Here I will present the diagnostic criteria for invasion into lamina propria (pT1) in urothelial cancer and illustrate histologic patterns of this process, which have also been the subject of a recent review.1

Stage is the most powerful prognostic indicator in urothelial carcinoma, and a major defining parameter in the management of this disease.1a The TNM staging system defines pT1 tumors as those invading into the lamina propria, but not the muscularis propria2. Although it has been demonstrated in several studies that pT1 tumors bear a less favorable prognosis than pTa (non-invasive) neoplasms3-6, clinically they are usually lumped together under the term “superficial” bladder tumors. Beside the fact that tumors classified in these two stages traditionally have been managed conservatively, another possible factor contributing to the clinicians’ rationale in grouping pTa and pT1 tumors as “superficial” is the pathologists’ inability to always accurately recognize lamina propria invasion. On the contrary, those tumors with involvement of the muscularis propria and beyond (pT2-4, or “invasive” tumors) are usually managed with aggressive surgical therapy (i.e. cystectomy). While an argument in favor of cystectomy for lamina propria invasive tumors of high grade has been made7, 8, others have focussed on attempting to identify additional pathologic prognostic markers in lamina propria invasive disease (pT1). This has made accurate histopathologic recognition of invasion into lamina propria even more important, and has inevitably raised an important question as to the best system to sub-stage pT1 disease.

I will further discuss the issue of substaging of pT1 disease as well as some staging issues in bladder cancer.
Most small bladder tumors (i.e. < 1 cm in size) can frequently be excised by cold cup biopsies. This procedure yields specimens in which the cellular architecture is mostly preserved, and in whom orientation is easier to maintain after embedding. The resulting H+E sections show the urothelial neoplasm, the lamina propria and superficial muscularis propria with orientation maintained, thus facilitating assessment of invasion. Larger tumors (>1cm) usually require hot loop resection (“transurethral resection of bladder tumor”, or TURBT), in which the urologist attempts to include a generous sample of the underlying muscle layer to enable adequate pathologic staging. The specimens rendered by this procedure are often fragmented, heavily cauterized and difficult to orient. Sections from these specimens are usually fouled with thermal artifact, tangential sectioning, and disruption of the tumor architecture. While examining both types of specimens, it is important to note the presence or absence of muscularis propria, in order to assess involvement by neoplasia, and to provide feedback to the urologist regarding adequacy of resection.

The subepithelial connective tissue is a compact layer of fibrovascular connective tissue. In most instances it is divided by a thin layer of smooth muscle fibers (muscularis mucosae) into a lamina propria proper, which is superficial, and a submucosal layer, located between the muscularis mucosae and muscularis propria. It was not until recently that the muscularis mucosae layer of the urinary bladder was described, alerting pathologists and urologists of the importance of recognizing it and differentiating it from the underlying compact smooth muscle bundles of muscularis propria. Muscularis mucosae fibers are usually thin, often discontinuous, wispy and wavy fascicles of smooth muscle, which are frequently associated with large caliber blood vessels, and surrounded by loose fibroconnective tissue. Most studies have identified some degree of this layer in 94-100% of cystectomy specimens, and in about a third of specimens from biopsies or TURBT. Muscularis propria fascicles, on the other hand, are usually thick and compact, divided into distinct bundles surrounded by perimysium. Occasionally, muscularis mucosae bundles may undergo hypertrophy especially after biopsy or at the base of the tumor, and in such situations the distinction between muscularis mucosae and muscularis propria, especially in biopsy or TURBT specimens, may be difficult.

NATURE OF THE SPECIMENS COMMONLY SUBMITTED FOR PATHOLOGIC EXAMINATION

HISTOLOGY OF THE SUPERFICIAL BLADDER WALL
Recognition of lamina propria invasion by urothelial carcinoma is occasionally one of the most challenging diagnoses in surgical pathology. Often faced with distorted, cauterized, and tangentially sectioned specimens, the pathologist should follow strict criteria to diagnose lamina propria invasion (Table 1). While evaluating tumors for invasion, it is important to focus in the following features:

- **Histologic grade of tumor,**
- **characteristics of the invading epithelium,**
- **the stromal response,**
- **the histologic pattern of invasion,** and
- **awareness of possible pitfalls.**

**Histologic grade.**

Lamina propria invasion should be carefully looked for in all high-grade papillary carcinomas. While invasion is not necessarily an unexpected finding in low grade tumors, it is much more common in high grade lesions. In Jordan et al.’s series, 96.5% of invasive carcinomas were grade III (1973 World Health Organization [WHO] classification). Similarly, of 53 patients with pT1 disease in Malmström et al.’s series, 37 (70%) were grades 2b and higher (modified Berkvist system), which roughly equate to the high grade papillary urothelial carcinomas of the 1998 World Health Organization/International Society of Urologic Pathology (WHO/ISUP) classification. Thus, while clear cut histologic signs of invasion are required for the diagnosis of invasion into lamina propria, the level of suspicion should be higher in those cases with a high histologic grade.

