



ELSEVIER

Contents lists available at ScienceDirect

Journal of Cardiovascular Computed Tomography

journal homepage: www.elsevier.com/locate/jcct

Review article

Image reconstruction in cardiovascular CT: Part 2 – Iterative reconstruction; potential and pitfalls

U. Tayal^a, L. King^b, R. Schofield^a, I. Castellano^b, J. Stirrup^c, F. Pontana^d, J. Earls^e, E. Nicol^{a,*}^a Department of Cardiovascular CT, Royal Brompton Hospital, London, UK^b Joint Department of Physics, The Royal Marsden, London, UK^c Department of Cardiology, Royal Berkshire Hospital, Reading, UK^d Department of Cardiovascular Imaging, Lille University Hospital, France^e George Washington University Hospital, Washington DC, USA

ARTICLE INFO

Keywords:

Cardiovascular CT
Iterative reconstruction

ABSTRACT

The use of IR in CT previously has been prohibitively complicated and time consuming, however improvements in computer processing power now make it possible on almost all CT scanners. Due to its potential to allow scanning at lower doses, IR has received a lot of attention in the medical literature and has become a successful commercial product. Its use in cardiovascular CT has been driven in part due to concerns about radiation dose and image quality. This manuscript discusses the various vendor permutations of iterative reconstruction (IR) in detail and critically appraises the current clinical research available on the various IR techniques used in cardiovascular CT.

1. Background

It has been claimed that “Iterative reconstruction (IR) has the ability to reduce image noise in CT without compromising diagnostic quality, which permits a significant reduction in effective radiation dose”.¹ IR algorithms have the potential to improve CT image quality by reducing image noise and reducing blooming artefact when compared with filtered back projection (FBP). This in turn may facilitate diagnostic image quality at reduced acquisition doses. However, in cardiovascular CT (CCT), there is a paucity of robust evidence to support these claims and trial data comes from a limited number of clinical trials with variable methodology and usually small cohorts. In this paper, we briefly re-review some of these important methodological concepts before moving on to evaluate the clinical applications of IR with a focus on CCT.

2. Iterative reconstruction overview

The weakness of filtered back projection (FPB) is documented in part one of this series²; the presence of noise in the acquisition process (whether from scattered X-rays, quantum variation in X-ray flux, electronic or structural noise) is augmented by the filtering step in the FBP

algorithm used to create the final cross-sectional images from the raw projection data.

IR techniques have been available since the advent of the first CT scanners, but these initial algebraic reconstruction techniques (ART), and simultaneous iterative reconstruction techniques (SIRT) were quickly dropped in favour of FBP due to the excessively large computation time required to reconstruct images. These early techniques^{3–5} are beyond the scope of this paper.

In recent years, the availability of increasing processing power has meant that IR techniques are now viable options for the raw data volume that modern CT scanners generate. IR is often marketed as a dose reduction tool, but this is somewhat misleading; current IR techniques aim to reduce image noise or facilitate reconstruction of diagnostic images acquired at lower dose, with comparable noise levels to traditional FBP techniques. There are a variety of different IR techniques, but description or comparison of different IR processes is challenging due to a lack of common nomenclature and the proprietary nature of the techniques, although broad categorisation is possible (Table 1). A broadly generic schematic of iterative reconstruction techniques used in IR image reconstruction is shown in Fig. 1.

Initial IR solutions (from the mid to late 2000s) usually involved post-processing of image data (including propagated noise) after FBP

* Corresponding author. Department of Cardiovascular CT, Royal Brompton Hospital, London, SW3 6NP, UK.

E-mail addresses: u.tayal@rbht.nhs.uk (U. Tayal), Laurence.king@rmh.nhs.uk (L. King), rebeccaschofield@doctors.org.uk (R. Schofield), Elly.Castellano@rmh.nhs.uk (I. Castellano), James.Stirrup@royalberkshire.nhs.uk (J. Stirrup), Francois.PONTANA@chru-lille.fr (F. Pontana), jpearls@yahoo.com (J. Earls), e.nicol@nhs.net, e.nicol@rbht.nhs.uk (E. Nicol).

<https://doi.org/10.1016/j.jcct.2019.04.009>

Received 31 January 2019; Received in revised form 4 April 2019; Accepted 15 April 2019

Available online 16 April 2019

1934-5925/ © 2019 Published by Elsevier Inc. All rights reserved.

Table 1
Broad categorisation of vendors' commercial iterative reconstruction solutions.

Vendor	Canon	General Electric	Philips	Siemens
Image domain techniques				
Image and raw data domain techniques	AIDR3D (Adaptive Iterative Dose Reduction)		iDose4	IRIS (Iterative Reconstruction in Image Space) SAFIRE (Sinogram-Affirmed Iterative Reconstruction)
Statistical forward projection techniques	FIRST (Forward projected model-based Iterative Reconstruction Solution)	ASIR (Adaptive Statistical Iterative Reconstruction) ASIR-V [hybrid IR] VEO [full optics modelling]	IMR (Iterative Model Reconstruction)	ADMIRE (Advanced Modelled Iterative Reconstruction)

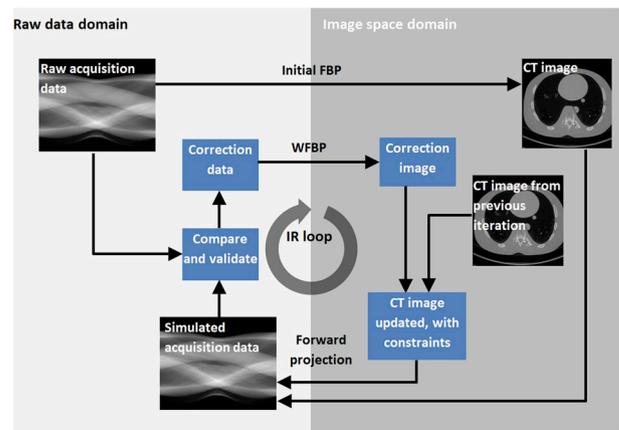


Fig. 1. Generic schematic of steps used in iterative image reconstruction algorithms. IR = iterative reconstruction, FBP = filtered back projection, WFBP = weighted filtered back projection. Additional noise identification and reduction techniques may occur in image and raw data domains and varying degrees of system and physics modelling may be considered during forward projection. Exact techniques for each step vary between vendors and implementations.

reconstruction; essentially the application of an algorithm to decrease image noise by reducing pixel-to-pixel variation in CT number in the final image. These early “smoothing algorithms” had the potential to remove clinically important fine detail and edge information, such as coronary plaque,⁶ so often employed frequency-dependent functions, where pixel value variations, existing in the typical frequencies where noise exists, were smoothed out, but with less aggressive smoothing in regions where edges in the image were detected. These techniques operate in the image-space (or image domain), i.e. applied to FBP reconstructed images, rather than the raw data, and vendors often described these smoothing techniques as “iterative” when applied to an image set progressively over several iterations.

