


# The role of contrast-enhanced computed tomography to detect renal stones

Alice Odenrick <sup>1,2</sup>, Nikolaos Kartalis,<sup>1,2</sup> Nikolaos Voulgarakis,<sup>1,2</sup> Fabian Morsbach,<sup>1,2</sup> and Louiza Loizou<sup>1,2</sup>

<sup>1</sup>Division of Radiology, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, 14186 Stockholm, Sweden

<sup>2</sup>Department of Abdominal Radiology, Karolinska University Hospital, Huddinge, 14186 Stockholm, Sweden

## Abstract

**Purpose:** To investigate the detectability of renal stones in corticomedullary and nephrographic phases on contrast-enhanced computed tomography (CT).

**Methods:** All consecutive patients between January 2012 and February 2016 undergoing CT of the kidneys according to our department's standard four-phase protocol and having at least one stone in the NC-phase (NCP) were included. Fifty patients with altogether 136 stones were eligible. Two radiologists in consensus evaluated the NCP from each examination and documented the number, location, and size of stones. Three abdominal radiologists blinded to the findings of the NCP reviewed independently the corticomedullary and nephrographic phases on two different occasions. They reported the number and location of stones in each kidney. For the inter-observer agreement the intra-class correlation coefficient (ICC) was estimated. The detection rate of renal stones was calculated for the three radiologists and compared between the two contrast-enhanced phases and the results were analyzed with concern to the size of the stones.

**Results:** The ICC was 0.86. There was no statistically significant difference between corticomedullary and nephrographic phases ( $p = 0.94$ ). The detection rate for stones measuring 3–5 mm was 82–88% and 98% for stones  $\geq 6$  mm.

**Conclusion:** The detectability of renal stones  $\geq 6$  mm on contrast-enhanced CT is extremely high. This means that stones with a higher risk of not passing spontaneously can be safely diagnosed.

**Key words:** Kidney—Calculi—Multidetector computed tomography—Contrast Media

## Abbreviations

|       |                                     |
|-------|-------------------------------------|
| CT    | Computed tomography                 |
| CE    | Contrast-enhanced                   |
| CEP   | Contrast-enhanced phases            |
| CM    | Contrast media                      |
| CMP   | Corticomedullary phase              |
| DE-CT | Dual-energy CT                      |
| EP    | Excretory phase                     |
| ICC   | Intra-class correlation coefficient |
| IV    | Intravenous                         |
| I     | Iodine                              |
| MDCT  | Multidetector computed tomography   |
| NGP   | Nephrographic phase                 |
| NC    | Non-contrast                        |
| NCP   | Non-contrast phase                  |

Nephrolithiasis is a common disorder that has a reported incidence of 12% in industrialized countries [1]. The prevalence is higher in developed countries and is globally increasing [2]. Colicky flank pain is the most common presenting symptom of urolithiasis [2]. Previous studies have shown that even renal stones that do not cause obstruction still can cause flank pain and that in the absence of another cause, either clinical or evident on CT, these stones are likely to be the cause of the symptoms [3–5]. Therefore, these non-obstructing stones may cause chronic symptoms that lead to multiple visits to the emergency department and repeated radiological examinations [4].

Treatment depends on the size and location of the stones, renal function, hemodynamic status, and the patients' symptoms [6]. Small renal stones (up to 5 mm in

size) have a high probability (almost 70%) of spontaneous passage [7] and are treated conservatively (observation, oral medication, medical expulsive therapy) [6]. For larger stones the probability of spontaneous passage is less than 50% [7]; in those cases, treatment options include minimally invasive methods (such as extracorporeal shockwave lithotripsy, ureteroscopy, percutaneous nephrolithotomy) or rarely surgery (laparoscopy, open surgery) [6].

Non-contrast (NC) multidetector computed tomography (MDCT) of the abdomen and pelvis has been considered the method of choice for renal stone detection [4, 6–10]. NC-MDCT also has the capability to detect other renal and extrarenal pathologies and it is more effective, faster, and less expensive compared to intravenous (IV) urography [11]. The reason the examination is carried out without IV contrast is based on the assumption that the high attenuating stone will be difficult to detect during either the corticomedullary or nephrographic phase when the surrounding renal parenchyma also enhances and becomes high attenuating [4].

A previous study showed that when a NC-MDCT is performed because of flank pain, up to one-third of the cases show unsuspected findings that are not related to stone disease [8]. Various renal diseases such as infections and neoplasms, and even extrarenal pathologies such as diverticulitis, appendicitis, pelvic inflammatory disease, and malignancies can simulate renal colic [4, 8]. In those cases, omission of IV contrast may lead to wrong or delayed diagnosis.

Another advantage of contrast-enhanced (CE)-MDCT compared to NC-MDCT is the ability to differentiate between a phlebolith and a urinary stone [6]. A CE-MDCT examination can also visualize delayed renal enhancement which can be a sign of urinary tract obstruction [4]. Our hypothesis was that the use of IV contrast would not have a negative effect on renal stones detection at MDCT.

The purpose of this study was to investigate the detectability of renal stones in corticomedullary (CMP) and nephrographic phases (NGP) of CE-MDCT.

## Materials and methods

The regional ethics review board approved the fully HIPAA-compliant study and granted a waiver of patient informed consent.