**Invading epithelium.**

The invasive front of the neoplasm may show one of several features: single cells or irregularly shaped nests of tumor within the stroma, architectural complexity not conforming to the usual regularity of papillary neoplasms, or an irregular, disrupted, or absent basement membrane. Sometimes tentacular or finger-like extensions can be seen arising from the base of the papillary tumor. Frequently the invading nests appear morphologically different from the cells at the base of the non-invasive component of the tumor, with more abundant cytoplasm and often with a higher degree of pleomorphism.

**Stromal response.**

The lamina propria may react to invasion in one or more of the following forms:

1. **Desmoplastic or sclerotic stroma:** The stroma is cellular with spindled fibroblasts, variable collagenization, with or without inflammation.
2. **Retraction artifact:** In some cases, a retraction artifact that mimics vascular invasion is seen in tumors invading only superficially into the lamina propria. Often this finding is focal, and, in our opinion, is one of the early signs of invasion into lamina propria. It is especially conspicuous in the recently described micropapillary variant of urothelial carcinoma.
3. **Inflamed stroma:** Invasion may elicit a brisk inflammatory response. The lamina propria is heavily infiltrated by numerous inflammatory cells that
may obscure the interface between epithelium and stroma. This makes recognition of small nests or single cell invasion difficult to recognize.

iv. **Myxoid stroma:** Loose and hypocellular stroma with a myxoid background may occasionally be seen in some cases of invasive urothelial carcinomas.

v. **Pseudosarcomatous stroma:** Sometimes the tumor induces an exuberant spindle cell response, with proliferation of fibroblasts that may display significant, often alarming cellular atypia. This feature, although helpful in assessing for invasion, should not be mistaken for the spindle cell component of a biphasic sarcomatoid urothelial cancer. The proliferating stroma is usually nonexpansile, being limited to areas around the neoplasm, and is cytologically composed of cells which have a degenerate or smudged appearance on high-power examination.

vi. **Absent stromal response:** Frequently the stromal response to invading carcinoma may be absent. In these cases, as mentioned above, diagnosis of invasion should rely on the characteristics of the invading epithelium.

### HISTOLOGIC PATTERNS OF LAMINA PROPPRIA INVASION

Lamina propria invasive tumors may be classified from their morphologic perspective according to several patterns (Table 2). Awareness of these patterns may be important to the surgical pathologist in order to focus on particular areas of the tumor while assessing for invasion, thus facilitating its recognition, even when it is extremely focal. Not all patterns are associated with clinical significance.

**Carcinoma in situ (CIS) with microinvasion.**

Isolated or de novo CIS (i.e. in the absence of papillary and/or invasive neoplasm) is rare, representing approximately 1% of bladder neoplasms\(^19\). Microinvasion by CIS is defined by Farrow et al.\(^6\) as an invasive component measuring less than 5 mm in depth. In their study, these authors found microinvasion in 34% of a series of entirely submitted bladders harboring CIS, and in 5.8% of these cases metastatic disease developed, causing the patients’ demise. Their data suggest that microinvasion confers the ability to metastasize and cause death in a small number of cases. Amin et al.\(^20\) have proposed that the 5 mm criterion may be liberal, and suggest a 2 mm cutoff for this diagnosis. The clinicopathologic significance of this finding needs to be determined.\(^20a\)

**Papillary urothelial carcinoma with microinvasion.**

Microinvasion of papillary tumors can be similarly defined as in cases with CIS, and should be mentioned in the diagnosis, in order to document minimal, focal or early invasion.
Papillary urothelial carcinoma with invasion into stalk.

Very rarely papillary urothelial carcinomas may invade into the stalk of a tumor.\textsuperscript{20b} Appreciation of this pattern requires optimal orientation of the entire papillary tumor, which may not always be the case, especially in TURBT specimens.

