Curr Radiol Rep (2018) 6:36
https://doi.org/10.1007/s40134-018-0297-1

Dual-Energy CT Pulmonary Angiography: Quantification of Disease Burden and Impact on Management

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Published online: 7 August 2018

Abstract

Purpose of Review Computed tomography pulmonary angiography (CTPA) has become the imaging modality of choice for patients with suspected pulmonary embolism (PE). Post-processing techniques currently available for dual-energy CT pulmonary angiography (DE-CTPA) enhance image quality and provide additional value in the diagnosis of PE. The objective of this article is to summarize these recent developments and discuss the appropriate use of DE-CTPA post-processing applications.

Recent Findings DE-CTPA post-processing applications enable reconstruction of virtual monoenergetic images (VMI) and color-coded iodine-perfusion maps to increase contrast conditions and visualize lung perfusion defects in case of embolic occlusion of pulmonary arteries. Both techniques revealed a superior diagnostic performance for the detection of pulmonary emboli and assessment of the pulmonary perfusion compared to the standard image reconstructions.

Summary DE-CTPA is a well-established method for excluding or diagnosing PE. Continued developments in DE-CTPA post-processing techniques improve patient management and allow for a quantification of disease burden.

Keywords Dual-energy computed tomography · Computed tomography pulmonary angiography · Pulmonary embolism · Pulmonary perfusion · Diagnostic accuracy

Introduction

Among all cardiovascular diagnoses with potentially life-threatening complications, pulmonary embolism (PE) is one of the most frequent. Therefore, accurate and reliable diagnosis of acute PE is crucial for rapid treatment and guidance of patient management [1]. Computed tomography pulmonary angiography (CTPA) has become the premier modality for imaging of patients with suspected PE [2]. However, limitations regarding the accurate diagnosis of small peripheral emboli still arise during routine clinical use of CTPA, often due to suboptimal opacification caused by incorrect bolus timing, breathing-related effects, or low cardiac output [3–7]. Moreover, suboptimal contrast attenuation of the small pulmonary arteries can occur even when the administration and timing protocol is optimized [8–10].

Dual-energy CT pulmonary angiography (DE-CTPA) offers several post-processing techniques that facilitate an optimized evaluation of patients with suspected PE. Several studies have demonstrated that image quality of vascular dual-energy CT (DECT) can be substantially improved with monoenergetic imaging. Moreover, DE-CTPA enables the reconstruction of iodine-perfusion maps that aid in the diagnosis of PE through detection of lung perfusion defects in case of embolic occlusion [11]. Recent

This article is part of the Topical collection on *Computed Tomography*.

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improvements in detector technology are used to lower the dose of contrast media and radiation, including high-pitch and low-tube voltage image acquisitions [12].

Pulmonary CT Angiography

Pulmonary CT Angiography Acquisition Protocols

CTPA enables rapid and accurate exclusion or diagnosis of PE. The main goal of CTPA is to provide high-contrast attenuation in the pulmonary arteries, minimizing motion and streak artifacts with short scanning acquisition times and minimal residual contrast in the superior vena cava [6, 7]. The administrated volume of contrast material should ideally be patient-specific and account for body habitus. Usually, a dedicated contrast bolus tracking software is used, placing a region-of-interest (ROI) in the center of the pulmonary trunk to obtain adequate contrast conditions of the pulmonary arterial circulation.

In many institutions, CTPA is performed during inspiratory breath-hold. However, several studies promoted expiratory CT scanning to reduce artifacts that result from variable inflow of unenhanced blood from the inferior vena cava [8, 9]. In a prospective clinical trial by Raczeck et al., the authors suggested performing CTPA in the resting expiratory position to achieve the highest possible attenuation in the pulmonary arteries [13]. The results of this study are also in line with several physiologic considerations that suggest a breath-hold near end-expiration to achieve high levels of pulmonary resistance and thus good arterial opacification [14, 15].

The differential diagnosis of chest pain is a complex problem in the emergency department and remains a challenge for the treating physician. In this context, triple-rule-out CT angiography can provide a simultaneous assessment of the coronary arteries, aorta, and pulmonary arteries for patients presenting with acute chest pain. This method is most appropriate for patients with a low risk for acute coronary syndrome and symptoms that may also be attributed to acute pathologic conditions of the aorta or pulmonary arteries [16]. Injection of contrast media for triple-rule-out CT angiography is tailored to provide high levels of arterial enhancement simultaneously in the coronary arteries, the aorta, and the pulmonary arteries. Scanning parameters include prospective ECG gating to reduce radiation exposure. In addition, triple-rule-out CT can provide comparable image quality to that of coronary CT angiography (CCTA) and CTPA [17, 18].