### *Study population*

All consecutive patients between January 2012 and February 2016 that underwent MDCT of the kidneys according to our department's four-phase standard protocol and with at least one renal stone confirmed in the NCP were included in the study. The study popula-

tion included mainly patients undergoing investigation of macroscopic hematuria or patients with treated renal malignancy undergoing follow-up investigation. No ureteral stones were included in the study. We excluded patients: (1) where the calcification was located in the walls of a vessel or a cyst, (2) where due to technical reasons, the contrast enhancement of the renal cortex was poor, (3) where the dose of IV contrast media was lower than the standard dose [ $< 0.5$  g iodine (I) per Kg body-weight] due to renal dysfunction, (4) where medullary nephrocalcinosis was suspected, and (5) where the stones were located in the ureter.

Cyst and vascular calcifications were omitted deliberately since their detection was not the aim of our study. Cyst and vascular calcifications can easily be diagnosed and differentiated from renal stones in the contrast-enhanced phases (CEP) which were those that the readers investigated. However, they are not as easily defined as such in the unenhanced CT which was used as the standard of reference for detecting renal stones. Thus, in order to avoid false negative cases, they were excluded. Also, in the few cases of medullary nephrocalcinosis it was not possible to measure and define specific stones in the kidney because of the diffuse appearance with innumerable tiny non-well defined high attenuating foci and that is why these cases were excluded.

A total of 50 patients were eligible (37 men and 13 women, median age 71). From these, one patient had a single-kidney. Two kidneys were excluded, one kidney because it had multiple calcifications in the parenchyma after previous pyelonephritis and the other because it had a large staghorn calculus that was fragmented making it impossible to count. Therefore, a total of 97 kidneys and 136 stones were included. There was a median of 1 stone per kidney, with a range from 0 to 9 stones. The median stone diameter was 4 mm, with a range from 1 to 40 mm.

### *Examination techniques, image acquisition and scanning protocols*

All examinations were performed in the radiology department at our hospital on a 64-MDCT scanner either GE Healthcare (GE lightspeed VCT and GE HD 750, GE healthcare, Milwaukee USA) or Siemens Healthcare (Siemens Somatom definition flash, Siemens healthcare, Forchheim Germany). The kernel used was soft tissue (GE) and I30 medium smooth (Siemens). All patients were examined according to our department's four-phase protocol that includes NCP, CMP, NGP, and excretory phase (EP) (Table 1).

### *Imaging assessment*

The NCP—alone or in combination with the CE-phases, when needed—was considered the standard of reference for detecting renal stones [4, 6–10]. One radiologist

**Table 1.** Protocol MDCT kidney

| Protocol                         | MDCT kidney   |
|----------------------------------|---|
| Oral contrast                    | 500 mL water, 30 min prior to examination   |
| Intravenous contrast media (CM)  | <i>Visipaque</i> 320 mgL/mL or <i>Iomeron</i> 400 mgL/mL  |
| (a) Volume (mgI/kg body weight)  | (a) 500   |
| (b) Injection duration (s)       | (b) 25  |
| (c) NaCl flush                   | (c) 100 mL with the same injection time as CM   |
| Scan start and field             |   |
| (a) Non-contrast phase (NCP)     | (a) Diaphragm down to trochanter minor  |
| (b) Corticomedullary phase (CMP) | (b) 10 s after bolus tracking reached 160 HU in the aorta at the level of the first lumbar vertebra |
| (c) Nephrographic phase (NGP)    | (c) 45 s after CMP administration begins  |
| (d) Excretory phase (EP)         | (d) 480 s after the injection started   |
| Scanning parameters              |   |
| (a) Slice thickness              | (a) 0.625 mm  |
| (b) Pitch                        | (b) 1   |
| (c) Tube voltage (kV)            | (c) 120 kV  |
| (d) Tube current (mA)            | (d) ATCM  |
| Reconstructions                  |   |
| (a) Slice thickness              | (a) 5 mm  |
| (b) Interval                     | (b) 2.5 mm  |

**Table 2.** Detection rate of renal stones in CMP and NGP for each reader and totally

|          | Detection rate           |                          |
|----------|--------------------------|--------------------------|
|          | CMP % (number of stones) | NGP % (number of stones) |
| Reader 1 | 75 (102)                 | 78 (106)                 |
| Reader 2 | 79 (108)                 | 81 (110)                 |
| Reader 3 | 96 (131)                 | 92 (125)                 |
| Total    | 84 (341)                 | 84 (341)                 |

CMP, corticomedullary phase; NGP, nephrographic phase

during residency (2 years of experience) in consensus with one radiologist (5 years of post-residency experience) evaluated the NCP by using all three reformations (axial, sagittal and coronal) from each examination and noted the number, location and size of stones. In this study (regarding the CEP as well as the NCP) we defined a renal stone as a round or oval, high attenuating focus measuring more than 1 mm in size located in renal calyces or pelvis and not in the wall of a vessel or a cyst. The size was measured in two dimensions: the largest diameter and the diameter perpendicular to that. For the statistical analysis, the largest diameter was taken into consideration.

