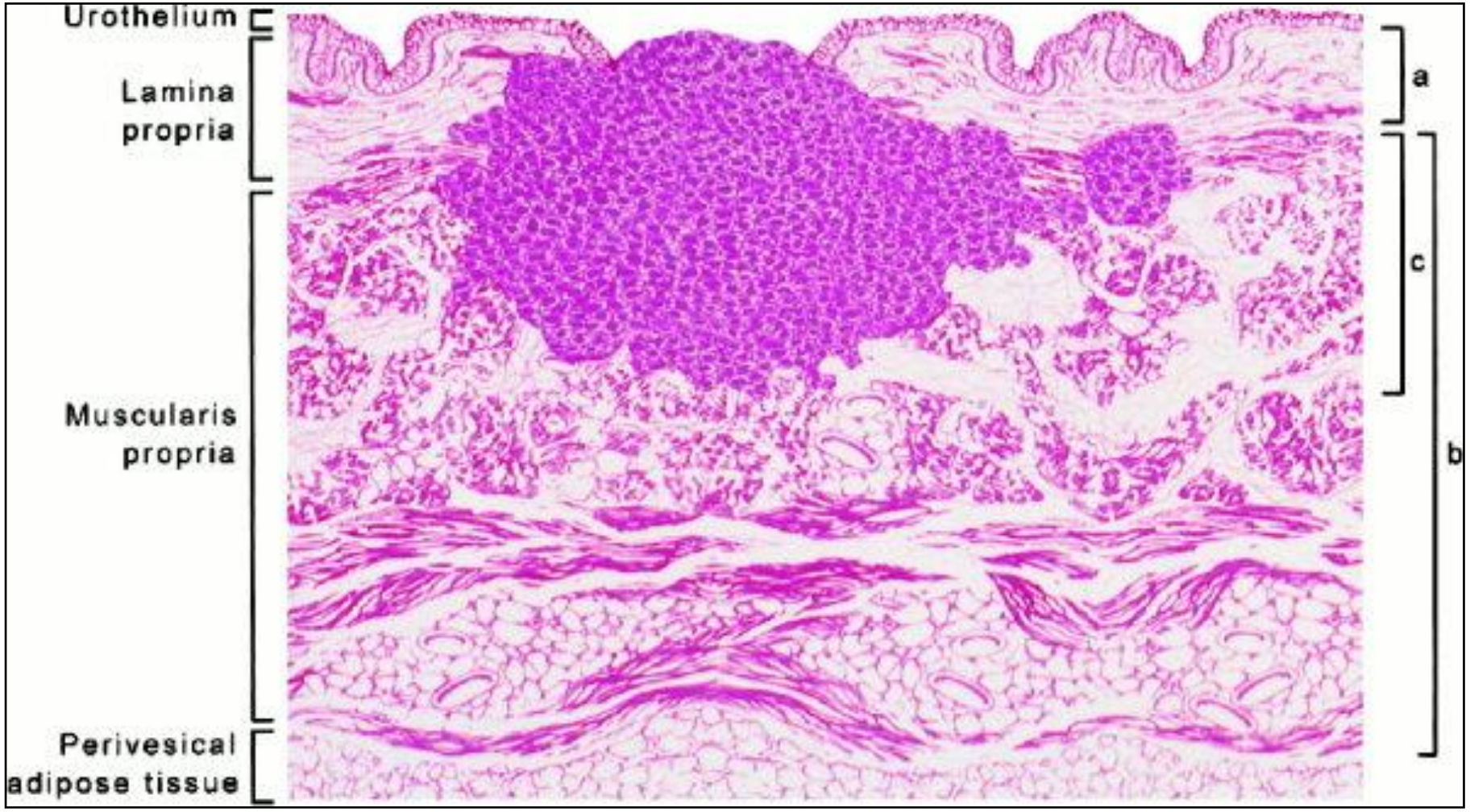
Cáncer de Vejiga T1. Aspectos anatomopatológicos recientes y subestadificacion utilizando patología digital.

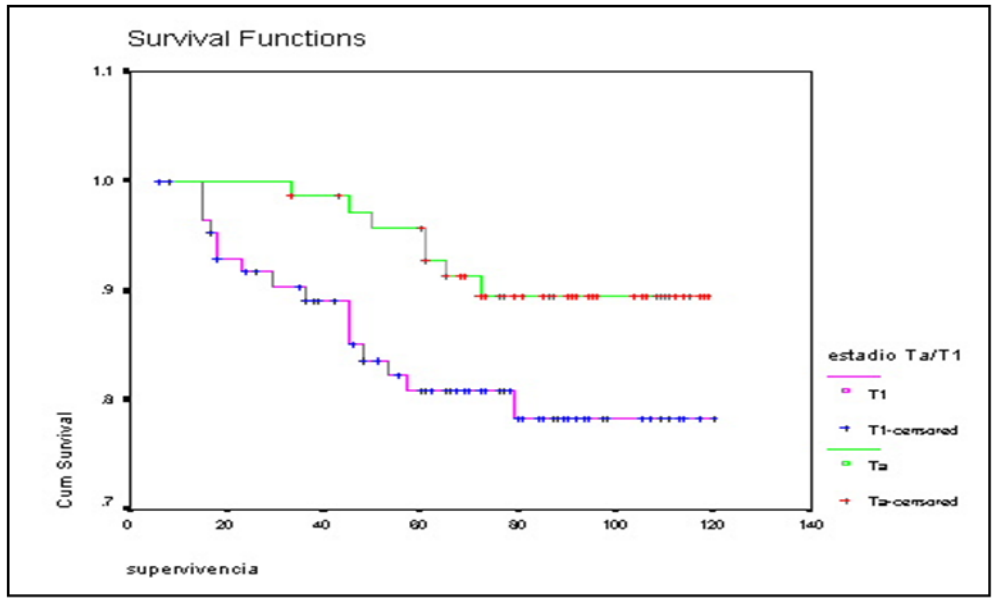
Antonio Lopez-Beltran

Background: Bladder wall invasion



T1- assessment and substaging

Definition T1 (AJCC/TNM 2017): Tumor invading subepithelial connective tissue



Background
- Lamina propria: Anatomic landmarks

T1 assessment
- Reproducibility

T1 substaging
- Methodological issues
- Clinical significance
- Substaging using Dig Path

