TECHNICAL

Reducing radiation dose for multi-phase contrast-enhanced dual energy renal CT: pilot study evaluating prior iterative reconstruction

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Abstract

Purpose Prior iterative reconstruction (PIR) uses spatial information from one phase of enhancement to reduce image noise in other phases. We sought to determine if PIR could reduce radiation dose while preserving observer performance and CT number at multi-phase dual energy (DE) renal CT.

Methods CT projection data from multi-phase DE renal CT examinations were collected. Images corresponding to 40% radiation dose were reconstructed using validated noise insertion and PIR. Three genitourinary radiologists examined routine and 40% dose PIR images. Probability of malignancy was assessed [from 0 to 100] with malignancy assumed at probability ≥ 75. Observer performance was compared on a per patient and per lesion level. CT number accuracy was measured.

Results Twenty-three patients had 49 renal lesions (11 solid renal neoplasms). CT number was nearly identical between techniques (mean CT number difference: unenhanced 2 ± 2 HU; enhanced 4 ± 4 HU). AUC for malignancy was similar between multi-phase routine dose DE and lower dose PIR images [per patient: 0.950 vs. 0.916 ($p = 0.356$); per lesion: 0.931 vs. 0.884 ($p = 0.304$)]. Per patient sensitivity was also similar (78% routine dose vs. 82% lower dose [$p \geq 0.99$]), as was specificity (91% routine dose vs. 93% lower dose PIR [$p > 0.99$]), with similar findings on a per lesion level. Subjective image quality was also similar ($p = 0.34$).

Conclusions Prior iterative reconstruction is a new reconstruction method for multi-phase CT examinations that promises to facilitate radiation dose reduction by over 50% for multi-phase DE renal CT exams without compromising CT number or observer performance.

Keywords Iterative reconstruction · Renal neoplasms · Radiation dosage · Computed tomography, x-ray

Introduction

Dual energy CT image acquisition can provide additional diagnostic information compared to single energy CT for diseases of the genitourinary tract, e.g., by classifying a renal stone as uric acid or calcium-containing, or by differentiating or characterizing renal neoplasms [1–5]. Two recent meta-analyses have concluded that of dual energy CT with iodine quantification yields a high and similar accuracy compared to single energy CT for evaluation of renal masses [6, 7]. Additionally, dual energy determination of iodine content can also be used to characterize renal masses when unenhanced imaging is not available [6, 8].

Complete characterization of the renal masses and the genitourinary tract (e.g., CT urography) is often performed with multi-phase imaging with a non-contrast scan followed by multiphasic imaging after injection of iodinated contrast. While dual energy acquisition can be used to lower radiation dose by creating virtual non-contrast images in the appropriate clinical context [9], multi-phase acquisition substantially increases radiation dose. Radiation dose reduction using dual energy techniques has been a concern in the past, but current acquisition methods are generally

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dose neutral compared to single energy techniques [9–11]. Iterative reconstruction can be used to lower the radiation dose for single or multi-phase CT exams, but does so based on the modeling the image noise and CT system for a single acquisition. Taking advantage of redundant spatial information common between multiple phases of acquisition may be another method to reduce image noise and provide an additional avenue towards radiation dose reduction. One such method is prior iterative reconstruction (PIR). PIR utilizes redundant information obtained from prior or subsequent phases to denoise CT images in other phases. It applies to multi-phase imaging and may be used with dual energy or single energy studies. Unlike many other noise reduction methods, it is bimodal, meaning it can be used in conjunction with other hybrid iterative reconstruction techniques [12].

The aim of this study is to assess the ability of PIR to facilitate radiation dose reduction in multi-phase contrast-enhanced dual energy renal CT without adversely affecting CT number or observer performance.

Methods

Ethical approval was attained from the Institutional Review Board, and this study was compliant with the Health Insurance Portability and Accountability Act. Consent was waived by our Institutional Review Board. Only patients that consented to the retrospective use of medical records for research purposes were included.

Image acquisition

Patients included in this study underwent clinically indicated contrast-enhanced, multi-phase renal CT and had archived CT projection data. DECT exams were performed on a second generation, dual source CT scanner (Definition Force, Siemens Healthcare). Only one examination from each patient was included with the earliest available used.

