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CT Urography: An Update in Imaging Technique

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Abstract For decades, traditional IVU studies have been the mainstay in the investigation of urinary tract calculi and obstruction. However, they have been largely superseded by non-contrast CT in the present day. The use of contrast material further expands the utility of CT in the evaluation of urinary tract disease, allowing detection and characterization of renal masses and urothelial lesions. In this review article, we discuss the development and current role of CT urography as the complete imaging investigation in the genitourinary system. Conventional multiphasic protocols and split-bolus techniques for radiation dose reduction are considered. We then focus on how recent technological advances have allowed dual-energy CT to play a complementary role in CT evaluation of the genitourinary system, allowing stone and renal mass characterization, as well as creation of virtual unenhanced datasets. The use of associated post-processing software applications in the clinical context is illustrated.

Keywords CT urography · Split-bolus · Dual-energy CT · Urinary stone characterization · Virtual unenhanced · Virtual non-contrast

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Introduction

Up until the time when the landmark article by Smith et al. was published in 1995 [1], intravenous urography (IVU) was the gold standard in the imaging evaluation of ureteral stones and urinary tract obstruction. Since then, non-contrast computed tomography (CT) of the urinary tract (CT KUB) has been accepted as being more precise and accurate. In that same year, Sommer et al. touched upon the value of reformatted CT images in the imaging evaluation of patients with suspected renal colic [2]. Looking back, even with the older generation CT scanners and their accompanying limitations, the value of multiplanar reformatted images was apparent.

In the subsequent year, Smith et al. further expounded on the utility of CT KUB in the workup of patients with acute flank pain, since other extraurinary etiologies of acute flank pain could be picked up as well [3]. In addition to that, Katz et al. elaborated on associated CT findings which supported the presence of acute obstruction, some of which are not seen on IVU [4].

As a cross-sectional imaging modality, CT has intrinsic advantages compared to radiographs. However, it also has the inherent disadvantage of higher radiation dose. Nevertheless, even with low-dose protocols with radiation doses similar to abdominal radiographs, it has been shown that the diagnostic quality is comparable with that of standard-dose protocols [5, 6]. In addition, CT KUB does not require intravenous administration of contrast medium, which removes the risk of nephrotoxicity. A retrospective study conducted by Ahmed et al. in a single-tertiary care centre spanning 6 years from 2002 to 2007 revealed a significant shift in choice of imaging in renal colic from IVU to CT KUB [7].

Yet, for over 80 years, IVU had been the tried and tested imaging modality and was found universally within protocols for the workup of renal colic. Given the trust and familiarity that had developed over a long time, it is understandable that some of our clinician colleagues still prefer IVU even in the current times. Possible reasons include the ease with which IVU images can be used to explain findings to patients, compared to cross-sectional CT images which require specialised training to interpret. Also, the usage of intravenous contrast medium and resulting opacification of structures allows better visualisation and appreciation of IVU images compared to non-contrast CT images.

On the background of a shift in preference towards CT, we now turn our attention to CT urography, which is essentially contrast-enhanced CT evaluation of the urinary tract.

CT Urography

CT urography (CTU) is defined as a diagnostic examination optimized for imaging the kidneys, ureters and bladder with thin-slice multidetector CT, administration of intravenous contrast medium and acquisition of images in the excretory phase [8]. It is now widely accepted as the most thorough imaging evaluation in the workup of hematuria, since the most common etiologies (calculi, renal mass and urothelial tumours) can be detected and characterized.

CTU is a contrast-enhanced multiphasic study and is similar to IVU in that respect. Like IVU, CTU generally comprises unenhanced, nephrographic and pyelographic phases. The acquisition of corticomedullary phase images is not routine, since it is well established that renal masses are more visible in the nephrographic phase compared to the corticomedullary phase [9]. Szolar et al. showed in their study of 93 patients with renal masses less than 3 cm in size that the nephrographic phase is superior to corticomedullary phase in depiction of small renal masses, due to statistically significant larger attenuation difference between lesion and renal medulla in nephrographic phase compared to corticomedullary phase [10]. In their study, 211 lesions were detected in corticomedullary phase, and 295 lesions were detected in nephrographic phase. Perhaps the most significant finding was that the number of medullary lesions picked up in nephrographic phase was 5.3 times that in corticomedullary phase (48 lesions in nephrographic phase and 18 lesions in medullary phase) [10]. Apart from potentially missing lesions, another major pitfall of the corticomedullary phase is the detection of pseudolesions (false positives), due to inhomogeneous enhancement of renal medulla or the appearance of normal renal medulla during this phase. In spite of these drawbacks, a small number of cases (3 %) in this study were actually better demonstrated on the corticomedullary phase compared to nephrographic phase. Nevertheless, the overall statistical evidence pointed to nephrographic phase being superior to corticomedullary phase in depiction of small renal masses. Although the renal veins and other abdominal visceral parenchyma are better evaluated in the corticomedullary phase, these are usually not required in the initial imaging evaluation of hematuria.

