

Urothelial carcinoma (i.e. transitional cell carcinoma) accounts for nearly 90% of primary bladder malignancies, with squamous cell carcinoma (6-8%) and rarely, adenocarcinoma, accounting for the remainder of cases. Staging of bladder cancers is accomplished using the TNM system. In this system, high grade flat tumor confined to the mucosa is designated Tis, while papillary carcinoma is designated Ta when confined to the mucosa, and T1 when limited to the submucosa. Tumors with involvement of the muscular wall of the bladder are designated as T2 or higher according to the depth of involvement (T2a, superficial (<50%); T2b, deep ( $\geq 50\%$ ), T3a, microscopic involvement of perivesical fat; T3b, macroscopic involvement of perivesical fat; T4: involvement of adjacent structures (T4a: prostate, uterus or vagina; T4b: pelvic wall or abdominal wall)<sup>1</sup>. Squamous cell and adenocarcinoma typically present as invasive malignancy. However, among urothelial carcinomas, approximately 75-85% are non-muscle invasive at presentation with 15-25% presenting as muscle-invasive masses (stage T2 or greater)<sup>2,3</sup>. The preoperative distinction between tumors of stage T1 and those of stage T2 or greater is of key importance in treatment planning for bladder cancer. Tumors <T2 are treated with transurethral resection (TUR), while stage T2 or greater tumors require surgical resection, with either partial or radical cystectomy, or treatment with adjuvant therapies including chemotherapy and/or radiation. In addition to pathology obtained at the time of biopsy, imaging can contribute to the preoperative determination of depth of invasion.

Multiparametric MRI is favored as the optimal imaging modality to assess local stage of bladder cancer due to its high soft tissue resolution. Careful attention to technique is necessary to ensure high quality images. The bladder should be well distended at the time of imaging, which can be accomplished by asking the patient to avoid voiding for 1-2 hours prior to the examination. Alternatively, if bladder imaging is performed as part of a complete urinary tract assessment (MR Urography) in which diuresis is performed, dedicated bladder sequences may be performed prior to the conclusion of the examination concurrent with peak bladder distention. The use of an antiperistaltic agent can be helpful in reduction of bowel motion. Saturation bands placed on the anterior abdominal wall will combat respiratory-related motion artifact when the phase encode direction is anteroposterior. Multiparametric MRI for bladder cancer evaluation can utilize T1 and T2W sequences for depiction of anatomy, along with diffusion weighted imaging (DWI) and dynamic contrast enhanced imaging (DCE). The latter two sequences can contribute both to anatomic staging and serve as potential biomarkers for tumor behavior. Additional imaging with lymphotrophic nanoparticle-enhanced MRI using ultrasmall paramagnetic iron oxide particles (USPIO) has also been shown to be of benefit in assessing lymph node involvement with MRI<sup>3</sup>.

“Anatomic” staging (T1 and T2WI): Urothelial carcinomas are seen at MR imaging as masses with either polypoid or sessile configuration. The signal intensity of urothelial carcinoma at T1WI prior to administration of gadolinium is mildly hyperintense to urine, but isointense to bladder muscle. At T2WI, urothelial carcinoma is seen as a mass which is hypointense to the fluid signal intensity of the urine, and mildly hyperintense to the bladder muscle. However, the SI of the tumor may be similar to the bladder wall, and overall staging accuracy of T2WI has been reported to range from 40-67% with overstaging more common than understaging using T2WI.<sup>4-7</sup>. Because of the spheroid configuration of the bladder, it is helpful to acquire high resolution T2WI in two or more planes (axial, coronal and/or sagittal) to best

display the relationship of the tumor to the bladder wall. DWI may also be performed in more than one plane to best depict the relationship of tumor to muscularis.

DCE: Urothelial carcinoma, mucosa and submucosa, enhance rapidly while bladder musculature enhances in a delayed fashion, a fact which can be exploited for tumor localization and to assess tumor anatomic features. The addition of DCE to T2WI at 3T improved sensitivity and accuracy for localization of bladder tumors, to 92% and 86-89%, respectively<sup>8</sup>. In addition, it has been noted that urothelial carcinoma enhances several seconds earlier than postbiopsy inflammatory tissue<sup>9</sup>. A high temporal resolution DCE strategy can be performed in postbiopsy patients in order to better demonstrate areas of residual tumor in the setting of postbiopsy granulation tissue. Submucosal linear enhancement (SLE), visualized as an uninterrupted linear enhancement feature at the base of a mucosal lesion, has been reported as indicative of stage T1 disease<sup>10</sup>. However, Takeuchi et al. found that tumor and submucosa had similar SI in 60% of cases<sup>4</sup>. Overall staging accuracy using DCE has been reported as 62-88%<sup>4,5,11,12</sup>.

DWI: An extensive body of literature has demonstrated value of DWI in the imaging evaluation of urinary bladder cancer. Restricted diffusion of water molecules in malignancy is thought to be due to increased cellularity and decreased extracellular space. Thus, bladder cancer demonstrates high signal intensity on high b-value (800-1000 s/mm<sup>2</sup>) images confirmed with low signal intensity on apparent diffusion coefficient (ADC) maps. Sensitivities for detection of bladder cancers using DWI have been reported as >90-100%<sup>13-15</sup>. In staging of urothelial carcinoma, DWI has been shown to improve the diagnostic performance of MRI when added to T2WI, with accuracy of distinguishing T1 from T2 or higher stage tumors ranging from 92-98%<sup>16</sup>. Other studies have shown staging accuracy of 80-88% for T2WI+DWI<sup>6,17,18</sup>. DWI can be of benefit in establishing stage by distinguishing tumor, with its characteristic finding of high SI on high b-value images and low SI at ADC map, from fibroinflammatory change which can be present at the base of some tumors and can simulate invasive disease<sup>4</sup>. In addition, specific morphologic features have been observed and reported that can facilitate accurate staging using DWI, including the so-called “inchworm” sign demonstrating the stalk of a papillary tumor (an MR correlate for stage T1 disease)<sup>6</sup>.

In addition to its role in bladder tumor staging, there is an expanding body of evidence that multiparametric MRI may be helpful in prognosis and assessment of response to treatment, through the use of DWI and DCE as biomarkers for tumor behavior<sup>3</sup>. ADC value has been shown to relate to tumor aggressiveness as denoted by histopathological phenotype<sup>19-21</sup> and other clinical prognostic factors, including immunohistochemical biomarkers<sup>15,22,23</sup>. In addition, ADC values have been found to differ between chemotherapy-sensitive and chemoresistant muscle invasive tumors<sup>24,25</sup>. More avid and rapid enhancement has been shown at DCE-MRI to correlate with tumor recurrence<sup>26</sup>. DCE has also been shown to differ in responders and nonresponders to chemotherapy and to correlate with disease specific survival in these patients<sup>27,28</sup>.

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