Subtraction techniques enable single-energy iodine mapping of pulmonary perfusion: An educational exhibit

Poster No.: C-2139
Congress: ECR 2014
Type: Educational Exhibit
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Keywords: Embolism / Thrombosis, Diagnostic procedure, Experimental, CT-Angiography, Thorax, Pulmonary vessels, Emergency
DOI: 10.1594/ecr2014/C-2139

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Learning objectives

- To describe the principles of CT subtraction imaging for creating iodine maps as a surrogate for pulmonary perfusion
- To provide a pictorial review of the spectrum of morphology of lung perfusion defects, typical artifacts, and pitfalls of subtraction imaging.
- To review the spectrum of morphology of lung perfusion defects on subtraction imaging
Background

We recently implemented subtraction imaging as a technique to calculate iodine maps of the lungs from pre- and post-contrast CT datasets. This technique was successfully applied in the workup of patients with suspected acute pulmonary embolism (PE). We optimized our scanning protocol by using faster scanning time, lower radiation dose, and a subtraction algorithm that includes segmentation, registration, and motion correction. In this exhibit we will introduce this technique, its pitfalls and clinical utilization.

Pulmonary Perfusion

Pulmonary perfusion is defined as the delivery of blood to the capillary bed [1]. Many pathological conditions cause alterations in the amount of pulmonary perfusion but absolute quantification of perfusion remains problematic. Iodine maps derived from CT provide semiquantitative measures of perfusion and are able to demonstrate perfusion differences between various parts of the lungs.

- Pulmonary embolism (PE) is one of the most common causes of focally reduced lung perfusion [2]. Severe obstruction or occlusion of pulmonary arteries will cause typical segmental perfusion defects. Perfusion defects are mandatory for the diagnosis of chronic thromboembolic pulmonary hypertension. In acute PE, defects may be absent if vessel obstruction is incomplete.
- In chronic obstructive pulmonary disease (COPD), impairment of gas exchange will lead to hypoxic pulmonary vasoconstriction and subsequent focally reduced perfusion [3]. Similar effects are seen in other processes that lead to focal hypoxia.
- Tumors may cause hypoperfusion, either directly by obstructing pulmonary arteries, or indirectly, by obstructing a bronchus and causing focal hypoxia.

Iodine Maps

Iodine maps display the local iodine concentration in a contrast-enhanced CT. This is usually achieved by using dual energy CT (DECT) techniques that have been implemented for the assessment of acute PE. Iodine maps from DECT are created by base material decomposition using iodine and soft tissue or water as base materials.

These iodine maps demonstrate perfusion abnormalities that reflect histopathological changes in acute and subacute PE [4]. Perfusion imaging has been shown to increase
sensitivity for PE, in particular for small emboli at a subsegmental level or in more distal vessels and to improve prediction of prognosis and therapy monitoring [5,6].

As an alternative, similar iodine maps can be created by subtracting a pre-contrast-scan from a contrast-enhanced (post-contrast) scan. Already in 2005, animal experiments showed that subtraction techniques can be used to obtain perfusion maps within one breathhold [7]. Because of faster scanning times, decreased radiation doses, and advances in image registration, this technique is now feasible in humans using different breathholds.
Findings and procedure details

For subtraction imaging, we use one pre-contrast scan and one post-contrast scan from a 320 detector-row CT scanner at an identical kilovoltage in patients with suspicion of PE. Software registers both volumes, corrects for motion differences, and thereafter subtracts the pre-contrast from the post-contrast scan. Resulting iodine maps reflect iodine distribution in the pulmonary vessels and parenchyma at a high contrast-to-noise ratio.

**Scanning Protocol**

Subtraction imaging consists of a pre-contrast scan followed by a contrast-enhanced scan using bolus tracking in the pulmonary trunk. Both scans use the same scanner settings except for a lower dose and a higher noise index for the pre-contrast scan. Breathing instructions are identical for pre- and post-contrast scans and do not differ from those used in standard pulmonary CTA.

