



## Accuracy of Computed Tomography for Identifying Locally Advanced Disease in Patients with Muscle-Invasive Bladder Cancer

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### ABSTRACT

**Introduction:** To retrospectively evaluate the utility of computed tomography (CT) scanning in identifying patients with locally advanced bladder cancer.

**Methods:** We performed an Institutional Review Board-approved review of 858 patients that underwent radical cystectomy (RC) from 2000 to 2008 at our institution. We selected patients with muscle-invasive bladder cancer (MIBC) who underwent up-front RC without neoadjuvant chemotherapy and who were assessed by preoperative CT scan. We limited this analysis to 48 CT scans obtained prior to transurethral resection. All CT scans were blinded and retrospectively re-read by a dedicated genitourinary radiologist (CSN) to identify tumor location, the presence of wall thickening, and evidence of extravesical disease (stranding or nodularity) or lymph node metastases. These radiologic findings were compared with pathologic findings.

**Results:** Pretransurethral resection CT scans were able to accurately identify tumor location in 66.7% of patients (sensitivity = 88.9%, specificity = 33.3%) while lymph node assessment was accurate in 58.3% (sensitivity = 75%, specificity = 62.5%). However, only 16.7% of patients with pathologic T3b disease were actually identified on CT as having radiologic evidence of extravesical disease. Specific radiologic signs suggestive of local disease extension, such as wall thickening, stranding, and nodularity correlated poorly with true pathologic T3b disease.

**Conclusion:** CT scanning has limits in its ability to accurately identify extravesical disease and lymph node spread in patients with MIBC. Investigations into additional or alternative means of clinical staging for bladder cancer patients are incredibly crucial.

### INTRODUCTION

The survival of patients with bladder cancer varies greatly based on the stage of their disease [1]. Unfortunately, physicians are notoriously poor at staging patients with invasive disease [2-8]. It remains critically important to be able to identify those patients with locally advanced disease (such as extravesical extension of tumors or clinically node-positive disease) in order to appropriately prognosticate survival and to identify patients who would gain the most benefit from up-front chemotherapy.

Current staging of bladder tumors is based on visual assessment of the tumor on cystoscopy, pathologic assessment via transurethral resection (TUR) specimens, exam under anesthesia (EUA) to assess for evidence of a 3-dimensional mass, and computed tomography (CT) imaging. Both older and newer studies have reported that CT imaging is limited by its poor accuracy in detecting local tumor extension and lymph node metastases [9,10]. Here we sought to further evaluate the ability of CT imaging to identify locally advanced disease in a rather homogeneous population of patients with cT2 bladder

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cancer by comparing a blinded review of preoperative imaging to pathologic features.

## METHODS

Using an Institutional Review Board-approved protocol, we queried our prospectively collected database and identified 858 consecutive patients who underwent radical cystectomy (RC) for urothelial carcinoma of the bladder from January 2000 to December 2008. We isolated patients designated having cT2N0M0 disease following their TUR and EUA; those patients with a palpable 3-dimensional mass on EUA and those who received chemotherapy prior to surgery were excluded in order to study a homogeneous cohort. Patients who underwent imaging immediately following TUR (< 30 days) were also excluded in order to avoid bias from confounding extravescical inflammation or extravasation commonly seen after resection.

All CT images were then de-identified and reviewed by a dedicated genitourinary radiologist (CSN), who was blinded to the pathologic features and clinical outcome. The CT images were acquired from various institutions, using a variety of helical and multidetector scanners, and thus there was no uniform protocol that was used. Axial CT images of 2.5 mm to 10 mm sections were reviewed. Endpoints of interest included tumor location, radiographic suspicion of locally advanced disease, and individual radiographic signs potentially predictive of extravescical disease or lymph node metastases.

The presence or absence and location of focal bladder wall thickening greater than that of the adjacent bladder wall, intraluminal bladder wall nodules/nodularity, and/or focal post-contrast enhancement of the bladder wall was documented, and the bladder location recorded and taken to represent the site of tumor(s). Local extension of disease was considered if there was stranding and/or nodularity in the adjacent perivesical fat. For this study, pelvic lymph nodes were considered to be positive for disease if  $\geq 0.5$  cm in the short axis.

