Treatment of Muscle Invasive Cancer

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BCAN Patient Forum
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Dan L. Duncan Cancer Center at Baylor College of Medicine

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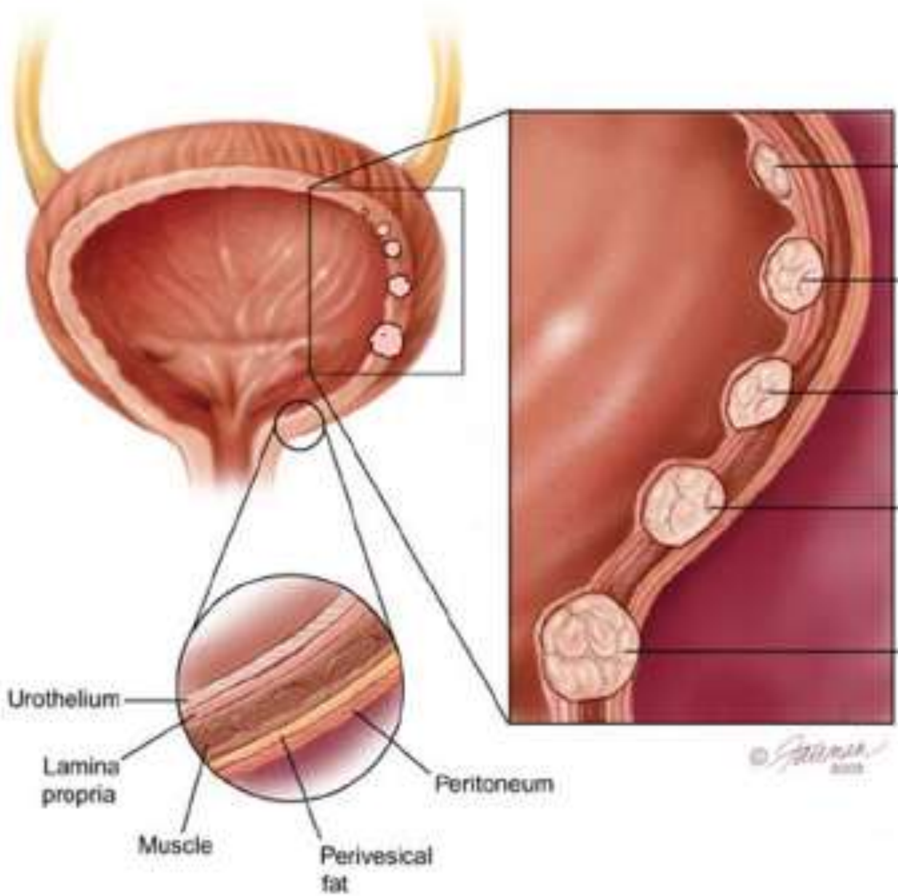
Staging



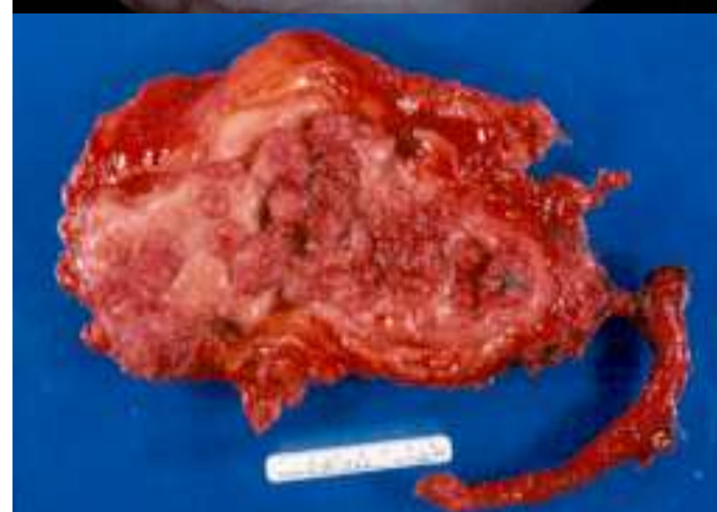
Non-muscle invasive (NMI-BC)

Muscle invasive (MI-BC)

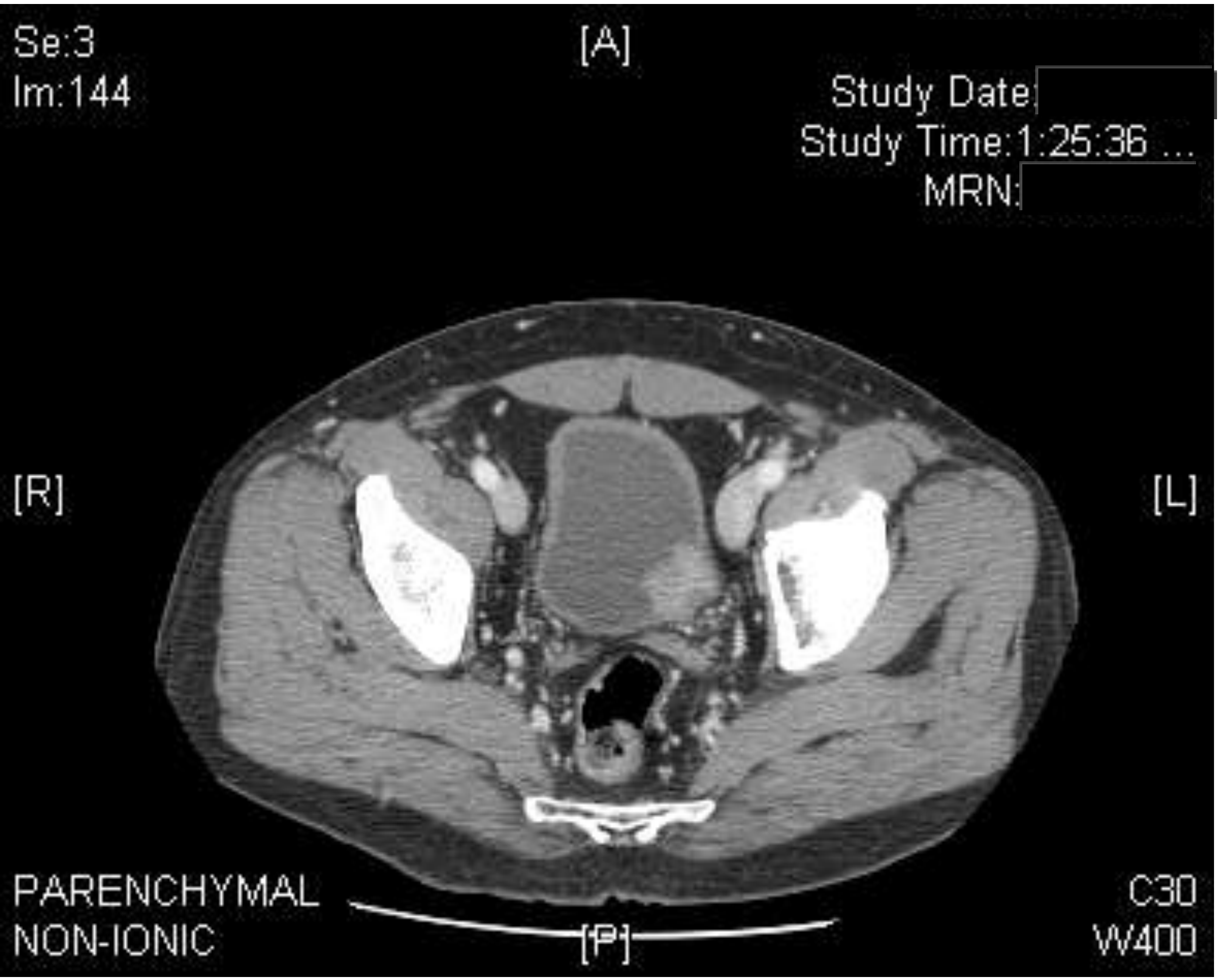
Overview of Bladder Cancer
Clinical Aspects

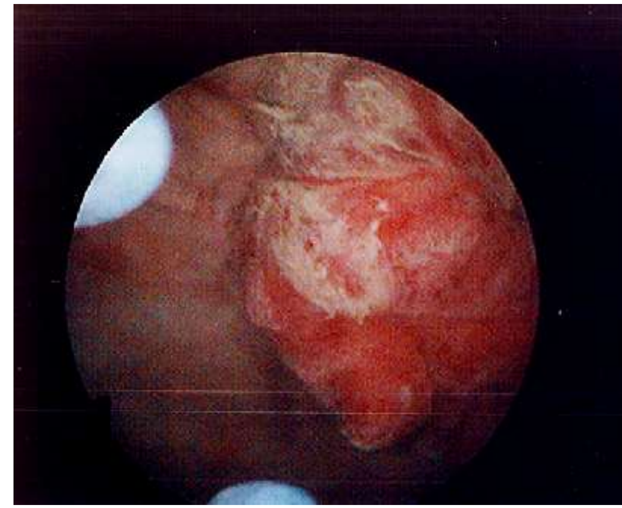
Low-grade: superficial, less likely to invade or metastasize, frequently reappears after resection but amenable to therapy, low mortality

High-grade: propensity to invade and metastasize, high mortality when invasive, but good response to treatment if detected early

