Mini Review

Corresponding author
Zhonghua Sun, PhD, FSCCT
Professor
Department of Medical Radiation Sciences, School of Science
Curtin University
GPO Box U1987, Perth
WA 6845, Australia
Tel. +61-8-9266 7509
Fax: +61-8-9266 2377
E-mail: z.sun@curtin.edu.au

ABSTRACT

This article discusses a hot topic on double low-dose protocol of computed tomography pulmonary angiography (CTPA) in the diagnosis of pulmonary embolism, with a special focus on a recent paper published in the British Journal of Radiology about the feasibility of this technique. Three aspects will be discussed in this review: First, both kVp and contrast medium can be reduced without affecting image quality when compared to the standard CTPA protocol; second, a low-pitch protocol is comparable to the high-pitch spiral image acquisition with similar image quality achieved, but at lower radiation dose; and finally, the double low-dose CTPA protocol can achieve diagnostic images in patients with body mass index up to 35 kg/m².

KEYWORDS: Computed tomography pulmonary angiography; Contrast medium; Optimization; Image quality; Pulmonary embolism; Radiation dose.

ABBREVIATIONS: CTPA: Computed Tomography Pulmonary Angiography; PE: Pulmonary Embolism; VIE: Virtual Intravascular Endoscopy; CIN: Contrast-Induced Nephropathy; BMI: Body Mass Index; CNR: Contrast-to-noise ratio.

Computed tomography pulmonary angiography (CTPA) has become the method of choice for the diagnostic assessment of patients with suspected pulmonary embolism due to technological advancements in CT imaging. Modern CT scanners with superior spatial and temporal resolution enable detection of segmental and subsegmental thrombus in the pulmonary arteries with high accuracy. In addition to 2D axial images, CTPA allows for generation of different image reconstructions including unique intraluminal views of the thrombus in the pulmonary arteries (Figures 1 and 2). Increased detection of pulmonary embolism seems to be associated with increased use of CTPA, in particular in the emergency department.

Although there are no guidelines available about the minimum acceptable yield of CTPA, it is generally agreed that a diagnostic yield of CTPA less than 10% indicates overuse of CTPA as a diagnostic tool. Sharma and Lucas recently reported their single center experience of CTPA in the diagnosis of pulmonary embolism over a period of 8 years. Authors found a direct correlation between increased number of CTPA scans and percentage of positive pulmonary embolism (the positive diagnostic yield ranges from 12% to 28.1%), suggesting that the use of CTPA is clinically appropriate. Mountain and colleagues in their multi-center study showed similar findings with association of increasing use of CTPA with increased rates of
pulmonary embolism diagnosis. Their study involved 14 clinical sites (15 emergency departments) across Australia and New Zealand consisting of more than 7000 CTPA scans with >94% performed on ≥64-slice CT. The overall diagnostic yield of CTPA at these 14 clinical sites was 14.5% (range: 9.3 to 25.3%) with significant variations in the diagnostic yield among the clinical sites. Of these clinical centers, four sites were found to have significantly lower yield which is less than the acceptable rate of 15.3%. Despite the yield variation in this multi-center study, increased use of CTPA is significantly correlated with pulmonary embolism (PE) diagnosis, thus, justifying its clinical value.17