For the unenhanced phase, the main objectives are to detect radiopaque urinary calculi and to help in characterization of renal lesions (e.g. baseline unenhanced attenuation value, presence of fat/calcium). For the nephrographic phase, the main objectives are to detect and characterise renal lesions and to detect subtle enhancing urothelial lesions (which may be iso-attenuating on unenhanced phase or obscured by contrast on pyelographic phase). For the pyelographic phase, the main objective is to detect urothelial lesions.

IVU has been largely supplanted by CTU in the evaluation of hematuria. CTU has many advantages over IVU. Firstly, it has been shown to be more effective than IVU in the detection of urinary tract calculi. Secondly, it is well established that CTU is better than IVU (and ultrasound) in the assessment of renal masses. Thirdly, advances in CT technology and the re-emergence of dual-energy CT have unlocked many useful applications, transforming CTU into a very powerful diagnostic tool. Present day dual-energy CT scanners and available advanced image visualisation software have made feasible several dual-energy applications such as stone characterization, generation of virtual non-contrast image sets and analysis of enhancement kinetics in renal lesions with the use of colour-coded iodine images. These will be discussed later in the article.

Evaluation of Urothelial Lesions

There has been scepticism with regard to the ability of CTU in detecting urothelial tumours. However, Tsili et al. showed the excellent accuracy of CTU in the detection of pelvicalyceal and ureteric transitional cell carcinoma [11]. The ability to detect urothelial malignancies was even highlighted as a main benefit of CTU [11]. But the variability of ureteral distension and opacification (due to peristaltic contractions) in CTU is well known, and there remains a theoretical risk of missing a urothelial malignancy within an unopacified ureter. Interestingly in this same study, Tsili et al. showed a 100 % negative predictive value of urothelial malignancy within an unopacified ureter (albeit in a small sample size where 22 out of 75 patients had incomplete distension/opacification of ureters). In 2012, Cowan emphasized the outstanding diagnostic accuracy of CT urography compared to other modalities (including IVU, ultrasound and retrograde ureteropyelography) and recommended CTU as the first imaging test for the evaluation of hematuria in patients at high risk of urothelial cell carcinoma [12•].

As detection of urothelial tumours logically depends on optimal distension and opacification of the pelvicalyceal systems and ureters, several methods have been used in an attempt to achieve complete distension of the collecting systems (e.g. oral hydration, saline infusion, diuretic administration, prone positioning and usage of compression devices). Some of these are more controversial than others. For example, the usage of external compression devices (like in IVU) necessitates additional CT acquisitions and increases radiation exposure.

Radiation Dose

The biggest drawback with CTU is the exposure to a larger amount of radiation dose, which accompanies multiple CT acquisitions. Several techniques have been developed to reduce the overall radiation dose that the patient receives.

For the unenhanced phase, low-dose protocols have been shown to be comparable to standard-dose acquisitions since the large difference in attenuation between calculi and soft tissue allows good contrast despite increased image noise that comes with dose reduction [5, 6].

The use of dual-energy CT permits virtual non-contrast (VNC) images to be post-processed from a single-contrast-enhanced CT acquisition, which potentially removes the need for a true non-contrast (TNC) CT acquisition. However, post-processing algorithms are currently not as robust as desired (e.g. stones <4 mm may be missed), and improvements as well as further studies are needed for wider acceptance and clinical application [13]. The use of VNC images will be further touched upon later in this article.

A split-bolus technique is another method employed to reduce radiation doses. The objective is to acquire images in a combined nephropyelographic phase. To achieve this, two boluses of intravenous contrast medium are administered in sequence after acquisition of unenhanced CT images. The first smaller bolus is given, followed by a delay of about 10 min, after which a larger second bolus is given, and CT images are acquired in the nephrographic phase. Due to the first smaller bolus and 10-min delay, contrast opacification of the collecting systems is seen (along with enhancement of renal parenchyma due to the second bolus). Since it allows two phases to be acquired simultaneously, the split-bolus technique effectively reduces the radiation dose. A possible downside to this technique is the possibility of missing subtle urothelial lesions which are not obvious on unenhanced scan (iso-attenuating) and obscured by contrast on the combined nephropyelographic phase.

Of course, there is potential in combining both VNC and split-bolus techniques with resulting marked reduction in radiation doses, and preliminary studies show promising results [14•, 15•].

Protocol/Technique

There is as yet no universally accepted protocol and at our institution, we employ a two-acquisition strategy for CTU studies. Our CTU protocol comprises acquisition of images in the unenhanced phase and a second acquisition of images after triple-bolus contrast administration. The outcome is a set of unenhanced images and a set of post-contrast images of combined phases (vascular, corticomedullary, nephrographic and excretory phases). On this post-contrast series, both the upper and lower urinary tracts, as well as vasculature, are enhanced [16].

