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Dual energy CT in patients with polycystic kidney disease

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Abstract
Objectives To evaluate the diagnostic efficacy of dual source–dual energy CT (DECT) in the detection of neoplasia in patients with polycystic kidney disease (PKD).
Methods A total of 21 patients with PKD underwent DECT on a dual source system, using kVp settings of Sn140/100 or 140/80. Colour-coded iodine maps and virtual unenhanced images were used to determine enhancement within cysts and to differentiate haemorrhagic from simple cysts. A cut-off of 15 HU was used as a threshold for malignancy. In patients with malignancy, histopathology was the gold standard; otherwise, patients underwent follow-up imaging for 150–908 days.
Results On the basis of measured enhancement, 13 enhancing masses were seen in 4 patients (12 renal cell cancers and 1 adenoma); follow-up imaging showed no malignancy in 18 patients. Cysts did not enhance by more than 15 HU, whereas masses showed a mean enhancement of 45 (25–123) HU. Average radiation exposure was 9.6 mSv for the biphasic protocol and 5.8 mSv for DECT only.
Conclusion DECT greatly facilitates the detection of malignancy in patients with polycystic kidney disease, at the same time reducing radiation exposure by omission of a true unenhanced phase.
Key Points
- *Identification of tumours within polycystic kidneys can be difficult.*
- *Dual energy computed tomography (DECT) provides two separate sets of images.*
- *Iodine maps and virtual non-enhanced (VNE) images can then be calculated.*
- *DECT facilitates screening for potential renal tumours in polycystic kidneys.*

Keywords Dual energy · CT · ADPKD · Polycystic · Kidney

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Introduction

State-of-the-art imaging in patients with known or suspected renal masses widely relies on multidetector-row computed tomography (MDCT) and magnetic resonance imaging (MRI), with MDCT being the most frequently performed examination. Whereas MRI benefits from high soft tissue contrast and the absence of ionising radiation, MDCT provides high spatial resolution and short acquisition times as well as lower associated costs. Standard renal MDCT protocols contain true non-enhanced (TNE), nephrographic and urographic (delayed) phase CT imaging. The characterisation of renal masses by CT is based on the ability to measure the presence or absence of contrast enhancement of suspicious renal masses. Unenhanced images are being used as a baseline for the quantification of enhancement, followed by a contrast-enhanced acquisition. Detection of intralesional fat and calcium also relies on unenhanced images. Generally, renal masses will be considered benign if they do not enhance by more than 10 Hounsfield units (HU). If, however, attenuation increases

by more than 20 HU, a lesion is regarded as malignant unless it fulfils clear diagnostic criteria for an angiomyolipoma or oncocytoma. The detection of enhancement within a renal mass is based on a comparison of measured CT numbers on pre- and post-contrast-enhanced nephrographic phase images. Comprehensive renal mass imaging therefore requires at least a biphasic examination of the abdomen and causes considerable radiation exposure to the patient.

Dual energy CT (DECT) relies on the simultaneous acquisition of CT data at different tube kilovoltages. From the raw data, two separate sets of images, namely low and high kVp data sets, are reconstructed. So-called weighted average images can be generated by using a three-material decomposition model [1]; furthermore, iodine maps and virtual non-enhanced (VNE) images can be calculated. It has been shown that VNE images approach the quality and HU stability of TNE images [2].

In the abdomen, several applications of DECT have been described so far [3]. The technique plays an important role in imaging of the kidneys because it allows for fast and reliable characterisation of renal masses [4]. On the basis of these results, DECT has the potential to facilitate the detection and characterisation of malignant tumours in patients with polycystic kidney disease, as it enables the direct visualisation of enhancement in solid and cystic structures. Patients with polycystic kidneys and end-stage renal disease (ESRD) have to undergo repeated imaging, as the risk of malignancy is significantly elevated [5].