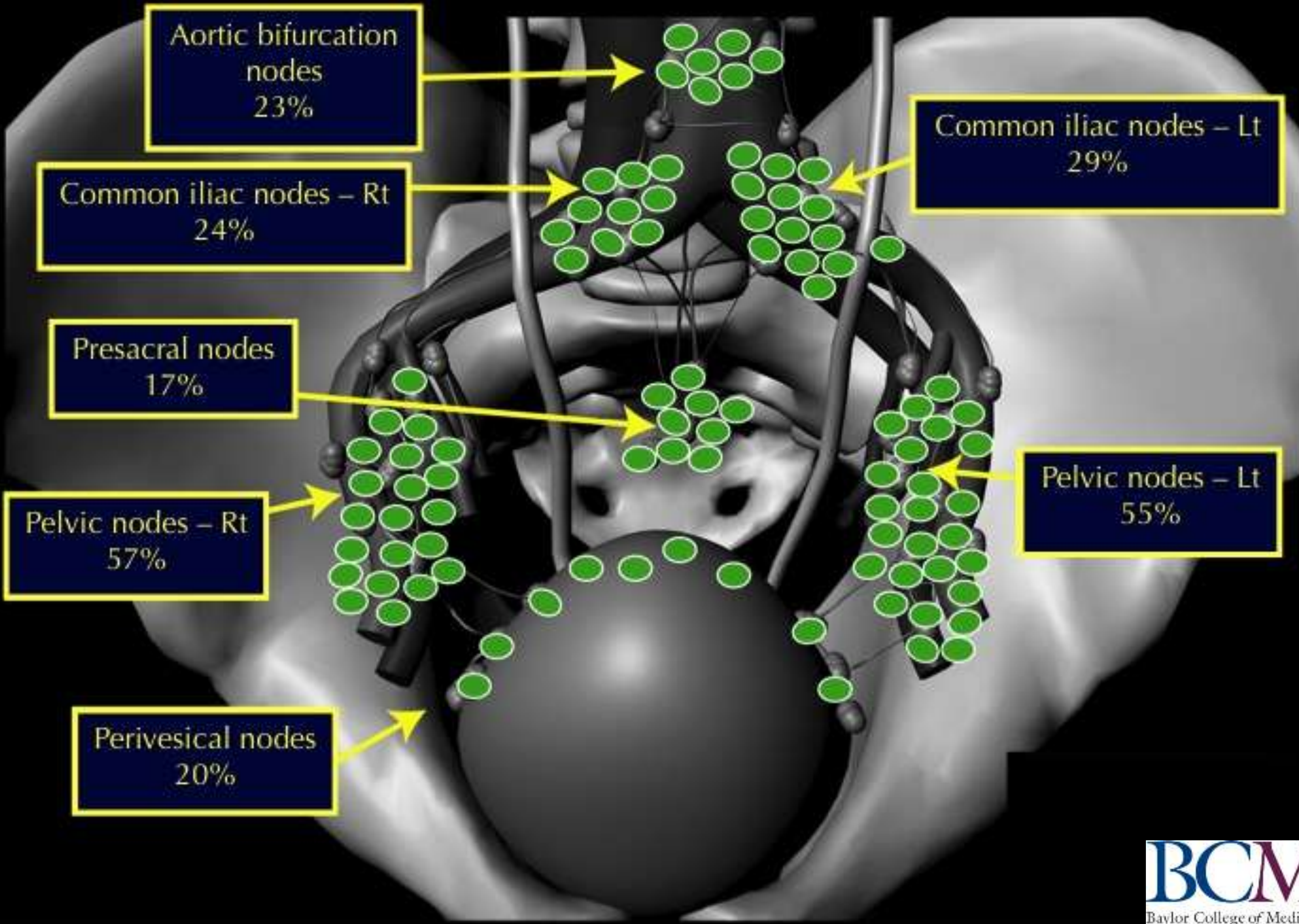


Invasive Bladder Cancer





Positive Lymph Node Distribution in 84 patients



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Natural History

- 15-20% of patients with Ta, T1 or Tis non-muscle invasive cancer progress to muscle invasion
- 80% of patients with muscle invasive cancer present de novo
- 40-50% have spread outside the bladder at time of diagnosis
- Requires integration of systemic and loco-regional treatment

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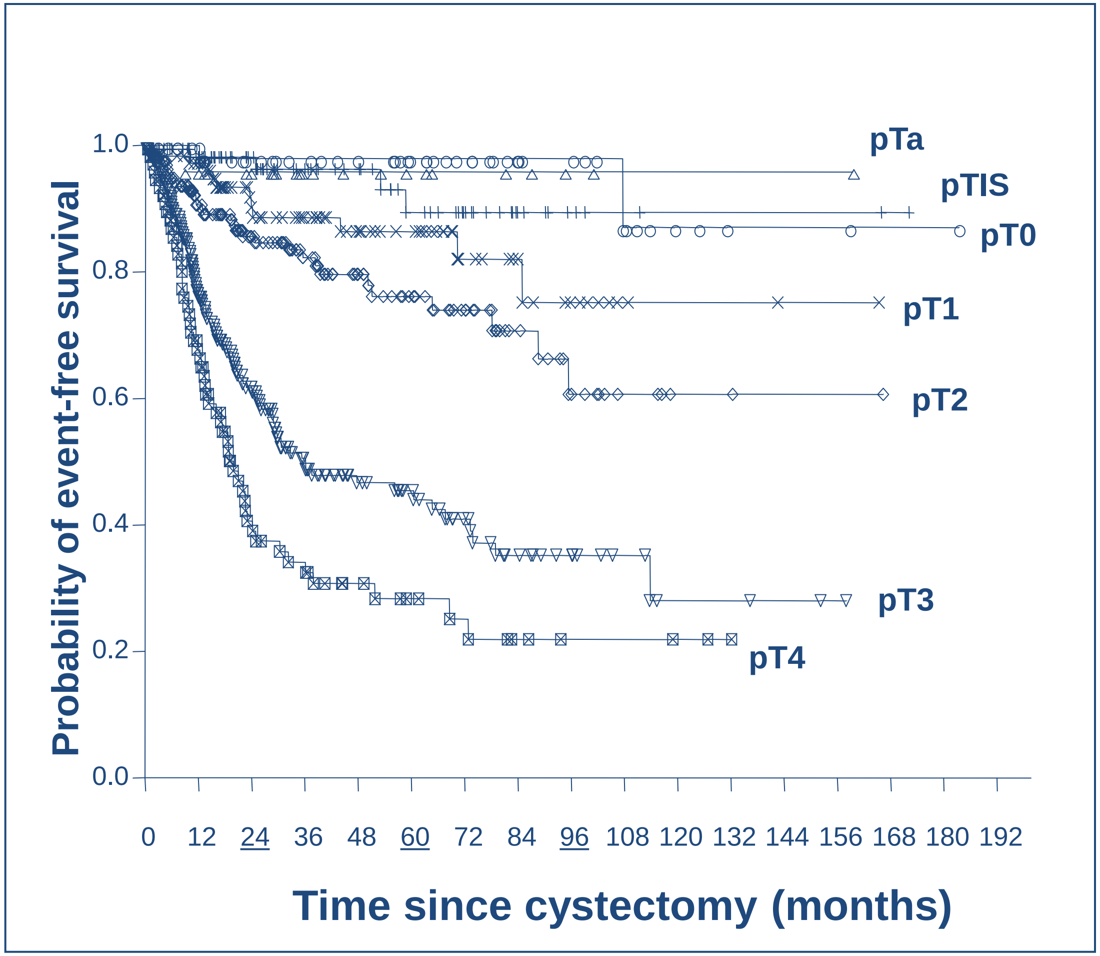
Treatment Goals

- Sterilize the regional tumor
- Control occult regional and distant metastases
- Preserve functional voiding per urethra
- Minimize treatment related morbidity

Disease-Specific Survival According to pT Stage at Cystectomy



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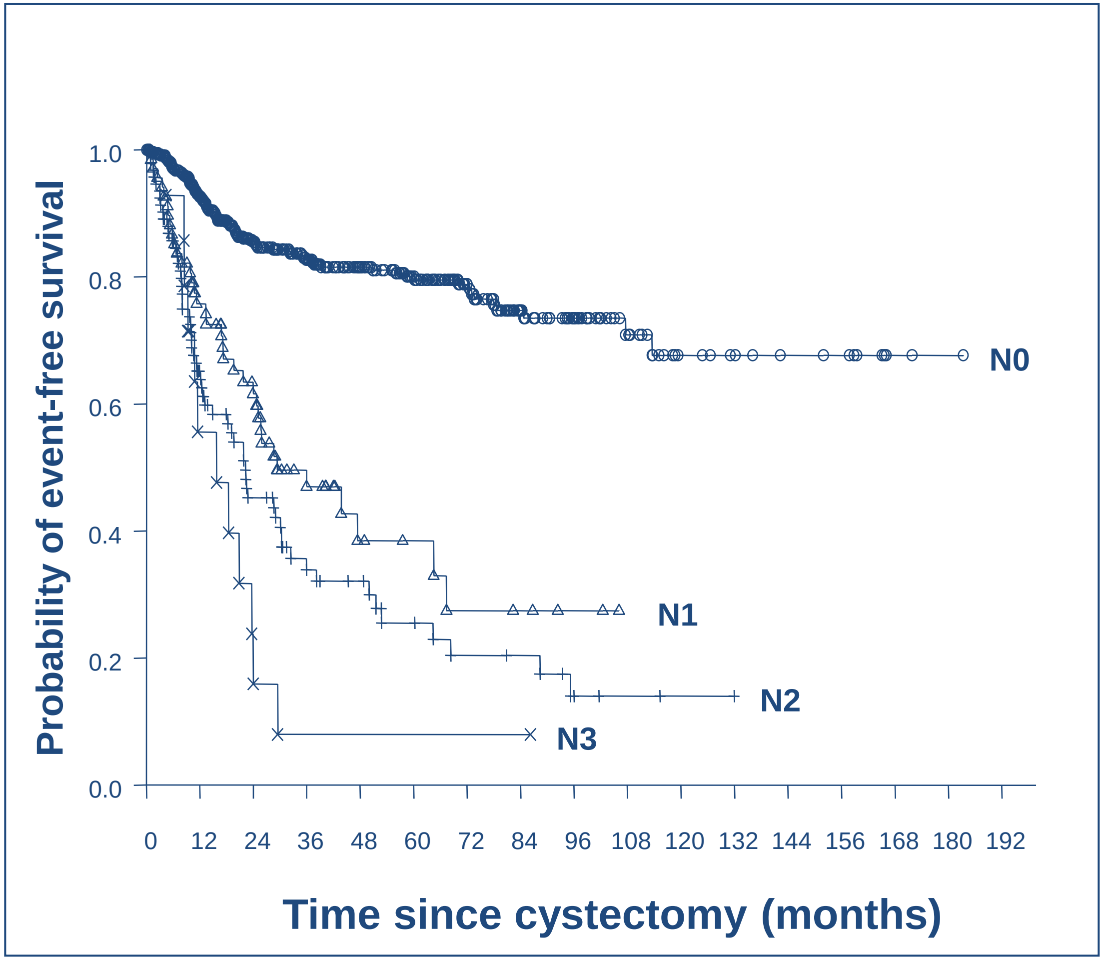
Disease-Specific Survival According to Node Stage at Cystectomy