The increased use of CTPA raises concerns about subjecting patients to excessive radiation exposure and contrast-induced nephropathy (CIN).7,13,20 CT is a well-recognized modality with high radiation dose, although significant dose reduction has been achieved in recent years with implementation of many dose-reduction strategies. This has been widely reported in cardiovascular CT imaging, such as coronary CT angiography,21-24 abdominal aortic imaging,25,26 and CTPA.27,30 Similarly, CIN has been drawing more attention in the recent literature due to routine use of contrast medium injection during CT scans including CTPA. Thus, reduction of contrast medium volume is equally
There are three observations from Boos study that bear discussions. First, the double low-dose CTPA is feasible in acquiring images for diagnostic assessment of pulmonary embolism with use of low kVp and low contrast medium. Of various dose-reduction strategies, low kVp is highly recommended and it is widely used in many CT angiographic applications, in particular, in cardiovascular CT imaging area. According to the society of cardiovascular computed tomography guidelines, selection of kVp is correlated with patient’s BMI, with low kVp (100 or 80 kVp) used in patients with smaller BMI. Reduction of kVp shows particular value in CT angiography because of the association between vessel visualization and iodine enhancement. This is confirmed in Boos’ study by showing an increase in vascular CT attenuation when kVp is reduced. The CT attenuation measured in main pulmonary trunk and left lower segmental pulmonary artery was found to be significantly higher in Group A than that in Group B (414.3±149.4 HU vs. 259.6±139.3 HU and 256.0±75.0 HU, p<0.0001) with no significant difference in signal-to-noise ratio (SNR) and contrast-to-noise-ratio (CNR) between the two groups (p>0.05). Most of the studies tested lowering kVp value with 80 or 100 kVp on CTPA examinations while achieving diagnostic images with low radiation dose, while Boos and colleagues in their study further lowered the kVp to 70 without affecting image quality. It is well known that lowering tube voltage is associated with increased image noise, but this can be compensated by iterative reconstruction, which is confirmed by Boos study.

Contrast medium has detrimental effects on renal function, thus, reduction of contrast medium during CT angiography has attracted increasing attention in the literature. Previous protocols using 80-100 ml contrast medium followed by 30-60 ml saline flush are being replaced by low volume of contrast medium, as shown in Boos and others’ studies. Further lowering contrast volume to even 40 or 20 ml has also been reported in some studies Saade et al compared two groups of patients

| Parameters                                  | Group A 35 patients | Group B 35 patients |
|---------------------------------------------|---------------------|---------------------|
| Data acquisition mode                       | Simultaneous dual-source protocol | Dual-source, high-pitch helical protocol |
| Pitch value                                 | 0.9                 | 2.2                 |
| kVp                                         | 70                  | 120 kVp in 29 patients, 100 kVp in 6 patients |
| mAs                                         | 269±91 (range: 100-397) | 144±35 (range: 82-211) |
| Volume of contrast medium (ml)              | 40                  | 70                  |
| Body mass index (kg/m²)                     | 26.8±3.9            | 26.8±4.2            |
| Effective radiation dose (mSv)              | 2.0±0.6             | 3.9±1.1             |
| Subjective image quality assessment         | 3.7±0.6             | 3.7±0.6             |
| SNR<sub>Trunk</sub>                         | 14.6±6.0            | 13.9±3.7            |
| SNR<sub>LLSA</sub>                          | 15.1±8.9            | 12.0±4.5            |
| CNR<sub>Trunk</sub>                         | 12.4±5.7            | 11.6±3.3            |
| CNR<sub>LLSA</sub>                          | 12.9±8.5            | 10.0±4.1            |

SNR: Signal-to-noise ratio, CNR: Contrast-to-noise ratio, LLSA: Left lower segmental pulmonary artery, Trunk: Pulmonary trunk.
undergoing CTPA with mean contrast volume being 33 ml and 29 ml, respectively. Their results showed significant improvement in the visualization of pulmonary vessels with use of low contrast medium. Another study by Lu et al. reported their experience of further lowering the contrast medium to 20 ml with tube voltage of 80 kVp and high-pitch protocol. Of 100 patients with suspected pulmonary embolism, 50 patients were scanned with the CTPA protocol of 100 kVp, pitch of 1.2 and 60 ml of contrast medium, while another 50 patients with the protocol of 80 kVp, pitch of 2.2 and 20 ml of contrast. Comparable image quality and diagnostic accuracy was found between two groups with no significant differences, while the double low-dose protocol using 20 ml contrast medium resulted in 50% radiation dose reduction.

