

RAMA MULTIDISCIPLINARY TEAM APPROACH IN

BLADDER CANCER



ไม่มีค่าลงทะเบียน

12.00-13.05	อาหารเที่ยง / เปิดงานประชุม
13.05-13.30	Urologists play vital role in non muscle invasive bladder cancer
13.30-14.05	Imaging in the Diagnosis, Staging, and Follow-Up of Urinary Bladder cancer
14.05-14.40	Optimal sequencing in treatment M-invasive bladder cancer :Urologists and Oncologists
14.40-14.50	พัก อาหารว่าง
14.50-15.25	The role of radiotherapy in urinary bladder cancer: current status.
15.25-15.50	Bladder cancer- Challenges in systemic treatment for advance disease
15.50-16.30	Case discussion / ปิดประชุม

ศุกร์ 30/ 3 /2018 ห้องประชุม 810 เวลา 12.00- 16.30



Imaging Pathways of Urinary bladder cancer

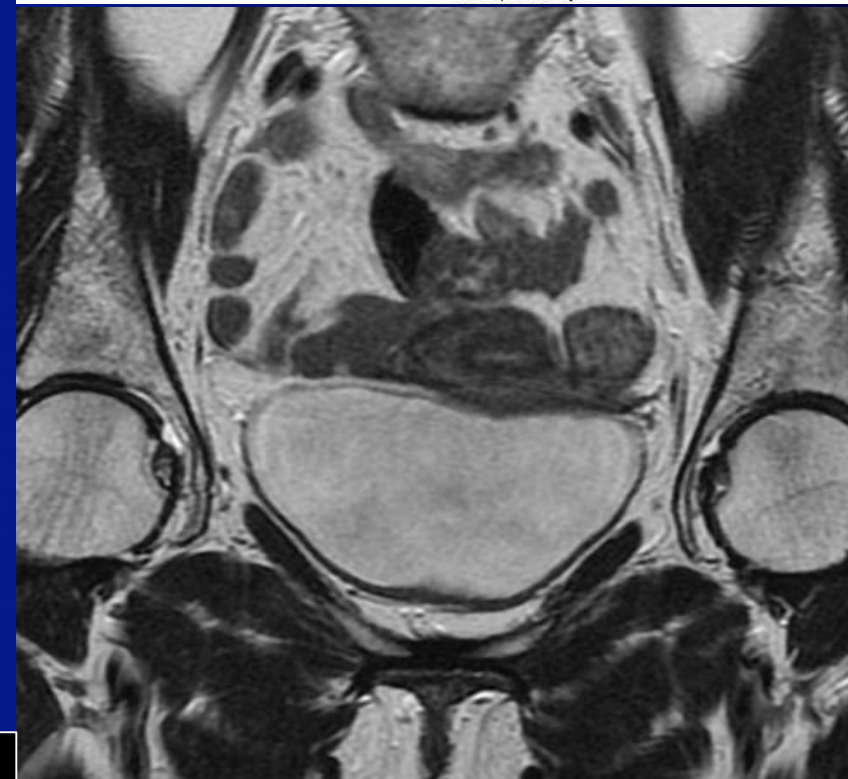
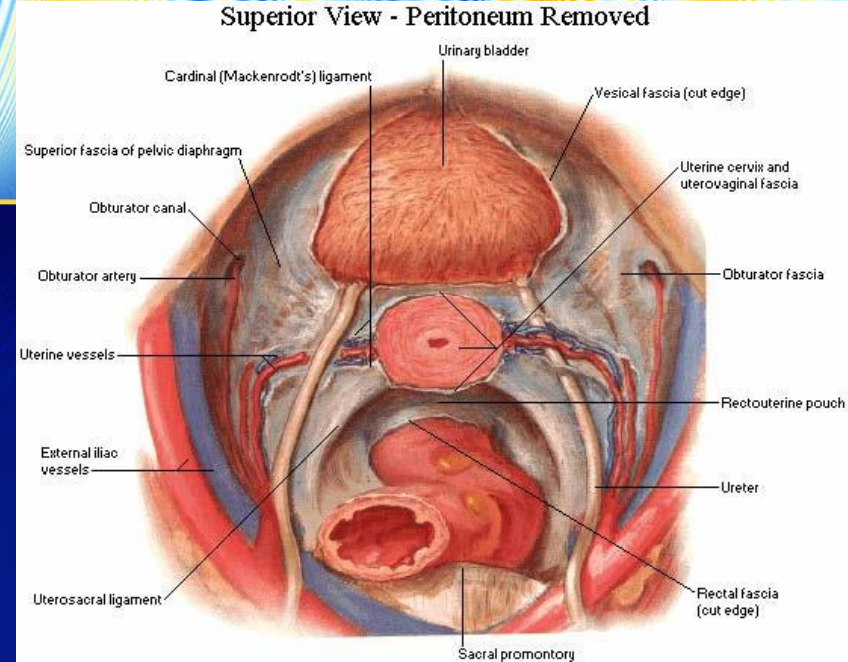
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Imaging Pathways of Urinary bladder cancer

- Anatomy
- Diagnosis
- Staging
- Follow up

Anatomy of urinary bladder

- Extraperitoneal organ
- Dome:
 - Cover by peritoneum
 - Prone to rupture with distention and trauma
- Space of Retzius (Ant perivesical space)
 - Extraperitoneal space
 - Between transversalis fascia and peritoneum