Treatment Options for Muscle Invasive Cancer

- Radical transurethral resection
- Partial cystectomy
- Radical cystectomy
- Pelvic lymphadenectomy
- Chemotherapy may be given before (neoadjuvant) or after surgery (adjuvant)
- Radiation usually together with chemotherapy

Radical Cystectomy
How Much to Take?

- Male: Bladder, prostate, seminal vesicles
  - Prostate, seminal vesicle sparing???
- Female: Bladder, ovaries, uterus/cervix, anterior vagina
  - Recent studies show low incidence of gyn organ involvement (J Urol 168:147, 2002)
  - Preservation of vagina/uterus – provides support for neobladder and pelvic floor (J Urol 168:587, 2002)
- Pelvic lymph nodes: Minimum must include bilateral external iliac, hypogastric, obturator
  - Extended includes: Pre-sacral and common iliac

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Nerve-Sparing Cystectomy

- Lessons from Hopkins experience
  - Safe – no increase in local recurrence rate
  - Effective – 42% potent with intercourse
    - Age dependent
- Who do I offer this to?
  - Potent and sexually active
  - Clinically organ confined cancer – T2 or less
  - No evidence of intra-operative local extension

Schoenberg, et al J Urol 155:490, 1996

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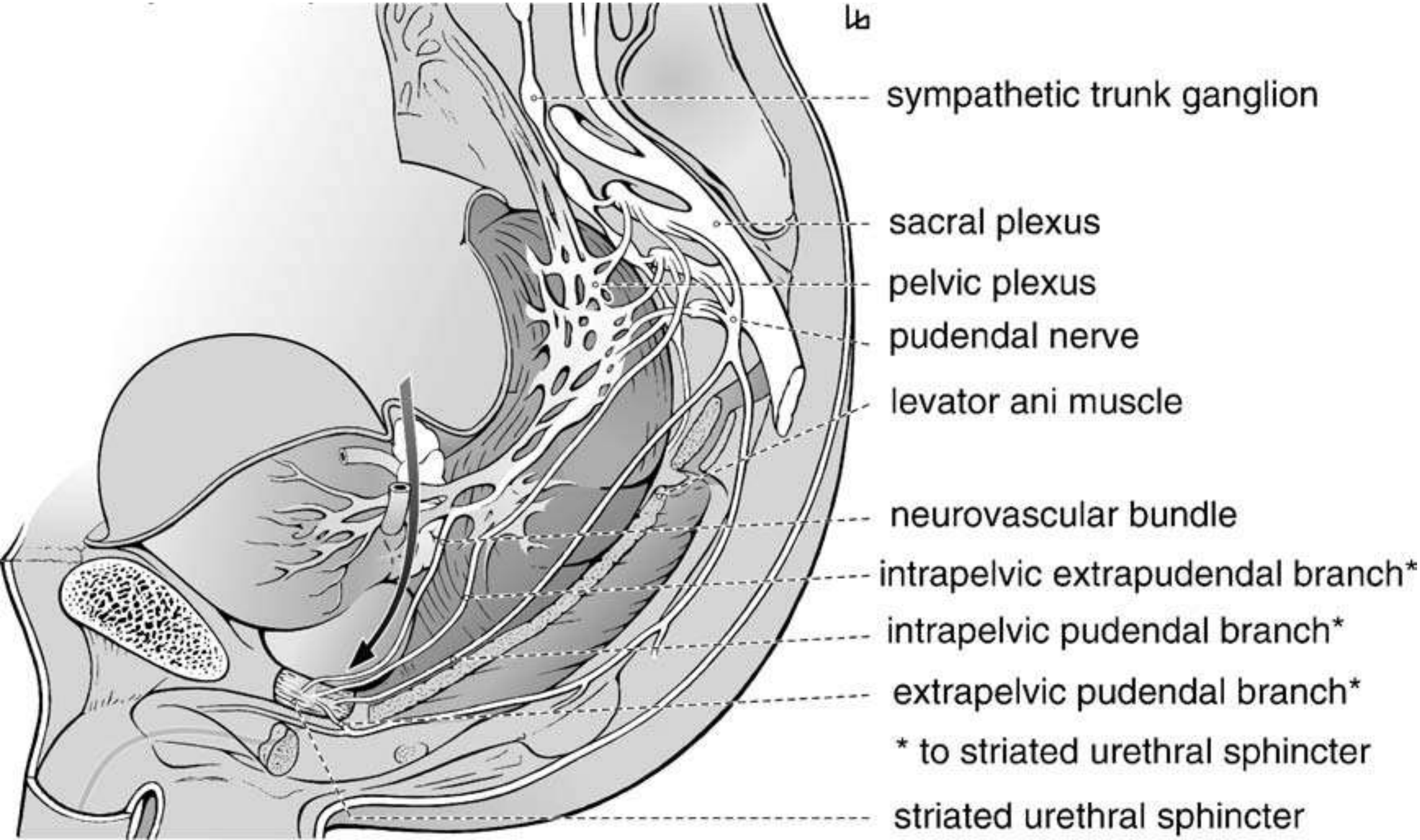
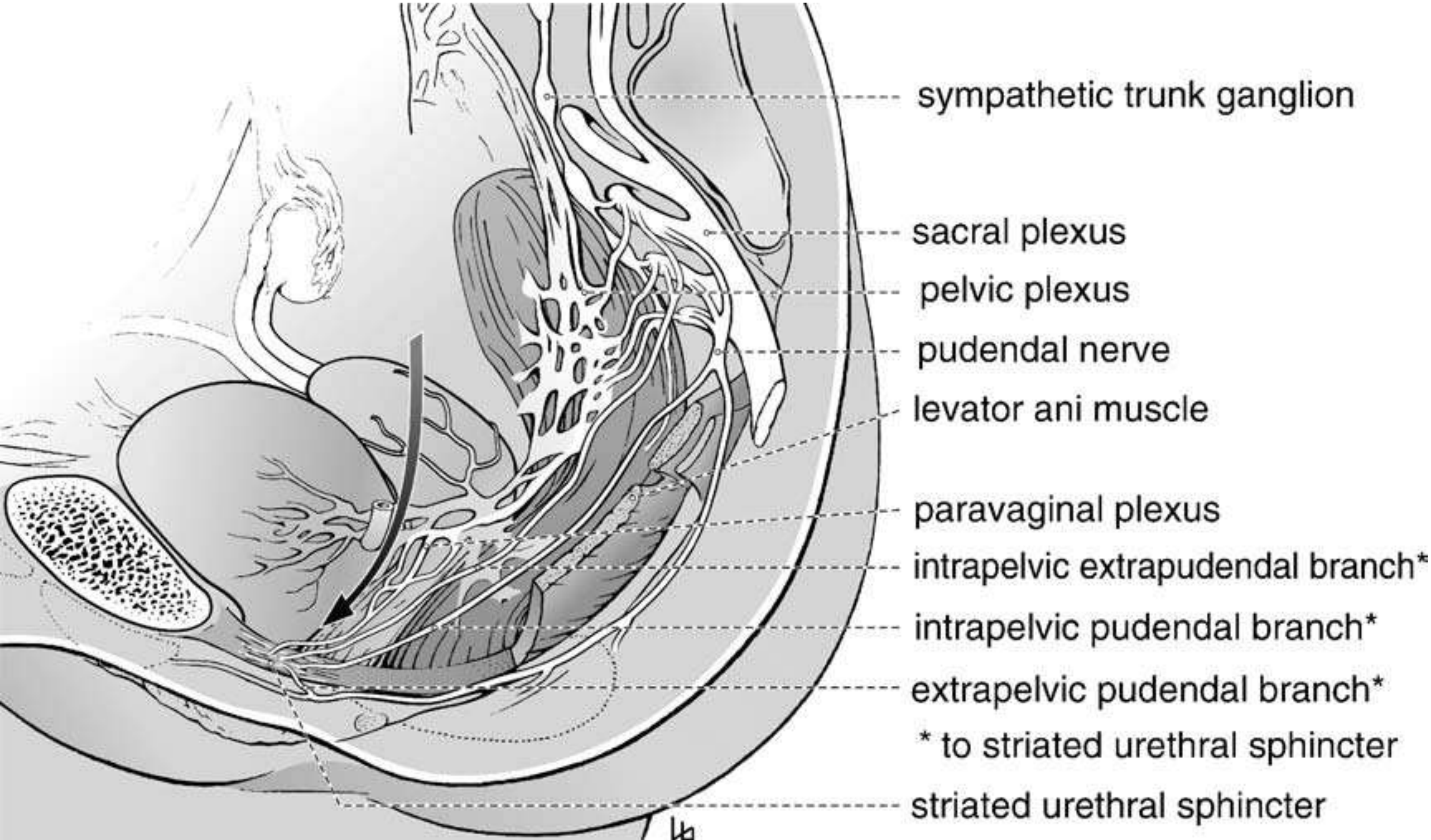
Nerve-sparing Male

