

Secondary Malignant Tumors of the Urinary Bladder

Direct extension • Systemic lymphoma • Rare distant metastases

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning outcomes

- Distinguish secondary involvement from a primary bladder neoplasm.
- Recognize direct extension, systemic lymphoma and rare distant metastasis.
- Integrate morphology, clinical history, imaging and focused immunophenotyping.
- Avoid applying primary bladder staging to a tumor originating elsewhere.

What “secondary bladder tumor” means

- Malignancy involving the bladder but originating outside the bladder.
- Origin may be a neighboring pelvic organ or a distant anatomic site.
- Bladder involvement does not automatically mean a primary urothelial cancer.

Site of involvement ≠ site of origin

Three routes to the urinary bladder

DIRECT EXTENSION

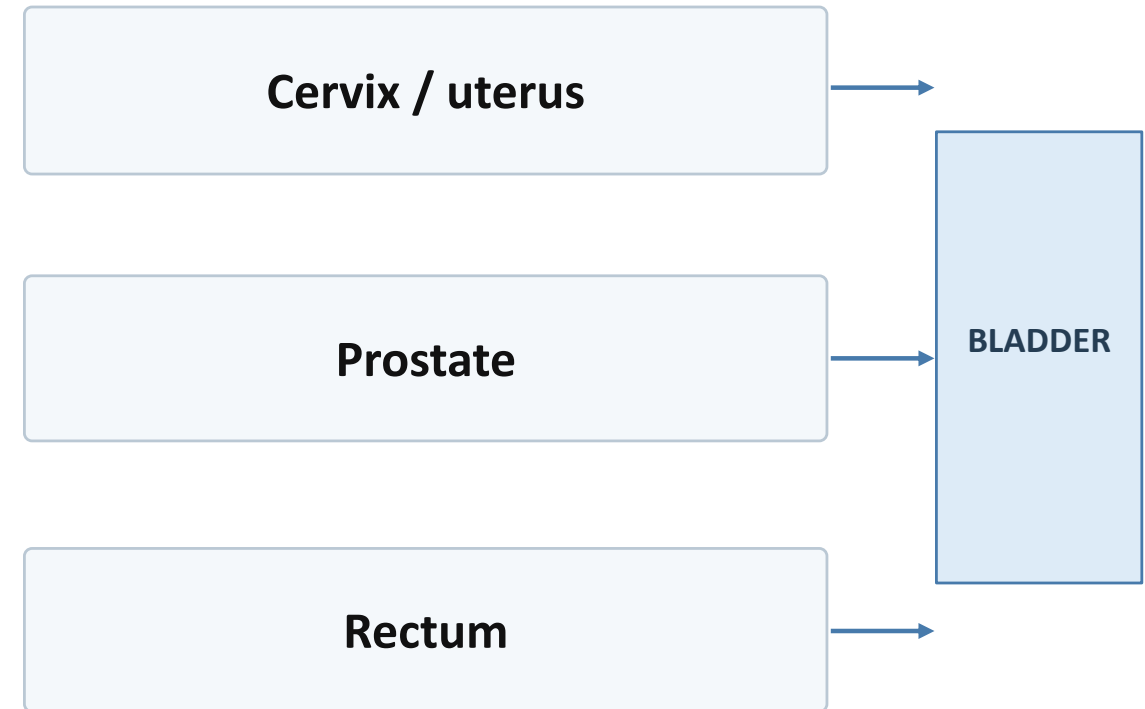
SYSTEMIC LYMPHOMA

**DISTANT SOLID-TUMOR
SPREAD**

- Direct extension from an adjacent primary malignancy: Predominant pattern.
- Bladder involvement by lymphoma as part of systemic disease.
- Distant spread of solid tumors: Possible but very uncommon.