<table>
<thead>
<tr>
<th><strong>Scanner</strong></th>
<th>Aquilion ONE ViSION Edition (Toshiba Medical Systems)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Collimation</strong></td>
<td>320 x 0,5 mm</td>
</tr>
<tr>
<td><strong>Rotation time</strong></td>
<td>275 ms</td>
</tr>
<tr>
<td><strong>Tube potential</strong></td>
<td>100 or 120 kV, dependent on patient size</td>
</tr>
<tr>
<td><strong>Automatic exposure control</strong></td>
<td>Pre-contrast scan: noise index = 30 Post-contrast scan: noise index = 22,5</td>
</tr>
<tr>
<td><strong>Scan range</strong></td>
<td>Whole lung</td>
</tr>
<tr>
<td><strong>Image reconstruction</strong></td>
<td>Iterative, AIDR 3D strong, filter F09</td>
</tr>
<tr>
<td><strong>Contrast injection</strong></td>
<td>70 ml Iobitridol 300 (Iomeron 300) at a 5 ml/s, bolustracking in the pulmonary trunk</td>
</tr>
</tbody>
</table>

Table 1: Scanning protocol

**Radiation Exposure**

We evaluated the radiation exposure of this technique in 50 consecutive patients examined for suspected PE. Available patient weights varied from 51 to 133 kg in this group. 2 Patients were scanned twice due to problems with bolus triggering: 1 Patient because of a Fontan circulation (110 kg, DLP 552 mGycm) and 1 obese patient (133 kg;
DLP: 815 mGycm). For the total procedure we found a median dose length product of 171 mGy cm (range: 84 - 815 mGy cm), which corresponds to an effective radiation dose of approximately 2.9 mSv (range, 1.4 - 13.9 mSv) if we use a conversion factor of 0.017 mSv/mGycm for chest CT.

Postprocessing

For processing, we used recently developed software (Sure subtraction™, Toshiba Medical Systems; FDA report K130960) that processes the data using the following steps (compare Figs. 1 and 2):

• Segmenting the lungs for further processing
• Registering and correcting for changes in location and volume of pulmonary structures between pre-and post-contrast acquisitions
• Subtracting the registered scans to create an iodine map
• Removing vessels and interpolating gaps (optional)
• Performing noise-reducing filtering
• Superimposing a color-coded iodine map over the contrast-enhanced data

Interpretation

Image Quality and Artifacts

Perfusion images are interpreted in correlation with the pulmonary CTA images. First, the quality of the CTA and the perfusion data is assessed:

• Low contrast enhancement of the pulmonary vessels (< 200 HU) leads to lower enhancement values and less signal-to-noise.
• Beam hardening artifacts due to intravenous contrast in the superior vena cava may cause streaks and hyperdense bands in the perfusion maps (Fig. 3).
• Photon starvation artifacts in the lung apices due to low-dose scanning will lead to darks bands in the lung apices (Fig. 4).
• Registration artifacts due to too large differences in inspiration between pre- and post-contrast scans will not cause double contours but a mottled effect of the perfusion maps (Fig. 5).
• Pulsation may cause high- or low-density streaks around the heart that are distinguishable from artifacts by their typical shape on coronal sections (Fig. 6).

These factors might hamper image evaluation but are frequently only disturbing and do not cause problems with diagnostic interpretation.
Assessment of Perfusion Images

Evaluation includes adaptation of the color scale if necessary, and interpretation of normal and abnormal findings:

- Note that the color scale reflects absolute HU differences and, as a default, starts at 0 HU and ends at a maximum of 100 HU enhancement. The scale can be adjusted manually to account for differences between patients in actual pulmonary enhancement.
- For clinical interpretation, no adaptation is required in the vast number of scans.
- However, the scale should preferably be set so that the lower end (black) corresponds to zero.
- Black areas indicate total loss of perfusion (Fig. 7), while darker blue areas indicate reduced perfusion.
- Presence of an anterior-posterior gradient is normal (Fig. 2).
- Atelectasis reduces the amount of air in the lungs and so increases (micro)vascular density and perfusion (Fig. 8).
- Irregular perfusion may be due to various kinds of lung disease (compare Figs. 9 and 10). In general, focally reduced perfusion is a consequence of impairment of gas exchange that lead to hypoxic pulmonary vasoconstriction.

