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REVIEW ARTICLE

Dose reduction with iterative reconstruction for coronary CT angiography: a systematic review and meta-analysis

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Objective: To investigate the achievable radiation dose reduction for coronary CT angiography (CCTA) with iterative reconstruction (IR) in adults and the effects on image quality.
Methods: PubMed and EMBASE were searched, and original articles concerning IR for CCTA in adults using prospective electrocardiogram triggering were included. Primary outcome was the effective dose using filtered back projection (FBP) and IR. Secondary outcome was the effect of IR on objective and subjective image quality.
Results: The search yielded 1616 unique articles, of which 10 studies (1042 patients) were included. The pooled routine effective dose with FBP was 4.2 mSv [95% confidence interval (CI) 3.5–5.0]. A dose reduction of 48% to a pooled effective dose of 2.2 mSv (95% CI 1.3–3.1) using IR was reported. Noise, contrast-to-noise ratio and subjective image quality were equal or improved in all but one study, whereas signal-to-noise ratio was decreased in two studies with IR at reduced dose.
Conclusion: IR allows for CCTA acquisition with an effective dose of 2.2 mSv with preserved objective and subjective image quality.

INTRODUCTION

The number of CT examinations has increased rapidly over the past decades leading to increased radiation exposure.[1] This is especially a concern for coronary CT angiography (CCTA) since, retrospectively, electrocardiogram (ECG)-gated CCTA used to be associated with relatively high radiation doses of >10 mSv.[2] These high CCTA radiation doses have led to the development of new techniques such as prospective ECG-triggering, high-pitch spiral acquisition and, more recently, iterative reconstruction (IR) to reduce radiation dose.[3] Despite these advances, radiation dose remains an important issue for CCTA because the number of indications and eligible patients has increased rapidly over the past few years.[4–6]

IR offers the possibility to reduce radiation dose and was already used on the first CT systems.[7,8] However, owing to the limited computational power at that time, it could not be used in clinical practice. With recent improvements in computer processing, IR has become feasible in a clinical setting. Currently, the most commonly used reconstruction technique is filtered back projection (FBP), which is a fast reconstruction technique that suffers from impaired image quality when radiation dose is lowered. IR is a noise-suppressing technique that allows for a decrease in radiation dose compared with FBP while maintaining image quality.[9]

Recently, new IR algorithms were introduced which led to a surge in the number of publications. Therefore, we present the results of a systematic review and meta-analysis to determine the achievable radiation dose reduction for prospective ECG-gated CCTA acquisitions using IR. Furthermore, the effect of IR on objective and subjective image quality was investigated.

METHODS AND MATERIALS

Search

A systematic search in PubMed and EMBASE was performed on 2 May 2014 for studies investigating IR for CCTA without a publication date limitation. English language restriction was applied. Synonyms for "IR techniques" and "CT" were combined. The search syntax is provided in Appendix A. Duplicates were removed. Hereafter, a manual search of the reference lists of included articles and review articles was performed after which review articles were removed.

Inclusion and exclusion criteria

All articles were screened by two authors (AH and MW). In case of discrepancy, a consensus had to be reached between authors on whether to include the study. Original research articles concerning IR techniques for CCTA using prospective ECG-triggering were included. Studies comparing routine dose acquisitions with FBP to reduced dose acquisitions with IR using the same CT system, contrast medium and dose modulation techniques were included, whereas studies investigating only one dose level without comparison to FBP were excluded. Furthermore, studies only investigating non-enhanced CCTA, *ex vivo*, *in vitro* and animal studies as well as studies performed in children were excluded. Case reports and reviews were excluded as well. Case reports were defined as studies including less than five patients.

Data extraction

Data were extracted to a standardized data sheet, which included first author, title, publication date, journal, study design, participant characteristics, reconstruction technique, scan indication, type of scan, type of CT system, and reported dose and image quality measurements.

The primary outcome was the effective dose reduction with IR. The effective dose was calculated as the dose–length product (DLP) times the conversion factor for chest CT ($0.014\,\mathrm{mSv\,mGy^{-1}\,cm^{-1}}$).[10] This conversion factor was chosen because it was the most commonly used conversion factor in the included articles. In case a different conversion factor was used, the effective dose was recalculated using the DLP. If the effective dose was reported without conversion factor or DLP, the corresponding author was contacted. The corresponding authors were also contacted if both the effective dose and the DLP were not reported.