(Burkhard, et al Crit Rev Oncol Hematol 57:255, 2006)

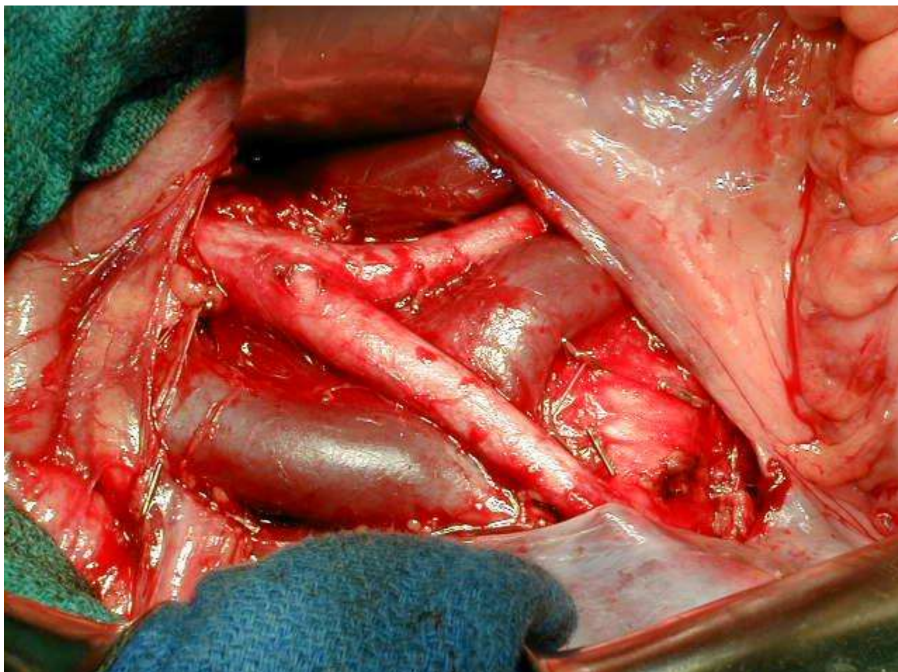


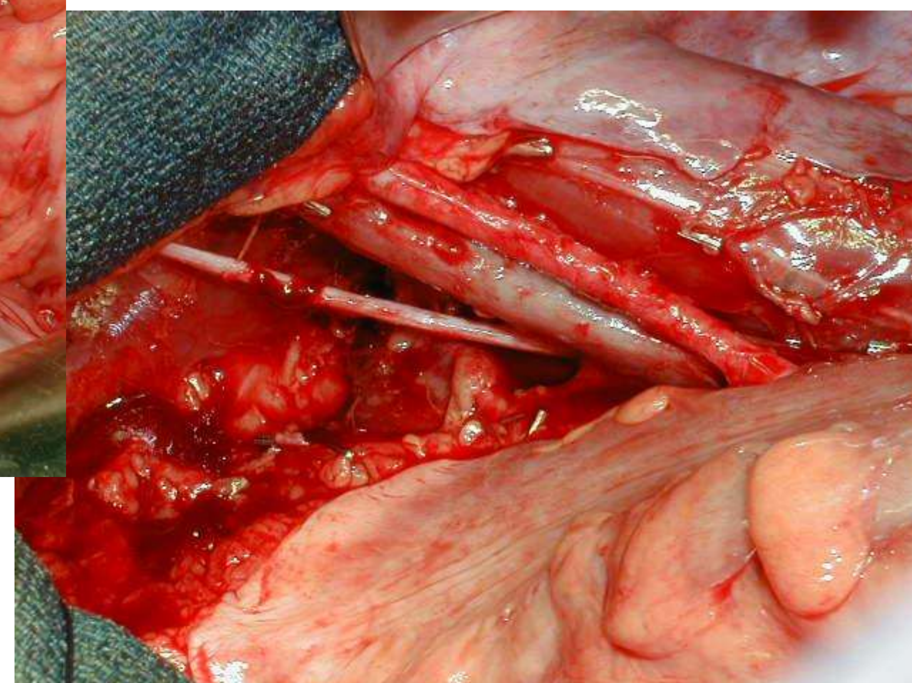
Nerve-sparing Female

(Burkhard, et al Crit Rev Oncol Hematol 57:255, 2006)



Extent of Lymph Node Removal





SWOG 1011 – Randomized Trial of Extended vs. Standard Lymph Node Dissection

T2,T3,T4a
Radical Cystectomy
(Neoadjuvant Ctx allowed)

RANDOMIZE

Standard PLND
External/internal iliac, obturator nodes

Extended LND
Standard + CI, pre sacral, distal IVC and aorta (optional)

N+ Adjuvant Chemotherapy

Male and Female Anatomy

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When is Radical Cystectomy Recommended

- To treat non-muscle invasive cancer that does not respond to intravesical therapy
- Muscle invasive cancer that has not spread outside the pelvis
- Healthy patient who can safely undergo the operation

Radical Cystectomy
Staging and Preparation

- Chest Xray, computed tomography (CT) scans, MRI, PET scan, Bone scan
  - Need to determine if there is spread to the lymph nodes and other organs – liver, lung and bone
- Pick a urinary diversion – Need to “re-route the plumbing” after bladder removal
- Meet with ostomy nurse - enterostomal therapist

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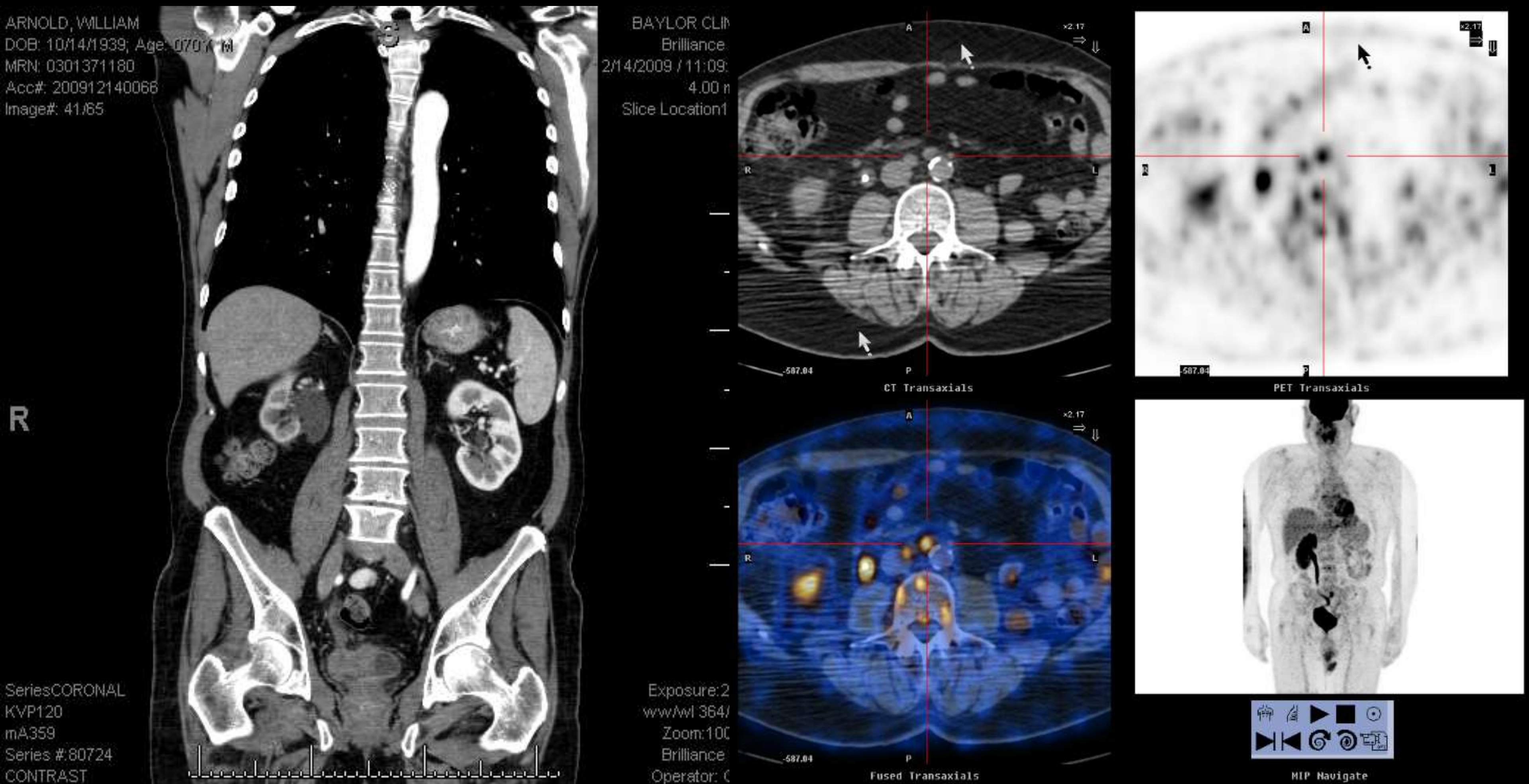

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Radical Cystectomy

- Choose a surgeon and a center that does a lot of them
- Both cancer outcome and recovery depend on making the right choice
  - Experience matters
  - Complications
  - Surgeon and hospital volume

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Radical Cystectomy

Does robotic surgery matter?