After acquisition of the unenhanced image series, 30 ml of intravenous contrast medium is injected via a power injector at a rate of 2.0 ml/s. This is followed by a saline bolus (80 ml at a rate of 2.0 ml/s). The patient is then encouraged to hydrate orally. Ten minutes after injection of the first contrast bolus, a second bolus comprising a 90-ml mixture of contrast (35 %), and saline (65 %) is injected intravenously at a rate of 2.0 ml/s via power injector. After a pause of 54 s, a third bolus comprising an 80-ml mixture of contrast (50 %), and saline (50 %) is administered intravenously via power injector at a rate of 3.0 ml/s. Acquisition of the post-contrast-enhanced image series is performed after the third bolus has been completely given. The first contrast bolus results in opacification of the collecting systems, ureters and bladder (excretory phase), while the second and third boluses contribute to the vascular, corticomedullary and nephrographic phases.

Our protocol is summarised in Fig. 1.

Dual-Energy CT

Dual-energy CT has been around for years, since the 1970s. However, it is not till fairly recently in about 2006 that its practical use in the clinical setting started to receive serious attention. Dual-energy CT essentially involves the acquisition of images at two separate X-ray photon energy spectra. The lower energy spectrum (commonly 80 kVp) yields images that have intrinsically low signal-to-noise ratios and historically were too noisy for clinical usage. More recently, however, the newer generation CT scanners are capable of producing low kVp images that are of diagnostic quality, thus opening the door to practical clinical applications for dual-energy CT. The primary advantage of dual-energy CT is its ability to differentiate materials based on the

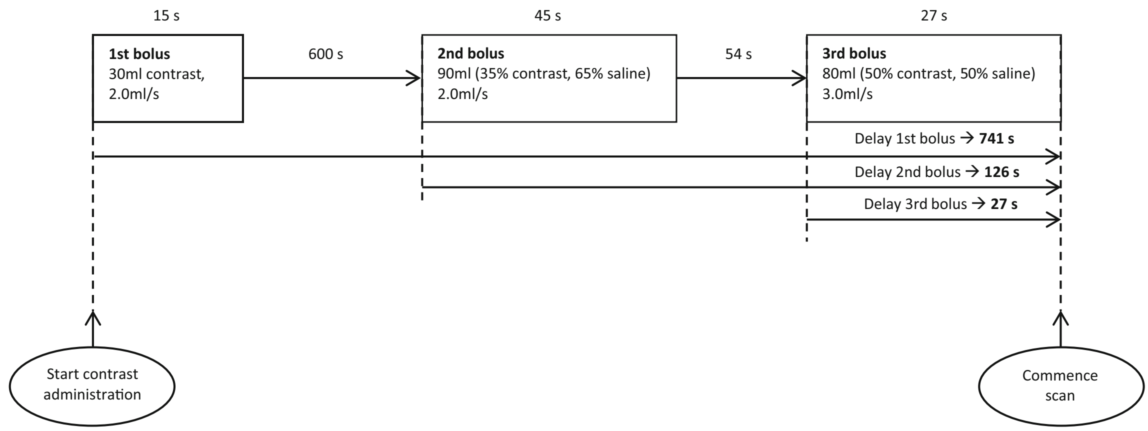

Fig. 1 Schematic diagram of a triple-bolus scanning protocol for acquisition of a single-post-contrast scan with combined phases. By the time of scanning, the first contrast bolus has resulted in opacification of the collecting systems, ureters and bladder (excretory phase), while the second and third contrast boluses cause enhancement of renal parenchyma and vessels (renal arteries and veins). The total time delay from start of contrast administration to acquisition of scan is 741 s

differences of their attenuation at different photon energy spectra. Thorsten provided an excellent review on the general principles of dual-energy CT, and the reader is directed to his article for an overview [17].

Post-processing algorithms create material-specific and non-material-specific images, and these have useful applications with regard to the evaluation of the genitourinary system [18]. Non-material-specific images basically simulate conventional CT images. They are created by blending of the low kVp and high kVp images to achieve an average kVp image set. Blending can be linear or nonlinear, the latter used for enhancement of image quality by maximising contrast and minimising noise [18].

The creation of material-specific images is what sets dual-energy CT apart from conventional CT, since additional information can be derived and potentially impact upon clinical management. During post-processing of post-contrast dual-energy CT images of the genitourinary system, detection and subtraction of iodine (producing 'iodine overlay' and VNC images respectively) create material-specific images. Non-iodine material-specific images can also be produced and utilised for example in characterisation of renal calculi.