Secondary outcome was the influence of IR on objective and subjective image quality. Noise, contrast-to-noise ratio (CNR) and signal-to-noise ratio (SNR) were investigated. Image quality was specified as improved, equal or deteriorated compared with FBP. Improved was defined as a statistically significant improvement of image quality with IR compared with FBP. Non-significant differences were classified as the same, and a significant decrease in image quality was classified as deteriorated. If multiple IR levels were studied, the IR level with the most favourable outcome was used for further analysis.

From each article, the mean and standard deviation (SD) of the effective dose were extracted. If only the median and the interquartile range (IQR) were reported, the mean and SD were recalculated. The median was considered to be equal to the mean if the number of patients exceeded 25.[11] The IQR was converted to the SD using the formula $1.35 \times \mathrm{SD} = \mathrm{IQR}$.

Statistical analysis

Statistical analysis was performed using SPSS® v. 20.0 (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL) [for Microsoft® Windows® (Microsoft, Redmond, WA)] and the RStudio statistical environment v. 0.98.1025 (RStudio, Inc., 2009–13) with "meta" package v. 3.7-1.[12] For every study, a mean and 95% confidence interval (CI) was calculated. Heterogeneity was assessed by the I^2 statistic, and random effect models were used in case of large interstudy variance ($I^2 \geq 65\%$). Results were presented as mean with 95% CI. Both the normal dose data with FBP and the reduced dose data with IR were calculated and pooled. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

Study selection

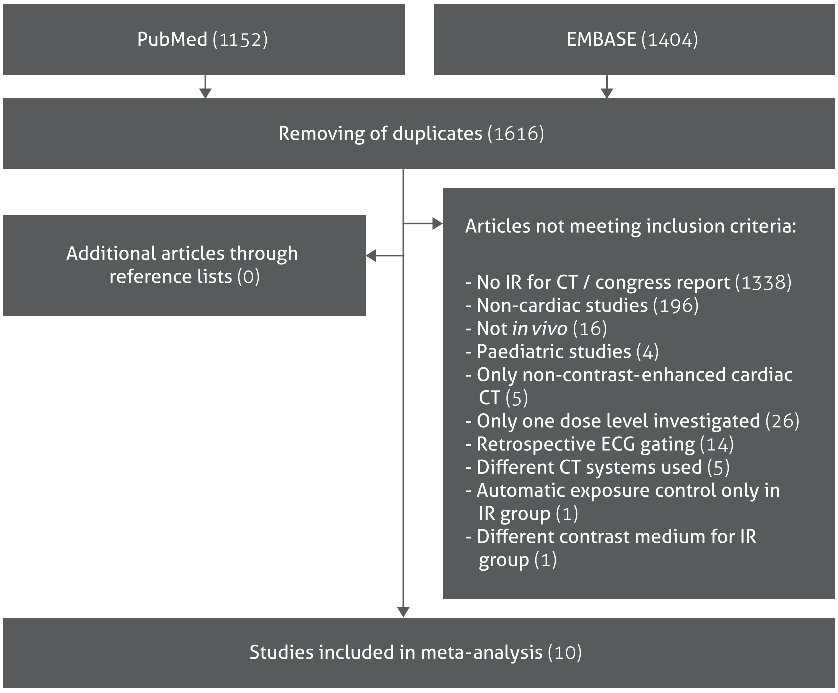
In total, 2556 articles were identified. A flowchart is provided in Figure 1. After removing of duplicates, 1616 articles were screened based on title and abstract. 1606 articles were excluded, because the articles did not investigate IR for CT ($n = 1338$), were non-cardiac ($n = 196$), were not *in vivo* ($n = 16$), were paediatric studies ($n = 4$), only concerned non-contrast-enhanced coronary CT ($n = 5$), only 1 dose level was investigated ($n = 26$), used retrospective ECG-gating ($n = 14$), used different CT systems for the FBP and IR groups ($n = 5$), used automatic exposure control only in the IR group ($n = 1$) or used a different contrast medium for the IR group ($n = 1$). Articles investigating one dose level are mentioned in Appendix B. 10 articles remained with a total of 1042 patients. One corresponding author was contacted because the reported information about radiation dose was insufficient.[13]