The next generation of IR techniques (AIDR3D, iDose4 and SAFIRE) were more complex but still heavily relied on FBP reconstructed images with adjunctive iterative statistical processing applied in the image-space and/or in the raw data domain of the sinogram. Statistical analysis of the distribution of signal in the sinogram can identify regions where signal is poor, and noise is high. Weighting factors can then be applied to the sinogram data so that data from regions of high signal and low noise are given higher weighting in the FBP reconstruction than low signal, high noise projections. This reduces the noise contribution from poorer quality projection data. This approach is more effective at removing image artefacts than processes in image space alone, however with these techniques there remains a risk that clinically relevant (non-artefactual) information may be lost following the application of these techniques to, remove noise and artefacts and “improve” overall image quality.

The most complex IR techniques (ASIR, ASIR-V, VEO, FIRST, ADMIRE) now forward-project the reconstructed image (from initial FBP or IR-generated images) to create a simulated sinogram. By comparing this simulated sinogram with the true sinogram of the acquired raw data, a deduction can be made as to where the initial reconstructed image fails to match the object that was scanned. A correction image is then synthesised, the reconstructed image is corrected, and then forward projected again for comparison against the acquisition sinogram. The process iterates a set number of times, or until convergence is reached between the simulated sinogram and the real sinogram of the acquisition. This process of forward-projection, comparison and correction is integral to model-based IR (MBIR) techniques.

The success of MBIR techniques relies on the accuracy of the forward-projection. Theoretically, the algorithm could take into account the modelling of system noise (statistical and electronic), physics (beam

hardening, X-ray scatter, absorption properties of the patient and the detector characteristics) and the specific “optics” of the system - this includes geometric corrections to account for the finite size of the focal spot where the X-rays are generated in the tube; dimensions of the detector; and voxel dimensions with different path lengths of the X-ray (dependent on the angle of travel) through the voxel volume. However, MBIR is computationally intensive: depending on the degree of system modelling undertaken, the reconstruction of a scan volume can take tens of minutes to produce, even with dedicated computers,⁷ thus potentially slowing clinical workflows. In practice, therefore, MBIR algorithms have to achieve a balance between acceptable reconstruction times and the sophistication of the system model. However, MBIR techniques are powerful and have the potential to further reduce image noise and artefacts, and to improve spatial resolution, especially when system optics are modelled accurately. MBIR techniques are usually specific to a single scanner model, as the geometry, detector and X-ray tube properties for any given scanner are scanner, not just vendor, dependent.

3. Methodology

To assess the literature on IR in cardiovascular CT a PubMed search was performed. Using the terms ‘iterative reconstruction’, ‘model based iterative reconstruction’, ‘cardiovascular CT’, ‘CT coronary angiography’, ‘filtered back projection’, ‘statistical iterative reconstruction’, ‘CT calcium score’, and ‘dose reduction’ research articles concerning IR techniques and cardiovascular CT were identified. Abstracts of all studies were reviewed, and studies were selected for full review if they involved either clinical or phantom studies using iterative reconstruction techniques to evaluate any modality of cardiovascular CT.

4. Clinical application

To date, the focus of research in the field of IR has mainly focused on facilitating lower radiation dose acquisition, with technological validation studies assessing both the effect on dose and image quality. However, now that IR techniques are increasingly used in routine cardiovascular CT, it is increasingly essential to understand the potential advantages and limitations of IR algorithms beyond technical assessment and assess the methodological validity of studies reported to date.

Despite the promise of diagnostic image quality at reduced radiation dose, there are important limitations of IR; these include image appearance and reconstruction time. IR reconstructed images, especially with the stronger settings, are often said to appear ‘over-smoothed’ or ‘plastic’ (Fig. 2A and B).⁸ In addition, whilst the time for more advanced IR algorithms to work has been reduced significantly due to advances in processing power, many are still not compatible with the usual clinical workflow. If the final CT coronary angiogram (CTCA) images appear too different (either over smoothed or plastic) this may be distracting and unfamiliar and have the potential to affect image interpretation. This may be key for diagnostic confidence, especially when imaging small structures, such as the coronary arteries⁹ but may be overcome with increasing familiarity. To make images visually more acceptable, some vendors have opted produce IR image sets that are then blended back with a conventional FBP-created image, maintaining some of the traditional texture of the final image.

4.1. Radiation dose

The most notable reported benefit of IR in CT is its ability to facilitate acquisition of scans at a lower radiation dose. The simplest way to reduce dose in CT imaging is to reduce the X-ray tube current (mA), however, this approach leads to increased image noise. Using IR, radiation dose reduction is largely facilitated through image optimisation of the noisier acquired image; specifically, noise reduction and removal of artefacts. It is therefore argued that IR allows the use of lower tube

currents to enable ‘low dose’ CT (Fig. 3). However, there is no universal definition of ‘low dose’ CT, in general or cardiac radiology, and there is limited data comparing the dose reduction possible, whilst maintaining diagnostic image quality, between IR algorithms. It is possible that the radiation dose reduction benefits of IR may not materialise in all patients, clinical scenarios or specific algorithms.

A systematic review and meta-analysis of the dose reduction for coronary CT angiography (CCTA) performed in 2016 identified 10 studies in adults where the technological parameters were methodologically sound (i.e. same CT scanner, contrast agent used and dose modulation) and more than one IR level was compared with FBP.¹⁰ These studies did however include those with different subjects in each study arm. This review reported a mean reduction in CCTA acquisition dose from 4.2 mSv to 2.2 mSv. It is interesting to note that the median dose for CCTA in a subsequent UK national survey was a DLP of 200mGycm,¹¹ equivalent to 2.8 mSv, using the same conversion factor ($k = 0.014$), again raising the question of whether lower dose acquisition without IR may be equally acceptable and that the addition of IR is maybe not what facilitates the dose reduction.

Furthermore, a critical assessment of published manuscripts in this field reveals that many studies have compared a “high dose” acquisition, with a “low dose” acquisition with IR in different patients (with inherent bias) and in these studies; those where FBP and IR is compared in the same patients, IR is often analysed with no adequate control arm i.e. against low dose acquisition without IR.^{8,12–15} Experimental study designs used to compare FBP to IR in CCT also include: the use of phantom studies to define the optimal combination of dose and IR strength before assessing it in a clinical patient cohort¹⁶; the use of reconstructed data from only one source of dual source scanner¹⁷; or discarding 50% of the data¹⁸ to form the low dose cohort. Further confounding the comparison of FBP and IR, many of the scan protocols have permitted a lower acquisition kV depending on patient BMI in the IR arm compared to the FBP arm leading to further potential intrinsic bias in terms of dose (which may be the same or different) and image quality (which will be different).^{14,19,20} This undermines many of the claims that IR is beneficial, as again it may just be that the reduced kV scans with better iodine conspicuity are just as interpretable as the high kV ones, even without the addition of IR.

