VQ SPET with CT, has high inter- and intra- observer concordance for lobar differen-

tial semi-quantitation of volume, ventilation and perfusion.

The authors declare that they have no conflicts of interest.

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