Autosomal dominant polycystic kidney disease (ADPKD) and acquired polycystic kidney disease are the most common polycystic kidney diseases in adults. Other conditions like autosomal recessive kidney disease, von Hippel–Lindau (vHL) disease or tuberous sclerosis can also lead to the formation of multiple cysts, but they play a minor role in older patients. ADPKD patients express either the PKD1 or the PKD2 gene locus on chromosome 16 or 4, respectively. They develop multiple bilateral renal cysts, but cysts can also occur in other organs like the liver or pancreas. Cysts tend to increase by number and size over the lifetime of the patients. Consequently, their kidneys can reach an enormous size and cause significant mass effect. As there is constant growth, cysts continuously replace the normal kidney parenchyma, thereby causing renal insufficiency. Eventually, this process can lead to end-stage renal disease (ESRD), when the glomerular filtration rate (GFR) reaches a value of no greater than 15 mL/min, making dialysis or a transplantation necessary. In PKD type 2 disease, cysts tend to occur about 15 years later in comparison to PKD type 1 (ESRD mean age 69.1 vs. 53.0 years) [6].

Although the risk of malignancy is generally elevated in ADPKD patients on the basis of the disease itself, chronic renal failure (CRF) additionally leads to an increase in renal cell carcinoma incidence [5]. Furthermore, CRF itself is often associated with the development of multiple bilateral cysts, especially in patients on dialysis. This acquired-type cystic disease can also be a cause of polycystic kidney disease. In two prospective studies, the lifetime incidence of renal cell carcinoma in these patients has been shown to be 4 % and 7 %, respectively [7].

We undertook this study in order to show that DECT allows for the accurate identification of malignant renal masses in the presence of multiple cysts in patients with polycystic kidney disease.

Materials and methods

Patient population

Between May 2007 and March 2011, dual energy CT was performed in 21 patients (12 male; 9 female) with known polycystic kidneys if a suspicious or unclear lesion was seen on routine ultrasound, as part of the present institutional review board (IRB)-approved, Health Insurance Portability and Accountability Act (HIPAA)-compliant study. All patients showed at least 10 cysts on each side and significant renal enlargement. Patients were referred for annual routine follow-up abdominal CT in known polycystic kidney disease or for symptoms like abdominal pain or gross haematuria.

Imaging protocol

All imaging was performed on one of two dual source multidetector row CT systems, Siemens Somatom Definition Dual Source (DS), $n=8$, or Siemens Somatom Definition Flash (FLASH), $n=13$ (Siemens Healthcare, Forchheim, Germany). Both systems consist of 2 X-ray tubes and their corresponding detectors that are mounted in one gantry. Patients were positioned on the CT table in the supine position. The first-generation system has a smaller field of view (FOV) on one of its detectors (26 cm), whereas the second-generation system provides a FOV of 33 cm on this detector. The larger detectors are identical and cover 50 cm.

First, TNE images of the abdomen were acquired from the dome of the liver to the iliac crest in an inspiratory breath hold using a detector configuration of 64×0.6 (FLASH 128×0.6) mm, a tube potential of 120 kVp, 240 quality reference mAs, and online dose modulation. In this vendor-specific software, the quality reference mAs value describes image noise characteristics which are similar to CT images acquired at 240 effective mAs per slice.

For the dual energy acquisition, the imaging protocol was adapted to the device type (see Table 1). Nephrographic phase images were acquired 80 s after intravenous injection of a non-

Table 1 Imaging parameters for the two dual source CT systems

	Definition DS (tubes A/B)	Definition Flash (tubes A/B)
Slices	2×64	2×128
Angular offset (°)	90	95
FOV (cm)	50/26	50/33
Spectra (kVp)	80/140	100/Sn140
Filter (mm)	3 Al, 0.9 Ti	3 Al, 0.9 Ti, 0.4 Sn (B tube only)
Tube Current–time product (mAs)	96/404	204/150
Modulation	CareDose4D (x,y,z-axis)	CareDose4D (x,y,z-axis)
Collimation (mm)	14×1.2	32×0.6
Pitch	0.55	0.6
Rotation time (s)	0.5	0.5

Definition DS first-generation dual source CT, *Definition Flash* second-generation dual source CT

ionic contrast agent (1.35 mL/kg patient body weight; Ultravist 370, Bayer Diagnostics, Berlin, Germay). For each of the two phases, dose–length products were recorded from the patient protocol. These values were used for the estimation of the individual effective radiation doses in millisieverts (mSv), using appropriately normalised conversion factors.