Study characteristics

The baseline characteristics are provided in Table 1. Studies were published in 2011 ($n = 1$), 2012 ($n = 3$), 2013 ($n = 5$) and 2014 ($n = 1$). Different IR techniques were used namely Adaptive Statistical Iterative Reconstruction (ASIR; GE Healthcare, Milwaukee, WI, $n = 3$), Sinogram-Affirmed Iterative Reconstruction (Siemens Healthcare, Erlangen, Germany, $n = 3$), iDose (Philips Healthcare, Best, Netherlands, $n = 2$), Iterative Reconstruction in Image Space (Siemens Healthcare, $n = 1$) and Adaptive Iterative Dose Reduction (Toshiba Medical Systems Co Ltd., Otowara, Japan, $n = 1$). One study compared Model-Based Iterative Reconstruction-Veo (GE Healthcare) with ASIR,[22] since FBP was replaced by ASIR as the clinically implemented routine reconstruction method. CT systems used were Aquilion One™ (Toshiba Medical Systems Co Ltd., $n = 1$), Brilliance iCT (Philips Healthcare, $n = 2$), Discovery™ HD 750 (GE Healthcare, $n = 3$) and Somatom® Definition Flash (Siemens Medical Systems, Forchheim, Germany, $n = 4$).

The median number of patients per study was 74 (range 20–338). In total, data of 1042 patients were included in this study. Most studies ($n = 7$) used different study populations to compare FBP with IR; however, three studies compared different dose levels in the same patients.[18,20,22] This was achieved by using data from only one source of a dual-source CT scanner[20] or by making additional scans of the same patient.[18,22] Mean body mass index (BMI) varied between studies from 23.9 to $33.8\,\mathrm{kg\,m^{-2}}$ with heart rates of 57–74 beats per minute. The contrast rate and volume was the same between the FBP and IR groups in all studies. In three studies, tube current modulation was used.[18–20]

Figure 1. Flowchart of included studies. ECG, electrocardiogram; IR, iterative reconstruction.



Effective dose

Interstudy variance was high for effective dose pooling (I^2 98.9%), therefore random effects models were used. In three studies, the effective dose was (re)calculated using the DLP, because the effective dose was not provided or calculated with a different conversion factor.[16,18,20] The pooled routine effective dose using FBP was 4.2 (95% CI 3.5–5.0) mSv. At reduced dose level using IR, the pooled effective dose was 2.2 (95% CI 1.3–3.1) mSv (Figure 2). Standard effective dose varied highly between studies from 1.2 to 9.6 mSv, whereas differences were smaller with IR (0.2–4.4 mSv). The relationship between routine effective dose and reduced effective dose for each CT system is illustrated in Figure 3.

Image quality

Objective image quality was scored using image noise ($n = 10$), CNR ($n = 6$) and/or SNR ($n = 8$). Subjective image quality was scored by two observers in all studies, mostly by using a Likert scale. The results are shown in Table 1.

Noise was improved ($n = 4$) or equal ($n = 5$) with IR at reduced dose compared with FBP at routine dose in all but one study.[20] CNR was equal ($n = 5$) in all but one study, whereas SNR was improved ($n = 1$), equal ($n = 5$) or deteriorated ($n = 2$) with IR at reduced dose.

Subjective image quality was improved ($n = 3$) or equal ($n = 6$) in all but one study.[20] Furthermore, Renker et al[14] and Takx et al[20] reported that IR resulted in a reduction of blooming artefacts. The study of Takx et al[20] was the only study reporting a decrease in both objective and subjective image quality which was possibly due to the large dose reduction (80%, compared with a median dose reduction of 50% in the other included studies).

DISCUSSION

This meta-analysis showed that dose reduction is feasible using IR techniques for CCTA with preserved image quality compared with conventional FBP techniques.

