Clinical Radiology 74 (2019) 650.e13–650.e18

Contents lists available at ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Image quality and radiation dose of renal perfusion CT with low-dose contrast agent: a comparison with conventional CT using a 320-row system

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ARTICLE INFORMATION

Article history:
Received 4 April 2018
Accepted 20 March 2019

AIM: To compare perfusion computed tomography (CT) with reconstructed image from source data using low-dose contrast agent and conventional 320-row CT for the evaluation of renal tumours.

MATERIALS AND METHODS: Twenty-eight patients underwent conventional CT (C-CT) and 26 patients underwent perfusion CT with low-dose (40 ml) contrast agent. Image noise, arterial visualisation, the sharpness of the corticomedullary junction (CMJ), and overall image quality were each assessed using a four-point scale. The tumour detection rate for lesions <4 cm (n=66) was also evaluated. Quantitative image parameters including image noise and the contrast-to-noise ratios (CNRs) of the renal artery and CMJ were measured. The volume CT dose index (CTDI), dose–length product (DLP), and size-specific dose estimate (SSDE) were also recorded.

RESULTS: Although the image noise of perfusion CT was higher than that of C-CT and the overall image quality of perfusion CT was lower than that of C-CT, the arterial visualisation score of perfusion CT was significantly higher than that of C-CT. The CMJ sharpness scores of the two techniques were equivalent. Sensitivity and positive predictive values were also equivalent with respect to tumour detection. The CNRs of both the left and right renal arteries were significantly higher on perfusion CT than on C-CT. The CTDI, DLP, and SSDE of perfusion CT were significantly lower than those of C-CT.

CONCLUSION: Perfusion CT using low-dose contrast agent preserved arterial visualisation and the tumour detection rate and achieved a low radiation dose despite image quality degradation and image noise.

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https://doi.org/10.1016/j.crad.2019.03.017
0009-9260/

Introduction

Various imaging methods have been developed for the evaluation of renal tumours. Among them, computed tomography (CT) plays a main role in the diagnosis and evaluation of tumour extent including distant metastasis as well as vascular anatomy. As a new functional imaging technique, perfusion CT depicts regional tumour perfusion and vascular permeability, which are indirect parameters of tumour angiogenesis, and thereby provides vital information regarding the tumour microenvironment.[1-4]

The second-generation 320-row CT unit combines faster gantry rotation, wide volume coverage (16 cm), a larger generator, and a new iterative reconstruction algorithm.[5] Perfusion CT using 320-row CT with low-dose contrast agent and radiation doses can not only provide tumour perfusion data, but also be used in diagnostic quality studies. For the evaluation of intracranial arteries, perfusion CT angiography reconstructed from perfusion CT source data yields image quality and vascular visualisation similar to conventional CT angiography at an acceptable radiation dose.[6] Similarly, images reconstructed from renal perfusion CT could be a substitute for conventional dynamic CT. There have been no reports comparing renal perfusion CT and conventional dynamic CT from the standpoint of routine diagnostic ability. The purpose of this study was to clarify the pretreatment diagnostic utility of perfusion CT for the evaluation of renal anatomy and tumour detection.

Materials and methods

Patients

This retrospective clinical study was approved by the ethics committee of Kyushu University Hospital. The requirement for informed patient consent was waived. From April 2014 to August 2017, 125 consecutive patients with renal tumour (<4 cm in maximum diameter) who underwent CT and were scheduled to receive cryoablation were evaluated. Patients were excluded for the following: preoperative CT without contrast medium administration due to impaired renal function or non-dedicated preoperative CT protocol without arterial phase (n=41), a scanner size other than 320 rows, e.g., a 64-row scanner (n=29), and dialysis patients with renal atrophy (n=1). Dedicated conventional preoperative CT (C-CT) was performed from April 2014 to September 2016 while perfusion CT was employed from October 2016 to August 2017. A total of 54 patients with 66 renal tumours were enrolled in this study. Twenty-eight patients (19 male and nine female patients; mean age, 67.3 years) with 36 renal tumours (mean diameter, 22.8 mm) were scanned with C-CT, and 26 patients (20 male and six female patients; mean age, 66.3 years) with 30 renal tumours (mean diameter, 22.9 mm) were scanned with perfusion CT (Table 1).