For each DE exam, tube A varied from 70 to 100 kV depending on the patient lateral width, while tube B remained at 150 kV. All single energy acquisitions were performed at 120 kV (usually unenhanced, see below). Automatic exposure control (CareDose 4D, Siemens Healthcare) was utilized to adjust for body composition and size. Average CTDIvol per phase was 16.3 mGy. Other parameters remained constant, with a collimation of 128×0.6, gantry rotation of 0.5 s, and pitch of 0.6 or less. Omnipaque 300 mg I/ml was utilized for the contrast-enhanced scans with a volume of 120 ml.

Image noise was inserted into CT projection data using a validated noise model that took into account tube current modulation, bow-tie filter effects, and scanner geometry.

This method has demonstrated excellent agreement to actual low dose studies [13]. A target dose level corresponding to 40% of routine dose level was chosen prior to the study based on visual assessment of a few sample studies. Image sets at noise levels correlating to 60%, 50%, 40%, and 25% radiation dose levels were reviewed. The authors felt 40% dose images allowed optimal dose reduction while maintaining image quality. For all CT exams in this study, image noise was inserted separately into CT projection data corresponding to high and low tube energies (or into the single energy acquisition). Noise-inserted projection data were then loaded back onto the CT system to reconstruct images.

Routine and lower dose images were reconstructed using clinically relevant parameters, i.e., BR40 kernel, ADMIRE level 2, 3 mm slice thickness, and 2 mm increment in the axial plane. PIR was then applied to the lower dose image reconstructions. Additional DE image series including a linearly blended (0.6) image series, a 50 keV monoenergetic image series, as well as a virtual non-contrast and iodine only image series for both doses were generated subsequently (Syngo Via, Siemens Healthcare).

Reader interpretation

Three readers, independent to the study design, were recruited from the genitourinary radiology staff at our institution with 3, 7, and 23 years of experience post fellowship training.

Prior to image evaluation, patient exams were reviewed by the first author (PN) to specify renal lesions that would be assessed. Screenshots were taken of the specific lesions and arranged in a presentation with exact series and image number provided. Reader sessions were performed at the same workstation with a high spatial resolution monitor (U2711 monitor, Dell, Austin, Tex; 27-inch viewable area, pixel resolution: 2560×1440) and a custom image review application. This allowed the readers to adjust windowing and scroll through the entire image set. Reader sessions occurred with a minimum intervening period of 3 weeks to deter recognition of images. Both full dose and 40% dose images with PIR were assessed in each session. Images from each patient were viewed only once per session and were viewed in random order.

Readers were blinded to all clinical information and radiation dose level. Once the target lesion was identified by the reader using the supplied information, a number of questions were asked. The reader was asked to predict the presence of malignancy on a per patient and a per lesion basis. The prediction of the presence of malignancy was scored on a continuum from 0 being definitely benign to 100 being definitely malignant. Readers were told that a score 0 represented complete confidence the lesion is benign; ≤ 25 indicating the lesion is unlikely to be a neoplasm; ≥ 75

indicating the lesion is likely to be a neoplasm; 100 representing complete confidence that the lesion can only be a neoplasm. Where a score of 75 or greater was given by the reader, this was taken as a prediction of malignancy. The reader was also asked to rate diagnostic image quality on a standard Likert scale from 1 to 5 (1 = non-diagnostic due to excessive noise or artifacts; 2 = diagnosis questionable due to excessive noise or artifacts, moderate decrease in confidence; 3 = diagnostic with moderate but acceptable noise or artifacts; 4 = mild noise, no change in confidence; 5 = routine diagnostic image quality).

The reference standard for each renal lesion was based on pathological analysis, when available. Where this was not possible or indicated, diagnosis was based on clinical evaluation and follow-up imaging. Patients were excluded if they were not followed up past a minimum of 1 year. Lesions were classified as non-neoplastic based on pathological specimen if available, evidence of cystic nature on subsequent imaging modalities (US/MRI) and stability on imaging over a 2 year period. Lesions were classified as neoplastic based on pathological specimen and evidence of solid nature on subsequent imaging or significant growth/increased complexity on follow-up imaging.