Anatomy of urinary bladder

Consist of

- Urothelium mucosa (a)
 - More sensitive to extreme temperature change than pain
- Submucosa
- Lamina propria (b)
- Smooth muscle (c = Detrusor muscle)
 - Inner longitudinal
 - Middle circular
 - Outer longitudinal
- Adventitia (d)

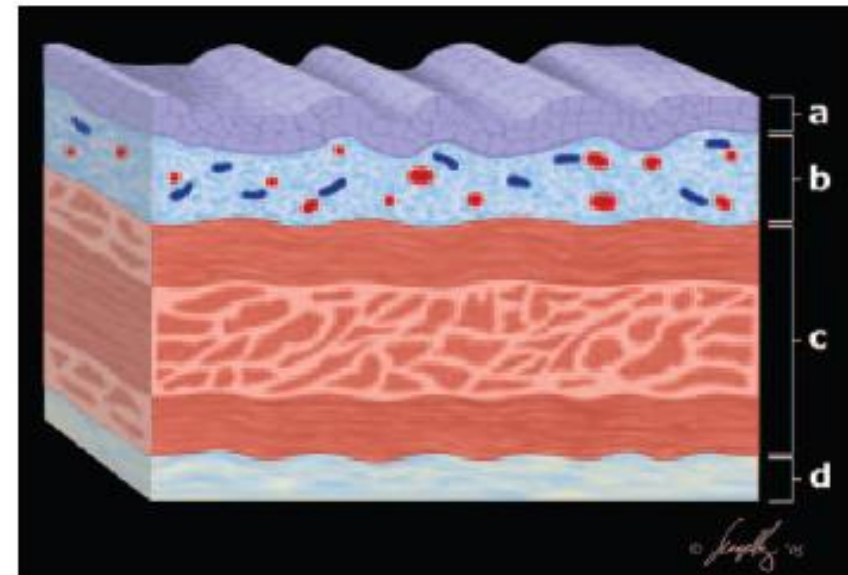
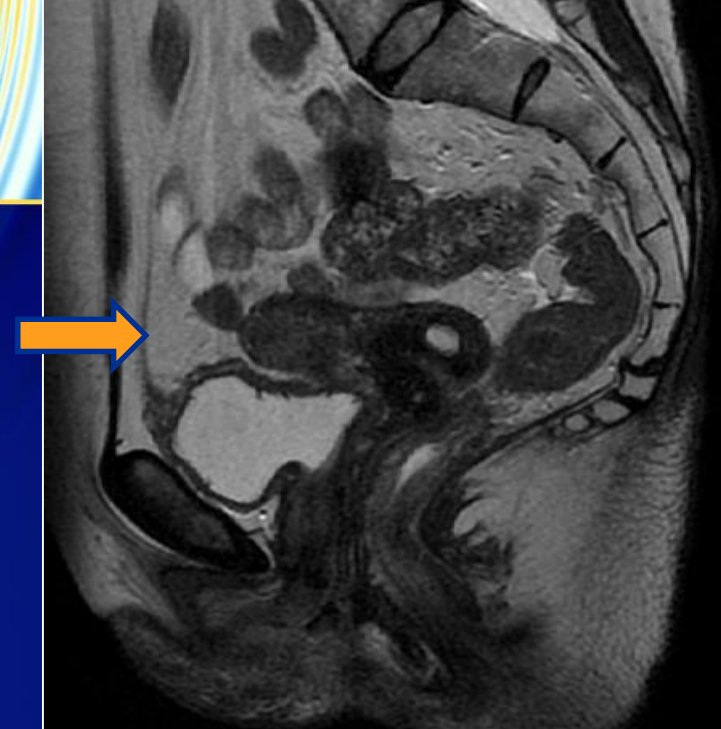


Figure 1. Normal bladder wall. Diagram shows the urothelium (a), lamina propria (b), muscularis propria (detrusor muscle) (c), and adventitia (d). (Reprinted, with permission, from reference 1).

Anatomy

Urachus

- Median umbilical ligament
- Midline musculofibrous band (5-6 cm) extend upward from ant dome toward umbilicus
- Vestigial remnant of obliterated umbilical arteries and allantois
- 70 % lined by TC (adults)



Urachus

- Length 3-10 cm
- Diameter 8-10 mm
- Three layered tubular structures
 - **Inner:** transitional epi (70 %), columnar epi (30%)
 - Surround by CNT
 - **Outer:** muscular layer continuity with detrusor muscle
- May merge one or both obl um a
- May deviation from midline