CT protocol

All CT images were obtained on a 320-section CT system (Aquilion ONE, Canon medical systems, Otawara, Japan) reconstructed with three-dimensional (3D) adaptive iterative dose reduction (AIDR 3D; Table 1).

C-CT

After unenhanced images through the liver to the kidney were obtained, 600 mg iodine/kg (maximum volume 100 ml) of a non-ionic iodinated contrast agent (Iopamiron 370; Bayer, Osaka, Japan) was injected with a fixed duration of 30 seconds at a variable injection rate followed by a saline flush using an automated power injector. Arterial phases including the entire abdominopelvis were scanned with a bolus-triggered technique (with a 1 second monitoring frequency starting 10 seconds after contrast medium injection, an increase of 100 HU in the descending aorta as the trigger threshold, and initiation of scan immediately after the trigger). The corticomedullary phases (diaphragm to kidney) were obtained 20 seconds after the arterial phases. The nephrographic phase (diaphragm to pelvis) and excretory phases (diaphragm to kidney) were acquired at 90 and 240 seconds after contrast medium injection, respectively. During the nephrographic phase, the chest was scanned simultaneously in 11 cases. The imaging parameters were as follows: 120 kVp tube voltage, automatically set tube current, 0.5 second rotation time, detector

Table 1
Patient characteristics and CT protocol.

	Conventional CT	Perfusion CT
No. of patients	28	26
Age	67.3	66.3
Gender (male/female)	19:9	20:6
No. of lesions	36	30
Mean diameter of the lesions	22.8	22.9
Mean eGFR (ml/min/1.72 m^2)	66.1±5.7	66.4±4.9
CT		
Contrast agent (mg iodine/ml)	370 or 300	370
Volume of contrast agent	300 mg iodine/kg	40+60 ml
Injection rate	Fixed (30 seconds)	5 ml/s
Tube voltage (kVp)	120	100
Tube current (mAs)	Automatically set	90
Rotation time (s/rotation)	0.5	0.5
Data acquisition from the start of contrast medium injection (s)		
Arterial phase	bolus triggered technique	10–34
Corticomedullary phase	20s after arterial phase	40–64
Nephrographic phase	90	72–96
Delayed phase	N/A	96–104
Excretory phase	240	N/A
Additional conventional scan	No	Yes (+60 ml of contrast medium)
Number of chest scans included	11	21
Iterative reconstruction (AIDR 3D)	weak	Standard

collimation of 0.5 mm, pitch factor of 0.813, and 1 mm section thickness with 1 mm section interval.

Perfusion CT

The contrast agent was injected using a power injector through a 20 G intravenous line into the cubital vein with a start delay of 10 seconds. A total of 40 ml (Iopamiron 370; Bayer) was injected in 8 seconds (5 ml/s) followed by a saline flush. The imaging parameters were as follows: 100 kVp tube voltage, 90 mAs tube current, 0.5 second rotation time, detector collimation of 0.5 mm, and 1 mm section thickness with 1 mm section interval. The perfusion CT protocol consisted of 27 dynamic volumes (Table 2); the total acquisition time was 124 seconds: every 2 seconds for the first 13 rotations (arterial phase), every 4 seconds for the next seven rotations (corticomedullary phase), every 8 seconds for the next four rotations (nephrographic phase), and every 10 seconds for the last three rotations (delayed phase). From these multiple scans, the images that most clearly revealed the renal arteries, corticomedullary junction (CMJ), renal parenchyma, and ureter were selected as the representative images for the arterial phase, corticomedullary phase, nephrographic phase, and delayed phase, respectively. Consequently, after an additional injection of 60 ml contrast agent, the chest to abdominopelvic area (n=21) and abdominopelvis (n=5) was scanned for evaluation of distant metastasis (additional conventional images). The parameters of this additional imaging were as follows: 120 kVp tube voltage, automatically set tube current, 0.5 seconds rotation time, detector collimation of 0.5 mm, pitch factor of 0.813, and 1 mm section thickness with 1 mm section interval.