Well-established invasion into underlying lamina propria.

In the overwhelming majority of cases, invasion is seen at the base of the papillary neoplasm. With respect to the muscularis mucosae layer within the lamina propria, invasive tumors may be classified as follows:

- i. Invasive up to the muscularis mucosae
- ii. Invasive beyond the muscularis mucosae (into the submucosa), but not in the muscularis propria.
- iii. Lamina propria invasion not further specified (no muscularis mucosae present).

This classification may in fact have clinical implications, as I will present below.

Urothelial carcinoma with endophytic or broad front growth pattern.

A more controversial pattern, and certainly a problematic one while assessing for invasion, is seen in large papillary tumors which display a prominent endophytic growth, and thus “invade” the lamina propria with a pushing border, much akin to cutaneous and mucosal verrucous carcinoma.\textsuperscript{20} Unless this pattern is accompanied by true destructive stromal invasion (as defined above), the likelihood of metastasis in tumors with this histology is minimal, because the basement membrane is not truly breached. Another form of endophytic growth is when the carcinoma has a basic inverted architecture-like inverted papilloma of the bladder but has clear-cut cytologic atypia placing it into the carcinoma category. The distinguishing features are summarized in Table 3.

Problems and Pitfalls in the Diagnosis of pT\textsubscript{1} Invasion

Diagnosis of lamina propria invasion is often difficult, and the problem is well exemplified in the data from the French Association of Urology Cancer Committee study\textsuperscript{21}, which revealed that seven experienced pathologists could agree on lamina propria invasion in only 61\% of cases after 3 assessments. In 10\% of cases, no consensus was achieved despite four evaluations. In another study by Abel et al.,\textsuperscript{22} 15\% of lesions initially diagnosed as pT\textsubscript{1} were downstaged to pT\textsubscript{a}, and 22\% of urothelial carcinomas diagnosed with muscle invasion were downstaged to pT\textsubscript{1} or pT\textsubscript{a} by a “dedicated” pathologist. In order to improve the concordance rates among pathologists, it is imperative to be aware and understand the possible pitfalls in the diagnosis of lamina propria invasion (Table 4).\textsuperscript{22a} The most common ones follow.

Tangential sectioning and poor orientation.

Transurethral resection of bladder tumor specimens are excised in a piecemeal fashion. This renders fragmented specimens, which are usually poorly oriented. Furthermore, due to their complex architecture, papillary tumors are inevitably tangentially
sectioned in multiple planes, resulting in isolated nests of tumor cells within connective tissue. Smooth, round, and regular contours favor tangential sectioning, whereas irregular, jagged nests with haphazard arrangement favors stromal invasion.

**Thermal injury.**

Thermal injury or cautery artifact produces severely distorted morphology in TURBT specimens, and is a frequent source of distress for the pathologist. Unfortunately, pathologists have no control over this problem, although deeper levels may occasionally display better preserved areas. When this is not helpful, the pathologist should express the inability to render a definitive diagnosis due to thermal effect.

**Obscuring inflammation.**

Papillary tumors may show variable, often brisk inflammation at the tumor-stromal interface, which may obscure isolated cells or nests of invasive tumor.

**CIS involving von Brunn’s nests.**

Flat lesions, when they involve von Brunn’s nests may mimic lamina propria invasion by the mere presence of high-grade cells in a submucosal location. This is especially problematic in prominent nests or those that have been distorted by an inflammatory process.

**Muscle invasion indeterminate for type of muscle.**

In these cases invasive tumor is seen juxtaposed to muscle fibers, but due to obscuring factors (i.e. inflammation, tangential sectioning, cautery artifact, strong desmoplastic response, or poor orientation), the pathologist is unable to determine whether the muscle involved belongs to the muscularis mucosae or the muscularis propria. It is recommended that when faced with this situation, the pathologist should clearly state their uncertainty in establishing the depth of invasion, rather than to commit to a particular type of muscle involvement - muscularis mucosae (pT1) or muscularis propria (pT2). This distinction is critical, as muscularis propria invasion is currently regarded as the crossroads between conservative management and aggressive therapy.

