How Much Dose Can Be Saved in Three-Phase CT Urography? A Combination of Normal-Dose Corticomedullary Phase With Low-Dose Unenhanced and Excretory Phases

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OBJECTIVE. The purpose of this study was to investigate the degree to which the total radiation dose for CT urography can be lowered by selective reduction of the dose in the unenhanced and excretory phases when images in these phases are systematically evaluated alongside normal-dose corticomedullary phase images.

SUBJECTS AND METHODS. Twenty-seven patients (mean age, 74 ± 9 years) underwent single-bolus CT urography with acquisition in the unenhanced, corticomedullary, and 5-minute excretory phases. The scanning parameters for normal-dose CT urography were as follows: 16 × 0.75 mm, 120 kV, and automatic exposure control technique reference tube loads of 100, 120, and 100 effective mAs (mAs_{eff}). The patients also underwent low-dose unenhanced and excretory phase scanning, in which the dose was escalated stepwise from a volume CT dose index ($CTDI_{vol}$) of 1.7 to 6.6 mGy (reference 20–40–60–80 mAs_{eff}). Images were analyzed for quality and diagnostic confidence. If low-dose scans of three patients were inadequate, the study continued to the next dose level. When 20 patients were successfully included in the unenhanced and excretory phase groups, the study ended. Doses were calculated with a CT patient dosimetry calculator.

RESULTS. Combined with the normal dose for corticomedullary phase scanning, doses of $CTDI_{vol}$ 1.5 mGy for the unenhanced phase and $CTDI_{vol}$ 2.7 mGy for the excretory phase were sufficient. The effective dose for three-phase CT urography was lowered from 16.2 to 9.4 mSv, a decrease of 42%. Diagnostic confidence in low-dose images was equal to that in normal-dose images when low-dose unenhanced and excretory phase images were read alongside normal-dose corticomedullary phase images.

CONCLUSION. With a three-phase CT urographic protocol, significant dose reductions in the unenhanced and excretory phases can be achieved when these phases are combined with a normal-dose corticomedullary phase.

Keywords: CT urography, dose escalation, hematuria, radiation dose

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Patients examined with CT are exposed to relatively high radiation doses and a potentially increased lifetime risk of developing radiation-induced cancer [1]. It is the radiologist's responsibility to continually work to lower the radiation dose according to the ALARA (as low as reasonably achievable) principle [2]. Therefore, radiologists must adapt image quality to diagnostic needs. A CT urographic examination traditionally consists of three acquisitions [3]. Scanning is performed before contrast administration (unenhanced phase); early after IV contrast injection (nephrographic phase) with an 80- to 120-second postinjection delay or, as in this study, in the corticomedullary phase, with a 20- to 30-second postinjection delay; and a late, or excretory, phase 5–15 minutes after IV contrast injection. Previous research [4] has shown that ultralow doses can be used in the unenhanced phase and calculi in the urinary tract will not be overlooked. Another group [5] found that decreasing the tube load to 70 mAs_{eff} (volume CT dose index [$CTDI_{vol}$], 5.3 mGy) is possible in the excretory phase.

Because diagnosis with CT urography is reached by combining the information from the various phases, all three scans obtained with this technique do not have to have optimal image quality. It is sufficient that the image quality be excellent in one of the three acquisitions (Fig. 1). A reduced dose, resulting in more image noise, can be accepted in the other phases, such as the unenhanced and excretory phases, if these images are systematically reviewed together with normal-dose corticomedullary or nephrographic phase images of the whole abdomen and pelvis.