Subjective image analysis

Subjective image quality was assessed independently by two radiologists (D.K. and N.F. with 19 and 14 years of experience, respectively) in a blinded manner. The reviewers were allowed to assess 1 mm section thickness/interval images of all phases of the C-CT group and same section thickness/interval images reconstructed from perfusion CT source data. They were not allowed to observe the additional conventional images in the perfusion CT group. The reviewers rated the visual image noise according to a four-point score (1, present and unacceptable; 2, present and interfering with the depiction of the structure; 3, present but not interfering with the depiction; 4, minimal or absent), and rated renal artery visualisation according to a four-point score (1, poor=insufficient vessel depiction; 2, fair=suboptimal arterial enhancement; 3, good=adequate for confident diagnosis; 4, excellent=sufficient vessel depiction). They also evaluated the sharpness of the CMJ depiction and the overall image according a four-point score (1, unacceptable; 2, acceptable; 3, good; 4, excellent), respectively. Interobserver agreement (kappa) values between the two radiologists were calculated.

Of 54 patients with 66 renal tumours, 52 patients with 52 renal masses underwent biopsy and 48 renal masses were proven to be RCC (clear cell carcinoma, 46 masses; papillary carcinoma, two masses). The other 18 renal masses including four masses with non-diagnostic pathology and 14 masses without biopsy were judged as RCC by two board-certified abdominal radiologists (Y.A. and A.N., each with 23 years of experience) in a comprehensive way from a constellation of CT, ultrasound, and magnetic resonance imaging (MRI) as a standard reference. Reviewers were asked to mark the tumour location and record it using commercially available presentation software (Microsoft Office PowerPoint 2010; Microsoft Corporation, Redmond, WA, USA). Hypervascular solid tumours followed by delayed washout indicated clear cell carcinomas, in contrast hypovascular solid tumours were considered to be other types of RCC such as papillary renal cell carcinomas; however, the reviewers were not asked to differentiate these subtypes. The study coordinator (Y.A.) evaluated the recorded lesions. CT performed 3 months after cryoablation was also referred for false-positive cases. The sensitivity and positive predictive values were calculated.

Objective analysis

Arterial and corticomedullary phases with 1-mm section thickness/interval were evaluated by a board-certified abdominal radiologist (Y.A., with 23 years of experience). Circular or oval regions of interest (ROIs; typical size, 20 mm^2) were placed on the bilateral renal arteries in the arterial phase and the renal cortex in the corticomedullary phase, as well as on the erector spinae muscle (ESM). The image noise (standard deviation of CT attenuation of the erector spinae muscle), signal-to-noise ratios (SNRs) of bilateral renal arteries and renal cortex, and contrast-to-noise ratio (CNRs) of bilateral renal arteries and renal cortex were assessed. The SNR of the renal arteries was calculated with the equation

$$SNR = RA_{max} / ESM_{mean},$$

where RA_{max} is the maximum CT value of the renal artery and ESM_{mean} is the mean CT value of the ESM. The SNR of the renal cortex was calculated with the equation

$$SNR = RC_{mean} / ESM_{mean},$$

where RC_{mean} is the mean CT value of the renal cortex. The CNRs of the renal arteries and renal cortex were calculated with the equation

$CNR = (RA_{max}\text{-}ESM_{mean})/ESM_{mean}$ and $(RC_{mean}\text{-}ESM_{mean})/ESM_{mean}$, respectively.

Table 2
Protocol for renal perfusion CT.

Phase	No. of scans	Cycle time (s)	Accumulated time since start of injection (s)
Start of injection			0
1 Arterial	13	2	10–34
2 Corticomedullary	7	4	40–64
3 Nephrographic	4	8	72–96
4 Delayed	3	10	104–124

Radiation dose report

For each patient who underwent CT including chest area (n=11 and 22 in C-CT group and perfusion CT group, respectively), the volume CT dose index (CTDI) and the dose–length product (DLP) values were recorded as provided automatically by the CT machine. A size-specific dose estimate (SSDE) was calculated using the sum of the anteroposterior and lateral dimensions at the level of mid-abdomen.[7]

Statistical analysis

All numeric values are reported as means ± standard deviations. The Wilcoxon signed-rank test was used for assessment of subjective and objective image quality analysis. The scale for kappa coefficients for interobserver agreement was as follows: kappa value <0.20, poor agreement; 0.201–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; 0.81–1.00, near-perfect agreement. Student's t-test was used to compare CTDI, DLP, and SSDE values. The level of significance was set at $p<0.05$ for all tests. JMP 11.0.0 software (SAS Institute, Cary, NC, USA) was used for the analysis.