Low-Tube-Voltage and High-Pitch Pulmonary CT Angiography

Low-tube-voltage CT scanning is an effective method for reducing radiation dose and enhancing contrast attenuation [19–21]. However, this approach is also accompanied by a higher level of image noise due to the lower energy of the photons. Therefore, further reductions of the tube voltage are not feasible in all patients and modification of the scanning parameters should be performed on a patient-specific basis [21, 22]. Furthermore, the improved vascular signal allows for contrast material reduction, which also decreases the risk of contrast-related acute kidney injury [20, 23, 24]. Several studies reported a similar, even improved, diagnostic accuracy for the detection or exclusion of PE [19, 20, 25]. Compared with the standard 120-kV CTPA, imaging with 100 kV resulted in a 37% reduction in radiation exposure and increased the evaluation of central and peripheral pulmonary arteries [19, 21].

High-pitch CTPA scanning is available for more recent scanner generations and can enhance temporal resolution, as well as image quality with a simultaneous reduction in radiation dose. Considering patients who are unable to comply with breath-hold commands, improved temporal resolution decreases motion artifacts for a better evaluation of cardiovascular structures [22, 26]. However, image noise also increases with high-pitch acquisitions; therefore, this approach requires iterative reconstruction of the CT raw data to ensure adequate image quality. Several studies have examined high-pitch low-tube-voltage scanning and revealed substantial reductions in radiation dose without compromising diagnostic accuracy [27–29]. In addition, CTPA acquired in free-breathing yields similar image quality compared to acquisition during inspiratory breath-hold for the diagnosis of PE [30].

Dual-Energy CT Pulmonary Angiography

Dual-Energy CT Post-processing Applications

The basic concept of DECT is defined by the acquisition of two different X-ray-beam energies to obtain two different spectral datasets. This spectral information facilitates material differentiation and provides qualitative information regarding tissue composition. Recent enhancements in detector technology and improved algorithms have emphasized the potential benefits of DECT post-processing in cardiothoracic imaging [31]. Since DECT has demonstrated to be dose neutral compared to standard single-energy CT (SECT), DECT is used more frequently in many clinical areas [31–33].

The most common, non-material-specific method for post-processing of DECT data is linear blending. This algorithm combines data from the low- and high-energy images in a single dataset, taking advantage of both the high-contrast contribution from the low-energy dataset and the low noise levels from the high-energy dataset. Shifting the blending ratio toward lower tube voltages results in increased iodine attenuation, but also usually results in higher image noise. Moreover, non-linear blending functions have been developed, including binary blending, slope blending, Gaussian, and modified sigmoid, to maximize the contribution from the high-contrast low-energy dataset [34–36]. Yet, DECT images are routinely obtained in clinical practice using a linear blending ratio.

In addition, DECT enables methods to discriminate between specific materials (e.g., fat, calcium, iodine, and water). Using dedicated mathematical algorithms, these methods can selectively identify the iodine contribution of an image from the absorption characteristics of three idealized materials, for example, soft tissue, iodine, and air. The material decomposition analysis has shown favorable results in oncological imaging regarding tumor characterization and therapy response [37, 38]. Moreover, the iodine contribution can be subtracted from the dataset, generating virtual non-contrast (VNC) images with image quality comparable to that of a conventional non-enhanced acquisition [39, 40]. Additionally, DECT energy-specific post-processing methods allow for reconstruction of virtual monoenergetic images (VMI). These images have many clinically relevant applications, including beam-hardening correction, optimization of image quality, and metal artifact reduction [41, 42]. For imaging of the pulmonary arteries, dual-energy perfusion maps and virtual monoenergetic images are the two main methods used for an advanced evaluation of patients with suspected PE.

Dual-Energy CT Perfusion Maps

Dual-energy perfusion maps display the iodine-perfused lung tissue, similar to pulmonary scintigraphy, and enable visual assessment of parenchymal perfusion defects distal to vessels affected by PE (Fig. 1). The iodine contribution is super-imposed on the standard grayscale images as a color map. Notably, DE-CTPA perfusion maps are static images that indirectly display the blood volume. This is contrary to time-resolved dynamic CT perfusion imaging, which is used clinically for the assessment of cerebral perfusion and arterial anatomy in stroke patients, for instance [43]. Although this approach was previously investigated for CTPA, it has not found its way into the clinical routine [44, 45]. DECT iodine-perfusion maps support the identification and assessment of non-obstructive emboli and may provide value in the subsequent risk stratification [46]. Reconstruction of 3D perfusion images may also help to visualize reduced perfusion images (Fig. 2).