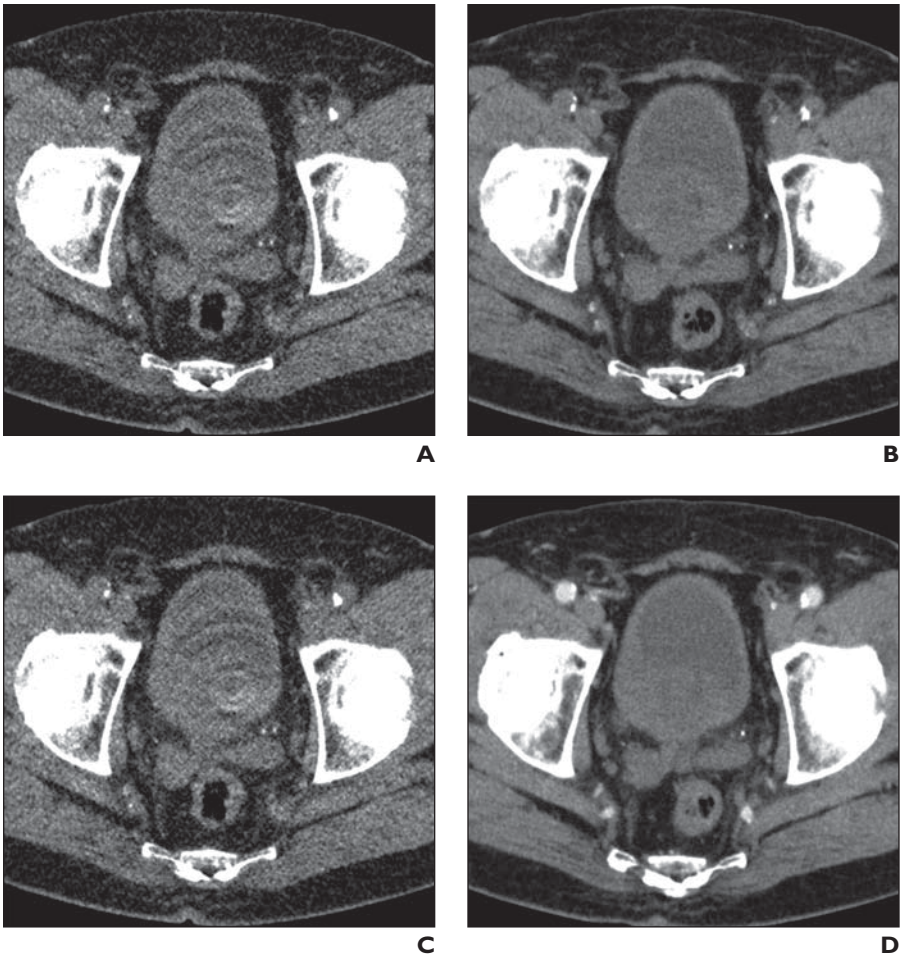


Fig. 1—77-year-old man with gross hematuria. Only one phase needs excellent image quality, and those images are used as anatomic roadmap for review of scans from phases with reduced image quality. There is no need for excellent quality of unenhanced scan (**B**) if corticomedullary scan (**D**) is used for anatomic reference in review of noisy reduced-dose images (**A** and **C**).
A, Low-dose unenhanced CT scan (volume CT dose index [$CTDI_{vol}$], 1.5 mGy).
B, Normal-dose unenhanced CT scan ($CTDI_{vol}$, 7.0 mGy).
C, Low-dose unenhanced CT scan ($CTDI_{vol}$, 1.5 mGy).
D, Normal-dose corticomedullary phase CT scan ($CTDI_{vol}$, 9.4 mGy).

The unenhanced phase is used to detect urinary tract calculi and provide baseline attenuation values for densitometry of lesions. The excretory phase is needed to evaluate renal excretion of IV contrast medium and to detect pathologic changes in the renal parenchyma to assist in detection of tumors in the collecting system, ureter, and bladder. The corticomedullary or nephrographic phase is needed to detect tumors in the kidneys, collecting system, ureters, and bladder and to provide information about vascular anatomy and renal function. Because the corticomedullary phase provides the most important information for patients undergoing workup for suspected upper urinary tract malignancy, it was decided that the radiation dose in the dose-escalation study would be reduced in the unenhanced and excretory phases and remain unchanged in the corticomedullary phase.

The normal-dose corticomedullary phase can be used for anatomic correlation of information on noisy low-dose unenhanced and excretory phase images. In addition, the excretory phase is not the only phase in which urothelial cell carcinoma can be detected. Urothelial cell carcinoma becomes enhanced soon after contrast administration [6–8] and can be detected in the corticomedullary or nephrographic phase or if the urinary tract, including the bladder, is well distended with urine, which acts as a negative contrast medium.

The CT urographic protocol chosen in this study was the standard CT urographic protocol used at our institution. It differs from that used at most centers, where the nephrographic phase is used instead of the corticomedullary phase [3]. Our decision to perform a corticomedullary phase acquisition was based on earlier research focusing on renal cell carcinoma [9–11]. When focus in recent years turned to urothelial cell carcinoma, the corticomedullary phase proved useful in detecting urothelial cell carcinoma in the upper urinary tract and bladder. Several reports describe urothelial cell carcinoma as strongly enhancing with contrast material [6–8] in the early phase after contrast administration. A prospective study with patients undergoing workup because of gross hematuria was performed with an unenhanced, corticomedullary, nephrographic, and excretory phase protocol. Preliminary results (Helenius M, oral communication, 2011) have shown that bladder tumors are most enhancing in the corticomedullary phase. Furthermore, imaging the whole urinary system in the early phase after contrast administration—in the corticomedullary or nephrographic phase—improves detection of nodal metastasis and facilitates local tumor staging.

The aim of this study was to investigate the degree to which the total CT urographic radiation dose can be lowered by selectively reducing the dose in the unenhanced and excretory phases when the images from these phases are systematically evaluated alongside normal-dose corticomedullary phase images. A secondary aim was to verify that attenuation measurements on low-dose images are comparable to measurements on normal-dose images.

Subjects and Methods

The faculty ethics review board approved the study. Written informed consent was obtained from all patients.

Study Design

This single-center crossover open-label dose-escalation study was performed to determine the efficacy of low-dose radiation in the unenhanced and excretory phases of CT urography. Patients who met the inclusion criteria and who signed informed consent documents received additional low-dose scanning at one of four low dose levels as part of the dose-escalation protocol. Because patients also underwent normal-dose scanning in the unenhanced and excretory phases, they acted as their own controls. One patient at a time was recruited to each dose tier. The efficacy data were reviewed every time a patient completed imaging. The study advanced to the next dose tier if sufficient efficacy was not observed for the low radiation dose in three

patients. To minimize the risk to the patients due to the increased radiation dose, only patients older than 45 years with a body mass index (weight in kilograms divided by the square of height in meters) less than 30 were included. Patients not eligible for IV contrast administration owing to reduced kidney function were excluded from participation.

Patients

Twenty-seven patients (20 men, seven women; mean age, 74 ± 9 [SD] years; range, 56–89 years; mean body mass index, 25 ± 3; range, 18–28) referred to our department for CT urography were included in the study. Twenty of the patients were referred for CT for analysis of macroscopic hematuria, four patients because of urinary tract infection, two patients for follow-up CT because of known renal abnormalities (atypical cyst and tumor), and one patient because of advanced stone disease.

CT Urographic Technique

The CT urographic examinations were performed with a 16-MDCT scanner (Siemens Sensation 16, Siemens Healthcare) with an Akron x-ray tube. The standard CT urographic protocol consisted of three phases: unenhanced, corticomedullary, and 5-minute delayed excretory. All phases included acquisition from the top of the kidney to the pubic symphysis. An angular automatic tube current modulation system (CARE Dose, Siemens Healthcare) was used. The scanning parameters were as follows: tube voltage, 120 kV; tube load, 100, 120, and 100 reference effective mAs (mAs_{eff}) for the unenhanced, corticomedullary, and excretory phases ($CTDI_{vol}$, 8.3, 9.9, and 8.3 mGy); rotation time, 0.5 second; collimation, 16 × 0.75 mm; pitch, 1; image reconstruction with slice thickness and increment, axial 5/5 mm and 1/1 mm, coronal 5/5 mm. The reference effective tube current–time setting is the input parameter for the CARE Dose software; the actual delivered dose usually deviates slightly from this number.