Results

All patients underwent DECT for the evaluation of unclear findings or incomplete examinations due to very large kidneys on ultrasound. On the basis of DECT findings, four patients (19 %) underwent partial nephrectomy. Seventeen patients underwent follow-up imaging using DECT (n=9), MRI (n=7) or CEUS (n=1) for an average of 254 days (range 150–908 days). Follow-up examinations did not reveal malignancy till the end of this study in these patients. We found the following pathological conditions in 21 patients included in this trial: multiple cysts and renal cell cancer (RCC) was detected in 3; in 3 other patients, DECT was used as a follow-up examination after partial nephrectomy for previous RCC; in 5 patients, multiple simple cysts were seen, and complex or haemorrhagic cysts in 10, one of which also had an enhancing mass (adenoma according to histopathology). For detailed findings, see Table 2; Figures 1 and 2 show examples of simple and haemorrhagic cysts as well as RCC in two ADPKD patients.

The mean effective radiation exposure was 4.7 mSv for the unenhanced acquisition, 5.8 mSv for the dual energy acquisition and 9.6 mSv for the biphasic protocol. As we changed our standard renal mass protocol during the course of the study [4], 6 out of 21 patients did not receive an unenhanced acquisition.

Table 2 Patient population

Patient	Age (years)	Sex	Date of CT	Treatment/follow-up	No. of cysts	Malignancy	Findings
1	60	Male	November 2007	FU January 2008	More than 20 each side	No	Polycystic kidneys
2	65	Make	May 2009	FU February 2011	Multiple	Yes	Multiple cysts
3	82	Male	June 2007	No	More than 30 each side	No	ADPKD
4	78	Male	May 2007	No	10 each side	No	Multiple cysts
5	41	Male	September 2009	No	More than 50 each side	No	ADPKD
6	74	Male	January 2008	No	10 each side	Yes	Multiple cysts
7	45	Female	January 2009	No	Innumerable	No	ADPKD
8	45	Female	March 10	FU April 2010	More than 50 each side	No	Multiple cysts
9	52	Male	November 2007	FU June 2010	Innumerable	No	ADPKD
10	54	Male	April 2009	No	Innumerable	No	ADPKD
11	73	Female	January 2008	FU July 2010	15 cysts each side	Yes	Multiple cysts
12	81	Female	November 2009	NE January 2010	15 cysts each side	Yes	Multiple cysts
13	52	Female	June 2010	FU August 2011	Innumerable	No	ADPKD
14	36	Female	November 2009	FU September 2010	Innumerable	No	ADPKD
15	40	Male	July 2009	NE July 2009	Innumerable	Yes	ADPKD
16	69	Male	August 2010	FU July 2011	Innumerable	No	ADPKD
17	81	Male	March 2009	NE March 2009	Innumerable	Yes	ADPKD
18	38	Male	August 2010	NE September 2010	Innumerable	No	ADPKD
19	41	Female	September 2010	FU February 2011	Innumerable	No	ADPKD
20	43	Female	March 2011	No	Innumerable	No	ADPKD
21	65	Female	March 2011	No	10 each side	No	Multiple cysts