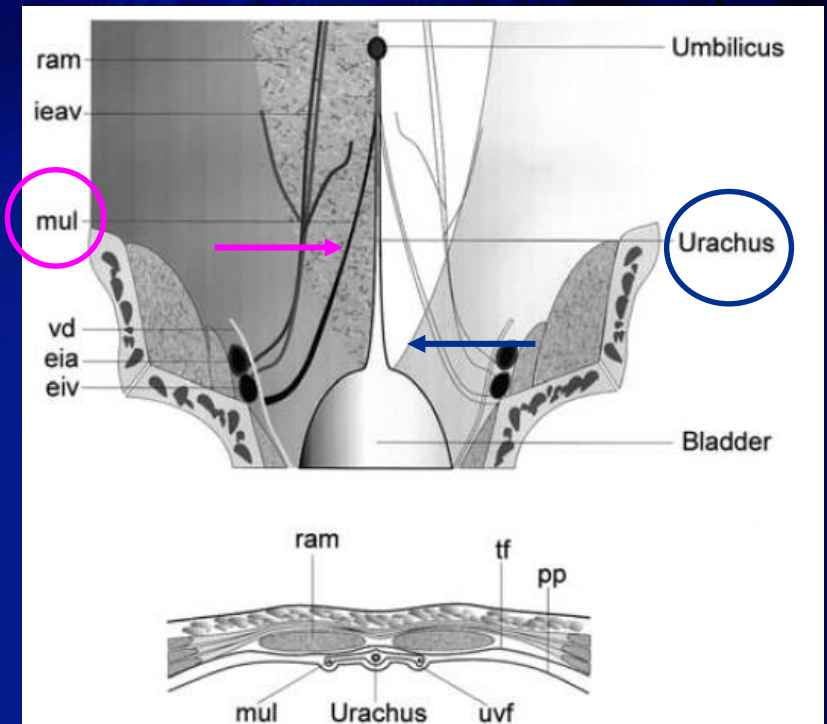
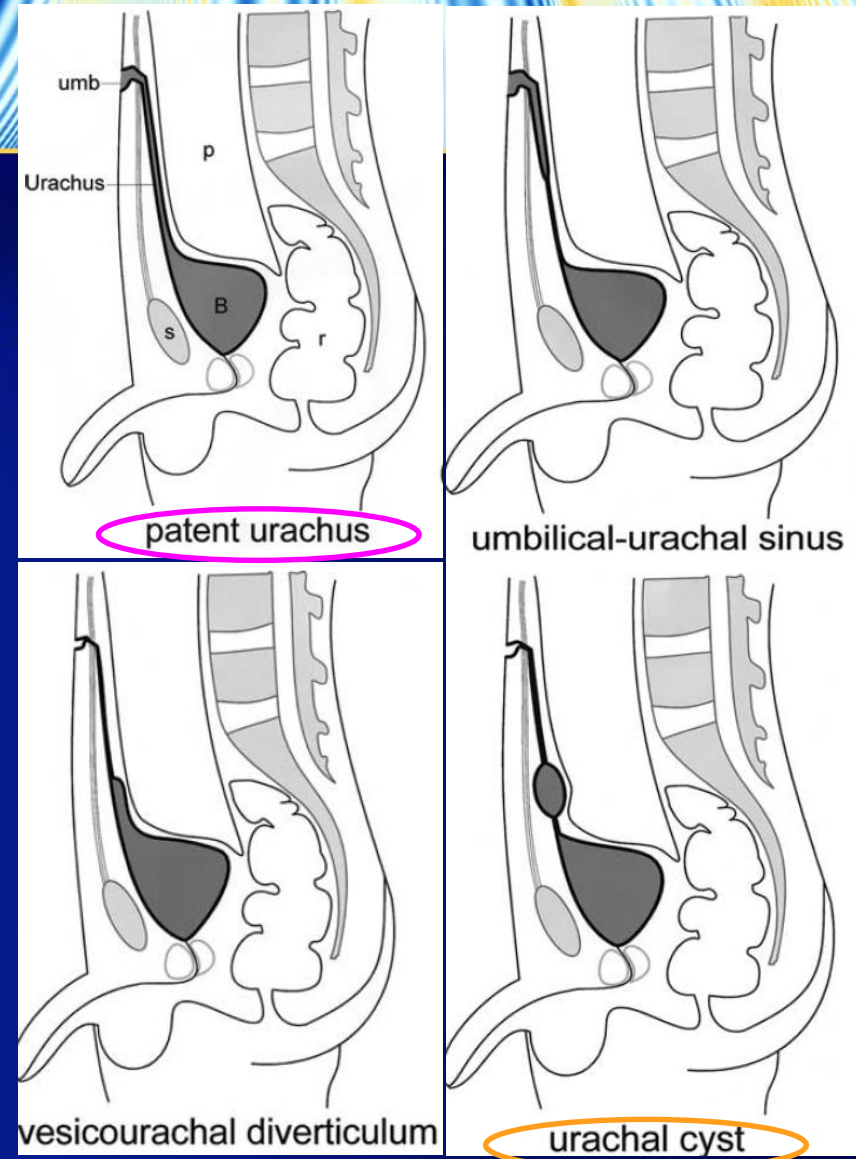


Figure 2. Drawings of the lower anterior abdominal wall as seen from inside the peritoneal cavity (top) and in the transverse plane (bottom) show the urachus extending from the dome of the bladder to the umbilicus along with the medial umbilical ligaments (obliterated umbilical arteries) (*mul*), which lie within the perivesical space between the transverse fascia (*tf*) and the parietal peritoneum (*pp*) and are surrounded by the umbilicovesical fascia (*uvf*). *eia* = external iliac artery, *eiv* = external iliac vein, *ieav* = inferior epigastric artery and vein, *ram* = rectus abdominus muscle, *vd* = vas deferens.