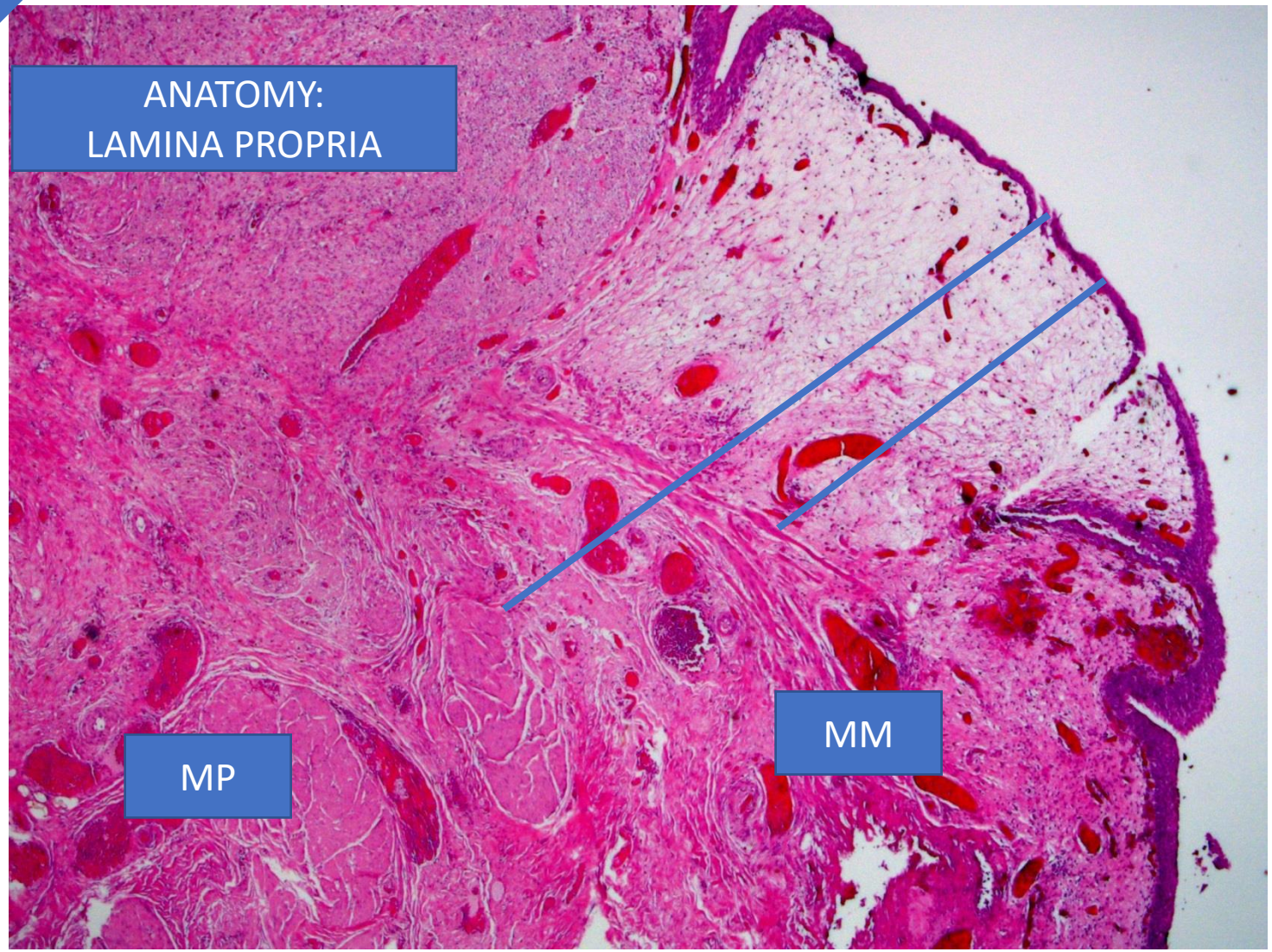
Conclusion

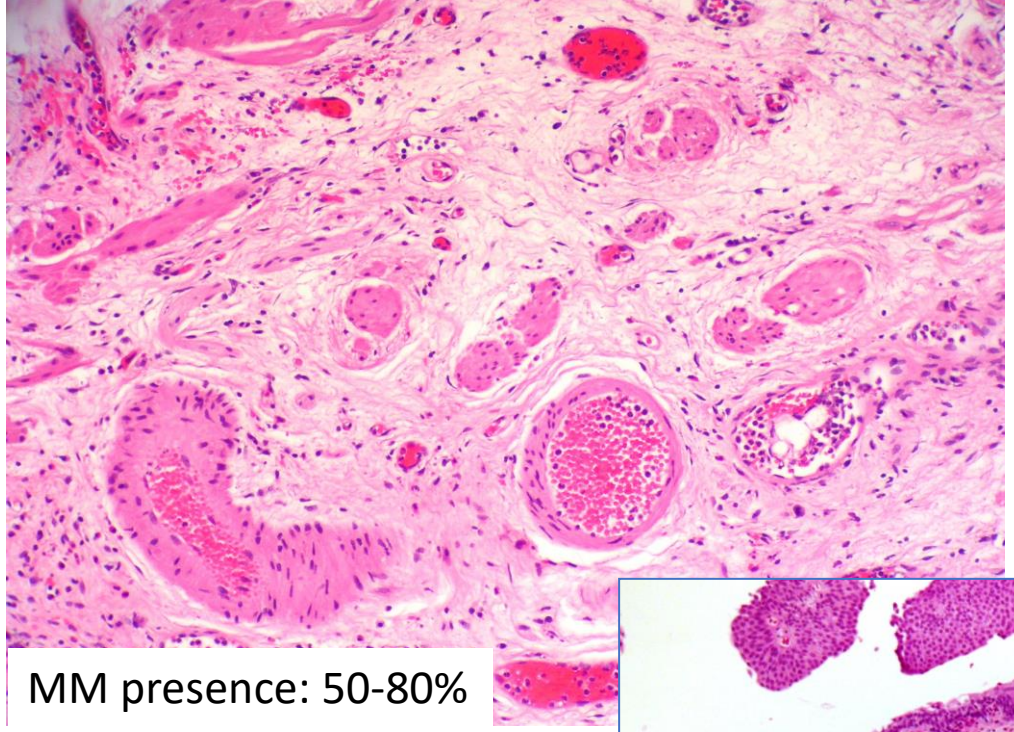
Take-home messages

Background

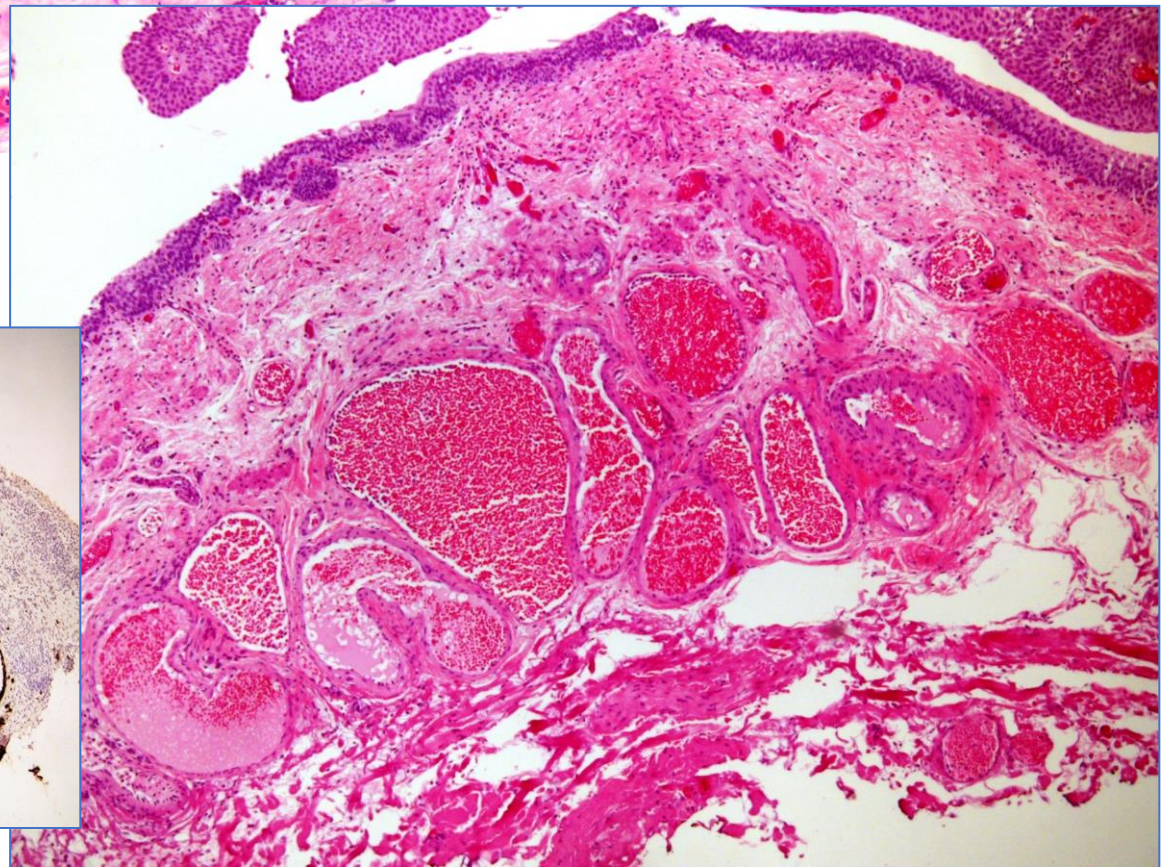
- Lamina propria: Anatomic landmarks

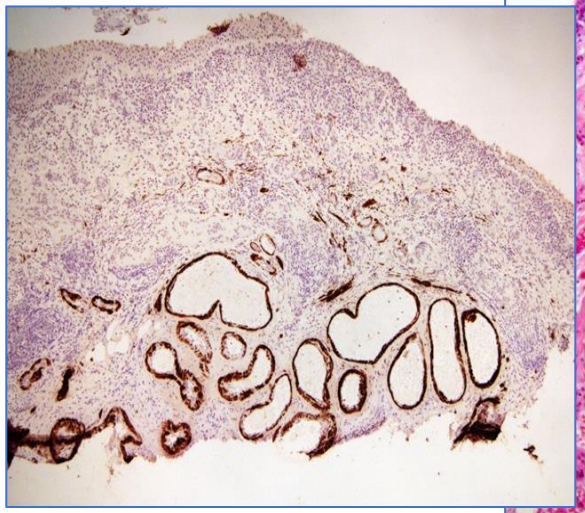
Definition T1 (AJCC/TNM 2017): Tumor invading subepithelial connective tissue

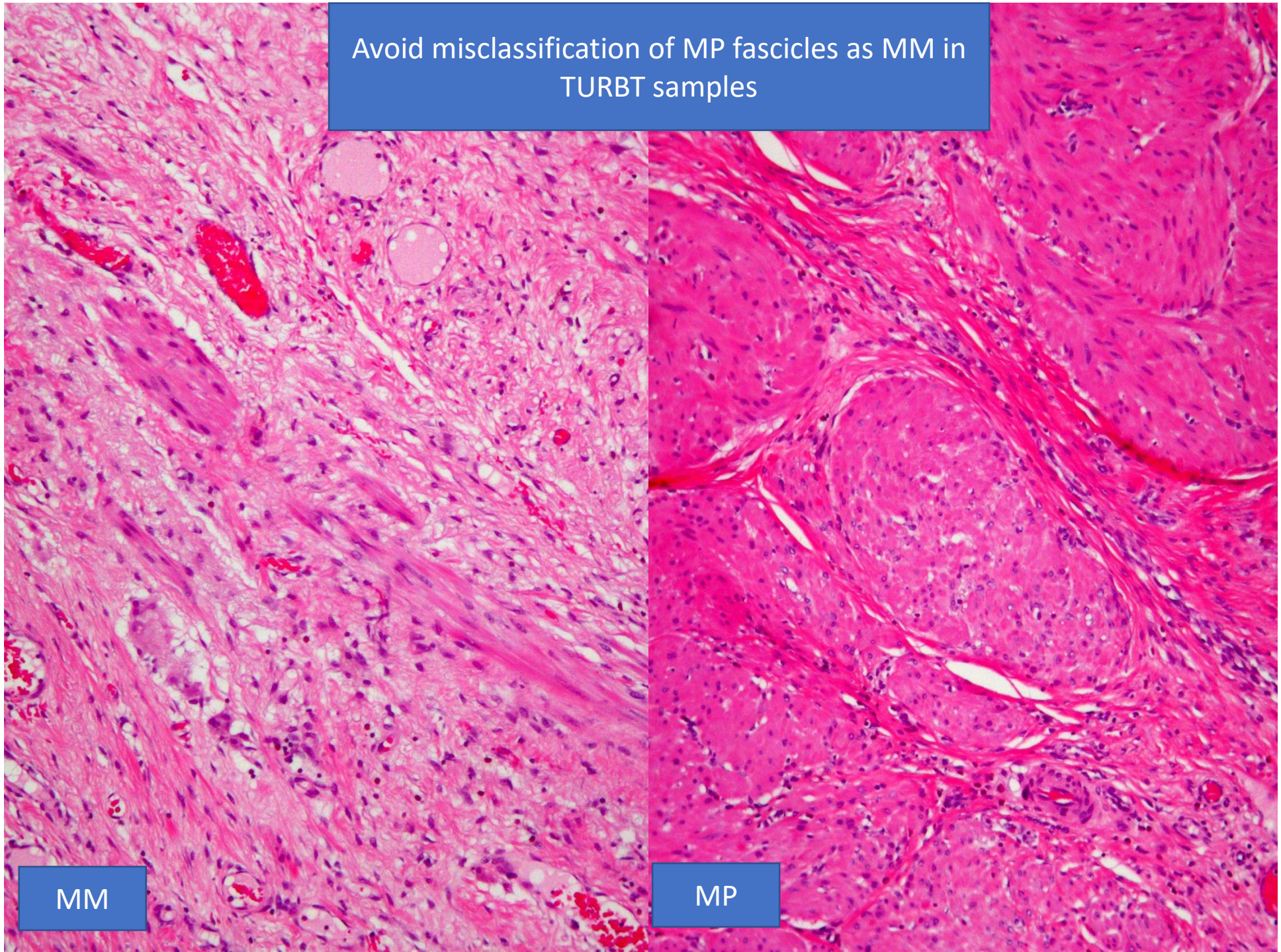


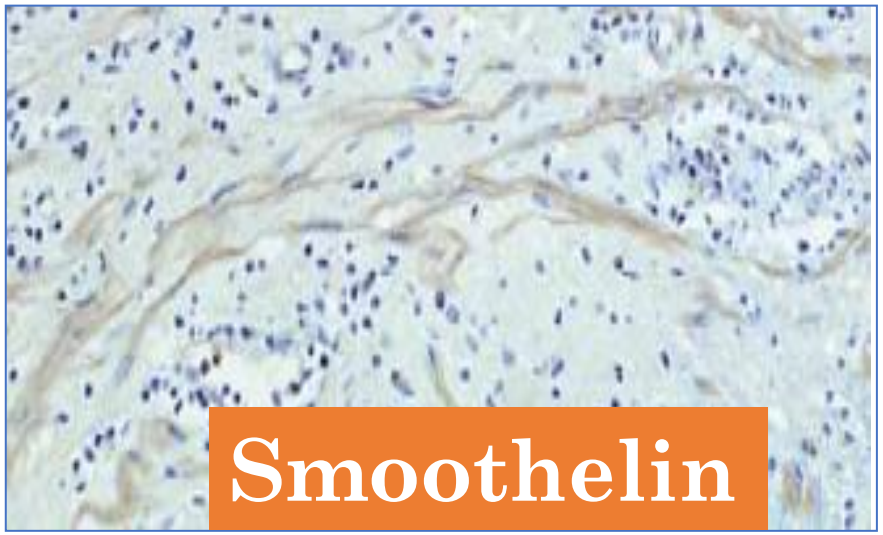


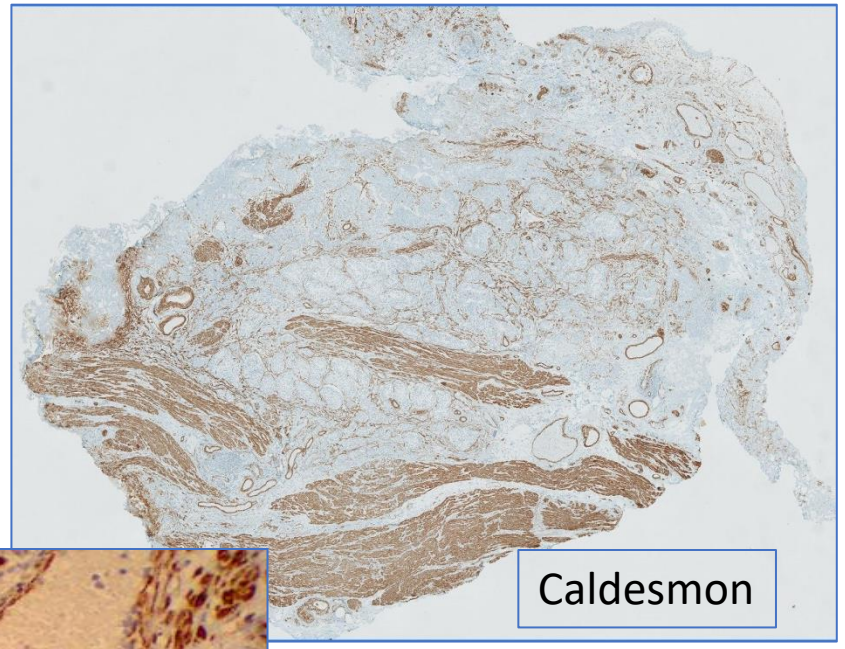
MM presence: 50-80%

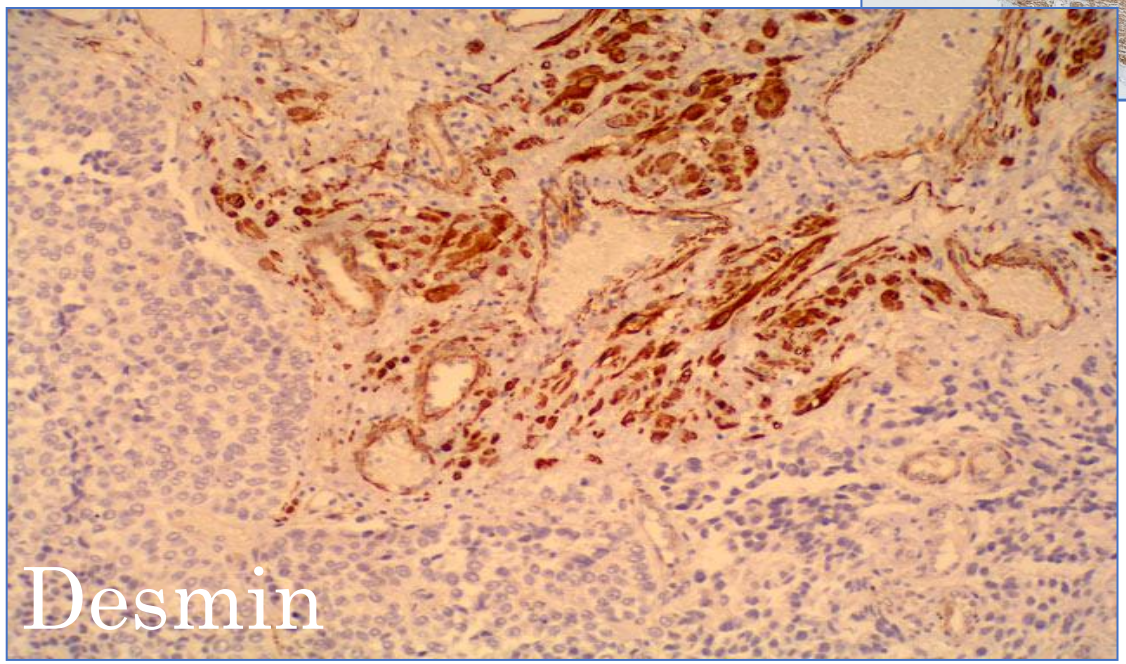





Avoid misclassification of MP fascicles as MM in TURBT samples
MM
MP



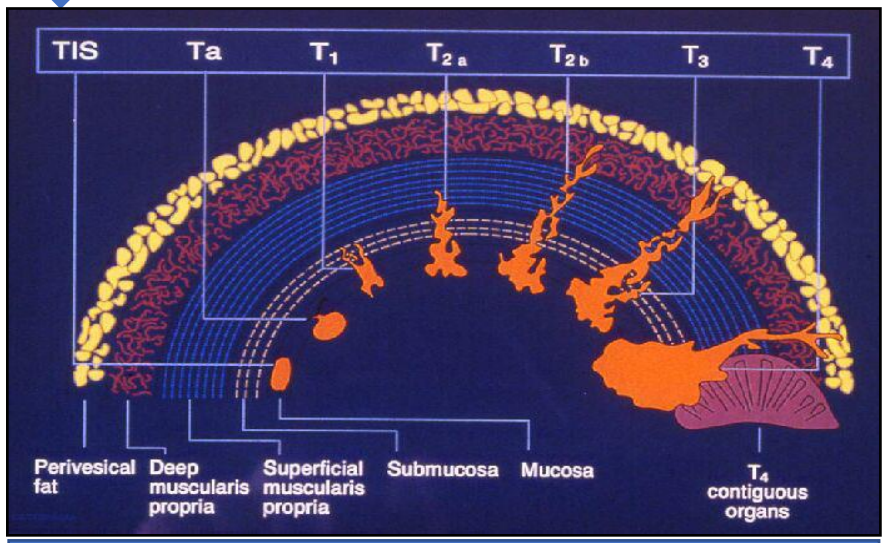




Vimentin: + MM and -MP

T1 assessment

- Reproducibility



- Bladder cancer is staged by the TNM system.
- The T categories are determined by depth of invasion into the layers of bladder wall and adjacent structures.
- T1 substaging seems to be a good predictor of outcome after TURBT
- Optimal method yet to be determined