Three radiologists (reader 1 with 6 years and reader 2 and 3 each with 5 years of post-residency experience) reviewed independently the CEP on two occasions blinded to the findings of the NCP. On the first occasion,

**Table 3.** Detection rate of renal stones in CMP and NGP stratified by stone size

|        | Detection rate           |                          |
|--------|--------------------------|--------------------------|
|        | CMP % (number of stones) | NGP % (number of stones) |
| ≤ 2 mm | 57% (60)                 | 65% (68)                 |
| 3–5 mm | 88% (134)                | 82% (126)                |
| ≥ 6 mm | 98% (147)                | 98% (147)                |

CMP, corticomedullary phase; NGP, nephrographic phase

they assessed the images obtained in the CMP, and on the second occasion, the NGP. Between these two occasions there was a time interval of at least 1 week in order to minimize recall bias. They scored the number of stones in each kidney and reported the location. The radiologists received written instructions and information about the definition of renal stones as described above. They were informed that all patients—though not all kidneys—included had at least one renal stone. The evaluation time was unlimited. The reviewers had access to axial, coronal and sagittal images for each patient. They were allowed to freely adjust window and level setting. The detection rate of renal stones was calculated for each radiologist and compared between the two CEPs and the results were analyzed with regard to the size of the stones. The correlation between the detection rate and the size of the stones divided into three different subgroups, namely, less than or equal to 2 mm, 3–5 mm, and larger than or equal to 6 mm was analyzed.

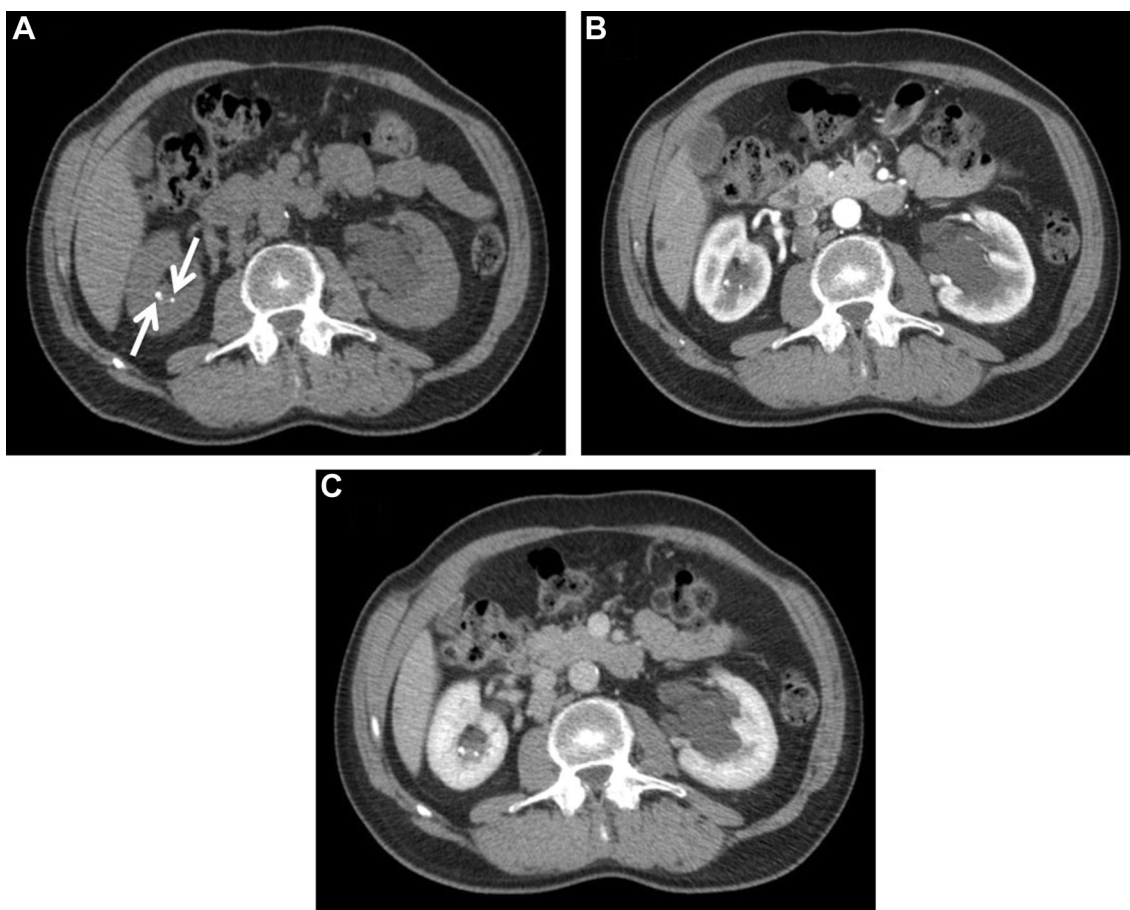
### Statistical methods and data management

The inter-observer reliability was calculated and analyzed according to the method described by Bland and Altman, which yields inter- and intra-class correlation, ICC and the reliability based on the internal consistency was also measured by Crombach's alpha [12, 13]. ICC less than 0.4 considered as poor, 0.4–0.59 as fair, 0.6–0.74 as good, and 0.75–1.0 as excellent. In addition to that, descriptive statistics and detection rates were used to characterize the data. All analyses were carried out on the SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

## Results

The ICC was calculated at 0.86, which means excellent agreement [14].

