Evaluation of virtual unenhanced CT obtained from dual-energy CT urography for detecting urinary stones

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Objective: The aim of our study was to determine if virtual unenhanced CT (VUCT) is equivalent to unenhanced CT (UCT) for detecting urinary stones.

Methods: Our institutional review board approved this retrospective study, which was compliant with the Health Insurance Portability and Accountability Act. A total of 80 stones were detected in 32 patients among 146 consecutive patients undergoing dual-energy CT urography. The number and size of stones were recorded on nephrographic VUCT (NVUCT) and excretory VUCT (EVUCT) images, respectively. UCT was a reference of standard for the number and size of stones. Image quality of VUCT was qualitatively assessed using a five-point scale. Repeated-measures analysis of variance with post-test was used for statistical analysis.

Results: 62 stones in 29 patients were detected on NVUCT and 59 stones in 27 patients were detected on EVUCT. The size of stones detected on NVUCT or EVUCT was significantly smaller compared with stones on UCT ($p < 0.05$). The size of stones detected on UCT, NVUCT and EVUCT ranged from 1.4 to 19.2 mm (mean, 4.6 mm), 0 to 19.2 mm (mean, 3.6 mm) and 0 to 18.7 mm (mean, 3.6 mm), respectively. 18 stones were missed on NVUCT and 21 were missed on EVUCT. The sizes ranged from 1.4 to 3.2 mm (mean, 2.1 mm) and 1.4 to 3.2 mm (mean, 2.2 mm) on UCT, respectively. VUCT was inferior to UCT regarding image quality ($p < 0.05$).

Conclusion: VUCT missed a significant number of small stones probably owing to poor image quality compared with UCT. Subsequently, VUCT cannot replace UCT for detecting urinary stones.

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Urolithiasis is a common cause of haematuria. Unenhanced CT (UCT) is considered a gold standard for diagnosing this disease entity because it is more sensitive to detecting urinary stones than simple radiography and ultrasound [1–3]. Therefore, UCT is an essential CT protocol that should be included for CT urography.

Dual-energy CT (DECT) imaging can reconstruct virtual unenhanced CT (VUCT) images from contrast-enhanced CT images. As VUCT is equivalent to UCT in characterising renal masses, radiation dose to patients can be reduced during CT scans using dual-energy sources [4, 5]. DECT is also useful in evaluating composition of urinary stones, uric acid stones can be differentiated from calcified stones [6–10]. However, there are few *in vitro* or *in vivo* reports about the validity of VUCT in detecting urinary stones [11–13]. Still, it is unclear whether or not VUCT can be an alternative imaging to UCT for diagnosing urolithiasis.

The purpose of our study was to determine whether or not VUCT is equivalent to UCT in detecting urinary stones.

Methods and materials

This retrospective study was approved by our institutional review board and informed consent was waived.

Patients

Between September 2009 and March 2010, a total of 146 patients (male-to-female ratio, 73:73; age range, 23–87 years; mean age 56 years) underwent CT urography due to one of the following chief complaints: microscopic haematuria ($n=60$), gross haematuria ($n=25$), flank discomfort ($n=46$) or pain ($n=15$). Of these patients, stones were detected in 32 and urothelial cancer was detected in 2 patients. Urolithiasis in 32 patients (male-to-female ratio, 18:14; age range, 23–78 years; mean age, 55 years) was confirmed by CT urographical findings that a renal calcification was located within the urinary tract.

Patients' height and weight were recorded to calculate the body mass index (BMI). BMI was obtained as weight in kilograms divided by the square of the height in metres.

CT imaging

CT urography was performed by a DECT scanner (Somatom Definition Flash, Siemens Medical Solutions,

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Forchheim, Germany). This system consists of two X-ray tubes mounted on a gantry at 90° and two corresponding detectors [14]. One detector (detector A) covers a 50-cm field of view (FOV) and the other detector (detector B) covers a 32-cm FOV [14]. All patients underwent three-phase CT imaging to scan the area between the liver and symphysis pubis. First, a UCT scan was acquired and then nephrographic and excretory CT scans were performed at 100 s and 8 min ($n=29$) or 12 min ($n=3$) after intravenous injection of 120 ml contrast material (ultravist 300; Bayer Schering Pharma, Berlin, Germany) at the rate of 3 ml s⁻¹. Prior to the 8 min excretory CT, furosemide was administered to 29 patients. In three patients undergoing 12 min excretory CT, no furosemide or saline was administered.