The creation of VNC images can eliminate the need for true unenhanced images (Fig. 2), and this has been alluded to earlier in the article. In patients with known renal masses, it has been shown that high quality VNC images can be produced and reasonably replace true unenhanced images for the purpose of mass characterisation on CT and in the process reduce radiation dose significantly [19]. Nevertheless, this technique is not yet widely accepted and not in routine clinical use. Takahashi et al. showed that VNC images created from the pyelographic phase allowed reasonable delineation of urinary calculi; however, this was

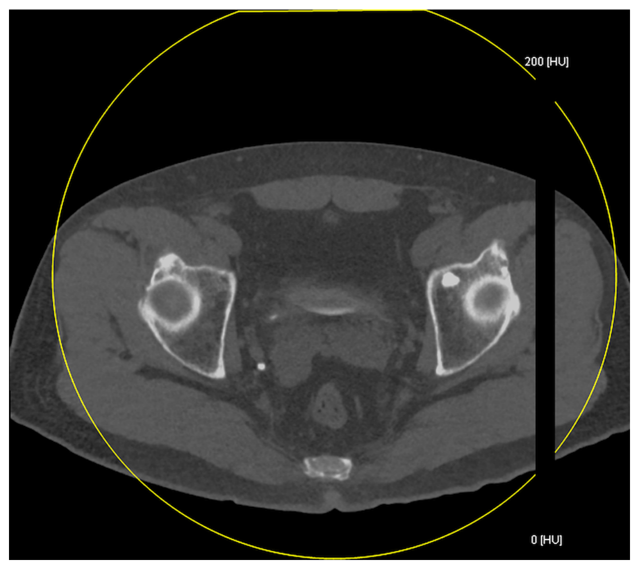

Fig. 2 Virtual non-contrast axial image in a 54-year-old male who presented with right abdominal pain demonstrating presence of a 5-mm right distal ureteric calculus. Virtual non-contrast images can potentially replace true unenhanced scans and allow significant reduction in radiation doses; however, there are limitations that prevent its widespread clinical use currently. Note the layering of unsubtracted iodine in the dependent portion of the imaged urinary bladder. Although not in this case, unsubtracted iodine may mimic urinary calculi (false positive)

limited for smaller calculi (1–2 mm) [20]. Another study by Toepker et al. shows that calculi appear slightly smaller on VNC as compared to TNC images—in this study, the average calculus size identified in VNC images was 92.5 % of that seen in TNC images [21]. In our experience, apart from being smaller, urinary calculi also appear less dense in VNC images as compared to TNC images. The limitations of VNC images in depicting urinary calculi with

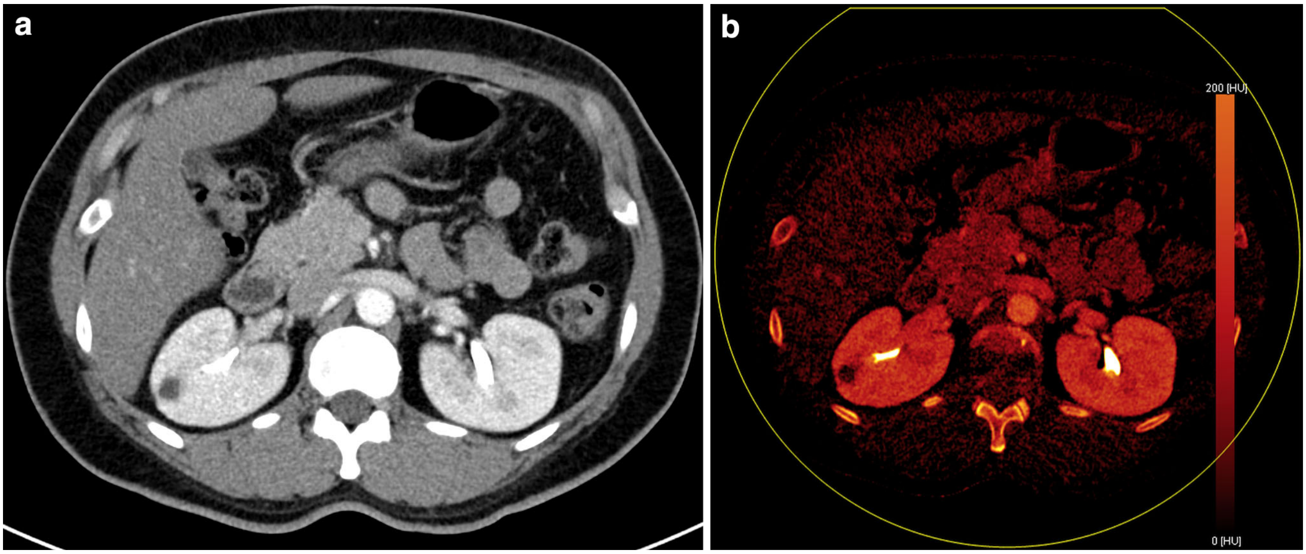

Fig. 3 **a** Triple-bolus contrast CT scan done in a 35-year-old female with hematuria shows a simple cyst in the right kidney. **b** On the 'iodine overlay' images generated on post-processing software, the cyst shows no iodine uptake, confirming absence of intralesional enhancement

