SUO CURRICULUM OUTLINE *(2013 Update)*

Topic	**Author**
1. Clinical Research	Matthew Resnick
2. Bladder Cancer	Peter Black
3. Upper Tract Urothelial Carcinoma	Alex Kutikov
4. Renal Cell Carcinoma	Brian Lane
5. Testicular Cancer	Todd Morgan
6. Penile Cancer	Matthew Resnick
7. Prostate Cancer	Dan Barocas
8. Other Urologic Malignancies	Stephen Boorjian and Scott Eggener
a. Adrenal cancer	
b. Urethral cancer	
c. Paratesticular tumors	
d. Genitourinary sarcomas	

Clinical Research and Evidence Based Practice

***Overall Unit Objective*:**

At the end of this unit the SUO fellow should be familiar with the principles of clinical research, in particular as they relate to the design, ethics and statistical analysis of research study both from the perspective of the clinical investigator and that the urological oncologist seeking to apply the current best evidence to the care of an individual patient.

***Overall Learner Objectives*:**

Upon completion of the unit the fellow should be able to:

1. Design and interpret appropriate studies to address different types of clinical research questions.
2. Describe and understand integral components of clinical trials and observational studies.
3. Describe the strengths and weaknesses of various study designs
4. Define the ethical challenges and regulatory requirements for conducting clinical research.
5. Efficiently search the medical literature for the current best evidence.
6. Appraise clinical studies for their validity by recognizing potential sources of bias.
7. Interpret study results and appropriately apply them to the care of an individual patient.

Suggested Resources:

1. Designing Clinical Research: An Epidemiological Approach by Stephen B. Hulley et al. (2006)
2. User's Guide to the Medical Literature by Gordon Guyatt et al (2008)
3. Intuitive Biostatistics by Harvey Motulsky (1995)
4. Users' Guide to the Urological Literature series in Journal of Urology (2007-09)

Sections:

- **A. Evidence Based Medicine**
  - **a. Introduction**
    - i. Hierarchy of Evidence

ii. "Evidence alone is never enough"

b. How to Search the Medical Literature

i. Pre-appraised evidence
ii. Primary evidence
iii. Other search tools

c. How to interpret a study of therapy/prevention (Randomized controlled Trials, Cohort)

i. Core concepts
    1. Random error and precision
    2. Systematic error and accuracy
    3. Surrogate endpoints
    4. Composite endpoints
    5. Heath-related quality of life
    6. Direct and indirect costs
    7. Number needed-to-treat/harm (NNT/NNH)
    8. Adjustment for confounding in observational research (multivariable analysis, propensity score analysis, instrumental variable analysis)
ii. Validity Assessment (Randomization, allocation concealment, comparability at baseline, blinding, completeness of follow-up, early stopping for benefit)?
iii. Result Interpretation (Effect size and effect size precision)?
iv. Generalizability (Inclusion/exclusion criteria, balance of benefits and harm)

d. How to Interpret a Study of Harm (Cohort, Case-control Studies and Case Series)

i. Are the results valid (Inception cohort, Adjustment, Identification bias, Assessment bias, Completeness of follow-up)?
ii. Results interpretation (Strength of exposure and precision of estimate)?
iii. Applicability (Inclusion/exclusion criteria of study, length of follow-up, Magnitude of risk)
iv. Understand the issues confounding (known and unknown) in observational research
    1. Develop basic knowledge of methods to address confounding in observational research

e. How to Use a Study about Prognosis (Cohort Studies):

i. Core concepts:
    1. Inception cohort
    2. Risk factor versus prognostic factor
    3. Confounding variables
    4. Incidence and prevalence
    5. Odds ratio/Risk ratio
    6. Adjusted analysis
    7. Survival analysis
    8. Are the results valid (Representativeness and homogeneity of sample, Completeness of follow-up, objective and unbiased outcome assessments)
ii. Results Interpretation (Likelihood of outcomes over time, Precision of estimates)?
iii. Applicability (Inclusion/exclusion criteria, Adequacy of follow-up)