CT number was assessed on full dose and 40% dose images. For this purpose, the 0.6 linear blend images were used. A region of interest marker was placed in the abdominal aorta and renal cortex in the non-contrast phase and corticomedullary phase of the examination. Region of interest markers were placed in the infrarenal abdominal aorta to include the entire intraluminal area without including the vessel wall. Markers were placed in the midpole renal cortex at greatest cortical thickness to include the entire cortex. Care was taken to avoid any artifact or anatomic anomalies.

Statistical analysis

CT number was compared using Student's T test. Inter-rater reliability was calculated using free marginal multi-rater Kappa [14]. ROC analysis was completed for both the routine and reduced doses using the continuous scale reader confidence scores. AUC values were compared between the two dose levels using DeLong's test. Sensitivity and specificity values were calculated using the previously mentioned cutoff to define a diagnosis of malignancy or non-malignancy. These values were compared between the two dose levels by McNemar's test. AUC, sensitivity, and specificity analyses were all completed using both the individual lesion-level and overall patient-level scores for each individual reader as well as an aggregated overall value. Subjective image quality ratings were compared between dose levels by Fisher's exact test.

Statistical analyses were performed using RStudio version 3.4.2 (R Project for Statistical Computing, Vienna, Austria)

and JMP software (JMP®, Version 12. SAS Institute Inc., Cary, NC, 1989–2007).

Results

Twenty-three patients who underwent dual energy contrast-enhanced multi-phase renal CT between February 2015 and April 2017 for whom archived projection data were available and who consented to the retrospective use of medical records for research purposes form our study cohort. Forty-nine renal lesions were identified in twenty-three patients. Mean patient age was 64 years (range 25 to 91 years). There were 10 male patients and 13 female patients. In 21 patients, a four-phase CT urogram study was performed with non-contrast, corticomedullary, nephrographic and excretory phase studies. A three phase study without excretory phase was performed in the remaining two patients. All phases for each patient were performed in dual energy mode except for precontrast series in five patients, and 1 nephrographic and 1 delayed phase acquisition (in separate patients). There were 21 lesions diagnosed ultimately as simple renal cysts, 8 lesions diagnosed as hemorrhagic cysts, and 11 diagnosed as solid renal neoplasms (Figs. 1, 2, 3). The two remaining lesions were diagnosed as functional residual renal tissue following extensive investigation over 5 years. There were seven with renal calculi. Of the 49 lesions, five were confirmed via pathological analysis from surgical resection, 33 lesions were confirmed based on further morphological evaluation via ultrasound or MRI imaging, and ten lesions required continued follow-up. Mean follow-up time was 65 months with a range of 39 to 107 months.

While PIR did appropriately reduce noise for the 40% dose images, it did not change CT number (Table 1). The mean CT number in the aorta between the routine dose and lower dose PIR images was less than 2 HU for both unenhanced images as well as contrast-enhanced images in the corticomedullary phase, and this difference was < 4 HU in measurements of the renal cortex.

The mean area under the curve (AUC), sensitivity, and specificity for identification of renal neoplasm are outlined in Table 2 (Fig. 4). There was no statistically significant difference in overall estimates for sensitivity, specificity, and AUC between the routine dose dual energy and 40% dose PIR. Similarly, there were no statistically significant differences for any of the three readers for any performance metric ($p > 0.149$). Inter-rater agreement using free marginal multi-rater Kappa was 0.78 (Confidence interval 0.64–0.92) in the standard dose and 0.92 (Confidence Interval 0.83–1) in the 40% dose cohort, indicating similar agreement across dose levels.