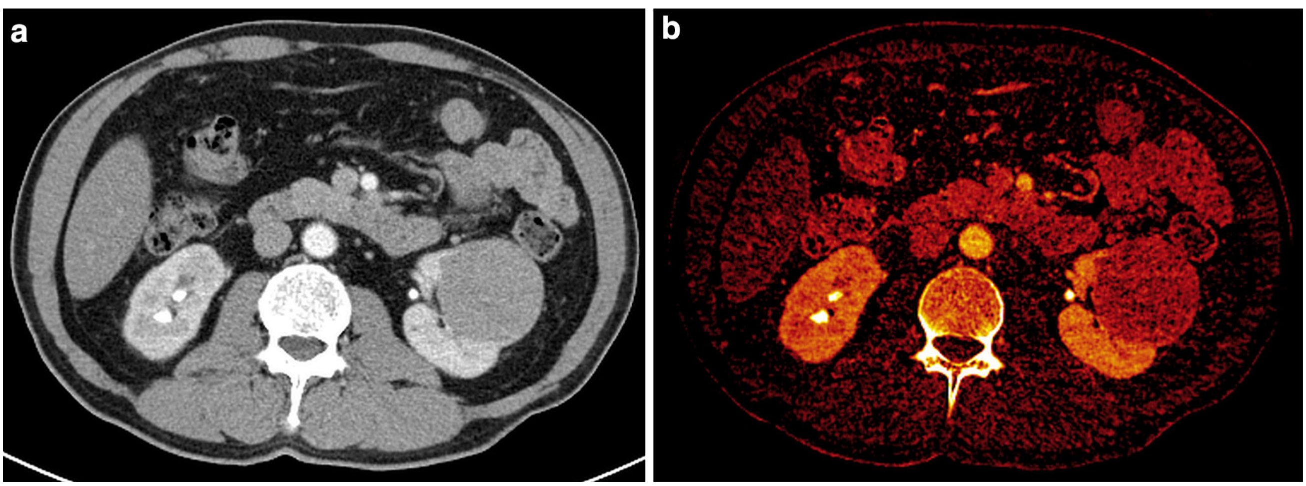

Fig. 4 A 60-year-old male was evaluated for hematuria. **a** A sizeable well-defined hyperdense cystic lesion is seen in the left kidney on triple-bolus contrast CT scan. **b** The 'iodine overlay' image shows iodine uptake, indicating presence of enhancement. Comparison between true unenhanced (not shown) and post-contrast images revealed significant post-contrast intralesional attenuation increase of about 50HU, confirming a surgical lesion. The ability of dual-energy CT to detect iodine permits characterisation of incidental hyperdense renal cysts on single-phase post-contrast CT scans

regard to stone size and density result in threshold sizes and density values being required for their reliable depiction on VNC images [20, 22]. In addition to these limitations, common rim artefacts outlining the collecting systems may obscure small stones (false negative), while unsubtracted iodine may give rise to the impression of a small stone (false positive) [20]. Although currently promising, VNC images cannot entirely replace TNC images due to slight but significantly poorer image quality. Nevertheless, new generation dual-source dual-energy CT scanners with higher tube power can produce VNC images of sufficient quality that will likely eliminate the need for TNC images in future when such scanners are more widely used [23].

'Iodine overlay' images are produced by superimposing colour-coded regions (where iodine is detected) on grey-scale non-material-specific images. This permits easy visualisation of contrast enhancement and allows lesion characterisation. A rather commonly encountered scenario is the incidental indeterminate hyperdense renal cystic lesion which has been picked up on a single-phase post-contrast CT scan. The traditional strategy is to organise a multiphasic CT scan of the kidneys so as to determine