**Invasion into fat does not indicate extravesical spread.**

Fat may be normally present in the lamina propria, therefore, tumor invasive into fat should not automatically equate to involvement of perivesical fat.²²b

**Deceptively bland variants of urothelial carcinomas.**

When limited to the lamina propria, deceptively bland patterns of invasive urothelial carcinoma may make the recognition of pT1 disease extremely difficult. For example, microcystic urothelial carcinoma²³ can easily mimic cystitis cystica, and the recently described “nested” pattern may be easily confused with von Brunn’s nests.²⁴ Attention should be paid to general features useful in assessing invasion, such as cytologic atypia, infiltrative architecture, desmoplasia and architectural complexity, especially since they may be subtle in superficial biopsies.
Overdiagnosis of vascular invasion.

As mentioned earlier, a peculiar stromal retraction artifact in lamina propria invasive tumors may mimic vascular invasion. Caution is hence warranted and strict criteria should be used (Table 5).

Applying strict morphologic criteria for the diagnosis of lamina propria invasion should minimize diagnostic discrepancies among pathologists. Admission of the inability to definitively identify invasion is appropriate in difficult cases with suboptimal tissue preservation or orientation.

### SUBSTAGING OF pT1 DISEASE

Several studies have evaluated the issue of substaging pT1 urothelial carcinomas (Table 6). Most of them use the muscularis mucosae as an anatomic landmark to assess the depth of invasion. In the absence of muscularis mucosae (seen in 18-83% TURBT specimens only), large vessels may be used as a substitute for muscularis mucosae. Others have divided cases between those tumors that involve the stromal core of the papillae and those that invade the lamina propria proper.20b

In 1990 Younes et al.25 found a 75% all-cause 5-year survival for tumors invading above or into the muscularis mucosae, compared to a 11% survival for those tumors invading below the muscularis mucosae. Similarly, Hasui et al.26, Angulo et al.12, and Holmang et al.27 were able to find different progression rates, 5-year all-cause survival, and cancer specific survival, respectively, for those tumors with invasion above and below the muscularis mucosae. In 1998, Hermann et al.28 found that tumors with invasion beyond the muscularis mucosae had a worse prognosis than those with invasion in the tumor stalk or above the muscularis mucosae. In a multivariate analysis, depth of invasion was the only significant parameter that predicted outcome. The main problem with this method of substaging pT1 urothelial carcinomas is that the muscularis mucosae, as mentioned before, is not a consistent histologic finding in bladder tumor resection specimens. Most of the above mentioned authors have at least partially overcome this problem by using the large blood vessels in the submucosa as a substitute anatomical landmark when muscularis mucosae was not present. For example, Angulo et al.12 were able to identify muscularis mucosae in 39% of their cases, and used the blood vessels landmark in a remaining 26%. Thus, in 35% of their cases, substaging could not be performed. Platz et al.13 identified muscularis mucosae in only 33% of their cases and Sozen et al in 55% of cases.26b Furthermore, by using the same substitute anatomical landmark in the rest of the cases, they did not find any prognostic significance in substaging pT1 disease. These realistic problems, which are probably encountered not infrequently in everyday practice, have prompted recent questioning of the validity of substaging pT1 disease based on the muscularis mucosae.

In 1999, Cheng et al.29 proposed a system of substaging pT1 tumors based on the micrometrical measurement of the depth of invasion. They studied a series of 55 patients with stage T1 urothelial carcinomas diagnosed on TURBT specimens and eventually treated by cystectomy. By using a micrometer to measure the depth of invasion from the mucosal basement membrane, they found a significant correlation between depth of invasion and survival.
invasion in the TURBT specimen and final pathologic stage on cystectomy. By using 1.5 mm of depth of invasion, they were able to predict advance stage in the cystectomy with a sensitivity of 81%, a specificity of 83%, and a positive and negative predictive value of 95% and 56%, respectively.

The collective data implies that deep lamina propria (i.e. submucosal) invasion, whether assessed by the relation of the tumor to the muscularis mucosae, or by direct micrometric measurement, identifies a subset of patients with pT1 disease with a more adverse prognosis. In Younes’ data25, the 5-year survival of patients with pT1c disease (i.e. invasion beyond the muscularis mucosae) was similar to those with pT2 disease (14% vs. 20%, respectively).