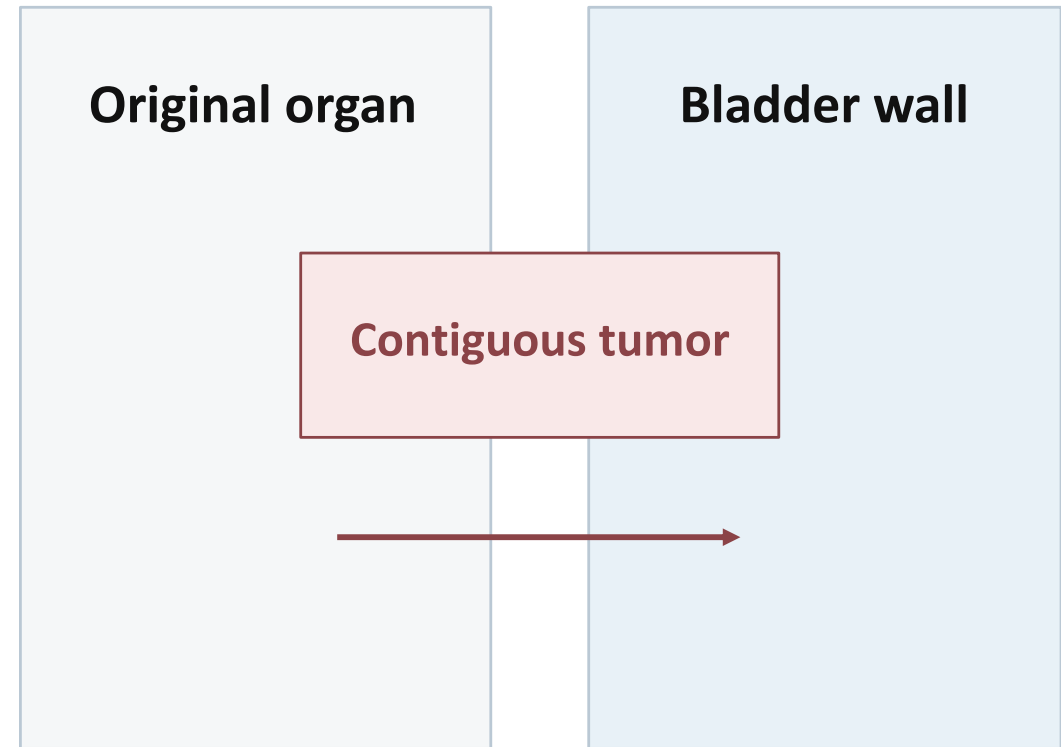
Direct extension is the main mechanism

- Cervix, uterus, prostate and rectum as the principal adjacent sources.
- Contiguity is the defining spatial relationship.
- Recognition changes the assigned primary site and diagnostic communication.



A pelvic-organ interface

- A malignant process crosses from its organ of origin into the bladder region.
- Tumor at the interface may be sampled as a “bladder mass.”
- A bladder biopsy alone may not reveal the direction of spread.



Schematic of direct extension

Why the clinical history matters

- Prior pelvic carcinoma increases suspicion for secondary bladder involvement.
- Review histologic type, treatment history and current anatomic imaging.
- A new bladder lesion can still be an independent primary: Compare evidence.

PAST / PRESENT MALIGNANCY



BLADDER LESION



INTEGRATED ORIGIN ASSESSMENT

How uncommon are secondary tumors?

- Secondary neoplasms constitute a small minority of bladder malignancies.
- Reported percentages vary with specimen selection and case definitions.
- Do not substitute a series-specific estimate for population incidence.

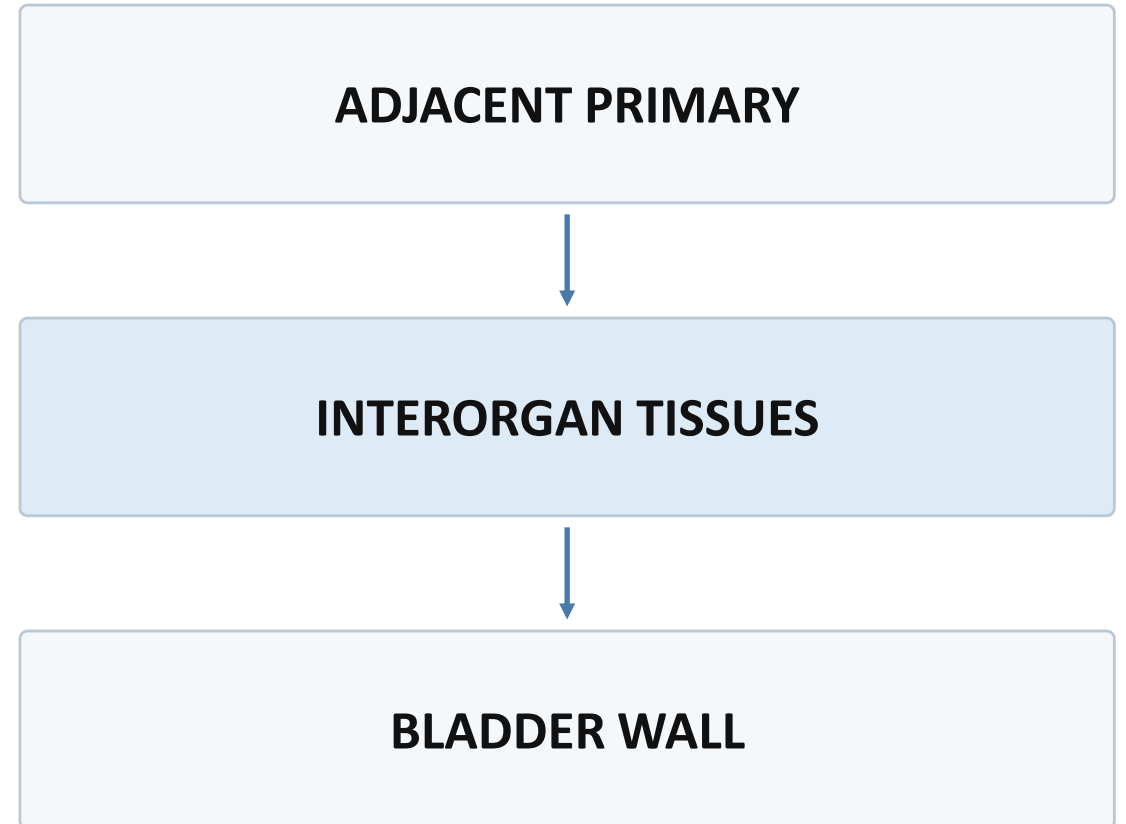
Rare as a group; Direct spread predominates within the group

Contiguous spread versus distant metastasis

Question	Direct extension	Distant metastasis
Anatomic continuity	Expected	Absent or not demonstrable
Usual context	Locally advanced adjacent primary	Systemically disseminated malignancy
Principal proof	Imaging / operative continuity	History, imaging, histology $\pm$ IHC
Key caution	Not an independent bladder primary	Not inferred from morphology alone

Conceptual sequence of direct invasion

- Original malignancy enlarges toward an adjacent tissue interface.
- Tumor reaches the bladder wall and may subsequently involve its lining.
- Depth and direction must be established from the actual specimen and imaging.



Wall layers: A useful orientation

- Urothelium and lamina propria form the luminal side.
- Muscularis propria lies deeper; Perivesical tissues are external.
- Layer involvement alone does not prove whether a tumor began in the bladder.