SUMMARY OF PUBLISHED DATA

- 61% agreement; 10% NO consensus after 4 rounds
- 15% of pT1 down-staged as pTa
- 22% of pT2 down-staged to pT1 or pTa
- 80% agreement; 88% after a 2nd round
- 35% pT1 to pTa; 3% to pT2-T3
- 2nd TURBT found: 2-28% pT1 to be at least pT2

- **pT1 (experts) study**: (Histopathology 2013)
- Full agreement (44%)
- Majority consensus (72%)
- *Kappa* ~ 50%

Pathology (January 2021) 53(1), pp. 67–85

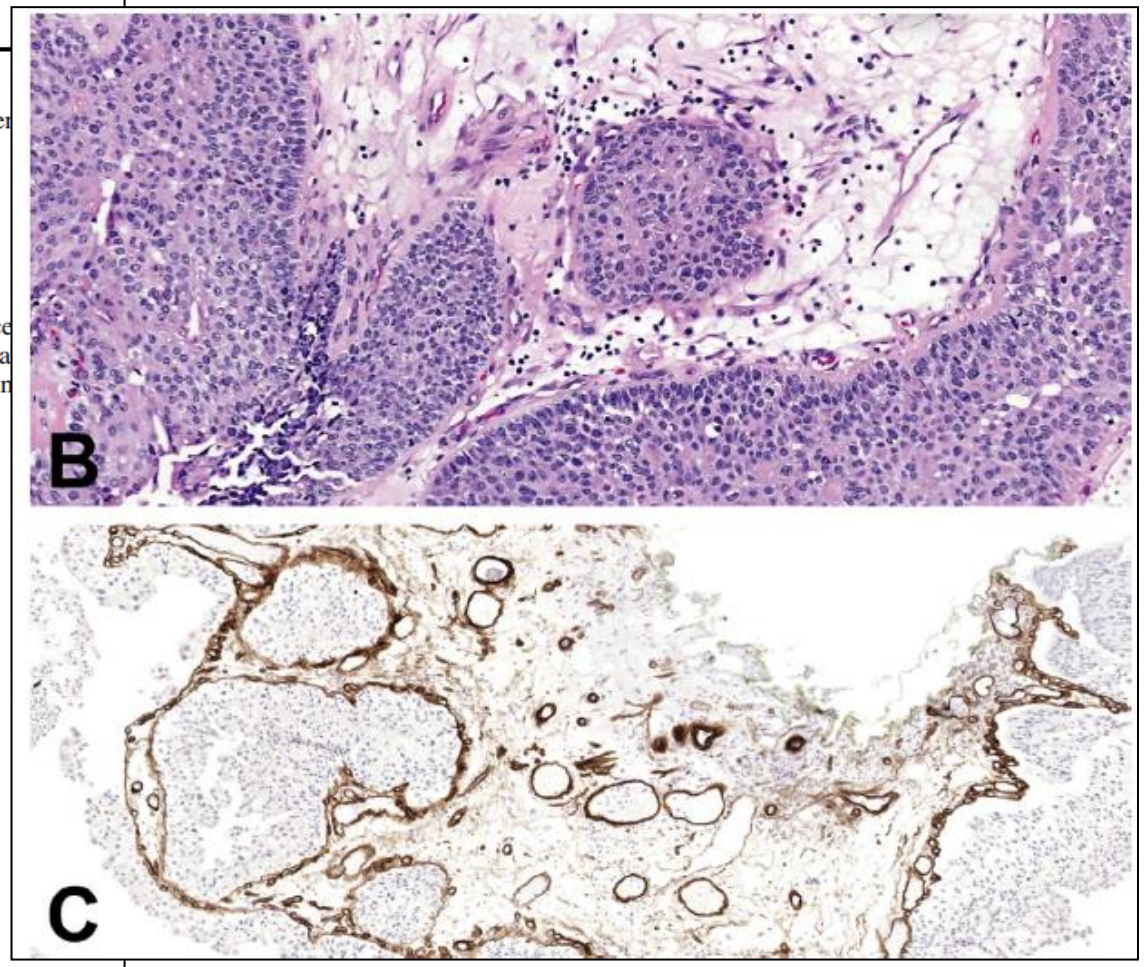
UROLOGICAL PATHOLOGY

Stage T1 bladder cancer: diagnostic criteria and pitfalls

ANTONIO LOPEZ-BELTRAN[1], LIANG CHENG[2,3]

Table 1 Main issues of focus for the diagnosis of subepithelial connective tissue invasion

- Characteristics of smooth muscle in the bladder wall
- Stromal–epithelial interface (histological appearance of basemer membrane)
- Histological grade
- Characteristics of the invading epithelium
  - Single cells
  - Cords of cells in single file pattern
  - Irregularly shaped or variably sized nests
  - Interrupted, irregular, or absent basement membrane interface
  - Angulated or jagged borders of finger-like epithelial prolifera
  - Invasive component with frequent high-grade cytology lackin polarisation
  - Invasive front with cytoplasmic eosinophilia ('paradoxical differentiation')
- Stromal responses
  - Desmoplasia with proliferative hypercellular stroma
  - Myxoid changes
  - Brisk inflammation
  - Retraction artifacts around single cells or tumour nests
  - Rarely limited or no associated stromal reactions
- Histologic patterns of invasion
  - Superficial early invasion (microinvasion)
    - Carcinoma *in situ* with microinvasion
    - Papillary urothelial carcinoma with microinvasion
  - Urothelial carcinoma with established invasion
    - Invasion at the tumour base
    - Invasion at the papillary stalk
  - T1 bladder carcinoma with variant histology
- The role of immunohistochemistry in diagnosis of invasion
  - Keratins (pancytokeratin, cytokeratin 20)
  - Smoothelin, desmin, vimentin
- Molecular biomarkers
- Reporting of biopsy and transurethral resection specimens

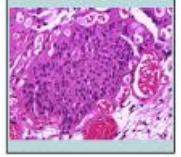


T1 Diagnostic Approach: Pitfalls

- Round to irregular nests
- Basement membrane (BM) preservation
- Parallel array of thin-walled vessels that evenly line the BM

AND

Smooth, round, and regular contours favor tangential sectioning

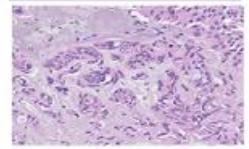


FAVOR

Non-invasive nests. Most probably tangetial sectioning (Ta)

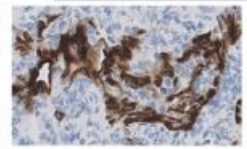
T1 Diagnostic Approach: Pitfalls

- Cautery artifacts
- Brisk inflammation
- Stromal reactions



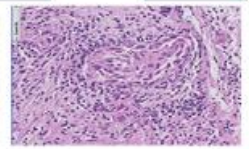
AND

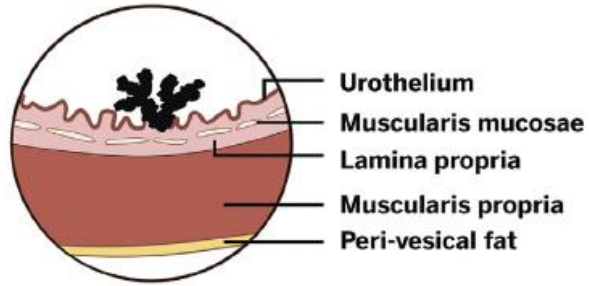
Pankeratin IHC defines the presence of epithelial nests and/or single cells and its morphology (round, angular, or jagged borders)



FAVOR

Invasive Cancer (T1)





T1 Diagnostic Approach: Cytology and Architectural Patterns

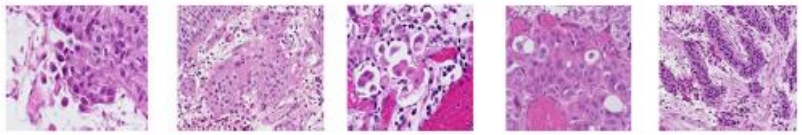
- Single cells
- Cords in single file
- Irregularly shaped variable sized nests
- Angulated or jagged borders
- Finger-like projections

AND

- High grade cytology
- Loss of cell polarity
- Cytoplasmic eosinophilia (paradoxical differentiation)
- Retraction artefact in single cells or nests
- Interrupted, irregular or absent BM interface

FAVOR

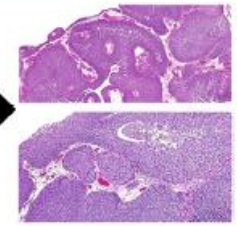
Invasive Cancer (T1)



T1 Variant Histology: Areas of Difficulty

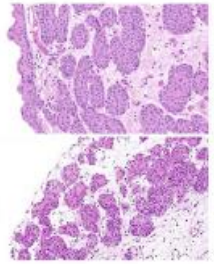
Inverted growth:

- Anatomic landmark MM/MP
- Epithelial/stromal interface
- If concerning invasive component present, then similar diagnostic criteria apply
- Ancillary study may be helpful



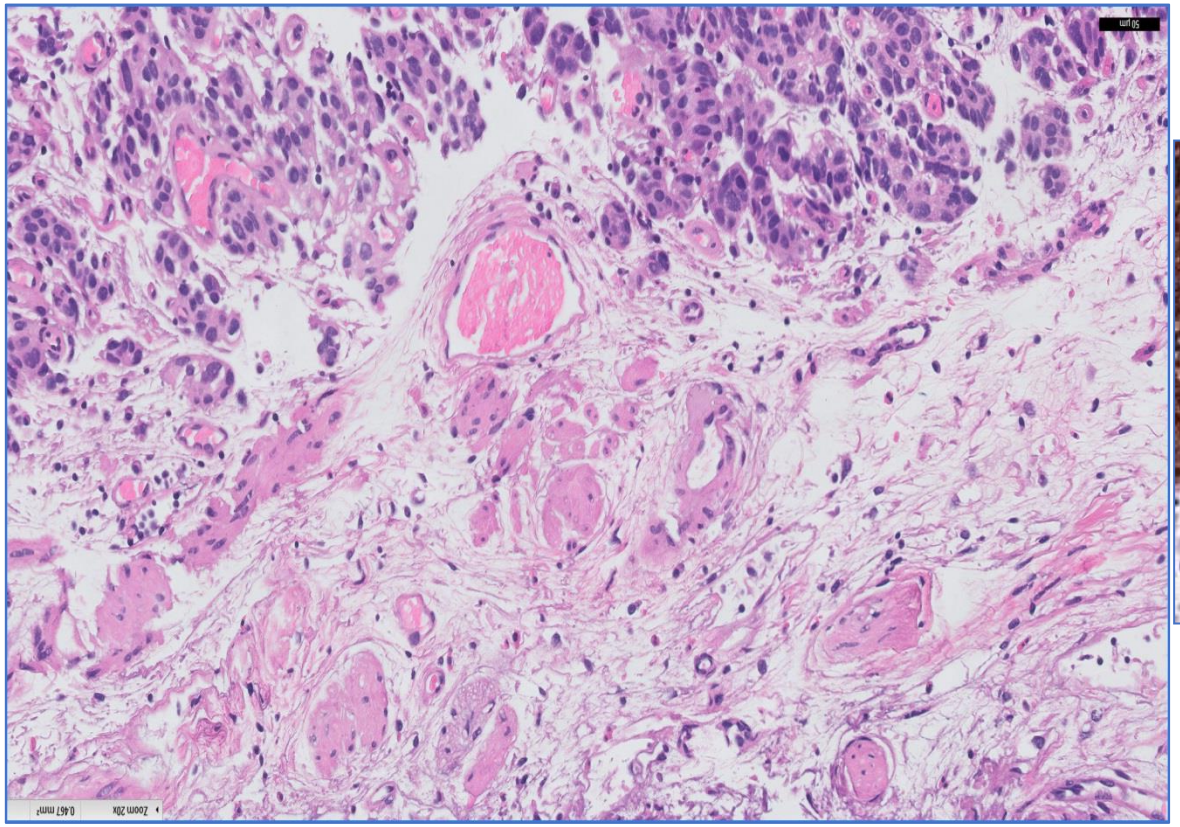
Nested UC vs von Brunn nests:

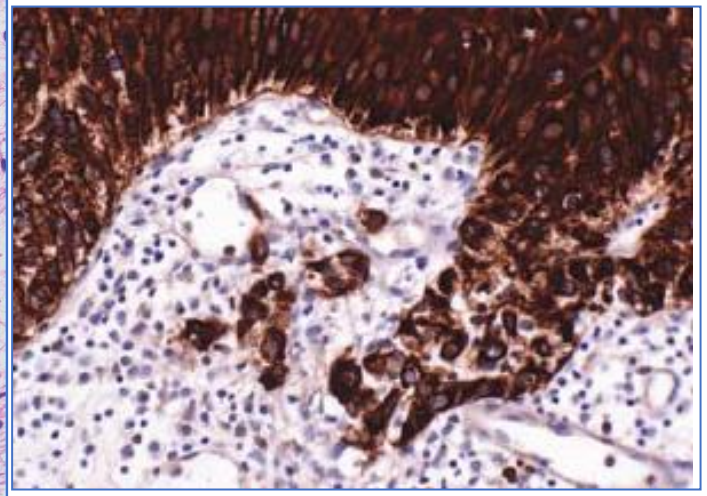
- Anatomic landmark MM/MP
- Epithelial/stromal interface
- Cytologic atypia
- Confluent growth
- *TERT* promoter mutation
- High/Intense p53 staining