Reader appraisal of image quality is outlined in Fig. 5. There was no statistically significant difference between
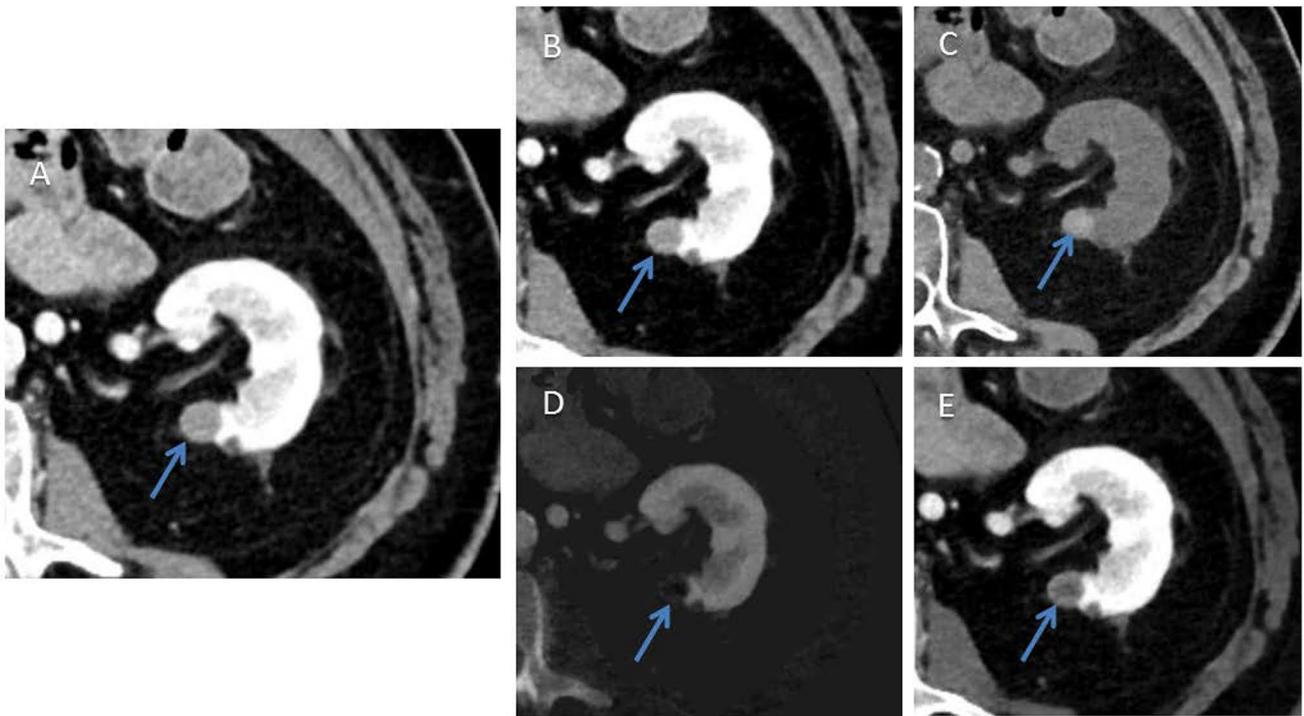
Fig. 1 Dual energy, mixed kV contrast-enhanced CT images from the nephrographic phase demonstrating a hemorrhagic cyst (blue arrow) at standard dose (**a**), 40% dose with PIR (**b**), 40% dose virtual non-contrast (**c**), 40% dose iodine only (**d**), and 40% dose 50 keV (**e**)

diagnostic image quality between routine dose and lower dose PIR images for any of the radiologists ($p = 0.342$, $p = 0.095$, $p = 0.545$). None of the radiologists scored image quality as 1 with lower dose PIR, with the vast majority of scores in the four or five categories.

Discussion

This study indicates that using PIR, a decrease in the radiation dose of over 50% is achievable for contrast-enhanced multi-phase, dual energy, renal CT while maintaining observer performance, and CT number. Simulated dose reduction was performed retrospectively using previously validated noise insertion software. To our knowledge no other study of PIR performance has been described in the literature.

The principle of performing imaging at a radiation dose that is as low as reasonably achievable is difficult to follow. Scientific developments have been significant in recent years in the field of radiation dose and noise reduction. As a result, offering a service to the patient that is diagnostically sound requires constant evaluation and reevaluation. How this evaluation is performed is debated. Often the primary

endpoints in radiation dose reduction studies consist of subjective visual analysis of image quality [15–17]. There are issues, however, with subjective visual evaluation including lack of correlation to observer performance and evidence, as a radiologist's appreciation of an image is based on various internal and idiosyncratic factors [1, 18–21]. We feel the use of use independent observer assessment combined with objective and subjective endpoints adds weight to our findings.