Urothelium

Lamina propria

Muscularis propria

Perivesical soft tissue

Site of origin versus anatomic extent

OBSERVED SITE

PRIMARY ORGAN

EXTENT OF DISEASE

- “Tumor in bladder tissue” is an observation.
- “Primary bladder carcinoma” assigns its origin.
- “Rectal carcinoma involving bladder” assigns both origin and extension.

Primary bladder staging has a defined scope

- Robbins prints the AJCC 8th-edition pTNM table for primary urinary bladder carcinoma.
- Its T categories describe local extent of a bladder-origin tumor.
- An extravesical primary invading bladder is staged under the appropriate primary site.

Do not assign a bladder-primary pT category solely because bladder is infiltrated.

The meaning of “T4” is origin-dependent

Bladder primary → adjacent organ

Adjacent-organ primary → bladder

- Bladder-primary T4 includes direct spread from the bladder into specified adjacent structures.
- The reverse scenario—an adjacent primary entering bladder—is different.
- Document the primary site before selecting a staging framework.

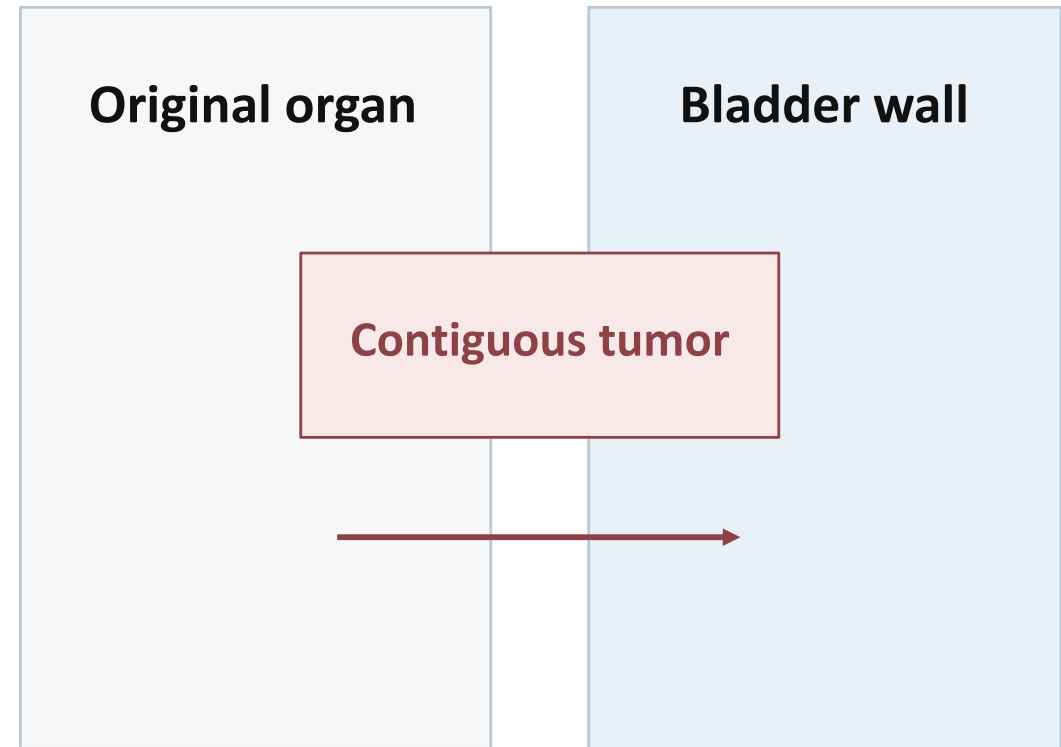
Naming the lesion in a pathology report

- Prefer “carcinoma involving urinary bladder, consistent with [known primary]” when supported.
- Specify whether source attribution is definitive or only favored.
- Avoid an unsupported label of “primary bladder cancer.”

Origin assignment is a conclusion, not a specimen label.

Cervical carcinoma extending to bladder

- The cervix is explicitly listed as a major contiguous source by Robbins.
- Correlation with an established cervical tumor and pelvic imaging is essential.
- Morphologic overlap with primary bladder squamous carcinoma may complicate biopsy interpretation.



Schematic of direct extension

Cervix: Diagnostic reasoning

- Compare the bladder lesion with previous cervical pathology when available.
- Determine whether radiology shows contiguous cervical-to-bladder extension.
- Use targeted ancillary tests only after defining the morphologic question.