Second, use of a low-pitch CTPA protocol is not associated with higher radiation dose when compared to the high-pitch mode. Pitch value has a direct impact on radiation dose as it is traditionally believed that higher the pitch, lower the radiation dose. However, increasing pitch to a higher level is not recommended due to increase in image noise resulting from suboptimal spatial resolution. With latest CT scanners the potentially high radiation dose associated with a low-pitch protocol could be countered by reducing the tube current time product (mAs), thus improving image quality by decreasing the image noise. This is observed in Boos’ study. The mean mAs in Group A was significantly higher than that in Group B (268±91 mAs vs. 144±35 mAs, p<0.0001). Despite higher mAs being used in Group A, the 70 kVp protocol led to lower radiation dose with improved image quality of pulmonary arteries. High-pitch and low kVp (80 kVp) protocol has been reported in a number of studies demonstrating the further dose reduction to less than 1 mSv (mAs), thus improving image quality by decreasing the image noise. This is observed in Boos’ study. The mean mAs in Group A was significantly higher than that in Group B (268±91 mAs vs. 144±35 mAs, p<0.0001). Despite higher mAs being used in Group A, the 70 kVp protocol led to lower radiation dose with improved image quality of pulmonary arteries. High-pitch and low kVp (80 kVp) protocol has been reported in a number of studies demonstrating the further dose reduction to less than 1 mSv without compromising diagnostic image quality.

However, lowering kVp and increasing pitch level will increase image noise, thus may impair diagnostic performance of CTPA, hence, it is not widely implemented in clinical practice. It has been reported that better image quality was achieved with a pitch of 2.0 when compared to the CTPA protocol using a pitch of 3.0. The mean effective dose was 2.0 mSv and 3.9 mSv for double low-dose and high-pitch CTPA protocols in Boos study, and this is higher than that reported in Lu’s study which used high-pitch CTPA protocol in normal weight patients. Given the improved image quality of pulmonary vasculature, even in large patients with BMI up to 35 kg/m², the radiation dose of 2.0 mSv is acceptable from a clinical perspective.

Finally, the double low-dose protocol of CTPA allows for acquisition of images in patients with large BMI, according to this study. BMI is one of the main factors that should be considered during CTPAs as in most of the situations, kVp and mAs are adjusted based on patient’s BMI because of its impact on the radiation dose and image quality. Of these reported double low-dose CTPA studies, most of them were performed in patients with normal BMI (mean value <25 kg/m²). In contrast, Boos and colleagues presented diagnostic quality images in large patients as well, although they did not include extremely obese patients. The limitations of previous studies including only normal sized patients or with missing data on BMI have been overcome by Boos’ study, with findings offering additional value to the current literature.

In summary, Boos and colleagues in their study have demonstrated the feasibility of using double low-dose protocol comprising 70 kVp and 40 ml of contrast medium during CT pulmonary angiography. This protocol leads to significant reduction of radiation dose and contrast medium dose when compared to the high-pitch spiral dual-source CT pulmonary angiography. In addition, this study also confirms that low-dose CT pulmonary angiography is able to produce diagnostic images in patients with body mass index up to 35 kg/m². Due to limited small sample size in this study, further research based on a large cohort of patients with assessment of both image quality and diagnostic accuracy is warranted.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. Mayo J, Thakur Y. Pulmonary CT angiography as first-lineimaging for PE: Image quality and radiation dose considerations. AJR Am J Roentgenol. 2013; 200(3): 522-528. doi: 10.2214/ AJR.12.9928

2. Wittram C. How I do it: CT pulmonary angiography. AJR Am J Roentgenol. 2007; 188(5): 1255-1261. doi: 10.2214/ AJR.06.1104

3. Den Exter AL, van der Hulle T, Klok FA, Huisman MV. Advances in the diagnosis and management of acute pulmonary embolism. Thromb Res. 2014; 133(Suppl 2): S10-S16. doi: 10.1016/S0049-3848(14)50002-3

4. Righini M, Le GG, Aujesky D, et al. Diagnosis of pulmonary embolism by multidetector CT alone or combined with venous ultrasonography of the leg: A randomised non-inferiority trial. Lancet. 2008; 371(9621): 1343-1352. doi: 10.1016/S0140-6736(08)60594-2