f. How to Use a Study about Diagnosis (Cohort Studies):

i. Core concepts
    1. Reference (gold) standard

2. Sensitivity and specificity, reviewer operator characteristic (ROC) curve
3. Probability revision (Pre-test and post-test probability)
4. Likelihood ratios
5. Test and treatment threshold

ii. Validity Assessment (Blinded comparison, spectrum bias, verification bias)
iii. Result interpretation (Likelihood ratios, sensitivity/specificity/positive and negative predictive value
iv. Applicability (Reproducibility, impact)

g. How to Use a Review Article (Systematic Reviews)

i. Core Concepts
1. Systematic versus narrative review
2. Meta-analysis
3. Summary statistic
4. Heterogeneity/homogeneity

ii. Validity assessment (Focused question, comprehensive search, assessment of study quality, reproducible study procedures)
iii. Results assessment (Homogeneity, Effect size estimates and precision)?
iv. Applicability (Relevance of endpoints to patient, benefit to risk ratio)

h. Clinical Practice Guidelines

i. Are the Recommendations Valid (AGREE criteria)?
ii. Method and basis of study inclusion in guideline development (expert opinion vs evidence based)
1. Scope and purpose
2. Stakeholder involvement
3. Rigor of development
4. Clarity and presentation
5. Applicability
6. Editorial independence

iii. Institute of Medicine (IOM) standards for developing trustworthy Clinical Practice Guidelines (CPGs)
1. Establishing transparency
2. Management of conflict of interest (COI)
3. Guideline development group composition
4. Clinical practice guideline-systematic review intersection
5. Establishing evidence foundations for and rating strength of recommendations
6. Articulation of recommendations
7. External review
8. Updating

iv. Interpretation of Recommendations (Clarity and strength)
v. Applicability

i. Develop basis for considering guideline implementation (Dissemination science)

B. Biostatistics

a. Types of statistical analyses

i. Statistical estimation
ii. Statistical hypothesis-testing

iii. Statistical modeling

b. P-values and confidence intervals

i. Binomial distribution
   1. Proportions
   2. Confidence interval of a proportion

ii. Gaussian (normal) distribution
   1. Mean
   2. Standard deviation
   3. Confidence interval and standard error of a mean

iii. Familiarity with reasons to use parametric and non-parametric tests

c. Statistical Significance and hypothesis-testing

i. Type I and II errors
ii. Alpha
iii. Beta
iv. Power

d. Sample size calculation

i. One mean
ii. Difference between two means
iii. One proportion
iv. Two proportions
v. Two survival curves

e. Correlation and Regression

i. Correlation
   1. Interpreting correlation coefficients
   2. P-values

ii. Regression
   1. Simple linear regression
   2. Multiple regression
   3. Logistic regression
   4. Nonlinear regression

f. Common statistical tests

i. Comparing two groups – The fellow should have a working knowledge of the appropriateness of basic statistical testing
   1. Student T-test
   2. Mann Whitney test
   3. Paired-t test
   4. Wilcoxon rank sum test
   5. Chi-Square test
   6. Fisher's exact test
   7. McNemar Chi-Square test
   8. Mantel-Haenszel Chi-Square test

ii. Comparing three or more groups
   1. Analysis of Variance (ANOVA)
   2. One-way ANOVA
   3. Multiple comparison post tests (i.e. Bonferroni, Tukey)
   4. Repeated measures ANOVA
   5. Nonparametric ANOVA
   6. Two-way ANOVA

iii. Correlation
   1. Spearman rank correlation
   2. Pearson correlation

iv. Multiple linear regression
v. Logistic regression
vi. Survival analysis
    1. Kaplan-Meier analysis
        a. Log-rank test
    2. Cox proportional hazards regression
    3. Competing-risks analysis
vii. Nonlinear regression