The detection rate for renal stones in CMP and NGP, by reviewer and totally, are represented in Table 2. Table 3 shows the detection rate for each phase stratified by size. There was no statistically significant difference between CMP and NGP for detecting renal stones ( $p = 0.94$ ). The first, second, and third reader detected 102, 108, and 131 out of the 136 stones respectively in the CMP and 106, 110, and 125 respectively in the NGP. The



**Fig. 1.** Two stones in the right kidney measuring 3 respectively 5 mm in size that was found by all readers in both contrast-enhanced phases (B, C). **A** Non-contrast phase. **B** Corticomedullary phase. **C** Nephrographic phase.

detection rate was 82–88% for stones in the size of 3–5 mm and 98% for stones equal or larger than 6 mm.

Figures 1, 2, 3, 4, and 5 show different examples of how the readers interpreted the examinations in various cases (Figs. 1, 2, 3, 4, 5).

Reader 1 missed 34 stones in the CMP and 30 stones on NGP. Reader 2 missed 28 stones on the CMP and 26 stones on the NGP. Reader 3 missed 5 stones on the CMP and 11 stones on the NGP.

On the CMP reader 1 had 3 false positive, reader 2 had 7 false positives, and reader 3 had 26 false positives. The corresponding numbers of false positives on the NGP were 3, 5, and 25 false positives, respectively. The total number of false positives was 36 stones in the CMP and 33 stones in the NGP.

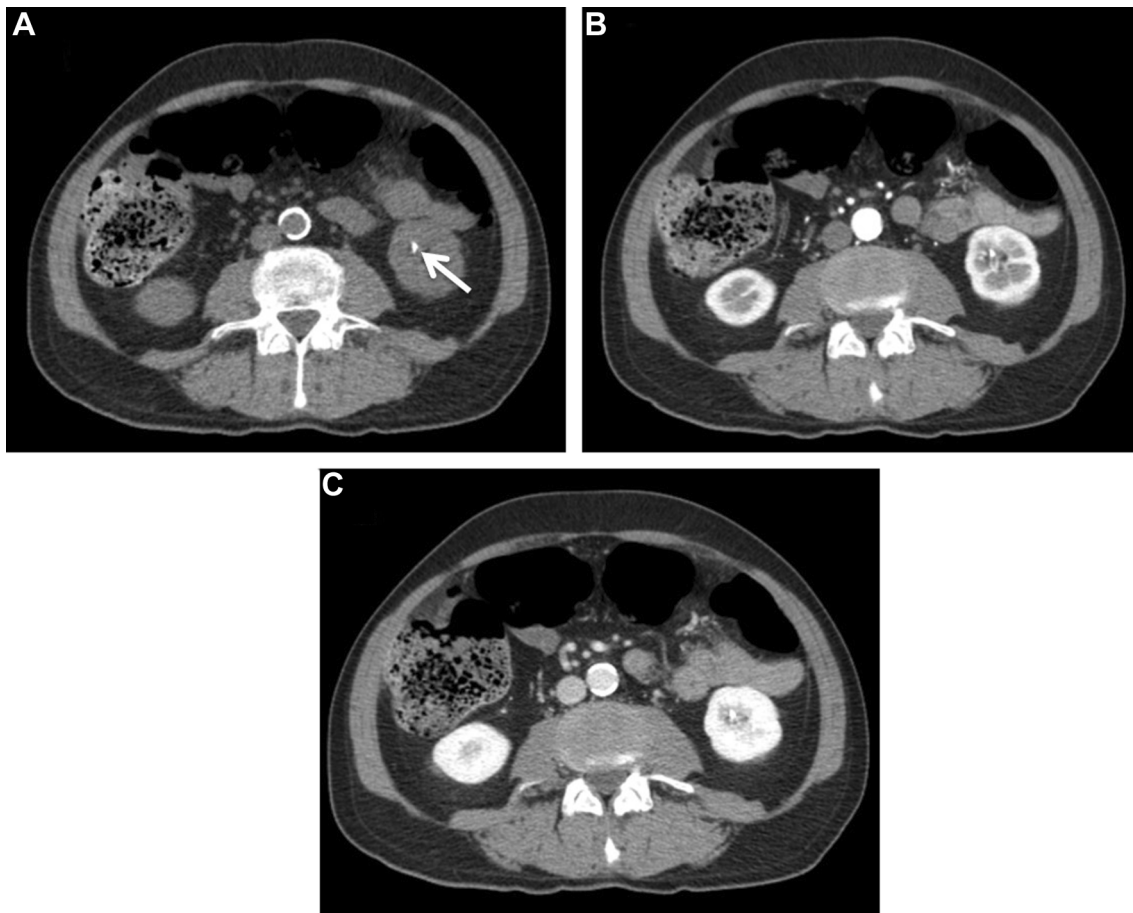
## Discussion

This study has shown that the IV administration of iodine-based contrast media in abdominal CT does not preclude the detection of renal stones, especially those that are clinically more relevant. CE-MDCT –irrespective of the performed phase. i.e., CMP or NGP– can reliably (in 98% of cases) detect renal stones that measure