Results

Subjective image quality analysis

Image noise was significantly more prominent for perfusion CT than for C-CT. The mean score for overall image quality was significantly higher with C-CT than perfusion CT. In contrast, for arterial visualisation, the mean score was significantly higher with perfusion CT than C-CT in reader 1 (4±0.1 versus 3.8±0.1; 95% confidence interval [CI]: 3.9–4.1 versus 3.7–3.9) and tended to be slightly higher with perfusion CT than C-CT in reader 2 (3.9±0.1 versus 3.8±0.1; 95% CI: 3.8–4.1 versus 3.7–4). The mean score of sharpness of CMJ was equivalent between perfusion CT and C-CT (Table 3).

Diagnostic performance for identifying RCC

Sensitivities of 97.2% and 93.3% for C-CT and perfusion CT, respectively, were obtained for observer 1, and 91.7% and 96.6% for observer 2. The PPV was 94.6% and 100% in C-CT and perfusion CT, respectively, for observer 1, and 94.3 and 96.6% for observer 2. Data are shown in Table 4. Representative cases are presented in Fig 1.

Objective image quality analysis

Image noise was higher in perfusion CT than in C-CT. The SNRs of the left and right renal arteries and renal cortex were significantly higher in perfusion CT than in C-CT. CNRs of left and right renal arteries were significantly higher in perfusion CT than in C-CT. The CNR of the renal cortex tended to be higher in perfusion CT than in C-CT, but the difference did not reach significance.

As for radiation dose, CTDI and SSDE values were significantly lower in perfusion CT than in C-CT. The difference in DLP between the two groups showed a similar trend but did not reach significance. Details are shown in Table 5.

Discussion

To the authors' knowledge, this is the first comparison of perfusion CT and C-CT for pretreatment work-up of renal tumours. The present study revealed that radiation and contrast agent dose can be reduced using perfusion CT. Perfusion CT offers better SNR/CNR and visualisation of renal arteries in comparison with C-CT. Almost the same SNR/CNR, visual score of the renal cortex, and tumour detection rate were provided in perfusion CT compared with C-CT, even though image noise was higher and the overall image quality was worse in perfusion CT than in C-CT.

In perfusion CT, the flow rate of contrast agent is higher (5 ml/s) than in C-CT (highest rate, 3.3 ml/s). In perfusion CT,

Table 4
Diagnostic performance for identifying RCC.

	C-CT		Perfusion CT	
	Observer 1	Observer 2	Observer 1	Observer 2
Sensitivity	97.2 (35/36)	91.7 (33/36)	93.3 (28/30)	96.6 (29/30)
PPV	94.6 (35/37)	94.3 (33/35)	100 (28/28)	96.6 (29/30)

PPV, positive predictive value.

Table 3
Subjective image quality.

	Observer 1			Observer 2			
Variable	C-CT	Perfusion CT	p-Value	C-CT	Perfusion CT	p-Value	kappa
Image noise	3±0.1 (2.9–3.1)	2.4±0.1 (2.3–2.6)	<0.001	3±0.07 (2.9–3.1)	2.4±0.08 (2.1–2.5)	<0.001	0.409
Vascular visualisation	3.8±0.1 (3.7–3.9)	4±0.1 (3.9–4.1)	0.013	3.8±0.06 (3.7–4.0)	3.9±0.07 (3.8–4.1)	0.278	0.738
Sharpness of CMJ	3.6±0.1 (3.3–3.9)	3.5±0.1 (3.3–3.8)	0.322	3.7±0.1 (3.4–3.9)	3.5±0.1 (3.3–3.7)	0.061	0.585
Overall Image quality	3.7±0.1 (3.5–3.9)	2.5±0.1 (2.3–2.7)	<0.001	3.5±0.1 (3.3–3.7)	2.6±0.1 (2.4–2.8)	<0.001	0.578

Data are mean ± standard deviation and data in parentheses are 95% confidence intervals.
CMJ, corticomedullary junction.