PRIOR CERVICAL PATHOLOGY



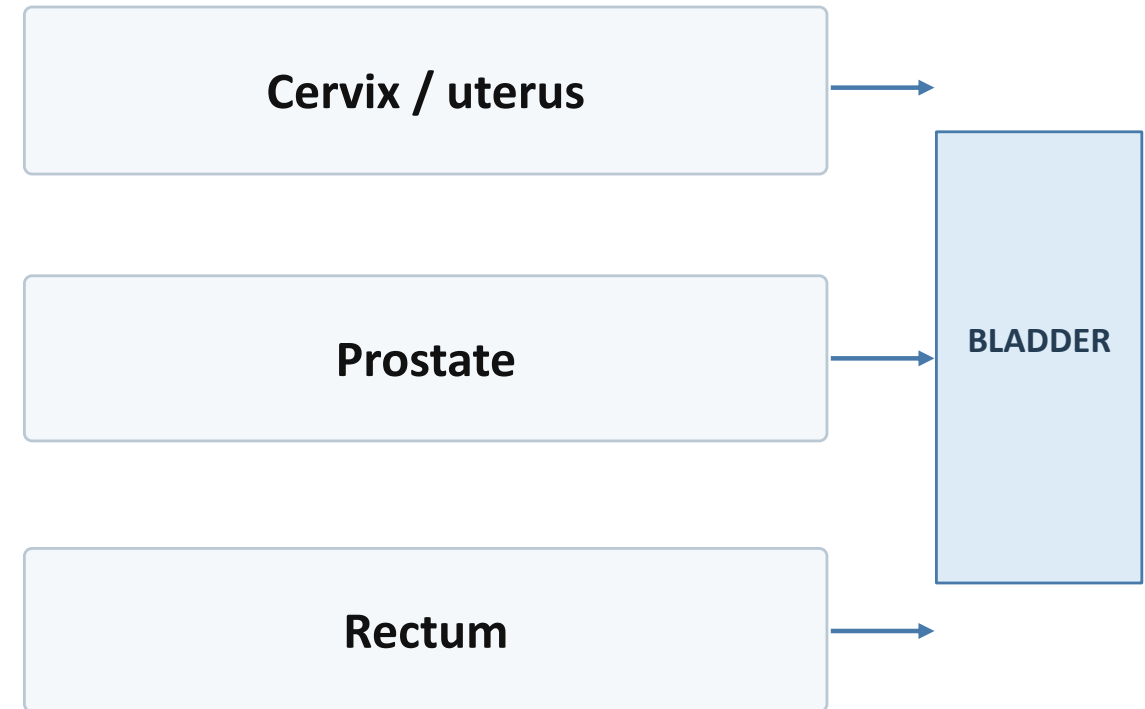
CONTINUITY ON IMAGING



TARGETED PATHOLOGY REVIEW

Uterine malignancy involving bladder

- The uterus is another adjacent source included.
- Endometrial/corpus and other uterine primaries require organ-specific correlation.
- A glandular lesion in bladder cannot be assigned uterine origin by appearance alone.



Uterus: The site-assignment problem

- Record the known uterine tumor histotype and prior pathology.
- Ask whether the lesion is continuous with the uterine/pelvic mass.
- Compare tumor morphology and immunophenotype only within the clinical context.

ORIGINAL UTERINE TUMOR



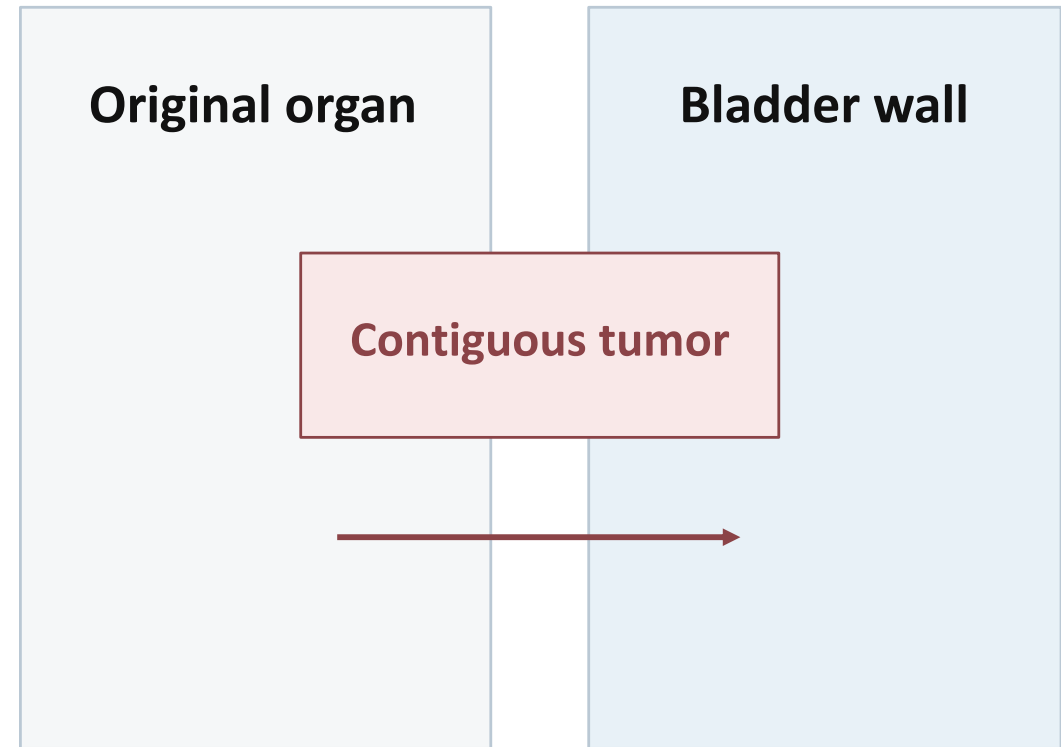
PELVIC ANATOMY



BLADDER BIOPSY

Prostatic carcinoma involving bladder

- Prostate is a principal adjacent source in the Robbins description.
- Bladder neck/trigone involvement may present as a bladder lesion.
- In a male with a suspicious gland-forming tumor, prostatic origin must be considered.



Schematic of direct extension

Prostate: Origin clues to integrate

- Relevant history: Prostate carcinoma, treatment, and disease distribution.
- Morphology: Assess for glands or patterns matching known prostate cancer.
- Ancillary tests such as PSA/PSAP may support prostatic differentiation; Interpret with controls.