Urachus

- Congenital anomalies (4 types)
 - Patent urachus (50 %)
 - Umbilical-urachal sinus (15 %)
 - Vesicourachal diverticulum (3-5 %)
 - Urachal cyst (30 %)
- Acquired urachal remnant
 - Close normally after birth
 - Re-open in asso with pathologic condition
- Acq urachal remnant disease
 - Infection
 - Tumor



Bladder diverticulum

- May be a result form outlet obstruction
- Rare: Congenital deficiency in bladder musculartuer adj to UVJ
 - Smooth walled sac formed by **herniation of bladder mucosa & submucosa through muscular wall**
 - **Consist only urethelium (not surrounded by detrusor muscle)**
- Location
 - Near UVJ: “Hutch diverticulum”
 - Bladder dome: like urachus (Rare)
- Small to very large, single or multiple
- **High incidence of tumor than bladder lumen**
 - Stasis of carcinogen laden urine
 - Not surround by detrusor muscle → rapid tumor spreading outside



Hutch diverticulum (cystogram and CT) cystogram demonstrate reflux into the left ureter and a diverticulum adjacent to the ureter.

Bladder tumor

Benign tumor

- Rare, 1 % all bladder neoplasm
- Most mesenchymal in origin
 - Leiomyoma
 - Pheochromocystoma
 - Papilloma
 - Neurofibroma

Malignant tumor

- Primary urothelium (95 %)
 - 90-95 % : TCC component
 - 4-8 % : Entirely composed of Squamous cell
 - 1-2 % : Only adenomatous cells
- Secondary bladder tumor

Urothelial Neoplasm Containing Transitional Cell Components

- “Urothelial cancer” ≠ transitional cell cancers
- 25-37% urothelial neoplasms contain areas with other histologies (clear cell, glandular, lymphoepithelial, micropapillary, plasmacytoid, cyclomatoid, and squamous)
- M/C in bladder
 - Large surface area (compared with renal collecting system and ureters)
 - Reservoir of urine (longer contact with carcinogen)
 - > 50 % at lateral bladder wall → trigone → dome

Urothelial cancer

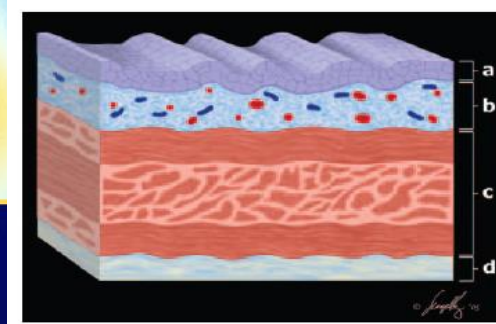


Figure 1. Normal bladder wall. Diagram shows the urothelium (a), lamina propria (b), muscularis propria (detrusor muscle) (c), and adventitia (d). (Reprinted, with permission, from reference 1).

- Mucosa → muscular layer (muscularis mucosa) → perivesical lymphatics and capillaries
- May direct extension into prostatic urethra, seminal vesicles, or vagina
- Pelvic lymph node involvement
- Hematogeneous spreading to lung and bone

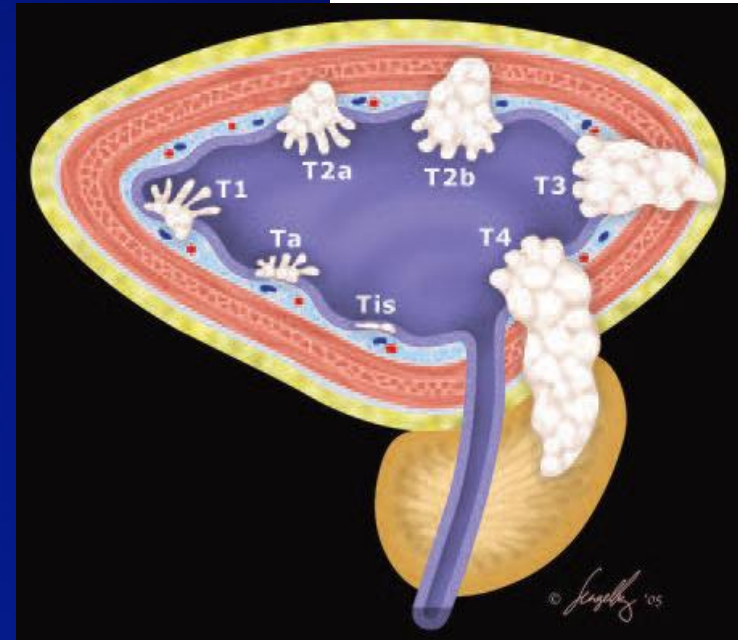


Diagram shows the stages of tumor invasion in bladder cancer. Tumors are considered superficial if they do not extend beyond the lamina propria (T1 or less). Once the muscle layer (muscularis propria) has been invaded (T2a or greater), the tumor is considered invasive.

AJCC Cancer Staging Manual

Eighth Edition

Table 6 – Updates in the American Joint Committee on Cancer staging of urinary bladder cancer

Category	Details
T1	Attempt for subcategorization in TUR recommended
T2	Staging of diverticular cancers has no T2
T4	Prostatic stromal invasion clarified that must be transmural from bladder; subepithelial stromal invasion staged as T2 (urethral)
N1	Perivesical LN added
M1	Divided into nonregional LN only (M1a) and non-LN distant metastases (M1b)
Prognostic stage group III	Divided into IIIA and IIIB based on number of regional LN and involvement of common iliac LNs
Prognostic stage group IV	Divided into IVA and IVB corresponding to the M1a and M1b division

LN = lymph node; TUR = transurethral resection.