Perfusion defects are characterized by their shape and location. Findings are interpreted in correlation with pulmonary CTA.

- Total occlusion leads to a total loss of enhancement in the affected region (black on perfusion images), while reduced perfusion retains some blood flow (dark blue) (see Fig. 7).
- Segmentally distributed perfusion defects correlate to (subtotal) vascular occlusion, such as in PE (Fig. 11).
- More patchy perfusion warrant the search for pulmonary parenchymal abnormalities such as emphysema (see Fig. 10).
- CTA must confirm the diagnosis of PE if emboli are present. In all other cases, alternative reasons for reduced perfusion such as vascular compression (Fig. 10a), or segmental hypoxia due to parenchymal or bronchial pathlogy, needs to be ruled out (see Fig. 9).
- Large emboli may cause extensive perfusion abnormalities, especially in the lung periphery (Figs. 7 and 12).
- In case of multiple emboli, assessing the effect on pulmonary perfusion can be difficult on CTA only. Perfusion images directly demonstrate the amount of relative hyper- and hypoperfusion of the lung parenchyma (Fig. 13).
- Areas of pulmonary infarction may show a hypervascular rim between non-perfused infarcted tissue and perfused pulmonary parenchyma (Fig. 14).
Fig. 1: The SureSubtractionTM 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: The iodine map is superimposed as a color overlay over the pulmonary CTA dataset. Note presence of an anterior-posterior gradient in this normal scan.

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**Fig. 3:** Streak artifacts due to beam hardening by highly concentrated contrast in the superior vena may present as a star-like pattern (a), or as dense regions on axial images (b) that correspond to a typical high-density band on coronal images (c).

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**Fig. 4:** Photon starvation artifacts causing dark bands in the lung apices due to low-dose scanning at 100 kV and 51 mAs in a patient without PE.

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**Fig. 5:** Suboptimal registration with consequent inadequately suppressed vessels. Note the mottled appearance of the perfusion maps posteriorly in the right lower lobe and in the whole left lower lobe.

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**Fig. 6:** Horizontal bands due to cardiac pulsation in a patient without PE. Despite the difference in position of the diaphragm between pre- (a) and post-contrast scans (b), registration is sufficient (c).
Fig. 7: Multiple bilateral emboli (a,b) with complete loss of perfusion (black) in the left lower lobe and reduced perfusion (dark blue) in the right lower lobe (c).
Fig. 8: Focal incomplete atelectasis at the right lung base (a, c) leads to corresponding areas of hyperperfusion (b, d) due to higher microvascular density in the regions of air loss.

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**Fig. 9:** Patient with dyspnea. CTA demonstrates normal pulmonary arteries in the left lower lobe (a) with basal atelectasis and bronchopathy (b). Perfusion maps demonstrate marked hypoperfusion in the affected region.

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**Fig. 10:** Patient with dyspnea. CTA demonstrates severe emphysema (a) that corresponds to patchy perfusion defects on iodine maps (b, c)

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**Fig. 11:** Right sided hilar tumor with encasement of the pulmonary artery and no PE. The tumor causes perfusion defects due to vascular compression.

Fig. 12: Perfusion defects correlated to presence of PE. Bilateral central PE at CT angiography (a) with large perfusion defects at subtraction imaging, especially at the left side (b).

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Fig. 13: Extensive bilateral PE at CT angiography (a) with almost total occlusion of left lower lobe arteries and the lingular artery (c). Iodine maps show that more extensive defects occur in the lingula and middle lobe than could be suspected form CTA (b, d).

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Fig. 14: Pulmonary infarct in the right lower lobe (a) due to bilateral PE at CT angiography (b). Perfusion maps reveal multiple wedge-shaped total perfusion defects and a hyperperfused rim around the pulmonary infarct (c).

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Conclusion

This exhibit demonstrates that subtraction imaging enables construction of good-quality iodine maps of the pulmonary parenchyma. These iodine maps allow for detection of pulmonary perfusion defects in patients with suspicion of pulmonary embolism, but also provide a tool for other diseases that lead to local perfusion abnormalities.
References