Filtered back projection was the first reconstruction method utilized in earlier CT scanners. It offers attenuation values within an area by computing simultaneous equations from information taken through the x-ray beam at different angles. This method was obviously successful as to which its longevity alludes with adequate speed and efficiency compared to other methods [22].

Iterative reconstruction, in its various forms, has demonstrated its ability to improve image quality over FBP in multiple recent studies. The benefit is predominantly seen in studies which utilize high image contrast such as chest CT [23–26] and CT colonography [27]. Its superiority in improving conspicuity of soft tissue lesions with lower contrast differences in the liver and kidney is less pronounced, however. Various studies, although demonstrating
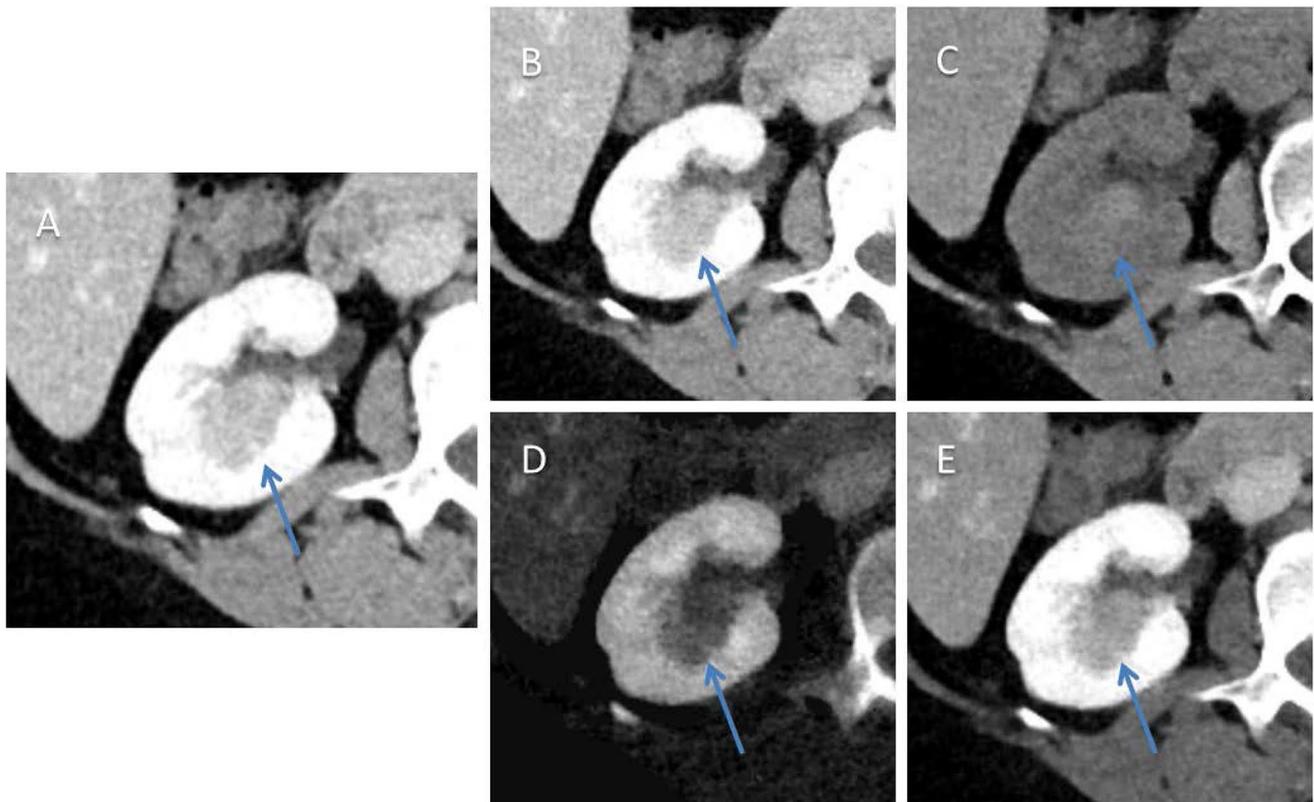
Fig. 2 Dual energy, mixed kV contrast-enhanced CT images from the nephrographic phase demonstrating a renal neoplasm (blue arrow) at standard dose (**a**), 40% dose with PIR (**b**), 40% dose virtual non-con- trast (**c**), 40% dose iodine only (**d**), and 40% dose 50 keV (**e**). Subse- quent biopsy demonstrated clear cell renal carcinoma, and the patient was treated with cryoablation of the renal mass

a significant reduction in dose, reported results short of the expected level [20, 28–30]. Indeed, low-contrast resolution may even be decreased using standard iterative reconstruc- tion methods [19, 20, 31].