PATIENT HISTORY



HISTOLOGIC COMPARISON



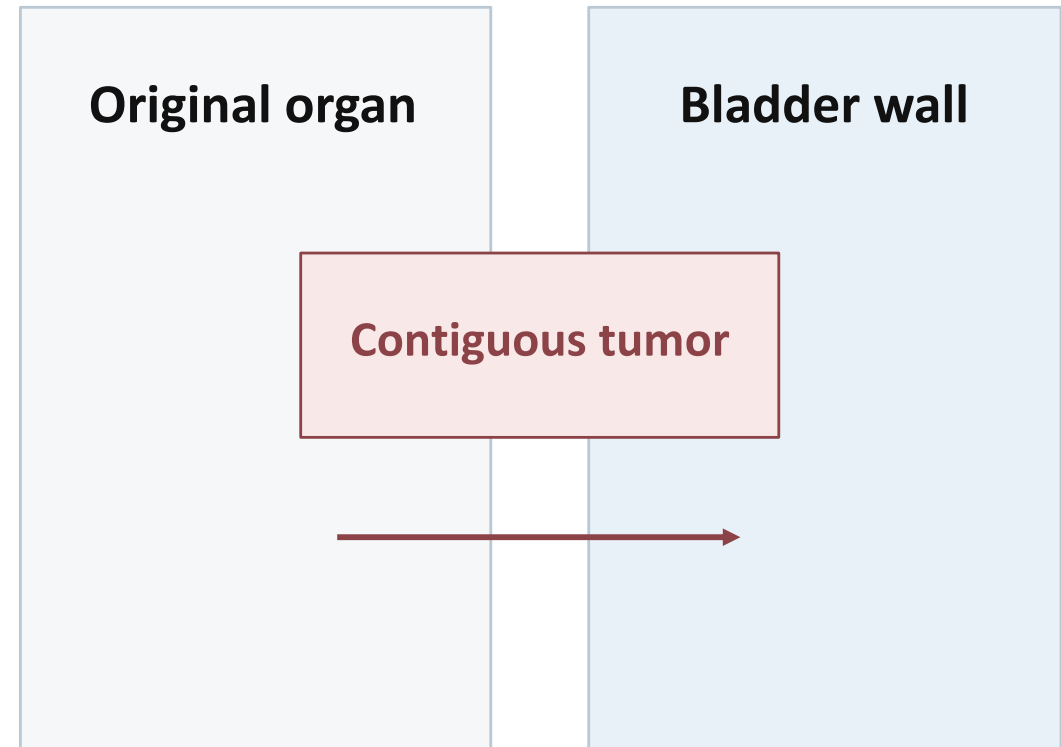
PROSTATE-LINEAGE IHC

Prostate versus urothelial carcinoma

Axis	Prostate-origin involvement	Primary urothelial carcinoma
History	Known or suspected prostate cancer	Bladder-centered tumor history
Morphology	Can show gland-forming carcinoma	Typically urothelial morphology
Ancillary focus	Prostate-lineage markers	Urothelial-lineage markers
Interpretation	Requires clinical and anatomic fit	Requires bladder-origin evidence

Rectal carcinoma directly invading bladder

- The rectum is explicitly listed among the major adjacent organs.
- Continuity may be established radiologically or in a combined resection.
- Bladder biopsy can contain colorectal-type adenocarcinoma without proving the route.



Schematic of direct extension

Colorectal adenocarcinoma: Morphology overlaps

- Colorectal carcinoma commonly forms malignant glands.
- Primary bladder adenocarcinoma may show highly similar enteric morphology.
- Gland formation and mucin are not, by themselves, site-specific.

Enteric morphology ≠ proof of colorectal origin.

Colorectal source: Integrated evidence

- Correlate with colonoscopy and cross-sectional imaging when appropriate.
- Compare prior colorectal tissue with the bladder specimen.
- Use an IHC panel recognizing overlap with primary bladder adenocarcinoma.

ANATOMIC EVIDENCE



PAIRED MORPHOLOGY



PANEL INTERPRETATION

Four adjacent sources at a glance

Primary site	Likely diagnostic issue	Most helpful context
Cervix	Squamous-pattern mimic	Cervical tumor / pelvic continuity
Uterus	Glandular-pattern mimic	Prior uterine tumor / pelvis
Prostate	Glandular carcinoma in bladder	Prostatic history / lineage markers
Rectum	Enteric glandular mimic	Colorectal pathology / anatomic continuity

Systemic lymphoma may involve the bladder

SYSTEMIC LYMPHOMA

BLADDER INVOLVEMENT

LINEAGE + EXTENT

- Robbins explicitly includes lymphoma as part of systemic disease.
- A bladder lesion need not originate from urinary tract epithelium.
- Clinical staging must address systemic distribution and lymphoid classification.

Lymphoma: A distinct lineage problem

EPITHELIAL NEOPLASM

HEMATOLYMPHOID NEOPLASM

- Lymphoid malignancy and carcinoma follow different diagnostic pathways.
- Epithelial markers alone cannot establish the nature of all poorly differentiated tumors.
- Morphology plus hematolymphoid markers establish the appropriate work-up.

Systemic versus primary bladder lymphoma

- A lymphoma in a bladder biopsy is not automatically a primary bladder lymphoma.
- Published series describe both primary bladder cases and systemic involvement.
- Clinical distribution and previous lymphoma history determine classification.

Bladder involvement is not equivalent to bladder origin.

Solid-tumor metastases: Uncommon route

DISTANT PRIMARY

SYSTEMIC DISSEMINATION

BLADDER DEPOSIT

- Metastatic dissemination of solid tumors to bladder as very rare.
- A noncontiguous bladder deposit is possible in disseminated malignancy.
- Correlate all suspected cases with disease distribution and original tumor.

Reported distant primary sites

- Published secondary-bladder series include stomach, breast, lung and cutaneous melanoma.
- These are reported possibilities, not a probability table for an individual patient.
- Prior malignancy and current distribution guide the shortlist.