Implement date of January 1, 2018

Urinary bladder cancer (AJCC 8th edition)

- Subdividing T1 in transurethral resection
 - Upstaging of T1 in radical cystectomy
 - 50% upstage to \geq T2
 - 33% upstage to non-organ confined stage
 - A cut-off of **2.3-mm** in greatest length is significantly associated with risk of progression to muscle invasion
- Intraurethral prostate stromal invasion:
 - T2 (per urethral staging and not bladder staging)
 - Separate T category (per bladder staging)
 - Remain unclear how a concurrent urethral T2 will impact a $>$ T2 bladder proper cancer
 - Emphasis in reporting should be given to the higher stage between the two.
- Bladder diverticula (not contain muscularis propria) \rightarrow no T2 in staging diverticular cancer
- Perivesical LN: independent predictor of survival
 - Included perivesical LN among regional LNs under N category (level of evidence II)
- LN+ ve beyond the **common iliac** as **M1a** and all other non-LN met \approx M1b

Excretory urography and cystography

- Detection
 - Insensitive in bladder cancer
 - Fine urothelial detail and pinpoint small upper tract tumors (multicentric lesions)
 - 60 % cancer detection rate
 - Nearly complete replacement by CT Urography
 - 2 % of bladder cancer: Metachronous (average 70 months)
 - 20% of upper tract tumor: antecedent bladder tumor
 - Still sometimes used for detailed imaging of the upper urinary tract
- Staging
 - Inability to show extravesical disease

Ultrasound

- Detection
 - Soft tissue mass projecting into the lumen
 - Increased vascularity on color Doppler/power Doppler images
 - Lower detection rate compared with CT & cystoscopy
 - Small lesions <5 mm
 - Position of lesion - worse in anterior wall
 - Inability to evaluate extent of invasion into bladder wall or extravesical extension, nor evaluation of the entire GU tract
- Staging
 - Little value



Ultrasound examination of urothelial cancer.

- Longitudinal image through the bladder demonstrates a small mass protruding into the bladder lumen.
- Color Doppler sagittal and power Doppler longitudinal images through the lesion demonstrate increased vascularity.

CT and CT urography

- Detection
 - Excellent sensitivity
 - Tumor morphology
 - Asymmetrical thickening
 - Mass-liked projecting into lumen (smaller defected bladder cancer tend to be papillary, tiny filling defect)
 - Diffuse thickened wall (rare)
 - CTU: Undetected **small and flat lesion** (carcinoma in situ) and at **base location** (volume averaging from prostate)
 - The sensitivity & specificity of CTU for tumor detection :**79-93% and 91-99%**

CT Virtual cystoscopy (CTVC)

- New 3D reconstruction technique
- Can be done using contrast-filled bladder (part of CTU) or air-filled bladder (require catheterization)
- Recent meta-analysis (26 studies with 3084 investigation) compared to gold standard cystoscopy
- CTVC : most sensitive and specific diagnostic modality (sen 93.9%, spec 98.1 %) for tumor detection compared to US, CT, MRVC
- Major limitation: inability to detect flat lesions accurately and inability to provide tissue samples for histologic diagnosis

-Battista G, Sassi C, Corcioni B, Bazzocchi A, Golfieri R, Canini R. Latest developments in imaging of bladder cancer. Expert Rev Anticancer Ther. 2010;10(6):881-94.

- Qu X, et al. Comparison of virtual cystoscopy and ultrasonography for bladder cancer detection: a meta-analysis. Eur J Radiol. 2011;80(2):188-97. (Level II evidence)

CT and CT urography

- Staging
 - Absence of grossly obvious tumor extension
 - Cannot determine muscularis mucosae invasion
 - Difficult to detect perivesical spread of tumor (increased stranding due to tumor or edema)
 - The reported accuracy in detecting extravesical spread varies from 40-92%, with a tendency to understage
 - Detect pelvic side wall invasion (obliterate fat plane)
 - Lymph node involvement (by size criteria)
 - Accuracy of CT: 73-92%
 - Tendency to understage nodal involvement
 - CT-MRI unable to detect metastasis spread in normal size node or enlarged node from benign process
 - Metastasis: liver (47%), lung (45%), bone (32 %), peritoneum (19%), pleura (16%)


CT and CT urography

- N Staging
 - 191 BCa patients who underwent radical cystectomy
 - A total of 184 out of 3317 resected lymph nodes were diagnosed as metastatic lymph nodes
 - The probability of metastatic nodes significantly increased with more advanced T stages
 - Once lymph nodes are detected on imaging, the characteristic signs should be paid attention to. The short diameter > 6.8 mm may indicate metastatic lymph nodes in BCa

Li et al. *Chin J Cancer* (2018) 37:3
<https://doi.org/10.1186/s40880-018-0269-0>

Chinese Journal of Cancer

ORIGINAL ARTICLE Open Access

 CrossMark

Computed tomography and magnetic resonance imaging evaluation of pelvic lymph node metastasis in bladder cancer