5. Ghannina W, Almas V, Aballi S, et al. Management of suspected pulmonary embolism [PE] by D-dimer and multi-slice computed tomography in outpatients: An outcome study. J Thromb Haemost. 2005; 3(9): 1926-1932. doi: 10.1111/j.1538-7836.2005.01544.x

6. Mos IC, Klok FA, Kroft LJ, Roos AD, Dekkers OM, Huisman MV. Safety of ruling out acute pulmonary embolism by normal computed tomography/pulmonary angiography in patients with an indication for computed tomography: Systematic review and meta-analysis. J Thromb Haemost. 2009; 7(9): 1491-1498. doi: 10.1111/j.1538-7836.2009.03518.x
7. Carrier M, Righini M, Wells PS, et al. Subsegmental pulmonary embolism diagnosed by computed tomography: Incidence and clinical implications. A systematic review and meta-analysis of the management outcome studies. J Thromb Haemost. 2010; 8(8): 1716-1722. doi: 10.1111/j.1538-7836.2010.03938.x

8. Stein PD, Chenevert TL, Fowler SE, et al. Gadolinium-enhanced magnetic resonance angiography for pulmonary embolism: A multicenter prospective study [PIOPED III]. Ann Intern Med. 2010; 152(7): 434-433. doi: 10.7326/0003-4819-152-7-201004060-00008

9. Sun Z, Al Dosari S, Ng C, al-Muntashari A, Almaliky S. Multislice CT. Virtual intravascular endoscopy for assessing pulmonary embolism: A pictorial review. Korean J Radiol. 2010; 11(2): 222-230. doi: 10.3348/kjr.2010.11.2.222

10. Schoepf UJ, Costello P. CT angiography for diagnosis of pulmonary embolism: State of the art. Radiology. 2004; 230(2): 329-337. doi: 10.1148/radiol.230201489

11. Sharma S, Lucas CD. Increasing use of CTPA for the investigation of suspected pulmonary embolism. Postgrad Med. 2017; 129(2): 193-197. doi: 10.1080/00325481.2017.1281084

12. van Es J, Douma RA, Schreuder SM, et al. Clinical impact of findings supporting an alternative diagnosis on CT pulmonary angiography in patients with suspected pulmonary embolism. Chest. 2013; 144(6): 1893-1899. doi: 10.1378/chest.13-0157

13. Ong CW, Malipatil V, Lavercombe M, et al. Implementation of a clinical prediction tool for the diagnosis of pulmonary embolism at CT angiography: Implications for appropriate-ness, cost, and radiation exposure in 2003 patients. Radiology. 2010; 256(2): 625-632. doi: 10.1148/radiol.10091624

14. Chandra S, Sarkar PK, Chandra D, Ginsberg NE, Cohen RI. Finding an alternative diagnosis does not justify increased use of CT-pulmonary angiography. BMC Pulm Med. 2013; 13: 9. doi: 10.1186/1471-2466-13-9

15. Mamlouk MD, vanSonnenberg E, Gosalia R, et al. Pulmonary embolism at CT angiography: Implications for appropriate-ness, cost, and radiation exposure in 2003 patients. Radiology. 2010; 256(2): 625-632. doi: 10.1148/radiol.10091624

16. Mitchell AM, Jones AE, Tumlin JA, Kline JA. Prospective study of the incidence of contrast-induced nephropathy among patients evaluated for pulmonary embolism by contrast-enhanced computed tomography. Acad Emerg Med. 2012; 19(6): 618-625. doi: 10.1111/j.1553-2712.2012.01374.x

17. Mountain D, Keijzers G, Chu K, et al. RESPECT-ED: Rate of pulmonary embolism (PE) and sub-segmental PE with modern computed tomographic pulmonary angiograms in emergency departments: A multi-center observational study finds significant yield variation, uncorrelated with use or small PE rates. Plos One. 2016; 11(12): e0166483. doi: 10.1371/journal. pone.0166483