Several studies showed that dual-energy perfusion deficits correlate with both CT-based morphologic and scintigraphic functional parameters [46, 47]. Moreover, Okada et al. showed, in comparison with traditional CTPA alone, the addition of dual-energy perfusion maps can enhance the detection of peripheral pulmonary clots and may have prognostic value for the clinical outcome [48].

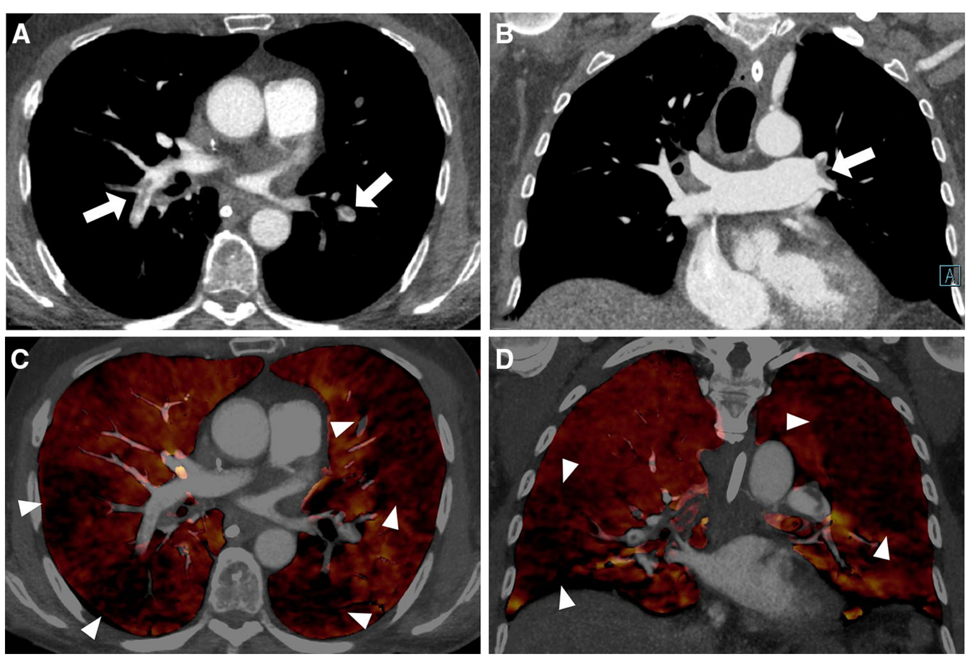


Fig. 1 Dual-energy CT pulmonary angiography of an 82-year-old woman who presented with shortness of breath. Axial (**a**) and coronal (**b**) standard CT images show left central and bilateral segmental pulmonary embolism. Axial (**c**) and coronal (**d**) color-coded dual-energy perfusion maps show wedge-shaped perfusion defects on both sides (arrowheads)