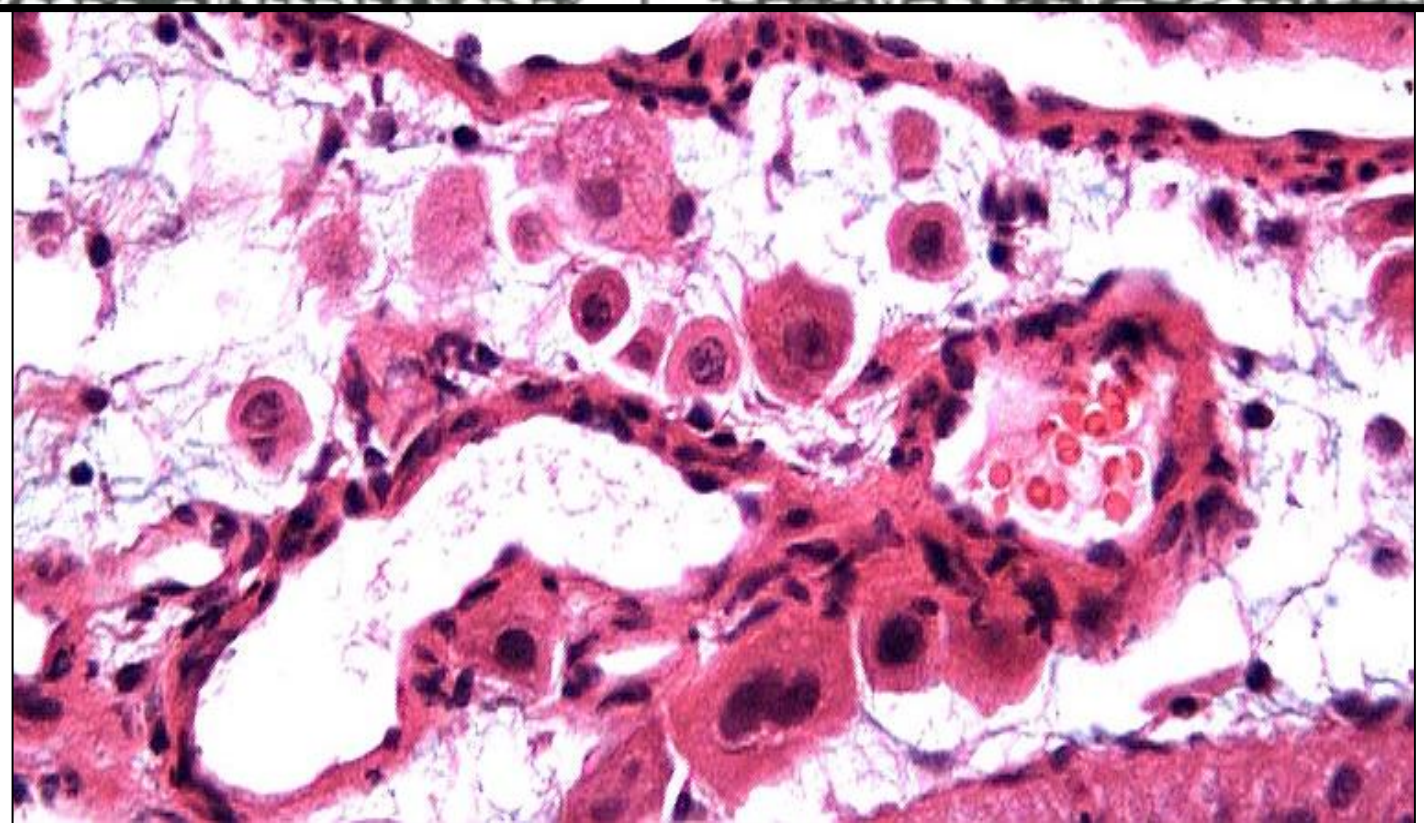


T1 substaging

- Methodological issues and clinical significance







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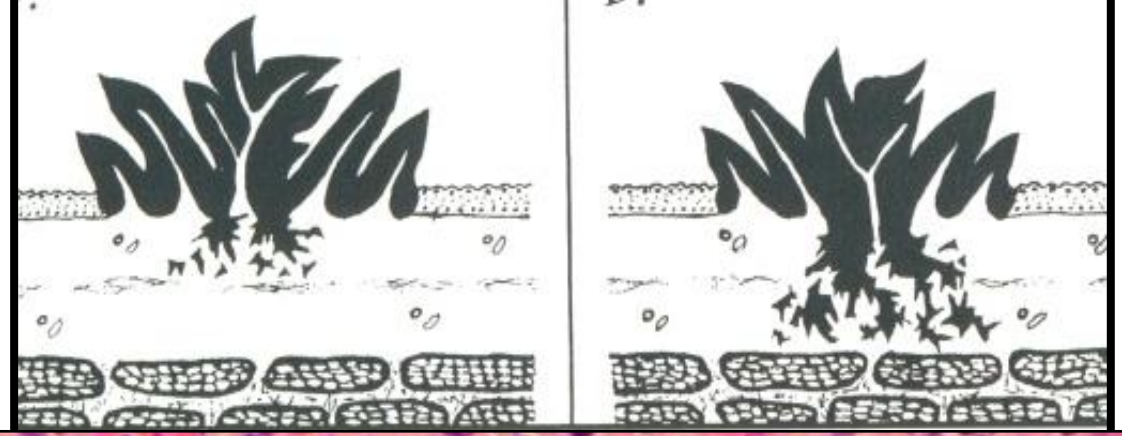
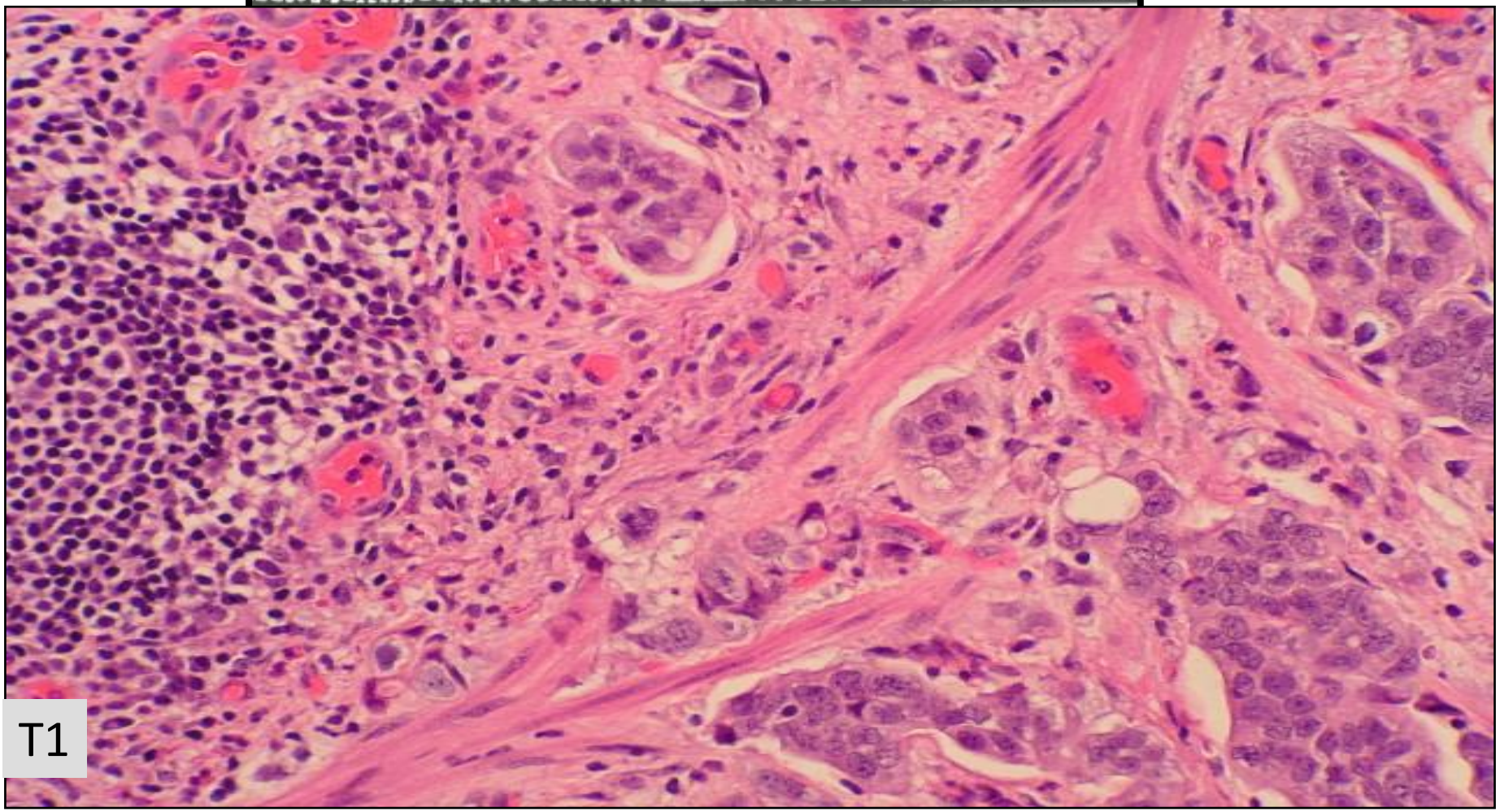
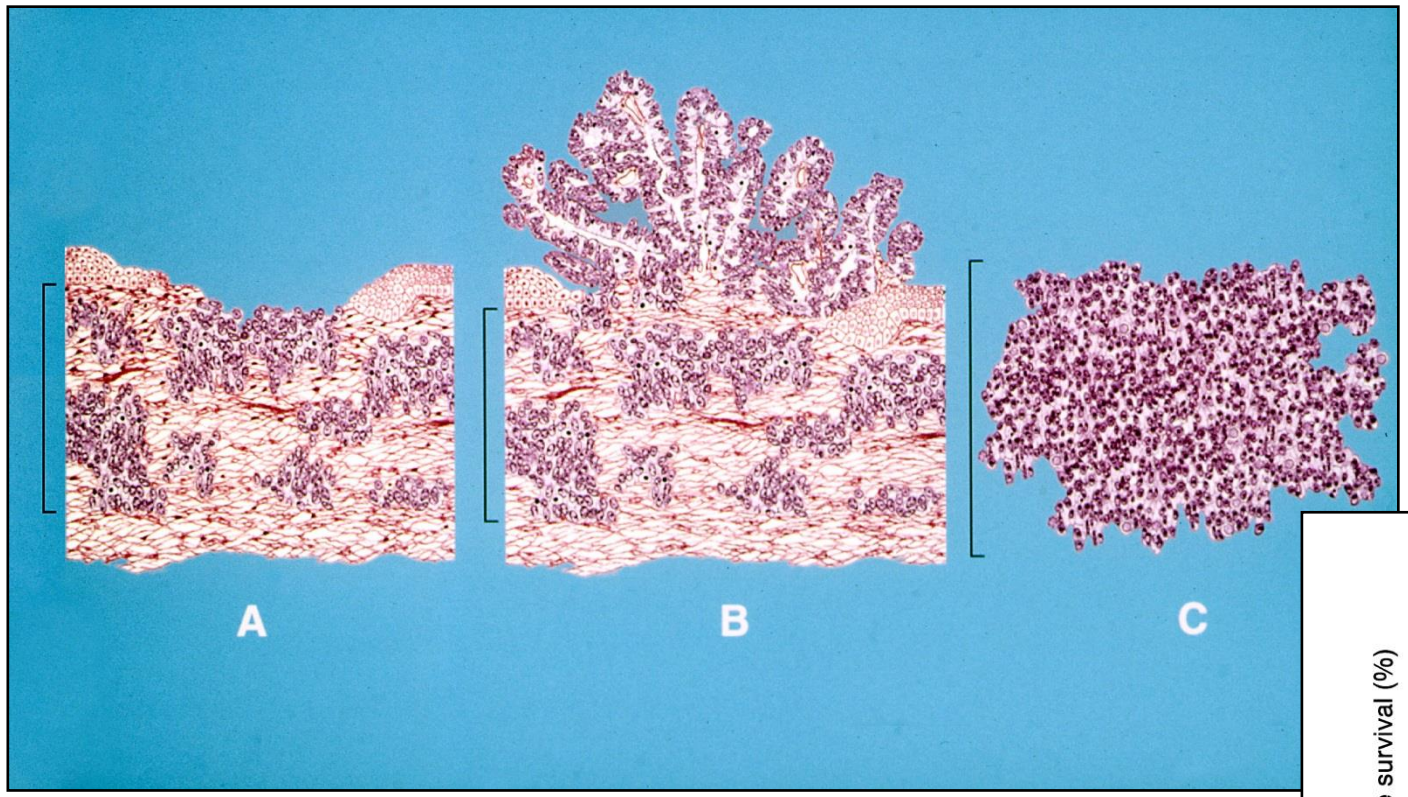
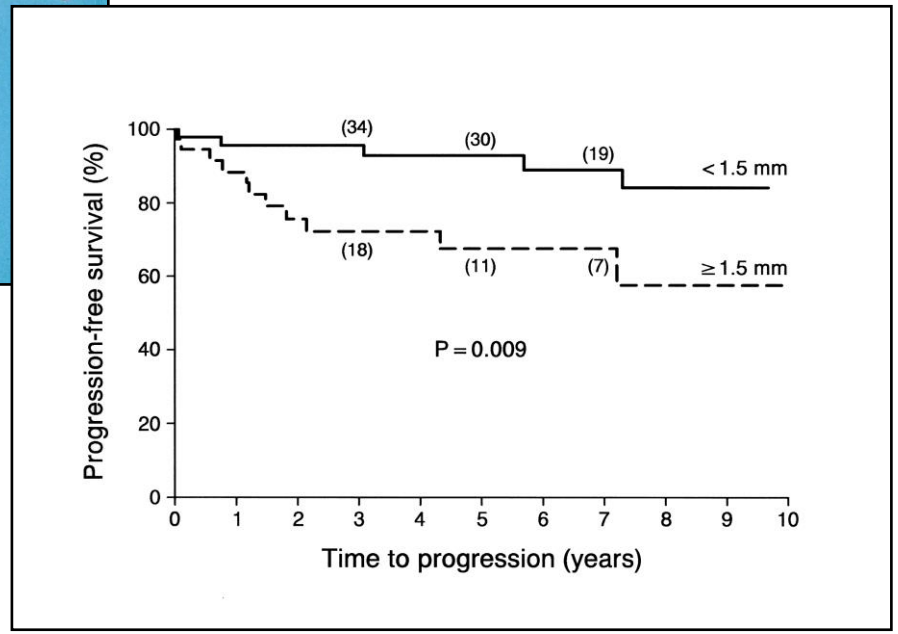