- No proof yet that cancer outcomes are the same as open surgery
- May be less bleeding
- May take longer
- Very complex operation and requires lots of robotic experience
- Need results of clinical trials in centers of excellence

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Bladder Sparing
Radiation Based Treatment

MaximumTURBT

↓

XRT (40Gy)
+
Concomitant Chemotherapy

↓

Cystoscopic response evaluation

CR → **Consolidation Chemo-radiation (64Gy) +/- adjuvant chemo**

Non-CR → **Radical Cystectomy +/- adjuvant chemo**

Courtesy of Jason Efstathiou, MD, PhD (MGH Radiation Oncology)

Selection is Key

<u>Tumor presentations with the highest success rates:</u>

- Solitary T2 or early T3 tumors < 6 cm
- No tumor-associated hydronephrosis
- Tumors allowing a visibly complete TURBT
- Invasive tumors not associated with extensive *carcinoma in situ*
- Adequate renal function to allow cisplatin concurrent with radiation
- TCC histology

Urinary Diversion

- Ileal conduit – bag on the outside
- Neobladder – option for both men and women – void through the urethra
- Continent stoma
  - Intestinal bladder on the inside
  - Catheterize through a small stoma
  - .

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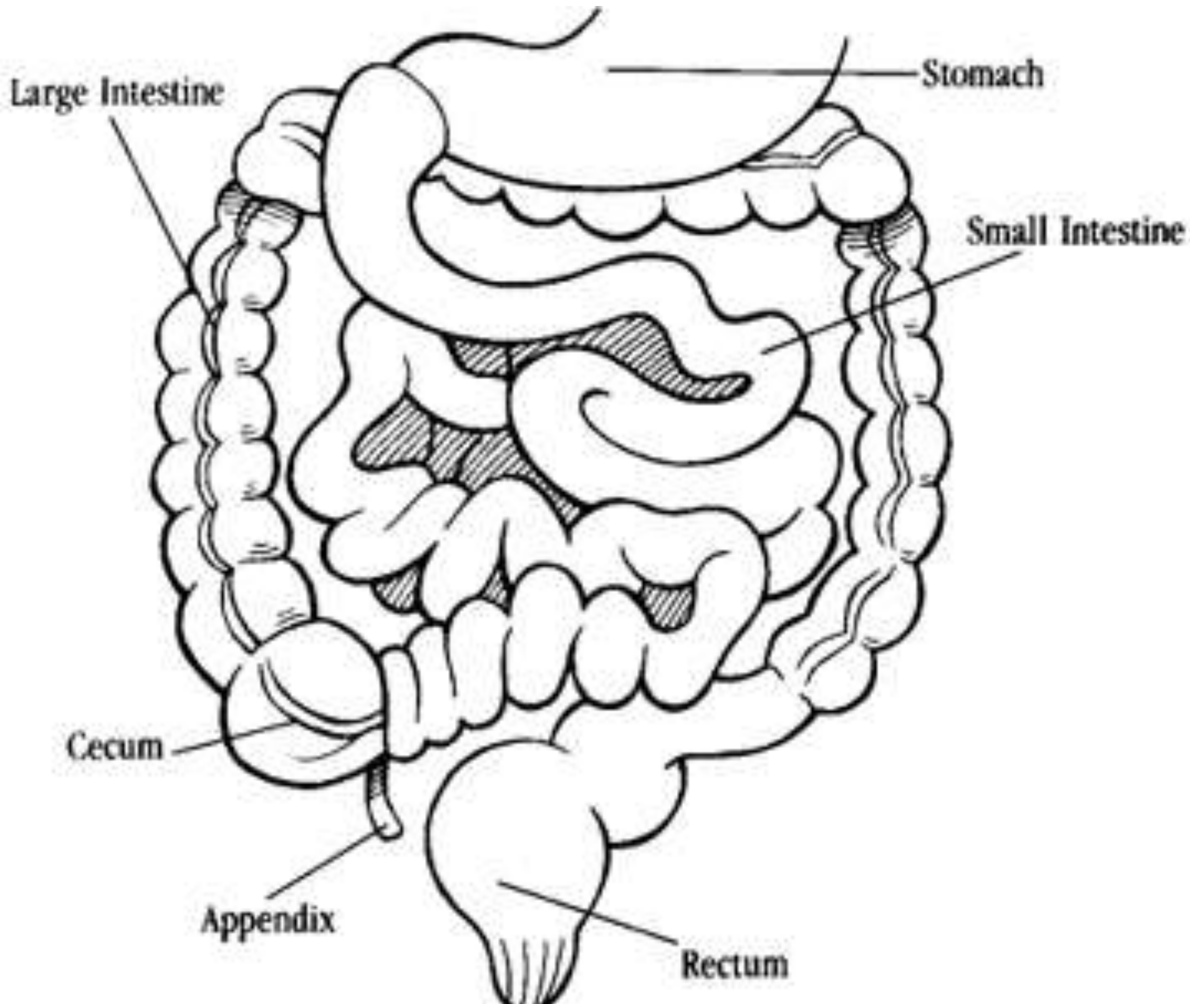

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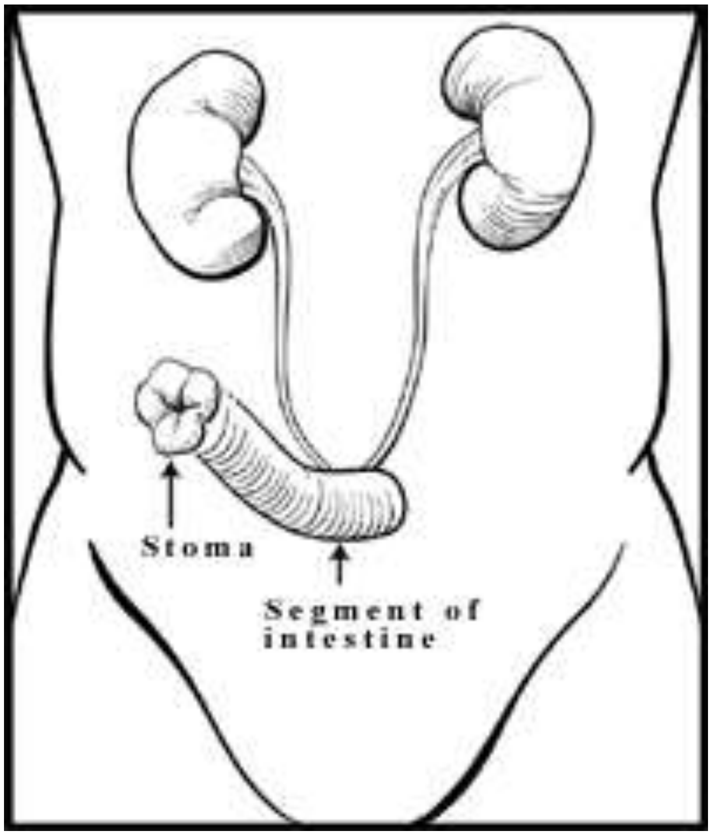
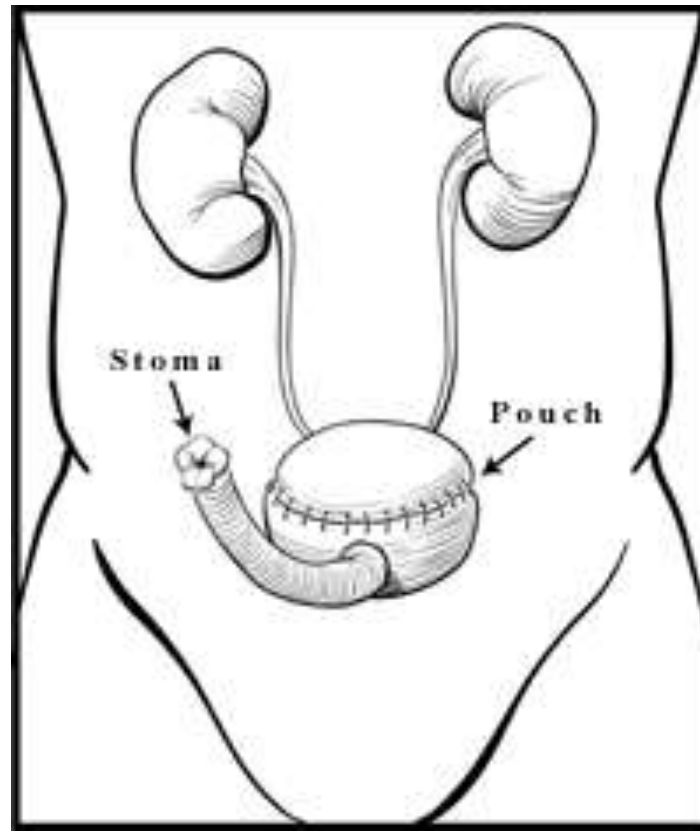
Conduit