Our results, indicating an achievable dose reduction of 48%, are in the range of dose reductions reported in a prior systematic review.[23] 49 studies were included, and reported achievable dose reduction varied from 23% to 76%. In that review, data were not pooled and only the percentage of achieved dose reduction for each study was reported. In this previous review, CCTA was not specifically studied since the review focused on all body regions. Also, no meta-analysis was performed. Furthermore, a lot of included studies concerned *ex vivo* data, new IR algorithms have become available and a substantial number of new studies have been published about IR for CT since the publication of the aforementioned review.[23]

In the present review, the effective dose reported in individual studies was pooled. Furthermore, only effective dose was used with the most commonly used conversion factor to achieve a uniform quantity to report dose. As can be seen in the forest plots (Figure 2), effective doses varied widely between studies. In addition, the 95% CI was high in some studies. This is partly due to the variation in BMI between study samples, but also shows the differences in routine scan protocols between hospitals.

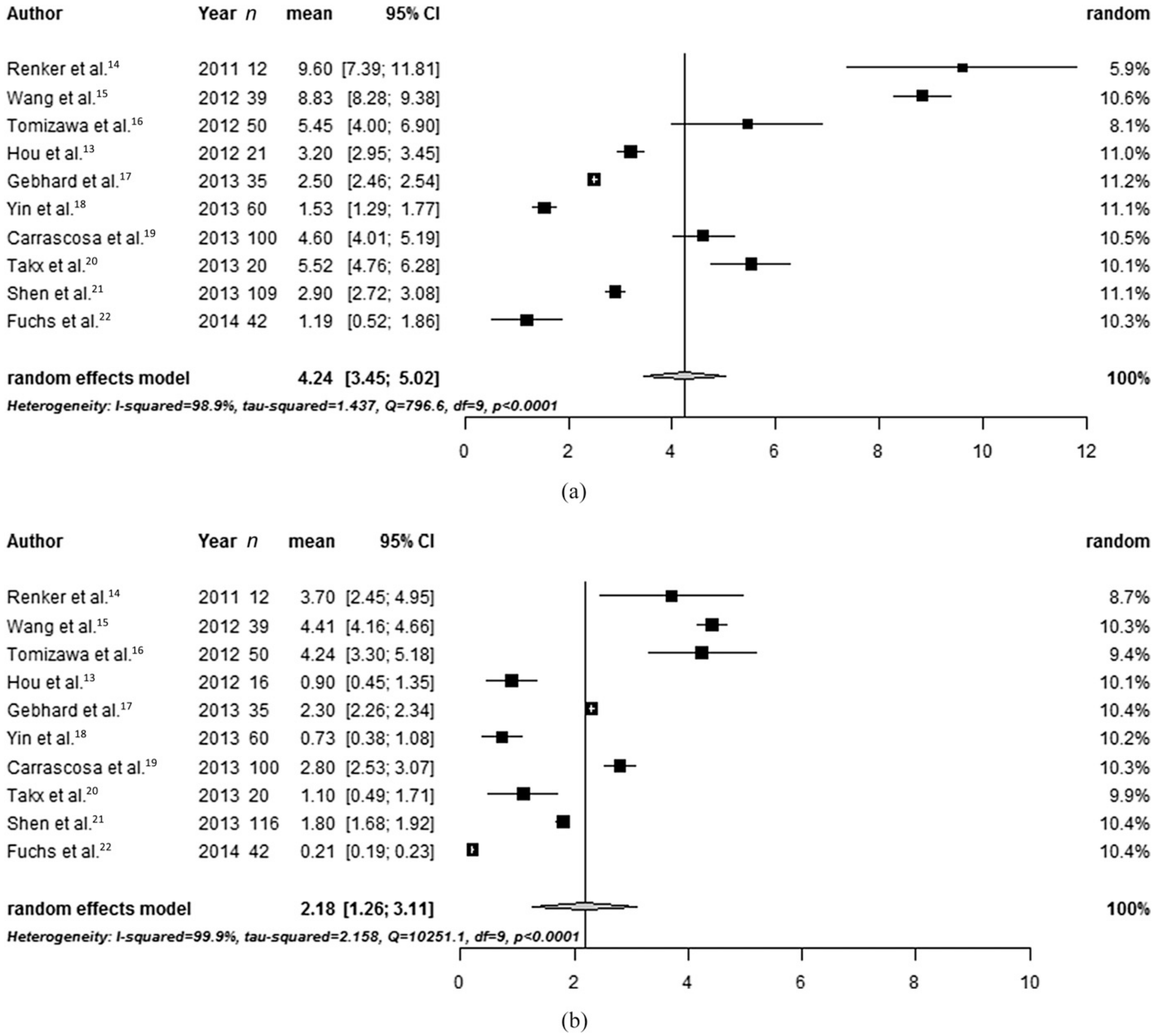
Most studies did not report whether the dose of the localizer and bolus-tracking images were included in the effective dose, which might have influenced results. However, the additional dose of the localizer and bolus-tracking images might be small and therefore less likely to have influenced the dose significantly.

Table 1. Baseline characteristics of the included studies

Study characteristics				Image quality				Routine dose group					Reduced dose group				
Study	Total number of patients	IR technique		Noise	CNR	SNR	Subjective image quality	BMI (routine dose group, kg m^{-2})	Number of patients	Tube current	Tube voltage (kV)	Mean effective dose (normal, mSv)	BMI (reduced dose group, kg m^{-2})	Number of patients	Tube current	Tube voltage (kV)	Mean effective dose (reduced, mSv)
Renker et al[14]	24	IRIS	Somatom® Definition Flash	+	NR	NR	+	30.7	12	NR	120	9.6	30.2	12	NR	80/100	3.7
Wang et al[15]	78	SAFIRE	Somatom Definition Flash	±	±	±	±	31.7	39	354–430 mAs	120	8.8	32.3	39	286–370 mAs	100	4.4
Tomizawa et al[16]	100	AIDR	Aquilion One™	+	±	±	±	24.0	50	483 mA	120	5.5	23.9	50	289 mA	120	4.2
Hou et al[13]	110	iDose	Brilliance iCT	±	±	±	±	25.1	21	210 mAs	120	3.2	25.5	16	65 mAs	120	0.9
Gebhard et al[17]	70	ASIR	Discovery™ HD 750	+	±	±	+	33.8	35	646 mA	116	2.5	32.9	35	633 mA	112	2.3
Yin et al[18]	60	SAFIRE	Somatom Definition Flash	±	±	±	±	NR	60	320–400 mAs	80–120	1.5	NR	60	160–200 mAs	80–120	0.7
Carrascosa et al[19]	200	iDose	Brilliance iCT	±	NR	NR	±	27.2	100	203 mAs	119	4.6	26.3	100	196 mAs	109	2.8
Takx et al[20]	20	SAFIRE	Somatom Definition Flash	−	−	−	−	33.1	20	331 mAs	100–120	5.5	33.1	20	66 mAs	100–120	1.1
Shen et al[21]	338	ASIR	Discovery HD 750	±	NR	−	+	25.5	109	600 mA	120	2.9	25.2	116	300 mA	120	1.8
Fuchs et al[22]	42	ASIR/MBIR	Discovery HD 750	+	NR	+	±	25.2	42	450–700 mA	100–120	1.2	25.2	42	150–210 mA	80–100	0.2

−, decreased with IR; +, improved with IR; ±, no difference; AIDR, Adaptive Iterative Dose Reduction; BMI, body mass index; CNR, contrast-to-noise ratio; IR, iterative reconstruction; IRIS, Iterative Reconstruction in Image Space; MBIR, Model-Based Iterative Reconstruction; NR, not reported; SAFIRE, Sinogram-Affirmed Iterative Reconstruction; SNR, signal-to-noise ratio.
The Somatom Definition Flash was obtained from Siemens Medical Systems, Forchheim, Germany; Aquilion One™ was obtained from Toshiba Medical Systems Co. Ltd, Ottowara, Japan; Brilliance iCT was obtained from Philips Healthcare, Best, Netherlands; Discovery™ HD 750 was obtained from GE Healthcare, Milwaukee, WI.

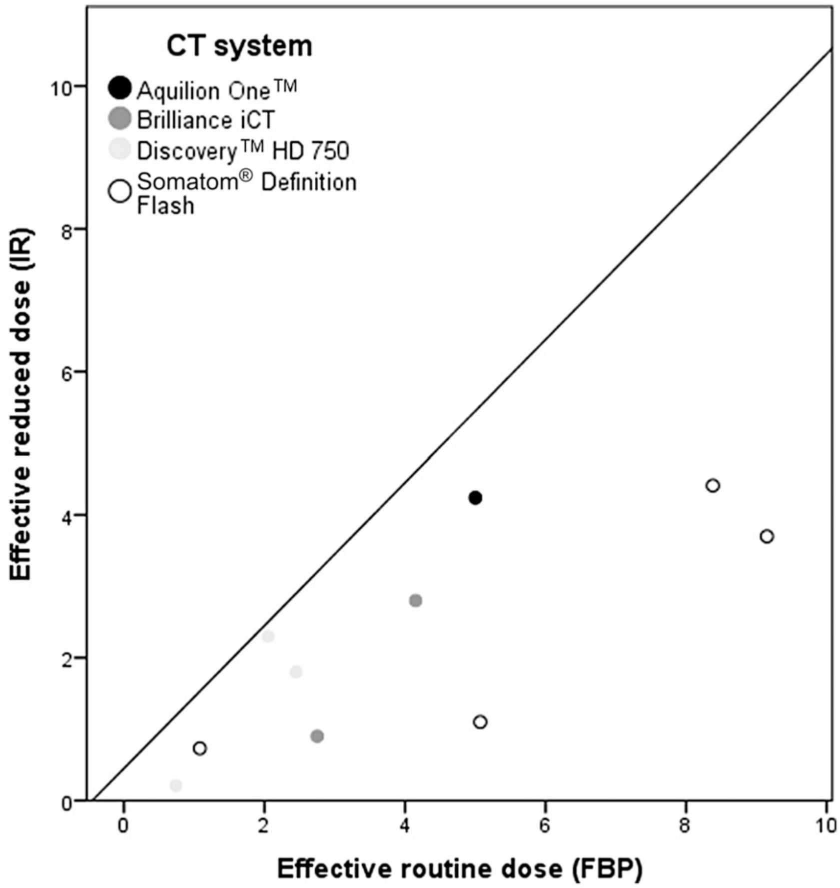
Figure 2. Forest plot of routine effective dose with filtered back projection (upper panel) and the reduced effective dose using IR (lower panel) with pooled estimate. n = number of patients. CI, confidence interval.



All major vendors have developed and are marketing a variety of slightly different IR algorithms. One study found an ultra-low dose of 0.2 mSv in patients with a mean BMI of 25.2 kg m^{-2} using Model-Based Iterative Reconstruction, which is a model-based IR algorithm.[22] All other studies investigated less advanced hybrid IR algorithms. Therefore with the development of model-based IR algorithms, the radiation dose is expected to decrease even further.

This study has several limitations. First, owing to our strict inclusion and exclusion criteria, we excluded many articles. By only including articles using the same CT system, contrast medium and scan parameters (except for variation in tube voltage and/or current to create dose reduction) for both the routine dose scan and the reduced dose scan, it was possible to investigate the true potential of IR. Second, there are different quantities to report dose but only the effective dose was used in the present study. Volume CT dose index might be more appropriate, because it is independent of anatomical length and dose conversion factors. In this review, the effective dose was used since most studies only reported DLP and/or effective dose. We felt this was appropriate because using a standard conversion factor eliminated the influence of different conversion factors. A conversion factor of 0.014 was used because this was the most commonly used factor in the included articles. However, this factor was designed for chest rather than cardiac CT and a different conversion factor might therefore be more appropriate. Efforts were made to ensure effective dose data concerned only CCTA studies and did not include non-enhanced acquisitions; however, this cannot be guaranteed and could be a potential limitation. Third, we used an English language restriction.

Figure 3. Relationship between normal effective dose and reduced effective dose in studies comparing multiple dose levels. FBP, filtered back projection; IR, iterative reconstruction. The Somatom Definition Flash was obtained from Siemens Medical Systems, Forcheim, Germany; Aquilion One™, was obtained from Toshiba Medical System Co. Ltd, Ottowara, Japan; Brilliance iCT was obtained from Philips Healthcare, Best, Netherlands; Discovery™ HD 750 was obtained from GE Healthcare, Milwaukee, WI.