T1

pT1 substaging is significant in patients' survival? Micrometric approach

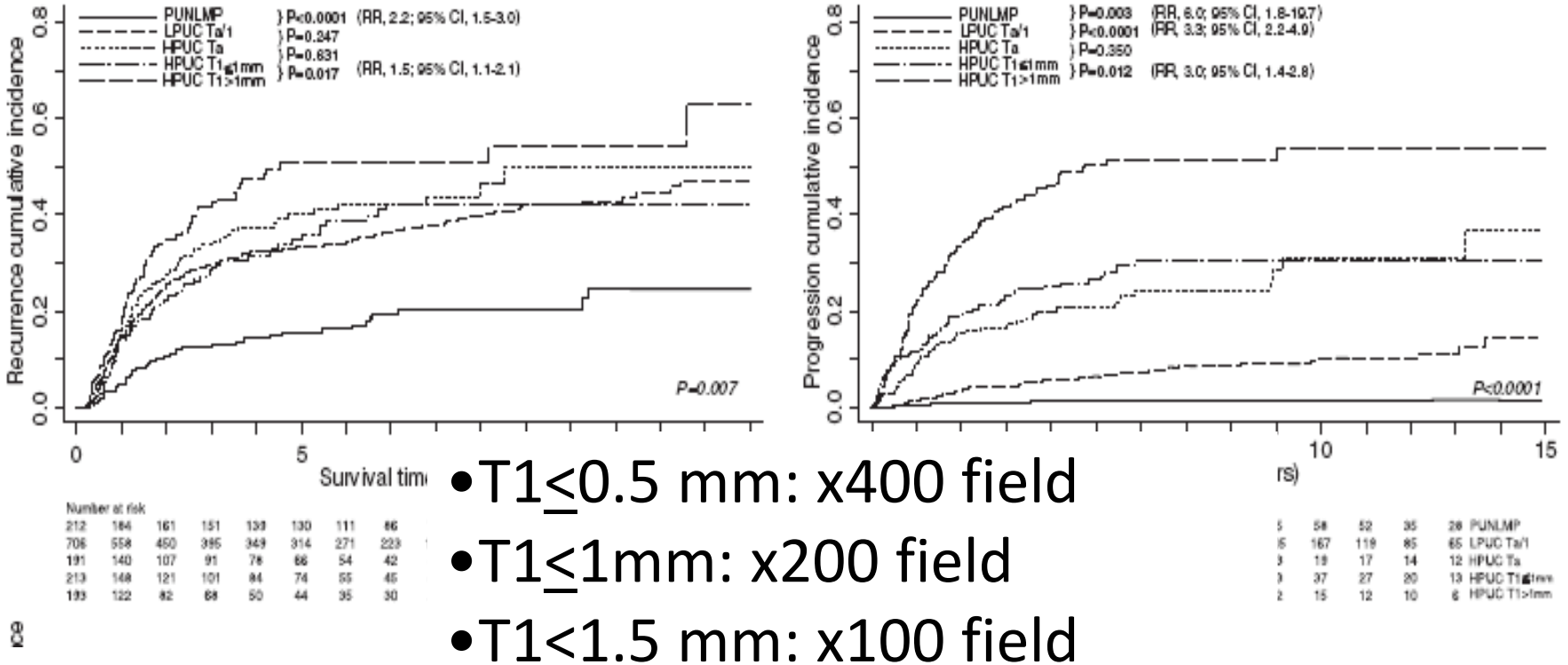




Prognostic Significance in Substaging of T1 Urinary Bladder Urothelial Carcinoma on Transurethral Resection

Wei-Chin Chang, MD, Yen-Hwa Chang, MD, PhD,† and Chin-Chen Pan, MD*‡*

tumors treated by transurethral resection were studied. Substaging was performed using 0.5, 1.0, and 1.5 mm as thresholds to distinguish extensive from focal invasion. Correlations to



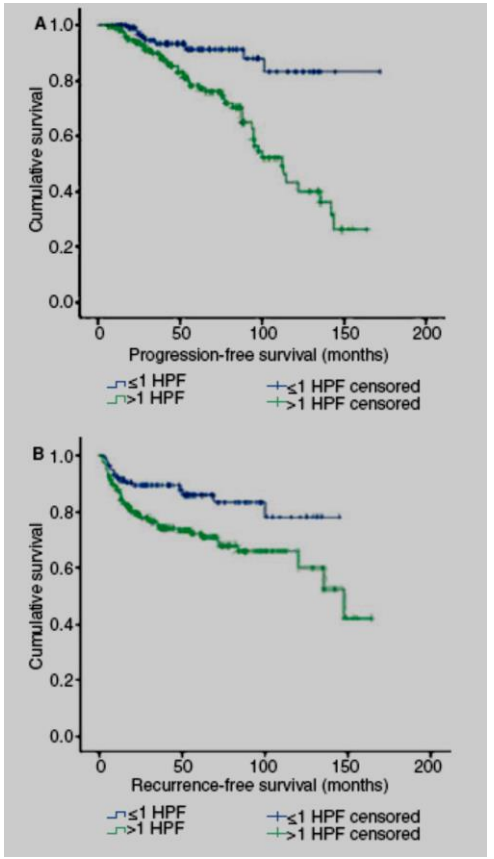
- T1≤0.5 mm: x400 field
- T1≤1mm: x200 field
- T1≤1.5 mm: x100 field

Histopathology 2011, **59**, 722–732. DOI: 10.1111/j.1365-2559.2011.03989.x

Substaging by estimating the size of invasive tumour can improve risk stratification in pT1 urothelial bladder cancer—evaluation of a large hospital-based single-centre series

Simone Bertz, Stefan Denzinger,[1] Wolfgang Otto,[1] Wolf F Wieland,[1] Robert Stoehr, Ferdinand Hofstaedter[2] & Arndt Hartmann

Methods and results: Specimens of 309 patients with pT1 urothelial carcinoma were re-evaluated histologically, including size of infiltrating tumour area estimated as equal to or smaller than one high-power field (HPF) or larger than one HPF, and tumour infiltration in relation to the muscularis mucosae (pT1a/b). Results were correlated with clinical follow-



Recent proposals for T1 substaging

Histopathology

Histopathology 2017, 71, 406–414. DOI: 10.1111/his.13247

Stalk versus base invasion in pT1 papillary cancers of the bladder: improved substaging system predicting the risk of progression

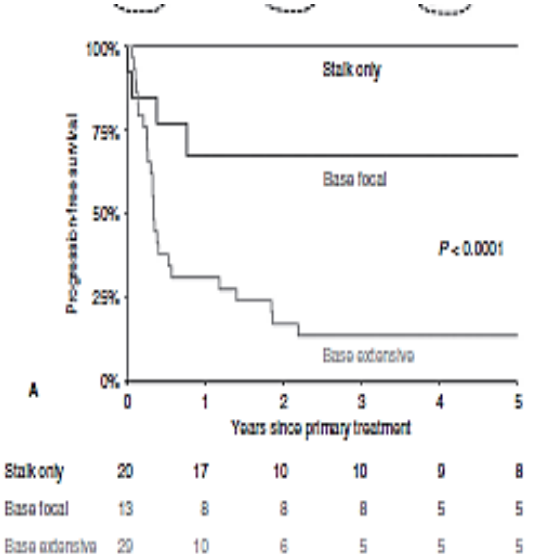
Margaret Lawless,[1] Roman Gulati[2] & Maria Tretiakova[1]

[1]*Department of Pathology, University of Washington School of Medicine, Seattle, WA, USA, and* [2]*Fred Hutchinson Cancer Research Center, Seattle, WA, USA*

Aims: Pathological stage pT1 bladder cancers constitute a clinically heterogeneous group. However, current staging guidelines for superficially invasive cancers do not acknowledge the variability in type and extent of lamina propria invasion in papillary urothelial carcinomas (PUCs), and historically proposed substaging systems showed either high interobserver variation or limited value in predicting patient outcomes. The aim of this study was to reappraise pT1 PUC substaging, with the objective of identifying a novel scheme that is reproducible and prognostically meaningful.

Methods and results: pT1 PUCs diagnosed during 1999–2015 were retrospectively reviewed and characterized as focal invasion confined to the papillary stalk, focal invasion of the tumour base, or extensive invasion of the tumour base. Cases with concurrent flat carcinoma *in situ*, angiolymphatic invasion, absent muscularis propria or clinically advanced disease were excluded. We calculated cumulative incidence rates of recurrence, progression and death by tumour subtype, and evaluated differential risks by using log-rank tests and Kaplan–Meier curves stratified by type and extent of invasion. Among 62 patients satisfying the inclusion criteria, 22 of 29 patients with base-extensive invasion progressed, whereas four of 13 with base-focal and none of 20 with stalk-only invasion progressed. There was strong evidence that base-extensive patients had a higher risk of progression and death resulting from bladder cancer than base-focal or stalk-only patients ($P < 0.0001$). However, tumour subtype was not significantly associated with risk of recurrence ($P = 0.21$).

Conclusions: We propose an innovative substaging approach for reporting the site and extent of lamina propria invasion in patients with pT1 PUC, allowing patient stratification for risk of progression.

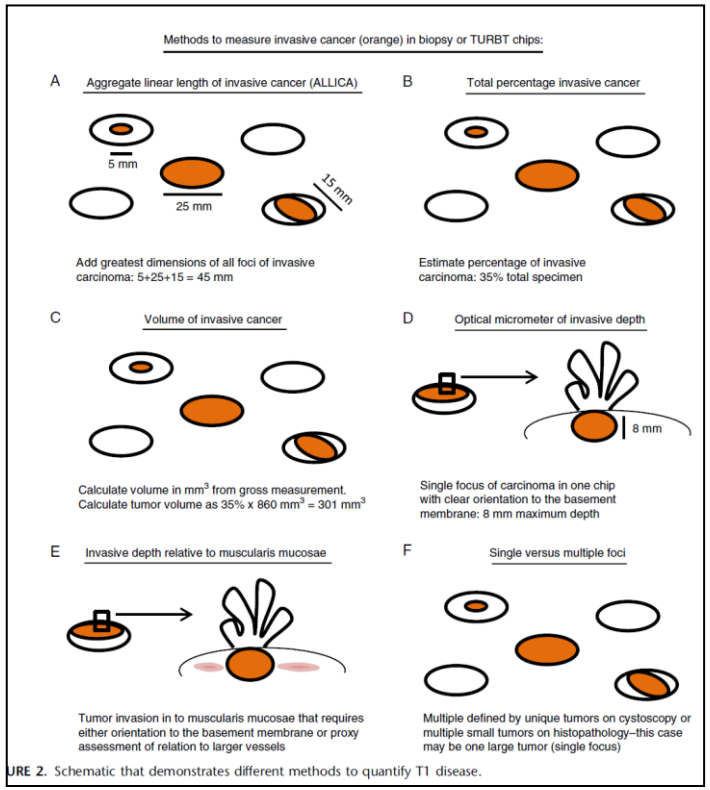


Recent proposals for T1 substaging

Analysis of T1 Bladder Cancer on Biopsy and Transurethral Resection Specimens

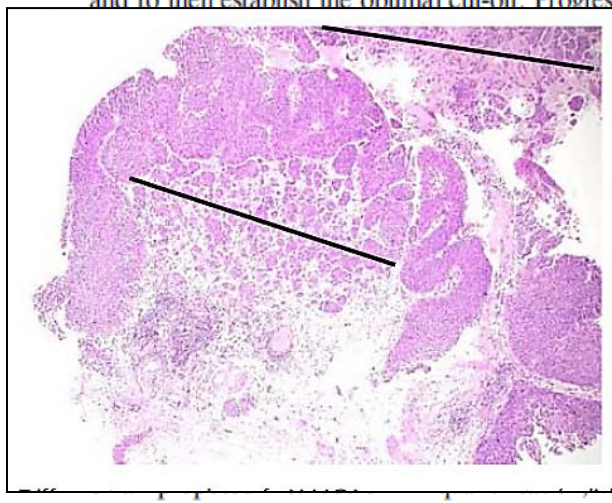
Comparison and Ranking of T1 Quantification Approaches to Predict Progression to Muscularis Propria Invasion

Mariah Z. Leivo, MD, Debashis Sahoo, PhD,† Zachary Hamilton, MD,‡ Leili Mirsadraei, MD,* Ahmed Shabaik, MD,* John K. Parsons, MD, PhD,‡ Andrew K. Kader, MD,‡ Ithaar Derweesh, MD,‡ Christopher Kane, MD,‡ and Donna E. Hansel, MD, PhD*‡*



URE 2. Schematic that demonstrates different methods to quantify T1 disease.

Abstract: Urothelial carcinoma of the bladder invasive into lamina propria on biopsy or transurethral resection of bladder tumor, termed "T1" disease, progresses to muscularis propria invasion in a subset of patients. Prior studies have proposed histopathologic metrics to predict progression, although methods vary widely and it is unclear which method is most robust. This poses a challenge since recent World Health Organization and American Joint Commission on Cancer editions encourage some attempt to substratify T1 disease. To address this critical problem, we analyzed T1 specimens to test which T1 quantification method is best to predict progression and to then establish the optimal cut-off. Progression was analyzed



uscularis propria
deling controlled
s suggest that ag-
CA) measured by
($P = 3.067 \times 10^{-6}$)
LLICA retained
d contribution of
e best cut-off for
2.3 mm and using
the latter severely
After comparison
e recommend the
adoption of the ALLICA measurement and a cut-off of ≥2.3 mm as the best predictor of progression, acknowledging that additional nonhistopathologic methods may be required to increase broad applicability and further reduce the false-positive threshold.