4.2. Effect of IR on image quality

Reduced radiation dose is of little clinical benefit if diagnostic accuracy and image quality are compromised. Studies have varied in their approach to the assessment of IR image quality and accuracy. In the studies that have focused on coronary artery calcium scoring (CACS), the main investigational question has been the effect of IR on the CACS itself, usually with FBP and IR algorithms being assessed at the same acquisition dose, often with the use of phantoms. This is very different to studies looking at IR on CTCA studies where high dose FBP acquisitions are usually compared to lower dose acquisitions with the use of IR algorithms.

4.3. Effect of IR on coronary calcium score

CACS is a robust and well validated technique used to estimate coronary artery atherosclerotic plaque burden; a standard CACS that allows the calculation of an Agatston score²¹ is performed using FBP at 120 kV. There have been several studies evaluating the effects of IR algorithms on CACS, at either the same dose with added noise to mimic a lower dose acquisition,²² the same dose²³ or lower dose acquisitions.^{24–26} These studies consistently show that IR techniques lead to lower CACS compared to standard FBP algorithms, irrespective of IR algorithm or vendor.^{22–25} One study comparing FBP with hybrid IR and model-based IR in 63 patients showed that the median CACS were lower in all IR groups, compared with FBP, but with no statistical difference at the different levels of IR used.²³ However, some evidence

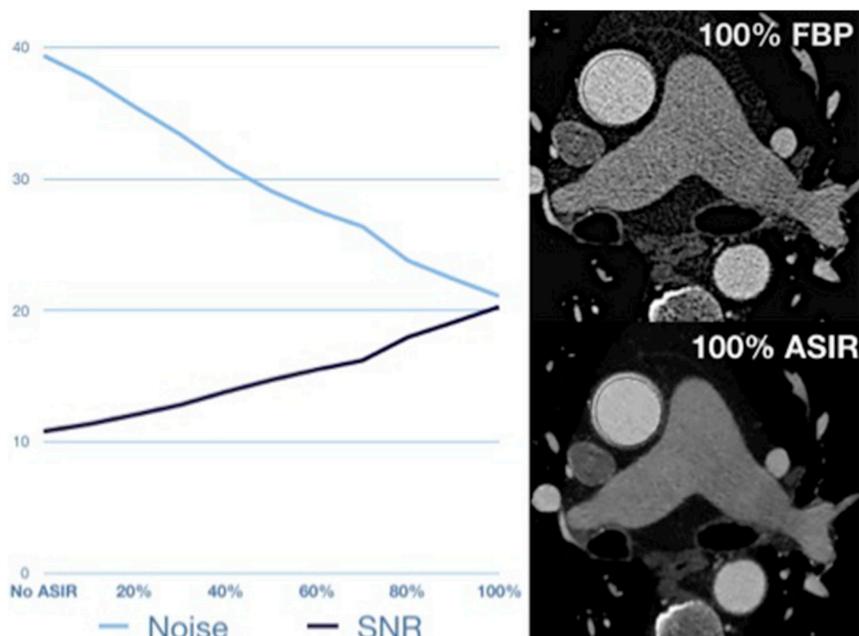


Fig. 2. A) Use of higher strength iterative reconstruction decreases image noise substantially and simultaneously increases signal to noise ratio. B) IR reconstructed images, especially with the stronger settings, are often said to appear ‘over-smoothed’ or ‘plastic’. In the ASIR reconstructed images shown here, the images become increasingly over-smoothed with use of more IR, despite the obvious advantage of noise reduction.

suggests that there may be a threshold dose reduction below which CACS may not be adversely affected. Using hybrid IR or model-based IR this may be as much as 60% (1 mSv vs. 0.4 mSv). With greater dose reduction, the IR derived Agatston score differed by up to 15% compared to the FBP reconstruction.²⁶

This alteration in the CACS need not be a cause for concern, if the reporting clinician, and referrer, are aware of the impact of IR on the CACS. Clearly the widely used CACS nomograms used for assessment of coronary artery disease and risk stratification are based on standard FBP data and should not be used for IR based CACS. Furthermore, the use of IR derived CACS may underestimate cardiovascular risk in the patient population, though patient and simulation studies suggest this

effect will be modest.^{23,27} In summary, whilst adjusting for the effect on Agatston score, the use of IR in calcium scoring protocols may be beneficial and may not significantly alter the CACS up to a 60% dose reduction.

4.4. CT coronary angiography (CTCA)

Several studies have compared CTCA image quality (either by visual assessment or SNR/CNR analysis) at standard dose FBP reconstruction compared to reduced dose acquisition with the addition of IR. Many, but not all, have shown that reduction in acquisition dose, with the addition of IR reconstruction algorithms, maintains image quality, but

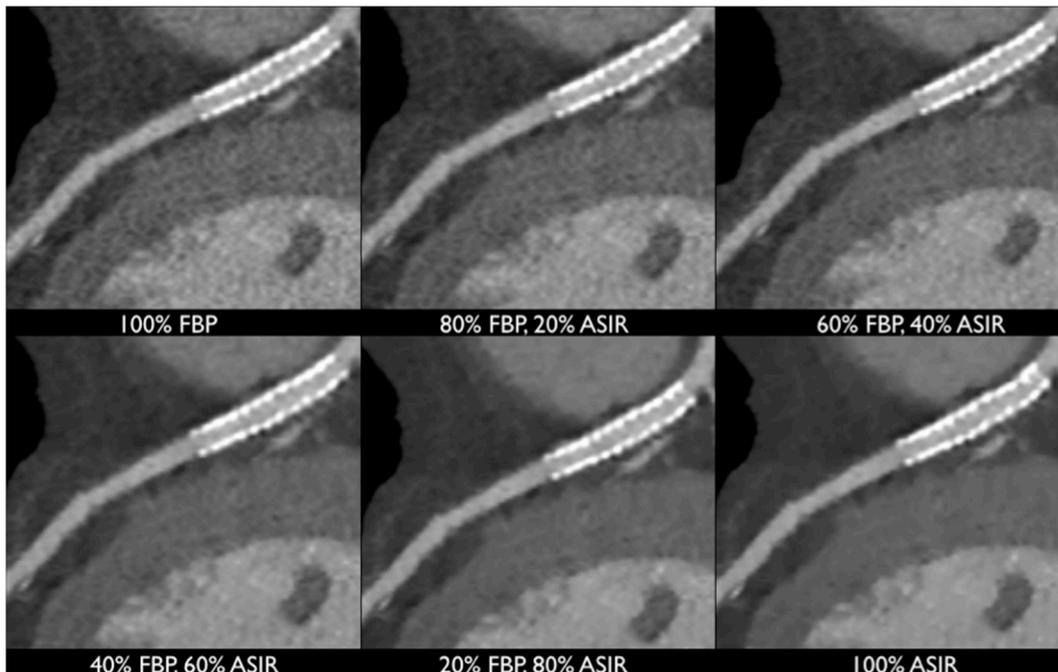


Fig. 2. (continued)