The recent WHO/ISUP Consensus Conference Committee recognized and encouraged the need to express some assessment of the degree or extent of invasion in the pathology report; however, at this point it is felt that substaging of pT1 tumors should not be universally adopted, due to the above-mentioned unresolved issues.17,33

CONCLUDING REMARKS

In summary, the aggregate data on “superficial” bladder neoplasms seem to suggest that grouping of pT1 tumors with pTa tumors, together into the category of “superficial” urothelial neoplasia, is not entirely appropriate. Although their treatment and follow-up is often similar, their biologic potential is different, with reported progression rates for pT1 disease ranging from 22% to 53%. Invasion into the lamina propria, whether occurring in CIS or papillary neoplasia, confers the ability to metastasize and cause death; hence, strict criteria should be applied when assessing for presence of invasion. In addition, lamina propria invasive tumors have a higher risk of recurrence and disease progression, requiring closer clinical surveillance. Further study is required to fully evaluate the significance of substaging of pT1 tumors and the most appropriate method, which can be reliably practiced by the surgical pathologist to document the extent and depth of invasion.
### Table 1

**Criteria for Diagnosis of Invasion into Lamina Propria by Urothelial Carcinoma**

<table>
<thead>
<tr>
<th>Histologic grade:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasion seen much more frequently, although not exclusively, in high grade (1998 WHO/ISUP classification) lesions.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Invading epithelium:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irregularly shaped nests</td>
</tr>
<tr>
<td>Single cell infiltration</td>
</tr>
<tr>
<td>Irregular or absent basement membrane</td>
</tr>
<tr>
<td>Tentacular finger-like projections</td>
</tr>
<tr>
<td>Invasive component with higher nuclear grade and/or more cytoplasm (or morphologically different) than overlying non-invasive component</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stromal response:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desmoplasia or sclerosis</td>
</tr>
<tr>
<td>Retraction artifact</td>
</tr>
<tr>
<td>Inflammation</td>
</tr>
<tr>
<td>Myxoid stroma</td>
</tr>
<tr>
<td>Pseudosarcomatous stroma</td>
</tr>
<tr>
<td>Absent stromal response</td>
</tr>
</tbody>
</table>

WHO/ISUP= World Health Organization/International Society of Urologic Pathology Consensus Classification of Bladder tumors

### Table 2

**Histologic Patterns of Invasion into Lamina Propria by Urothelial Carcinoma**

- Carcinoma in situ with microinvasion
- Papillary urothelial carcinoma with microinvasion
- Papillary urothelial carcinoma with invasion into stalk
- Well-established invasion into lamina propria
  - *Invasion up to muscularis mucosae*
  - *Invasion beyond muscularis mucosae*
  - *Lamina propria invasion not further specified (no muscularis mucosae present)*
- Urothelial carcinoma with endophytic or broad front growth pattern with destructive stromal invasion
**Table 3**

Differences between inverted papilloma and TCC with inverted papilloma-like growth.

<table>
<thead>
<tr>
<th></th>
<th>Inverted Papilloma</th>
<th>TCC with Inverted Papilloma-like growth</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surface</strong></td>
<td>Smooth dome shaped or focally exophytic, cytologically unremarkable, usually intact surface.</td>
<td>Variable, usually exophytic papillary lesion.</td>
</tr>
<tr>
<td><strong>Growth Pattern</strong></td>
<td>* Endophytic expansile sharply delineated lesion.</td>
<td>Endophytic, may coexist with “broad front” inverted growth pattern, lesional circumscription variable.</td>
</tr>
<tr>
<td></td>
<td>• Ramifying cords and trabeculae of even width.</td>
<td>Ramifying cords and trabeculae with irregularity of width and with transition into solid areas.</td>
</tr>
<tr>
<td></td>
<td>• Destructive invasion of lamina propria or muscularis propria absent by definition.</td>
<td>Invasion into lamina propria or muscle may be present.</td>
</tr>
<tr>
<td><strong>Cytologic Features</strong></td>
<td>• Orderly polarized cells with tendency to spindle and palisade at the periphery.</td>
<td>Maturation, spindling or palisading minimal to absent.</td>
</tr>
<tr>
<td></td>
<td>• Diffuse and severe cytologic atypia absent.</td>
<td>Cytologic features are grade dependent (urothelial carcinoma, low grade or high grade).</td>
</tr>
<tr>
<td><strong>Biologic Potential</strong></td>
<td>Benign</td>
<td>Recur (usually new occurrences) or progress (depends on grade and stage)</td>
</tr>
</tbody>
</table>