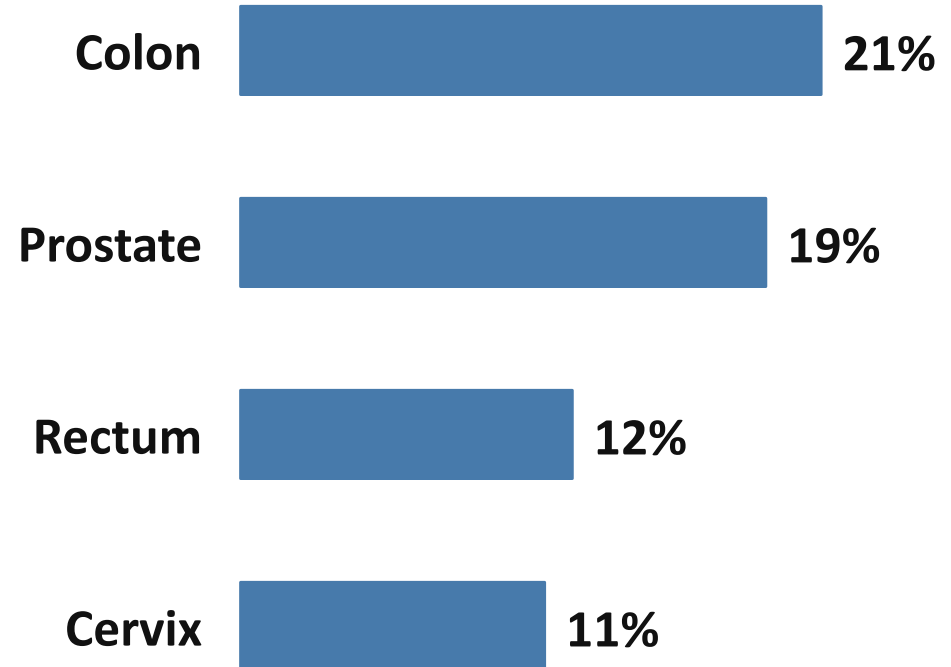
Do not confuse rarity with impossibility

- A rare route can still be the correct explanation for an individual biopsy.
- Clinical history may radically shift pretest probability.
- Atypical histology should prompt comparison with known distant primaries.

Uncommon ≠ excluded

Retrospective distribution: 282 cases

- In one historic pathology series of 282 secondary bladder tumors, colon, prostate, rectum and cervix were leading sites.
- Percentages are proportions within that selected secondary-tumor series.
- They must not be interpreted as incidence among all bladder neoplasms.



Percentage of the 282 secondary bladder tumors in this series

Interpreting small, heterogeneous series

- Case mix depends on institution, period and surgical/autopsy inclusion.
- Direct invasion and distant spread can be combined in published analyses.
- Compare denominators and definitions before contrasting studies.

A reported proportion requires its denominator.

Clinical presentation: Hematuria

- Hematuria is a recognized presentation of bladder tumors, including secondary lesions.
- Hematuria alone does not distinguish primary from secondary disease.
- The history of an extravesical malignancy should influence evaluation.

Other urinary manifestations

- Irritative voiding complaints or obstructive symptoms may accompany secondary involvement.
- Symptom type reflects the bladder region and degree of involvement.
- Clinical features are nonspecific and cannot independently establish origin.

Imaging asks an anatomic question

- Is the bladder mass continuous with an adjacent-organ tumor?
- Is there a bladder-centered lesion without demonstrable pelvic continuity?
- What additional sites of malignancy are involved?

CONTIGUITY



BLADDER LOCATION



SYSTEMIC DISTRIBUTION

Cystoscopy localizes but does not assign origin

- Cystoscopy may identify a mucosal lesion or deformation.
- Endoscopic appearance is not a reliable lineage test.
- Interpret the sampled lesion alongside pelvic imaging and prior pathology.

An endoscopic “bladder tumor” is an anatomic finding.

Specimen type changes what can be inferred

Small biopsies may lack surrounding organ interface and full wall orientation.

Specimen	Common strength	Common limitation
Biopsy	Confirms lesional histology	Limited architecture / continuity
TURBT	More tissue and muscle sampling	May still lack original interface
En bloc resection	Potential proof of continuity	Needs careful mapping / orientation

A practical pathology sequence

- First: Identify whether the lesion is epithelial, lymphoid or another lineage.
- Second: Characterize morphology and compare previous tumor material.
- Third: Choose focused ancillary stains, then reconcile imaging and history.

MORPHOLOGY



SOURCE COMPARISON



CORRELATED TESTING

Morphology can suggest, not guarantee, origin

- Many secondary tumors lack a unique histologic signature.
- Adenocarcinoma is a particularly difficult diagnostic category.
- Diagnostic confidence rises when morphology matches clinical-anatomic evidence.

Histology is necessary; Context may be decisive.

The gland-forming differential

PRIMARY BLADDER

SECONDARY PELVIC

OTHER GLANDULAR

- Primary bladder adenocarcinoma.
- Colorectal adenocarcinoma secondarily involving bladder.
- Prostatic or gynecologic primary involving bladder.
- Urothelial carcinoma with glandular differentiation in selected cases.