PIR is a novel bimodal method of iterative reconstruc- tion. By utilizing redundant data in multi-phase acqui- sitions, it allows a significant reduction in noise. It can be applied with other standard reconstruction methods, such as SAFIRE, as employed in our study. PIR requires additional software, available from a single vendor with post-processing requiring only seconds before images can be reconstructed. When compared to standard iterative reconstruction methods we found a dose reduction of 60% was achievable, while maintaining observer performance. This is obviously beneficial in an organ such as the kidney where only moderate reduction in noise could be achieved with standard techniques. Maintenance of observer per- formance was proven using multiple endpoints. Objec- tively CT number demonstrated no significant difference between the routine and lower dose CT images with PIR.

Subjective image quality, appreciated by three different GU radiologists also did not demonstrate any significant difference. PIR itself has limitations because it requires spatial co-registration of data, so organs (like the bowel or bladder) that are changing positions drastically dur- ing phases would not be amenable to PIR-based noise reduction. PIR has not been previously assessed in any published literature and therefore comparison to any other literature is not possible.

There are limitations to this study. The study population is small. Practical limitations restricted the amount of stud- ies where raw data were available. This results in limited assessment of certain subgroups such as renal calculi. The patients and lesions were also not picked in a random fash- ion. This may introduce an element of selection bias.

The choice of dose reduction was set at 60% based on visual assessment and comparison between various dose levels. This choice was not scientifically chosen. Various dose levels may lead to similar or more significant findings. The methodology of noise insertion also, although validated,
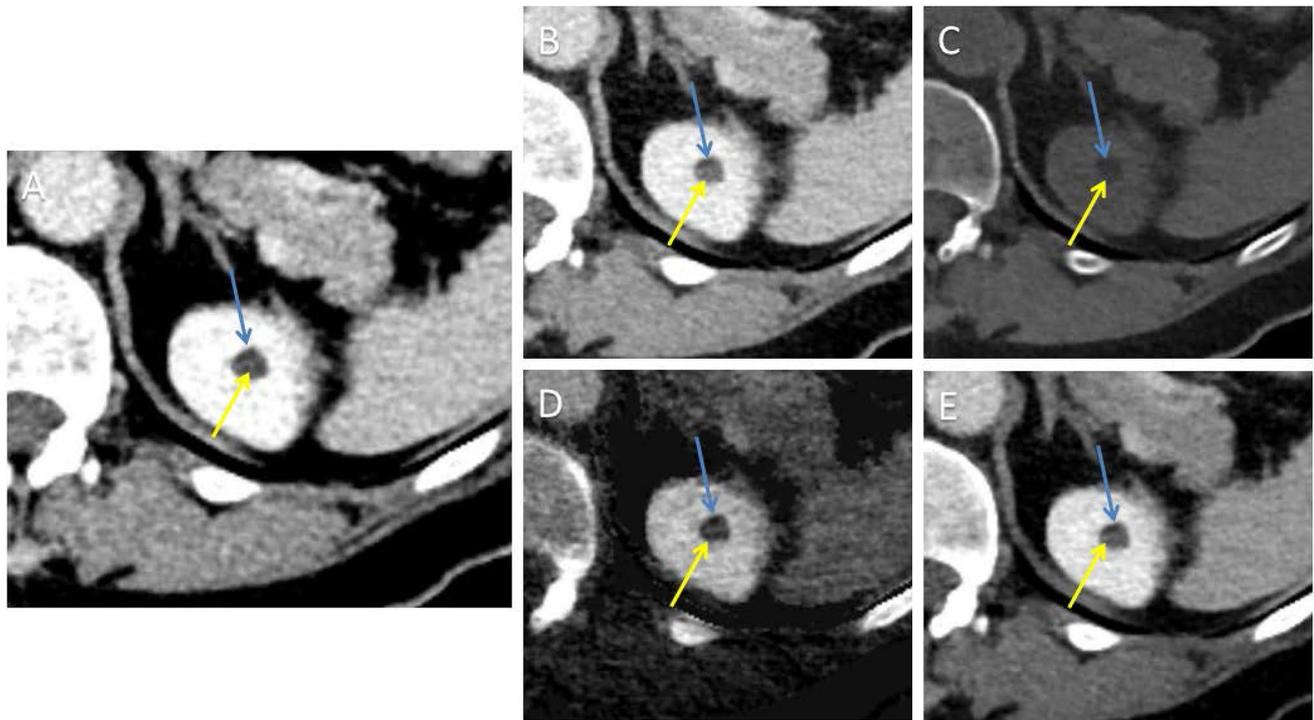
Fig. 3 Dual energy, mixed kV CT demonstrating a simple cyst (blue arrow) with thin septation (yellow arrow) at standard dose (**a**), 40% dose mixed kV with PIR (**b**), 40% dose virtual non-contrast (**c**), 40% dose iodine only (**d**), and 40% dose 50 keV (**e**). Images obtained in the corticomedullary phase