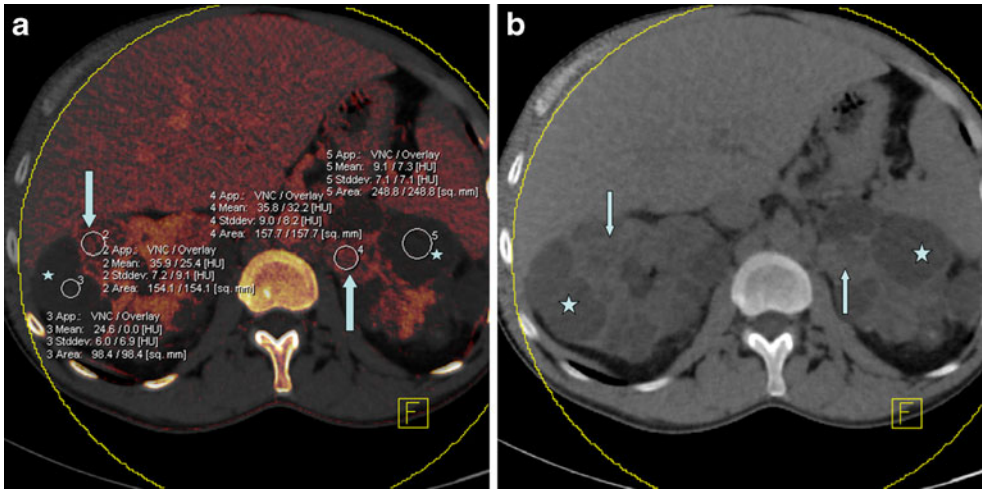

Fig. 1 Dual energy CT in a 40-year-old man with known autosomal dominant polycystic kidney disease (ADPKD) allows for direct visualisation of contrast enhancement based on a single-phase CT examination. Colour-coded image (**a**) shows the absence of enhancement in two simple cysts (*asterisks*), whereas two malignant-appearing masses enhance by 25 and 32 HU ("overlay" values in the image, *arrows*). The virtual non-enhanced (VNE) image (**b**) shows that simple cysts appear to be homogeneously hypodense (*asterisks*), whereas masses display soft tissue attenuation (*arrows*)

Discussion

As patients with polycystic kidney disease (PKD) and especially those with additional ESRD are at an increased risk of developing RCC [5], which can only be treated with curative intent if detected early, they need constant follow-up imaging.

In this patient population it is of key importance to keep radiation exposure to a minimum, as the risk of radiation-induced malignancy increases with the number of CTs [8]. All patients in this study underwent routine ultrasound imaging with (n=8) or without (n=13) intravenous contrast; although ultrasound is a radiation-free test and therefore ideally suited for repeat examinations, it did not reveal conclusive results in our patient population. Twelve patients had undergone one to four MRI examinations in the past. MRI tends to be problematic in PKD patients as a result of motion and breathing artefacts and misregistration between contrast- and non-contrast-enhanced sequences that may limit the diagnostic accuracy in the detection of subtle enhancement.

Our preliminary results in this selected patient population with PKD show the potential of DECT to significantly reduce the radiation exposure to the patient, at the same time improving the diagnostic accuracy of the examination. DECT is able to differentiate benign from malignant renal masses on the basis of a single-phase CT examination (nephrographic phase) as opposed to a normal biphasic acquisition (unenhanced and nephrographic phases) of single energy CT, thereby saving a considerable amount of radiation.

When imaging patients with PKD, the most important diagnostic criterion for the detection of malignancy is contrast enhancement of potential masses. Traditionally, this can only be assessed by means of comparative Hounsfield unit measurements on pre- and post-contrast-enhanced acquisitions which tends to be tedious and difficult as