6 mm or more, that correspond to stones with a higher risk of non-spontaneous passage [6, 7]. Furthermore, a high proportion (82–88%) of stones between 3 and 5 mm is confidently diagnosed after the IV administration of contrast media. It is well known that more severe entities, which demand different and in some cases immediate treatment, can mimic colicky renal stone pain [8]. Aortic dissection may present with similar symptoms and can be overlooked if NC-MDCT is performed. Appendicitis, diverticulitis, or other inflammatory or even malignant diseases of the pelvis enter into the spectrum of differential diagnosis. Entities such as these are more confidently diagnosed after the injection of IV contrast media in the venous phase [4]. Also, a CE-MDCT makes it easier to differentiate between vessel calcifications and renal stones [6]. For all these reasons, it is suggested that a CE-MDCT should be preferred rather than an unenhanced MDCT in all patients proceeding to the emergency department due to abdominal pain. Of course, unenhanced CT can be considered in patients with a known renal stone disease and typical clinical findings.

According to our study, almost half (37–45%) of the 1–2 mm renal stones can be overlooked. The clinical





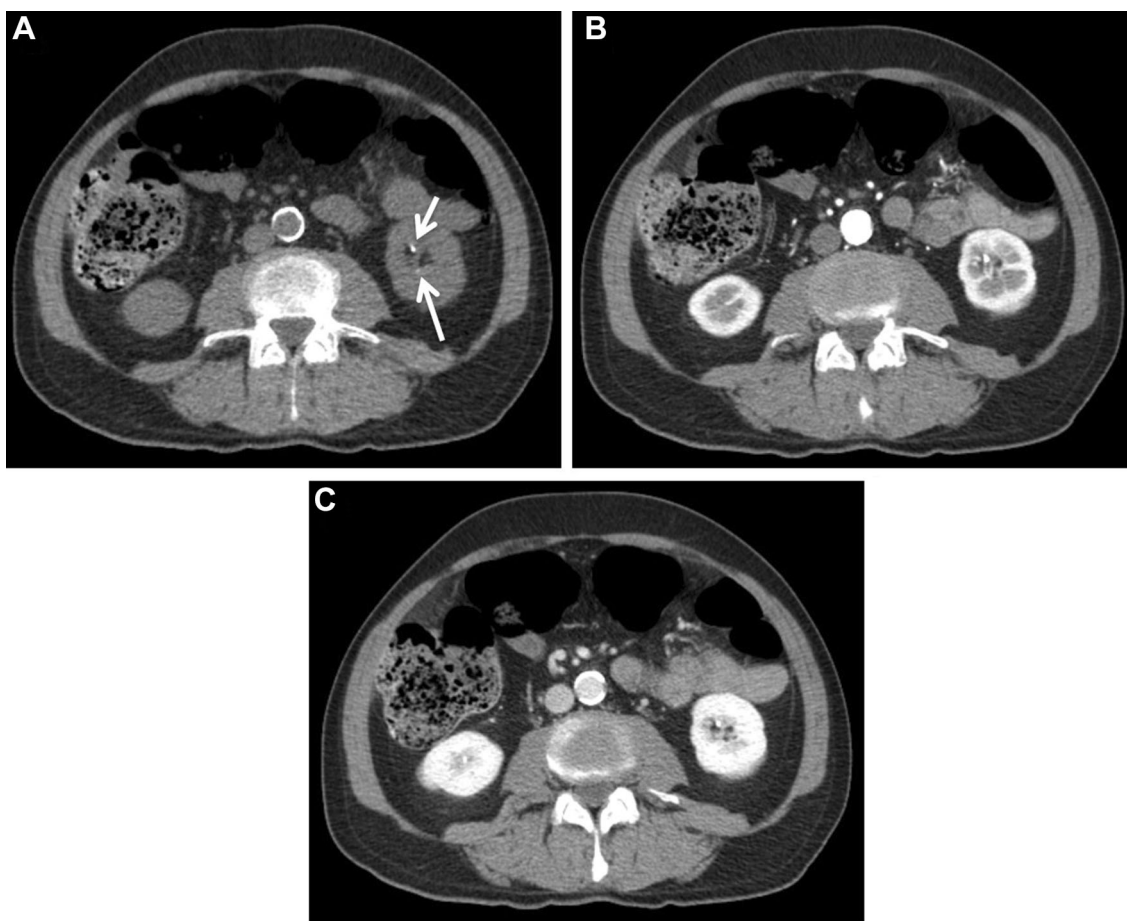
**Fig. 2.** One stone in the left kidney measuring 5 mm that was found by all three readers in both contrast-enhanced phases (**B**, **C**). **A** Non-contrast phase. **B** Corticomedullary phase. **C** Nephrographic phase.

importance of this finding is contested. Small non-obstructing stones are usually not recognized as the cause of pain by the physicians [3]. However, some studies [4, 5, 15] have shown that stones of 1–2 mm in size sometimes can cause symptoms when located in the renal calyces. The radiological findings should always be correlated to the clinical findings. The assumption behind the symptoms is that these small non-obstructing renal stones may cause mucosal irritation, intermittent calyceal obstruction, or in the case of papillary stones, obstruction of the collecting ducts [4]. However, the pain characteristics in these cases differ from those of larger stones, since the pain is more chronic and mild [3, 4].

