

The availability of multi-detector CT (MDCT) with faster acquisitions and improved spatial resolution has had a significant impact on the field of urological imaging. The quality of renal parenchymal and upper tract imaging evaluation has markedly improved, making this evaluation mandatory in the work-up of renal and urothelial tumors (1-3), upper tract infections (4), urolithiasis (5, 6), and trauma (7-9), as well as pre-transplantation evaluation (10). Nowadays, the value of conventional “urography” is being reconsidered in multiple clinical settings, but is single excretory phase CT-urography adequate for evaluation of the upper tracts? The main pitfall of this newer technique is the frequent incomplete opacification of the ureters (11, 12). Several studies have been conducted to improve CT protocols: abdominal compression and prone position have not shown a significant improvement (12, 13); only hyperdiuresis has shown some efficacy with improved ureteral distension and opacification. This may be achieved by injection of a small dose of diuretics (14,15), infusion of an isotonic saline solution (12, 13, 15), or by ingestion of water (16). Because we believed that furosemide injection would be more appropriate and reproducible, we have sought to assess its efficacy in the evaluation of the upper tracts using MDCT compared to a standard protocol without hyperdiuresis.

Materials and Methods

Patients

Prospective evaluation conducted from February to October 2005. A total of 67 patients were included (34 males/33 females; mean age of 51 (18-86) years). All patients were referred to CT for work-up of upper tract or renal pathology (CT-urogram), or evaluation of other GU pathology potentially involving the upper tracts (CT abdomen and pelvis with excretory phase): hematuria (n=8), renal stone (n=8), GU infection (n=4), renal
trauma (n=1), proteinuria (n=1), renal mass (n=2), staging (n=11) or follow-up (n=7) of urothelial tumors; work-up of hemopathy (n=16), chronic inflammatory syndrome (n=4), or sepsis (n=3). Exclusion criteria were the presence of obstruction and/or a serum creatinine level above 15 mg/l.

The patient population was randomized into 3 separate but similar and homogeneous groups: Group 1 or "control" group without use of furosemide (11 males/10 females; mean age=52 ± 19 years), Group 2 with injection of 20 mg of furosemide (11 males/12 females; mean age=50 ± 18 years) and Group 3 with injection of 10 mg (half dose) of furosemide (12 males/11 females; mean age=50 ± 18 years). Five patients with single kidney were in the furosemide groups and one patient with single kidney was in group 1. One patient in the furosemide group had a Bricker type ureteral anastomosis.

A single patient was excluded because of hydroureteronephrosis from a bladder tumor.

Protocol
The CT examinations were performed on a 40-detector row CT (Philips Brilliance 40, Philips Medical Systems, Best, Netherlands). Each CT examination included at least a noncontrast acquisition and an excretory phase contrast-material-enhanced acquisition (7 min 30 sec) covering the entire upper tracts. All acquisitions were performed with breath hold using the following parameters: 140 kV; automatic tube current modulation based on patient body habitus; gantry rotation time of 0.5 sec; 40x0.625 mm with pitch of 0.676 and increments of 0.8 mm; slice thickness of 1.5 mm; 512x512 matrix; mean acquisition time per series of 13 sec. All patients were injected with a weight-adjusted (400 mg/kg) volume of non-ionic iodinated contrast material (iohexol, Omnipaque 300®) using a power injector (Stellant, Medrad, USA) at a rate of 3 ml/sec. In addition, contrast volume guidelines were implemented: minimum of 90 ml iohexol for patients <70 kg, and maximum of 150 ml iohexol for patients >100 kg (table I).

Furosemide was hand-injected immediately prior to the administration of iodinated contrast material. The dose was adjusted depending on the group.

Data analysis
The excretory phase acquisitions were separated from the other images, de-identified by a resident (CC), and then sent to an independent workstation with real time MPR and MIP capabilities (Extended Brilliance Workspace). Images were reviewed by two experienced radiologists (LL, JD) blinded to patient group. From a total of 128 upper tracts (67 examinations), both radiologists independently evaluated the following items:

1. The degree of upper tract opacification along 8 segments: calices, pelvis, ureteropelvic junction, proximal ureter, lumbar ureter, ureter crossing the iliac vessels, pelvic ureter and ureterovesical junction.

