Targeted Delayed Scanning at CT Urography: A Worthwhile Use of Radiation?¹

Kalesha Hack, MD²
Patricia A. Pinto, BSc
Marc J. Gollub, MD

Purpose: To determine whether ureteral segments not filled with contrast material at computed tomographic (CT) urography ever contain tumor detectable only by filling these segments with contrast material.

Materials and Methods: In this institutional review board–approved, HIPAA-compliant retrospective study, with waiver of informed consent, databases were searched for all patients who underwent heminephroureterectomy or ureteroscopy between January 1, 2001, and December 31, 2009, with available CT urography findings in the 12 months prior to surgery or biopsy and patients who had undergone at least two CT urography procedures with a minimum 5-year follow-up between studies. One of two radiologists blinded to results of pathologic examination recorded location of unfilled segments, time of scan, subsequent filling, and pathologic or 5-year follow-up CT urography results. Tumors were considered missed in an unfilled segment if tumor was found at pathologic examination or follow-up CT urography in the same one-third of the ureter and there were no secondary signs of a mass with other index CT urography sequences. Estimated radiation dose for additional delayed sequences was calculated with a 32-cm phantom.

Results: In 59 male and 33 female patients (mean age, 66 years) undergoing heminephroureterectomy, 27 tumors were present in 41 partially nonopacified ureters in 20 patients. Six tumors were present in nonopacified segments (one multifocal, none bilateral); all were identifiable by means of secondary signs present with earlier sequences. Among 182 lesions biopsied at ureteroscopy in 124 male and 53 female patients (mean age, 69 years), 28 tumors were present in nonopacified segments in 25 patients (four multifocal, none bilateral), all with secondary imaging signs detectable without delayed scanning. In 64 male and 29 female patients (mean age, 69 years) who underwent 5-year follow-up CT urography, three new tumors were revealed in three patients; none occurred in the unfilled ureter at index CT urography. Estimated radiation dose from additional sequences was 4.3 mSv per patient.

Conclusion: Targeted delayed scanning at CT urography yielded no additional ureteral tumors and resulted in additional radiation exposure.

¹From the Department of Radiology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave, Room C76F, New York, NY 10065. Received March 15, 2011; revision requested April 25; final revision received October 3; accepted February 2, 2012; final version accepted March 30. Address correspondence to M.J.G. (e-mail: gollubm@mskcc.org).

²Current address: Department of Medical Imaging, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada.

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Computed tomographic (CT) urography has essentially replaced excretory urography as the initial investigation of choice in the evaluation of hematuria and possible ureothelial tumors in most imaging centers (1–5). An ongoing concern with CT urography is nonopacification of the ureter, which could limit the evaluation of small tumors that might manifest solely as intraluminal filling defects. At present, there is no consensus on the most effective CT urography protocol to achieve maximal ureteral opacification. In many centers, such as our own, the examination is monitored and additional delayed sequences are performed if nonopacified ureteral segments are present. A concern relevant to this practice is the higher radiation dose, which is estimated to be 1.5 times that of conventional excretory urography (4). The use of delayed scanning sequences increases the imaging time and cost expenditure, as well as the radiation dose.

In several studies, researchers have investigated the effectiveness of various modifications in technique to improve ureteral opacification, including abdominal compression, intravenous saline infusion, oral hydration, and intravenous furosemide administration (4,6–10). Other investigators have sought ways to limit radiation dose, including the use of split-holus techniques, thereby decreasing the number of scans obtained in each patient (6). It remains unclear, however, whether incomplete ureteral opacification results in missed tumors. Such data are needed to weigh the benefits of obtaining additional delayed scans to achieve complete ureteral opacification, given the additional time and radiation that this practice incurs.

The purpose of this study was to determine whether ureteral segments not filled with contrast material at CT urography ever contain tumor detectable only by the filling of these segments with contrast material. The secondary aim was to evaluate the radiation dose associated with additional delayed scans.