In addition to normal-dose CT urography, the patients included in the study underwent low-dose scanning in the unenhanced and excretory phases. All scans were acquired from the diaphragm to the pubic symphysis. The following low-dose reference tube loads were used: 20 mAs_{eff} ($CTDI_{vol}$, 1.7 mGy), 40 mAs_{eff} ($CTDI_{vol}$, 3.3 mGy), 60 mAs_{eff} ($CTDI_{vol}$, 5.0 mGy), and 80 mAs_{eff} ($CTDI_{vol}$, 6.6 mGy). With the exception of the reduced tube load, all scanning parameters were identical for the low-dose unenhanced and low-dose excretory phase scans. In the excretory phase, patients were randomized to low-dose (n = 14) or normal-dose (n = 13) scans to be obtained first.

Seven of the 27 patients underwent additional scanning in the low-dose unenhanced and low-dose excretory phases with a tube load of 20 mAs_{eff}. Thirteen patients underwent additional low-dose unenhanced scanning with a tube load of 20 mAs_{eff} and low-dose excretory phase scanning with a tube load of 40 mAs_{eff}. Seven patients underwent additional scanning in the low-dose excretory phase with a tube load of 40 mAs_{eff} only.

Contrast Material

A dose of 80 mL iopromide 300 mg I/mL (Ultravist, Bayer Schering Pharma) was administered at a rate of 3–4 mL/s with a double-barrel power injector (Stellant D, Medrad). The corticomedullary acquisition started automatically when the attenuation value in the region of interest (ROI) placed in the aorta at the level of the diaphragm reached 200 HU. For adequate distention of the collecting systems, the patients received oral hydration with water, 800 mL over 120 minutes before the examination. Patients were asked not to void before the CT examination and received IV diuretics (10 mg furosemide) at the start of the examination.

Effective Dose

The effective dose to the standard patient was calculated with the ImPACT CT patient dosimetry calculator (version 1.0.2, ImPACT). In the program, the start of the operator-planned scan was set to the diaphragm in the virtual patient (position 44), and the end of the scan was set to the pubic symphysis (position 2). The planned scanning length was thus set at 42.0 cm per phase. An additional average overrange of 3.0 cm per phase (1.5 cm on each side) was incorporated into the dose calculations, increasing the scan range from position 45.5 to position 0.5 [12]. Angular automatic tube current modulation was used in the xy plane. Therefore, the effective tube current–time product varied between patients. The mean value of the effective tube current–time product in each phase was used in the calculations.

Endpoint Assessment

The primary endpoint was to compare the quality of CT urographic images obtained with the low radiation dose with that of images obtained with the standard dose. The reviewer evaluated the images according to a protocol used to assess image quality and diagnostic confidence. The unenhanced and excretory phase scans were evaluated separately and on separate dates to avoid intrarater bias. The evaluation was performed by consensus of two radiologists with 5 and 20 years of experience in radiology. Reader 1 performed the attenuation measurements at a later point in time, and the same ROI placement was used for the different scans of each patient. The size of the ROI in the liver varied slightly between patients depending on the anatomy. In each patient, however, the same ROI area was used on the different scans. The size of the ROI was kept as large as possible. This feasibility study was focused on the diagnostic confidence of the radiologist (reading low-dose images and reading normal-dose corticomedullary phase images for anatomic correlation). The number of patients was too small for conclusions on diagnostic accuracy.

Subjective Evaluation of Image Quality

First, the low-dose images were scored on a 2-point scale (0, not visible; 1, visible) according to a modified version of the European Commission image quality criteria [13] for visualization of anatomic structures. These images were then evaluated on a 2-point scale (0, no abnormality; 1, abnormality present) for the presence of urinary tract abnormalities (on the low-dose unenhanced images for calcifications, phleboliths, tumors, and signs of obstruction and on the low-dose excretory phase for filling defects, signs of obstruction, and abnormalities of the renal vein, caval vein, and liver) and for diagnostic confidence on a 5-point scale (1, nondiagnostic; 2, poor; 3, acceptable; 4, good; 5, excellent). Second, the normal-dose images in the unenhanced and excretory phases were judged according to the same protocol. Third, if discrepancies were found between the findings on the low- and normal-dose images in the unenhanced and excretory phases, the low-dose unenhanced and low-dose excretory phase images were evaluated together with the corticomedullary phase images to see whether the shortcomings of the low-dose images were nullified. If there was a discrepancy between the low-dose images and the normal-dose images and the error was not corrected after review of the low-dose images together with the corticomedullary phase images, then the examination was judged a failure. Finally, overall diagnostic confidence was scored on the aforementioned 5-point scale after review of the low tube current–time setting images together with normal-dose corticomedullary phase images.

In the review process, the urinary tract was divided into five segments: 1, renal calices and pelvis; 2, upper ureter (ureteropelvic junction to iliac crest); 3, middle ureter (ureter overlying iliac bone); 4, lower ureter (ureter below iliac bone to the ureterovesical junction); 5, bladder. The left and right sides were scored separately. In the unenhanced phase, visibility of the five urinary tract segments was scored on a 2-point scale (0, not identifiable; 1, identifiable), and in the excretory phase, the contrast filling was scored on a 2-point scale (0, not opacified; 1, opacified). In the unenhanced phase, it was not necessary to outline the entire segment of the ureter but was sufficient to identify the anatomic structure.

Objective Evaluation of Image Quality

Image quality on low- and normal-dose images was further evaluated by measurement of attenuation and noise, expressed as the SD of attenuation in Hounsfield units in two standardized ROIs placed in the same anatomic location in the liver (above the hepatic portal vein) on low- and normal-dose images. Attenuation and image noise measurements were performed on all focal renal lesions. To ensure that attenuation measurements on low- and normal-dose scans are comparable, the difference between attenuation measurements in each patient was calculated. The mean difference was presented with ± 1.96 SD.

Artifacts

Artifacts observed on the low-dose images were judged on a 5-point scale (1, no artifacts; 2, slight artifacts; 3, moderate degree of artifacts; 4, heavy artifacts making diagnosis difficult; 5, nondiagnostic due to artifacts).

Statistical Analysis

All 27 patients who were enrolled and treated with one of the escalating doses completed the study. Hence there were no differences between the intention-to-treat and the per-protocol populations. Diagnostic confidence was assessed as mean ± SD and range. Comparison of the diagnostic confidence score acquired with the low doses and high doses was performed with the Wilcoxon rank sum test. The Wilcoxon rank sum test was also used to compare diagnostic confidence acquired in reading the combination of the low-dose image with the corticomedullary phase information and diagnostic confidence acquired when only the high-dose images were considered. A p equal to 0.05 value was considered significant. Bland-Altman plots [14] were used to compare the accuracy and level of agreement for the high and low radiation doses. All analyses were performed with R software (version 2.11, R Foundation for Statistical Computing).

Results

Subjective Evaluation of Image Quality

Unenhanced phase—In the unenhanced acquisition group, 20 patients were included at the 20-mAs_{eff} reference level without loss of clinically important information in any patient. The actual delivered tube loads are summarized in Table 1. The corresponding calculated effective doses were 1.0 mSv in the low-dose unenhanced phase and 4.9 mSv in the normal dose unenhanced phase. None of the imaging of the 20 patients enrolled at the 20 mAs_{eff} reference level was judged a failure.

Fewer urinary tract anatomic structures were visualized on low-dose than normal-dose unenhanced phase images (Table 2). All structures were visualized when low-dose unenhanced images were viewed together with corticomedullary phase images. No urinary tract or vessel calcifications were missed in the low-dose unenhanced compared with the normal-dose unenhanced phase. In one case, a phlebolith close to the distal ureter seen in the low-dose unenhanced phase was misdiagnosed as being in the ureter. The mistake was obvious on normal-dose unenhanced phase images and when low-dose unenhanced phase images were viewed with corticomedullary phase images for correlation.

The mean diagnostic confidence score was 3.7 ± 0.9 (range, 2–5) after viewing of the low-dose unenhanced images, 4.8 ± 0.4 (range, 4–5) after viewing of the normal-dose unenhanced images, and 4.9 ± 0.3 (range, 4–5) after viewing of the low-dose unenhanced images in combination with the corticomedullary phase images. The diagnostic confidence was significantly lower for the low-dose than for the normal-dose unenhanced images ($p < 0.001$). Combining the low-dose unenhanced images and the corticomedullary phase images resulted in significantly better diagnostic confidence than considering the normal-dose unenhanced images only ($p < 0.05$) (Fig. 2).

Excretory phase—The reference dose level of 20 mAs_{eff} was abandoned after imaging of seven patients. The formal criteria for failure were not filled because the shortcomings of the low-dose excretory phase compared with normal-dose excretory phase were nullified when low-dose excretory phase images were judged with corticomedullary phase images for anatomic correlation. The image quality for three of seven patients was judged inadequate because image noise and artifacts in the pelvis made it impossible to exclude small filling defects in the urinary tract (Fig. 3). The diagnostic confidence score was 3.1 ± 0.9 (range, 2–4) after viewing of the low-dose excretory phase images, 4.3 ± 0.7 (range, 3–5) after viewing of the normal-dose excretory phase images, and 4.4 ± 0.5 (range, 4–5) after viewing of the low-dose excretory phase images in combination with the corticomedullary phase images. The diagnostic confidence was significantly lower for the low-dose than for the normal-dose excretory phase ($p < 0.01$). Combining the low-dose excretory and corticomedullary phase images was not significantly different from considering the normal-dose excretory phase images ($p = 0.53$) (Fig. 2).

Twenty patients were included at the reference dose level of 40 mAs_{eff} without loss

TABLE 1: Volume CT Dose Index and Effective Dose Calculated With CT Patient Dosimetry Calculator (ImPACT)

Phase	Actual Mean Tube Load (mAs_{eff})	Volume CT Dose Index (mGy)	Effective Dose (mSv)
Low-dose unenhanced	17.6	1.5	1.0
Normal-dose unenhanced	84.8	7.0	4.9
Corticomedullary	114.0	9.4	6.5
Low-dose excretory (40 mAs_{eff})	33.2	2.7	1.9
Normal-dose excretory	83.6	6.9	4.8

Note—Volume CT dose index values refer to actual delivered mean effective tube current–time product and not to the reference effective values set prospectively in CARE Dose (Siemens Healthcare). mAs_{eff} = effective mAs.

TABLE 2: Number of Urinary Tract Anatomic Structures Identified on Low- and Normal-Dose Unenhanced Images

Structure	Phase		
	Low-Dose Unenhanced	Normal-Dose Unenhanced	Low-Dose Unenhanced and Corticomedullary
Gerota fascia ($n = 40$)	27	40	40
Renal lesions (20 kidneys)	13	20	20
Upper ureter ($n = 40$)	38	40	40
Middle ureter ($n = 40$)	28	40	40
Lower ureter ($n = 40$)	27	40	40
Exact borders of bladder ($n = 20$)	15	20	20

Note—All structures were identified when low-dose unenhanced phase images were reviewed together with the normal-dose corticomedullary phase used for anatomic correlation.

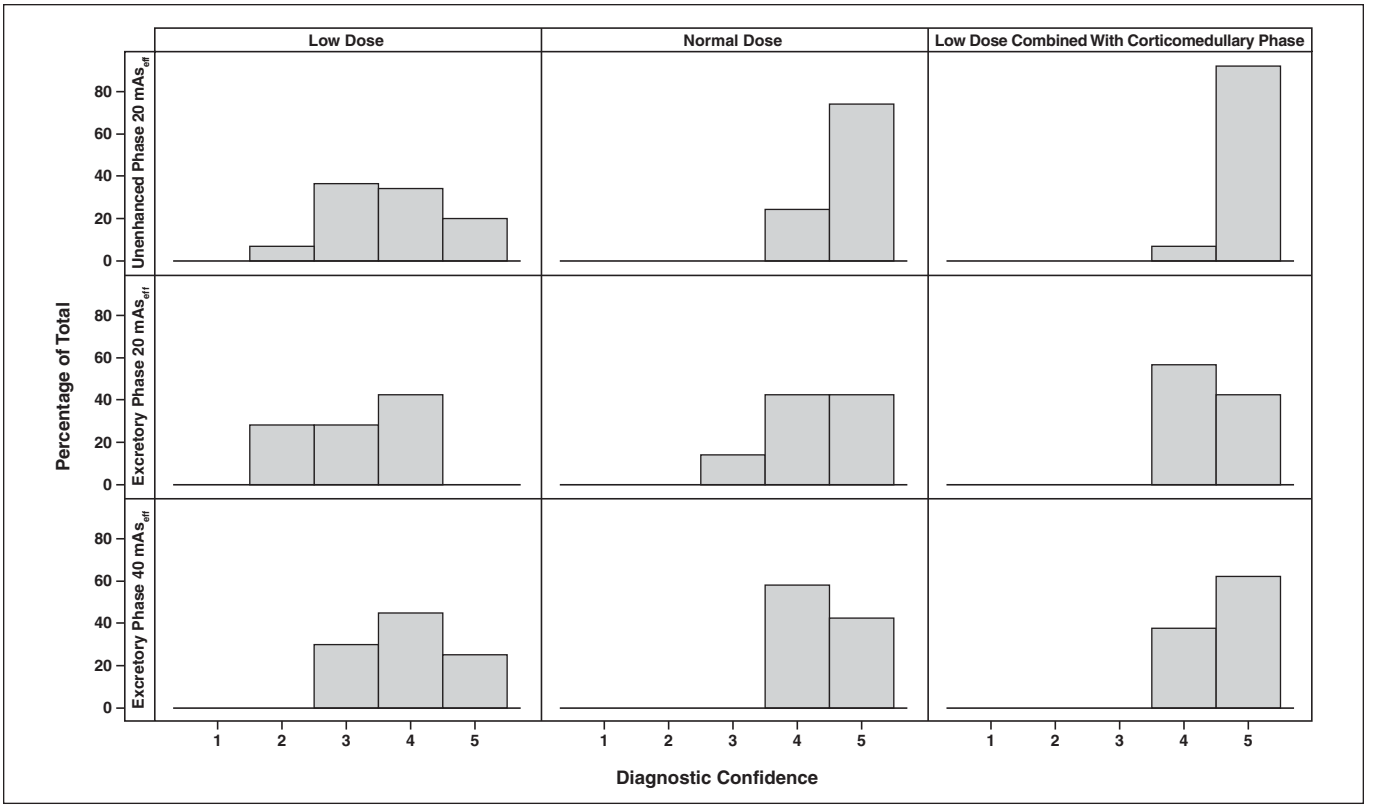


Fig. 2—Graphs show distribution of diagnostic confidence in imaging of patients with low radiation dose, normal dose, and low dose in combination with corticomedullary phase acquisition.

of information on any patient. Thirty-nine renal collecting systems were opacified on both low-dose and normal-dose excretory phase images and were reviewed according to the study protocol, as were 36 upper ureter segments, 31 middle segments, and 27 lower segments. In the 39 systems evaluated, there were no tumors in the renal pelvis or ureter. Bladder tumors were diagnosed in four patients. One small bladder tumor (diameter < 1 cm) was not seen on the low-dose excretory phase images but was diagnosed on the normal-dose excretory phase images and the low-dose excretory phase images in combination with the corticomedullary phases images. In this case, the degree of bladder distention was suboptimal, and contrast layering between urine and excreted contrast material was present. The diagnostic confidence after the low-dose excretory phase was 4.0 ± 0.7 (range, 3–5), after the normal-dose excretory phase was 4.4 ± 0.5 (range, 4–5), and after the low-dose excretory in combination with the corticomedullary phase was 4.6 ± 0.5 (range, 4–5). The diagnostic confidence was significantly lower for the low-dose excretory than for the normal-dose excretory phase ($p < 0.001$). Combining the low-dose excretory phase and corticomedullary phase images resulted in significantly better diagnostic confidence than only considering the normal-dose excretory phase images ($p < 0.01$) (Fig. 2).

Objective Evaluation of Image Quality

The attenuation measurements in the liver and renal cysts on the low- and normal-dose unenhanced images and low- and normal-dose excretory phase images are presented in Table 3. The reduced image quality, due to noise, on the low-dose unenhanced and excretory phase images compared with the normal-dose unenhanced and excretory phase images was seen as an increased mean value of the individual SD in the ROIs.

In the comparison of attenuation measurements performed on low- and normal-dose unenhanced images, the mean difference in the liver was 2.8 ± 2.1 HU (range, –1 to 7 HU) and in renal cysts was 2.9 ± 2.7 HU (range, –3 to 8 HU). The mean attenuation value in both the liver and in the renal cysts was higher in the low-dose unenhanced phase. The attenuation values were also slightly higher on the low-dose images in the excretory phase. The mean difference was 1.4 ± 2.5 HU (range, –4 to 6) in the liver and 0.9 ± 3.5 HU (range, –5 to 9) in renal cysts. The differences in attenuation measurements in renal cysts and liver parenchyma between low- and normal-dose scans are shown in Bland-Altman plots in Figure 4.

The mean ROI area in the liver was 22.5 ± 6.6 cm^2 (range, 8.7–36 cm^2) on the low-dose unenhanced images and 21.8 ± 7.3 cm^2 (range, 8.4–37 cm^2) on the normal-dose unenhanced images. In the excretory phase the area was 25 ± 8.5 cm^2 (range, 10.8–47 cm^2) on the low-dose images and 22.9 ± 8.3 cm^2 (range, 10.1–50) cm^2 on the normal-dose images.