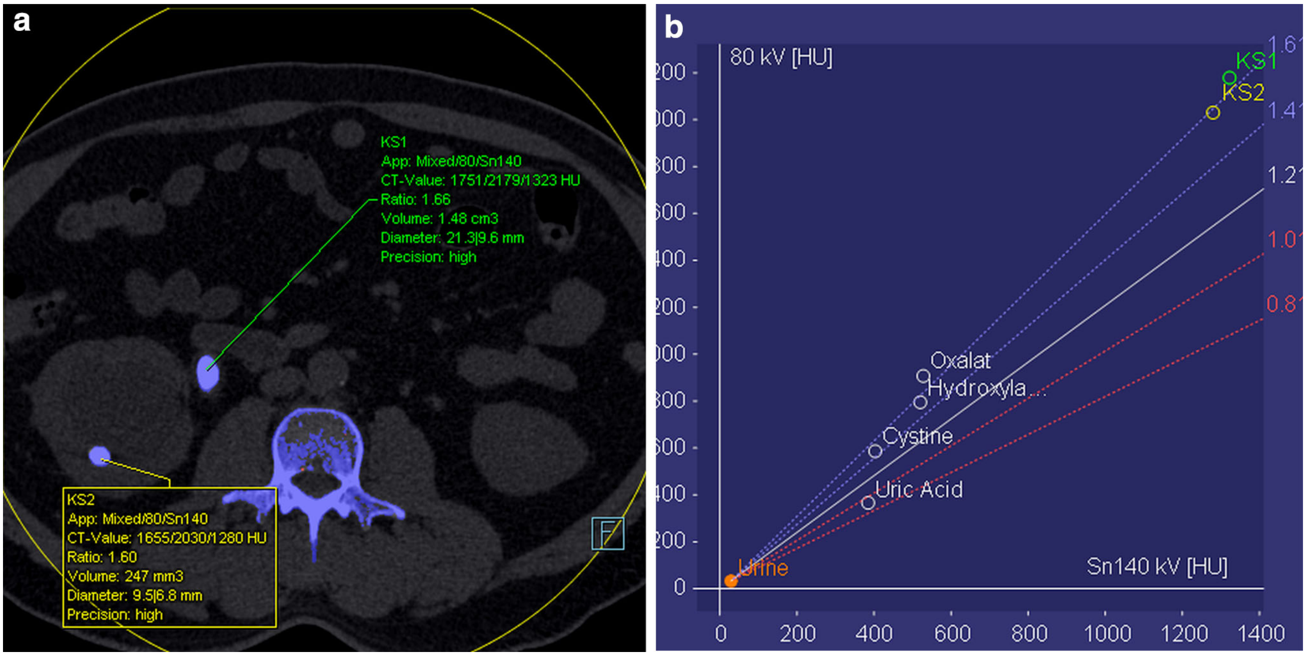

Fig. 5 A 44-year-old male presented with right flank pain. Dual-energy CT KUB showed an obstructing right pelviureteric junction stone and a non-obstructing right renal stone. **a** In analysis of stone composition, post-processing software assigns colour to the stones (*blue*) based on their attenuation values at different photon spectra (**b**). In this case, both stones are non-uric acid stones and are likely composed of calcium oxalate (Color figure online)

whether the lesion enhances (by comparing pre and post-contrast attenuation values) and to look for other features which might indicate malignancy. If the initial single-phase scan was performed using a dual-energy CT scanner, post-processing software allows the generation of 'iodine overlay' images which permits evaluation for the presence of enhancement within the lesion (Figs. 3, 4). This allows distinction between complicated cysts (of hyperdense attenuation) and truly enhancing cystic lesions and eliminates the need for further CT characterization, and along with it increased patient anxiety, radiation dose and healthcare costs [24•]. Benign renal cysts have no enhancement by definition and should have no iodine uptake. Recently, some researchers have discovered that renal cysts can in fact demonstrate tiny amounts (up to 0.5 mg/ml) of iodine uptake, whereas a truly enhancing lesion shows an iodine concentration higher than this threshold value of 0.5 mg/ml [25, 26]. Quantitative measurement of iodine concentration can therefore serve as a problem solving tool in the characterisation of commonly encountered renal lesions which are 'pseudoenhancing' or 'too small to characterise' [25, 26].

Another clinical application of dual-energy CT is in the characterisation of urinary calculi. In the past, attempts at characterizing renal calculi using conventional CT were not very successful. Each type of calculus has a range of attenuation values depending on its composition, and since there is much overlap between the attenuation ranges, such an approach was not accurate enough for clinical application. Dual-energy CT, however, allows differentiation of the calculi compositions based on the differences in their attenuation values at different photon spectra (Figs. 5, 6). The use of dual-energy CT to distinguish urate-containing from non-urate-containing renal calculi has been studied and shown to have accuracies approaching 100 % [27, 28]. Such great accuracy is attributed to the large difference in effective atomic numbers between urate-containing and non-urate-containing renal calculi. With more recent advances in technology, characterization of renal calculi into five categories (namely urate, cystine, struvite, calcium and brushite and apatite) has been made possible. In their study, Qu et al. showed that the use of additional tin filtration in dual-source dual-energy CT resulted in better differentiation between the 5 categories of renal calculi [29].

Advanced Imaging Visualisation Techniques

The use of post-processing software allows more powerful and complete interpretation of CT images. Multiplanar reconstruction (MPR) images can be dynamically manipulated and assessed in real-time (Fig. 7). Dynamic MPR evaluation greatly enhances visualisation of anatomical structures and lesions since it allows the images to be viewed in any slice thickness and literally any plane, not

