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CURRENT ROLE OF DUAL-ENERGY COMPUTED TOMOGRAPHY IN PREDICTING THE CHEMICAL COMPOSITION OF THE URINARY STONES AND RADIATION CONCERNS.

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ABSTRACT

Dual-energy CT (DECT) has shown excellent outcomes in differentiating the chemical composition of the urinary stones with a great accuracy. Several in-vivo and ex-vivo studies have validated the results. Simultaneous dual-source scans with two x-ray tubes of 80 and 140 kV[45, 14], a single-source scan with dual-layer detector[37, 38] and Rapid switching technique are the commonly used data acquisition techniques, with each having some merits and demerits over each other. The ability of dual-energy CT to differentiate two materials depends on the characteristic CT number ratio of each material.The difference between the CT number ratios for any two materials is determined by the separation between the low and high energy spectra and the effective atomic numbers of the materials.[15] Both material-specific and diagnostic images are created from a single acquisition. The installation of a tin filtration equipment on the newer generation dual energy scanners have resulted in better spectral separation and has made it easy to further differentiate the non-uric acid stone types. Radiation exposure is a prime concern regarding the use of DECT. The amount of radiation exposure to the patients depends on the scanning technique used as well as the part of body to be covered. The implementation of radiation protection strategies during dual energy scanning, such as automated tube current modulation, iterative reconstruction techniques, and designing of improved detector can decrease electronic noise and thus may help to further reduce the radiation dose of DECT.

KEYWORDS: Urolithiasis; Dual-energy CT; DECT; Radiation.

INTRODUCTION

Urinary stone is a very common pathological entity leading to acute flank pain, affecting about one tenth of the overall population and has a high recurrence rate.[1-5] A rising curve is seen in the number of urinary stone patients, probably due to change in dietary habits and working lifestyle. Pediatric population has also witnessed increased incidence of stone disease. Patients typically present with acute loin pain which is colicky in nature that over time may radiate to the inguinal or external genitalia during the course of passage of the stone down the ureter.[6, 7] Associated symptoms may be nausea, vomiting and painful micturition .Hematuria may be present in most of the cases.

Pathogenesis

Multiple predisposing causes have been suggested for the formation of urinary stones. Genetics, positive family history, food intake, hyperparathyroidism, employment, geographical location and urinary tract infections have been identified to be responsible for the increased probability of stone formation. Patients with metabolic disorders such as gout, renal tubular acidosis and hypercalcuria have a greater risk for new stone disease or recurrence of stones.[8] A thorough clinical assessment may suggest metabolic disturbances in over 90% of patients with urolithiasis. Increased intake of sodium chloride and animal protein has also been studied to favor stone growth. Lesser uptake of daily fluid also accelerates the process of stone formation. Cystine stones have been linked to an autosomal recessive disease called Cystinuria. Struvite or magnesium ammonium phosphate stones are prone to develop in infected urine, while formation of uric acid is enhanced in an acidic medium. Diabetes mellitus, obesity and elevated levels of serum urate are risk factors uric acid stones.

Many theories have been in the literature regarding the pathophysiology of stone formation. The theory of super saturation states that urinary stones can be formed as a consequence of crystallization and aggregation of highly concentrated urinary components. Another theory suggest that the precipitation or formation of Randall's plagues in the renal parenchyma have been associated with calcium oxalate and brushite stone occurrence.

Renal anomalies such as horse shoe kidney, medullary sponge kidney polycystic kidney are considered as secondary causes for urolithiasis. They tend to stagnant the urine which causes recurrent urinary tract infections and thus provides micro environment for stone growth.

Stone composition

The chemical composition of the urinary stones is quite variable, the most common being calcium oxalate stones (60%), followed by uric acid stones (5-10%). Cystine, struvite and brushite stones are relatively less frequent.[9]

Diagnosis

Urolithiasis is mainly a clinical diagnosis suggested by the typical presentation of the patient together with the proper medical history combined with renal angle tenderness and hematuria. A clinical scoring scheme STONE[10] standing for size, timing, origin(race), nausea/vomiting and erythrocytes (red blood cells) has been used in the emergency medicine. This calculates a risk quotient for obstructive uropathy and the need for further imaging in these patients. Urinalysis is often the initial laboratory examination. Urine biochemical parameters such as urinary sodium, calcium oxalate and uric acid may provide important clues for the stone composition.[11] But nearly 50% of the symptomatic patients are required to undergo imaging studies to further validate the diagnosis.

Treatment and Management

Medical management includes hydration with intravenous fluids, pain management with intravenous analgesics and operative procedures if required .Stones <5mm in size are treated conservatively, due to high likelihood of spontaneous passage. Medical expulsion therapy (MET) involves the prescription of some regimes that are considered to facilitate the passage of stone. Calcium channel blocker (Nifedipine) and Alpha blockers (Tamsulosin) have shown promising results in this regard. Larger stones are either treated with medical dissolution therapy or through surgical interventions such as extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), ureteroscopy (URS) or open surgery.

ESWL is a minimally invasive day care procedure which is generally used for stones up to 2 cm in size. Extra corporeal shockwave lithotripsy uses externally focused high-intensity acoustic pulses to break a stone in place. It can be used for stones in various locations but is less compatible with lower pole stones, staghorn stones and with the anatomical anomalies of the urinary tract.[12] Success rate of ESWL depends on stone (size, number, composition, and location), renal anomalies, obesity, bony deformities and on the efficacy of lithotripters. Renal hematoma formation, flank pain and trauma to adjacent tissues are known complications. Due to high success rate and because no anesthesia is required, ESWL is the most common surgical procedure, currently used for treatment of stones.

PCNL is generally used for stones greater than 2 cm in size. A small incision of about 1 cm is made at the flank area to get access to the renal pelvis; a percutaneous needle is than passed through it up to the location of the stone. Subsequently a guide wire and a dilator are introduced, while the needle is retracted. A nephroscope is then inserted and the stone is retrieved straight away if small or is first fragmented than extracted. It is useful for large, lower pole stones, and staghorn stones.[12] Most commonly reported complications after PCNL consist of significant bleeding, infection and persistent urinary leakage.[12.13] Hydrothorax can also occur if PCNL is done through the 11th intercostal space.

URS is commonly used for distal ureteral calculi.[13] URS is a more invasive procedure and requires anesthesia. It is optimal for stones up to 1 cm in size located in the kidney or ureter. A ureteroscope is inserted through the urethra up the ureter to the stone. A rigid endoscope may be used in the case of distal ureteral stones, while flexible endoscope is required for proximal ureteral and renal stones. Once the stone is approached, it is either crushed into smaller pieces with the help of a holmium laser or is removed intact if it is small, using a Dormia basket or are left to be passed spontaneously. The stone-free rate for URS is very high (78% to 97%).[14] The procedure is generally performed on an outpatient basis. Possible complications associated with URS include pain, urinary tract infection, ureteral injury, and ureteral stricture Open surgery are rarely performed these days and are opted for complex stones or for patients with underlying renal anomalies where ESWL, PCNL or URS cannot be used.

Imaging Techniques for Stone detection

Imaging in urolithiasis has been evolving over the years due to the technological advancement and a better understanding of the disease process. Imaging plays an important role in establishing the diagnosis, planning management and performing interventions, assessing therapeutic efficacy and for the surveillance of established disease for patients with urolithiasis. The cost of the dianostic imaging, its safety, availibility and good accuracy are the key determinants which requires consideration while evaluating a patient presenting with flank pain.

Plain X-ray KUB, ultrasonography and Intravenous pyelography and computed tomography (CT) are the commonly requested investigations by the urologist.

X-ray Kidney, ureter, bladder (KUB) is limited to the diagnosis of radio-opaque urinary stones as it is unable to detect the radiolucent stones. KUB is also less specific, as it cannot make easy distinction between phleboliths from ureteric stones.

KUB provides stone size measurements, comparable to CT, therfore can be particularly useful in follow-up studies after treatment, so that both the cost and radiation of further CT imagings can be reduced.

Ultrasonography (USG) is a cost effective, contrast free and radiation free technique that is considered optimal for the initial diagnosis of renal stones. As it has no radiation hazards, it is most suitable for imaging pediatric as well as pregnant patients. It can detect urinary stones in the pelvicalyceal system, but is not sufficient for depecting stones in distal ureter as well as at ureterovesical junction. The direct visibility of ureteral stone can be hampered by the overlying bowel gas and the relative depth of the ureter within the pelvis. Furthermore, stone visualisation may be complicated in obese patients by the presence of large amount of fatty tissue.

Intravenous urogram (IVU) gained immense popularity for detecting the renal system. It can give important information about the physiological and functional aspects of the kidney and the urinary tract, including the site, degree and nature of obstruction as well as presence or absence of various possible congenital anomalies. However due to the requirement of bowel preparation, toxicity of the contrast medium causing allergic reactions and anaphylactiod reactions, and due to its contraindications in renal dysfunction, insulin insufficiency, multiple myeloma, congestive heart failure and pregnancy ,has led to its decreased use during the years.[16]

Non-enhanced helical CT (NCCT) is now the preferred method for evaluating patients with urinary stone.[17] It has replaced IVU in recent years due to its better sensitivity, specificity, accuracy and speed.[18-20] NCCT also provides helpful information regarding the differential diagnosis of urolithiasis such as appendicitis, diverticulitis ,colitis or gynecological pathologies such as hemorrhagic cyst or ovarian torsion. CT has found to provide an alternative diagnosis in nearly 20-40% of the patients presenting with symptoms suggestive of urolithiasis.[21-23]

Stone size, burden, anatomic location and stone composition are the main criteria which affect the treatment plan and outcome.[24] Among these stone composition stands out as a very crucial determinant in advocating the treatment plan. Stones composed of cystine or calcium oxalate monohydrate have a firm composition that limits the success of extracorporeal shock wave lithotripsy (ESWL).[15, 25-27] These stones may be more effectively treated with ureterorenoscopy (URS) or percutaneous nephrolithotomy (PCNL).[15, 28] Uric acid stones on the other hand show a good response to chemolysis by citrates.[29] In addition cystine stones have a high recurrence rate, so requires specific metabolic evaluation and follow-up. Thus it is wise to have a prior knowledge of the stone type so that the treatment could be tailored specifically thus avoiding unnecessary invasive procedures.

Traditional techniques for stone analysis are x-ray diffraction, infrared spectroscopy and polarization microscopy, with X-ray diffraction being the most accurate.[30] The major disadvantage of these techniques is that the chemical analysis of the stones is performed only after the stones are extracted and thus they offer no help in selecting optimal treatment approach for the patient.

CT uses the attenuation value (Hounsfield units) of stones to provide some information about their composition.[31-33] Several in vivo[32,33] and in vitro[31,32,34] studies showed that CT can differentiate between uric acid and calcium stones by their different attenuation, as uric acid stones have lower HU values.

However considerable overlap of attenuation values precludes accurate characterization of stone composition with single-source CT[35] as no definite cut-off values have been stated for differentiating the various stone types. The accuracy of correctly identifying all the sub types of urinary stones is reported to be 64–81%, due to significant overlap in attenuation measurements at single-energy CT.

DECT: Though the concept of dual-energy computed tomography was visualized about thirty years ago Alvarez and Macouski[36], it gained importance in recent times due to technical advancement both in scanners as well as post processing software. Currently it is seen as an alternative to NCCT.[33]

The two important mechanisms that are responsible for the attenuation of tissues and materials in computed tomography are Compton scattering and the photoelectric effect; also depending on the energy of X-ray photons. The photoelectric effect is mainly dependent on atomic number (z) and energy (E), whereas Compton Effect is independent of atomic number and is weakly dependent on electron density. CT attenuation does not change significantly with beam energy for the soft tissues, but it varies considerably for materials with large atomic numbers such as iodine or bone, which have stronger attenuation at low tube voltage settings. This allows, the chemical characterization of stones possible using dual energy CT, based on their different chemical character.[37]

The ability of dual-energy CT to differentiate two materials depends on the characteristic CT number ratio of each material. CT ratio is defined as the ratio of the CT number of a given material in the low-energy image to the CT number of the same material in the high-energy image.[15] The difference between the CT number ratios for any two materials is determined by the separation between the low and high energy spectra and the effective atomic numbers of the materials.[15]
DE Ratio = HU lower kVP / HU higher kVp

The accuracy of material discrimination by dual- energy CT is improved by reducing the spectral overlap between low and high energy X-rays and accurate spatial and temporal registration between the low and high energy spectra.[38,39] Spectral separation can be increased by using different tin filtration on the two X-ray tubes.

Several in vitro and in vivo studies have investigated the ability of DECT to accurately differentiate uric-acid stones from non-uric acid stones.[40-43] However there is a clinical need to further differentiate the non -uric acid stones. Kulkarni et al used a single source dual-energy scanner to find its accuracy in differentiating UA stones from non-UA stones both in vivo and ex-vivo. They found the material density images to be 100% sensitive and accurate in detecting UA and non-UA stones. They used the effective atomic number of the stone to sub-classify the non-UA stones and were able to accurately separate all of the struvite, cystine and calcium stones in their phantom study, but only in 83% of calcium stones in the patient study. They concluded that sub-classification of pure non-UA stones can be made accurately, but in case of mixed stones, only the major component can be determined.[44]

Types of dual-energy Scanners and Data acquisition Techniques.

There are several methods of acquiring dual energy CT data: simultaneous dual-source scans with two x-ray tubes of 80 and 140 kV[45], a single-source scan with dual-layer detector[37,38] Rapid switching technique, Sequential dual-energy CT and Twin-beam dual-energy CT.

The Seimens Medical Solution SOMATOM Definition Scanner was the first DECT scanner available. This uses a dual source technique, with two x-ray tubes arranged at 90 degrees. These work simultaneously at the two required energy levels (usually 80 and 140 kVp).

The second technique as used by GE Heatlhcare Discovery 750 HD uses one x-ray tube that rapidly switches between 80 and 140 kVp. This is called as "Fast kv switching" and has a time interval of 0.4 milliseconds.

The third configuration, seen in the Philips Healthcare Brilliance 64, involves a single source but a dual layer multi-detector. This detector has two layers: the first layer absorbs most of the low energy spectrum. These images are then reconstructed separately from the two layers, alleviating the need to have two separate beams.

Dual-source dual energy (DSDT) scanners are most commonly deployed presently.

(DSDT) scanner has two X-ray tubes which generate X-rays at low- and high-energy, and two detector chains which capture the low- and high-energy spectra separately. The high-energy X-rays are generated at 140 or 150 kVp and low-energy X-rays can be generated at 70–100 kVp.[46] Additional filtration of the high-energy X-rays can be done using tin filter to increase the spectral separation from low-energy X-rays.[47] The tube potential of the low-energy X-rays can be varied depending on patient body habitus to achieve better penetration. Since two X-ray tubes are used, the tube current (mA) can be individually optimized for each acquisition enabling use of automated tube current modulation. The tube operating at higher tube potential has full scan field of view of 50 cm, whereas the second tube operating at lower tube potential has a smaller scan field of view which is 33 cm or 35 cm on the second and third generation dual-source dual-energy CT scanners, respectively.[48, 46] Since the low- and high-energy scans are obtained at slightly different times and angles, a slight delay in temporal registration and 90 degree offset of phase of low- and high-energy data would be present.[48,46]

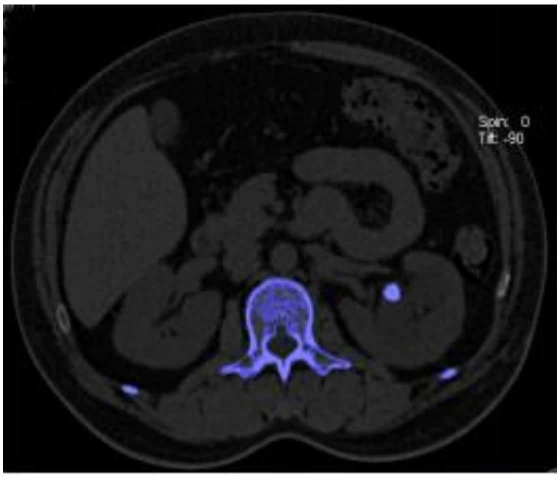
Dual energy Post Processing

Dual-energy CT scan data can be processed to generate three types of image sets.

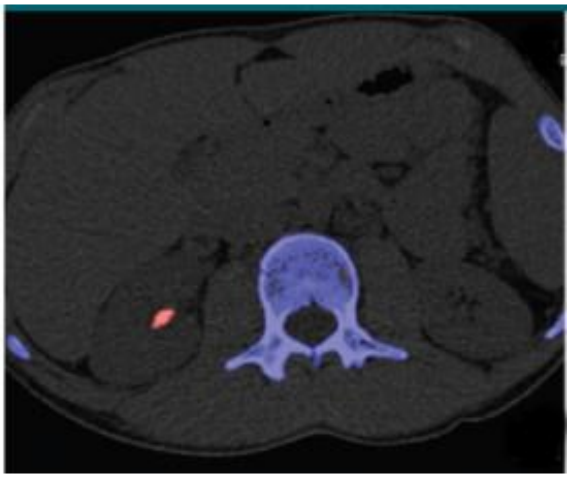
1. Images providing structural information with attenuation values similar to conventional single-energy CT commonly referred to as the “120 kVp images”. These images are used for routine diagnostic interpretation.
2. Material-specific images which can remove or highlight specific materials.
3. Virtual monochromatic images which display energy-dependent attenuation.

In addition to these, the images at low and high kVp can be generated and viewed on some of the dual-energy scanners. Material-specific information from dual-energy data is generated by using material decomposition algorithms which identify and quantify specified materials based on measured change in attenuation between low- and high-energy scans. Material-specific information with dual-source dual-energy CT is generated using ‘‘three-material decomposition algorithm’’ in which the HU values of two known substances (tissue and fat) at both low- and high-energy are fixed while the third substance is varied. The most common third substance is iodine, although any other substance with known chemical composition such as calcium can be used.

Dual energy post-processing software algorithms assume a mixture of water, calcium, and uric acid for every voxel and color-code voxels that show a dual energy behavior similar to calcium, in blue and one that is similar to uric acid in red (Figure 1) .Voxels that show a linear density behavior at both tube potentials remain gray. Using dual energy CT, differentiation of pure uric acid, mixed uric acid and calcified stones is possible.[49] Furthermore, the differentiation of struvite and cystine is possible by adapting the slope of the three-material decomposition algorithm.[49]



(a)



(b)

Figure 1: Axial images in (a) 20-year-old man and (b) 32-year-old man. Dedicated DECT Post processing software can be used to distinguish between uric acid and non-uric acid urinary stones. Uric acid stones are usually coded in red colour whereas non-uric acid stones are encoded blue.

Limitations of DECT

Current limitations of dual-energy CT in stone characterization include the decreased accuracy in characterizing small stones measuring <3 mm and stones with mixed composition, as it would be difficult to obtain accurate dual-energy ratios with calculi <3 mm, and attenuation profile of mixed stones would be different from the predefined thresholds of stones with known composition used for material decomposition algorithms.[50, 51]

However it has been found that stones <4mm tend to pass spontaneously in 80% of the cases, whereas stones >7mm mostly require intervention.[40]

Radiation Concerns

Radiation exposure is a prime concern regarding the use of DECT. Many studies have raised the issue regarding the risk of cancer related to radiation exposure from the various radiological diagnostic imaging as well as interventional procedures and. Dose considerations also becomes important in the context of detecting urolithiasis given the high risk of disease recurrence, which can necessitate further follow up radiological investigations over the life time of a patients with urolithiasis. The amount of radiation exposure to the patients depends on the scanning techniques and protocols used as well as on the region of body studied.[52] Using radiation protection strategies during dual energy scanning, such as automated tube current modulation, iterative reconstruction techniques, and novel detector designs that can decrease electronic noise may help to reduce the radiation dose.[51, 53] It has also been recommended to start with acquisition of a low dose abdominal scan with dose modulation as per the patient’s habitus. After the stone has been located by the radiologist, a subsequent short DECT acquisition is to be performed in the ROI, while the patient is still on the table. This approach has shown to reduce the effective dose by 2-4 msv. The mean radiation dose in a routine-dose DECT examination for stone composition analysis ranges from 6.0 to 26.2 Gy. Efforts have been made to minimize the x-ray radiation dose in CT examinations using dual-energy technologies for kidney stone characterization purposes, including using a low-dose scan technique with the volume CT dose index (CTDI vol) as low as 8.3mGy.Recently several authors have shown that even low dose DECT can effectively estimate the stone composition.

Thomas et al[49] demonstrated that a low-dose dual-source DECT renal calculus protocol (140 kV, 46 mA; 80 kV, 210 mA) were able to distinguish calcified and non -calcified stones in all patients with reduced tube currents (3.43-5.30 mSv). Another study by Thomas et al reported that 38 of 40 patients were correctly categorized by using a low-dose DECT protocol (140 kV, 23 mAs and 80 kV, 105 mAs) with a mean ED of 2.7 mSv. Eiber et al[54] approached by using a targeted DE single-source multidetector computed tomography with a mean ED of 4.95 mSv. The study by Ascenti et al.[43] Consisted of a combined lower-dose single-energy CT of the whole urinary system and focal dual-energy CT of the anatomic region containing the stone. They were able to correctly diagnose all the 24 stones (100%specificity) even by reducing the radiation dose levels by 50%, compared to standard dual-energy acquisition and achieved a mean effective dose of 3.46Msv. In the study by Wilhelm et al[55] the tube current was decreased by 38% of the standard DECT dose level, resulting in significant dose reduction without compromising stone detection and compositional analysis results. In a recent study by Xiangran Cai et al[56], they were able to precisely differentiate calcified, uric acid, and cystine stones with 96.6% accuracy while allowing for patient dose savings of up to 50% (1.81 mSv) using 135 kV, 50 mA and 80 kV, 290 mA scan protocols. Mahalingam et al[57] used a second generation 128 slice DS-DECT scanner (80kV, 105mAS and 140kV, 41mAs) in their study. They were able to obtain a 3 fold reduction in radiation dose compared to standard-dose DECT (45-7mSv).

CONCLUSION

Dual-energy analysis of stone composition is an important adjunct in imaging of urinary stones that has a high accuracy which may be utilized to improve the patient treatment and management. Moreover adoption of proper scanning protocols usage of advanced post processing techniques together with refinement in technology, the amount of radiation dose can be further reduced.

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CONFLICT OF INTEREST

All the authors declare that they do not have any conflict of interest.

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