2. Density measurement over the renal pelvis for each upper tract from a 10 mm thick MIP image to assess the density of opacification (fig. 2).

Statistical analysis
A descriptive analysis of data was first performed for control and summary purposes (box-plots, means and standard deviation). Then, mean values for the different parameters were compared between all three groups using a variance analysis.
Table II
Mean scores per upper tract segment.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calices</td>
<td>2.66±0.48</td>
<td>2.76±0.47</td>
<td>2.84±0.32</td>
<td>0.51</td>
</tr>
<tr>
<td>Pelvis</td>
<td>2.86±0.32</td>
<td>2.98±0.10</td>
<td>2.80±0.52</td>
<td>0.27</td>
</tr>
<tr>
<td>Ureteropelvic</td>
<td>2.78±0.56</td>
<td>2.93±0.31</td>
<td>2.67±0.77</td>
<td>0.36</td>
</tr>
<tr>
<td>Proximal ureter</td>
<td>2.85±1.28</td>
<td>2.89±0.37</td>
<td>2.61±0.78</td>
<td>0.19</td>
</tr>
<tr>
<td>Lumbar ureter</td>
<td>2.55±0.72</td>
<td>2.86±0.46</td>
<td>2.63±0.71</td>
<td>0.10</td>
</tr>
<tr>
<td>Crossing over iliac vessels</td>
<td>1.42±1.17</td>
<td>2.69±0.80</td>
<td>2.41±0.87</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Pelvic ureter</td>
<td>1.59±1.16</td>
<td>2.80±0.51</td>
<td>2.48±0.76</td>
<td>0.0002*</td>
</tr>
<tr>
<td>Ureterovesical</td>
<td>1.52±1.28</td>
<td>2.86±0.37</td>
<td>2.54±0.83</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

Note: Groups 2 and 3 have a score significantly superior for the pelvic ureter from its origin (crossing of iliac vessels) to its termination (ureterovesical junction).

Results

Degree of opacification

Results summarized in table II correspond to mean scores for each segment for each group. A significant difference (p < 0.05) between the 3 groups exists only for opacification of the distal segments: ureter crossing the iliac vessels, pelvic ureter and ureterovesical junction (table III). After injection of 20 mg of furosemide, opacification of all segments of the upper tracts with a score of 3/3 was noted in 52.2% of patients and opacification of all segments of the upper tracts with a score of 2/3 or 3/3 was noted in 82.6% of patients as opposed to 30.4% and 43.5% respectively after injection of 10 mg of furosemide and 0% and 19% respectively in patients without injection of furosemide.

Density of opacification

The mean renal pelvis density was 1310 ± 398 HU for the group without furosemide, 265 ± 90 HU for the group with 20 mg of furosemide and 255 ± 77 HU for the group without furosemide (table III). No significant difference was noted between groups 2 and 3, but a significant difference was noted between these groups (2 and 3) and group 1. Bladder opacification was never homogeneous in group 1 patients, but it was homogeneous in 13 of 24 cases for group 2 patients and in 13 of 22 cases for group 3 patients.

