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ORIGINAL ARTICLE

Ventilation/perfusion SPECT or SPECT/CT for lung function imaging in patients with pulmonary emphysema?

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Abstract

Purpose To evaluate the utility of attenuation correction (AC) of V/P SPECT images for patients with pulmonary emphysema.

Materials and methods Twenty-one patients (mean age 67.6 years) with pulmonary emphysema who underwent V/P SPECT/CT were included. AC/non-AC V/P SPECT images were compared visually and semiquantitatively. Visual comparison of AC/non-AC images was based on a 5-point likert scale. Semiquantitative comparison assessed absolute counts per lung (aCpLu) and lung lobe (aCpLo) for AC/non-AC images using software-based analysis; percentage counts (PC = (aCpLo/aCpLu) × 100) were calculated. Correlation between AC/non-AC V/P SPECT images was analyzed using Spearman's rho correlation coefficient; differences were tested for significance with the Wilcoxon rank sum test.

Results Visual analysis revealed high conformity for AC and non-AC V/P SPECT images. Semiquantitative analysis of PC in AC/non-AC images had an excellent correlation and showed no significant differences in perfusion ($\rho = 0.986$) or ventilation ($\rho = 0.979$, $p = 0.809$) SPECT/CT images.

Conclusion AC of V/P SPECT images for lung lobe-based function imaging in patients with pulmonary emphysema do not improve visual or semiquantitative image analysis.

Keywords Attenuation correction · V/P SPECT/CT · Pulmonary emphysema

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Introduction

Over the last decades, the advent of ventilation/perfusion single photon emission computed tomography (V/P SPECT) has improved the diagnostic value of lung imaging by nuclear medicine methods [1, 2]. Further benefits are described for the use of hybrid scanners such as PET/CT and SPECT/CT [3–5].

For patients with chronic obstructive pulmonary disease and pulmonary emphysema lung function imaging is seen to be a domain of quantitative CT [6–8].

But chronic obstructive pulmonary disease and pulmonary emphysema also can be seen as a new indication for V/P SPECT and/or V/P SPECT/CT for identifying the least functional lung lobe—especially prior to pulmonary volume reduction therapy.

The low-dose CT generated with this technique can be used to generate attenuation correction (AC) for SPECT images and additionally can give—however, limited—morphologic information.

Hybrid imaging techniques combining morphological and metabolic information by fusing image data are known to improve the localization and differentiation of normal and abnormal tracer uptake in circumscribed lesions [9–12]. Therefore, AC images generated with the aid of CT data have an undisputed benefit. The benefit of AC in V/P SPECT images for patients who do not undergo SPECT/CT for detecting, localizing, or differentiating circumscribed lesions remains to be proven.

The present study was designed to evaluate the impact of AC on V/P SPECT images for lung lobe-based function imaging in patients with pulmonary emphysema prior to volume reduction treatment.

Materials and methods

Study participants and enrolment

This study was a retrospective analysis. The institutional review board approved the entire study. Each patient gave written informed consent for V/P SPECT/CT imaging prior to the examination. All study participants suffered from pulmonary emphysema and chronic obstructive pulmonary disease (COPD) in the high global initiative for chronic obstructive lung disease (GOLD) classification. All patients were candidates for lung volume reduction treatment. For treatment planning, they underwent standardized V/P SPECT/CT at our institution to identify the least functional lung lobe before treatment. Patients with pulmonary malignancy and inflammation were excluded from this retrospective analysis.

Study outcome

Primary study outcome was to evaluate the influence and necessity of AC in V/P SPECT images for evaluating tracer uptake in the lung of patients with pulmonary emphysema to identify the least functional lung lobe.

V/P SPECT/CT protocol

V/P SPECT/CT was performed on a hybrid dual-head Siemens Symbia TruePoint T6 SPECT/CT system (Siemens Medical Solutions, Erlangen, Germany), which has a crystal thickness of 9.5 mm and a 53.3 cm axial by 38.7 cm transversal diameter SPECT field of view (FOV) and a 6-slice CT scanner. The following 1-day standard protocol was used: acquisition was performed in a 128 × 128 matrix, zoom of 1.0, pixel size of 4.8 mm, and noncircular orbit (auto contour) with 30 projections over 180° (continuous acquisition). A low-energy high-resolution collimator was used with dual-energy windowing and a lower scatter energy window (10 % width) for scatter estimation. Thirty steps, each of 15 s duration, were used for the ventilation and for the perfusion study. The total acquisition time was approximately 20 min, which was well tolerated by all patients. The seated patient inhaled about 60 MBq Tc-99m Technegas (Tema 10000, Cyclomedica GmbH, Germany). Then, the ventilation SPECT, including a low-dose CT, was performed in the supine position. After the ventilation SPECT/CT scan, 100–120 MBq of 99mTc-labeled macroaggregated human albumin (Malinckrodt Medical BV, The Netherlands) was slowly injected intravenously while the patient took deep breaths. Then, the perfusion tomogram including a second low-dose chest CT was performed in the supine position. CT scan was acquired at mid-inspiration, and the SPECT scan using a shallow breathing pattern to minimize respiratory artifacts and mismatch between CT and SPECT.

AC/non-AC

First the SPECT and then the CT projection images were acquired using a tube voltage of 130 kV, effective 10 mAs with activated adaptive dose modulation CARE Dose4D (Siemens Medical Solutions, Erlangen, Germany) using a 40 × 50 cm FOV. CT raw data were used to perform attenuation correction (AC) and low-dose diagnostic CT. AC reconstruction was performed with a smooth kernel, a B08s filter with 5.0 mm, and 512 × 512 matrix. The diagnostic low-dose CT was performed with a medium kernel, a B40s filter with 5.0 mm, and 512 × 512 matrix. After reconstructing the CT raw data for AC, an attenuation map was created and the SPECT data were reconstructed using Flash 3D, a tomographic reconstruction algorithm based on maximum likelihood [13] reconstruction was applied using ordered subsets (OSEM) [14]. This enables both scatter and CT-based attenuation correction using 4 subsets and 8 iterations. Non-AC images were generated from SPECT raw data using a Butterworth filter (of order 5 and cut off 0.4 cm^{-1}) and filtered backprojection method (FBP).

Visual V/P SPECT analysis

Two board-certified nuclear medicine physicians with 7 and 20 years of experience, respectively, visually assessed all V/P SPECT images in consensus. The observers read AC and non-AC V/P SPECT images for each patient and compared their conformity in terms of lung lobe-based tracer uptake in ventilation and perfusion images using the following 5-point likert scale: 1 = very low correlation (low correlation for focal and segmental uptake in the lung); 2 = low correlation (low correlation for segmental uptake in the lung and moderate correlation for focal uptake); 3 = moderate correlation (moderate correlation for segmental uptake in the lung and for focal uptake); 4 = high correlation (excellent correlation for segmental uptake in the lung and moderate correlation for focal uptake); 5 = very high correlation (excellent correlation for focal and segmental uptake in the lung). Figure 1 gives an example of visual analysis of AC (Fig. 1a) and non-AC (Fig. 1b) perfusion SPECT images. Tracer uptake in-/homogeneity was not assessed.

Semiquantitative V/P SPECT analysis

To objectively verify visual assessment of AC/non-AC V/P SPECT images, we performed a semiquantitative analysis using PMOD version 3.4 (Technologies Ltd., Zurich, Switzerland). Three-dimensional regions of interest (ROIs) were drawn manually on every lung lobe using the CT images for identifying fissures between the lung lobes (Fig. 2a). The ROIs were transferred to the SPECT images, which had been co-registered with the CT scans (Fig. 2b, c). In this way, AC and non-AC V/P SPECT images were segmented based on low-dose CT (Fig. 2d) information for determining numeric tracer uptake values per pulmonary lobe and per lung. Absolute counts per pulmonary lobe (aCpLo) and lung (aCpLu) were calculated automatically by PMOD using the lung/lung lobe volumes. Investigation of aCpLo and aCpLu served as a parameter to clarify the influence of AC on count density. Percentages of counts (PC = (CpLo/CpLu) $\times$ 100) were calculated and used for semiquantitative analysis of pulmonary lobe function.

Statistical analysis

The association between AC and non-AC SPECT images in semiquantitative software-based analysis and visual analysis was compared using Spearman's rho correlation coefficient. The differences between PC and aCpLo in AC and non-AC SPECT images were tested for significance using the Wilcoxon rank sum test. Statistical significance was accepted at $p < 0.05$. Statistical analysis was performed with the SPSS software package (SPSS 20.0.0; SPSS Corporation, Chicago, USA).

Results

Twenty-one patients ($n = 12$ men, $n = 9$ women) with a mean age of 67.6 years (median 68, range 58.0–74.0 years) with clinically confirmed pulmonary emphysema and COPD GOLD IV were included in this study.

AC and non-AC SPECT images were rated to show very high correlation in the visual analysis in 76 % and high correlation in 62 % of the V/P SPECT images (Fig. 3).

These results could be confirmed by semiquantitative analysis comparing PC in AC and non-AC V/P SPECT images, which had an excellent correlation and showed no significant difference for perfusion ($\rho = 0.986$) or ventilation ($\rho = 0.979$, $p = 0.809$; Table 1).

The impact of AC on V/P SPECT image count density is reducible looking at the absolute counts:

In AC and non-AC V/P SPECT images aCpLo correlated only moderately for perfusion ($\rho = 0.511$) and ventilation ($\rho = 0.515$) and were significantly different ($p < 0.001$; Table 2).

By subtracting PC and aCpLo values for AC and non-AC V/P SPECT images, the deviation of these values can be visualized (Fig. 4a, b).

Discussion

Hybrid imaging combining morphological and metabolic information by fusing image data is known to improve the localization and differentiation of normal and abnormal tracer uptake in circumscribed lesions [9–12]. This applies to hybrid scanning, including SPECT/CT and PET/CT. CT data—in addition to providing morphological information—can be used to generate attenuation-corrected SPECT or PET images. The purpose of this study was to

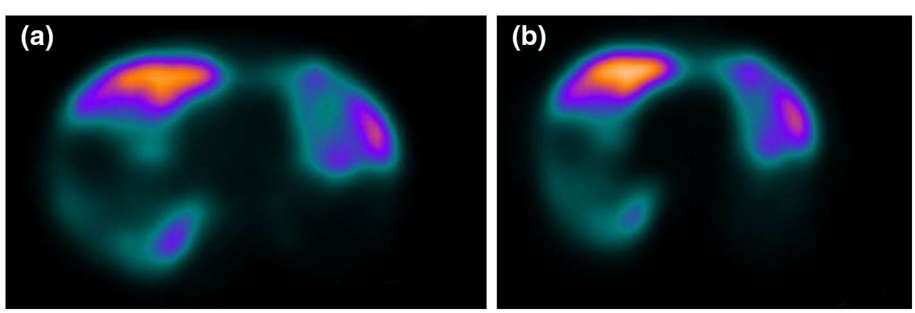

Fig. 1 A 74-year-old woman with severe pulmonary emphysema. Imaged by AC perfusion SPECT (**a**) and non-AC perfusion SPECT (**b**) images, which were compared in visual analysis using a 5-point likert scale

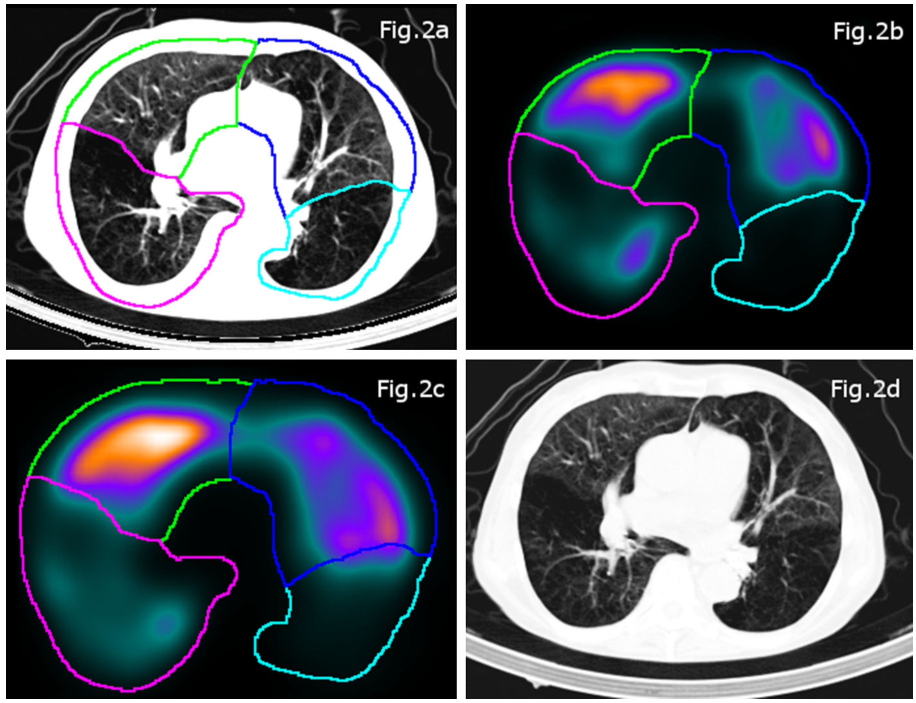

Fig. 2 AC and non-AC perfusion SPECT images of the same patient subjected to software-based analysis. **a** Low-dose CT with lung lobe circumscribing ROIs, **b** AC perfusion SPECT, **c** non-AC perfusion SPECT, **d** correlating low-dose CT

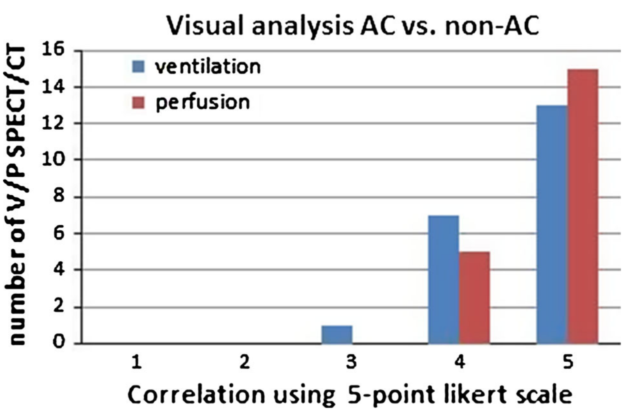

Fig. 3 High to very high interobserver conformity in visual analysis of AC and non-AC V/P SPECT images using a 5-point likert scale

analyze the benefit of AC for lobe-based pulmonary function imaging using V/P SPECT/CT in patients with pulmonary emphysema.

Our visual analysis revealed a very high to high conformity between AC and non-AC V/P SPECT images. These results could be objectified by our semiquantitative analysis: PCs correlated well between AC and non-AC V/P SPECT images. So, we can conclude that non-AC V/P SPECT images analyzed visually or semiquantitatively by assessing the percentage count density per lung lobe in patients with pulmonary emphysema are comparable with AC V/P SPECT images.

Lung function imaging by SPECT without included CT need not be seen as a disadvantage for imaging patients with pulmonary emphysema. But we strongly recommend SPECT imaging including ventilation and perfusion examination for the detection of reverse mismatches of tracer uptake, which can be used for pulmonary emphysema assessment [15]. Further, ventilation SPECT can be used for pulmonary embolism. We also recommend that V/P SPECT be complemented by a functional in- and expiration CT for a dedicated lung fissure imaging, which is an important diagnostic tool to estimate the success of endobronchial valve treatment. It is known that complete lung fissures have a positive impact on this treatment [16–18]. aCpLo and aCpLu are not useful for describing lung function in patients with pulmonary emphysema using V/P SPECT because the tracer distribution is not an absolutely accurate measure of physiologic lung function but merely provides a rough estimate. This is due to the influence of changes in posture on physiologic lung function and nuclide distribution in pulmonary V/P SPECT examinations [3] such as the influence of adjoint objectives density. Nevertheless, we analyzed aCpLO and aCpLu and obtained a moderate correlation with a significant difference for AC and non-AC V/P SPECT images with the aim to clarify the influence of attenuation correction on count density. In our study, we did not perform gated SPECT of the lungs [19–22], which means that motion artifacts are present.

Our results contradict various insights reported in the literature. For instance, Suga et al. [23] showed improvement in lung perfusion SPECT images in a fielded-based lung analysis using attenuation correction. A possible explanation for the divergent results is the use of field-based

Table 1 PC in non-AC minus PC in AC V/P SPECT images without significant difference ($p = 0.809$)

	RUL	RML	RLL	LUL	LLL	All lobes
(PC non-AC) − (PC AC) perfusion	1.31 (1.26; 0.0–4.83)	1.29 (0.96; 0.04–5.73)	1.56 (1.42; 0.08–4.75)	1.18 (1.11; 0.10–3.41)	1.19 (0.66; 0.01–4.2)	1.31 (1.11; 0.01–5.73)
(PC non-AC) − (PC AC) perfusion	1.60 (1.52; 0.21–5.04)	1.62 (1.03; 0.01–7.23)	1.17 (0.86; 0.03–3.69)	1.43 (1.52; 0–5.18)	1.6 (1.52; 0.01–5.64)	1.48 (1.19; 0–7.23)

Data are given as mean (median; min–max)

RUL right upper lung lobe, *RML* right middle lung lobe, *RLL* right lower lung lobe, *LUL* left upper lung lobe, *LLL* left lower lung lobe

Table 2 aCpLo in non-AC minus aCpLo in AC V/P SPECT images were significantly different ($p < 0.001$)

	RUL	RML	RLL	LUL	LLL	All lobes
(aCpLO non-AC) − (aCpLo AC) perfusion	85.73 (72.29; 60.58–191.07)	83.8 (75.34; 48.91–161.66)	87.62 (71.74; 59.41–182.92)	88.54 (72.27; 64.74–176.26)	82.75 (71.82; 62.35–173.78)	85.69 (72.3; 48.91–191.07)
(aCpLO non-AC) − (aCpLo AC) ventilation	102.09 (75.36; 61.18–278.34)	104.29 (77.22; 55.9–527.62)	92.2 (73.8; 62.08–236.96)	97.1 (75.98; 58.6–224.27)	97.33 (71.49; 60.85–236.51)	98.6 (75.21; 55.9–527.26)

Data are given as mean (median; min–max)

RUL right upper lung lobe, *RML* right middle lung lobe, *RLL* right lower lung lobe, *LUL* left upper lung lobe, *LLL* left lower lung lobe

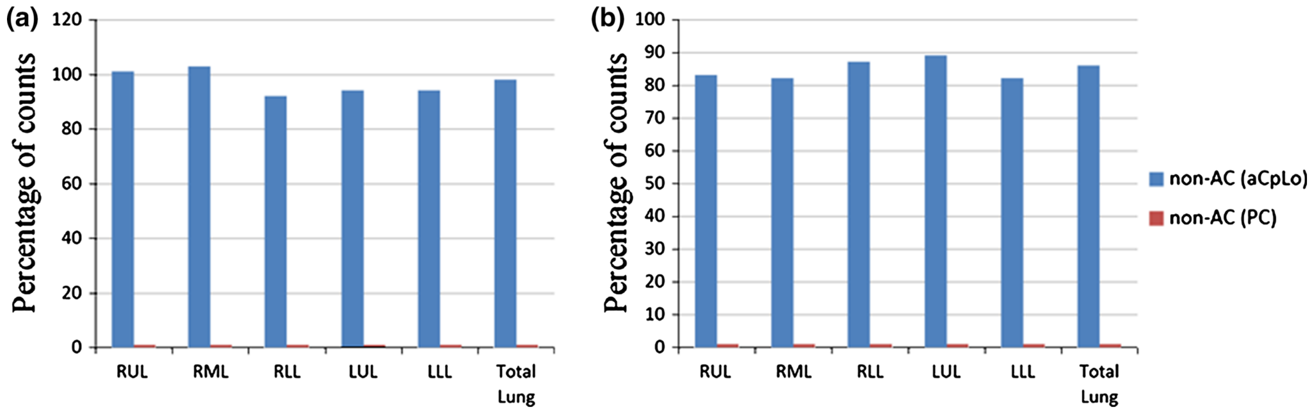

Fig. 4 Clear differences shown for aCpLo in AC and non-AC ventilation (**a**) and perfusion (**b**) SPECT images. Minimal difference shown for PC in AC and non-AC ventilation (**a**) and perfusion (**b**). *RUL* right upper lung lobe, *RML* right middle lung lobe, *RLL* right lower lung lobe, *LUL* left upper lung lobe, *LLL* left lower lung lobe

analysis of AC perfusion SPECT images only [23]. In the present study, we did not focus on the impact of AC on tracer uptake in-/homogeneity, which is an interesting issue described in the literature. For example, Gustafsson et al. showed in healthy subjects that inhomogeneity of SPECT images decreases with attenuation correction, but inhomogeneity persists even when averaged lung density correction is done. This is not only attributable to statically caused noise and non-uniformity of the camera [24].

It has to be mentioned that V/P SPECT/CT—compared to quantitative CT—is not a standard examination for the evaluation of patients with pulmonary emphysema [6–8]. This is why heterogeneity evaluation has so far been less of a concern in interpreting SPECT images and needs to be improved.

We can conclude that visual and/or semiquantitative analysis of pulmonary lobe-based function imaging in patients with pulmonary emphysema does not profit from AC of V/P SPECT images. Despite this, it is important to note that the present study focuses on a special instance and the results should be reconfirmed by subsequent studies. At this moment, there is still a limitation regarding the use of non-AC SPECT images for clinical diagnosis and the readers should be aware of this.

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