Received:
23 July 2016

Revised:
9 January 2017

Accepted:
8 March 2017

<https://doi.org/10.1259/bjr.20160632>

Cite this article as:

Han D, Ma G, Wei L, Ren C, Zhou J, Shen C, et al. Preliminary study on the differentiation between parapelvic cyst and hydronephrosis with non-calculous using only pre-contrast dual-energy spectral CT scans. *Br J Radiol* 2017; **90**: 20160632.

FULL PAPER

Preliminary study on the differentiation between parapelvic cyst and hydronephrosis with non-calculous using only pre-contrast dual-energy spectral CT scans

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Objective: To investigate the value of using the quantitative parameters from only the pre-contrast dual-energy spectral CT imaging for distinguishing between parapelvic cyst and hydronephrosis with non-calculous (HNC).

Methods: This retrospective study was approved by the institutional review board. 28 patients with parapelvic cyst and 24 patients with HNC who underwent standard pre-contrast and multiphase contrast-enhanced dual-energy spectral CT imaging were retrospectively identified. The parapelvic cyst and HNC were identified using the contrast-enhanced scans, and their CT number in the 70-keV monochromatic images, effective atomic number (Z_{eff}), iodine concentration (IC) and water concentration in the pre-contrast images were measured. The slope of the spectral curve (λ) was calculated. The difference in the measurements between parapelvic cyst and HNC was statistically analyzed using SPSS® v. 19.0 (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL) statistical software. Receiver-operating

characteristic analysis was performed to assess the diagnostic performance.

Results: The CT numbers in the 70-keV images, Z_{eff} and IC values were statistically different between parapelvic cyst and HNC (all $p < 0.05$). The sensitivity, specificity and accuracy of these parameters for distinguishing between parapelvic cyst and HNC were 89.2%, 73.3% and 82.1%; 86.5%, 43.3% and 67.2%; 91.9%, 40.0% and 68.7%; and 64.9%, 73.3% and 83.6%, respectively, and the combined specificity was 92.9%. There was no statistical difference in λ between the two groups ($p > 0.05$).

Conclusion: The quantitative parameters obtained in the pre-contrast dual-energy spectral CT imaging may be used to differentiate between parapelvic cyst and HNC.

Advances in knowledge: The pre-contrast dual-energy spectral CT scans may be used to screen parapelvic cysts for patients who are asymptomatic, thereby avoiding contrast-enhanced CT or CT urography examination for these patients to reduce ionizing radiation dose and contrast dose.

INTRODUCTION

The parapelvic cyst is a rare disease in the clinic with a detection rate in autopsy of about 1.25–1.5%.¹ It is believed to originate from the secondary lymphatic obstruction,² and most of the patients were occasionally found without any symptoms.³ However, when the cyst is large enough, it may lead to hypertension, haematuria, hydronephrosis or secondary infection, and even acute renal failure.^{4,5} Parapelvic cyst is easy to be mistaken for hydronephrosis by ultrasonic diagnosis and hospitalization. CT urography (CTU) was always performed in these patients to look for the reason for “hydronephrosis”. Although the parapelvic cysts can be diagnosed by CTU, the extra ionizing radiation and contrast load outweigh the

clinical benefit because asymptomatic parapelvic cysts usually do not require intervention. Studies have shown that CTU may increase X-ray exposure.⁶ Moreover, some patients who have contraindications, such as iodine allergy or renal insufficiency, so they cannot be underwent to contrast-enhanced CT or CTU. Although renal pelvis or ureteral dilation supports the diagnosis of hydronephrosis, it is not a sign of every patient.⁷ In particular, there were no significant high-density positive stones in the ureter of a part of some patients with dilated renal calyx and pelvis. In the conventional non-contrast CT scans, the parapelvic cyst and hydronephrosis with non-calculous (HNC) have a similar appearance, making them difficult to be identified. Recently, a dual-energy spectral CT imaging mode was introduced

Figure 1. Flowchart. CTU, CT urography; HNC, hydronephrosis with non-calculous.

which produces virtual monochromatic images, spectral curve, effective atomic number (Z_{eff}) and material decomposition (MD) images to provide more information for the diagnosis of disease. The purpose of this study was to explore the diagnostic value for differentiating parapelvic cyst from HNC using the quantitative parameters from only the pre-contrast dual-energy spectral CT images in reducing both the radiation dose and contrast dose.

METHODS AND MATERIALS

Patients

This retrospective study was approved by our institutional review board. The radiology information system application (Huahai; Huahai Co., Ltd, Xi'an, China) was used to conduct a review of a medical imaging database. Radiology information system search parameters specified the imaging modality as CT and free-text search keywords of “Low density” AND “renal pelvis” AND/OR “hydronephrosis”. A total of 78 reports were returned from this search (Figure 1).

One author (TPH), an associate chief physician with 13 years' experience, reviewed dictated reports and images from the search. The inclusion criteria were: (a) the lesion was limited to Class I according to the Bosniak⁸ classification (the renal cystic lesions of other categories are often accompanied by calcification, a high density in cyst, a rough cyst wall or soft tissue nodules and other signs and are easy to be separated from hydronephrosis; therefore, these types of lesions were not included in the study) and (b) all the lesions were homogeneous cystic lesions in the renal pelvis and could be clearly separated from renal parenchyma. The exclusion criteria were: (a) uneven density and abnormal soft tissues in the lesion; (b) extrarenal pelvis/ampulla-type pelvis (although these two kinds of lesions often manifest as a kind of low density of the renal hilus, the minor calyces were not dilated); (c) positive ureter stones were seen in the scan range; (d) history of urinary tumours; and (e) operation history of renal pelvic region. The flowchart is shown in Figure 1.

Finally, 52 patients (27 females and 25 males; age range, 18–86 years with median of 58 years) with a total of 67 kidneys were included in this study. These patients were diagnosed with parapelvic cyst (28 cases, bilateral lesions in 9 cases; total of 37 kidneys) or HNC (24 cases, bilateral lesions in 6 cases; total of 30 kidneys) by the contrast-enhanced and CTU scans. The main clinical symptoms were primary symptom, urinary tract irritation sign, haematuria, hypouricemia, abdominal pain or abdominal distension; some patients had no obvious symptoms. The characteristics and clinical information of the two groups are shown in Table 1. The date of the examinations selected ranged from October 2015 to June 2016.

CT examinations

CT scans were performed in a 64-slice CT scanner (Discovery CT 750 HD, GE Healthcare, OH); all patients provided written

Table 1. The patient characteristics and clinical information comparison between the two groups

Parameter	Parapelvic cyst ($n = 28$)	HNC ($n = 24$)	Test value	p -value
Patient characteristics				
Age (years)	61.61 $\pm$ 12.71	52.25 $\pm$ 16.64	2.30 ^a	<0.05
Gender (F/M)	12/16	13/11	0.66	>0.05
Bilateral incidence	9/28 (32.1%)	6/24 (25.0%)	0.32	>0.05
Medical history				
Accidental discovery of ultrasonography/CT	10/28 (35.7%)	3/24 (12.5%)	3.71	>0.05
History of non-urinary system	18/28 (64.3%)	21/24 (87.5%)	3.71	>0.05
Symptom/sign				
Symptoms of urinary system	3/28 (10.7%)	10/24 (41.7%)	6.60	<0.05
Symptoms of non-urinary system	14/28 (50.0%)	11/24 (45.8%)	0.09	>0.05
Symptomless	11/28 (39.3%)	3/24 (12.5%)	4.71	<0.05

F, female; HNC, hydronephrosis with non-calculous; M, male.

History of non-urinary system, history of tumour (16/6); other non-tumour history (2/15); symptoms of urinary system, urinary irritation (2/3), haematuria (1/3) and hypouricemia (0/4); symptoms of non-urinary system, primary symptom (13/8) and abdominal pain or abdominal distension (1/3).

^aFor the t -value, and the other is χ^2 value.

informed consent before contrast-enhanced CT and CTU examinations. Before the examination, patients were asked to hold urine and were trained to hold their breath after inspiration. The patients were scanned in the supine position. The unenhanced and the three contrast-enhanced scans in the cortical phase, medulla phase and excretion phase were performed using dual-energy spectral imaging mode with a gemstone spectral imaging (GSI) scanning protocol GSI-1: 630 mA, rotation speed 0.5 s/rotation, pitch 1.375:1. The pre-contrast and excretion phase scan ranges were from the upper left kidney to the upper margin of the pubic symphysis, and the cortical phase and medulla phase scan ranges were from the upper left kidney to under the right kidney. These patients were injected with a non-ionic iodinated contrast agent (ioversol, 350 mg I/ml; Jiangsu Hengrui Medicine Co. Ltd, China) at a dose of 1.0 ml kg^{-1} of body weight *via* the antecubital vein at a rate of 4.0 ml s^{-1} by using a dual-tube power injector (Ulrich, Germany). After the contrast agent was injected, 40 ml of normal saline was injected at the same rate. The bolus triggering technique was used at the cortical phase, monitoring points on the abdominal aorta at the upper left pole of the upper left kidney (threshold was 150 HU). The delay times for the medulla phase and excretion phase were 35 s and 6–8 min after the cortical phase was complete. Both monochromatic images with energies

from 40 keV to 140 keV and MD images using water and iodine as base material pairs were reconstructed using standard reconstruction algorithm with 1.25 mm slice thickness. All images were transferred to an AW4.6 post-processing workstation (GE Healthcare) for analysis.

Quantitative analysis

The reconstructed non-enhanced spectral CT images were loaded into an AW4.6 workstation and were analyzed using the GSI viewer software package. The quantitative parameters of the two groups of GSI pre-contrast images were evaluated by one radiologist (LQW with 4 years' experience, in CT abdominal imaging), and he was blinded to the results of contrast-enhanced and CTU examinations. Regions of interest (ROIs) were drawn on the parapelvic cyst or HNC and renal parenchyma on the same side of the lesion in the 70-keV pre-contrast images and in water-based and iodine-based MD images, avoiding the edge of the lesions. The ROI size of was about $20\text{--}200 \text{ mm}^2$. The CT numbers from the 40-keV, 70-keV and 140-keV monochromatic images, Z_{eff} , iodine concentration (IC) from the iodine-based MD images, water concentration (WC) from the water-based MD images on lesion and ipsilateral renal parenchyma were measured. The slope of the spectral curve (λ) was calculated using the CT number of 40 keV and 140 keV with the formula:

Figure 2. A 68-year-old female: (a) the 70-keV pre-contrast virtual single-energy image shows an irregular low-density shadow in the renal pelvis; (b–e) the iodine-based material decomposition (MD) image, water-based MD image, effective atomic number and spectral curve are shown. (f) The CT urography shows the contrast agent did not enter the low-density shadow; the renal pelvis is compressed, confirmed as parapelvic cyst.

Figure 3. A 43-year-old female: (a) the 70-keV pre-contrast virtual single-energy image shows an irregular low-density shadow in the renal pelvis; (b-e) the iodine-based material decomposition (MD) image, water-based MD image, effective atomic number and spectral curve are shown. (f) The CT urography shows the contrast agent into the expansion of the renal calyx and pelvis, confirmed as hydronephrosis with non-calculous.

$\lambda = (HU_{40\text{ keV}} - HU_{140\text{ keV}})/(140 - 40)$. The above ROIs were selected from the slice with the largest lesion size and placed again on the above and below slices. Average value was calculated using the measurements from the three consecutive slices.

Statistical analysis

The above parameters were expressed as mean $\pm$ standard deviation ($\bar{x} \pm s$) and were analyzed using SPSS® v. 19.0 (IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL) statistical

software, with $p < 0.05$ indicating statistically significant difference. The single-sample K-S and Levene's tests were used to test the goodness of fit and homogeneity of variance of the measurements, respectively. The independent samples t test was used to test the parameters of the two groups which were consistent with normal distribution and homogeneity of variance; otherwise, the Mann-Whitney U test was used, presented as $M (Q_1, Q_3)$. The receiver-operating characteristic curves were drawn with parameters which were statistically significant. The best

Table 2. Quantitative assessment of the CT number in 70-keV monochromatic image, effective atomic number (Z_{eff}), slope of the spectral curve (λ), iodine concentration (IC) and water concentration (WC) for the pre-contrast spectral CT imaging for the ipsilateral kidney parenchyma in the presence of different types of lesions

Group	CT number in 70 keV (HU)	Z_{eff}	λ	IC (mg ml^{-1})	WC (mg ml^{-1})
With parapelvic cyst ($n = 37$)	29.06 ± 4.32	7.82 (7.72, 7.93)	0.30 ± 0.14	4.02 ± 1.76	1019.92 ± 5.04
With HNC ($n = 30$)	29.71 ± 5.61	7.73 (7.69, 7.86)	0.26 ± 0.11	3.40 ± 1.50	1022.54 ± 6.17
Test value	0.54	-1.53^a	1.28	1.54	-1.92
p -value	>0.05	>0.05	>0.05	>0.05	>0.05

HNC, hydronephrosis with non-calculous.

^aFor the Z -value, and the other is t -value.

Table 3. Quantitative assessment of the CT number in 70 keV, effective atomic number (Z_{eff}), slope of the spectral curve (λ), iodine concentration (IC) and water concentration (WC) values between the parapelvic cyst and hydronephrosis with non-calculous (HNC) in pre-contrast spectral CT images

Group	CT value in 70 keV (HU)	Z_{eff}	λ	IC (mg ml^{-1})	WC (mg ml^{-1})
With parapelvic cyst ($n = 37$)	6.50 ± 5.20	7.75 (7.70, 7.83)	0.24 ± 0.11	3.10 ± 1.39	998.82 ± 6.37
With HNC ($n = 30$)	-0.30 ± 7.17	7.64 (7.60, 7.76)	0.18 ± 0.13	2.32 ± 1.62	994.41 ± 6.45
Test value	4.10	-2.14^a	1.87	2.14	2.80
p -value	<0.001	<0.05	>0.05	<0.01	<0.01

^aFor the Z -value, and the other is t -value.

diagnostic threshold was determined according to the maximum Youden index ($YI_{\text{max}} = \text{sensitivity} + \text{specificity} - 1$), and the area under the curve was calculated to analyze the diagnostic performance. To improve the specificity of differentiating the two lesions, a combined specificity was calculated: combined specificity = Test A specificity + $(1 - \text{Test A specificity}) \times \text{Test B specificity}$, where Test A and Test B represent the two parameters with the higher specificity, and in our study these parameters were CT number in 70 keV and WC.

RESULTS

CT performances

All the lesions were homogeneous cystic lesions in the renal pelvis and could be clearly separated from renal parenchyma. There was no enhancement at the cortical phase and medulla phase during the contrast-enhanced scans, and no entering of contrast into the parapelvic cyst at the excretion phase. The adjacent renal pelvis and renal calices were compressed and had clear separations with the cyst (Figure 2). In the case of HNC, the renal pelvis, renal calices and ureter were filled with the contrast agent (Figure 3). The upper ureteral dilation degrees of the two groups of these patients were 0.52 (0.40, 0.71) and 0.57 (0.44, 1.04), $Z = -1.41$, $p > 0.05$.

The quantitative parameter comparison of the ipsilateral kidney parenchyma of lesions in pre-contrast spectral CT imaging

The quantitative measurements for the ipsilateral kidney parenchyma of lesions are listed in Table 2 to investigate whether there was a systematic bias in the measurements. All measurements were statistically the same for the kidney parenchyma, whether the patient had parapelvic cyst or HNC, indicating that there was no systematic bias for the measurement system.

The quantitative parameter comparison between parapelvic cyst and hydronephrosis with non-calculous

The quantitative parameter comparison between parapelvic cyst and HNC is listed in Table 3. There were statistically significant differences in CT number in 70 keV, Z_{eff} , IC and WC values between parapelvic cyst and HNC. The trend of the average spectral curve of the two lesions was similar; there was no significant difference for λ between the two groups (Table 3, Figure 4).

Effectiveness analysis of quantitative parameters for the differential diagnosis between parapelvic cyst and hydronephrosis with non-calculous

There was no significant difference between the two groups with λ ; therefore, the diagnostic performance was not evaluated. We used the contrast-enhanced CT scans to identify parapelvic cyst and HNC. The receiver-operating characteristic curves with CT number in 70 keV, Z_{eff} , IC and WC were generated and are shown in Figure 5. Their diagnostic performance is shown in Table 4, and the combined specificity that was calculated by CT number in 70 keV and WC 92.9% (Figure 6).

DISCUSSION

General ultrasound is particularly suitable for the diagnosis of renal cystic disease and early screening of patients who are asymptomatic. However, because of its special position, parapelvic cyst sometimes cannot be accurately diagnosed even if there are some indirect sonographic features.¹ At the same time, the false-positive rate of ultrasonic diagnosis in hydronephrosis was 11–26%;⁹ therefore, parapelvic cyst is sometimes misdiagnosed as hydronephrosis by ultrasonic diagnosis.^{10,11} In CTU, parapelvic cysts are not associated with the collection system. Contrast agents can enter the renal pelvis or ureter but not the parapelvic cyst in the excretion phase of CTU, and this feature was used to identify parapelvic cysts in our study.

There was no significant difference in dual-energy spectral CT-related parameters of the ipsilateral kidney parenchyma for the two lesion groups, indicating no measurement bias in the system. So, it can be considered that the measurement of parapelvic

Figure 4. The average spectral curves of the two types of lesions. HNC, hydronephrosis with non-calculous.

Figure 5. The receiver-operating characteristic of the CT number in 70 keV, effective atomic number (Z_{eff}), iodine concentration (IC) and water concentration (WC) for identifying parapelvic cyst and hydronephrosis with non-calculous.

cysts and HNC was in the same background. Owing to the fact that the conventional single-source CT X-ray beam is polychromatic, which leads to beam hardening artefacts,^{12,13} the CT number is not accurate enough and affects both the parapelvic cyst and HNC. The true single-energy CT number refers to the attenuation of the monochromatic X-rays produced by a specific energy level through the detected materials. The dual-energy spectral CT imaging mode produces virtual monochromatic images through the energy spectrum analysis of the two energy spectrums obtained during a single rotation to reduce beam hardening artefacts and provide more accurate CT attenuation number measurements. In addition, the dual-energy spectral CT imaging mode uses the space- and time-coherent data sets of two different energy spectrums with the single-source, fast peak kilovoltage switching method to reduce the interference of autonomous and involuntary movement. Several studies^{12,14,15} have shown that virtual monochromatic images of the dual-energy spectral CT reduce beam hardening artefacts. The virtual monochromatic images (40–140 keV) generated by the dual-energy spectral imaging mode can eliminate (or reduce) the CT number shift caused by the beam hardening artefact and provide a more accurate CT attenuation value than the conventional polychromatic X-ray regardless of the shape of the model.¹⁶ The research of He et al¹⁴ also further shows that the 70-keV

monochromatic images had the lowest mean CT number shift under severe beam hardening conditions. Previous phantom studies have shown that for a given radiation dose, 70-keV virtual monochromatic image was similar to the traditional 120-kV image in image display effect. The 70-keV virtual monochromatic image has lower image noise and higher contrast-to-noise ratio than the conventional 120-kVp polychromatic images. Virtual monochromatic images have the potential to replace 120-kVp CT as the standard CT imaging modality.¹⁷ However, many studies about renal cyst pseudoenhancement also show that regardless of the reconstruction algorithm, lesion size and location and the enhancement degree in kidney parenchyma, the virtual monochromatic images can eliminate pseudoenhancement and 70 keV is the optimal energy level for renal cyst diagnosis.^{13,18,19} The pathogenesis of simple renal cysts and parapelvic cysts is almost the same.²⁰ Therefore, in our study also, the 70-keV virtual monochromatic images were chose to perform quantitative measurements.

There were significant differences in the CT number in the 70-keV virtual monochromatic images for the two lesion groups, according to the formula:

$$HU = K[(\mu_x - \mu_{\text{water}}) / \mu_{\text{water}}],$$

where K is a constant, μ_x is the linear attenuation coefficient of the measured substance and μ_{water} is the linear attenuation coefficient of water. Therefore, CT number is related to μ_x , and μ_x is proportional to the density of the measured substance. Although the composition of the two lesion types is mainly water, the other components of the cystic fluid are different. The hydronephrosis and urine compositions are similar with water and solid substances dissolved in it. These solid substances are composed of electrolyte and non-protein nitrogen that have lower molecular weight, lower density and smaller linear attenuation coefficient. On the other hand, the fluid in the cyst is serous fluid, similar to serum, containing electrolyte, urea nitrogen, sugar, protein and creatinine,²¹ in which the protein is biological macromolecules and has relatively higher density and larger attenuation coefficient. However, the averaging effect and the existence of beam hardening artefacts in the polychromatic images in conventional CT negatively impacts the CT number measurement accuracy and reduces the low contrast resolution. The CT number measurement in conventional CT cannot reflect the small difference between the parapelvic cyst and hydronephrosis, as indicated in the research work of Ding et al.²² Our study results indicated that the use of virtual monochromatic

Table 4. The diagnostic performance of the CT value in 70 keV, effective atomic number (Z_{eff}), iodine concentration (IC) and water concentration (WC) for differentiating between parapelvic cyst and hydronephrosis with non-calculous

Parameter	AUC	YI _{max}	Threshold	Sensitivity (%)	Specificity (%)	Accuracy (%)
CT number in 70 keV (HU)	0.785	0.63	2.11	89.2	73.3	82.1
Z_{eff}	0.653	0.30	7.66	86.5	43.3	67.2
IC	0.643	0.32	1.81	91.9	40.0	68.7
WC	0.701	0.38	997.01	64.9	73.3	83.6

AUC, the area under the curve; YI_{max}, the maximum Youden index.