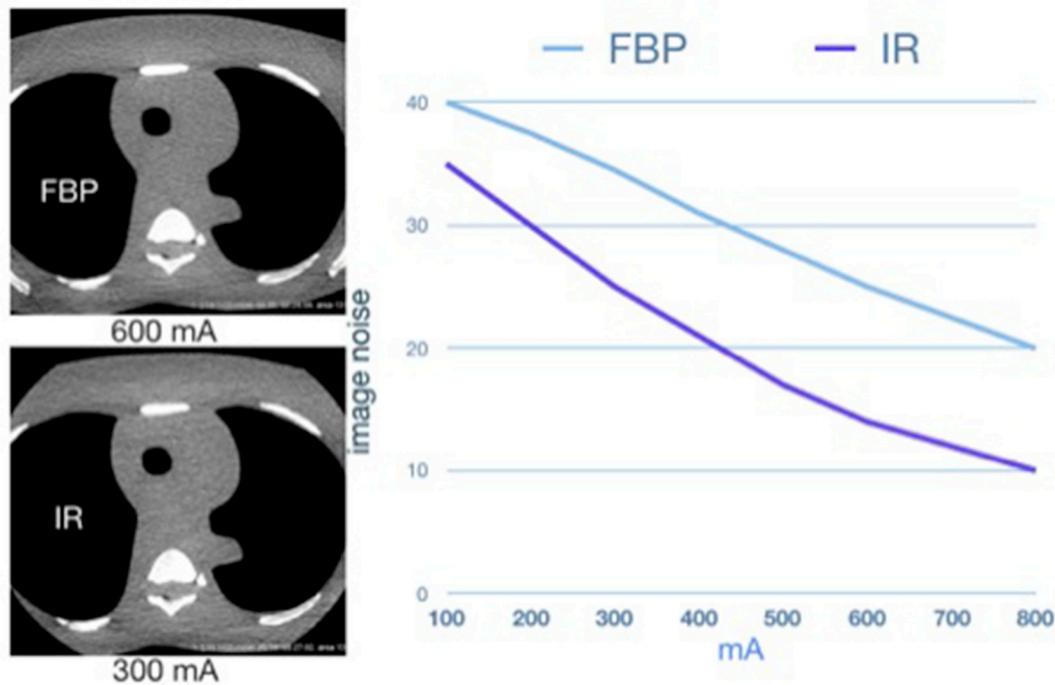


Fig. 3. Iterative reconstruction is often used primarily to lower radiation dose. In the example shown here, there is a substantial drop in noise when going from FRBP to IR. The noise and SNR of a 600 mA image reconstructed with FBP is similar to an image acquired at 300 mA and reconstructed with IR.

importantly a lower limit is often reached where the lowest dose, noisiest acquisitions cannot be fully compensated for with IR algorithms. The level of this low dose threshold is however inconsistent between studies.

As an example, in one study of 110 patients undergoing CTCA on a 256 slice MDCT, subjective and objective image quality of IR reconstructed images at reduced tube current with lower doses on consecutive patients (1.8 mSv, 1.4 mSv, 1.2 mSv, 0.9 mSv) was compared to a FBP reconstructed group (dose 3.2 mSv).²⁸ In the IR datasets, image quality was maintained at all doses; however, image sharpness and study acceptability were lower at 0.9 mSv. The 1.2 mSv dataset was deemed the optimal for maintaining luminal sharpness whilst lowering effective dose. Intra-individual comparison studies lack the confounding factors of subject variability and have also demonstrated maintenance of image quality and diagnostic accuracy at lower doses with IR.²⁹ Two studies comparing standard of practice CTCA with ultra-low dose CTCA using MBIR, with an 80% and 50% effective dose reduction respectively (1.2 mSv vs. 0.2 mSv³⁰ and 1.5 mSv versus 0.7 mSv³¹), demonstrated no significant difference in image quality. The effect of IR alone on the diagnostic accuracy of CTCA studies is difficult to quantify in isolation. Nevertheless, a meta-analysis of 10 studies involving 1042 patients¹⁰ showed that subjective estimates of noise and image quality were equal or improved in most studies using IR compared to FBP^{32,33}; however, the method of IR may be critical, especially at the very low doses. In a comparison of FBP reconstructions versus increasing contributions of statistical IR (40% and 100%) and MBIR in 91 patients, the largest noise reduction was identified with MBIR³⁴ with a higher specificity to detect coronary artery disease using MBIR in a subset of 36 patients who also underwent invasive coronary angiography.³⁴

In a direct head to head comparison of FBP and IR in 60 patients who underwent invasive coronary angiography and then 2 separate CTCA scans, the diagnostic accuracy of IR studies did not differ to that of FBP studies. On a per patient level, the sensitivity and specificity for diagnosing > 50% coronary artery stenosis were 100% and 93.1% with FBP and 96.8% and 89.7% with IR ($p > 0.05$).³¹ Whilst not statistically significant, the per patient specificity of detecting coronary stenoses

was lower with IR compared to FBP possibly suggesting that there may be a discrepant diagnostic performance between the two reconstruction techniques, that a larger study may detect. Given the ethical considerations of performing repeated CT studies in the same individuals,³⁵ this data may not be easily forthcoming.

Studies using IR algorithms demonstrate that image noise and subjective image quality significantly increased with increasing levels of IR³⁶ whilst others demonstrate a reduction on diagnostic confidence with increasingly noisy images and higher strengths of IR.³⁷ In summary, many of the studies to date comparing standard dose FBP acquisition and IR reduced dose acquisition CTCA have found at least comparable, if not improved, image quality. This appears particularly true of MBIR algorithms, when compared to earlier statistical algorithms. However, even in the MBIR studies, one of the most challenging methodological flaws is a lack of true controls i.e. low dose acquisitions reconstructed with FBP. This is surprising as it is straightforward to reconstruct an IR image set and an FBP image set as long as the scanner has both reconstruction options available.

Whilst subjective and objective image quality and the effect of IR on the assessment of stenosis severity are important, the qualitative and quantitative effect of IR algorithms on plaque analysis is also particularly relevant for coronary imaging. The presence of a high plaque burden and vulnerable plaque features (such as low attenuation plaque, positive remodelling and spotty calcification) are associated with increased cardiovascular risk.³⁸ Given the data from CACS studies, it follows that there may be a significant effect on visualising calcified and mixed plaque lesions. Therefore, the ability to accurately and reproducibly delineate stenosis severity and plaque composition may be affected using IR algorithms.