Materials and Methods

Subjects

This study was approved by our institutional review board and was performed in compliance with the Health Insurance Portability and Accountability Act. Patient consent was waived for this retrospective review. We searched the clinical records and the picture archiving and communication system, or PACS, database for (a) all patients who underwent heminephroureterectomy between January 1, 2001, and December 31, 2009, who also underwent CT urography in the 12 months prior to surgery (in one patient who underwent more than one CT urography examination in the 12 months preceding surgery, only the CT urography study acquired nearest to the date of surgery was included); (b) all patients who had undergone ureteroscopy and biopsy and who underwent CT urography up to 12 months prior to biopsy (patients who underwent only a brush biopsy were excluded because no pathologic report was generated [n = 12], patients with “inadequate biopsy findings” on the pathologic report were also excluded [n = 8], and if patients underwent more than one CT urography examination in the 12 months preceding ureteroscopy and biopsy, only the CT urography study performed closest to the biopsy date was included [n = 10]); and (c) patients who had undergone at least two CT urography studies with a minimum 5-year follow-up interval between studies. Exclusion criteria included surgery or biopsy in the interval between follow-up CT urography studies. No patients were excluded.

Imaging Techniques

All CT urography studies were performed with an eight-, 16-, or 64-detector row CT scanner (GE Healthcare, Waukesha, Wis). The imaging protocol included an unenhanced scan from the top of the kidneys to the pubic symphysis by using 2.5-mm axial sections, followed by contrast material–enhanced scans in the parenchymal phase and the delayed phase (also known as the excretory phase). A dose of 150 mL of contrast material (Omnipaque 300; GE Healthcare) was used in all patients. The CT urography imaging protocols varied slightly between 2001 and 2010 and are summarized in the Table.

<table>
<thead>
<tr>
<th>Date Range</th>
<th>Imaging Protocol</th>
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<tr>
<td>2001–2005</td>
<td>Unenhanced scan, followed by contrast material–enhanced scans in the parenchymal phase and delayed phase</td>
</tr>
<tr>
<td>2006–2010</td>
<td>Unenhanced scan, followed by contrast material–enhanced scans in the parenchymal phase and delayed phase</td>
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Scans in progress were routinely reviewed by a radiologist to determine the need for additional delayed scanning. Additional delayed scans were limited to the unopacified segments of the ureter to avoid unnecessary radiation.

Advances in Knowledge

- Delayed excretory CT urography sequences performed in 92 patients to attempt complete ureteral filling resulted in detection of no new tumors that were not already revealed with earlier sequences.
- Delayed excretory CT urography sequences performed to attempt complete ureteral filling resulted in a mean additional radiation exposure equivalent to 4.4 mSv.

Implication for Patient Care

- In patients undergoing CT urography for detection of neoplasms, routine additional excretory phase imaging to attempt complete ureteral opacification is not advised, given the low likelihood that the sole manifestation of a tumor will be a filling defect in an otherwise normal ureter.
### Image Evaluation

Images were reviewed independently by one of two board-certified body-imaging fellows, one of whom was an author of this article (K.H.). Each had 4 years of radiology training and had access to patient age, clinical indication for the scan, prior imaging studies, and radiology reports. All images were reviewed without knowledge of pathology reports to determine the presence or absence of unopacified segments and secondary signs. After all images had been assessed, the reviewers evaluated the pathologic findings on a separate occasion, without being able to access the picture archiving and communication system images. Locations of tumors on the pathologic reports were noted, if available, and the reviewers subsequently recorded whether tumors at pathologic examination were located in the same one-third as the unopacified ureter. For cases in which tumor occurred in an unopacified segment, it was also recorded if secondary signs were present at imaging. As an additional precaution, for the cases in which tumor was present in an unopacified ureter and secondary signs were present, the initial radiology report was reviewed to determine whether the finding had been identified by the radiologist who evaluated the images initially. In all cases of secondary signs recorded by the reviewers, the finding considered a secondary sign was mentioned by the radiologist who evaluated the images initially, who could not have had knowledge of the pathology report. This was done as a check to ensure that the reviewers did not “overcall” secondary signs and potentially underestimate missed tumors.