Image Artifacts

In addition to the increased image noise, ring artifacts in the pelvis were a problem on the low-dose images. The artifacts in the small pelvis were especially troublesome, the presence of a metal hip prosthesis causing additional beam-hardening artifacts. The levels of artifacts were 2.9 ± 1.0 (range, 1–5) in the low-dose unenhanced phase, 2.6 ± 0.9 (range, 2–4) in the low-dose excretory phase at 20 mAs_{eff}, and 1.7 ± 0.9 (range, 1–4) in the low-dose excretory phase at 40 $mAs_{eff.}$

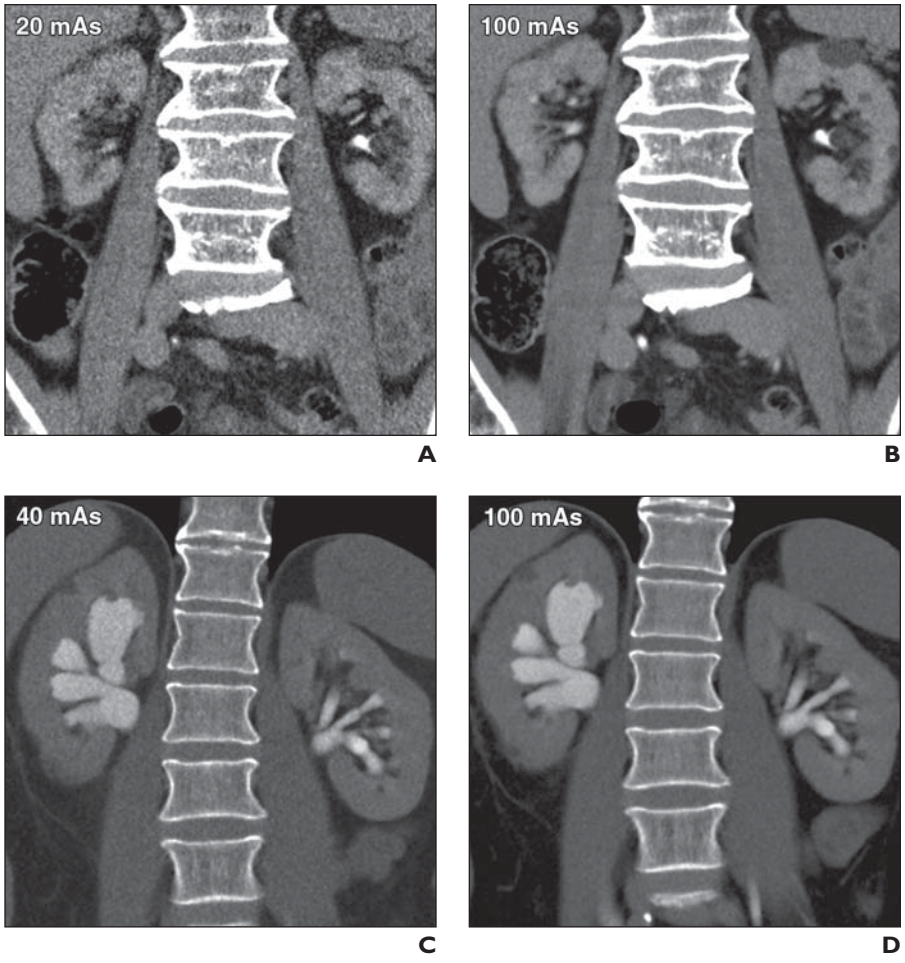


Fig. 3—Examples of image quality in excretory phase at different dose levels. Increased image noise made it difficult to safely rule out small urothelial cell carcinomas in collecting system on 20-mAs excretory phase images. When image quality was judged inadequate owing to image noise and artifacts in pelvis, 20-mAs_{eff} level was abandoned in imaging of three of seven patients.
A and **B,** 80-year-old woman with gross hematuria. Excretory phase CT scan obtained at 20 mAs_{eff} (**A**), excretory phase CT scan obtained at 100 mAs_{eff} (**B**).
C and **D,** 72-year-old man with gross hematuria. Excretory phase CT scan obtained at 40 mAs_{eff} (**C**), excretory phase CT scan obtained at 100 mAs_{eff} (**D**).

Effective Dose

The total effective dose from CT urography was reduced 42%, from 16.2 to 9.4 mSv (Table 1) with a combination of normal-dose corticomedullary phase (reference dose, 120 mAs_{eff}) with low-dose unenhanced (reference dose, 20 mAs_{eff}) and excretory phase (reference dose, 40 mAs_{eff}) acquisition.

Discussion

The last decade has seen dramatic improvement in CT technology. The introduction of MDCT has resulted in advancement of *xyz* axis spatial resolution (isotropic scanning), shorter scan times, and increased patient throughput [15, 16]. Thus CT is a key technique in uroradiology, and CT urography has replaced excretory urography at many centers.

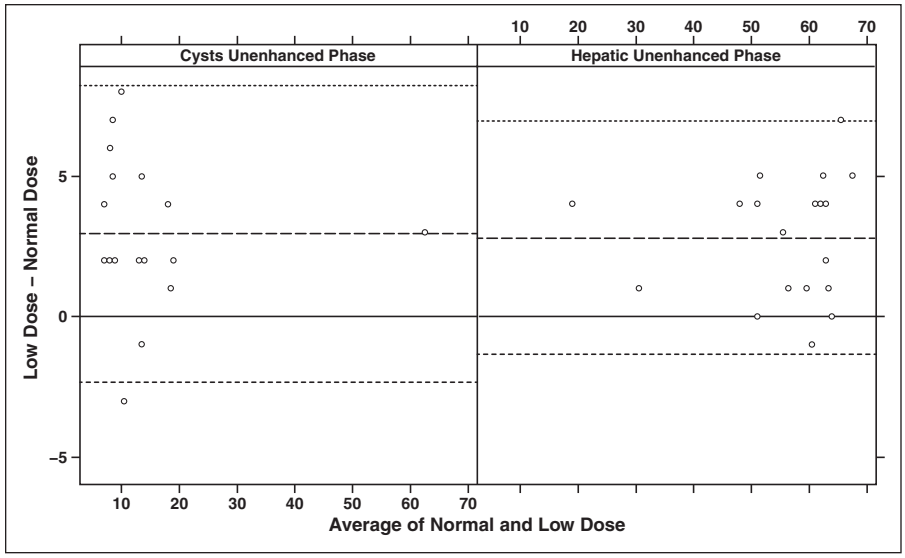
The major disadvantage of CT is the high patient radiation dose compared with that in other imaging modalities. Therefore, it is important to focus research on justification of CT urography and optimizing CT scan protocols and scanning tube load parameters according to the ALARA principle. In this study, a novel concept was adopted whereby low-dose images in the unenhanced and excretory phases were systematically evaluated together with normal-dose corticomedullary phase images, that is, combined low- and normal-dose CT urography. With the combination of image information from all three phases, the tube load was lowered considerably, and the total effective dose decreased from 16.2 to 9.4 mSv without loss of clinically important information.