(From ref 20 Amin et al)•
Table 4

Pitfalls in the diagnosis of lamina propria invasion by urothelial carcinoma

- Tangential sectioning
- Thermal artifact
- Obscuring inflammation
- Carcinoma in situ involving von Brunn’s nests
- Invasion into muscle, indeterminate for type of muscle (muscularis mucosae vs. muscularis propria)
- Invasion into adipose tissue within lamina propria (overdiagnosis of extravesical invasion)
- Deceptively bland urothelial carcinomas
- Microcystic variant of urothelial carcinoma (invasive)
- Broad front or inverted growth raising the question of invasion
- Nested variant of urothelial carcinoma (invasive)
- Overdiagnosis of vascular invasion

Table 5

Criteria And Pitfalls For Vascular-Lymphatic Invasion In Urothelial Neoplasms.

Criteria For Vascular-Lymphatic Invasion

- Presence of unequivocal endothelial lining
- Nests attached to wall of lumen containing blood constituents (red blood cells, inflammatory cells or thrombus)
- Nests attached to and conforming to the shape of the vessel
- Peritumoral location of vascular invasion (not intratumoral invasion)
- Tumor cells in the space near large artery or vein (vascular route)
- Immunohistochemical confirmation (Factor VIII, Ulex europaeus, or CD31)

Pitfalls In Recognition Of Vascular-Lymphatic Invasion

- Pitfall in recognition of endothelial/venular spaces
  - Retraction of stroma (particularly conspicuous in micropapillary tumors)
- Pitfall in recognition of large vessel invasion
  - Carry-over due to fragmentation of neoplasm

(From ref 14 Amin et al)
Table 6
Proposed Substaging Systems for pT1 Urothelial Carcinoma

<table>
<thead>
<tr>
<th>Authors</th>
<th>Substaging system</th>
<th>Outcome</th>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panago et al. 20b</td>
<td>T1a: Invasion into papillary core</td>
<td>82%</td>
<td>Recurrence free rate</td>
</tr>
<tr>
<td></td>
<td>T1b: Lamina propria invasion</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td>Younes et al. 25</td>
<td>T1a: Invasion above muscularis mucosa</td>
<td>75%</td>
<td>5 year all-cause survival</td>
</tr>
<tr>
<td></td>
<td>T1b: Invasion at muscularis mucosa</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Hasui et al. 26</td>
<td>T1a: Invasion above muscularis mucosa</td>
<td>7%</td>
<td>Progression rate</td>
</tr>
<tr>
<td></td>
<td>T1b: Invasion below muscularis mucosa</td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td>Angulo et al. 12</td>
<td>T1a: Invasion above or at muscularis mucosa</td>
<td>86%</td>
<td>5-year all-cause survival</td>
</tr>
<tr>
<td></td>
<td>T1b: Invasion below muscularis mucosa</td>
<td>52%</td>
<td></td>
</tr>
<tr>
<td>Platz et al. 13</td>
<td>T1a: Invasion above muscularis mucosa</td>
<td>65%</td>
<td>10-year cancer-specific survival</td>
</tr>
<tr>
<td></td>
<td>T1b: Invasion at muscularis mucosa</td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T1c: Invasion below muscularis mucosa</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>Holmang et al. 27</td>
<td>T1a: Invasion above muscularis mucosa</td>
<td>23%</td>
<td>Disease-specific demise</td>
</tr>
<tr>
<td></td>
<td>T1b: Invasion at or below muscularis mucosa</td>
<td>45%</td>
<td></td>
</tr>
<tr>
<td>Hermann et al. 28</td>
<td>T1a: Invasion limited to stalk of papillae</td>
<td>78%</td>
<td>5-year all cause survival</td>
</tr>
<tr>
<td></td>
<td>T1b: Invasion above muscularis mucosa</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T1c: Invasion at or below muscularis mucosa</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td>Cheng et al. 29</td>
<td>Depth of invasion measured by micrometer</td>
<td>&lt;1.5 mm</td>
<td>Prediction of pT2+ disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;1.5 mm</td>
<td>95%</td>
</tr>
<tr>
<td>Sozen et al. 28b</td>
<td>T1a: Invasion above muscularis mucosa</td>
<td>NA</td>
<td>Stage statistically significant</td>
</tr>
<tr>
<td></td>
<td>T1b: Invasion below muscularis mucosa</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

Modified from Cheng et al 29 and Jimenez et al 1

References:


