Lung perfusion imaging of acute pulmonary embolism using subtraction computed tomography angiography: correlation with vascular obstruction indices

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Authors: M. Brink¹, A. Verschoor¹, M. Engels¹, Y. Heijdra¹, L. J. Oostveen¹, C. M. Schaefer-Prokop², M. Prokop¹; ¹Nijmegen/NL,²Amersfoort/NL
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Aims and objectives

Distribution of intravascular administered iodine in the lungs can be used as a marker for pulmonary perfusion. Pulmonary embolism (PE) is one of the most common causes of focally reduced lung perfusion [1]. Severe obstruction or occlusion of pulmonary arteries will cause typical segmental perfusion defects that reflect histopathological changes.

Dual energy (DE) computed tomography angiography (CTA) has frequently been used to evaluate pulmonary perfusion by creating iodine maps. DE iodine maps are based on material decomposition, by using iodine and soft tissue or water as base materials. Perfusion defects on these maps correlate with severity and rate of occlusion of PE [2].

As an alternative to dual energy CT, similar iodine maps can be created by subtracting precontrast-scans from contrast-enhanced scans derived from mono-energy CT scanners as shown in Fig. 1 on page 3 [3]. Because of faster scanning times, decreased radiation doses, and advances in image registration, subtraction techniques are now feasible in humans using different breath holds. We implemented this subtraction technique at our centre and routinely evaluated all patients with suspicion of PE with subtraction imaging [4].

The purpose of this study was to assess clinical feasibility of subtraction imaging in patients with PE, and evaluate correlation of severity of perfusion findings with vascular obstruction.
**Fig. 1:** Figure 1. The subtraction software registers both scans to correct for motion and thereafter subtracts pre- and postcontrast scans. The resulting iodine map undergoes filtering and transfer to a heat scale.

Methods and materials

Patients:

The responsible institutional review board waived informed consent before implementation of subtraction imaging.

We retrospectively evaluated all patients of 18 years and older who underwent CTA for suspicion of PE at the emergency ward of one university hospital in the Netherlands between December 26th 2012 until August 11th 2014. Of these patients, we included all patients who had acute pulmonary embolism at CTA and who had subtraction imaging available.

Scanning protocol:

For subtraction imaging, we use one precontrast scan of the chest followed by a contrast-enhanced scan from a 320 detector-row CT scanner. These scans have identical scanner settings except for a lower dose setting for the precontrast scan (noise index = 30 for the precontrast scan as compared to 22.5 for the contrast-enhanced scan). Breathing instructions for both scans do not differ from those used in standard pulmonary CTA. Tube voltage is either 100 or 120 kV, depending on patient size. Seventy milliliters of intravenous iodine contrast is injected at a rate of 5 ml/s and bolus-tracking is used by placing a region if interest in the pulmonary trunk. Software registers both scanning volumes, corrects for motion differences and thereafter subtracts the precontrast from the contrast-enhanced scan. The resulting iodine maps are filtered and displayed on a color scale as shown in Fig. 1 on page 6.

Data collection:

One investigator (ME) collected patient characteristics, clinical data, treatment and follow-up from the electronic patient files. To evaluate radiation dose, computed tomography dose indices (CTDI) and total dose length product (DLP) of each scan were collected from the scanners console.

Based on clinical data, we assessed the simplified pulmonary embolism severity index (SPESI) score [5] as a measure of clinical severity of PE.

Outcome measures:

Both CTA images and subtraction images were evaluated in axial, coronal, and sagittal orientations on a dedicated workstation for severity of perfusion defects and vascular obstruction.
Vascular obstruction CTA was independently assessed according to Mastora by one observer (MB). The Mastora scoring system evaluates 5 central, 6 lobar, and 20 segmental pulmonary arteries independently for degree of vascular occlusion. This degree is visually assessed on a scale from 0-5 as a degree of obliteration of these arteries (0: no clot, 1: 1-24% obliteration, 2: 25-49% obliteration, 3: 50-74% obliteration, 4: 75-99% obliteration, 5: 100% occlusion). The sum of these scores gives a global obstruction score with a maximum of 155 [6].