In one study where raw image data was reconstructed using MBIR, hybrid IR and FBP, plaque characterisation was performed using automated software and categorised into calcified plaque (> 130 HU), non-calcified plaque with high attenuation (90–129 HU), intermediate attenuation (30–89 HU) and low attenuation (< 30 HU).³⁹ Overall plaque volume and calcified plaque volume were lower using MBIR compared to hybrid IR and FBP. Non-calcified, intermediate and low attenuation plaque volumes did not differ between reconstructions.³⁸

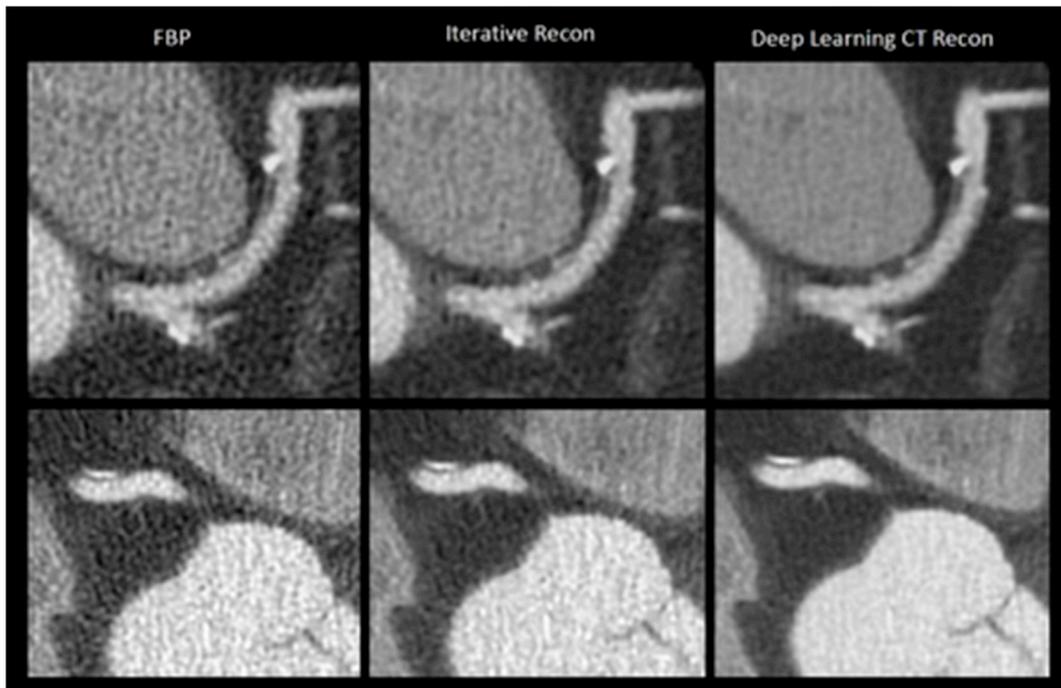


Fig. 4. Comparison of filtered back projection (FBP), iterative reconstruction, and deep learning reconstruction performed on the same CCTA data set. Note image noise is reduced and image noise quality appears optimal with the deep learning algorithm. This results in improved noise appearance especially in the epicardial fat as well as along the edges of the left coronary (top row) and proximal right coronary (bottom row) arteries. Images courtesy of GE Healthcare, Inc.

This effect may represent improved image quality and reduction of blooming artefact but also may lead to a loss of diagnostic accuracy in determining spotty calcification (an independent predictor of MACE.⁴⁰ Similar findings have been observed in a small study of 3 patients, comparing MBIR to adaptive statistical IR, with MBIR associated with reduced plaque volumes and plaque burden⁴¹; however, the study sample size precludes definitive conclusions from being drawn. When FBP and IR (adaptive-statistical (ASIR) and model-based (MBIR) reconstructed CTCA datasets are compared with intravascular ultrasound (IVUS), plaque was overestimated by $\sim 10\%$ regardless of the algorithm used.⁴² However not all study findings are consistent, with a study comparison of FBP with statistical IR reconstructions also showing no significant difference between plaque composition, volume, or cross-sectional area.⁴³

4.5. Effect of IR on coronary stent assessment

It has been argued that IR may offer superior imaging of coronary artery stents due to a reduction in image noise.⁴⁴ Several *in vivo* studies have evaluated this with statistical IR datasets associated with reduced stent noise, improved signal to noise ratio, and improved image quality. Stent volumes are lower with IR, possibly as a result of reduced beam hardening artefact,⁴⁵ with a 40% larger luminal area visualisation and reduced stent length seen.⁴⁶ Subjective image quality also appears to be better with IR than FBP but sensitivity, specificity, and positive and negative predictive values do not seem to significantly differ between FBP and IR algorithms.⁴⁷ Therefore, whilst the data appears to suggest an improvement of image quality it remains unclear as to whether this leads to increased diagnostic accuracy in the evaluation of coronary stent patency.

4.6. Effect of IR on valve assessment

CCT potentially offers advantages over other imaging modalities in being able to detect the cause of prosthetic valve dysfunction, such as thrombus or pannus, as well as identify complications of infective

endocarditis.^{48,49} To date there have been a limited number of studies evaluating the effect of IR on valve assessment. Both statistical⁵⁰ and MBIR⁵¹ algorithms have been used in the assessment of prosthetic heart valve disease in studies using IR *in vitro*, with improved objective image quality and either similar or reduced artefacts at lower acquired doses. Both hyper- and hypo-dense artefacts were reduced by use of MBIR in a non-pulsatile model at reduced dose,⁵⁰ but were equivalent using IR in a pulsatile phantom.⁵¹ Whilst phantom valve studies suggest similar findings to those in coronary imaging, the clinical performance of IR compared to FBP in valve disease has not yet been comprehensively evaluated beyond reports that IR acquired scans are possible at moderate radiation doses (DLP 569 ± 208 mGy.cm).⁵² The effect of IR models on the assessment of calcific disease, pannus and thrombus will all warrant further clinical validation particularly in areas such as aortic stenosis where calcium scores have been correlated to stenosis severity.⁵³

4.7. Future directions with artificial intelligence

Artificial intelligence techniques, specifically deep learning (DL) have been used for analysis of reconstructed images, including computer aided diagnosis/detection (CAD).⁵⁴ Deep convolutional neural network (DCNN), a type of deep learning, have been widely adapted for CAD and have shown performance accuracy.^{55–57} DCNN can also be used as filters that remove artefacts or used to remove specific objects that interfere with diagnosis.⁵⁸ However, deep learning techniques also have great potential to also improve the reconstruction of CT images.^{59,60}

Iterative reconstruction techniques, as discussed in this text, are limited in the number of parameters they can use model a complex phenomenon, the resulting visual impression of the images often differs from the classical look and feel of the images generated with FBP. The noise texture typically exhibits a plastic or unnatural look. Early evidence suggests that AI can improve reconstruction of CT images without some of the limitations imposed by IR. The power of deep learning is its ability to handle complex models and vast number of

parameters. Traditional IR algorithms rely on humans to minimize the size of parameters so that an optimal solution is trackable. This process restricts the number of parameters optimized to typically less than a hundred, which limits the complexity of model that can be incorporated into the reconstruction process and, eventually, limits the performance of the algorithm. The DL approach does not require the complex models of the real system to be simplified to a few parameters. These models are formed in the training process “as is”, and the number of parameters that can be handled is in the millions, avoiding the shortcomings faced by IR algorithms. Initial results of deep learning reconstruction (Fig. 4) show that the resultant images, even with a low radiation dose acquisition, can achieve excellent image definition with natural image noise texture.