Analysis of T1 Bladder Cancer on Biopsy and Transurethral Resection Specimens

Comparison and Ranking of T1 Quantification Approaches to Predict Progression to Muscularis Propria Invasion

Mariah Z. Leivo, MD, Debashis Sahoo, PhD,† Zachary Hamilton, MD,‡ Leili Mirsadraei, MD,* Ahmed Shabaik, MD,* John K. Parsons, MD, PhD,‡ Andrew K. Kader, MD,‡ Ithaar Derweesh, MD,‡ Christopher Kane, MD,‡ and Donna E. Hansel, MD, PhD*‡*

TABLE 3. Definition of T1 Measurement Criteria

Measurement	Description	Binary or Continuous	Benefits	Limitations
% of specimen with invasive tumor	Estimates the percentage of the invasive component in the entire specimen from 0% to 100%	Continuous	Quick; not dependent on specimen orientation	Subjective
Calculated volume of invasive tumor	Calculates volume by multiplying % invasive tumor component by mm^3 volume at gross examination	Continuous	Accounts for overall invasive tumor volume; not dependent on specimen orientation	Requires additional time; highly dependent upon accurate measurements at time of gross examination
ALLICA	Uses an optical micrometer to measure greatest dimension of each invasive tumor focus on biopsy or TUR and adds them together	Continuous	Optical micrometer increases measurement accuracy; not dependent on specimen orientation; objective	Requires additional time; unclear how each chip may relate to one another in 3 dimensions
Single or multiple foci	Multiple foci defined by presence of pT1 disease at different locations in bladder or clear-cut separate invasive foci in specimen	Binary	Quick	In larger tumors that involve multiple chips, it may be difficult to determine whether the origin was a single focus or multiple foci; dependent on clinical location assignment of multiple tumors
Above muscularis mucosae vs. into/below muscularis propria	Uses the muscularis mucosae anatomic landmark to determine limited depth invasive tumors versus greater depth	Binary	Quick; smaller tumors are readily substaged using this methodology whether orientation can be ascertained or else requires "surrogate" landmark of larger vessels	Muscularis mucosae not always visible due to discontinuous layer or destruction; highly dependent on orientation to the surface urothelium
Optical micrometer depth	Uses an optical micrometer to evaluate depth of invasive tumor from the basement membrane, using greatest depth of invasion as the greatest extent	Continuous	Optical micrometer increases measurement accuracy; eliminates need to identify muscularis mucosae	Requires additional time; highly dependent on orientation to the surface urothelium; lack of orientation may limit application to all specimens
Focal or extensive invasion	Estimates "focal" through identification of 1 or 2 small foci of invasion; "extensive" is more than focal	Binary	Quick; not dependent on specimen orientation	Subjective

TABLE 6. Predicted Optimal Cut-off Values for T1 Criteria

	Patients With Muscularis Propria Present		All Patients	
	Best Cut-off (30% False Positive)	Best Cut-off (10% False Positive)	Best Cut-off (30% False Positive)	Best Cut-off (10% False Positive)
Aggregate linear length of invasive tumor (mm)	2.3	25	2.4	25
Depth of invasion using optical micrometer (mm)	1	2.4	2.0	2.4
Percentage of specimen with invasive cancer	8	37	8	40
Focal vs. extensive	NA	NA	NA	NA
Above vs. into/below the muscularis mucosae	NA	NA	NA	NA
Calculated volume of invasive cancer (mm^3)	709	5810	336	5280
Single vs. multiple foci	NA	NA	NA	NA

NA indicates not available.

Critical Reviews in Oncology / Hematology 171 (2022) 103601

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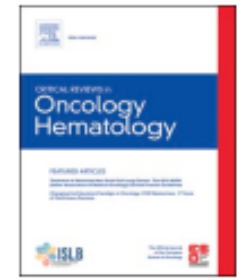
journal homepage: www.elsevier.com/locate/critrevonc



Artificial intelligence: A promising frontier in bladder cancer diagnosis and outcome prediction

Soheila Borhani [a,*], Reza Borhani [b], Andre Kajdacsy-Balla [a,**]

[a] Department of Pathology, University of Illinois at Chicago, Chicago, IL, United States
[b] Department of Electrical & Computer Engineering, Northwestern University, Evanston, IL, United States

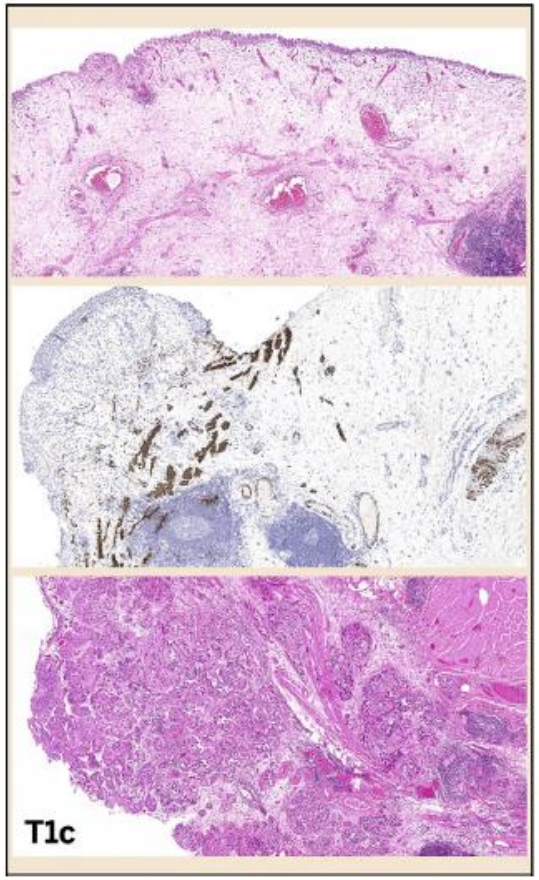
Approaches for T1 Bladder Cancer Substaging

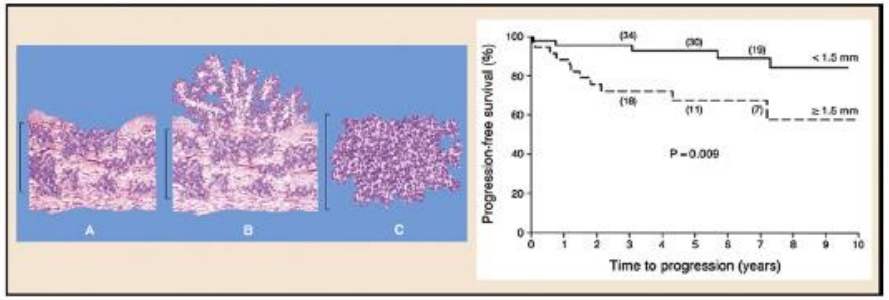
Anatomic Landmark

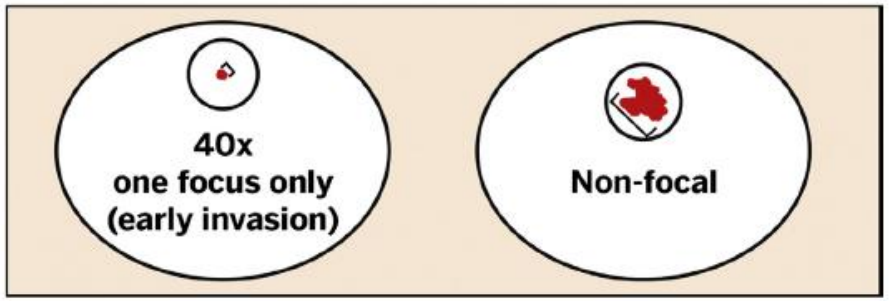
- Muscularis mucosae or
- "Large vessels"

Quantitative Measurements

- Micrometer measurements
- Focal vs non-focal
- Add all greatest dimensions of invasive foci







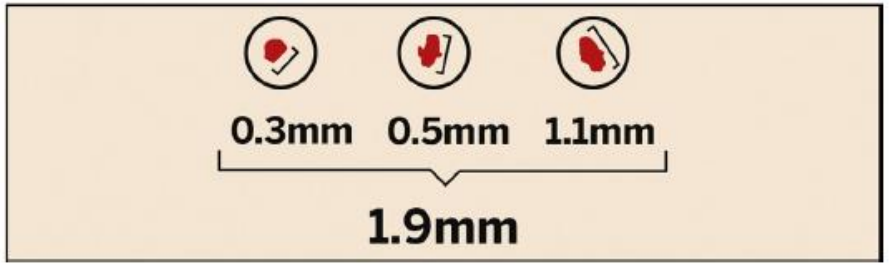


Fig. 14 Substaging of T1 bladder cancer. Different methodologies have been developed over the years, using the anatomical landmark of muscularis mucosae or by immunohistochemistry (e.g., smoothelin or desmin). Recent developments allow application of quantitative methods ba focal vs non-focal tumour extension using the ocular of a microscope (middle right), or adding all greatest dimensions

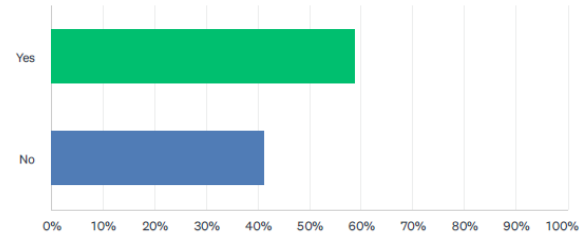
Lopez-Beltran & Cheng 2021

WG3: Substaging of T1 bladder cancer
Survey: Critical results regarding T1 substaging practice

- About 40% responders do not perform T1 substaging
- 48% vs. 52% responders>> Histoanatomic vs quantitative methods
- 50% responders think the method applied to assess T1 substaging will influence clinical decision in T1 bladder cancer

Q28 Do you consider sub-staging of T1 bladder cancer in transurethral resections to be of enough clinical relevance to deserve reporting in daily practice of pathology?

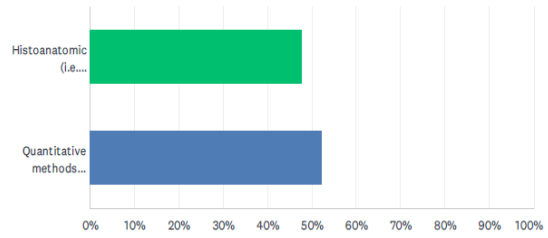
Answered: 153 Skipped: 2



ANSWER CHOICES	RESPONSES	
Yes	58.82%	90
No	41.18%	63
TOTAL		153

Q33 Concerning T1 substaging methods for transurethral resections, would you recommend an histoanatomic method or quantitative method?

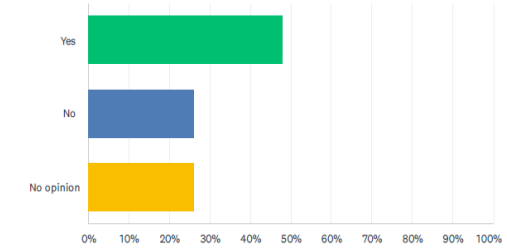
Answered: 151 Skipped: 4



ANSWER CHOICES	RESPONSES	
Histoanatomic (i.e. muscularis mucosae / vascular plexus)	47.68%	72
Quantitative methods (micrometer or high-power fields)	52.32%	79
TOTAL		151

Q37 Do you think the method applied to assess T1 substaging would influence clinical decisions in T1 bladder cancer?

Answered: 154 Skipped: 1



ANSWER CHOICES	RESPONSES	
Yes	48.05%	74
No	25.97%	40
No opinion	25.97%	40
TOTAL		154

Review of previous reports on depth of lamina propria involvement as a prognostic factor for disease progression in T1 bladder tumors

Year	Author	Staging system	Number of cases	Progression (%)	Survival (%)
1990	Younes et al. [6]	T1a (lamina propria)	15	NA	75
		T1b (into MM)	3		
		T1c (across MM)	14		11
1994	Hasui et al. [8]	T1a (Younes T1a)	60[a]	6.7	95
		T1b (Younes T1b and c)	28[a]	53.5	82
1995	Angulo et al. [21]	T1a (Younes T1a and b)	50[a]	NA	86
		T1b (Younes T1c)	49[a]	NA	52
1997	Holmäng et al. [9]	T1a (Younes T1a)	26	36	58
		T1b (Younes T1b and c)	38	58	42
1998	Smits et al. [10]	T1a		6	NA
		T1b	119 total[a]	33	NA
		T1c		55	NA
1998	Hermann et al. [22]	T1a	31[b]	NA	79
		T1b	60[b]	NA	70
		T1c	52[b]	NA	57
1999	Cheng et al. [11]	T1 above MM	23[a]	11	NA
		T1 into or below MM	21[a]	32	NA
2000	Kondylis et al. [7]	T1a into MM	32[b]	22	NA
		T1b beyond MM	17[b]	29	NA
2001	Bernardini et al. [20]	T1a (Younes T1a)	54[a]		NA
		T1b (Younes T1b and c)	40[a]	[c]	NA
2003	Trias et al. [12]	T1a (Younes T1a)	11	9	NA
		T1b (Younes T1b and c)	13	30.7	NA

Tumor Progression: Clinically meaningful

Table 1 Study characteristics of 40 studies assessing the prognostic value of T1 substaging in patients with bladder urothelial carcinoma