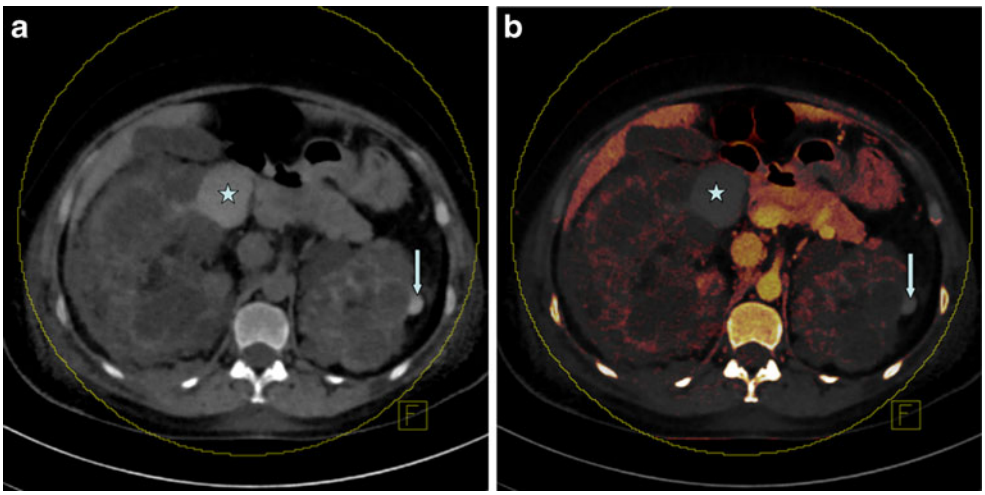

Fig. 2 Dual energy CT in a 41-year-old woman with known ADPKD. The VNE image (**a**) shows two hyperdense cysts (*arrow*, *asterisk*). The colour-coded image (**b**) proves the absence of enhancement in these two lesions, thereby excluding malignancy

images have to be compared side-by-side. Dual energy CT provides the ability to directly visualise enhancement of masses and cystic lesions in a colour-coded fashion. Furthermore, it allows for direct measurements of enhancement on the contrast-enhanced acquisition without the need to acquire unenhanced imaging [4].

For radiologists, the examination of polycystic kidney patients with CT not only involves high radiation doses that accumulate over the years, but it is also very tedious to compare the sometimes innumerable cysts on unenhanced and contrast-enhanced phase images with one other. It is necessary to check the iodine uptake of a suspicious renal lesion to differentiate between a malignant tumour and a haemorrhagic or complex cyst. Our patients, especially those with ADPKD, often had gigantic kidneys with more than 50 cysts. With DECT, a colour-coded display of the iodine distribution on the CT images could help the radiologist to determine the presence of enhancement within one or more of those multiple lesions. In addition, DECT allows for direct measurements of enhancement on a single set of CT images, obviating the need for comparison of pre- and post-contrast-enhanced densities on TNE and nephrographic phase images.

The direct visualisation of enhancement on DECT images makes it much easier and faster to differentiate a suspicious lesion from a simple cyst and consequently speeds up the workflow. Thus, DECT helps the radiologist to achieve a shorter reading time compared with the standard examination, and it also improves diagnostic confidence as malignant lesions can reliably be differentiated from benign findings.

On a regular dual phase CT of the kidneys, the phases are acquired one after another and there is potential that they are not perfectly aligned, or that motion artefacts occur. In patients with multiple renal cysts, anatomical mismatch can make it impossible to determine whether or not there is enhancement in a single cystic lesion. A DECT, however, only requires one phase for differentiation and thereby minimises anatomical mismatch.

One out of 21 patients was scheduled for bilateral nephrectomy and underwent preoperative DECT. In this case (no. 18 in Table 2), kidneys were grossly enlarged and showed innumerable simple and haemorrhagic cysts. One lesion at the right lower pole showed clear contrast enhancement and was reported as suspicious for malignancy; however, at histopathology, an adenoma with associated inflammatory changes was found which is generally regarded as a premalignant lesion, but there was no evidence of malignancy.

In summary, our study shows the potential of renal dual energy CT in patients with polycystic kidney disease. Because of the diverse imaging appearance of complex and simple renal cysts in close proximity to potential malignancy it is not always easy to correctly identify malignant renal masses in these patients. Dual energy CT facilitates this task by providing immediate information about enhancement and thereby about the nature of complex cystic and solid renal masses. On the basis of our preliminary results, we believe that renal DECT can be recommended as an innovative and reliable imaging test in patients with polycystic kidney disease.

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