18. Costantino MM, Randall G, Gosselin M, et al. CT angiography in the evaluation of acute pulmonary embolus. AJR Am J Roentgenol. 2008; 191(2): 471-474. doi: 10.2214/AJR.07.2552

19. Costa AF, Basseri H, Sheikh A, Stiell I, Dennie C. The yield of CT pulmonary angiograms to exclude acute pulmonary embolism. Emerg Radiol. 2014; 21(2): 133-141. doi: 10.1007/s10140-013-1169-x

20. Newman DH, Schriger DL. Rethinking testing for pulmonary embolism: Less is more. Ann Emerg Med. 2011; 57(6): 622-627. doi: 10.1016/j.annemergmed.2011.04.014

21. Shen Y, Sun Z, Xu L, et al. High-pitch, low-voltage and low-iodine concentration CT angiography of aorta: Assessment of image quality and radiation dose with iterative reconstruction. Plos One. 2015; 10(2): 0117469. doi: 10.1371/journal. pone.0117469

22. Shen Y, Fan Z, Sun Z, et al. High pitch dual-source whole aorta CT angiography in the detection of coronary arteries: A feasibility study of using Iodixanol 270 and 100 kVp with iterative reconstruction. J Med Imaging Health Inf. 2015; 5: 117-125. doi: 10.1166/jmihi.2015.1367

23. Wang H, Xu L, Zhang N, Fan Z, Zhang Z, Sun Z. Coronary CT angiography in coronary artery bypass grafts: Comparison between low concentration iodixanol 270 and Iohexol 350. J Comput Assist Tomogr. 2015; 39(1): 112-118. doi: 10.1097/RCT.0000000000000162

24. Wu Q, Wang Y, Kai H, et al. Application of 80-kVp tube voltage, low-concentration contrast agent and iterative reconstruction in coronary CT angiography: Evaluation of image quality and radiation dose. Int J Clin Pract. 2016; 70: B50-B55. doi: 10.1111/ijcp.12852

25. Sabarudin A, Mustafa Z, Nassir KM, Hamid HA, Sun Z. Radiation dose reduction in thoracic and abdomen-pelvic CT using tube current modulation: A phantom study. J Appl Clin Med Phys. 2015; 16(1): 319-328. doi: 10.1120/jacmp.v16i1.5135

26. Hansen NJ, Kaza RK, Maturen KE, Liu PS, Platt JF. Evaluation of low-dose CT angiography with model-based iterative reconstruction after endovascular aneurysm repair of a thoracic or abdominal aortic aneurysm. AJR Am J Roentgenol. 2014; 202(3): 648-655. doi: 10.2214/AJR.13.11286

27. Kaur M, Vijayananthan A, Kumar G, Jayarani K, Ng KH, Sun Z. Use of 100 kV versus 120 kV in computed tomography pulmonary angiography in the detection of pulmonary embolism: Effect on radiation dose and image quality. Quant Imag-
ing Med Surg. 2015; 5(4): 524-533. doi: 10.3978/j.issn.2223-4292.2015.04.04

28. Almutairi A, Sun Z, Poovathumkadavi A, Assar T. Dual-energy CT angiography of peripheral arterial disease: Feasibility of using lower contrast medium volume. Plos One. 2015; 10(9): e0139275. doi: 10.1371/journal.pone.0139275

29. Faggioni L, Neri E, Sbragia P, et al. 80-kV pulmonary CT angiography with 40 ml of iodinated contrast material in lean patients: Comparison of vascular enhancement with ioxaglate (320 mg I/ml) and iomeprol (400 mg I/ml). AJR Am J Roentgenol. 2012; 199(6): 1220-1225. doi: 10.2214/AJR.11.8122

30. Lu G, Luo S, Meinel FG, et al. High-pitch computed tomography pulmonary angiography with iterative reconstruction at 80 kVp and 20 ml contrast agent volume. Eur Radiol. 2014; 24(12): 3260-3268. doi: 10.1007/s00330-014-3365-9