Two previous studies, published with some years in-between, evaluated renal stones detection in similar ways to our study. Kawamoto et al. [1] studied the detectability of renal stones on arterial phase. They showed that all stones larger than 5 mm and 75% of all renal stones can be detected on the arterial phase, suggesting that patients with acute abdominal pain may benefit from the use of CE-MDCT [1]. The percentage of stone detection is even higher in the arterial phase according to our study (84%). This may partly be due to

technological advances during the last decade. For example, in the study of Kawamoto et al. they had been using a 16 channels scanner. In our study, the examinations had been performed on 64 channels MDCT scanner which is a more modern system and one can speculate that this may contribute to a higher detection rate because of the advantage of more sensible and broader detectors.

In a more recent study, Dym et al. calculated the sensitivity of CE-MDCT for renal stone detection in portal venous phase [4]. They concluded that CE-MDCT is highly sensitive for the detection of renal stones larger than or equal to 3 mm in diameter. The sensitivity for renal stone  $\geq 3$  mm was 95% and for renal stones  $\geq 5$  mm it was 98%. The result of that study is more consistent with our result [4]. To the best of our knowledge, our study is the first study to compare the CMP and NGP. We found no significant difference between the two phases regarding stone detection, so even if a CT in the arterial phase is indicated (i.e., to rule out aortic dissection) or in a later venous phase (i.e., appropriate to diagnose diverticulitis or appendicitis) we can confidently detect renal stones.



**Fig. 3.** Two stones in the left kidney. The bigger, more anterior stone, 5 mm in size, was found by all readers in both contrast-enhanced phases (**B**, **C**). The smaller, more

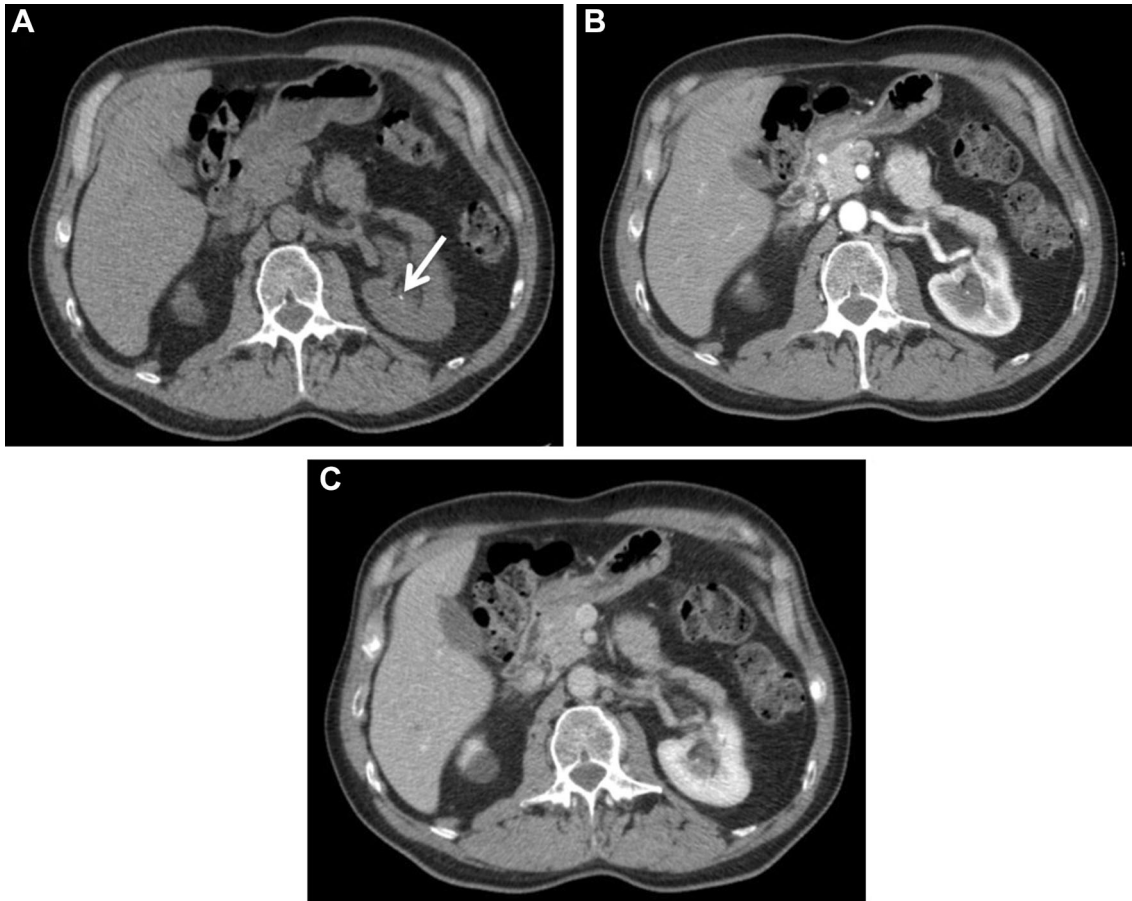
posterior stone, only 1 mm in size, was not detected by any of the readers. **A** Non-contrast phase. **B** Corticomedullary phase. **C** Nephrographic phase.