The rationale behind this study was that there are advantages to keeping the different scan phases separate and that it is possible to reduce radiation doses in the unenhanced and excretory phases if the resulting noisy low-dose images are systematically reviewed with normal-radiation-dose optimal-image-quality corticomedullary or nephrographic phase images as roadmaps. The hypothesis was tested in a dose-escalation study design. The results of this study show that it is possible to use three separate phases and reduce the dose to a $CTDI_{vol}$ of 1.5 mGy in the unenhanced phase and 2.7 mGy in the excretory phase without loss of information if the corticomedullary phase scan is obtained at a

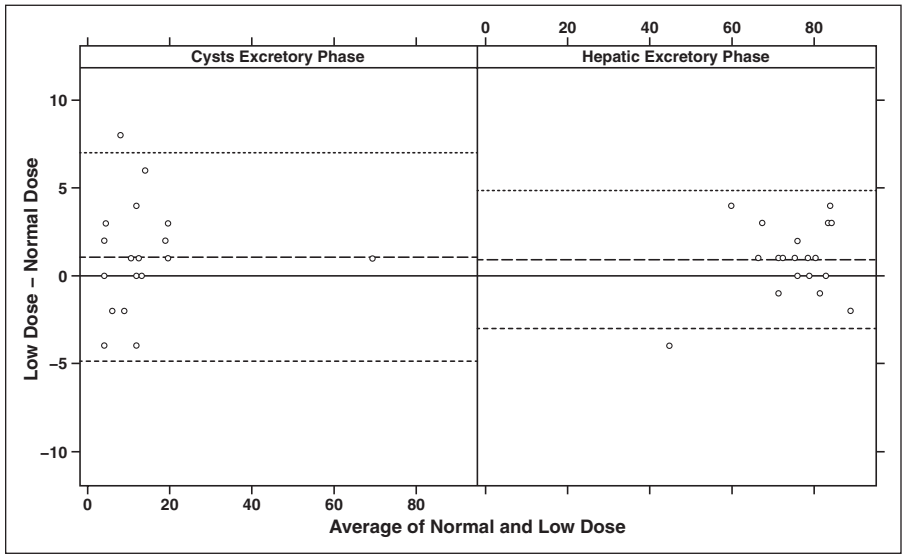
TABLE 3: Objective Evaluation of Image Quality

	Phase							
	Low-Dose Unenhanced, 20 mAs (n = 20)		Normal-Dose Unenhanced, 100 mAs (n = 20)		Low-Dose Excretory, 40 mAs (n = 20)		Normal-Dose Excretory, 100 mAs (n = 20)	
Structure	Mean Attenuation	Mean SD	Mean Attenuation	Mean SD	Mean Attenuation	Mean SD	Mean Attenuation	Mean SD
Liver	57 (21–70)	33 (19–46)	55 (17–65)	15 (9–20)	76 (43–88)	25 (16–32)	75 (47–90)	16 (10–20)
Cyst	16 (8–64)	31 (17–53)	13 (5–61)	14 (6–21)	14 (2–70)	22 (14–29)	13 (3–69)	13 (10–22)

Note—All values are Hounsfield units. Values in parentheses are ranges. Attenuation measurements on low-dose images must be reliable. Attenuation measurements were performed in the liver and in all focal renal lesions in the low- and normal-dose unenhanced and excretory phases. A total of 15 cysts were evaluated on normal-dose unenhanced scans and 23 cysts on normal-dose excretory phase scans. One of the cysts had high attenuation. The differences between low- and normal-dose measurements are shown in Figure 3.



A



B

Fig. 4—Bland-Altman plots show differences between attenuation measurements in liver and renal cysts on low- and normal-dose images. Circles indicate instances of 40–100 effective mAs (mAs_{eff}); dashed lines, mean of 40–100 mAs_{eff}; dotted lines, ± 1.96 SD.
A, Unenhanced phase.
B, Excretory phase.

$CTDI_{vol}$ of 9.4 mGy and is used for anatomic correlation. Use of this technique reduces the effective dose from 4.9 to 1.0 mSv in the unenhanced phase and from 4.8 to 1.9 mSv in the excretory phase. The total dose for CT urography is reduced 42%.

The $CTDI_{vol}$ levels in this study are even lower than those suggested by the European Society of Urogenital Radiology CT urography working group [3]. The society suggests that imaging in the unenhanced phase ought to be feasible with $CTDI_{vol}$ values of 2–3 mGy; corticomedullary phase, 7–8 mGy; and excretory phase, 4–5 mGy. The average effective dose from multiphase CT urography protocols ranged between 16 and 22 mSv in a pilot study of a multicenter CT urographic dose analysis (van der Molen AJ, et al., presented at the 2010 annual meeting of the American Roentgen Ray Society). Few reports can be found in which the effective dose from a split- or triple-bolus protocol is reported. Because one of three scans is discarded, the effective dose ought to be reduced by 30%. The effective dose from a triple-contrast-bolus two-phase protocol including an unenhanced phase is reported to be 13.2 mSv, that is, 3.4 and 9.8 mSv in the two phases [17].