Author	Year	Region	Recruitment period	Design	No.pT1 Pts	Sub-staged T1 Pts	Substaging system	Oncological end point
Hasui [23]	1994	Japan	1980–1991	Retrospective	88	88	MM invasion (T1a/T1b)	DR, DP
Holmäng [24]	1997	Sweden	1987–1988	Retrospective	121	113	MM invasion (T1a/T1b)	DP, CSS, OS
Smits [40]	1998	The Netherlands	1987–1990	Retrospective	133	124	MM invasion (T1a/T1b/T1c)	DR, DP
Cheng [22]	1999	USA	1987–1992	Retrospective	83	83	Depth of lamina propria invasion	DP
Kondylis [26]	2000	USA	1981–1997	Retrospective	55	49	MM invasion (T1a/T1b)	DR, DP
Shariat [39]	2000	USA	N/A	Retrospective	47	36	MM invasion (T1a/T1b)	DR, DP, OS
Bernardini [17]	2001	France	1973–1996	Retrospective	149	94	MM invasion (T1a/T1b)	PFS
Sozen [42]	2002	Turkey	1983–1997	Retrospective	90	50	MM invasion (T1a/T1b)	DR, DP
Orsola [32]	2005	Spain	1996–2001	Retrospective	97	85	MM invasion (T1a/T1b/T1c)	RFS, PFS
van der Aa [45]	2005	The Netherlands	N/A	Retrospective	63	53	Tumor infiltration depth (T1 m/T1e)	DP
Chaimuangraj [20]	2006	Thailand	1990–2004	Retrospective	192	192	Muscularis mucosa invasion	DR
Andius [13]	2007	Sweden	1987–1988	Prospective	121	121	MM invasion (T1a/T1b)†	PFS, CSS
Mhawech-Fauceglia [29]	2007	Switzerland	N/A	Retrospective	45	45	MM invasion (T1a/T1b)	DR, DP
Queipo-Zaragoza [37]	2007	Spain	1986–2003	Retrospective	91	83	MM invasion (T1a/T1b)	DP
Soukup [16]	2008	Czech Republic	2001–2005	Prospective	105	99	MM invasion (T1a/T1b)	DR, DP (PFS)
Orsola [14]	2010	Spain	N/A	Prospective	159	138	MM invasion (T1a/T1b)	DR, DP
Bertz [18]	2011	Germany	1989–2006	Retrospective	309	309	MM invasion (T1a/T1b), Infiltration depth (≤ 1 HPF/> 1 HPF)	CSS, RFS, PFS
Palou [34]	2012	Spain/Belgium	1985–1996	Retrospective	146	93	MM invasion (T1a/T1b/T1c)	DR, DP, CSM
Lee [27]	2012	Korea	1999–2009	Retrospective	183	183	MM invasion (T1a/T1b/T1c)	DR, DP, CSM
Chang [21]	2012	Taiwan	1991–2005	Retrospective	509	509	Muscularis mucosa invasion, Infiltration depth (3 cut-off values to substage the T1 tumors: 0.5 mm, 1.0 mm, and 1.5 mm)	DR, DP, CSD, OM
van Rhijn [46]	2012	The Netherlands/ Canada	1984–2006	Retrospective	129	129	MM invasion (T1a/T1b/T1c), tumor infiltration depth (T1 m/T1e)	DR, DP
Brimo [19]	2013	Canada	2004–2012	Retrospective	86	86	Muscularis mucosa invasion, Maximum tumor depth (mm)	DR,DP,WFS
Olsson [31]	2013	Sweden	1992–2001	Retrospective	285	211	MM invasion (T1a/T1b/T1c)	DR, DP
Nishiyama [30]	2013	Japan	1995–2010	Retrospective	79	79	Tumor infiltration depth (T1 m/T1e)	DR, DP
Rouprêt [38]	2013	France	1994–2010	Retrospective	612	587	MM invasion (T1a/T1b)	RFS, PFS, CSS
Soukup [41]	2014	Czech Republic	2002–2009	Retrospective	200	176	MM invasion (T1a/T1b)	RFS, PFS, CSS, OS
Hu [25]	2014	USA	1997–2005	Retrospective	39	23	Focality, Percentage of tumor invasion, and aggregate length of invasion	DR
D. E. Marco [44]	2014	Italy	2000–2006	Retrospective	40	40	MM invasion (T1a/T1b/T1c), tumor infiltration depth (T1 m/T1e)	CSS, DP
Lim [28]	2015	Korea	1998–2012	Retrospective	177	141	MM invasion (T1a/T1b/T1c)	RFS, PFS
Orsola [15]	2015	Spain	N/A	Prospective	200	200	MM invasion (T1a/T1b)	DR, DP
Patschan [36]	2015	Sweden	1997–2003	Retrospective	167	152	MM invasion (T1a/T1b/T1c)	PFS
Patriarca [35]	2016	Italy	2011–2007	Retrospective	450	314	MM invasion (T1a/T1b), tumor infiltration depth (T1 m/T1e), ROL substaging†	DR, DP
Colombo [8]	2018	Italy	2007–2011	Retrospective	502	250	MM invasion (T1a/T1b/T1c), microinfiltration and extended infiltration of LP (T1 m/T1e), ROL substaging	DR, DP

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Table 1 (continued)

Author	Year	Region	Recruitment period	Design	No.pT1 Pts	Sub-staged T1 Pts	Substaging system	Oncological end point
Fransen van de Putte [9]	2018	Europe/Canada	1982–2010	Retrospective	601	601	MM invasion (T1a/T1b), microinfiltration and extended infiltration of LP (T1 m/T1e)	PFS, CSS
Otto [33]	2018	Germany/The Netherlands	1989–2012	Retrospective	322	322	Metric T1 substage (tumor infiltration depth)	PFS, CSS, OS
Turan [43]	2018	Turkey	2009–2014	Retrospective	106	106	MM invasion (T1a/T1b), tumor infiltration depth (T1 m/T1e)	DR, DP

N/A not available, *LP* lamina propria, *MM* muscularis mucosa, *PFS* progression-free survival, *CSM* cancer-specific mortality, *CSS* cancer-specific survival, *OS* overall survival, *WFS* worsening-free survival, *DR* disease recurrence, *DP* disease progression, *RFS* recurrence-free survival, *OM* overall mortality, *HPF* high power field

[†]ROL substaging ROL1 < 1 power field (objective 20×, ocular 10×/field 22, diameter 1.1 mm) of invasion, approximately corresponding to invasion of the lamina propria 1 mm thick or less; ROL2: > 1 power field (objective 20×), approximately corresponding to invasion of the lamina propria more than 1 mm thick, or multifocal invasion with foci cumulatively amounting to invasion of the lamina propria more than 1 mm thick

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ORIGINAL ARTICLE

Prognostic value of T1 substaging on oncological outcomes in patients with non-muscle-invasive bladder urothelial carcinoma: a systematic literature review and meta-analysis

Mehdi Kardoust Parizi[1,2] · Dmitry Enikeev[3] · Petr V. Glybochko[3] · Veronika Seebacher[4] · Florian Janisch[1,5] · Harun Fajkovic[1] · Piotr L. Chłosta[6] · Shahrokh F. Shariat[1,3,7,8]

Abstract

Purpose To evaluate the prognostic value of substaging or
carcinoma of the bladder.

Methods A literature search using PubMed, Scopus, Web of
to identify relevant studies according to the Preferred Report
guidelines. The pooled disease recurrence (DR) and disease
using a fixed or random effects model.

Results Overall 36 studies published between 1994 and 201
pT1) stage were selected for the systematic review and meta
between tumor infiltration depth or muscularis mucosa (MM
included in the meta-analysis. MM invasion (T1a/b/c [or pT
with DR (pooled HR: 1.23, 95%CI: 1.01–1.49) and DP (p
(T1 m/e [or pT1 m/e] substaging system) was also associated
HR: 3.29, 95%CI: 2.39–4.51).

Conclusions T1(or pT1) substaging in patients with bladder cancer is of prognostic value as it is associated with oncologic outcomes. Inclusion of this factors into the clinical decision-making process of this heterogeneous tumor may improve outcomes, while avoiding over- and under-treatment for T1(or pT1) bladder cancer.

Conclusion

We found that T1(or pT1) substaging systems are strong predictors of oncological outcomes (DR, DR). Although T1(or pT1) substaging systems are promising and can be used as an aid in determining the most appropriate treatment modality and intensity of follow-up, optimal T1(or pT1) substaging system definition remains to be elucidated in future well-designed prospective studies.

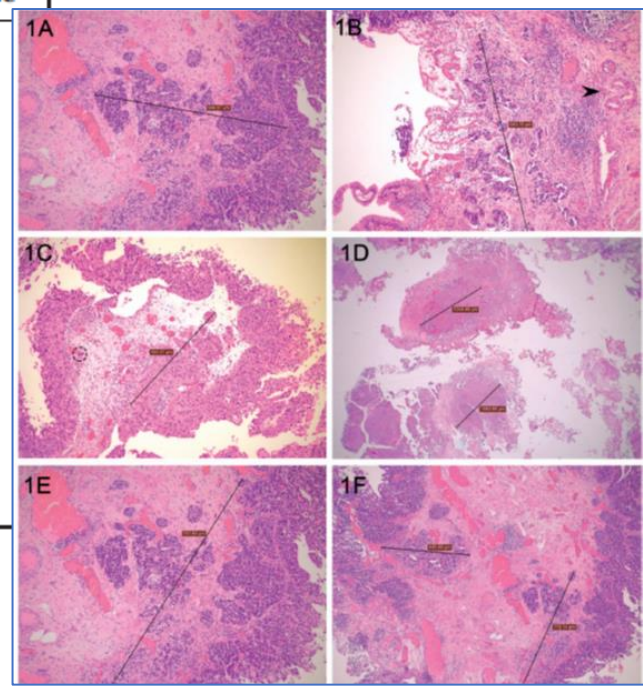
Subcategorization of T1 Bladder Cancer on Biopsy and Transurethral Resection Specimens for Predicting Progression

Anna Budina, MD, PhD; Sahar J. Farahani, MD; Priti Lal, MD; Anupma Nayak, MBBS, MD

Table 1. T1 Measurement Criteria in Predicting Progression Status

Criteria	Description	Univariate		Multivariate[a]	
		Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
Depth of invasion, µm	Measurement from the basement membrane to the deepest point of invasion	1.69 (1.07–2.66)	.02	1.69 (1.04–2.75)	.03
Largest invasive focus, µm	Measurement of largest contiguous focus of invasion in any direction	1.32 (1.07–1.64)	.01	1.36 (1.06–1.74)	.01
Aggregate linear length of invasion, µm	Measures greatest dimension of each invasive tumor focus in specimen and adds them together	1.08 (1.02–1.14)	.009	1.09 (1.02–1.16)	.009
Number of invasive foci	Counting of foci of pT1 disease either present at different location in bladder or separate invasive foci in specimen	1.29 (1.07–1.57)	.008	1.32 (1.05–1.66)	.01
Above versus into muscularis mucosae/vascular plexus	Use of muscularis mucosae or vascular plexus as anatomic landmark to determine depth of invasion	1.88 (0.51–6.95)	.35	1.84 (0.45–7.59)	.39
Focal or extensive invasion	"Focal" defined as 2 or fewer foci of invasion of <1 mm each; "extensive" defined as more than focal	2.00 (0.51–7.90)	.32	1.55 (0.33–7.28)	.58

[a] Adjusted for age, sex, ethnicity, tumor focality, presence of carcinoma in situ, immunohistochemical phenotype, and prior treatment status.