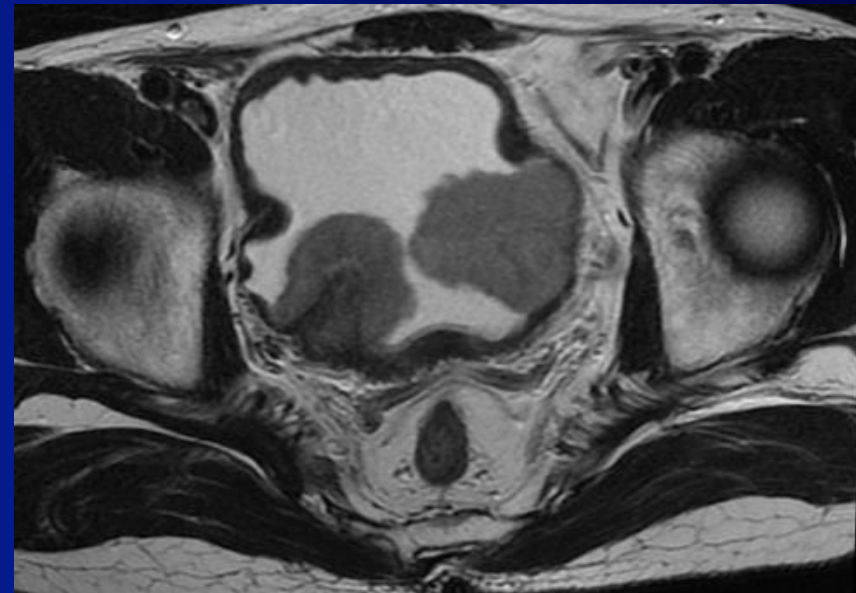
Yong Li^{1†}, Feiyu Diao^{2†}, Siya Shi¹, Kaiwen Li³, Wangshu Zhu¹, Shaoxu Wu³ and Tianxin Lin^{3*}

CT and CT urography

- Follow up after local treatment: (limitation of cystoscopy)
 - Thickened wall (inflammation, scar, tumor recurrence)
 - Detect large bladder mass
 - Evaluate metachronous tumors
- Follow up after radical cystectomy
 - 1/3 recurrence near **cystectomy site**
 - 2/3 recurrence in **pelvic nodes**

MRI

- Detection
 - High sensitivity (focal asymmetrical thickening, mass projecting into lumen, abnormal hyperenhancement with GBCM, restricted diffusion in DWI) include tumor in diverticulum
 - Focal thickening: inflammation/fibrosis, recurrent tumor (Same as CT)



MRI

- Staging:
 - Determine the depth of bladder wall invasion
 - Low signal T2 stripe of muscular layer
 - DWI (depth of high SI of tumor compares with lower SI bladder wall)
 - DCE (increased enhancement)
 - Local tumor staging, the accuracy of MRI varies from 62-85% (on average about 20% higher than CT)
 - Gadolinium enhanced MRI improves accuracy of extravesical extension to 73-100 %
- Overall accuracy 92 % (combine T1, T2, DWI)
- MRI nodal staging is based on size criteria (as for CT) , accuracy 73-92 %

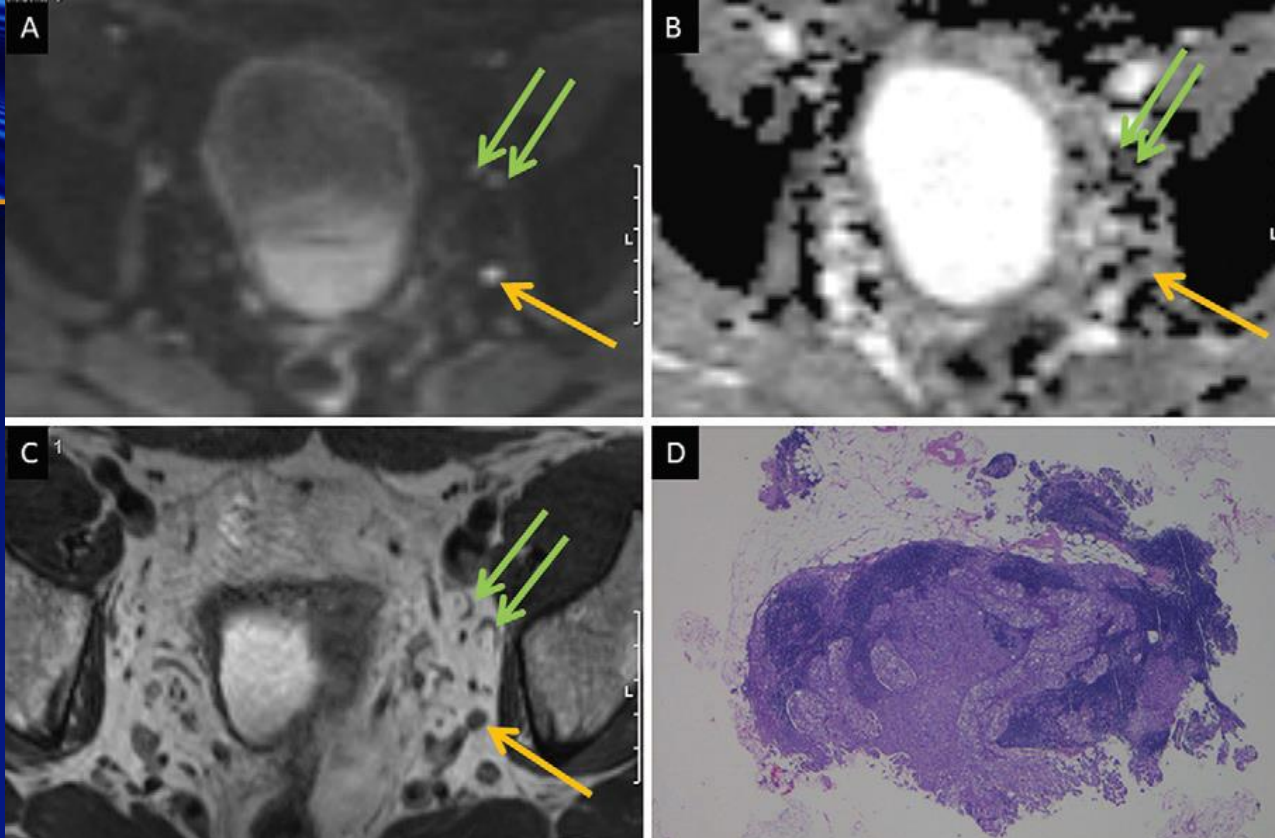
MRI

- Nodal metastasis
 - Novel contrast: ferumoxtran-10 and ultrasmall superparamagnetic particles of iron oxide (USPIO)
 - Limited commercial availability of USPIO
 - Occasional adverse events
 - Another image technique to improve LN staging
 - DWI-MRI
 - 64-79% pt with CA prostate or bladder = met in normal size node
 - Vast majority of missed LN met ≤ 5 mm
 - No significant difference in ADC value between malignant vs benign
 - Additional morphologic criteria (round, irregular ill-defined border, low T2 SI, fat hilum) \rightarrow improve diagnostic performance of DW MRI with **specificity of 95.4%**

- Deserno WM, Harisinghani MG, Taupitz M, Jager GJ, Witjes JA, Mulders PF, Hulsbergen van de Kaa CA, Kaufmann D, Barentsz JO. Urinary bladder cancer: preoperative nodal staging with ferumoxtran-10-enhanced MR imaging. *Radiology*. 2004;233(2):449-56. (Level II evidence)

- Thoeny HC, Triantafyllou M, Birkhaeuser FD, Froehlich JM, Tshering DW, Binser T, Fleischmann A, Vermathen P, Studer UE. Combined ultrasmall superparamagnetic particles of iron oxide-enhanced and diffusion-weighted magnetic resonance imaging reliably detect pelvic lymph node metastases in normal-sized nodes of bladder and prostate cancer patients. *Eur Urol*. 2009;55(4):761-9. (Level III evidence)

- Thoeny HC, Froehlich JM, Triantafyllou M, et al. Metastases in normal-sized pelvic lymph nodes: detection with diffusion-weighted MR imaging. *Radiology*. 2014;273(1):125-135.



Images in 48-year-old man with bladder cancer (stage pT3a) and incidentally detected prostate cancer (Gleason 3+3 = 6).

A, DW MR image (b value, 1000 sec/mm²) shows **hyperintense round structure in internal iliac region** on left side (yellow arrow).

B, ADC map shows **corresponding hypointense structure** (yellow arrow).

C, Reconstructed transverse T2-weighted image. The structure (yellow arrow) was correlated with a lymph node. This lymph node had a short-axis diameter of 4 mm and was diagnosed as positive by all readers.

D, Photomicrograph (hematoxylin-eosin stain) demonstrates that approximately 80% of this lymph node is occupied by solid growing urothelial carcinoma tissue, a finding compatible with **metastasis of bladder cancer**.

Note two **other less hyperintense structures** (green arrows in A–C) on images that also correspond to lymph nodes. These have lower signal intensity on DW MR image obtained with b value of 1000 sec/mm² and are similar in size to positive lymph node. These nodes were classified as true negative owing to the presence of fatty hilum on conventional MR image. ADC in fatty lymph nodes (67×10^{-5} mm²/sec) was lower than that in positive node (100×10^{-5} mm²/sec).

PET-CT

- 18 Fluorodeoxyglucose (FDG)-positron emission tomography (PET)
 - FDG avid tumor
 - Not widely use for know bladder cancer patient
 - Radio-isotope excreted normally in urine and accumulates in the renal collecting system and bladder
 - Utilized successfully, particularly to detect metastatic disease.
 - Nodal staging of bladder cancer: **excreted in urine which may obscure nearby lymph nodes**
- Various techniques trialed to overcome these limitations, such as using **non-urinary excreted tracers** such as 11C-choline and use of various tracers attached to anti-oncoantigen

Pure Squamous Cell Carcinoma

- Most in chr, recur bladder infection, calculi or both
- Higher incidence in bladder diverticula than in bladder lumen
- Increased risk in pt with schistosomiasis
- 25% Multifocal
- Tend to be poorly differentiated and invasive
- 5 year survival rate: 10%
- Radiographically, SCC cannot be differentiated from other bulky urothelial tumors

Pure Adenocarcinoma

- Adenocarcinoma: Composed exclusively of adenomatous cells
- Typical associated with metaplastic change in exstrophic bladders
- May in pt with cystitis glandularis and in urachal remnants
- 34% of bladder adenocarcinoma from urachal in origin

Urachal Carcinoma

- 70% mucin-producing adenocarcinoma (transitional epithelium lining the urachus **metaplasia** to glandular epithelium → produce mucin)
- 15% non mucin-producing adenocarcinoma
- TCC, SqCC, sarcoma (< 20 yo)
- SqCC: Ass urachal cyst and calculi urachal diver
- 40-70 YO Patients
- 65% in male

Urachal Carcinoma

- Ultrasound: Supravesical complex mass
- CT
 - Calcification detected by CT 70% of patient
 - Mass above or anterior bladder
 - May invade bladder or extend anterosuperiorly to umbilicus or both
 - Midline supravesical calcified mass: nearly dx urachal cancer
- Poor prognosis
- 5 year survival <15%
 - Late presentation of symptoms
 - Early local infiltration
 - Early development of bone and lung metastasis.