A potential reason for the low detectability rate for small renal stones is the relative thick slices. Reformations made with 5 mm thick slices and 2.5 mm overlap was used for reconstructing the axial, sagittal and coronal images. This reflects our daily clinical practice when investigating patients with abdominal pain presenting at the emergency room. Renal stones measuring less than 2.5 mm may be overlooked. A recent study from 2016 showed that thin axial images are highly sensitive for the detection of renal stones  $\geq 2$  mm on portal venous phase CT [16]. They compared the sensitivity on axial thin images (1–1.50 mm) to the sensitivity on 5-mm coronal MIP images. Regarding stones that were  $\geq 2$  mm the sensitivity on thin axial images was 98.5%. On coronal MIP images the corresponding number was 94% [16].

Lately the interest in dual-energy CT (DE-CT) has been increasing. Two previous studies investigated the detectability of urinary stones on virtual non-enhanced images generated at pyelographic-phase DE-CT [17, 18]. One of the studies [17] concluded that the detection of urinary stones had a moderate accuracy but that the detection of small (1–2 mm) stones was limited on virtual

non-enhanced images generated at pyelographic-phase DE-CT. The other study [18] concluded that high-attenuation ( $> 387$  HU) stones within the renal collecting system measuring more than 2.9 mm can be detected with good reliability (sensitivity 76%) at pyelographic-phase DE-CT after virtual elimination of contrast medium but the detection rate is not as good as with NC-MDCT. Today, DE-CT is routinely being used to characterize the composition of renal stones [7] based on the fact that uric acid stones have different x-ray attenuation properties on DE-CT than other types of stones such as calcium oxalate, hydroxyapatite or cystine stones [7].

This retrospective study has several limitations. A potential limitation was the absence of cases without stone disease; however, we aimed to evaluate the detectability of renal stones and not the diagnostic accuracy of contrast-enhanced CT. The reviewers were aware of this so there is a risk for bias to overcall in our study. Two of the three readers performed similarly regarding false negatives and false positives results. The third reader, however, had much higher rates of false positives results compared to the other two. This reflects



**Fig. 4.** One stone in the left kidney measuring 3 mm in size that was found by all readers in the corticomedullary phase (**B**) but missed by all readers in the nephrographic phase (**C**).

**A** Non-contrast phase. **B** Corticomedullary phase. **C** Nephrographic phase.

most probably individual variations in the threshold of stone detection. Too low a threshold leads to higher sensitivity and, correspondingly, lower specificity as is the case with the third reader in our study.

Another limitation that might influence our results is that the patient group was not homogenous since the examinations were performed for different indications. The majority of our study population was not investigated directly for suspicion of renal stones but rather for renal malignancies. The higher age group in our study would certainly have had an impact on the result if we investigated the prevalence in the general population of renal stone disease. But since the aim of our study was to investigate the detectability of renal stones in CMP and

NGP on CE-MDCT, we believe that the above factor had a limited, if any, impact on our result.

In conclusion, the detection rate of renal stones larger or equal to 6 mm is extremely high on contrast-enhanced CT. This means that stones with a higher risk of not passing spontaneously can be safely diagnosed. This could imply that there is a benefit of doing an examination with IV contrast from the beginning in cases where the patient's diagnosis is uncertain and renal stones is only one out of many differential diagnoses so not to miss any other clinical relevant finding. This can minimize the radiation dose given to the patient and faster conclude correct diagnoses and choose appropriate treatment.

