Dual energy computed tomography angiography in the peripheral arterial imaging: A systematic review of image quality, radiation dose and diagnostic value

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Abstract

To perform a systematic review of the diagnostic value of dual energy computed tomography angiography (DECTA) in peripheral arterial disease (PAD). PubMed, ProQuest, Medline and ScienceDirect were searched for studies evaluating DECTA compared to conventional computed tomography angiography (CTA) and digital subtraction angiography (DSA) in patients with PAD. Diagnostic value, image quality and radiation dose were analysed and compared. Nine studies comprising a total of 286 patients were found to meet selection criteria where DECTA was used to evaluate lower extremities. The mean estimates of sensitivity and specificity of DECTA were 95.8% (95% CI: 84 to 97.2%) and 79.8% (95% CI: 78 to 97%). Reduction of the contrast medium volume up to 50% was found to achieve an adequate image quality at the optimal keV setting. The mean effective dose for DECTA was 9.51 mSv (95% CI: 7.56 to 11.18 mSv). DECTA is a non-invasive and an accurate diagnostic procedure in the diagnostic assessment of peripheral arterial disease with high diagnostic value.

Keywords: Computed tomography, Dual energy computed tomography, Diagnostic value, Peripheral arterial disease, Virtual monochromatic images.

INTRODUCTION

Recently, the development of dual-energy computed tomography (DECT) allows for utilisation of this technology for differentiation of different materials, thus enhancing diagnostic accuracy when compared to the conventional CT [1, 2]. The main advantage of DECT is the use of various kiloelectron volt (keV) values ranging from 40 to 190 keV, which lead to the improvement of differentiating different materials, such as iodine mapping, and improvement of diagnosis of the cardiovascular disease [3]. Furthermore, the main characteristics of DECT lie in its ability to produce and display either monochromatic or material differentiation in an image [4], such as separating iodine from calcification and other materials [5]. This process is beyond the capability of traditional single-energy CT. Thus, use of DECT in clinical practice provides better image quality and may lower the radiation dose by eliminating the true unenhanced series as shown in DECT abdominal protocols [6-10]. The lower tube potential (kVp) in DECT has not only higher contrast attenuation than the high kVp images, but also it is associated with high contrast-to-noise ratio (CNR), therefore, achieving higher vascular enhancement with lower image noise [4].

The concept of using low kVp in DECT can be applied to evaluate the peripheral arterial disease (PAD). In addition, cardiovascular structure can be assessed with more accuracy when bone removal application is used in DECT [3, 11]. Virtual monochromatic images (MEIs) at the desired energy level can be produced by subtracting the iodine from the images [12]. Accurate detection and analysis of vessel wall calcification in the cardiovascular system, especially in lower extremities is one of the main challenges for the conventional CT angiography (CTA) due to blooming artefacts arising from heavy calcification [13, 14]. Therefore, the use of DECT might overcome this limitation of conventional CTA. Despite the advantages of DECT, radiation dose associated with DECT is still a major concern in the medical field [15]. Furthermore, use of contrast medium leads to potential risk of contrast-

induced acute kidney injury. Thus, reduction of contrast medium during DECT is another research direction in the current literature [2, 16].

Although a number of studies of using DECT application in lower extremities have been reported in the literature with promising results, findings among these studies are variable. To the best of our knowledge, there is no systematic review of the diagnostic value, image quality and radiation dose associated with DECT angiography (DECTA) in peripheral arterial disease. Thus, this systematic review is conducted to determine the diagnostic performance of DECT in PAD based on analysis of the current literature.

METHODS

Literature searching and data selection criteria

The literature search was performed by using different databases including PubMed, ProQuest, Medline and ScienceDirect. The keywords used for searching the eligible references included: dual energy computed tomography, DECT and cardiovascular disease, dual source computed tomography and cardiovascular disease, DECT and peripheral angiography, DECT and radiation dose and image quality, diagnostic value of DECT in cardiovascular disease. The reference lists of identified articles were also checked manually to obtain additional relevant articles. Article inclusion criteria are: 1) published between 2006 and October 2015 (DECT was introduced in 2006); 2) published in English language; 3) prospective and retrospective studies with at least 10 patients and with one DECT series performed and with (a) radiation dose or image quality comparison with conventional CTA or invasive angiography; or (b) diagnostic value (in terms of sensitivity and specificity) in comparison with conventional CTA or digital subtraction angiography (DSA). Exclusion criteria were: review articles, comments to the editor, phantom studies, case reports and conference abstracts.