Continent Catheterizable



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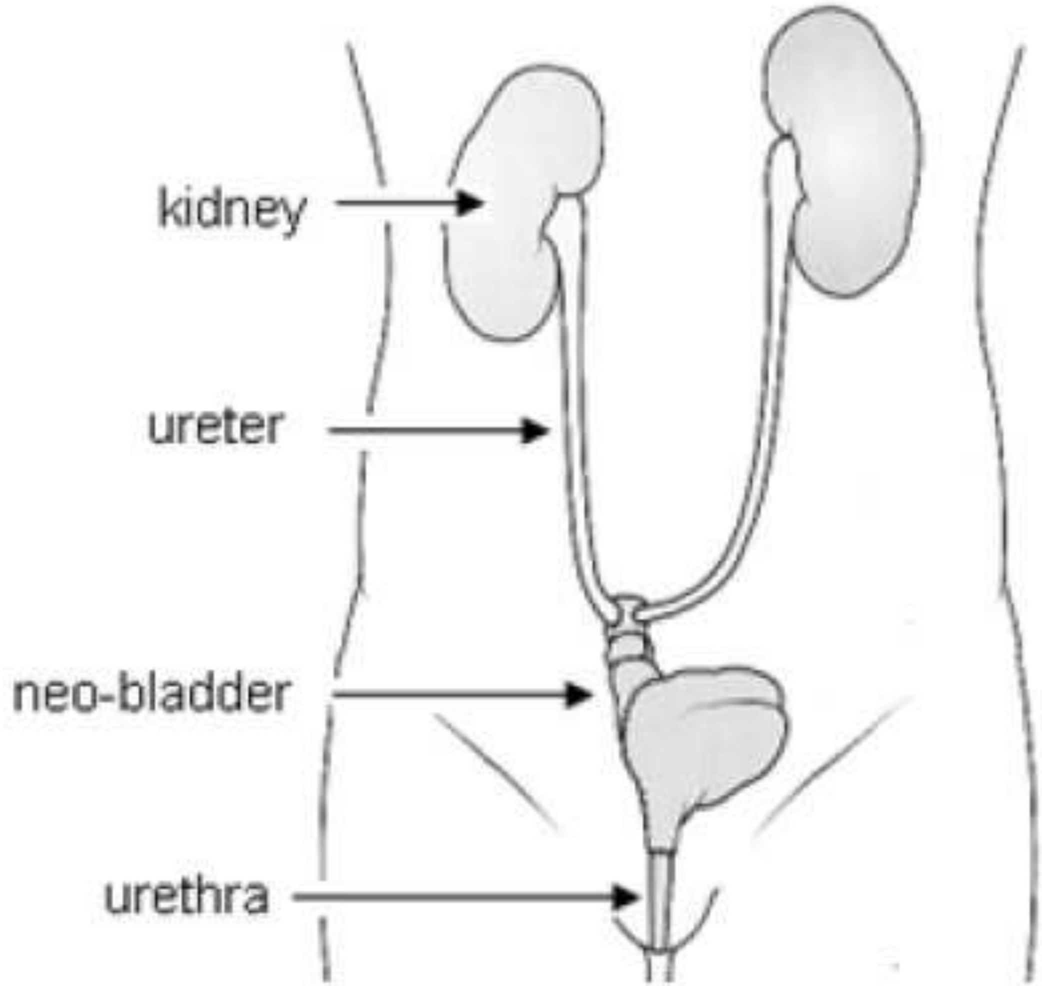
Neobladder



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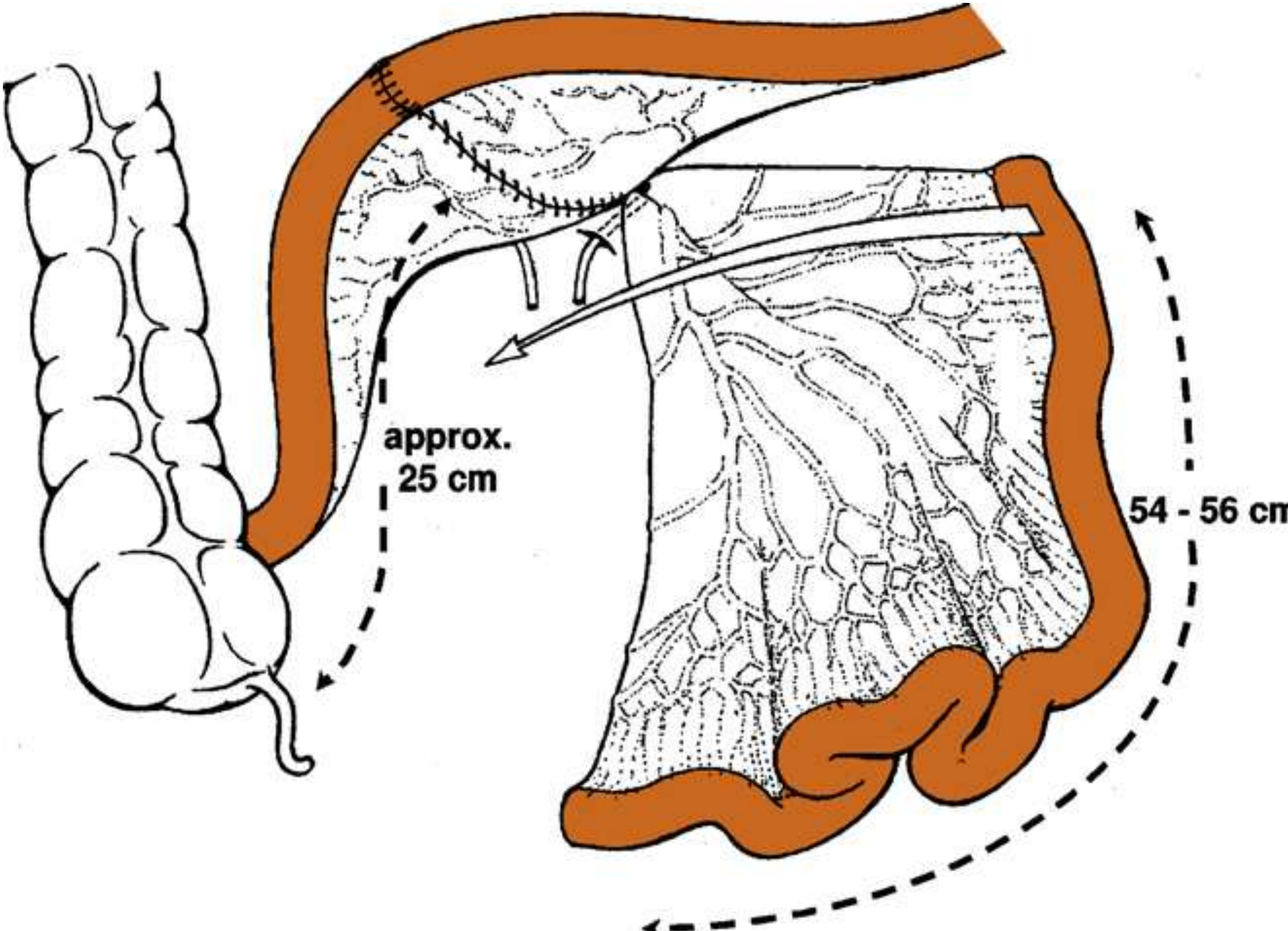
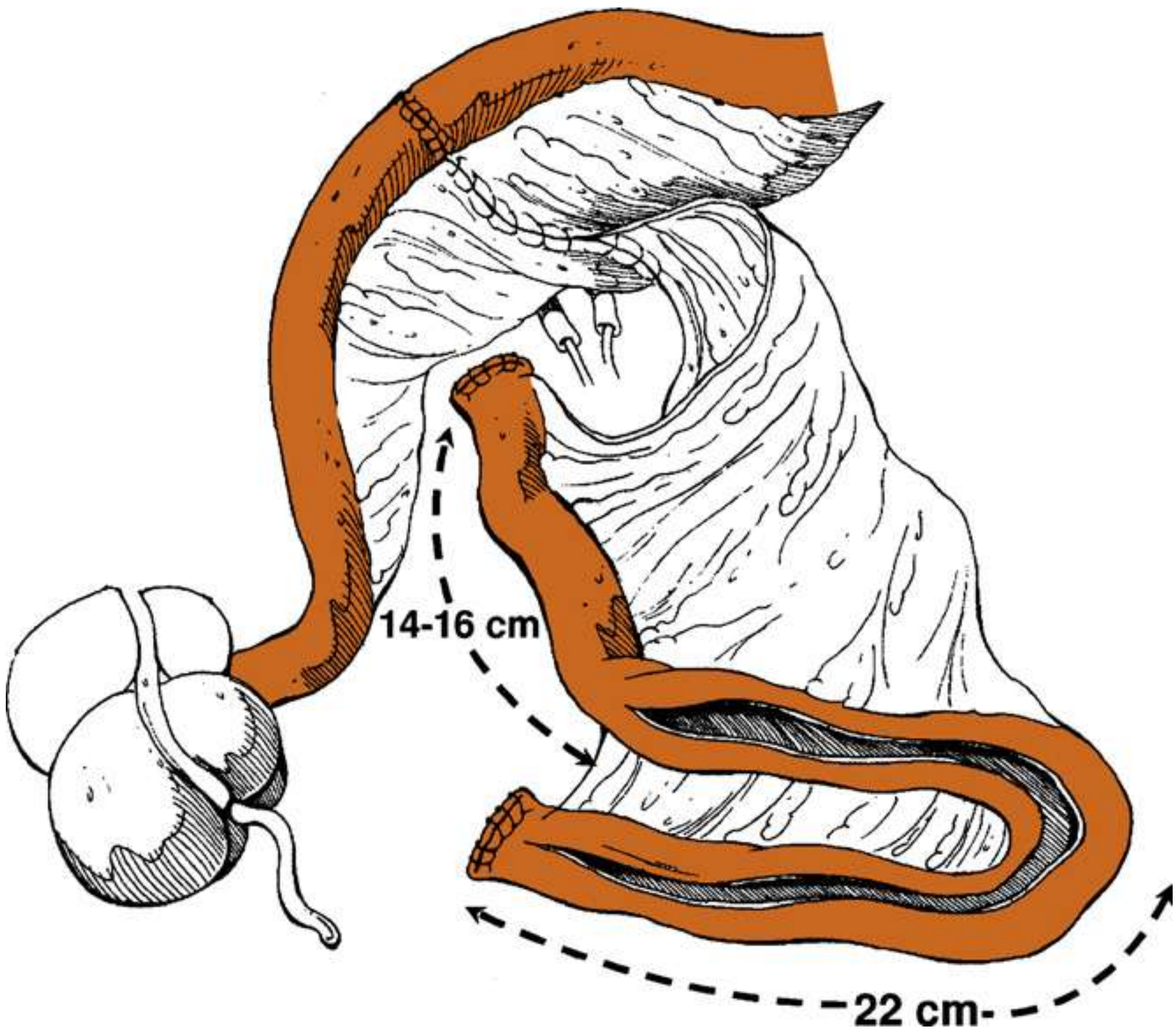