The parameters of the UCT scan include a potential of 120 kVp, a quality reference of 240 mAs, a pitch of 1.2 and a detector configuration of 64 × 0.6 mm. The parameters of the nephrographic and excretory CT scans were for tube A, a potential of 140 kVp and a reference value of 96 mAs and for tube B, a potential of 80 kVp and a reference value of 404 mAs. Both of the nephrographic and excretory phase CT scans had a pitch of 0.55 and a configuration of 14 × 1.2 mm. For all scans, gantry rotation speed was 0.5 s. With both tubes, an online dose modulation (Care DOSE 4D; Siemens Medical Solutions) was used and a reference value was limited by the maximum photon flux available on tube B.

Image post-processing and reconstruction

All three-phase CT scans were performed with a section thickness of 1.5 mm and were reconstructed to axial images of a slice thickness of 3 mm. The axial images of both NVUCT and EVUCT were also produced with a slice thickness of 3 mm. By using an application liver VUCT, images from which iodine has been subtracted can be calculated at a post-processing workstation (syngo MM-WP, version 2008A; Siemens Medical Solutions) [5].

For abdominal applications, standard soft-tissue attenuations used by the system are 65 HU and 45 HU for 80 kVp and 140 kVp, respectively, while typical values for fat are -110 HU and -95 HU, respectively.

Data analysis

The size, number and location of stones detected on UCT, NVUCT and EVUCT images were recorded and compared with one another. The size, number and location of stones missed on NVUCT and EVUCT images were also recorded using UCT findings as a standard. The number and detection rate of stones detected on NVUCT and EVUCT were obtained in terms of stone size. Stone detection rate was defined as follows: (the number of stones detected on VCT images) × 100 / (the number of stones detected on UCT images). The longest diameter of urinary stone was measured at the axial CT images.

Regarding image quality, NVUCT and EVUCT were qualitatively assessed in consensus by two radiologists who had more than 5 years of experience in interpreting urological imaging studies. Qualitative image quality of

VUCT was rated with a five-point scale compared with that of UCT as follows: 1, excellent (VUCT is equivalent to UCT); 2, good (VUCT is slightly inferior to UCT but the former can depict the same number of stones as the latter); 3, fair (VUCT is inferior to UCT and the former can depict some of the stones detected on the latter); 4, poor (VUCT is so inferior to UCT that the former can depict none of the stones detected on the latter); and 5, unable to interpret. Image quality of NVUCT or EVUCT was correlated with BMI to determine whether or not BMI affected the image quality of VUCT. The presence or absence of residual contrast material within the urinary tract was recorded to evaluate iodine subtraction of contrast-enhanced CT images.

Dose-length product (DLP) and effective dose on each CT scan were obtained to determine what radiation dose could be reduced. DLP were recorded from the patient protocol that was automatically displayed on each CT scan. Effective dose (mSv) was determined by multiplying the DLP (mGy cm) for each CT scan by a normalised-conversion factor for the lower abdomen (0.014 mSv / mGy cm) [15, 16].

Statistical analysis

As paired data sets were obtained from different CT scans that were performed in the same patient, repeated measures analysis of variance (ANOVA) with Bonferroni post-test were used to compare the size of stones and the score of image quality obtained from UCT, NVUCT and EVUCT.

The Mann-Whitney *U*-test was used to compare the size of detected and undetected stones or pelvocalyx and ureter stones. The size of stones missed on VUCT images was measured on UCT images. When the size of undetected stones was compared with that of detected stones, the latter as well as the former was based on the findings of UCT images.

Bivariate correlation analysis using Pearson's correlation coefficient (*r*) and *r*² was used to correlate BMI and image quality of NVUCT or EVUCT. A commercially available software program (PASW Statistics, version 17; Chicago, IL) was used for statistical analysis. A *p*-value < 0.05 was considered statistically significant.

Results

DECT successfully covered upper urinary tracts and the urinary bladder (Figure 1). Repositioning the patient's body or FOV was not required because almost all abdominal organs were covered. The number of stones detected on UCT, NVUCT and EVUCT images was 80 in 32 patients, 62 in 29 patients and 59 in 27 patients, respectively. Of 80 stones, 74 were detected in the pelvocalyx and 6 were detected in the ureter, respectively (Table 1). Bladder stones were not detected on DECT images. According to the findings of UCT images, the size of ureter stone (range, 3.8–8.5 mm; mean, 5.8 ± 2.0 mm) was significantly larger than that of pelvocalyx stone (range, 1.4–19.2 mm; mean, 4.5 ± 3.5 mm) (*p* < 0.05).