Study selection

Two reviewers independently assessed the title and abstract of the identified articles for eligibility based on the study design and procedure techniques. After this initial selection, the full texts of the potentially eligible articles were retrieved and assessed for eligibility by the same authors. Agreement on the final data and results were resolved by consensus. Potentially missed relevant articles were identified by checking the reference lists of the included articles.

Data extraction

A data extraction sheet was developed which included; the year of publication, number of subjects, their age, gender, body mass index (BMI), type of CT scanner, section thickness, reconstruction interval, gantry rotation time, beam collimation, pitch, tube voltage and current. Radiation dose parameters include: volume CT dose index (CTDIvol), dose length product (DLP), effective dose (E). Image quality based on the image noise, signal-to-noise ratio (SNR), and CNR data was also extracted. The accuracy of DECTA based on sensitivity and specificity was extracted from each study. Additionally, the use of contrast material for DECTA was extracted including the following details: contrast medium type, contrast concentration mg/ml, flow rate mL/s, method of dose calculation, and CT threshold (HU) for scan initiation.

Data analysis

Data were entered into SPSS V 22.0 for statistical analysis (SPSS Inc, Chicago., IL, USA). Categorical variables were presented as percentages or frequencies. Diagnostic value of sensitivity, specificity, image quality and radiation dose were analysed with mean values reported and compared using Student T test.

RESULTS

Study selection

The initial search yielded 335 articles from all the databases included in this study. A total of 18 studies met the selection criteria and only 9 studies [11, 14, 17-23] were found to be eligible for the analysis. Four studies were excluded as they evaluated the venography system, while another three evaluating the upper extremities were excluded as well, and remaining two did not use dual energy mode. Figure 1 is the flow chart showing the search process for identifying eligible studies. Two types of CT scanners were used in these studies, with 8 studies using Somatom definition 64-slice dual-source CT [11, 14, 17-22], and one using fast kilovoltage-switching 64-slice CT scanner [23]. The total number of patients included in these studies was 286 with mean age of 67.5 years. Of these 9 studies, only 4 reported the radiation dose [14, 17, 19, 24], however, none of the studies compared the radiation dose with the conventional CTA. For the scanning parameters used in these studies, the section thickness ranged from 1 mm to 1.5 mm and reconstruction interval ranged from 0.65 mm to 1.5 mm, with pitch value from 0.55 to 0.984. Patients' characteristics and scan parameters of DECT protocols are summarized in Table 1.

Image quality assessment

Image quality parameters were evaluated in these studies, which included image noise, SNR, CNR and ranking scales. Qualitative assessment of image quality using a four- and three-point ranking scale was performed in 4 studies, a three- point scale was used in three studies while in one study a four-point scale was used, and in the remaining study the information about qualitative assessment was unavailable. For quantitative evaluation of the lower extremities, out of nine studies, only three studies reported the SNR and CNR comparing MEIs with polychromatic images [20, 21, 23]. In a study conducted by Sudarski et al. authors

concluded that using low keV of 60 resulted in higher attenuation and CNR and SNR (513 HU, 87, 13.2, respectively) compared to the polychromatic images (333 HU, 57, and 8.75, respectively). However, a recent study by Almutairi et al. found that 65 keV yielded the highest SNR and CNR (14.61 and 21.75) respectively when peripheral arterial trees were valuated [23]. Also, one study reported the CNR was only additional to coefficient of variance as another parameter to evaluate the image quality compared to DSA and CTA [18]. In this study the CNR ranged from 45 to 64.6 for vessels above the knees, which was claimed to be higher than those in DSA and CTA. On the other hand, for the subjective image evaluation of image quality on a 3- point scale in two studies higher value using DECTA was achieved [20, 23]. The quality of bone removal using DECT application was reported in five studies with general agreement indicating that the bone removal with DECT was scored higher than conventional CTA.

Radiation dose

The radiation dose was reported only in 3 studies [11, 14, 23] with use of different approaches for calculating effective dose. Effective dose was estimated by multiplying the DLP with a conversion factor of 0.015 in two studies [11, 14] while the third study used a conversion factor of 0.0056 [23]. Thus, the mean effective dose for DECT protocols from these three studies was 9.51 mSv, ranging from 7.56 to 11.18 mSv. The reported $CTDI_{vol}$ was 6.6 and 7.48 mGy for studies using Somatom definition 64 DSCT scanners and 9.05 mGy for fast kilovoltage-switching 64-slice CT scanner. Tube current modulation was applied in three studies, however, radiation dose was not reported in these studies.