To date, AI reconstruction techniques have had limited clinical evaluation. However, they have been shown to further optimize IR algorithms and allow for implementing more complex functions.^{61–65} Recently presented DL based reconstruction techniques incorporating noise and artefact reduction filter by a DCNN⁶⁶ comparing the DL recon with hybrid IR reported reduced image noise (noise of a 100 mA image reconstructed with hybrid IR was the same as that of a 20 mA (80% dose reduction) images reconstructed with the DL technique). When noise quality was also taken into consideration an overall 30% dose reduction was deemed achievable. Emerging DL reconstruction techniques can be applied to CT in several different ways. They have potential to surpass IR techniques because of fewer mathematical and computational restrictions. Early results show that they have promise to facilitate reduced radiation dose acquisition, speed up reconstruction times, and improve overall image and noise quality.

5. Discussion

We have presented an overview of the use of IR in CCT imaging, and whilst there seems to be real potential, especially with MBIR, for improved image quality, possibly at lower acquisition doses, there are clearly important methodological limitations of the IR studies to date that clinicians need to be aware of. Most clinical research into the use of IR techniques in CCT has centered on the ability of IR to allow for acquisition of CCTA at significant dose reduction, without loss of image quality, and this has been a major focus and key marketing tool used by vendors.

It is clear from reviewing the IR studies undertaken to date in cardiovascular CT that there are several methodological and reporting issues that are prevalent in these types of studies, namely that reporting a percentage dose reduction isn't meaningful without the initial dose level, and that effective dose conversion factors for the thorax are not appropriate for cardiac exams. Reported DLP and CTD_{ivol} would enable better dose level comparison than effective dose. Reporting of CT acquisition protocols is also often poor i.e. incomplete information on technique, or incorrect or misleading nomenclature and in more than one paper the IR algorithm being studied was not named. As each vendor's implementations are different, conclusions from one vendor cannot necessarily be applied to another, making specific applicability of the findings challenging. We must apply appropriate critical analysis of this field whilst remaining positively vigilant and ensuring preservation of diagnostic accuracy in the context of the application of IR algorithms. To date relatively few studies have considered clinical assessment as a primary endpoint.

Most vendors are now on the 3rd or 4th iteration of IR, so, as with the evolution of CCT itself, there is an intrinsic lag time between the clinical take up of new technology and the research base to provide the evidence to support its use. The challenge around the clinical applicability of the evidence is further compounded by the lack of transferability of research conclusions between different types of IR, both within and between vendors. In addition to the data presented in this manuscript it is worth commenting on the fact that with a departure of image reconstruction from FBP to IR, there is potential that the

contribution of noise to an image can be reduced or mitigated to the extent that image noise is no longer strongly dependent on the kV or mAs, meaning the well-understood relationship between image noise and radiation dose no longer applies. This relationship will need to be explored for each IR technique offered by individual vendors, especially where IR techniques involve selective smoothing or noise reduction in the image or raw data domains, with the effect on spatial resolution and appearance of small details and edges assessed on a scanner by scanner basis. The role of various artificial intelligence algorithms show promise but again will require robust clinical scrutiny to ensure they are delivering the true benefits claimed by vendors.

6. Conclusion

The advent of, and the increasing clinical uptake of, iterative reconstruction in cardiac CT offers the scope to improve image quality, reduce image noise, and reduce radiation dose. However cardiac CT is uniquely challenging and patient risk stratification is dependent upon analysis of coronary calcification, plaque burden and composition and stenosis severity. These are all factors which are variably affected by iterative reconstruction techniques. There is a pressing need for a more critical evaluation of how various IR algorithms, including those utilizing artificial intelligence, affect diagnostic accuracy and the subsequent impact on patient management. Despite the focus on dose reduction, it is still unclear exactly which kV and mAs for a given body habitus is optimal with each IR algorithm. To achieve a true understanding of optimal combination of lowest possible radiation dose with best quality diagnostic quality a collaborative approach between industry and clinicians will be required, with larger, scientifically robust studies, free of significant confounders seen in most studies to date. Only then will we start to be able to fully appraise these new, potentially beneficial reconstruction algorithms.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Naoum C, Blanke P, Leipsic J. Iterative reconstruction in cardiac CT. *J CCT*. 2017;9(4):255–263.
2. Schofield R, King L, Tayal U, Stirrup J, Pontana F, Castellano I, Nicol E. *Iterative Reconstruction in Cardiovascular Radiology Part 1 – Understanding How CT Images Are Made*. *J CCT*. TBD; 2018.
3. Gordon R, Bender R, Gabor TH. Algebraic Reconstruction Techniques (ART) for three-dimensional electron microscopy and X-ray photography. *J Theor Biol*. 1970;29:471–481.
4. Gilbert P. Iterative methods for the three-dimensional reconstruction of an object from projections. *J Theor Biol*. 1972;36:105–117.
5. Anderson AH, Kak AC. Simultaneous algebraic reconstruction technique (SART): a superior implementation of the ART algorithm. *Ultrason Imag*. 1984;6:81–94.
6. Wang J, Li T, Xing L. Iterative image reconstruction for CBCT using edge-preserving prior. *Med Phys*. 2009;36:252–260. <https://doi.org/10.1118/1.3036112>.
7. Miéville, et al. Model-based iterative reconstruction in pediatric chest CT: assessment of image quality in a prospective study of children with cystic fibrosis. *Pediatr Radiol*. 2013;43:558–567.
8. Hou Y, Liu X, Xv S, Guo W, Guo Q. Comparisons of image quality and radiation dose between iterative reconstruction and filtered back projection reconstruction algorithms in 256- MDCT coronary angiography. *AJR Am J Roentgenol*. 2012;199(3):588e594.
9. Pontana F, Castellano I, Ismail T, Gartland N, Rubens M, Nicol E. Reduced-dose dual-source coronary computed tomography angiography (CCTA): is raw-data-based iterative reconstruction able to maintain diagnostic confidence? *Heart*. 2015;101(Suppl 4):A75.
10. Den Harder AM, Willemsink MJ, De Ruitter QM, et al. Dose reduction with iterative reconstruction for coronary CT angiography: a systematic review and meta-analysis. *Br J Radiol*. 2016;89(1058):20150068.
11. Castellano I, Nicol E, Roobottom C, Bull R, Williams MC, Harden S. A prospective national survey of coronary CT angiography radiation doses in the United Kingdom. *J Cardiovasc Comput Tomogr*. 2017 Jul - Aug;11(4):268–273. <https://doi.org/10.1016/j.jcct.2017.05.002> Epub 2017 May 8.
12. Gordic S, Desbiolles L, Sedlmair M, et al. Optimizing radiation dose by using advanced modelled iterative reconstruction in high-pitch coronary CT angiography. *Eur Radiol*. 2016;26:459–468.

13. Wang R, JU Schoepf, Wu R, et al. Image quality and radiation dose of low dose coronary CT angiography in obese patients: sinogram affirmed iterative reconstruction versus filtered back projection. *Eur J Radiol.* 2012;81(11):3141–3145.
14. Williams MC, Weir NW, Mirsadraee S, et al. Iterative reconstruction and individualized automatic tube current selection reduce radiation dose while maintaining image quality in 320-multidetector computed tomography coronary angiography. *Clin Radiol.* 2013;68(11):e570ee577.
15. Leipsic J, LaBount TM, Heibron, et al. Estimated radiation dose reduction using adaptive statistical iterative reconstruction in coronary ct angiography” the ERASIR study. *AJR.* 2010:655–660.
16. Hou Y, Zheng J, Wang Y, Yu M, Vembar M, Guo Q. Optimizing radiation dose levels in prospectively electrocardiogram- triggered coronary computed tomography angiography using iterative reconstruction techniques: a phantom and patient study. *PLoS One.* 2013;8(2):e56295.
17. Ebersberger, et al. CT evaluation of coronary artery stents with iterative image reconstruction: improvements in image quality and potential for radiation dose reduction. *Eur Radiol.* 2013;23:125–132.
18. Moscariello A, Takx R, Schoepf U, et al. Coronary CT angiography: image quality, diagnostic accuracy, and potential for radiation dose reduction using a novel iterative reconstruction technique-comparison with traditional filtered back projection. *Eur Radiol.* 2011;21:2130–2138.
19. Fuchs TA, Stehli J, Bull S, et al. Coronary computed tomography with a model-based iterative reconstruction using a radiation exposure similar to a chest x-ray examination. *Eur Heart J.* 2014;35:1131–1136.
20. Carrascosa P, Rodriguez-Granillo GA, Capunay C, Deviggiano A. Low-dose CT coronary angiography using iterative reconstruction with a 256-slice CT scanner. *World J Cardiol.* 2013;5(10):382e386.
21. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte Jr M, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol.* 1990;15(4):827–832. [https://doi.org/10.1016/0735-1097\(90\)90282-1](https://doi.org/10.1016/0735-1097(90)90282-1).
22. Rodrigues MA, Williams MC, Fitzgerald T, et al. Iterative reconstruction can permit the use of lower X-ray tube current in CT coronary artery calcium scoring. *Br J Radiol.* 2016:20150780.
23. Szilveszter B, Elzomor H, Karolyi M, et al. The effect of iterative model reconstruction on coronary artery calcium quantification. *Int J Cardiovasc Imaging.* 2016;32(1):153–160.
24. van der Werf NR, Willemink MJ, Willems TP, Greuter MJW, Leiner T. Influence of dose reduction and iterative reconstruction on CT calcium scores: a multi-manufacturer dynamic phantom study. *Int J Cardiovasc Imaging.* 2017;33(6):899–914.
25. Gassenmaier T, Allmendinger T, Kunz AS, et al. In vitro evaluation of a new iterative reconstruction algorithm for dose reduction in coronary artery calcium scoring. *Acta Radiol Open.* 2017;6(5):2058460117710682.
26. den Harder AM, Wolterink JM, Willemink MJ, et al. Submillisievert coronary calcium quantification using model-based iterative reconstruction: a within-patient analysis. *Eur J Radiol.* 2016;85(11):2152–2159.
27. Tesche C, De Cecco CN, Schoepf UJ, et al. Iterative beam-hardening correction with advanced modeled iterative reconstruction in low voltage CT coronary calcium scoring with tin filtration: impact on coronary artery calcium quantification and image quality. *J Cardiovasc Comput Tomogr.* 2017;11(5):354–359.
28. Hou Y, Xu S, Guo W, Vembar M, Guo Q. The optimal dose reduction level using iterative reconstruction with prospective ECG-triggered coronary CTA using 256-slice MDCT. *Eur J Radiol.* 2012;81(12):3905–3911.
29. Fareed A, Vavere AL, Zimmermann E, et al. Impact of iterative reconstruction vs. filtered back projection on image quality in 320-slice CT coronary angiography: insights from the CORE320 multicenter study. *Medicine (Baltim).* 2017;96(48):e8452.
30. Fuchs TA, Stehli J, Bull S, et al. Coronary computed tomography angiography with model-based iterative reconstruction using a radiation exposure similar to chest X-ray examination. *Eur Heart J.* 2014;35(17):1131–1136.
31. Yin WH, Lu B, Li N, et al. Iterative reconstruction to preserve image quality and diagnostic accuracy at reduced radiation dose in coronary CT angiography: an intraindividual comparison. *JACC Cardiovasc Imag.* 2013;6(12):1239–1249.
32. Shen J, Du X, Guo D, et al. Prospective ECG-triggered coronary CT angiography: clinical value of noise-based tube current reduction method with iterative reconstruction. *PLoS One.* 2013;8(5):e65025.
33. Takx RA, Schoepf UJ, Moscariello A, et al. Coronary CT angiography: comparison of a novel iterative reconstruction with filtered back projection for reconstruction of low-dose CT-initial experience. *Eur J Radiol.* 2013;82(2):275–280.
34. Benz DC, Fuchs TA, Grani C, et al. Head-to-head comparison of adaptive statistical and model-based iterative reconstruction algorithms for submillisievert coronary CT angiography. *Eur Heart J Cardiovasc Imag.* 2018;19(2):193–198.
35. Pontana F, Castellano I, Remy-Jardin M, Nicol E. The ethics of publishing dual exposure scans involving ionizing radiation when validated alternatives exist. *JACC Cardiovasc Imaging.* 2014;7(9):963–964. <https://doi.org/10.1016/j.jcmg.2014.03.016> Sep.
36. Benz DC, Grani C, Mikulicic F, et al. Adaptive statistical iterative reconstruction-V: impact on image quality in ultralow-dose coronary computed tomography angiography. *J Comput Assist Tomogr.* 2016;40(6):958–963.
37. Pontana F, Castellano I, Ismail T, et al. 131 Reduced-Dose dual-source coronary computed tomography angiography (CCTA): is raw-data-based iterative reconstruction able to maintain diagnostic confidence? *Heart.* 2015;101:A75.
38. Driessen RS, Stuijffand WJ, Rajmakers PG, et al. Effect of plaque burden and morphology on myocardial blood flow and fractional flow reserve. *J Am Coll Cardiol.* 2018 Feb 6;71(5):499–509. <https://doi.org/10.1016/j.jacc.2017.11.054>.