We then compared the radiologic impression and findings to the pathologic results. Summary statistics were used to describe demographical and clinical characteristics of the study population. Basic statistical measures were used to decipher the accuracy of CT imaging in detecting locally advanced bladder cancer.

## RESULTS

Using our stringent selection criteria for this study, we identified 48 patients with complete clinical and pathologic data who also had a pre-TUR CT scan available for review. For these patients, the median time from CT to TUR was only 3 days and from TUR to RC was 42. Despite this selection, 45.8% of our cT2 patients were found to be upstaged to pT3 disease pathologically and

Table 1. Comparison of preoperative radiographic impression to pathologic outcome.

Pathologic Stage (Number)	< rT3b	$\geq$ rT3b	Equivocal
pT0 (5)	4		1
pTis (7)	4	1	2
pTa (3)	3		
pT1 (5)	3	1	1
pT2 (6)	4	1	1
pT3a (8)	5	2	1
pT3b (12)	9	2	1
pT4a (2)	0		2

Pathologic Stage (Number)	rN0	rN+
pN0 (40)	29	11
pN+ (8)	4	4

16.7% were node positive (Table 1).

None of the patients were originally thought to have CT findings consistent with advanced disease, but for the purposes of this study the CT scans were re-evaluated for radiologic findings consistent with extravescical disease (i.e.,  $\geq$  rT3b) or nodal metastases (rN+). The repeat radiographic impressions indicated that 14.6% of patients had rT3b disease and 31.3% rN+ (Table 1). However, only 2 of 12 patients (16.7%) with pathologic T3b disease were correctly identified as having radiologic signs suspicious for extravescical disease. Furthermore, 5 of 7 patients (71.4%) thought to have rT3b disease and 11 of 15 (73.3%) thought to have rN+ disease were overstaged. Finally, 12 of 29 patients (41.4%) thought to have organ-confined disease (< rT3b and rN0) were understaged.

EUA is an underutilized but important part of the staging evaluation for muscle-invasive bladder cancer (MIBC). However, the accuracy of EUA can vary based on tumor location and body habitus, with poor sensitivity in obese patients. Here we found that EUA was unable to identify macroscopic tumor extension in 12 of the 48 patients (25%). However, tumor location was accurately identified by CT in 66.7% of patients (sensitivity = 88.9%, specificity = 33.3%), and lymph node assessment was correct in 58.3% (sensitivity = 75%, specificity = 62.5%) (Table 2).

We then evaluated the correlation of extravescical extension with bladder wall thickening, extravescical stranding, and

Table 2. Predictive ability of imaging to identify tumor and node location.

	Tumor Location (%)	Node Location (%)
Sensitivity	88.9	75
Specificity	33.3	62.5
Negative predictive value	16.7	92.6
Positive predictive value	95.2	28.6
Accuracy	66.7	58.3

extravesical nodularity as individual variables. As shown in Table 3, these criteria were not sufficient to accurately identify extravesical disease as only 28.2, 27.6, and 28.6% of patients with pT3b disease were found to have these radiographic findings, respectively. Furthermore, 28 patients had at least pT2 disease; among these, 11 of 23 (47.8%) with bladder wall thickening, 8 of 19 (42.1%) with extravesical stranding, and 2 of 5 (40%) with extravesical nodularity had extravesical disease.

## DISCUSSION

Accurate clinical staging is essential for the appropriate selection of therapy for all cancers, and it is especially pertinent to bladder cancer given that current staging paradigms result in pathologic upstaging (extravesical disease extension or lymph node positivity) ranging from 36 to 73% following radical cystectomy [3-6]. It is partly due to this limitation in clinical staging that many experts recommend the use of neoadjuvant chemotherapy (NAC) to all patients with MIBC [11-14]. Most, however, will agree that the true benefit of NAC is in patients who harbor occult nodal metastases and/or have tumors that extend beyond the confines of the bladder. Thus, the hope is that refinements in technology allow CT imaging to better delineate cases of locally advanced disease and therefore increase utilization of preoperative chemotherapy. At our cancer center, we have reported on the use of clinical parameters to risk-stratify these patients—namely, the presence of lymphovascular invasion on TUR specimens, hydronephrosis, variant histologic subtypes, and suspicion for extravesical disease on EUA—in an attempt to identify patients judged to be at the highest risk and who would likely benefit from NAC [15].