Diagnostic value of DECTA

The diagnostic value of DECTA was only reported in four studies [11, 14, 19, 22]. Comparison of diagnostic value between DECTA and conventional CTA was reported in one

study [14], thus only analysis of the mean diagnostic value of DECTA in PAD was conducted. Summary estimates of the overall sensitivity and specificity of DECTA were 95.87% (95% CI: 84 to 97.2%) and 79.8% (95% CI: 78 to 97%) respectively. With regard to diagnostic performance in the four subdivisions of the arterial tree in three studies that reported the data, the pooled sensitivity and specificity for aorta are 94.5% (95% CI: 89 to 100%) and 94% (95% CI: 88 to 100%), 88.4% (95% CI: 81 to 94.4%) and 92.9% (95% CI: 88 to 96.2%) for pelvis, 84.5% (95% CI: 67 to 100%) and 93.3% (95% CI: 88 to 97.8%) for thigh, and 95.9% (95% CI: 91 to 100%) and 58.9% (95% CI: 38.7 to 86.9%) for calf, respectively. Two studies evaluated the accuracy of bone removal algorithm with sensitivity and specificity ranging from 84 to 97.2% and 67 to 94% for stenosis greater than 50-74%, respectively. Moreover, one study evaluated the accuracy of maximum intensity projections and found that DECTA had 84% sensitivity and 67% specificity when compared with DSA [19]. Furthermore, another study evaluated the accuracy of selective CTA for the below knee arteries with sensitivity and specificity of 100% and 89%, respectively [22].

Contrast medium assessment

Table 2 shows details of contrast medium used in these studies during DECTA examinations. As shown in the table, the mean contrast volume and flow rate were 108.94 ml (66.47-160 ml) and 4.22 ml/s (3-5.5 ml/s) respectively. Furthermore, the contrast concentration used in DECTA was between 300 mg/ml and 400 mg/ml in all studies with the protocol of using a saline chaser following administration of contrast medium in 8 of them. Two approaches were used to monitor the contrast flow either by bolus tracking in two studies [18, 23] or specific threshold level in six studies [11, 14, 17, 19-21] with CT attenuation between 100 and 250 HU as the triggering threshold. Only one study involved comparison of the effect of different contrast volumes [23]. The remaining study used a selective CTA and injection of

contrast medium directly via catheter in the external iliac artery using a very ultra-low contrast volume (17.5 mL) [22].

DISCUSSION

Four key findings were found in this systematic review: first, improved image quality can be achieved with use of DECTA in PAD when compared to conventional CTA. Second, there is good diagnostic accuracy of DECTA in the diagnostic assessment of PAD. Third, contrast medium can be reduced by up to 50% without compromising image quality. Finally, radiation dose may be still higher in DECTA, despite its improved diagnostic performance.

Image quality degradation in conventional CT is due to the polychromatic fauna of the x-ray source and the ability of CT detector to distinguish the energy. Currently, there are two types of DECT in clinical practice: single source dual energy (achieving dual energy imaging with use of fast kilovolt dynamic switching) and dual source dual energy (achieving dual energy imaging with use of two x-ray tubes with different kVp). DECT is based on the MEI and might overcome the limitation of conventional CT, and further improve the image quality. In addition, post-processing flexibility of DECT data allows for a wide range of monochromatic energy levels, which allow for balancing image contrast and noise to obtain desirable diagnostic information for the clinicians. Therefore, the evaluation of peripheral arterial disease by DECT allows for acquisition of better image quality beyond what has been obtained by conventional CTA. Huang et al.[20] reported that DECT improved the vascular enhancement with ability to assess the severity of stenosis beyond CTA and DSA in peripheral disease. For MEIs, lower keV was found to improve the image quality of enhanced vessels because it is close to the K-shell of iodine material which is 33keV [4].