The size of stones measured on UCT, NVUCT and EVUCT images ranged from 1.4 to 19.2 mm (4.6 ± 3.4 mm),

Figure 1. 56-year-old male with a left calyx stone. (a) Excretory axial CT image shows that the abdominal organs are almost entirely covered even with a small detector (arrows) measuring 32 cm in diameter. The body mass index of this patient is 28 kg m^{-2} . (b) Unenhanced axial CT image (left) shows a left calyx stone (arrow) of 2.5 mm. However, this stone measures 2 mm on nephrographic virtual unenhanced axial CT image (right). In addition, the edge of the stone is somewhat unclear. Left posterior pararenal fascia (arrow-heads) is clearer on unenhanced CT image than on virtual unenhanced CT image.

1.3 to 19.2 mm ($4.7 \pm 3.8 \text{ mm}$) and 1.1 to 18.7 mm ($4.7 \pm 3.9 \text{ mm}$), respectively (Table 1). As the sizes of these stones were paired data, statistical analysis showed that the size of stones measured on UCT images were significantly larger than that of stones measured on NVUCT or EVUCT images ($p < 0.05$) (Figure 1). The size of stones measured on NVUCT images were not significantly different from that of stones measured on EVUCT ($p > 0.05$). According to these paired data, the size of stones measured on NVUCT and EVUCT images ranged from 0 to 19.2 mm ($3.6 \pm 3.9 \text{ mm}$) and 0 mm to 18.7 mm ($3.4 \pm 3.9 \text{ mm}$).

18 stones were missed on NVUCT and 21 were missed on EVUCT images. The sizes ranged from 1.4 to 3.2 mm ($2.1 \pm 0.4 \text{ mm}$) and 1.4 to 3.2 mm ($2.2 \pm 0.4 \text{ mm}$), respectively, as measured on UCT images (Table 2). 2 stones were missed on NVUCT alone, 5 were missed on EVUCT alone and 16 were missed on both CT scans (Figure 2). Of 80 stones, NVUCT or EVUCT was able to depict 59–62 stones with a detection rate of 74–78%. Of 40 stones that measured less than 3.2 mm in diameter, 19–22 (48–55%) were detected on NVUCT or EVUCT images alone. As the size of stones was smaller, the detection rate was lower (Table 3). Of 18 stones measuring less than 2.5 mm, 3–4 (17–22%) stones were detected on VUCT alone. The size of the stones not seen on VUCT but seen on UCT images was significantly smaller than the other stones detected on UCT images ($p < 0.05$). All of these missed stones were located in the pelvocalyx.

Of 32 NVUCT scans, 18 were graded as 2, 11 were graded as 3 and 3 were graded as 4. Of 32 EVUCT scans, 15 were graded as 2, 12 were graded as 3 and five were graded as 4, respectively. None of the NVUCT or EVUCT scans were graded as 1 or 5. Regarding image quality,

Table 1. The size, number and location of urinary stones detected on CT images

		UCT	NVUCT	EVUCT
Size (mm)	Unpaired	4.6 ± 3.4	4.7 ± 3.8	4.7 ± 3.9
	Paired	4.6 ± 3.4	3.6 ± 3.9	3.4 ± 3.9
Number	Detected	80	62	59
	Missed	0	18	21
Location	Pelvocalyx	74	56	53
	Ureter	6	6	6

EVUCT, excretory virtual unenhanced CT; NVUCT, nephrographic virtual unenhanced CT; UCT, unenhanced CT.

both of NVUCT and EVUCT were poorer than UCT ($p < 0.05$). The image quality of NVUCT was not significantly different from that of EVUCT ($p > 0.05$). In nine patients, contrast-filled pelvocalyx was seen on EVUCT images despite iodine subtraction. Two stones in two patients were not detected on EVUCT images because these stones could not be discriminated from the residual contrast material (Figure 3). However, no contrast material in any patients was seen on NVUCT images.

The mean DLP and effective dose incurred during DECT scan for CT urography was $841\text{--}2073 \text{ mGy cm}$ ($1165 \pm 243 \text{ mGy cm}$) and $11.8\text{--}29.0 \text{ mSv}$ ($16.3 \pm 3.4 \text{ mSv}$). The DLP on unenhanced, nephrographic and excretory CT scans was $244\text{--}593 \text{ mGy cm}$ ($319 \pm 66 \text{ mGy cm}$), $314\text{--}767 \text{ mGy cm}$ ($445 \pm 92 \text{ mGy cm}$) and $283\text{--}713 \text{ mGy cm}$ ($401 \pm 88 \text{ mGy cm}$), respectively. The effective dose on unenhanced, nephrographic and excretory CT scans was $3.4\text{--}8.3 \text{ mSv}$ ($4.5 \pm 0.9 \text{ mSv}$), $4.4\text{--}10.7 \text{ mSv}$ ($6.2 \pm 1.3 \text{ mSv}$) and $4.0\text{--}10.0 \text{ mSv}$ ($5.6 \pm 1.2 \text{ mSv}$), respectively. The mean effective dose of UCT scan accounted for 27.6% of that of DECT scan.

The body weight and height of 32 patients with urinary stones ranged from 45 to 98 kg ($63.9 \pm 11.0 \text{ kg}$) and 142 to 183 cm ($163 \pm 9.0 \text{ cm}$), respectively. BMI was calculated as $18.6\text{--}32.2 \text{ kg m}^{-2}$ ($24.0 \pm 3.3 \text{ kg m}^{-2}$). The correlation of BMI and image quality of NVUCT or EVUCT was so poor that r and r^2 were -0.074 and 0.005 for BMI and NVUCT ($p > 0.05$) and -0.112 and 0.013 for BMI and EVUCT, respectively ($p > 0.05$).

Discussion

Our results showed that more than 20% of stones detected on UCT are invisible on both NVUCT and EVUCT. The size of stones detected on NVUCT and EVUCT images tends to be smaller than that of stones detected on UCT. Image quality of NVUCT and EVUCT was poorer than that of UCT.

DECT scan is performed as simultaneous acquisition of data sets that are made at two different tube potentials. Two different photon spectra are produced in a single CT acquisition [14, 17, 18]. Tissue composition is therefore theoretically different according to the variation of tissue photon absorption at different photon energies. Because of a large atomic number, the attenuation

Table 2. The size of missed stones on nephrographic virtual unenhanced CT (NVUCT) and excretory virtual unenhanced CT (EVUCT) images

		Stones measured on UCT images		
		Range (mm)	Mean $\pm$ SD (mm)	p-value
NVUCT	Detected	1.9–19.2	5.3 $\pm$ 3.6	<0.0001
	Undetected	1.4–3.2	2.1 $\pm$ 0.4	
EVUCT	Detected	1.9–19.2	5.4 $\pm$ 3.6	<0.0001
	Undetected	1.4–3.2	2.2 $\pm$ 0.4	

SD, standard deviation; UCT, unenhanced CT.

of iodine is much higher at 80 kVp than at 140 kVp. Subtraction of iodine from the images is possible based on reconstruction of complete 80 kVp and 140 kVp image data from the raw data. VUCT images are created with dual-energy post-processing algorithms which are based on the three-material decomposition principles using soft tissue, fat and iodine in the abdomen [4, 17].

The VUCT data set can serve as an alternative to UCT data set and subsequently UCT scan is not necessary for DECT scan [19]. Graser et al reported that DECT can provide such high quality VUCT images that UCT images can be replaced for evaluating renal masses [5]. The attenuation of renal masses measured on VUCT images was not significantly different from that of renal masses measured on UCT images. However, they experienced an algorithm-related artefact from which calcifications within the mass or adjacent organs as well as iodine can be subtracted. These calcifications became less distinct or smaller on VUCT images compared with those on UCT images, which explains why the size of stones detected on VUCT images were smaller than the stones on UCT images owing to partial subtraction in our study. In addition, 45–62% of stones measuring ≤ 3.2 mm in diameter on UCT images were invisible on VUCT images owing to complete subtraction. This stone detection rate in our study is much lower than that of the previous studies, probably because of different stone sizes [11, 12]. The mean diameter (8.0 mm) of stones in Scheffel et al's study was much larger than the stones in our study (4.6 mm) [11]. Takahashi et al measured the short axis of

the stone in an *in vitro* study setting while we measured the longest diameter in an *in vivo* study setting [12].

Clinically, detection of small calyx stones is important in patients with haematuria. These stones are seldom symptomatic but are a common cause for microscopic haematuria. If these stones are not identified on unenhanced CT, contrast-enhanced CT should be performed to investigate hidden malignancy in older patients. If it is negative, more invasive examinations including cystoscopy, ureteroscopy and pyeloscopy should be added to the work-up of haematuria. Further improvement of iodine subtraction technique is essential so that VUCT can replace UCT for detecting urinary stones.

Our study has several advantages over previous reports using DECT. First, we used a larger detector B for evaluating urinary tract than previous studies [4, 5, 11]. As it could cover a 32-cm FOV, kidneys as well as the entire urinary tracts of all patients were successfully scanned without knowledge of clinical or radiological information on the location of the stone or tumour. However, DECT using a 26-cm detector B required information on lesion location in advance and the centre of the CT scan should be shifted into the region of interest to prevent the off-centred scan of DECT imaging [4, 5]. Second, VUCT images were obtained from both nephrographic and urographic contrast-enhanced CT images to compare detection rate of urinary stones. More stones were detected on NVUCT than on EVUCT images. Contrast material is rarely excreted into the urinary tract during nephrographic CT but during excretory CT. Takahashi et al reported that highly concentrated iodine within the urinary tract can make stones less visible at 80–140 kVp paired DECT [12]. As the urinary tract had more concentrated contrast material on excretory CT images than on nephrographic CT images, EVUCT seemed to miss more stones than NVUCT in our study. Unfortunately, we did not quantify the amount of contrast material excreted to the urinary tract. Therefore we did not show the correlation between concentration and attenuation of contrast material within the urinary tract. Our results suggest that VUCT should be reconstructed

Figure 2. 74-year-old male with a left calyx stone. Unenhanced axial CT image (left) shows a left calyx stone (arrow) measuring 2.7 mm in diameter. However, this stone is not seen on excretory virtual unenhanced axial CT image (right).

Table 3. The detection rate of urinary stones regarding the stone size

Size range (mm)	Number of stones (detection rate)		
	UCT	NVUCT	EVUCT
≥ 1.0 and < 2.5	18	4 (22%)	3 (17%)
≥ 2.5 and < 4.0	32	28 (88%)	26 (81%)
≥ 4.0	30	30 (100%)	30 (100%)

EVUCT, excretory virtual unenhanced CT; NVUCT, nephrographic virtual unenhanced CT; UCT, unenhanced CT.

Figure 3. 44-year-old male with a right calyx stone. Excretory axial CT image (left) shows an upper polar calyx (arrowheads) that is filled with excreted contrast material. No stone is seen on virtual unenhanced CT image (middle) as a small amount of the contrast material (arrowheads) is still seen despite subtraction of iodine from the excretory CT image. However, a small calyx stone (arrow) measuring 2 mm in diameter is seen on unenhanced axial CT image (right).

from nephrographic not excretory DECT data sets. Third, BMI was not correlated with qualitative image quality that was based on the number of stones detected on CT images. Scheffel et al reported that a false-negative result for urinary stones occurs only in obese patients [11]. However, our study shows that the detection of urinary stones is not related to BMI but to stone size or subtraction artefact. Last, DECT urography did not expose more radiation to patients than single-energy CT urography. Several studies reported that mean effective dose ranges 20–30 mSv at single-energy CT urography [20–22]. This dose is slightly higher than that in our study (16.3 mSv).

Our study has several limitations. First, it was conducted in a retrospective manner so there may be a selection bias in nature. Second, quantitative analysis was not performed for assessing image quality, although signal-to-noise ratio and contrast-to-noise ratio of UCT, NVUCT and EVUCT were calculated during our study. Although UCT images were qualitatively better than the other CT images, these ratios of UCT were lower than those of NVUCT and EVUCT. To avoid confusion, the results of quantitative analysis were not shown in our study. Therefore, further research is necessary regarding these discordant results of image quality. Third, our study did not discriminate uric acid stones from calcified stones. In fact, we were not able to focus on stone composition but on comparison of VUCT and UCT for detection of urinary stone because our study was retrospectively designed. Several studies reported that DECT is useful for evaluating the composite of urinary stones and that uric acid stones can be differentiated from calcified stones *in vitro* and *in vivo* [4, 6, 7, 12]. More *in vivo* studies are necessary to determine if VUCT helps not only detect a urinary stone but also assess the stone composition.

Conclusions

VUCT has a potential to detect urinary stones but a substantial number of small stones are missed due to technical failure of iodine subtraction from contrast-enhanced images and poor image quality relative to that

of UCT. Therefore, VUCT cannot totally replace UCT for detecting urinary stones even though radiation dose to patients can be significantly reduced. More improvement of post-processing algorithm for reconstructing VUCT images is necessary in order to ensure they are equivalent to UCT images regarding detection of urinary stones and image quality.

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