Discussion

Over the recent years, CT urography has played an increasing role in the evaluation of the urinary tract. This is in part explained by technical advances allowing helical CT acquisitions over the entire urinary tract in a single breath hold. CT is a well-established imaging modality for characterization of renal masses, evaluation of urolithiasis, or congenital malformations (1, 4, 10, 17, 18). Opacification of the upper tracts, which frequently is incomplete, especially in the distal segments, remains a limitation on CT (11, 12). The main cause for this incomplete opacification is ureteral peristalsis, which is overcome by obtaining radiographs at different times on conventional urography. This technique is difficult to reproduce on CT because acquisitions must be limited to reduce radiation exposure (19). Some authors have explored other techniques to optimize opacification of the upper tracts.
tracts (table IV). Recently, the idea of induced hyperdiuresis was introduced. 
The purpose of our study was to assess the value of furosemide induced hyperdiure-
sis on upper tract opacification at the excretory phase of CT urography, but also to 
assess the value of increasing the routinely prescribed dose of furosemide (10 mg) (14, 15, 20, 21). 
Since iso-osmolar or nearly iso-osmolar iodinated contrast materials are routinely 
used in clinical practice, the injected volume has little impact on diuresis, but at si-
milar diuresis, the iodine concentration will have an impact on upper tract opaci-
fication. Unlike other authors, we have injected all patients with a similar dose of 
iodine (400 mg/kg). In order to limit patient exposure, we have acquired a single 
helical series at the excretory phase using the automatic tube current modulation 
feature of our scanner. Based on a review of the literature, we have elected to ac-
quire the excretory phase series at 450 seconds post injection: Cailli et al. have re-
ported that a delay of 450 seconds was superior to a delay of 300 seconds for up-
per tract opacification (13). In a recent study by Kemper (21) where time delay 
for excretory phase acquisitions was patient-adjusted, the median time delay in 
51 patients was 418 seconds (mean: 447±118 sec).

The concept of inducing hyperdiuresis for improved upper tract opacification was first introduced around 2000 (14). Se-
veral techniques can be used: intravenous infusion of 250 ml of normal saline (1, 12-
14), oral ingestion of 1 liter of water (16), or intravenous injection of furosemide 
(14, 15, 20, 21) (table IV). Results of hyper-
rhythm from infusion of NS are var-
ed (1, 12, 13) and oral hyperhydration seems complicated to implement for pa-
tients referred for CT urogram (reproduc-
cibility, tolerance, poorly controlled effi-
cacy). The use of diuretics has been 
evaluated by several studies, including those by Nolte Ernsting (14, 20) using fu-
rosemide (a potent short acting diuretic 
inhibiting sodium and chloride reabsorp-
tion mainly at the ascending loop of Henle) with a dose of 10 mg injected 3 to 5 
minutes before administration of the iod-
inated contrast material. The only contra-
indications to its use are acute upper tract 
obstruction, dehydration, known hyper-
sensitivity to sulfas, and hepatic ence-
phalopathy. Complete upper tract opaci-
fication was noted in 95% of cases in a 
population of 16 (14). Two recent studies 
compared IV furosemide to IV adminis-
tration of 250 ml of NS for upper tract 
opacification. Both groups of authors 
agreed that IV furosemide alone was ne-
necessary and sufficient to improve upper 
tract opacification.

Among other techniques to improve upper tract opacification on CT urogram (table I), we did not believe that it was 
worthwhile to use abdominal compres-
sion. The recent report by Cailli et al. (13) 
showed that abdominal compression did 
not significantly improve upper tract opa-
cification, while it did improve disten-
sion. Prone acquisitions were not perfor-
med for similar reasons: lack of proven 
efficacy (12).

We have instead elected to evaluate the 
efficacy of furosemide on a larger patient 
population at the usual dose (10 mg) for 
Group 3, but also at a higher dose (20 mg 
– entire dose from a vial of Lasilix®) for 
Group 2.

Impact of hyperdiuresis

Furosemide provided improved upper 
tract opacification and distension in our 
patient population. Complete upper tract 
opacification was noted in 52.2% of 
patients after injection of 20 mg of fu-
rosemide versus 30.4% after 10 mg of fu-
rosemide and 0% of patients without fu-
rosemide. Opacification was complete or 
nearly complete (2/3 and 3/3) in more 
than 80% of series after 20 mg of fu-
rosemide versus 43.5% after 10 mg of fu-
rosemide and 19% without furosemide.

Unlike Silverman et al. (15) we have not 
obtained measurements of the renal 
pelvis to assess the degree of upper tract 
distension. However, this was observed 
subjectively but unanimously by the re-
viewers. The use of furosemide resulted in dilu-
tion of the excreted contrast in the upper 
tracts by a factor of nearly 5, from 
1310 HU in Group 1, to 265 HU in 
Group 2 and 255 HU in Group 3.