Several studies have been published on image quality using different keV settings in evaluation of PAD. Almutairi et al.[23] reported that 65 keV achieved an optimal image

quality in peripheral DECTA which is in accordance with a previous study based on phantom study that evaluated the peripheral arterial stents [24]. Another study by Sudarski et at.[21] demonstrated the best image quality of MEI at 60 keV for the lower extremities. This is supported by studies investigating spectral imaging in thoracic arteries with results showing that MEIs from 55 keV provided better image quality than standard chest CTA [2, 17, 25]. A recent study evaluated abdominal aorta aneurysm found higher accuracy at 55 keV compared with standard CTA. However, Pinho at al.[9] and Sudarski et al.[21] found the optimal image quality obtained at 70 keV in abdominal artery imaging. Furthermore, improvement of the noise and contrast in a pixel-by-pixel way can be achieved using non-linear image blending techniques in vascular imaging [26]. In a recent study by Lv et al.[27] researchers reported that using non-linear blending image in abdominal CTA the contrast enhancement was improved in a lower energy protocol. Despite these encouraging results, more studies are needed to confirm the use of MEIs and non-linear blending images in peripheral arterial imaging protocols.

The diagnostic value for CTA in the assessment of the peripheral arteries has been reported with high accuracy [28-30]. Recent advances in CT technology may further improve the diagnostic value. Therefore, using DECT applications for bone removal is more accurate and time efficient than conventional CTA applications. Several studies concluded that DECT bone removal applications are superior to conventional CTA [11, 14, 20, 23], however, none of these studies investigated the use of MEIs with bone removal in peripheral arterial protocols. Thus, further research is needed to clarify the quality of MEIs with bone removal application in the lower extremities.

The analysis of available data in this review shows that DECTA is an accurate diagnostic tool compared with the standard reference DSA, or CTA for detecting arterial lesions of the lower extremities, with overall good sensitivity and specificity. However, according to results from

most of the individual studies it shows that improvement of image quality using DECTA in peripheral arteries is highly significant. Brockmann et al.[14] reported a sensitivity of 97.2% and specificity of 94% when compared with DSA and CTA for diagnosing ≥50% stenosis. This is also supported by a study conducted by Meyer et al.[11] who evaluated the peripheral arteries by DECT with reported sensitivity of 93.1% and specificity of 78.2%. The lower accuracy of this review was mainly due to the results of the study by Kau et al.[19] who reported lower sensitivity of 84% (95% CI, 80 to 88%) and specificity of 67% (95% CI, 62 to 71%) when maximum intensity projections in DECT were compared to DSA. Thus, results of the diagnostic value of DECTA in this review need to be interpreted with caution.

Although the diagnostic accuracy was moderate as shown in this analysis, the selective CTA for assessing popliteal arteries conducted by Swanberg et al.[22] was reported to achieve a sensitivity of 100% and specificity of 89% at ultra-low contrast medium volume. Therefore, this new approach might lead to better evaluate specific arteries and stents with minimum radiation dose and contrast medium.

This review shows no consistency between these studies in terms of contrast flow rate and the contrast monitoring. Baxa et al.[31] assessed the use of low volume of the contrast material with a double-level test bolus method and concluded that the use of this method could achieve high image quality with low contrast material volume. A recent study compared different volumes of contrast medium and concluded that using low contrast volume was not different from the routine contrast volume in the image quality outcome [23]. Reducing the contrast medium volume by up to 50% with DECT was found to be useful and did not affect the overall image quality. Therefore, low contrast volume is highly recommended at low kVp during DECTA in PAD. This approach is supported by studies evaluating the contrast medium volume in pulmonary CTA [32, 33] and abdominal CTA [9], as low contrast volume with similar image quality was reported when compared to the high contrast volume. Thus, to

reduce the variances between patients, an individual contrast medium and scan time optimization in lower extremities is recommended.

Although radiation dose associated with CT is always a main concern, dose reduction technique was not evaluated in most of these studies that were analysed in this review. However, the obtainable dose values in some studies are found to be similar to or even lower than that of conventional CTA. Applying the latest methodology of calculating the effective dose with DECT in peripheral arterial studies may significantly reduce the radiation dose [23, 34]. Therefore, the low effective dose in peripheral arterial protocol was achieved by using the new methodology of estimating the lower limbs area with conversion coefficient *k* (0.0056 mSv/mGy) in DECTA. However, this approach was recently applied to the clinical area therefore, the calculated dose in the other studies seems similar to that was recorded from abdominal protocols. Apparently further studies with a focus on dose reduction are necessary.

There are some limitations in this review that should be acknowledged. First, the limited number of studies of DECTA in PAD did not allow us to perform a meta-analysis, thus, only a systematic review was conducted. Second, insufficient information is provided in some studies, such as lack of dose reports, or diagnostic value of DECTA in PAD. Furthermore, different ranking scales were used in these studies that were analysed, and objective assessment of image quality was available in only a few studies. Third, inconsistent protocols among these studies represent another important limitation of our analysis. Finally, the study heterogeneity that exists in these studies with various types of DECT scanning is another important limitation of our analysis.