39. Karolyi M, Szilveszter B, Kolossvary M, et al. Iterative model reconstruction reduces calcified plaque volume in coronary CT angiography. *Eur J Radiol.* 2017;87:83–89.
40. Motoyama S, Kondo T, Sarai M, et al. Multislice computed tomographic characteristics of coronary lesions in acute coronary syndromes. *J Am Coll Cardiol.* 2007;50:319–326.
41. Precht H, Kitslaar PH, Broersen A, et al. First experiences with model based iterative reconstructions influence on quantitative plaque volume and intensity measurements in coronary computed tomography angiography. *Radiography (Lond).* 2017;23(1):77–79.
42. Stolzmann P, Schlett CL, Maurovich-Horvat P, et al. Variability and accuracy of coronary CT angiography including use of iterative reconstruction algorithms for plaque burden assessment as compared with intravascular ultrasound-an ex vivo study. *Eur Radiol.* 2012;22(10):2067–2075.
43. Takx RA, Willemink MJ, Nathoe HM, et al. The effect of iterative reconstruction on quantitative computed tomography assessment of coronary plaque composition. *Int J Cardiovasc Imaging.* 2014;30(1):155–163.
44. Min JK, Swaminathan RV, Vass M, Gallagher S, Weinsaft JW. High-definition multidetector computed tomography for evaluation of coronary artery stents: comparison to standard-definition 64-detector row computed tomography. *J Cardiovasc Comput Tomogr.* 2009;3(4):246–251.
45. Ebersberger U, Tricarico F, Schoepf UJ, et al. CT evaluation of coronary artery stents with iterative image reconstruction: improvements in image quality and potential for radiation dose reduction. *Eur Radiol.* 2013;23(1):125–132.
46. Gebhard C, Fiechter M, Fuchs TA, et al. Coronary artery stents: influence of adaptive statistical iterative reconstruction on image quality using 64-HDCT. *Eur Heart J Cardiovasc Imag.* 2013;14(10):969–977.
47. Eisentopf J, Achenbach S, Ulzheimer S, et al. Low-dose dual-source CT angiography with iterative reconstruction for coronary artery stent evaluation. *JACC Cardiovasc Imag.* 2013;6(4):458–465.
48. Moss AJ, Dweck MR, Dreisbach JG, et al. Complementary role of cardiac CT in the assessment of aortic valve replacement dysfunction. *Open Heart.* 2016 Nov 2;3(2):e000494.
49. Kim IC, Chang S, Hong GR, et al. Comparison of cardiac computed tomography with transesophageal echocardiography for identifying vegetation and intracardiac complications in patients with infective endocarditis in the era of 3-dimensional images. *Circ Cardiovasc Imaging.* 2018 Mar;11(3) <https://doi.org/10.1161/CIRCIMAGING.117.006986> e006986.
50. Sucha D, Willemink MJ, de Jong PA, et al. The impact of a new model-based iterative reconstruction algorithm on prosthetic heart valve related artifacts at reduced radiation dose MDCT. *Int J Cardiovasc Imaging.* 2014;30(4):785–793.
51. Habets J, Symersky P, de Mol BA, Mali WP, Leiner T, Budde RP. A novel iterative reconstruction algorithm allows reduced dose multidetector-row CT imaging of mechanical prosthetic heart valves. *Int J Cardiovasc Imaging.* 2012;28(6):1567–1575.
52. Faure ME, Swart LE, Dijkshoorn ML, et al. Advanced CT acquisition protocol with a third-generation dual-source CT scanner and iterative reconstruction technique for comprehensive prosthetic heart valve assessment. *Eur Radiol.* 2018;28(5):2159–2168.
53. Thaden JJ, Nkomo VT, Suri RM, et al. Sex-related differences in calcific aortic stenosis: correlating clinical and echocardiographic characteristics and computed tomography aortic valve calcium score to excised aortic valve weight. *Eur Heart J.* 2016 Feb 21;37(8):693–699. <https://doi.org/10.1093/eurheartj/ehv560>. Epub 2015 Oct 27.
54. Erickson BJ, Korfiatis P, Akkuz Z, Kline TL. Machine learning for medical imaging. *Radiographics.* 2017;37(2):505–515.
55. Shen D, Wu G, Suk HI. Deep learning in medical image analysis. *Annu Rev Biomed Eng.* 2017;19:221–248.
56. Chartrand G, Cheng PM, Vorontsov E, et al. Deep learning: a primer for radiologists. *Radiographics.* 2017;37(7):2113–2131.
57. Suzuki K. A supervised 'lesion-enhancement' filter by use of a massive training artificial neural network (MTANN) in computer-aided diagnosis (CAD). *Phys Med Biol.* 2009;54(18):S31–S45.
58. Chen S, Suzuki K. Computerized detection of lung nodules by means of "virtual dual-energy" radiography. *IEEE Trans Biomed Eng.* 2013;60(2):369–378.
59. Wolterink JM, Leiner T, Viergever MA, Isgum I. Generative adversarial networks for noise reduction in low-dose CT. *IEEE Trans Med Imaging.* 2017;36:2536–2545.
60. Willemink MJ, Noël PB. The evolution of image reconstruction for CT—from filtered back projection to artificial intelligence. *Eur Radiol.* 2018 Oct 30. <https://doi.org/10.1007/s00330-018-5810-7> [Epub ahead of print].
61. Kopp FK, Catalano M, Pfeiffer D, Rummeny EJ, Noël PB. Evaluation of a machine learning based model observer for x-ray CT. *Proc SPIE.* 7 March 2018 <https://doi.org/10.1117/12.2293582>.
62. Wu D, Kim K, El Fakhri G, Li Q. Iterative low-dose CT reconstruction with priors trained by artificial neural network. *IEEE Trans Med Imaging.* 2017;36:2479–2486.
63. ChenY Liu J, Xie L, et al. Discriminative prior - prior image constrained compressed sensing reconstruction for low-dose CT imaging. *Sci Rep.* 2017;7:13868.
64. Kang E, Min J, Ye JC. A deep convolutional neural network using directional wavelets for low-dose x-ray CT reconstruction. *Med Phys.* 2017;44:e360–e375.
65. Yi X, Babyn P. Sharpness-aware low-dose CT denoising using conditional generative adversarial network. *J Digit Imaging.* October 2018;31(5):655–669 <https://doi.org/10.1007/s10278-018-0056-0>.
66. Higaki T, Nishimaru E, Nakamura Y, Tatsugami F, Yu Z, Zhou J, Prabhu Verleker A, Akino N, Awai K. Radiation dose reduction in CT using Deep Learning based Reconstruction (DLR): A phantom study. Presented at The European Society of Radiology Annual Scientific Meeting. 2018; 2018 <https://posterng.netkey.at/esr/viewing/index.php?module=viewing...task...pi...>