Severity of perfusion defects on the color-coded maps was quantified by assessing the P-score according to Thieme et al [2]. One observer (AV) visually graded the extent of wedge-shaped perfusion defects on each anatomic lobe (upper lobes, lower lobes, middle lobe, and lingula) as a percentage of defect (0: no defect, 1: subtle perfusion defect (1-25% of the lobe), 2: moderate defect (26-50% of the lobe), 3: severe defect (51-75% of the lobe), 4: subtotal defect (76-99% of the lobe), 5: complete defect (100%)). We multiplied these scores with a factor reflecting the number of lung segments of each lobe. The sum of these scores represents the P-score for the whole lung with a maximum of 100 [2].

Fig. 2 on page 6 gives an example of perfusion scores and vascular obstruction scores in a patient with acute PE.

**Statistical analysis:**

Normally distributed data were represented as means including ranges and 95% confidence intervals. For skewed values we used medians and full ranges. We used the spearman's coefficient of rank correlation to assess correlation between vascular obstruction score and perfusion score.
Fig. 1: Figure 1. The subtraction software registers both scans to correct for motion and thereafter subtracts pre- and postcontrast scans. The resulting iodine map undergoes filtering and transfer to a heat scale.


Fig. 2: A patient with partially obliterating, but also occluding PE. At CTA, vascular obstruction score was 96. Subtraction imaging showed typical wedge-shaped defects in 26-50% of the right upper lobe, 100% of the middle lobe, and 75-99% of the right lower lobe, 1-25% of the left upper lobe, 51-75% of the lingula, and 76-99% of the left lower lobe, ending up in a global perfusion score of 65.

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Between 26-12-13 until 11-8-2014, 396 CTA scans were performed in 381 patients to rule out PE. In 59 patients (15%), acute PE was present according to the radiological reports. In two of these patients, subtraction images were not available. One patient had 2 scans during the inclusion period. Only the first scan was included in the cohort.

The final cohort therefore consisted of 57 scans. In 1 patient dose length product was not available. Patient- and scanning-characteristics are displayed in table 1. At follow-up, 8 patients died. Two patients died due to PE and cardiovascular comprise. Six patients died because of other co-morbidity.

<table>
<thead>
<tr>
<th>Age</th>
<th>median 62 (range: 18-87)</th>
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<tbody>
<tr>
<td>Sex</td>
<td>54% male</td>
</tr>
<tr>
<td>SPESI score</td>
<td>mean 0.83 (range 0-3)</td>
</tr>
<tr>
<td>CT dose index precontrast scan</td>
<td>mean 2.5 mGy (range 0.8-8.1)</td>
</tr>
<tr>
<td>CT dose index contrast enhanced scan</td>
<td>mean 4.7 mGy (range 1-12)</td>
</tr>
<tr>
<td>Dose Length product of total scan acquisition</td>
<td>median 224 mGycm (range 89-683)</td>
</tr>
</tbody>
</table>

Table 1: Patient characteristics and radiation dose parameters

Mean Mastora score was 38 (range 1-125, 95% confidence interval 30-46). Forty-eight patients had perfusion defects (mean P-score: 21, range 0-75, 95% confidence interval 16-26) in 142 lobes. As illustrated in figure 3, we found a statistically significant correlation between P-score and vascular obstruction score (Spearman rho = 0.642), p < 0.005.
Fig. 3: Scatterplot: Correlation between vascular occlusion and obliteration and perfusion defects at subtraction imaging in 57 patients.

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Conclusion

In this cohort of patients with acute PE, we showed that subtraction imaging is feasible: Registration software enables subtraction of two lung volumes, even between different breath holds.

Although subtraction imaging includes two scans of the chest, median radiation dose is in the same range as the usual CT work-up of patients with PE [1] due to a very high noise index of the nonenhanced CT scan and application of iterative reconstruction.

We independently scored pulmonary perfusion defects on subtraction imaging and level of obliteration of pulmonary arteries in patients with PE. According to previous publications on PE and DE CT [1,2], we showed that general vascular obliteration correlates with perfusion defect scores.

In the future, more objective quantification and evaluation of perfusion maps in PE patients is mandatory to further investigate this correlation.

In conclusion, subtraction imaging is feasible in patients with PE. Findings on subtraction images seem to correlate with severity of PE and might serve as an indicator for pulmonary perfusion in acute PE.