In conclusion, this systematic review shows that DECT angiography may achieve the optimal image quality at low keV values. DECT is an accurate diagnostic imaging technology in the

assessment of peripheral arterial disease with moderate diagnostic value but with lower contrast medium, therefore, reducing the risk of contrast-induced acute kidney injury. Reduction of the contrast medium volume up to 50% can achieve an adequate image quality at the optimal keV setting.

CONFLICT OF INTEREST

The authors confirm that this is no conflict of interest.

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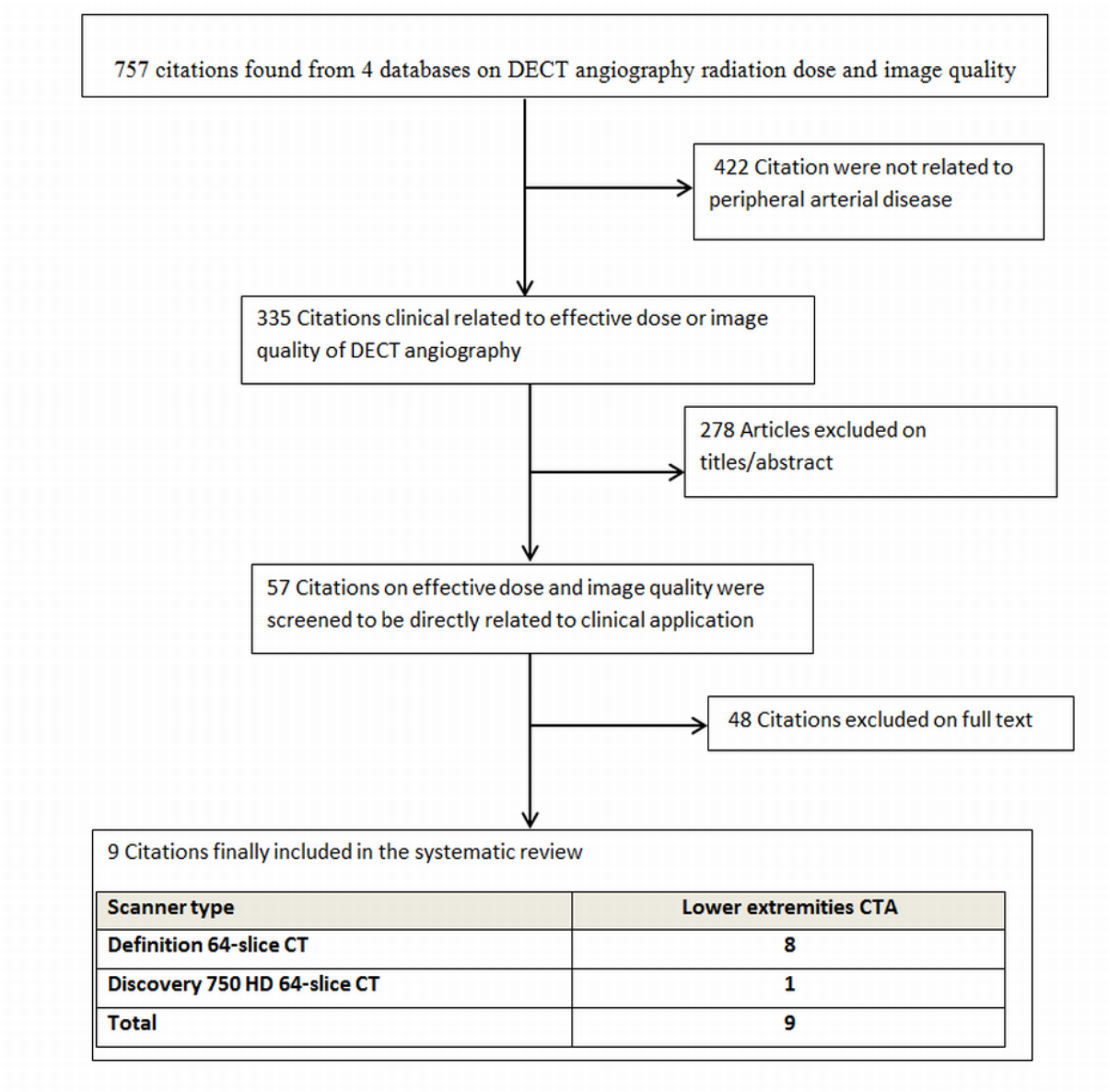
Figure and figure legend



Scanner type	Lower extremities CTA
Definition 64-slice CT	8
Discovery 750 HD 64-slice CT	1
Total	9

Figure 1. Flow chart showing searching strategy for identifying the eligible studies.