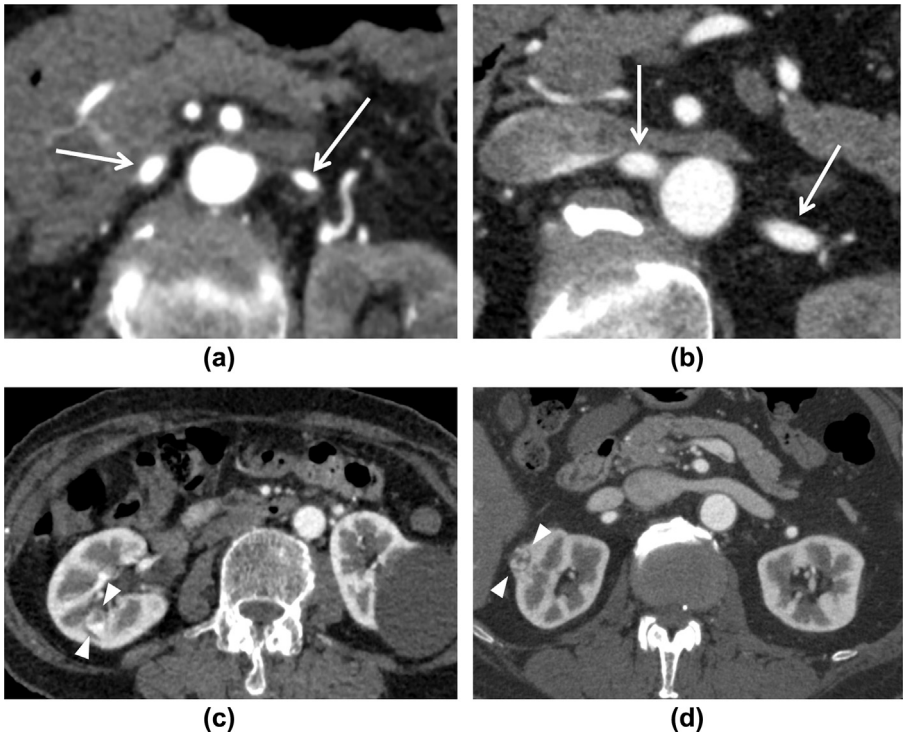

Figure 1 Renal arteries (arrow) are well visualised in perfusion CT image (a), but image noise was somewhat conspicuous compared with conventional CT (b). The CMJ was well recognised and the CMJ sharpness in the perfusion CT image (c) was equivalent to that in conventional CT (d). Small renal cell carcinomas (arrowhead) were depicted in perfusion CT (c) as well as in conventional CT (d).

Table 5
Objective image quality.

Variable	C-CT		Perfusion CT		*p*-Value
		95% CI		95% CI	
Image noise	14.6±0.52	13.5–15.6	20.6±0.51	19.6–21.6	<0.001
SNR					
Left renal artery	17.5±1.28	14.9–20.1	27.9±1.31	25.3–30.5	<0.001
Right renal artery	17.6±1.54	14.5–20.8	29.6±1.45	26.2–32.2	<0.001
Renal cortex	13.8±0.96	11.9–15.8	17.1±0.96	15.2–19.1	0.027
CNR					
Left renal artery	14.7±1.20	12.3–17.1	24.1±1.22	21.6–26.5	<0.001
Right renal artery	14.8±1.45	11.8–17.7	25.7±1.36	22.5–28.1	<0.001
Renal cortex	10.5±0.80	8.90–12.1	12.7±0.80	11.1–14.4	0.101
Radiation dose					
CTDI (mGy)	121.1±6.18	108.4–133.7	92.2±4.47	83.0–101.3	0.001
DLP (mGy·cm)	2608.7±165.2	2271.4–2946.0	2231.7±119.5	1987.6–2475.8	0.074
SSDE (mGy)	175.8±10.6	154.1–197.6	128.4–7.70	112.7–144.1	0.001

Radiation dose was evaluated at the CT studies including thorax.
SNR, signal-to-noise ratio; CNR, contrast-to-noise ratio; CTDI, volume CT dose index; DLP, dose–length product; SSDE, size-specific dose estimate; CI, confidence interval.

the highest and optimal arterial contrast can be selected from the multiple arterial images; in contrast, the arterial phase was obtained only in single timing in C-CT. Furthermore, low tube voltage affected the CT value of the renal artery. When the voltage is reduced, X-ray absorption of iodine increases. The attenuation values in the arteries increase with a constant intravascular iodine concentration.[8] The benefits of low-tube-voltage CT imaging have been reported for many clinical applications involving abdominal organs. Nakaura *et al.* reported that the low tube voltage/high tube current CT technique may enable substantial reduction (40%) of contrast medium volume and 20% reduction of radiation dose, without compromising image quality during multiphase hepatic dynamic CT in underweight to normal-weight adults.[9] Kanematsu *et al.* also reported that the low-iodine-load protocol at 80 kVp tube voltage could maintain the image quality of dual-phase renal CT angiographic imaging while reducing the iodine load by 51% compared with the high-iodine-load protocol at 120 kVp.[10] The present results are in concordance with

previous reports; however, image quality deteriorated, probably because a low tube current (90 mAs) was employed in the present perfusion CT.

In the detection of renal tumours <4 cm in diameter, perfusion CT and C-CT were comparable. The majority of RCCs were a clear cell subtype and showed hypervascularity. The low volume of contrast agent did not impair the qualitative and quantitative enhancement in the renal cortices because the apical part of the contrast bolus was dense enough to yield a very high attenuation value in the renal tumour and cortices by the combined use of a low tube voltage setting and new-generation iterative reconstruction algorithm (AIDR 3D).[10] AIDR 3D can improve spatial resolution with reduced noise levels.[11] Thus, the difference in enhancement between the tumour and the renal cortex or medulla was sufficient for discrimination on perfusion CT, as in C-CT.

Perfusion CT has been believed to have a high radiation burden because of the repetitive scans acquired over a period of time[1]; however, in the current study, CTDI, DLP, and SSDE values in perfusion CT were all lower than in C-CT. This is because low tube voltage and current with the iterative reconstruction were employed. The recent development of CT technology can provide satisfactory images without excessive radiation dose in perfusion CT.

The present study has several limitations. First, the perfusion CT data used in this study was originally gathered for other purposes, such as evaluation of tumour perfusion or kidney function, and this study design was retrospective in nature. Thus, the study protocol was not integrated. For example, some patients underwent chest CT and the others did not, which limits the radiation dose estimation. Second, regarding tumour depiction, this study included only patients with renal tumours; thus, the specificity, negative predictive value, and accuracy could not be evaluated. Third, fine anatomical structures, such as tumour extension to the Gerota's fascia, were not evaluated. Further studies to verify the clinical utility of reconstructed images from perfusion CT data in evaluating local tumour extension are necessary. Fourth, as it is self-evident that contrast enhancement of veins in perfusion CT would be inadequate because of the insufficient iodine mass administered,[10] the conspicuity of veins was not compared. For this limitation, additional conventional images should be obtained after the perfusion CT series so that enough information about veins can be provided if the renal function is preserved. Fifth, as perfusion CT can cover 16 cm in the craniocaudal direction, the orifice of an anomalous renal artery originating from an iliac artery could be missed.

In conclusion, even though the role of perfusion CT of the kidney remains a matter of debate, a reconstructed image with a low iodine dose can provide sufficient anatomical information for visualising the renal artery and cortex as well as tumour detection, with a significant reduction in radiation dose compared to C-CT.

Conflict of interest

Y. Asayama is a staff of joint research department in Kyushu University with Canon Medical systems corporation.

Acknowledgement

This study was supported by Canon Medical systems corporation.

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