Table 1 Comparison of CT number and noise in the aorta and renal cortex in routine dose and lower dose CT images reconstructed with PIR

	Mean CT # (std dev): aorta	Mean CT # (std dev): renal cortex	Mean noise (std dev): aorta	Mean noise (std dev): renal cortex
Unenhanced phase				
Routine dose	42.3 HU (5.2)	40.0 HU (37.7)	13.0 (5.1)	13.8(3.8)
40% dose with PIR	41.2 HU (6.4)	38.7 HU (28.3)	13.1 (5.1)	14.6 (5.8)
Absolute value of difference	1.9 HU (1.8)	2.6 HU (2.4)	1.5 (1.3)	1.67 (1.9)
Corticomedulary phase				
Routine dose	203.3 HU (76.2)	162.6 HU (68.8)	12.2 (2.7)	12.9 (2.8)
40% dose with PIR	202.8 HU (76.8)	158.9 HU (68.0)	12.5 (3.1)	13.6 (4.2)
Absolute value of difference	1.6 HU (2.0)	3.8 HU (3. 6)	1.04 (1.1)	1.55 (1.5)

Table 2 Sensitivity, specificity, and AUC in the standard dose and 40% dose groups, on a per patient and per lesion basis

	Dual energy routine dose Overall estimate (95% CI)	Dual energy 40% dose PIR Overall estimate (95% CI)	
Per lesion			
Sensitivity	0.788 (0.363, 0.910)	0.700 (0.309, 0.850)	$p=0.37$
Specificity	0.965 (0.568, 0.992)	0.965 (0.625, 0.992)	$p=0.37$
AUC	0.931 (0.868, 0.993)	0.884 (0.801, 0.968)	$p=0.30$
Per patient			
Sensitivity	0.778 (0.369, 0.899)	0.815 (0.350, 0.928)	$p=0.99$
Specificity	0.905 (0.506, 0.977)	0.929 (0.502, 0.999)	$p=0.99$
AUC	0.950 (0.902, 0.997)	0.916 (0.834, 0.999)	$p=0.36$
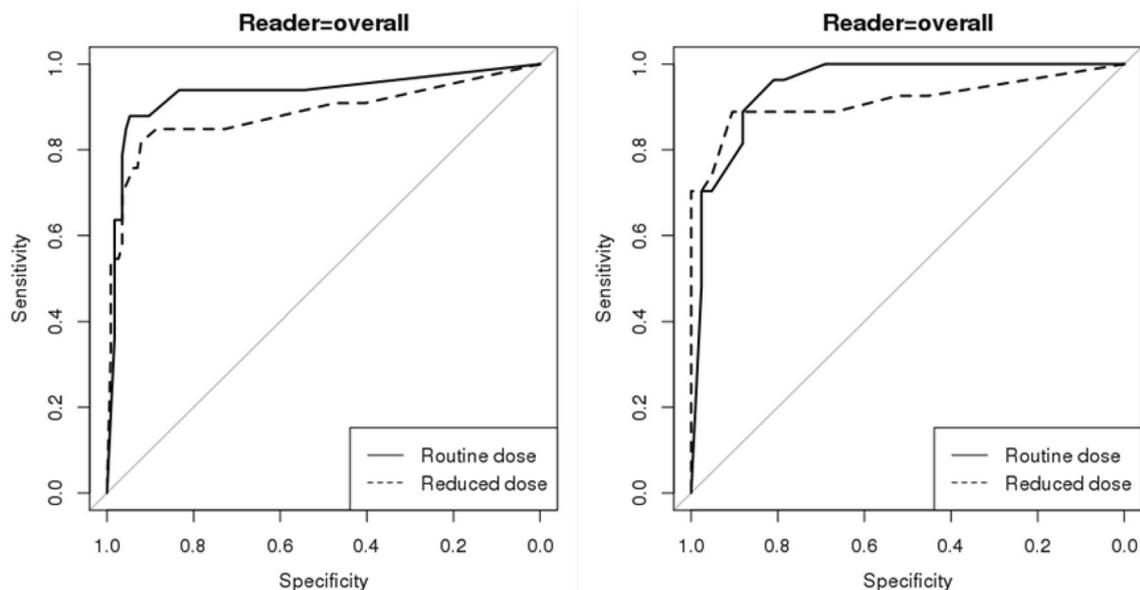
Fig. 4 Receiver operator characteristic curve on a per lesion (left) and per patient (right) basis
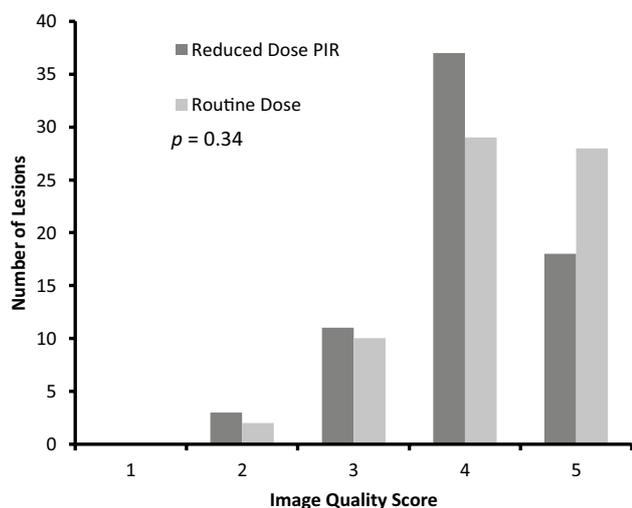