!!!VALIDATION STUDY¡¡¡

</= 1.4 mm

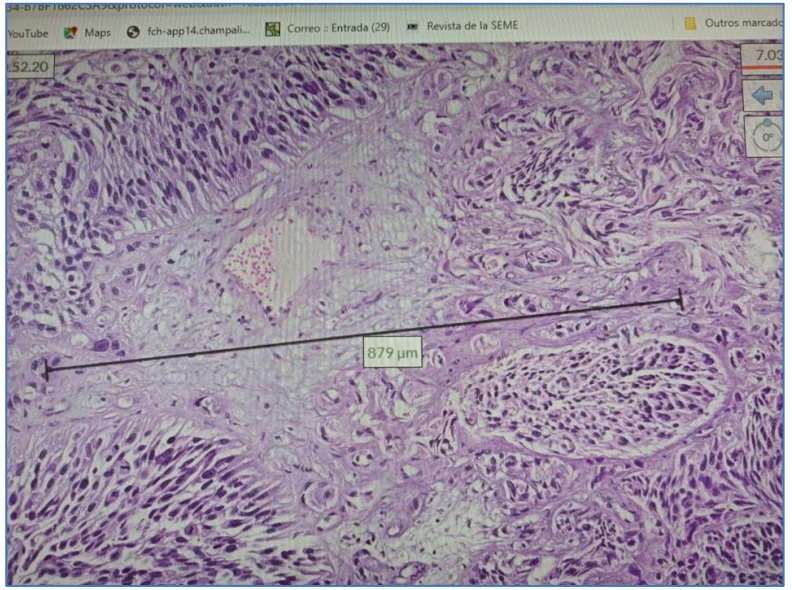
>/= 3.6 mm

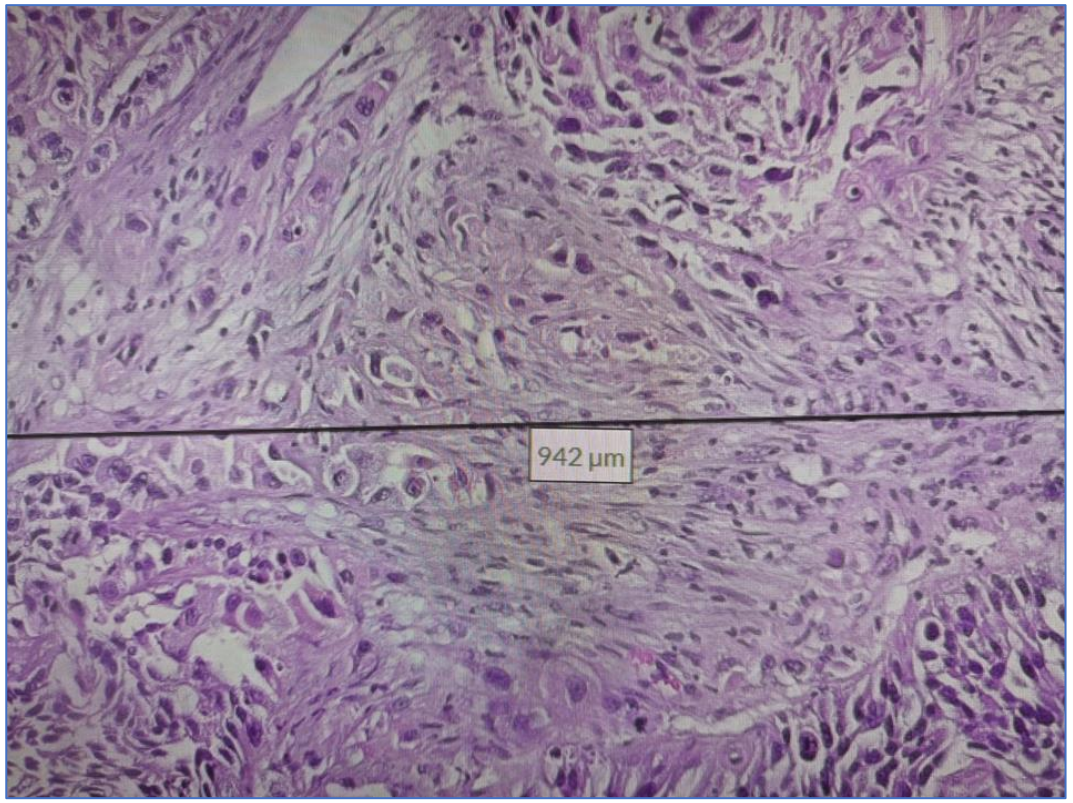
>/= 8.9 mm

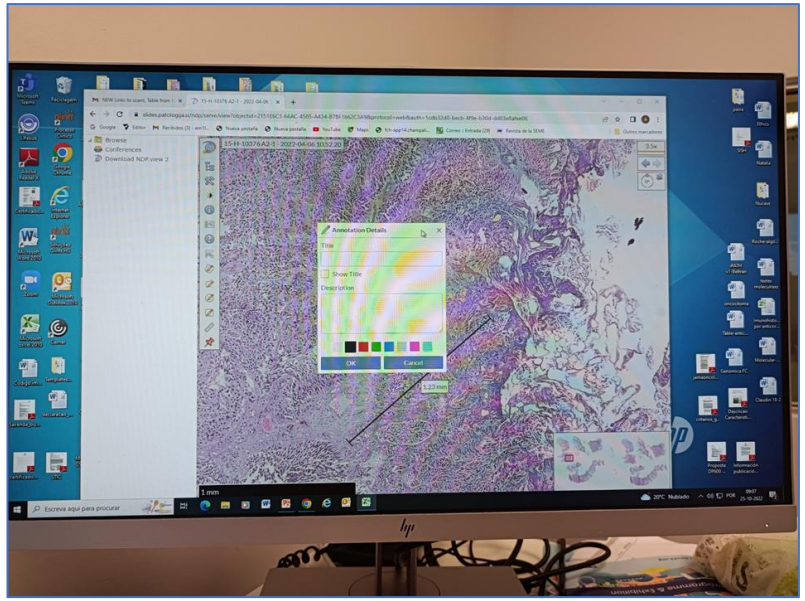
>/= 3 focos

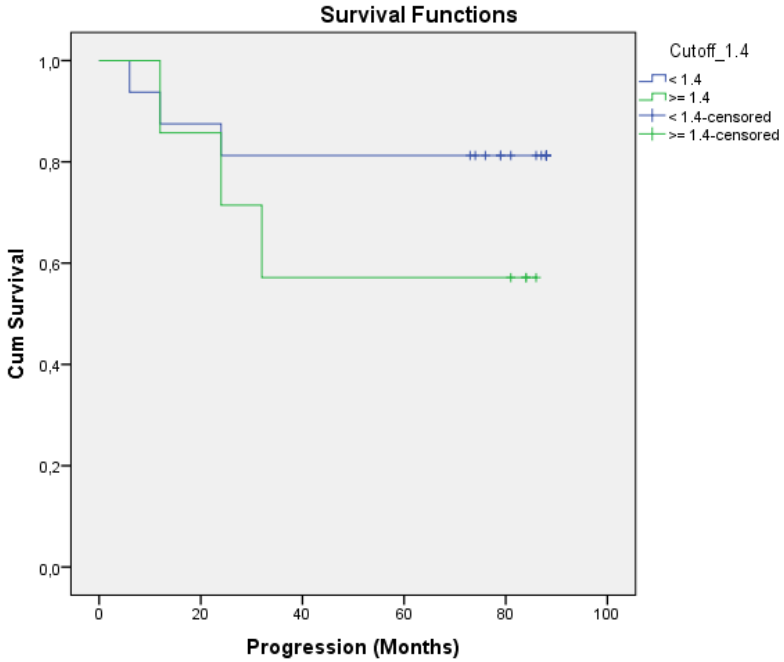
N=160/test N=36

TP/CSS





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< 1.4-censored
>= 1.4-censored
Cum Survival
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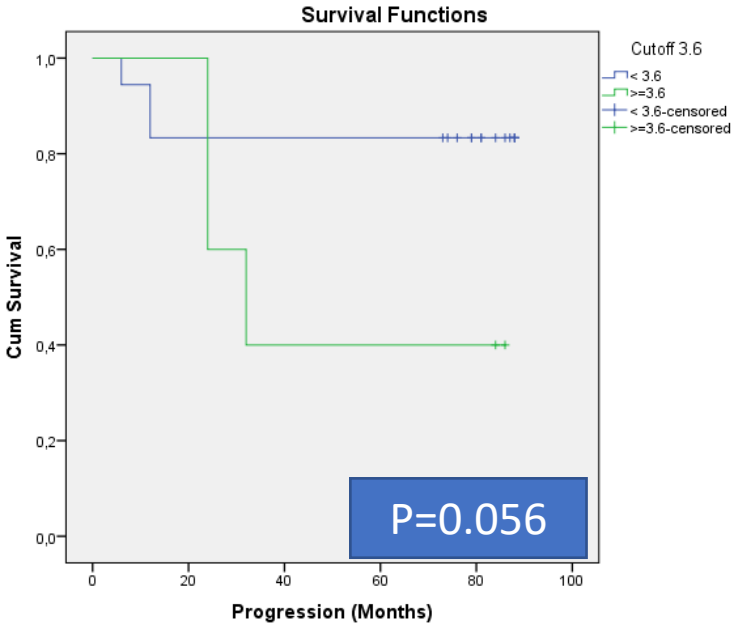
0,8
0,6
0,4
0,2
0,0
0
20
40
60
80
100
Progression (Months)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< 3.6-censored
>=3.6-censored
Cum Survival
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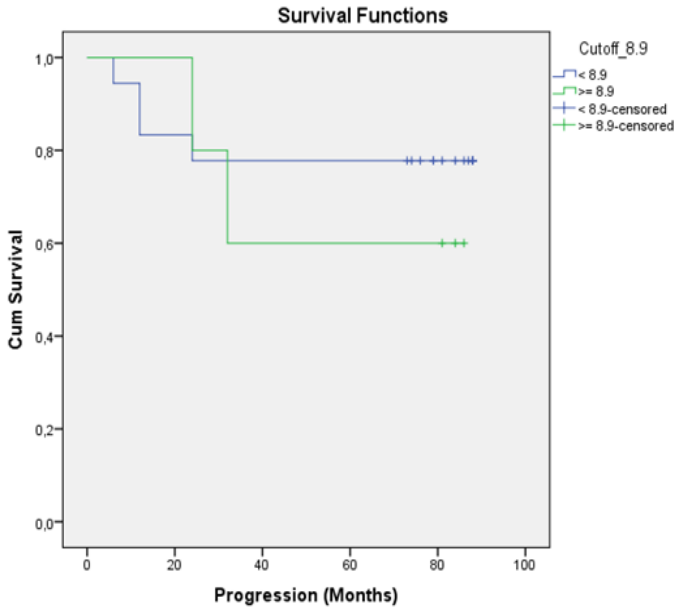
0,6
0,4
0,2
0,0
0
20
40
60
80
100
Progression (Months)
P=0.056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Cum Survival
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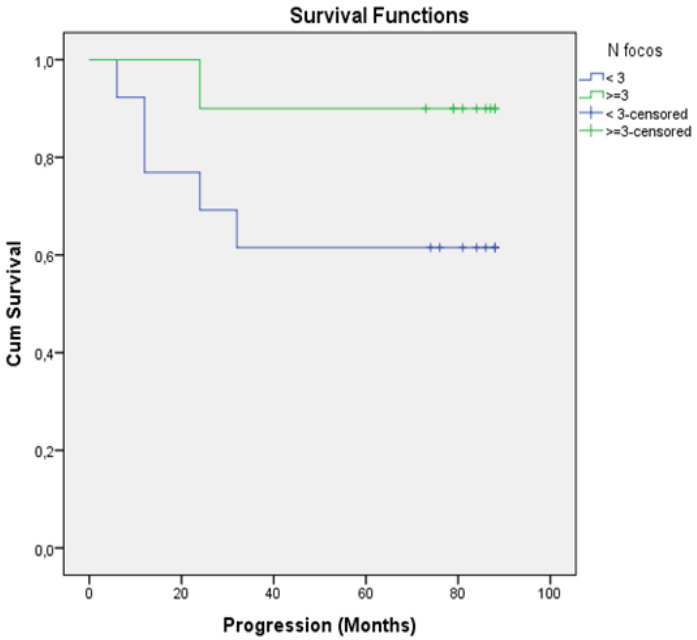
0,6
0,4
0,2
0,0
0
20
40
60
80
100
Progression (Months)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>=3-censored
Cum Survival
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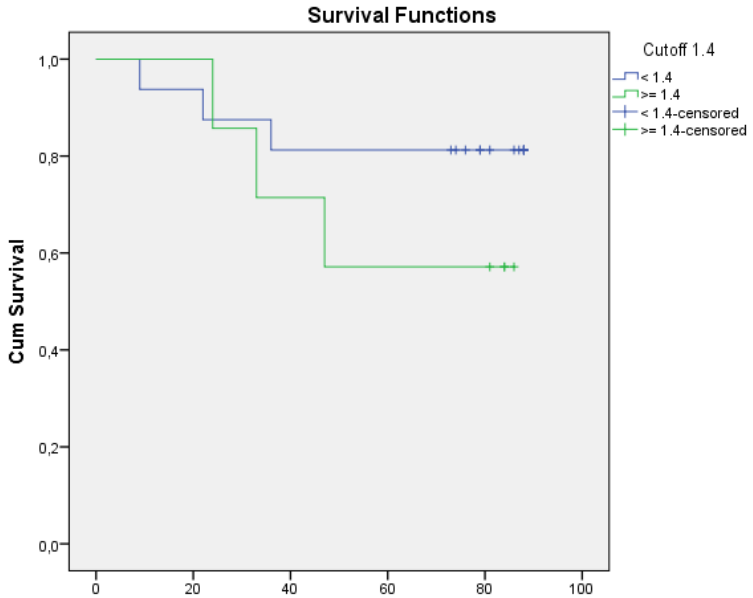
0,6
0,4
0,2
0,0
0
20
40
60
80
100
Progression (Months)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< 1.4-censored
>= 1.4-censored
Cum Survival
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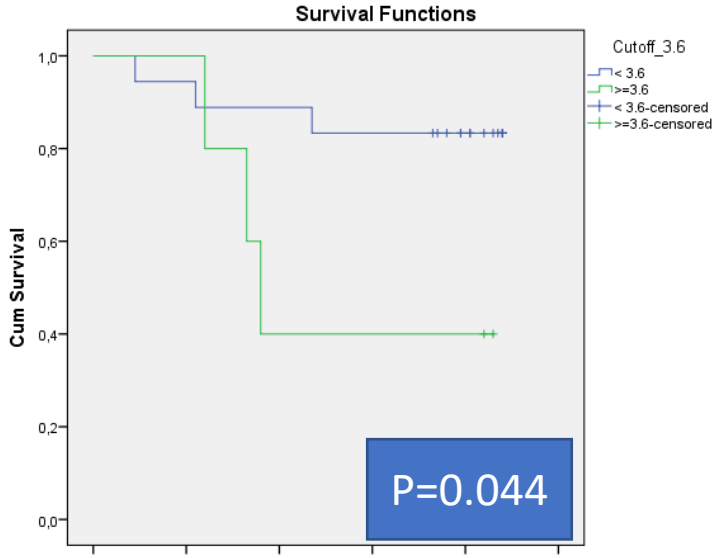
0,8
0,6
0,4
0,2
0,0
0
20
40
60
80
100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Cum Survival
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0,4
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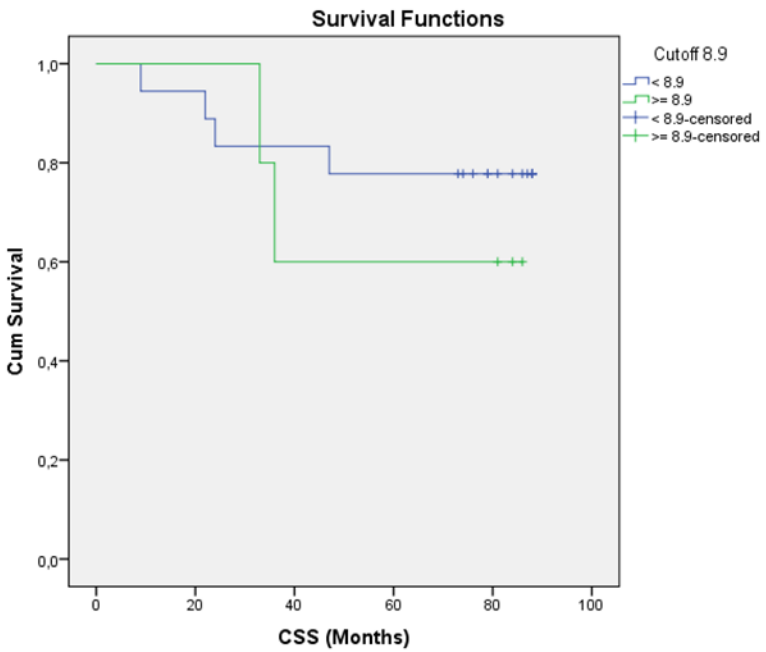
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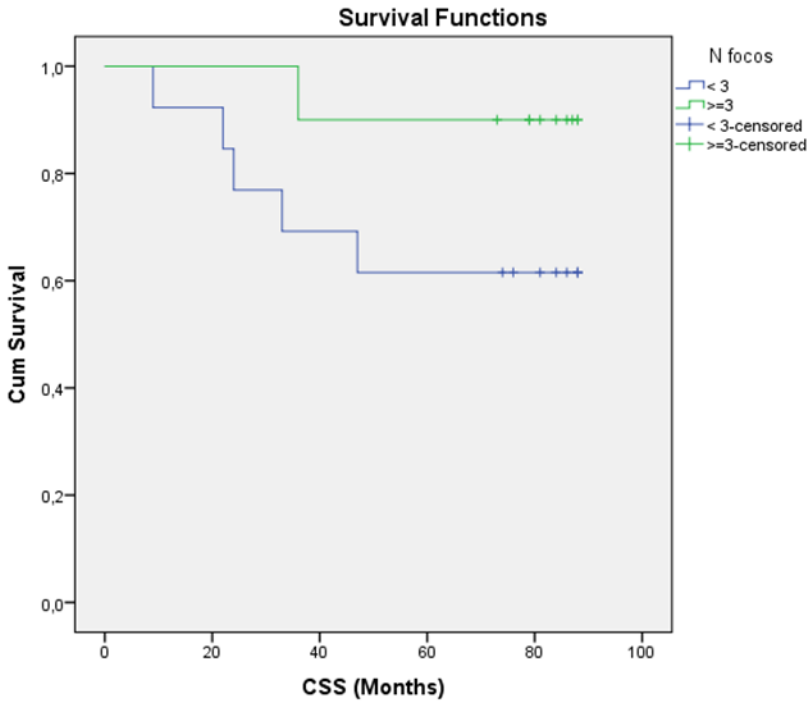
0,6
0,4
0,2
0,0
0
20
40
60
80
100
CSS (Months)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Cum Survival
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0,6
0,4
0,2
0,0
0
20
40
60
80
100
CSS (Months)

Conclusion

Take-home messages

- La utilización de herramientas de patología digital puede ayudar de manera eficiente en el procedimiento de subestadificación del carcinoma urotelial T1.
- La medición del foco de mayor tamaño puede proporcionar suficiente información en relación con la progresión tumoral y la supervivencia cáncer especifica del carcinoma urotelial T1.

¡THANKS!