Dhar, et al Eur Url 2007



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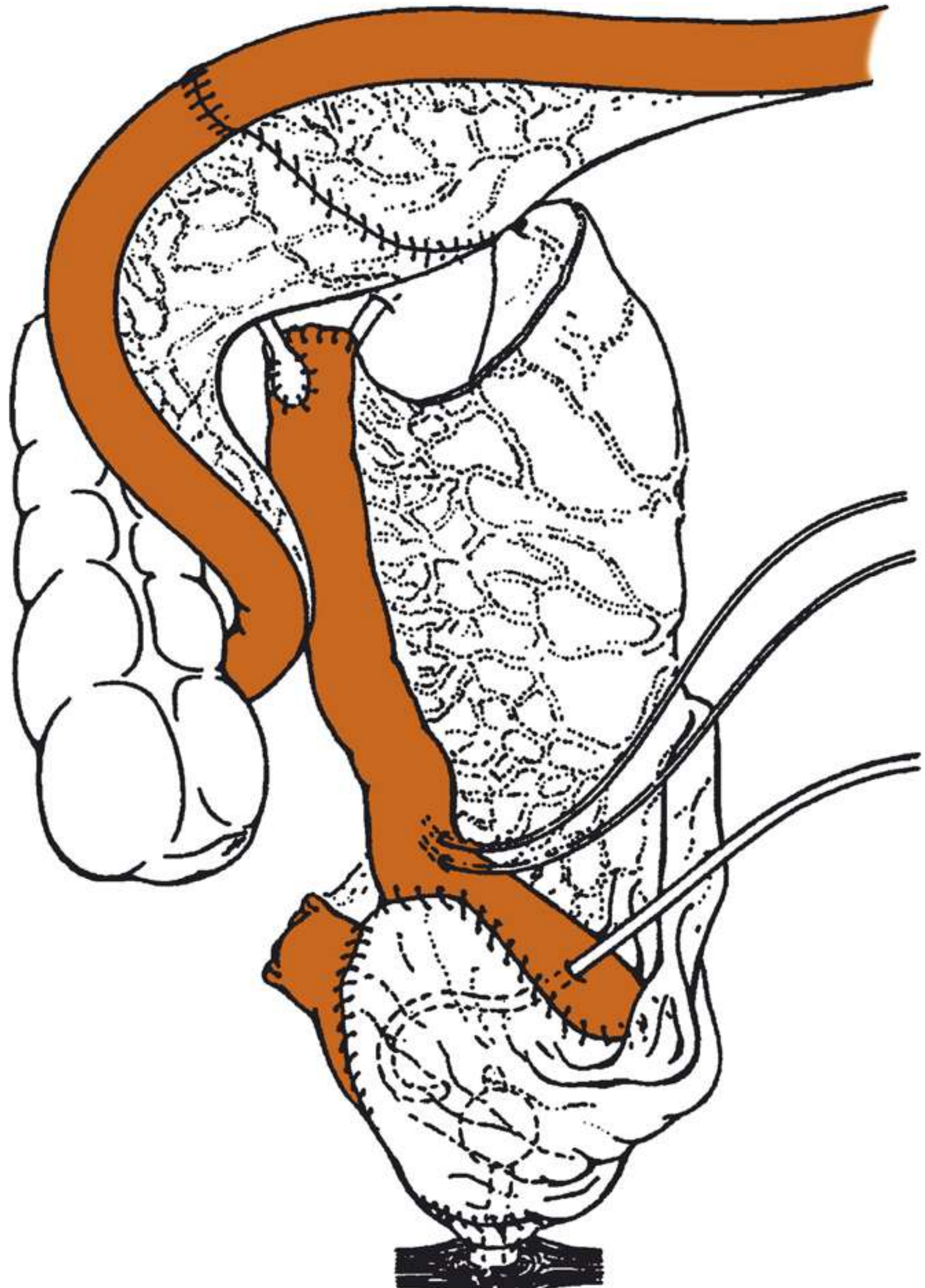
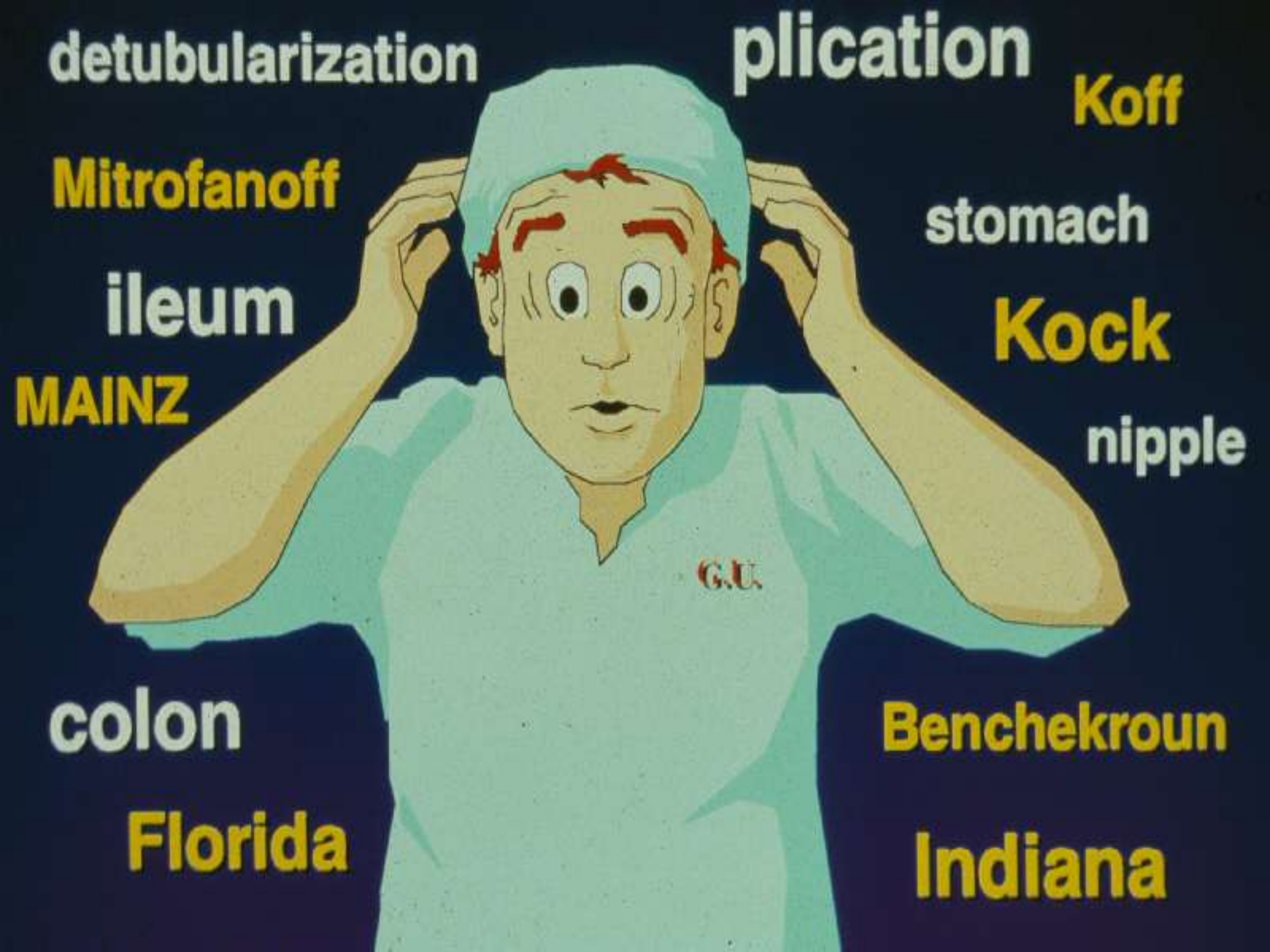