Table 1. Study characteristics of dual energy CT angiography in peripheral arterial disease.

Study /Year	Body part	No of patients	Mean age (yrs)	Male %	Scanner type	Technique used for DECT	Collimator Setting	Section thickness (mm)	Recon. Interval (mm)	Pitch	Algorithm	mA	Dose modulation	Rotation time (msc)
Meyer et al. 2008 [11]	Lower extremity	50	67	68	64 DSCT	2 tubes	2 x 32 x 0.6	1	0.6	0.7	NA	56/238	NA	500
Brockmann et al. 2008 [14]	Lower extremity	20	67	80	64 DSCT	2 tubes	14 x 1.2	1.2	1	0.6	D30f	90/382	NA	500
Yamamoto et al. 2009 [17]	Lower extremity	20	73	55	64 DSCT	2 tubes	2 x 32 x 0.6	1	0.65	NA	D30f	95/405	Yes	500
Sommer et al. 2009 [18]	Lower extremity	51	70.8	72	64 DECT	2 tubes	2 x 32 x 0.6	1.5	1	0.7	NA	80/340	Yes	500
Kau et al. 2011 [19]	Lower extremity	58	72	60	64 DSCT	2 tubes	14 x 1.2	1.5	1	0.6	NA	90/390	NA	500
Huang et al. 2012 [20]	Abdomen and lower extremity	25	64.7	52	64 DSCT	2 tubes	14 x 1.2	1.2	1.5	0.55	D20f	115/448	NA	500
Sudarski et al. 2013 [21]	Abdomen and lower extremity	18	67	72	64 DSCT	2 tubes	14 x 1.2	1	1.5	0.6	NA	80/440	NA	500
Swanberg et al. 2014 [22]	Lower extremity	10	73	9	64 DECT	2 tubes	2 x 32 x 0.6	1.5	1	0.7	D30f	55/Auto	No	500
Abdulrahman et al 2015 [23]	Lower extremity	34	52.1	25	64 DECT	Fast kVp switching	64 x 0.625	1	1	0.984	Standard	600	Yes	500

DSCT dual source computed tomography, DECT dual energy computed tomography, NA not available, mA Milliampere

Table2. Contrast protocols used in dual-energy CT angiography in peripheral arterial disease.

Study /Year	Body part	DECT protocol	Contrast medium	Contrast concentration mg/ml	Flow rate mL/s	Method of dose calculation	Threshold (HU) for initiating the scan
Meyer et al. 2008 [11]	Lower extremity	Run off	Iomeron	400	4	100 mL + 50 mL saline flush	250 HU +3s
Brockmann et al. 2008 [14]	Lower extremity	Run off	Imeron	300	4	140 mL + 40 mL saline flush	200 HU
Yamamoto et al. 2009 [17]	Lower extremity	Run off	Iopamidol	370	3.5	120 mL + 40 ml saline flush	150 HU +10s
Sommer et al. 2009 [18]	Lower extremity	Run off	Ultravist	370	5.5	100 mL + 60 ml (160mL) + 50 ml saline flush	Bolus triggering
Kau et al. 2011 [19]	Lower extremity	Run off	Iomeprol	400	4	1.5 mL/kg (120 mL + 50 mL saline flush) mean 118ml	150 HU +5s
Huang et al. 2012 [20]	Abdomen and Lower extremity	Run off	Iopamidol	300	3	100 mL + 50 mL saline flush	150 HU
Sudarski et al. 2013 [21]	Abdomen and Lower extremity	Run off	Imeron	400	5	120 mL	100 HU
Swanberg et al. 2014 [22]	Lower extremity	Run off	Iopamidol	400	NA	17.5 mL + 32.5 mL saline flush	7 mL CM + 13 mL NS in 10s followed by 10.5 mL CM + 19.5 NS in 30s

Abdulrahman et al. 2015 [23]	Lower extremity	Run off	Xenetix	350	4.75	1.5 and 0.75ml/kg + 40 mL saline flush (66.5 and 116 for two groups)	Bolus tracking

CM-contrast medium, HU-Hounsfield unit, NS-normal saline