Why enteric morphology is insufficient

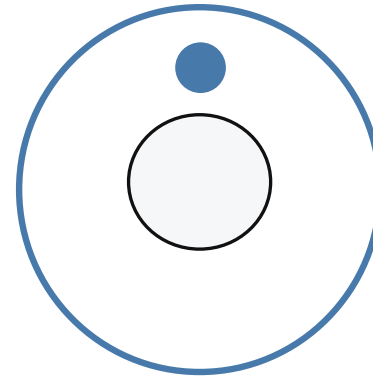
PRIMARY BLADDER ADENOCARCINOMA

**COLORECTAL ADENOCARCINOMA IN
BLADDER**

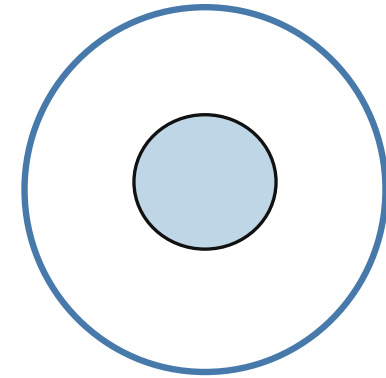
- Both bladder-primary and colorectal adenocarcinoma can show enteric gland formation.
- Mucinous and signet-ring features also overlap.
- A “looks like colon” impression is not proof of the primary site.

β -catenin: Pattern rather than simple positive/negative

- Nuclear staining favors a colorectal source in the Roy et al. Comparative cohort.
- Some primary bladder adenocarcinomas can show focal nuclear expression.
- Therefore β -catenin is a supporting observation, not a standalone origin test.



**Mainly membrane /
cytoplasm**



Nuclear accumulation

Original educational schematic; Not a micrograph

CK7, CK20 and CDX2: Substantial overlap

- CK20 and CDX2 expression can occur in both bladder-primary and colorectal adenocarcinomas.
- CK7 may add context but cannot resolve all difficult cases.
- A full panel and radiologic/endoscopic correlation remain necessary.

A marker identifying intestinal differentiation does not always identify intestinal origin.

Interpreting the mucosal surroundings

- Associated glandular metaplasia can provide useful context for bladder-primary adenocarcinoma.
- Biopsies may omit or destroy relevant surface urothelium.
- Secondary colorectal carcinoma may colonize the surface and mimic an in situ process.

Squamous-pattern differential

**PRIMARY SQUAMOUS BLADDER
CARCINOMA**

**CERVICAL CARCINOMA INVOLVING
BLADDER**

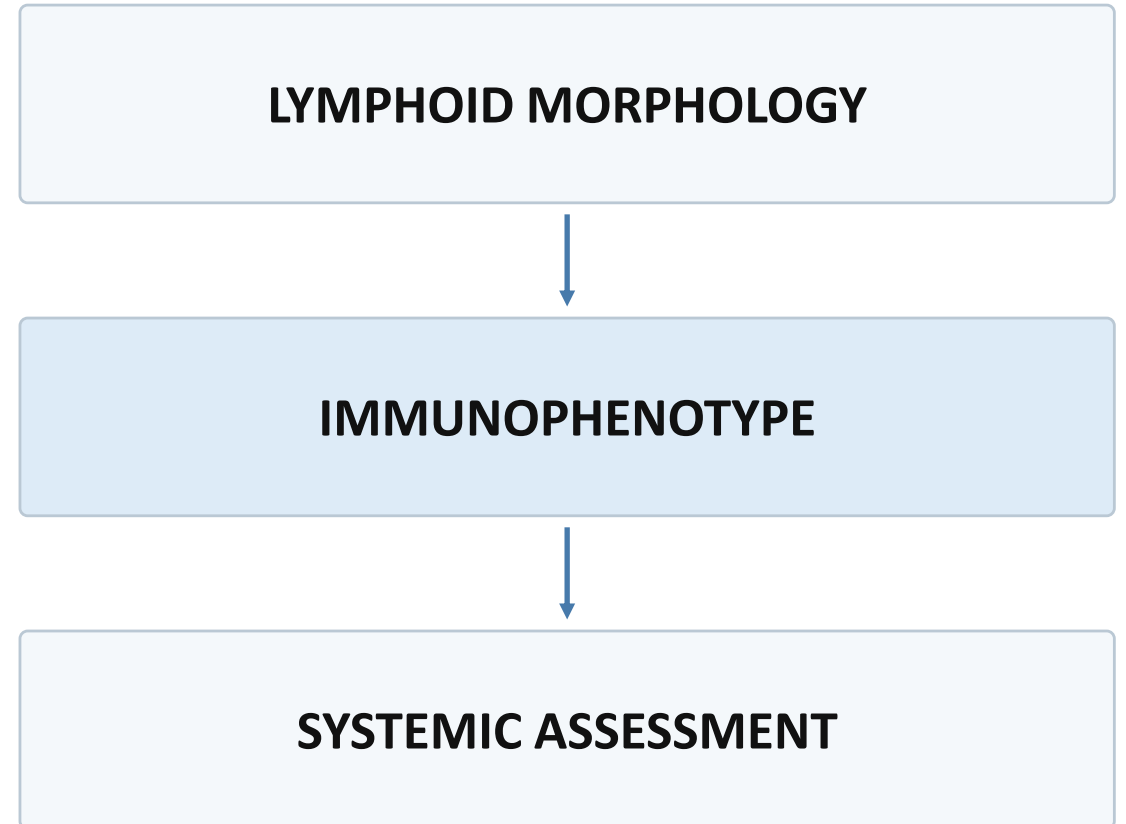
- A squamous carcinoma in bladder may be primary or extend from a gynecologic site.
- The presence of squamous differentiation is not enough to define origin.
- Known cervical disease and continuity are crucial context.

Prostate-lineage tests are hypothesis-driven

- Adenocarcinoma in a male bladder specimen may prompt evaluation for prostate origin.
- PSA and prostatic acid phosphatase are examples of supportive lineage markers.
- Read staining with morphology, history and the laboratory's validation context.