Dhar, et al Eur Url 2007


detubularization
plication
Koff
Mitrofanoff
stomach
ileum
Kock
MAINZ
nipple
G.U.
colon
Benchekroun
Florida
Indiana

Neobladder
Patient Selection

- Normal external sphincter
- No cancer at apical urethral margin in men or bladder neck/urethra in women
- Motivated patient
- Do not routinely exclude:
  - Elderly patients
  - Prior irradiation
  - P3b, P4 or N+ patients

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Neobladder Continence

Daytime	59/69 (86%)
< 65 y.o.	37/42 (88%)
> 65 y.o.	22/27 (81%)
Night	37/68 (54%)
< 65 y.o.	26/41 (63%)
> 65 y.o.	11/27 (41%)

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Neobladder
Experience in Women

- Patient selection critical
- Contraindications
  - Cancer at Bladder neck or urethra
- Preserve distal 2/3 of urethra and endopelvic fascia
- Increased incidence urinary retention requiring intermittent catheterization

Continent Cutaneous Diversion
Patient Selection

- Life expectancy > 1 year
- Strong self-image and desire to be “bag free”
- Manual dexterity
- Normal or nearly normal renal function
- Normal or nearly normal bowel function

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Continent Cutaneous Diversion

- Stoma site
  - Right lower quadrant typical
  - Umbilicus
    - Concealable
    - Very easy to perform
    - Great with obese patients
- Continence rates higher than with neobladder
- Lifelong requirement for intermittent catheterization

What you can do before and after surgery to help your recovery

- Stop smoking
- Exercise
- Healthy diet
- Evaluate and treat sexual dysfunction
- Optimize control of diabetes, blood pressure
- Cardiology evaluation
- Talk to other patients
- Attend a support group meeting

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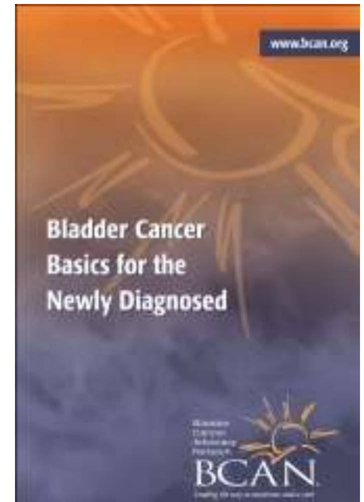
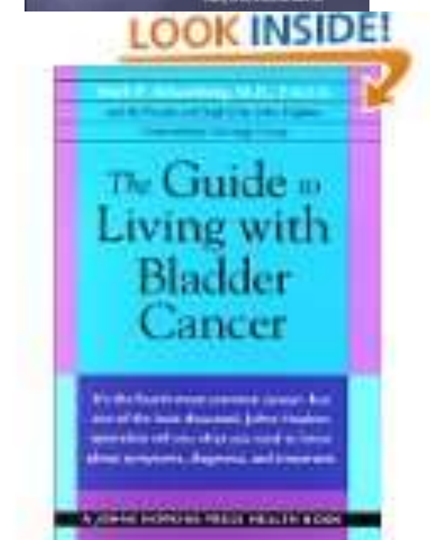
Post-operative Issues

- Older patient with co-morbidity
- Am I cured?
  - Will I need additional treatment
- Lots of tubes
- Control of urination
- Sexual function

Resources

- BCAN Brochure
- Guide to Living with Bladder Ca
- Talk to another patient
- Internet resources
  - American Cancer Society
    - www.cancer.org
  - National Cancer Institute (NCI)
    - www.nci.nih.gov
  - BCAN
    - www.bcan.org





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Clinical Trials

- Research database
- Tissue banking
  - Blood, urine, tumor tissue
- Targeted therapy drugs
- Imaging

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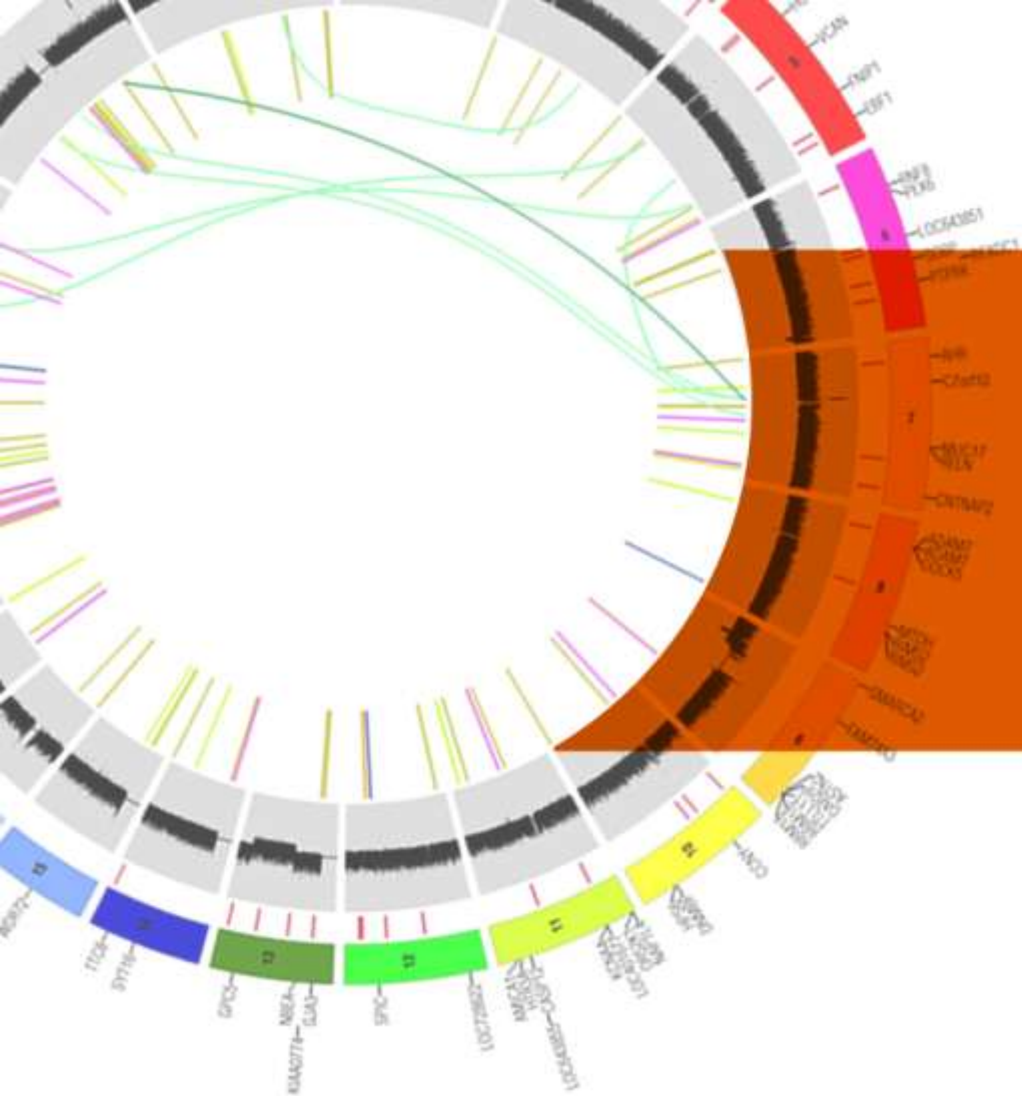


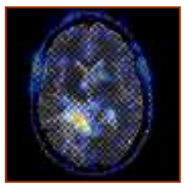
The Cancer Genome Atlas

The Cancer Genome Atlas

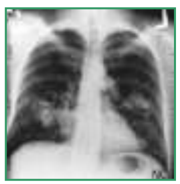
TCGA: "No Platform Left Behind"

25 forms of cancer

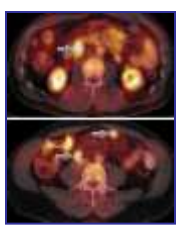
glioblastoma multiforme
(brain)



squamous carcinoma
(lung)



serous
cystadenocarcinoma
(ovarian)



Invasive Bladder Cancer

Biospecimen Core Resource with more than 150 Tissue Source Sites

6 Cancer Genomic Characterization Centers

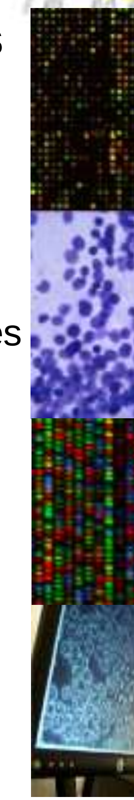
3 Genome Sequencing Centers

7 Genome Data Analysis Centers

Data Coordinating Center

Multiple data types

- Clinical diagnosis
- Treatment history
- Histologic diagnosis
- Pathologic report/images
- Tissue anatomic site
- Surgical history
- Gene expression/RNA sequence
- Chromosomal copy number
- Loss of heterozygosity
- Methylation patterns
- miRNA expression
- DNA sequence
- **RPPA (protein)**
- **Subset for Mass Spec**



Conclusions

- Radical cystectomy is safe and effective
- Surgeon and hospital experience matters
- Be informed and get healthy
- Talk to other patients and caregivers
- Consider clinical trial participation