Despite CT imaging demonstrating a respectable positive predictive value for identifying tumor extension into perivesical fat, it displayed a dismal specificity. Thus CT imaging adds minimal benefit for local tumor staging, which highlights the importance of incorporating EUA into the staging regimen to

Table 3. Predictive ability of specific radiographic signs to identify extravesical disease.

	Bladder wall thickening (%)	Extravesical stranding (%)	Extravesical nodularity (%)	Combined (%)
Sensitivity	91.7	66.7	16.7	100
Specificity	22.2	41.7	86.1	13.9
Negative predictive value	88.9	78.9	75.6	100
Positive predictive value	28.2	27.6	28.6	27.9
Accuracy	39.6	47.9	87.5	35.4

help identify locally advanced tumors. Nevertheless, CT imaging was able to exclude lymph node metastases in most patients (negative predictive value of 92.6%), indicating that it remains an important part of this aspect of staging.

Ideally, one would like to use preoperative cross-sectional imaging as the primary modality to accurately stage the extent of local tumor invasion and patterns of lymph node spread or distant metastases (bony or visceral). However, accuracy of CT for bladder cancer staging has been reported to be at best 50% with at least a 25% rate of understaging [9,10]. Since some of these series included patients that were treated prior to 2000, and CT scanning technology has advanced since then, we decided to re-evaluate the utility of CT scanning (from 2000 until now) in the hands of a dedicated genitourinary radiologist blinded to patient outcomes and pathologic features. Unfortunately, we have corroborated prior studies showing that cross sectional imaging with CT scans remains unreliable in identifying the presence of extravesical disease. Moreover, we found no reliable radiologic signs that consistently identified the extravesical extent of disease. Finally, identification of small-volume lymph node metastases is barely adequate with today's CT scans.

Our study cohort consisted of our most recent 12 years of patient data. However, our findings are primarily limited by the heterogeneity in the available CT imaging quality and technique. Some of our CT images were derived from scanning techniques as far back as 2000. Furthermore, only axial CT images were reviewed since the majority of scans were obtained from routine staging protocols rather than any kind of specialized or research thin-cut section protocols with the possibility of 3-D reformations. Nevertheless, we specifically did not exclude CT studies from other institutions in order to replicate real world



results.

We do recognize that the number of patients selected for this re-review can be considered small. However, we used strict criteria to avoid the biases of a post-TUR CT scan, and it is possible that we have not been able to demonstrate an improvement in staging due to the small number of CT scans reviewed; however, it is likely that inclusion of post-TUR scans would only lower the accuracy of CT scanning due to procedure-introduced artifacts.

Ultimately, CT imaging is not yet sensitive enough to distinguish between organ-confined and extravesical bladder cancer. Moreover, CT is especially difficult to interpret in the post-biopsy or transurethral setting secondary to inflammatory changes. Magnetic resonance imaging has been proposed as a better cross-sectional imaging modality to stage patients given the high tissue contrast with contrast enhancement and diffusion-weighted imaging. Unfortunately, studies have been unable to prove the significant clinical benefit of magnetic resonance over CT that justifies its use [16-20]. These limitations in cross-sectional imaging highlight our desperate need for better patient stratification, whether it is through molecular analyses of tumor characteristics on TUR specimens, circulating tumor cells, or molecular imaging.

## CONCLUSION

CT scanning has limits in its ability to properly identify extravesical disease or lymph node spread in patients with MIBC. Investigations into additional or alternative means of clinical staging for bladder cancer patients are incredibly crucial.

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