### Heminephroureterectomy Group

For these subjects, images obtained from the initial excretory phase were examined, and ureteral nonopacification was documented if there were at least two consecutive CT sections with no visible contrast material in the lumen of the ureter. The corresponding vertebral-body levels were recorded. Coronal images were used to determine whether the nonopacified segment was in the upper ureter (the ureteropelvic junction to the inferior endplate of the L2 vertebral body), the middle ureter (the inferior endplate of the L2 vertebral body to the pelvic brim), or the distal ureter (the pelvic brim to the ureterovesical junction). Subsequent excretory phase CT scans were then reviewed sequentially to determine whether the nonopacified segment ever opacified. It was also recorded whether secondary signs of urothelial neoplasm were present and in which segment of the ureter. Secondary signs were defined as any finding other than direct visualization of a filling defect in an opacified ureter. These included an enhancing mass, hydronephrosis proximal to an obstructing mass or hydronephrosis with an abrupt transition, continuous filling of the ureter proximal to a mass or hydronephrosis, abnormal focal urothelial thickening with or without urothelial enhancement, or periureteral fat stranding.

Pathology reports were reviewed to determine the side and location of tumors (upper, middle, or distal segment of the ureter, as per the pathologist). In cases in which a segment of ureter remained persistently nonopacified on the final excretory phase scan, tumors were considered missed if a tumor was present in the same one-third of the nonopacified segment of ureter at pathologic examination and no secondary...
signs of urothelial neoplasm were present. A tumor was considered not missed if secondary signs of urothelial neoplasm were present.

**Ureteroscopy and Biopsy Group**

Pathology reports for all ureteral lesions biopsied at ureteroscopy were reviewed, and the final pathologic examination results and locations of tumors were recorded. Tumors were considered missed if a nonopacified segment was present in the same one-third of the ureter and secondary signs of urothelial neoplasm were absent.

**Follow-up CT Urography Group**

All 93 CT urography studies were evaluated for persistent ureteral nonopacification in the most delayed phase. In cases in which there was a persistent nonopacified segment at initial study, CT urography images acquired at a minimum of 5 years of follow-up were reviewed to see if this originally nonopacified segment opacified with contrast material, thereby indirectly confirming absence of tumor in the initially nonopacified segment.

**Dose Calculations**

Radiation burden associated with additional delayed scanning was estimated for the primary (heminephroureterectomy) outcome group. Information from available dose reports for 20 patients from the overall study population from 2008 to 2009 (note that dose reports were not available before this time) was used to estimate the mean dose-length product for a single excretory phase scan and then multiplied by the normalized effective dose coefficient for the pelvis (II) to determine the estimated mean dose for a single excretory phase scan in the heminephroureterectomy cohort. The mean radiation dose per patient in the heminephroureterectomy cohort for additional scans was determined by multiplying the mean effective dose for a single excretory phase scan by the number of additional excretory phase scans and dividing by 47, the actual number of patients in this cohort who underwent additional scanning.

**Results**

Among 182 lesions biopsied in 177 patients (124 men and 53 women; age range, 39–92 years; mean age, 69 years), 28 tumors were present in nonopacified segments, all with secondary imaging signs detectable without delayed scanning. Eight patients had more than one tumor—seven unilateral and one bilateral.

**Heminephroureterectomy Group**

Ninety-two subjects underwent unilateral heminephroureterectomy within 1 year of CT urography, of whom 59 were male (age range, 38–85 years; mean age, 67 years) and 33 were female (age range, 39–82 years; mean age, 70 years) (Fig 1). The mean time between imaging and surgery was 2.5 months (range, 2 days to 11 months; median, 2.5 months). The mean age for the entire group was 66 years (range, 38–85 years). All but one patient had a history of transitional cell carcinoma of the kidney, ureter, or bladder. The remaining subject had prostate cancer and hematuria. Of the 92 ureters examined, 38 opacified completely in the initial excretory phase and demonstrated no tumor. Fifty-four ureters had unopacified segments, of which only 13 (24.1%) eventually opacified completely with additional delayed scanning. In 20 patients, 27 tumors were present in the remaining 41 persistently partially nonopacified ureters. Only six tumors were present in nonopacified segments. All six tumors were identifiable by means of secondary imaging signs, including enhancing mass (n = 3) and urothelial thickening (n = 3) (Fig 2). One of six tumors was multifocal. None were bilateral. For 21 of 27 tumors, the location of tumor was not specified in the pathology report. Of these unspecified tumors, 17 of 21 were multifocal, with an obvious renal pelvis...
were female (age range, 39–83 years; mean age, 70 years). The mean time between imaging and biopsy was 2.9 months (range, 1 day to 11 months). The mean age for the entire group was 71 years (range, 45–86 years). In 177 patients, the indications for imaging were transitional cell carcinoma in 129 (73%), hematuria in seven (4%), positive urine cytologic results in five (3%), and other (including injury, calculi, hydronephrosis, renal mass, and other tumor) in 36 (20%). There was a persistently nonopacified segment in 30 of 177 ureters. Twenty-eight tumors were present in nonopacified segments in 25 patients (four tumors were multifocal in one ureter; none were bilateral), all of which had secondary imaging signs. The secondary signs were an enhancing mass in 13 tumors (nine single masses in nine patients and four masses in one patient), continuous filling of the ureter above a mass with complete nonfilling below the mass in four tumors, and urothelial thickening with 11 tumors. No tumor was identified in a nonopacified segment without secondary signs. There was one case of false-negative findings at CT urography in a patient with positive urine cytologic results (Fig 4) in which results of CT urography with complete ureteral opacification and of intraoperative retrograde pyelography were both reported as negative, but multifocal papillary tumors were found near the ureterovesical junction at ureteroscopy.

It should be noted that there were 14 patients who were in both the surgical and ureteroscopy groups. Of those, eight had completely opacified ureters at CT urography, four had tumors that were not in an unopacified segment of ureter although unopacified ureteral segments were present at CT urography, one had multifocal atypia at pathologic examination but no tumor, and one had a dominant renal pelvis tumor with tumor in the ureter (location not specified at pathologic examination) with an unopacified distal segment (Figs 1, 3).

Unifocal tumor was not identified in any nonopacified segment without the presence of secondary signs. There were three cases with false-positive findings where ureteral filling defects corresponded to inflammatory change at pathologic examination.

**Ureroscopy and Biopsy Group**

At ureteroscopy, 182 lesions were biopsied in 177 patients (177 ureters) who had undergone CT urography within 1 year of biopsy (Fig 3). Of these, 124 patients were male (age range, 49–92 years; mean age, 67 years), and 53 were female (age range, 39–83 years; mean age, 70 years). The mean time between imaging and biopsy was 2.9 months (range, 1 day to 11 months). The mean age for the entire group was 71 years (range, 45–86 years). In 177 patients, the indications for imaging were transitional cell carcinoma in 129 (73%), hematuria in seven (4%), positive urine cytologic results in five (3%), and other (including injury, calculi, hydronephrosis, renal mass, and other tumor) in 36 (20%). There was a persistently nonopacified segment in 30 of 177 ureters. Twenty-eight tumors were present in nonopacified segments in 25 patients (four tumors were multifocal in one ureter; none were bilateral), all of which had secondary imaging signs. The secondary signs were an enhancing mass in 13 tumors (nine single masses in nine patients and four masses in one patient), continuous filling of the ureter above a mass with complete nonfilling below the mass in four tumors, and urothelial thickening with 11 tumors. No tumor was identified in a nonopacified segment without secondary signs. There was one case of false-negative findings at CT urography in a patient with positive urine cytologic results (Fig 4) in which results of CT urography with complete ureteral opacification and of intraoperative retrograde pyelography were both reported as negative, but multifocal papillary tumors were found near the ureterovesical junction at ureteroscopy.

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**Five-year Imaging Follow-up Group**

Ninety-three subjects underwent follow-up CT urography up to a minimum...
of 5 years, with no ureteral surgery or biopsy between studies. Of these, 64 were male (age range, 45–89 years; mean age, 69 years), and 29 were female (age range, 53–85 years; mean age, 71 years). The indication for follow-up CT urography was a previous history of transitional cell carcinoma. Only three of 93 patients developed interval urothelial neoplasms (none multifocal), none of which were located within a segment of ureter that was nonopacified at initial CT urography.

### Radiation Associated with Additional Delayed Scanning

Sixty-eight additional delayed scans (range, 1–3 scans per patient; mean, 1.4 scans per patient) were obtained in 47 patients from the heminephroureterectomy cohort (in 28, one additional scan was obtained; in 17, two additional scans were obtained; and in two, three additional scans were obtained).

From 20 available CT urography studies from the whole population from 2008 to 2009, we derived a mean dose-length product of 159.4 mGy · cm for a single additional excretory phase scan.

When multiplied by the normalized effective dose coefficient for the pelvis (0.019 mSv/mGy · cm), this yielded a mean dose of 3.0 mSv per additional delayed scan.

Overall, on the basis of the above estimation, the 68 additional delayed scans obtained resulted in an estimated total radiation dose of 204 mSv, or approximately 4.3 mSv per patient. By comparison, in the same group, the mean dose for imaging in the abdomen and pelvis during the parenchymal phase was 19.2 mSv.

### Discussion

In our study, no tumors were missed as a result of ureteral nonopacification. Secondary signs were present in all cases in which tumor existed in a ureteral segment that was nonopacified at CT urography. In addition, there was a single case of a false-negative CT urography finding in a patient with normal CT urography results with complete ureteral opacification and normal intraoperative retrograde pyelography results. This patient had multiple papillary tumors near the ureterovesical junction at ureteroscopy. This last case exemplifies how small tumors can be missed, despite complete ureteral opacification. There was moderate additional radiation exposure, approximately the equivalent per person of 20% of a single abdominopelvic CT scan.

CT urography has become a mainstay in the evaluation of patients with hematuria and urothelial tumors (2–5,9,10,12,13). The achievement of adequate ureteral opacification, one of the defining features that distinguishes CT urography from routine CT scanning, has been an ongoing challenge since the onset of CT urography (3–8,10,12–15). Various techniques used to optimize ureteral opacification are described in the literature (4,6–10). Although imaging protocols are center specific, it is common practice to monitor studies for ureteral nonopacification and to perform additional excretory phase imaging for nonopacified segments. Such was the practice at our institution at the time this study was performed. While we recognize that some tumors might be recognized solely as a
nonobstructing filling defect in a well-opacified ureter without secondary signs, such as thickening or abnormal wall enhancement, and we are not advocating that imaging in the excretory phase be abandoned altogether, we do wish to call into question the practice of performing additional delayed scanning in nonopacified ureters. In particular, the value of additional delayed scanning, in light of the low diagnostic yield we found, becomes questionable when one considers the associated increased radiation dose and the time required.

Our finding that ureteral nonopacification does not result in missed tumors is consistent with the findings of other investigators. It has previously been suggested that evaluation of nonopacified ureteral segments on axial images may be satisfactory in cases of incomplete ureteral distention and opacification (14). Findings in a recent study indicated that the positive predictive value of CT urography for urothelial tumors was the greatest for masses larger than 1 cm, followed by urothelial thickening, as opposed to filling defects in an opacified ureter (5). In fact, tiny filling defects in this group never represented tumor, but rather assorted benign entities, such as blood clots, prominent renal papillae, and crossing blood vessels. Overall, the relative importance of an intraluminal filling defect, as compared with secondary signs of malignancy, is not yet well established. In an early article about CT urography, 24 of 27 urothelial tumors were detected retrospectively at CT urography, most of which manifested as urothelial thickening (15). Investigators in a more recent study examined the importance of urothelial thickening and filling defects in the upper urinary tract at CT urography and found that only 15 of 24 endoluminal filling defects were tumors, as compared with nine of 14 areas of urothelial thickening (2). Further research is needed to establish the positive predictive value (for tumor) when an endoluminal filling defect is seen in an opacified ureter.

One of the recognized limitations of CT urography is the potential to miss small intraluminal masses and particularly carcinoma in situ (12,13,15,16). Rare cases of missed tumors have been reported in an incompletely opacified distal ureter (13). Also reported are false-negative cases in which known tumors were not detectable in opacified ureters at CT urography, even at retrospective review of the imaging findings (15). Therefore, while small intraluminal filling defects that possibly represent tumors could be missed owing to nonopacification, in our experience, such events are rare and may be within the intrinsic limitations of the test. As such, in the absence of secondary signs, such as enhancement and thickening, or risk factors, such as positive urine cytologic results or prior urothelial malignancy, the potential of missing a small lesion in a nonopacified segment of ureter may not warrant the added radiation and cost of additional delayed scanning.

The clinical implications of our results led to a change in practice at our institution. Specifically, we no longer perform routine additional delayed imaging for ureteral nonopacification at CT urography beyond the 18-minute scan. We are planning to analyze whether we can omit the 18-minute excretory scan, as well, such that only a single excretory phase would suffice for CT urography studies. We recommend judicious use of additional delayed imaging, which we believe has the potential to decrease the radiation dose associated with these studies without compromising diagnostic quality.

One limitation of our study was its retrospective design. Another limitation was the lack of specificity with regard to the described location of tumor within the ureter at pathologic examination and uroscopy. This made it difficult to correlate whether or not tumor was within a nonopacified ureteral segment. In addition, it is likely that the ex vivo length of the ureter does not necessarily correlate with the in vivo length. Consequently, exact correlation between tumor location at pathologic examination and imaging was often not possible. There were 17 of 21 cases of tumor in heminephroureterectomy specimens in which the tumor location was not well specified, but all cases revealed multifocal tumor, in which at least one dominant lesion with secondary signs was present in either the renal pelvis or the ureter. As these cases were multifocal, however, it can be presumed that missed additional tumors in a nonopacified segment would not have altered management.

Another limitation of our study was the disproportionate number of patients with prior transitional cell carcinoma who were undergoing close imaging surveillance, which is reflective of the fact that we are a tertiary care cancer center. Consequently, our results may not be applicable to a general screening population with hematuria.

Finally, our mean dose-length product estimate was based on 20 selected delayed phase scans from 2008 to 2009, owing to a lack of availability of doses prior to that time. As a result, we may have under- or overestimated the dose-length product if these patients were in any way atypical.

In summary, we found that in a group of patients undergoing CT urography at a tertiary care cancer hospital primarily for follow-up of bladder cancer, in no case did ureteral nonopacification result in a missed ureteral tumor. Given the added radiation associated with performing additional delayed scanning, we recommend obtaining only a single additional delayed scan for ureteral nonopacification. Further research and consideration can be dedicated to triaging patients into high- or low–pretest probability groups on the basis of factors such as urine cytologic results, clinical symptoms, risk factors for urothelial carcinoma, and prior history of renal calculi to determine the need for additional delayed scanning in cases of persistent ureteral nonopacification.

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