Lymphoma work-up differs from carcinoma

- Assess lymphoid architecture and cytology.
- Use hematolymphoid markers and a subtype-directed panel when indicated.
- Clinical hematology evaluation establishes whether disease is systemic.



Cytology: The same origin limitation

- Malignant cells in urine indicate a urinary tract sample containing neoplasia.
- Cytology alone may be unable to establish the extravesical primary organ.
- Tissue, prior tumor comparison and cross-sectional imaging may be necessary.

Selecting an immunohistochemical panel

- Start with the morphologic differential, not a large indiscriminate stain list.
- Ask whether the panel differentiates two plausible tissue origins.
- Use multiple convergent findings; Recognize shared marker expression.

DIFFERENTIAL



DISCRIMINATING MARKERS



CLINICAL INTEGRATION

Why one positive marker is not enough

- Many markers reflect differentiation rather than absolute site specificity.
- Signal location and distribution can be more informative than binary positivity.
- Discordant stains require reconsideration rather than forced classification.

Specificity depends on the diagnostic setting.

Route-to-diagnosis synthesis

Potential route	Most decisive discriminator	Typical limitation
Direct extension	Demonstrated anatomic continuity	Small biopsy omits interface
Systemic lymphoma	Immunophenotype + systemic work-up	Bladder-only sample
Distant deposit	Known distant malignancy + match	No single unique histology

Integrated diagnostic decision path

- Confirm lesion and identify its morphologic lineage.
- Search for a neighboring primary and demonstrate or exclude continuity.
- If noncontiguous, reconcile systemic history and targeted marker findings.
- State origin with the level of certainty the evidence permits.

Bladder specimen contains malignancy



Known adjacent primary + continuity?



Else: Assess systemic disease + IHC



Assign supported origin / uncertainty

Elements worth documenting in the final report

- Anatomic specimen/site and histologic tumor classification.
- Known primary and evidence supporting origin attribution.
- Extent of bladder wall involvement in the material sampled.
- Any uncertainty or recommendation for clinicoradiologic correlation.

Four recurring diagnostic pitfalls

- Calling every malignant bladder biopsy a primary bladder neoplasm.
- Treating enteric morphology or CDX2 expression as origin-specific.
- Ignoring prior pelvic malignancy or cross-sectional imaging.
- Applying the bladder-primary staging table to an adjacent-organ primary.

Case 1 — A rectal mass and bladder glands

Diagnostic problem

- Patient with a known rectal adenocarcinoma develops a posterior bladder lesion.
- Bladder tissue contains infiltrating adenocarcinoma with enteric morphology.
- Imaging suggests a continuous mass between rectum and bladder.
- What is the most defensible working diagnosis?

Case 1 — Interpretation

Reasoned resolution

- Favor rectal carcinoma involving bladder by direct extension.
- The imaging continuity provides evidence beyond enteric histology.
- Compare prior rectal tissue and report the primary origin explicitly.

Case 2 — Prostate history, bladder-neck mass

Diagnostic problem

- A man previously treated for prostatic carcinoma develops a bladder-neck lesion.
- Biopsy contains infiltrating glands; Mucosal findings are not defining.
- Which observations would separate prostatic involvement from bladder primary?

Case 2 — Interpretation

Reasoned resolution

- Review previous prostate tumor and current imaging of bladder neck/prostate.
- Apply an appropriate lineage-focused immunostain panel.
- Avoid assigning a bladder-primary stage without evidence of bladder origin.

Case 3 — Bladder lesion in systemic lymphoma

Diagnostic problem

- A patient with established systemic lymphoma has a new bladder mass.
- Tissue is predominantly composed of atypical lymphoid cells.
- What question takes priority over urothelial tumor grading?

Case 3 — Interpretation

Reasoned resolution

- Determine hematolymphoid lineage and lymphoma subtype.
- Compare with the established systemic lymphoma.
- Classify the lesion as systemic involvement if supported by distribution/history.

Case 4 — A distant primary with a bladder lesion

Diagnostic problem

- A patient with metastatic gastric carcinoma develops an isolated-appearing bladder nodule.
- The biopsy demonstrates adenocarcinoma.
- Does the biopsy alone establish a new bladder primary?

Case 4 — Interpretation

Reasoned resolution

- No: Metastatic gastric carcinoma is a documented, though unusual, possibility.
- Compare original tumor, imaging distribution and the complete immunophenotype.
- Classify only when the combined evidence supports the site of origin.

Diagnostic synthesis

- The predominant form of secondary bladder involvement is contiguous extension.
- Cervix, uterus, prostate and rectum are the principal adjacent sources.
- Systemic lymphoma and rare distant solid-tumor deposits broaden the differential.
- Origin attribution requires anatomic, morphologic and clinical integration.

Final diagnostic checklist

- Is there a known or suspected extravesical primary malignancy?
- Does imaging demonstrate anatomical continuity with an adjacent tumor?
- Does the bladder lesion match previous tumor morphology?
- Are targeted markers interpreted with their site-specific limitations?
- Does the final diagnosis communicate the supported site of origin?

Selected references

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026).
- Bates AW, Baithun SI. Histopathology. 2000;36:32–40. PMID 10632749.
- Roy S et al. Diagn Pathol. 2012;7:151. doi:10.1186/1746-1596-7-151.
- Wang L et al. Int J Clin Exp Pathol. 2018;11:5581–5591. PMID 31949645.
- El-Taji O et al. Transl Androl Urol. 2021;10:2427–2434. PMID 34295729.
- Bates AW et al. J Clin Pathol. 2000. PMID 10911804.