There are advantages to keeping the contrast phases separate in single-contrast-bolus three-phase CT urography: The protocol is more flexible for adapting delay times when unilateral obstruction is present; lesion characterization is safer because attenuation can be measured at three different times; and small urothelial cell carcinoma may be missed in the excretory phase or the combined nephrographic and excretory phases because of blooming artifact from concentrated contrast material, especially in the lower urinary tract and the calices. The blooming artifact in the bladder can be avoided by having patients urinate before the examination and by using a delayed excretory phase [18]. In the protocol in this study, however, in which CT urography is performed with a distended bladder, the artifact can be troublesome. Urothelial cell carcinoma also becomes enhanced with contrast medium in the corticomedullary and nephrographic phases [6] and is detectable on these scans. Therefore, in a CT urographic protocol with separate corticomedullary (or nephrographic) and excretory phase scans, the urothelium can be evaluated twice, which may improve the chance of urothelial cell carcinoma detection. Urothelial cell carcinoma can occur in the entire urinary collecting system: renal collecting system, ureters, and bladder [19]. Because urothelial cell carcinoma is early and strongly enhancing [7, 8, 20], serial attenuation measurements in the unenhanced, corticomedullary, and excretory phases can confirm the presence of urothelial cell carcinoma [6] or nonenhancing blood clots. Therefore, the whole urinary tract is imaged in the unenhanced, corticomedullary, and excretory phases for patients in whom urothelial cell carcinoma is strongly suspected.

The number of patients in this study was too small for conclusions about diagnostic accuracy. In the 27 patients included in the study, no abnormality was missed when all three scans (low-dose unenhanced and excretory phases, normal-dose corticomedullary phase) were read together.

Justification of CT urography is a key factor in dose containment, and the European Society of Urogenital Radiology CT urography working group puts emphasis on this issue. The Netherlands Society of Urology suggested an algorithm whereby CT urography should be the first-line diagnostic test only for patients at high risk of malignancy,

that is, for imaging of gross hematuria in patients older than 50 years and in patients with known or strongly suspected urothelial cell carcinoma [21]. For all other risk categories, corticomedullary phase CT urography is a problem-solving test if initial test results remain inconclusive and symptoms persist.

Several technical developments have been introduced since this study was performed. CT vendors now provide tools such as volumetric tube current modulation [22], adaptive collimation with automatic shutters to shield patients from overscanning [23], and increased computer power that allows use of 3D adaptive noise filters and iterative reconstruction (e.g., ASIR, GE Healthcare) [24]. These technical and software tools promise to enable even more dose reduction. In addition, modern dual-source CT scanners offer virtual unenhanced imaging. Virtual unenhanced imaging promises possible dose reduction as high as 30%, making unenhanced scans unnecessary. Early reports on virtual unenhanced imaging have been optimistic [25]. The biggest drawback of virtual unenhanced imaging is that small calculi might be missed [26]. Even small calculi can be important in patients with hematuria. Further studies on the detection of small calculi, their clinical significance, and the reliability of attenuation measurements are needed before the unenhanced phase can be safely eliminated.

The results of this feasibility study show that detection of calcifications in the unenhanced phase is not a problem on low-dose images. However, further studies with larger patient samples are needed to verify that small urothelial cell carcinoma is not missed in the excretory phase with reduced $CTDI_{vol}$ settings.

Correct attenuation measurements are essential in CT urography for accurate characterization of renal lesions as cysts or tumors. In the evaluation of contrast enhancement in MDCT, enhancement of 20 HU or more strongly suggests that a renal lesion is solid [27]. Enhancement of 10–20 HU is considered unequivocal, and further follow-up of the lesion with contrast-enhanced ultrasound or MRI should be pursued. In the current study, the attenuation measurements on the low-dose scans were slightly higher than those on normal-dose images (Fig. 4). In the unenhanced phase (20 mAs_{eff} compared with 100 mAs_{eff}), the mean difference was 2.8 ± 2.1 HU in the liver and 2.9 ± 2.7 HU in renal cysts. In the excretory phase (40 mAs_{eff} compared with 100 mAs_{eff}), the mean difference was 1.4 ± 2.5 HU in the liver and 0.9 ± 3.5 HU in renal cysts. There was more image noise on low-dose images, and expectedly, attenuation measurements on low-dose images increase uncertainty. The results of this study support the hypothesis that baseline attenuation measurements in the low-dose unenhanced phase are comparable to those in the normal-dose unenhanced phase.

There were limitations to this study. It was a feasibility study with a small number of patients, and therefore the results are preliminary. When the study was performed, only angular automatic tube current modulation was available to us. Because the abdomen is a fairly homogeneous structure, the results ought to be comparable to those obtained with current volumetric automatic tube current modulation techniques with dose modulation in the *xyz* axes.

The ring artifacts in the pelvis were troublesome, occurring whether or not low-dose scans were obtained after scanner calibration. Patients with suspected urinary tract malignancy are old, and a large number have undergone hip replacement. Metal beam-hardening artifacts were more pronounced on low-dose images. Two patients in the study had undergone hip replacement surgery, and one patient had metal rods in the lumbar spine after decompression surgery.

A dose-escalation study design was used in this project. The aim was to find a dose level at which image quality was sufficient in at least 85% of the patients. Twenty of 20 patients had sufficient image quality after imaging with a reference tube load of 20 mAs_{eff} in the unenhanced phase and 40 mAs_{eff} in the excretory phase. There is less than a 5% risk that 20 of 20 patients will pass the testing criteria, given that the true failure rate is 15%. It can therefore be concluded that a tube load of 20 mAs_{eff} in the unenhanced phase and of 40 mAs_{eff} in the excretory phase will be sufficient in more than 85% of cases. A dose-escalation study design is preferable in this situation because it has the chance of substantially reducing the number of subjects needed for the study. With a traditional study design, a total of 80 patients would have been needed to evaluate the efficacy of all four dose levels considered in this study. With the design used, only 27 patients were needed to find a sufficient dose. One limitation of the dose-escalation design is that the optimal dose level cannot be derived. For example, a higher radiation dose might provide additional information and improved diagnostic results. The dose-escalating design, however, was suitable in this study because the main aim was to identify the lowest possible dose to obtain sufficient image quality for most patients.

Conclusion

It is possible to reduce the total radiation for dose CT urography by 42% by selectively reducing the dose in the unenhanced and excretory phases and systematically evaluating the images obtained in these phases alongside those obtained in the normal-dose corticomedullary phase.

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