Fig. 5 Subjective image quality score in the routine dose and 40% reduced dose groups. Diagnostic image quality on a standard Likert scale from 1 to 5 (1 = non-diagnostic due to excessive noise or artifacts; 2 = diagnosis questionable due to excessive noise or artifacts, moderate decrease in confidence; 3 = diagnostic with moderate but acceptable noise or artifacts; 4 = mild noise, no change in confidence; 5 = routine diagnostic image quality)

may be criticized as inferior to a prospective approach. This method, however, permits comparison of identical anatomy with identical contrast enhancement at different dose levels, with no increase in radiation dose to the subjects.

Finally, no training manual was provided to the assessors to guide how they should score the various outcome measures. However, good inter-rater agreement was demonstrated between all three assessors indicating adequate homogeneity.

Conclusion

This pilot study suggests that PIR in multi-phase, dual energy renal CT studies allows a 60% reduction in radiation dose without demonstrating a significant decrease in observer performance or CT number. This method may even have the potential to allow dual energy exams to be performed at doses substantially lower than single energy CT exams without PIR while providing equivalent performance and additional diagnostic information.

Compliance with ethical standards

Conflict of interest Dr. Halaweish is an employee of Siemens Healthineers. Drs. McCollough and Fletcher receive grant support to their institution from Siemens Healthineers, which provided the offline computer workstation and prior iterative reconstruction software examined in this work.

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