A major limitation is the inability to determine whether the diagnostic accuracy remains acceptable at reduced dose levels. Since this was not reported in most studies, we were not able to investigate this. Therefore, the current meta-analysis only provides an overview of dose reductions reported in the literature and does not focus on diagnostic acceptability. However, it is difficult to investigate the diagnostic accuracy because of IR alone, since this is also influenced by factors as the used CT system and other dose-reduction techniques.

Ideally, different dose levels should be compared within patients. However, performing multiple scans in one patient can lead to difficulties with contrast enhancement. This explains why only two studies performed additional scans for research purposes in the same patients.[18,22] Another study tried to simulate a within-patient comparison by using data from one detector of a dual source CT system.[20]

This meta-analysis provides the possible dose reduction with IR as reported in the literature. However, the lowest possible dose remains unclear. Most studies only investigated one or two different dose levels, and we found that it is feasible to reduce the dose below 3 mSv using prospective ECG-triggering and state-of-the-art CT systems. Other dose-reduction techniques have been developed in the past years such as automatic tube current modulation, which was used in only three of the included studies. It is likely that radiation dose can be reduced even further by combining techniques. Future research investigating dose reduction with IR should focus on radiation doses of 3 mSv and lower. Furthermore, we recommend a uniform way of reporting radiation dose. Both volume CT dose index and DLP should be reported, making it possible to calculate the effective dose with a consistent conversion factor. In addition, authors should be clear about whether scout views and non-enhanced scans were included in the total reported dose.

In conclusion, this meta-analysis provides an overview of currently available dose reduction for CCTA with IR. Pooled data suggested that CCTA acquisition with an effective dose <3 mSv is possible with preserved image quality. Future research should determine if radiation dose can be reduced even further with model-based IR techniques.

CONFLICTS OF INTEREST

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APPENDIX A

SEARCH SYNTAX PUBMED

((((((iterative[Title/Abstract]) AND reconstruction[Title/Abstract])) OR (((iterative[Title/Abstract]) AND dose[Title/Abstract]) AND reduction[Title/Abstract])) OR (((((((((ASIR[Title/Abstract]) OR iDose[Title/Abstract]) OR IRIS[Title/Abstract]) OR AIDR[Title/Abstract]) OR IMR[Title/Abstract]) OR MBIR[Title/Abstract]) OR Veo[Title/Abstract]) OR SAFIRE[Title/Abstract]) OR ADMIRE[Title/Abstract]))) AND (((((CT [Title/Abstract] OR "Tomography, X-Ray Computed" [Mesh] OR "Cone-Beam Computed Tomography" [Mesh] OR "Four-Dimensional Computed Tomography" [Mesh] OR "Spiral Cone-Beam Computed Tomography" [Mesh] OR "Tomography Scanners, X-Ray Computed" [Mesh] OR "Tomography, Spiral Computed" [Mesh])))) OR ((computed[Title/Abstract]) AND tomography[Title/Abstract])) Filters: English

SEARCH SYNTAX EMBASE

(((iterative:ab,ti AND reconstruction:ab, ti) OR (iterative:ab,ti AND dose:ab,ti AND reduction:ab,ti) OR (ASIR:ab,ti OR iDose: ab,ti OR IRIS:ab,ti OR AIDR:ab,ti OR IMR:ab,ti OR MBIR:ab,ti OR Veo:ab,ti OR SAFIRE:ab,ti OR ADMIRE:ab,ti)) AND ((computed:ab,ti AND tomography:ab,ti) OR (CT:ab,ti OR 'tomography, x-ray computed':ab,ti OR 'cone-beam computed tomography':ab,ti OR 'four-dimensional computed tomography':ab,ti OR 'spiral cone-beam computed tomography': ab,ti OR 'tomography scanners, x-ray computed':ab, ti OR 'tomography, spiral computed':ab,ti))) AND [english]/lim

APPENDIX B

LIST OF EXCLUDED STUDIES INVESTIGATING ONE DOSE LEVEL

Leipsic J, LaBounty TM, Heilbron B, Min JK, Mancini GBJ, Lin FY, et al. Adaptive statistical iterative reconstruction: assessment of image noise and image quality in coronary CT angiography. *Am J Roentgenol* 2010; 195: 649–54.

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