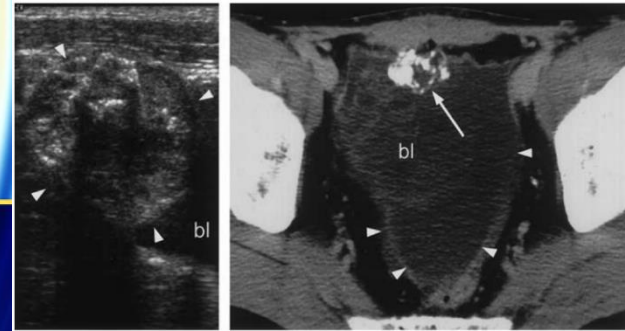
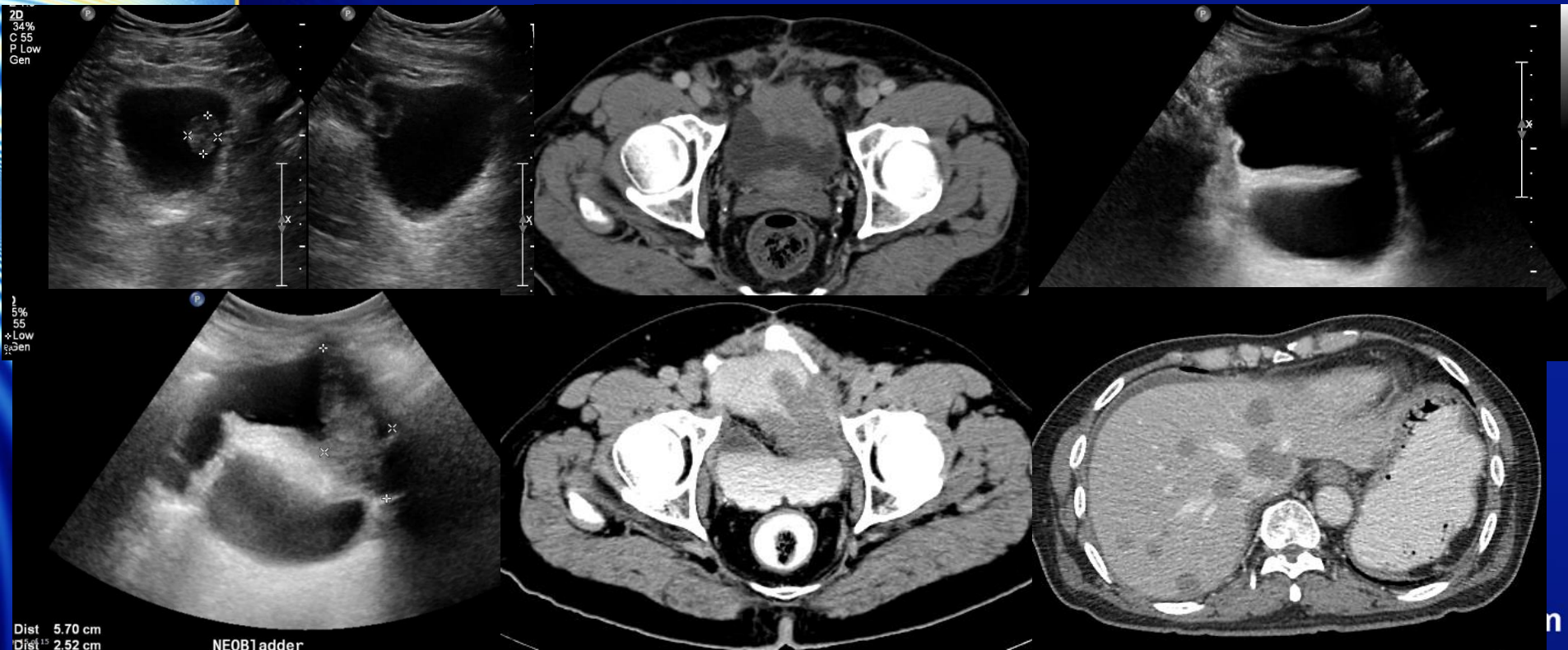


Figure 11. Mucinous adenocarcinoma arising from the urachal remnant in a 40-year-old man. **(a)** Sagittal US image shows a soft-tissue mass with multiple thick flecks of calcification (arrowheads) accompanied by posterior shadowing. **(b)** Unenhanced CT scan shows a densely calcified mass (arrow) projecting into the dome of the bladder (*bl*). A large amount of peritoneal fluid is seen surrounding the urinary bladder (arrowheads), a finding that suggests carcinomatosis.

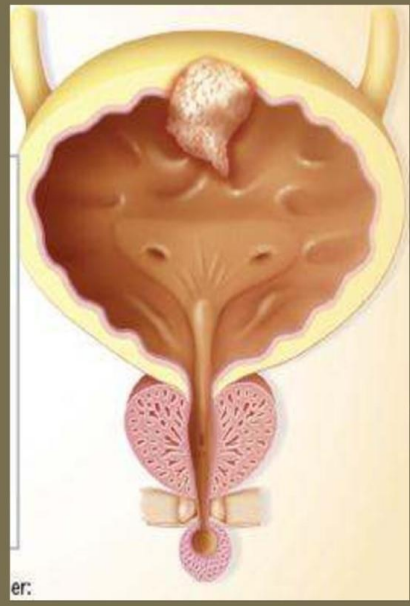
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Thank you for your attention