31. Boos J, Kropil P, Lanzman RS, et al. CT pulmonary angiography: Simultaneous low-pitch dual-source acquisition mode with 70 kVp and 40 ml of contrast medium and comparison with high-pitch spiral dual-source acquisition with automated tube potential selection. Br J Radiol. 2016; 89(1062): 20151059. doi: 10.1259/bjr.20151059

32. Sun Z, Wan YL, Hsieh IC, Liu YC, Wen MS. Coronary CT angiography in the diagnosis of coronary artery disease. Curr Med Imaging Rev. 2013; 9: 184-193. Web site. http://www.ingentaconnect.com/content/ben/cmir/2013/00000009/00000003/art00003. Accessed March 29, 2017.

33. Sun Z, Almoudi M, Cao Y. CT angiography in the diagnosis of cardiovascular disease: A transformation in cardiovascular CT practice. Quant Imaging Med Surg. 2014; 4: 376-396. doi: 10.3978/j.issn.2223-4292.2014.10.02

34. Halliburton SS, Abbara S, Chen MY, et al. SCCT guidelines on radiation dose and dose-optimization strategies in cardiovascular CT. J Cardiovasc Comput Tomogr. 2011; 5(4): 198-224. doi: 10.1016/j.jcct.2011.06.001

35. Laqmani A, Kurfurst M, Butscheidt S, et al. CT pulmonary angiography at reduced radiation exposure and contrast material volume: Comparison of 80 kV CT pulmonary angiography with hybrid iterative reconstruction with 80 kV CT pulmonary angiography: Comparison of 100- and 80-kV protocols in a matched cohort. Invest Radiol. 2008; 43: 871-876. doi: 10.1097/RLI.0b013e3181875e86

36. Szucs-Farkas Z, Schibler F, Cullmann J, et al. Diagnostic accuracy of pulmonary CT angiography at low tube voltage: Intra individual comparison of a normal-dose protocol at 120 kVp and a low-dose protocol at 80 kVp using reduced amount of contrast medium in a simulation study. AJR Am J Roentgenol. 2011; 197: W852-W859. doi: 10.2214/AJR.11.6750

37. Szucs-Farkas Z, Schaller C, Bensler S, Patak MA, Vock P, Schindera ST. Detection of pulmonary emboli with CT angiography at reduced radiation exposure and contrast material volume: Comparison of 80 kVp and 120 kVp protocols in a matched cohort. Invest Radiol. 2009; 44(12): 793-799. doi: 10.1097/RLI.0b013e3181bfe230

38. Szucs-Farkas Z, Kurmann L, Strautz T, Patak MA, Vock P, Schindera ST. Patient exposure and image quality of low-dose pulmonary computed tomography angiography: Comparison of 100- and 80-kV protocols. Invest Radiol. 2016; 51(9): 798-803. doi: 10.1097/RLI.0000000000001377

39. De Zordo T, von Lutterotti K, Dejaco C, et al. Comparison of image quality and radiation dose of different pulmonary CTA protocols on a 128-slice CT: High-pitch dual source CT, dual energy CT and conventional spiral CT. Eur Radiol. 2012; 22(2): 279-286. doi: 10.1007/s00330-011-2251-y

40. Saade C, Mayat A, El-Merhi F. Exponentially decelerated contrast media injection rate combined with a novel patient-specific contrast formula reduces contrast volume administration and radiation dose during computed tomography pulmonary angiography. J Comput Assist Tomogr. 2016; 40(3): 370-374. doi: 10.1097/RCT.0000000000000371

41. Tacelli N, Remy-Jardin M, Flohr T, et al. Dual-source chest CT angiography with high temporal resolution and high pitch modes: Evaluation of image quality in 140 patients. Eur Radiol. 2010; 20(5): 1188-1196. doi: 10.1007/s00330-009-1638-5

42. Wichmann JL, Hu X, Kerl JM, et al. 70 kVp computed tomography pulmonary angiography: Potential for reduction of iodine load and radiation dose. J Thorac Imaging. 2015; 30(1): 69-76. doi: 10.1097/RTI.0000000000000124