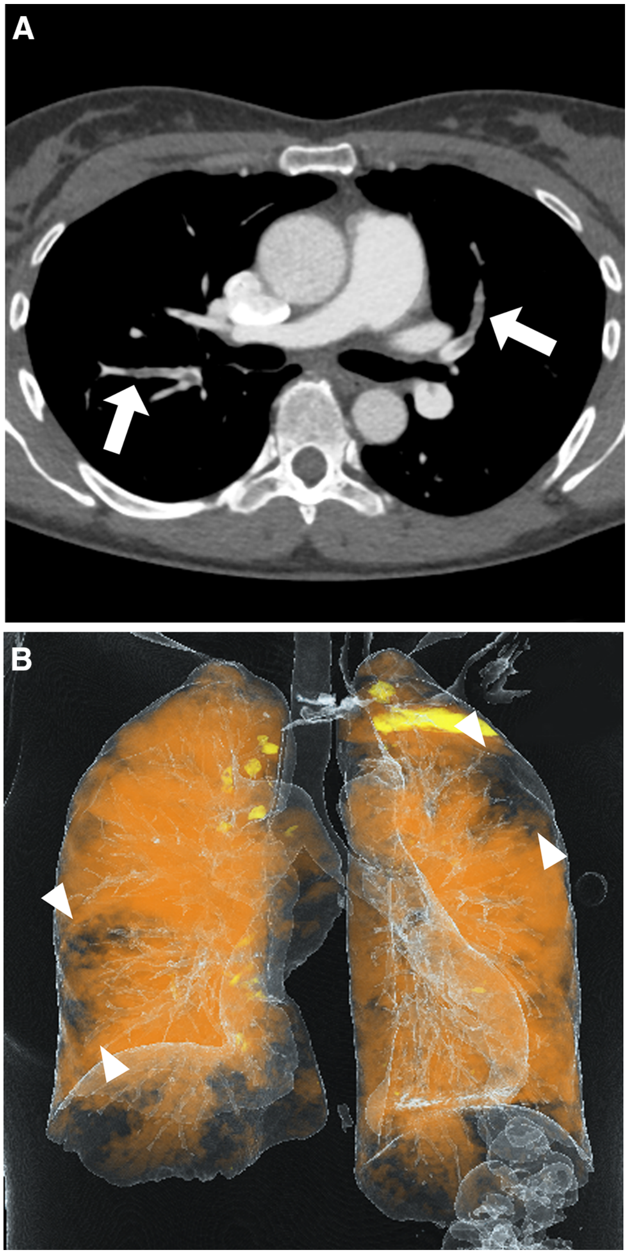


Fig. 2 Dual-energy CT pulmonary angiography performed in a 55-year-old woman with bilateral pulmonary embolism. Transverse standard image reconstructions **a** show filling defects on both sides (arrows). Reduced perfusion in the left upper lobe (arrowheads) is also visible on a 3D perfusion image (**b**)

Only a few studies have evaluated direct lung perfusion DECT using Xenon [49–51]. Xenon is an inert radiopaque gas that has similar photoelectric absorption characteristics as iodine. Due to its ability to decompose materials, DECT allows for separation of inhaled xenon from lung tissue at a single imaging point. However, xenon-enhanced DECT has not been introduced into routine clinical practice, so far.

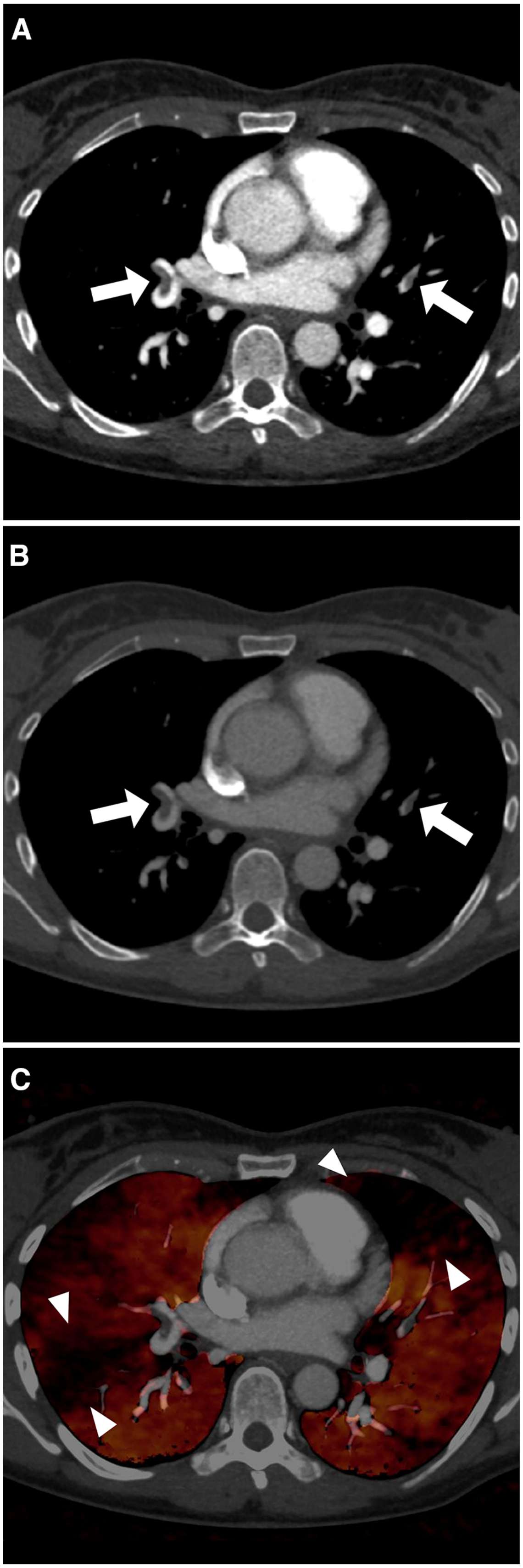
Virtual Monoenergetic Imaging

The calculation of VMI series is a well-established energy-selective post-processing technique based on material decomposition. Based on the material-specific information, the density of each voxel from the DECT data is extrapolated to a certain energy [52, 53]. Application of the VMI post-processing technique had initially been implemented for reduction of metal artifacts and beam-hardening correction [41, 54]. Recently, a noise-optimized virtual monoenergetic imaging (VMI+) algorithm was introduced, designed specifically to improve image quality at low-keV levels. Noise-optimized VMI+ reconstructions are generally based on a regional spatial frequency split technique of the high and the low-energy datasets [55]. Initial studies investigating this VMI+ technique showed improved quantitative image quality in DECT angiography of the aorta and vasculature of the lower extremities, in addition to improved detection of endoleaks and active arterial hemorrhages of the abdomen [56–59].