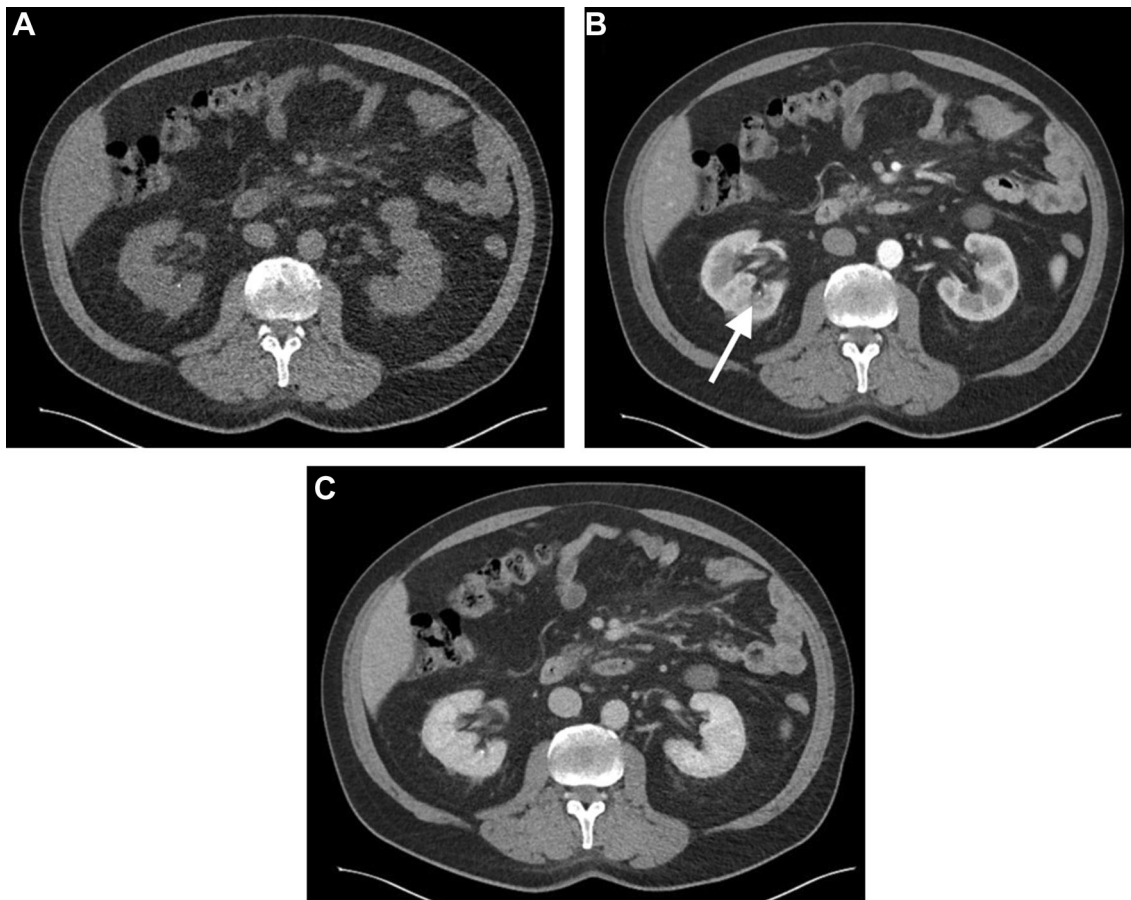


Fig. 5. One stone in the right kidney measuring 2 mm. This stone was found by all three readers in both contrast-enhanced phases (B, C). A Non-contrast phase. B Corticomedullary phase. C Nephrographic phase.

**Acknowledgements** Per Näsman, Center for Safety Research, Department of Transport Science, KTH Royal Institute of Technology Stockholm, Sweden.

**Compliance with ethical standards**

**Funding** Not available.

**Conflict of interest** The authors declare that they have no conflict of interest.

## References

- Kawamoto S, Horton KM, Fishman EK (2008) Detection of renal calculi on late arterial phase computed tomography images: are noncontrast scans always needed to detect renal calculi? *J Comput Assist Tomogr* 32:859–864
- Cheng PM, Moin P, Dunn MD, et al. (2012) What the radiologist needs to know about urolithiasis: part 1—pathogenesis, types, assessment, and variant anatomy. *AJR* 198:540–547
- Furlan A, Federle MP, Yealy DM, et al. (2008) Nonobstructing renal stones on unenhanced CT: a real cause for renal colic? *AJR* 190:125–127
- Dym RJ, Duncan DR, Spektor M, et al. (2014) Renal stones on portal venous phase contrast-enhanced CT: does intravenous contrast interfere with detection? *Abdom Imaging* 39:526–532
- Brandt B, Ostri P, Lange P, et al. (1993) Painful caliceal calculi. The treatment of small nonobstructing caliceal calculi in patients with symptoms. *Scand J Urol Nephrol* 27:75–76
- Cheng PM, Moin P, Dunn MD, et al. (2012) What the radiologist needs to know about urolithiasis: part 2—CT findings, reporting, and treatment. *AJR* 198:548–554
- Renard-Penna R, Martin A, Conort P, et al. (2015) Kidney stones and imaging: what can your radiologist do for you? *World J Urol* 33:193–202
- Rucker CM, Menias CO, Bhalla S (2004) Mimics of renal colic: alternative diagnoses at unenhanced helical CT. *Radiographics* 24:11–33
- Eisner BH, McQuaid JW, Hyams E, et al. (2011) Nephrolithiasis: what surgeons need to know. *AJR* 196:1274–1278
- Smith RC, Rosenfield AT, Choe KA, et al. (1995) Acute flank pain: comparison of non-contrast-enhanced CT and intravenous urography. *Radiology* 194:789–794
- Pfister SA, Deckart A, Laschke A, et al. (2003) Unenhanced helical computed tomography vs intravenous urography in patients with acute flank pain: accuracy and economic impact in a randomized prospective trial. *Eur Radiol* 13:2513–2520
- Bland MJ, Altman D (1986) Statistical methods for assessing agreement between two methods of clinical assessment. *The Lancet* 327:307–310
- Shrout PE, Fleiss JL (1979) Intraclass correlations: uses in assessing rater reliability. *Psychol Bull* 86:420–428
- Cicchetti Domenic V (1994) Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. *Psychol Assess* 6:284–290
- Jura YH, Lahey S, Eisner BH, et al. (2013) Ureteroscopic treatment of patients with small, painful, non-obstructing renal stones: the small stone syndrome. *Clin Nephrol* 79:45–49
- Corwin MT, Lee JS, Fananapazir G, et al. (2016) Detection of renal stones on portal venous phase CT: comparison of thin axial



- and coronal maximum-intensity-projection images. *AJR* 207:1200–1204
17. Takahashi N, Vrtiska TJ, Kawashima A, et al. (2010) Detectability of urinary stones on virtual nonenhanced images generated at pyelographic-phase dual-energy CT. *Radiology* 256:184–190
  18. Mangold S, Thomas C, Fenchel M, et al. (2012) Virtual nonenhanced dual-energy CT urography with tin-filter technology: determinants of detection of urinary calculi in the renal collecting system. *Radiology* 264:119–125