Additional advantages related to the in-
jection of furosemide are summarized in 
table V:

- probable increased sensitivity for detec-
tion of urothelial tumors from comple-
te upper tract opacification and improved 
distension;
- reduction of streaking artifacts seconda-
ry to the high density of excreted contrast 
in the upper tracts that may prevent detec-
tion of small endoluminal lesions. Intrave-
nous hyperhydration may also reduce the-
se artifacts (13), but to a lesser extent than 
furosemide (14);
- intraluminal density better suited for evalua-
tion of ureteral wall and lumen (lithiasis), 
decreasing the need for continuous window 
level and width adjustments. Because of furosemide, 
ureteral wall and lumen can be assessed 
using window settings similar to those 
required for renal parenchymal evalua-
tion. This is a time saving feature at the 
time of image interpretation and it also 
facilitates detection of renal stones 
(fig. 4c);
- improved 3D reconstructions: the dyna-
ic range of the upper tracts no longer overlaps that of bones, while being 
different than surrounding soft 
tissues, facilitating the generation of 3D 
images using automatic segmentation 
software (fig. 4);
- standardization and simplification of a 
CR urogram protocol: a 20 mg vial of furo-
semide is injected via the catheter placed
for the iodinated contrast injection. No additional preparation or manipulation is required. Abdominal compression devices are no longer needed.

Limitations

Our results demonstrate that upper tract opacification is significantly more complete on CT urogram when using furosemide, but opacification remains incomplete in some cases.

Density measurements over the renal pelvis were inferior to 200 HU (about 160 HU) in 5 of 23 cases in Group 2. This low density was independent from the injected volume of contrast: mean injected volume of 104 ml in Group 3 and 95 ml in Group 2. Also, this effect was not increased in patients receiving a double dose of furosemide (20 mg): mean density of 255 HU for Group 2 and 265 HU for Group 3. This phenomenon does not appear related to the CT protocol but could relate to the hydration status of the individual patients: fasting or non-fasting, inpatient (IV fluids) or out-patient... Fasting prior to scanning has an impact on renal excretion, which may have an impact on upper tract opacification. Since iodinated contrast materials no longer cause nausea and vomiting, this requirement could potentially be changed. Patient renal function also has an impact on upper tract density.

The density of excreted contrast through out the upper tracts was fairly homogeneous except for persistent increased density at the calices and bladder. This could be reduced by patient mobilization prior to excretory phase scanning.

Finally, furosemide was sometimes associated with heterogeneous nephrographic phase renal parenchymal enhancement (fig. 5), which did not interfere with image interpretation on excretory phase acquisitions. This heterogeneous appearance could be related to a differential recruitment of short and long nephrons.

The density of excreted urine facilitates detection of lithiases.

### Tableau V

Properties of furosemide and benefits on excretory phase CT urogram.

<table>
<thead>
<tr>
<th>Properties of furosemide</th>
<th>Benefits on CT urogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Distension of upper tracts</td>
<td>- improved distension and filling of pyelocaliceal structures, ureters and bladder, nearly completely opacified &gt; increased sensitivity for detection of urothelial tumors</td>
</tr>
<tr>
<td>- Diluted contrast material with decreased endoluminal density</td>
<td>- reduced streaking artifacts (contrast concentration too high)</td>
</tr>
<tr>
<td>- Homogeneous upper tract opacification</td>
<td>- facilitates image review with reduced need for continuous window settings adjustments</td>
</tr>
<tr>
<td>- Simplification and standardization of CT urogram protocol</td>
<td>- facilitates detection of lithiases</td>
</tr>
<tr>
<td></td>
<td>- time saving for technologist and patient</td>
</tr>
<tr>
<td></td>
<td>- reduced time to excretory phase scanning at 420-480 sec (versus 600-720 after the first contrast bolus)</td>
</tr>
</tbody>
</table>

### Conclusion

Our results support the use of 20 mg of furosemide as part of the CT urogram protocol, prior to injection of iodinated contrast material, with excretory phase acquisition at 450 seconds. This protocol resulted in significantly more complete upper tract opacification compared to the standard protocol (without furosemide), reduced and more homogeneous upper tract attenuation (266 HU±91) facilitating ureteral wall and lumen evaluation, and improved 3D reconstructions. This standardized protocol is simple. The