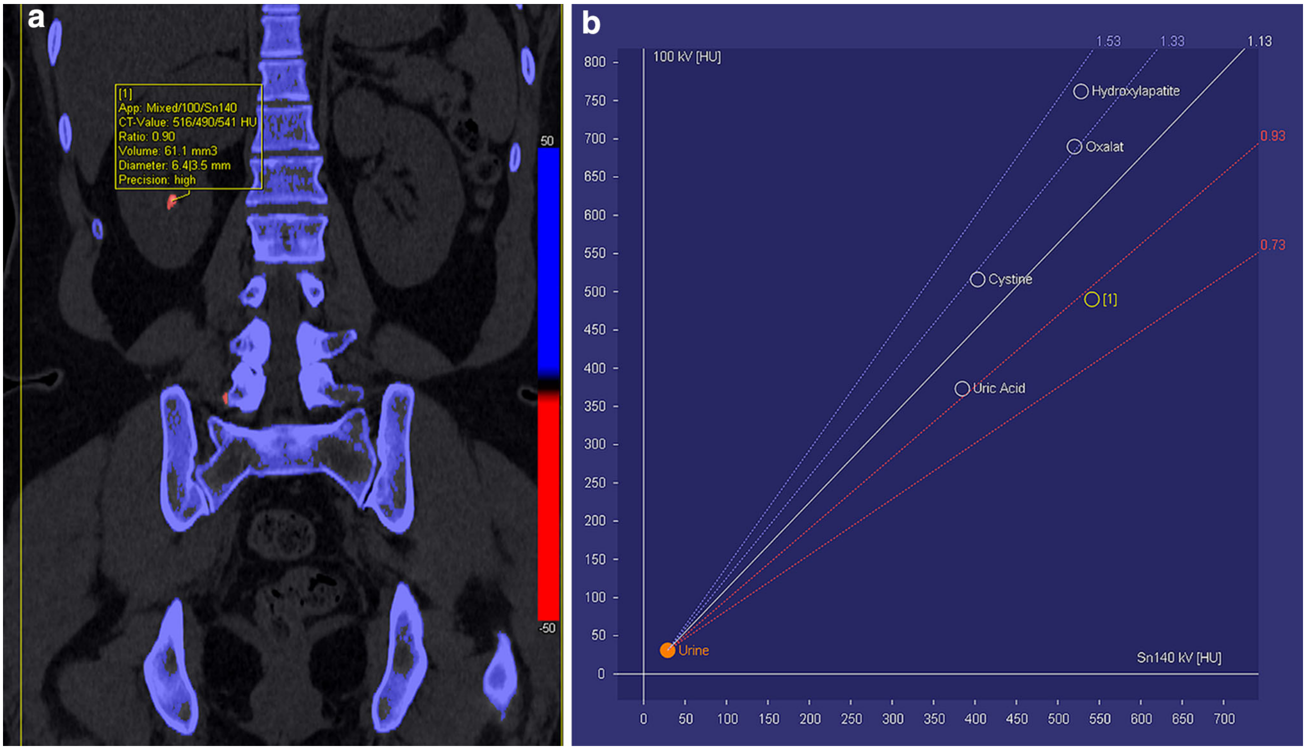

Fig. 6 A 50-year-old female was evaluated for hematuria. Dual-energy CT KUB revealed a right lower pole renal stone. **a** Stone analysis assigned colour to the stone (*red*) based on its attenuation values at different photon spectra (**b**). Note that the *colour* assigned depends on presets and is customisable. In this case, the stone is composed of uric acid. Due to the large difference in their effective atomic numbers, there is great accuracy in distinguishing uric acid stones from non-uric acid stones (Color figure online)

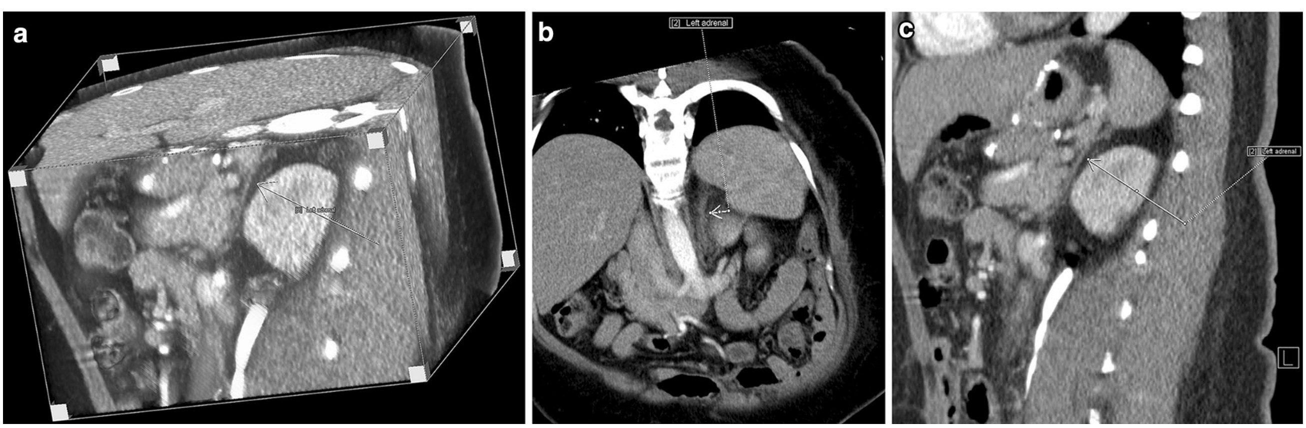

Fig. 7 **a–c** Dynamic MPR evaluation is an advanced imaging visualisation technique which can be performed on post-processing software. It enhances visualisation of anatomical structures, which can be displayed in virtually any plane. This patient had a CT scan done for evaluation of nonspecific abdominal pain. The images demonstrate a normal left adrenal gland with 'sheet-like' appearance. Apparently, bulky left adrenal gland on the conventional axial images was deemed insignificant and could have been contributed by partial volume effect

limited to the conventional axial, coronal and sagittal sections. This is useful not only in evaluating the genitourinary system but also other complex bodily systems.