Figure 6. Specificity of each parameter and the combined specificity; the combined specificity was calculated by CT number in 70 keV and water concentration (WC). IC, iodine concentration; Z_{eff} , effective atomic number.

images provided higher sensitivity for detecting the small difference in CT numbers in 70-keV virtual monochromatic images between parapelvic cyst and HNC.

The MD technique in dual-energy spectral CT uses the combination of two base materials to produce the same attenuation effect as the tested material. It provides more details for the anatomy and function of the unknown object, compared with the traditional single-source CT.²³ In theory, the attenuation curve of any material can be expressed by any two substances in the attenuation of expression, known as the base material pair. Usually, the base material pair does not represent the true composition of the evaluated material, but the same attenuation effect was simulated by the combination of the two materials; so, it was a relative expression of the materials to be examined. In clinical diagnosis, base material pairs with large difference in atomic number are often chosen. However, they can also be chosen according to different diagnostic purposes. At present, the most commonly used base material pair in clinical practice is water–iodine. In this study, we also used iodine–water as the base material pair, because the difference of X-ray linear attenuation coefficient between the two materials iodine and water was large and the water was the main component of the two kinds of diseases. Our results demonstrated that there was difference for these parameters between parapelvic cyst and HNC.

Z_{eff} is the effective atomic number of the element in the ROI and is weighted sum of the mixture. Studies have shown that the dual-energy spectral CT can accurately measure the Z_{eff} of the material.²⁴

Z_{eff} also reflects the structural difference of different materials and is often used in the identification of different component stones.²⁵ In our study, the difference of Z_{eff} between the two groups was statistically significant, but its diagnostic performance was not high. Our results indicated that the trend of the average spectral curve of the two lesions was similar, as shown in Figure 5; therefore, there was no significant difference in the λ between the two kinds of lesions.

None of the above four parameters of significant difference were very specific; if only one of these parameters was used, a small number of patients were misdiagnosed as hydronephrosis. Therefore, this study combined the specificities of the two parameters provided by the dual-energy spectral CT that produced the highest specificity (CT number in 70 keV and WC) for screening of parapelvic cyst. Compared with a single parameter, the combined specificity was increased to 92.9%, although the sensitivity was reduced. The pre-contrast dual-energy spectral CT can be used as a relatively safe and simple method. When a lesion was excluded from parapelvic cyst by the pre-contrast scan, the patient should be performed for further contrast-enhanced CT and CTU scan with relatively high accuracy.

There were some limitations in our study. First, this was a retrospective analysis with small number of patients, and patient selection bias may exist. Second, in this article, we evaluated only the quantitative parameters of spectral CT, and the morphological features of lesions may also help identify different types of lesions in clinical work; for example, the ureter on the same side of the lesion may expand when there is severe hydronephrosis. However, there was no significant difference in the degree of upper ureteral dilation between the two groups of patients in our study cohort. Third, this study used the multiphase enhanced CT scans or CTU as the gold standard, and there were no pathological results. Therefore, one could not completely eliminate the possibility of misdiagnosis. Fourth, the specificity obtained in this study is still relatively low at 73.3%. Although the combined parameter approach improved the specificity, it also negatively impacted the sensitivity. We are investigating whether the use of the general linear model can further improve both the sensitivity and specificity.

In conclusion, the multiple quantitative parameters obtained in the pre-contrast dual-energy spectral CT imaging may be used to differentiate between parapelvic cyst and HNC, providing opportunities to avoid contrast-enhanced CT or CTU examination in patients without symptoms, thereby reducing the dose of ionizing radiation and contrast agent load.

ACKNOWLEDGMENTS

We would like to thank Dr Jian Ying Li of GE Healthcare, China, for his technique support and editing the article.

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