Moreover, low-keV VMI+ reconstructions are also beneficial for DE-CTPA examinations (Fig. 3). Weiss et al. discovered that VMI+ improves diagnostic accuracy for the detection of incidental PE in oncological DECT follow-up and staging examinations. The authors observed that VMI+ reconstructions at 55 keV presented the highest subjective diagnostic confidence for the detection and exclusion of PE [60•]. Another study by Leithner et al. assessed the value of VMI+ and iodine-perfusion maps of DE-CTPA; they showed that the implementation of both 40-keV VMI+ series and iodine-perfusion maps improves reader confidence and diagnostic accuracy for segmental PE detection in suboptimal contrast conditions [61•].

Quantification of Disease Burden and Impact on Management

Assessment of the severity of PE is crucial for selecting the appropriate treatment strategy and ensuring ideal patient care. There are several methods available for assessing disease severity of PE with CTPA. The most widely used approach for this evaluation is the calculation of the right-ventricular-to-left-ventricular (RV/LV) diameter ratio [62–65]. Applied in numerous studies, this marker for right-ventricular dysfunction has shown to be a predictor of in-hospital mortality and adverse clinical events in patients with acute PE [62–64, 66]. Moreover, Qanadli et al. and Mastora et al. proposed that specific CTPA indices could quantify the location and degree of arterial obstruction in PE [61•, 62, 62]. Although these CTPA scoring systems may be useful for analyzing the effectiveness of treatment, their effect on prognosis in patients with severe pulmonary embolism is still debated in literature [67–69].



◀**Fig. 3** 64-year-old man undergoing dual-energy CT pulmonary angiography with suboptimal contrast conditions and pulmonary embolism on both sides (arrows). Noise-optimized virtual monoenergetic image reconstructions obtained at 40 keV show increased luminal attenuation (**a**). Standard linearly-blended M_0.6 image reconstructions are shown for comparison (**b**). Dual-energy iodine-perfusion maps display wedge-shaped perfusion defects (arrowheads; **c**)

The post-processing capabilities of DECT allow for further evaluation of disease burden in patients with PE. Introduced by Chae et al., the DE-CTPA perfusion defect score presented good correlation with RV/LV diameter ratio and CTA obstruction score, potentially aiding with the assessment of acute PE severity [70]. Another study investigated the impact of the size of perfusion defects as a predictor of right heart dysfunction and its correlation with d-dimer levels [71]. The authors of this study discovered only a weak correlation between perfusion defects and d-dimer levels, but patients with right heart dysfunction presented with significantly larger perfusion defects than patients without. Apfaltrer et al. showed that the extent of DE-CTPA perfusion defects correlates with adverse clinical outcome in patients with PE [72]. However, according to a study by Im et al., the volume of DECT lung perfusion defects provided no statistically significant value for prediction of death within 30 days in patients with PE [73•]. Therefore, further investigations are necessary to validate these first clinical experiences.

Conclusion

DE-CTPA is well-established as a fast and reliable technique in patients with suspected PE. Continued developments in CT system hardware and post-processing techniques enhance image quality and diagnostic accuracy for the detection or exclusion of PE. Moreover, DECT iodine-perfusion maps allow for an assessment of disease severity in patients with acute PE, although the added value of these methods for the prediction of adverse clinical events still remains under discussion.

Compliance with Ethical Guidelines

Conflict of interest Simon S. Martin, Marly van Assen, L. Parkwood Griffith, Maximilian J. Bauer, and Thomas J. Vogl each declare no potential conflicts of interest. Carlo N. De Cecco reports a grant from Siemens. Akos Varga-Szemes reports a grant from Siemens and is a consultant for Guerbet. Julian L. Wichmann reports personal fees from Siemens and GE Healthcare. U. Joseph Schoepf reports receives institutional research support from Astellas, Bayer, General Electric, and Siemens Healthineers. Dr. Schoepf has received honoraria for speaking and consulting from Bayer, Guerbet, HeartFlow Inc., and Siemens Healthineers.

Human and Animal Rights Statement All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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