To harness the power of this new technology, there has to be a paradigm shift in the way CT imaging data is handled and interpreted, which necessitates modifications to conventional workflow processes. In our institution, a client server environment exists which allows dual-energy imaging datasets to be completely evaluated with advanced imaging visualisation techniques. Relevant image snapshots can be acquired and also stored within PACS, as well as made available to the requesting clinicians for use in

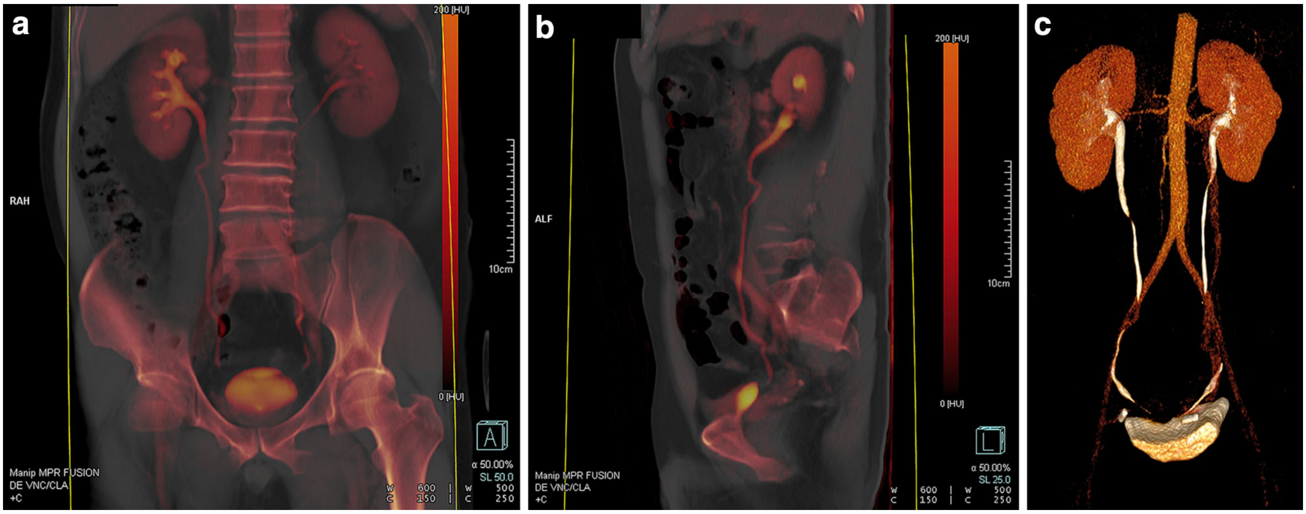

Fig. 8 A 43-year-old male presented with right flank pain. CT urography was performed and revealed an obstructing right distal ureteric calculus with resultant right hydroureteronephrosis. Dynamic MPR evaluation was performed on 'iodine overlay' images with manipulation of slice thickness, achieving overview 'big picture' images **a**, **b** which are excellent for explaining findings to patients. **c** Volume rendering technique (VRT) was performed on post-processing software for a CT urography study of a 46-year-old female with hematuria. This three-dimensional pseudo-IVU image can be used for explanation of findings to the patient. This scan was essentially normal. Note the presence of tubal ligation clips

patient management. Conventional CT images from the same datasets are simultaneously sent to PACS for archiving.

The overview 'big picture' images that traditional IVU studies provide is a feature that many clinicians like, since they can be used to explain findings to patients more easily. This IVU-like image can be achieved with dynamic MPR evaluation and manipulation of slice thickness. Volume rendering technique (VRT) is another post-processing technique which allows the construction of a three-dimensional image of the urinary collecting system in the excretory phase, which also resembles an IVU image. The manipulated image can then be used by the clinician for explanation of findings to patients (Fig. 8).

Conclusions

Multidetector CT is currently the imaging modality of choice in the evaluation of urinary tract disease and has largely supplanted IVU. CT urography is probably the most complete imaging investigation of the urinary tract in the present day. Higher radiation dose, however, as the major disadvantage of CT, is a problem amplified by the multiphasic nature of CT urography. Development of split-bolus techniques to combine scan phases within single acquisitions has resulted in significant reductions in radiation doses. Advances in CT technology have also lessened this problem, with lower radiation doses necessary to achieve diagnostic quality scans. In recent years, the emergence of dual-energy CT has made feasible many useful applications which complement CT urography and further lend support to the reduction of radiation doses. Associated advanced image visualisation tools not only support more comprehensive interpretation of images, but also serve as a means to display images in a fashion suitable for clinicians to convey findings to patients.

Compliance with Ethics Guidelines

Conflict of Interest Dr Keynes Tze-Anns' Low declares no potential conflicts of interest. Dr Hui Seong Teh is a section editor for *Current Radiology Reports*.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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