C. Designing a cohort study or clinical trial

i. Hypothesis testing
ii. Selecting the null and alternate hypothesis
iii. Selection of optimal study design
    1. Familiarity with the strengths and limitations of study designs (RCT, cohort, case-control, nested case-control, etc.)
iv. Identifying primary and secondary objectives
v. Sampling techniques (convenience, cluster, random, population based)
vi. Assessment of effect size and calculating sample size requirements
vii. Clinical trials
    1. Phase I, II and III trial design
    2. Underlying concepts for trial design
    3. Alternate trial designs
    4. Blinding
    5. Protocol development
    6. Recruitment strategies
    7. Toxicity criteria
        a. Standardized NIH common toxicity criteria
        b. Standardized scales for surgical complication assessment (i.e. Clavien-Dindo)
    8. Stopping rules
    9. Interim analyses and their importance
    10. Creation and composition of a Data Safety Monitoring Board
    11. Infrastructure and resources needed for starting up a clinical trial
    12. Interaction with FDA and other federal agencies
        a. Elements of an Investigational New Drug application
        b. Approval process for devices and tests
    13. Budgeting for clinical trials
    14. Co-operative groups and their role in clinical trial development

D. Databases

a. Publicly available databases
b. Basics of database structure
c. Advantages and disadvantages of using publicly available administrative datasets
    i. Recognizing strengths and limitations to the use of administrative data
d. How to set up an institutional database
    i. Bioinformatics – basic concepts
    ii. Setting up and accessing an institutional tissue repository
e. Institutional infrastructure needed for setting up a database
f. Designing forms and setting up process for building and maintaining a database

g. Pooling of institutional datasets
h. Available templates for building databases (eg. Caisis, RedCap)
i. Data protection and collaboration

E. Quality of life studies

a. Basis and importance of health-related quality of life (HRQOL) studies
b. Available instruments relevant for HRQOL studies in cancer
    i. Understand differences between general and disease-specific HRQOL instruments
    ii. Have basic familiarity with "off the shelf" general and disease-specific HRQOL instruments (SF-36, FACT, EPIC, UCLA-PCI, FACT-VCI, etc.)
c. Concepts in design and structure of HRQOL instrument
    i. Understanding basic concepts of scale development
    ii. Assessment of reliability and validity (face, content, construct, criterion)
d. Measurement of patient satisfaction
e. Measurement of utilities

F. Co-operative groups and funding

a. Oncology co-operative group structure and CTEP
b. SUO clinical trials consortium
c. How to get involved in a co-operative group
d. Benefits and pitfalls of co-operative group involvement
e. Funding opportunities for clinical research
f. Early career funding opportunities
g. Grant writing tips
h. Instructional courses and other resources for developing early career investigators

Bladder Cancer

1. Anatomy and pathology of bladder cancer

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

1. Recognize and demonstrate an understanding of the normal anatomy and physiology of the bladder
2. Understand the relationship of the anatomy of the bladder to surrounding organs, as pertains to gender-specific differences
3. Understand and identify the pathologic difference between normal bladder urothelium and bladder carcinoma
4. Identify the grade and stage of bladder cancer
5. Understand and identify the different histologic variants of bladder carcinoma

Contents:

1. Normal gross anatomy of the male and female bladder, including surgical relationships to pelvic floor, prostate, uterus, and vagina
2. Lymphatic drainage of the bladder, prostate, urachus, and urethra
3. Relationship of the bladder to the neuroanatomy of the pelvis
4. Histology of normal bladder and benign lesions of the bladder
    a. Normal urothelium

b. Papilloma
c. Inverted papilloma
d. Squamous and glandular metaplasia
e. Cystitis cystica
f. Cystitis glandularis
g. Nephrogenic adenoma
h. Malakoplakia
i. Inflammation

5. Histology of urothelial carcinoma grading[1]

    a. WHO / ISUP classification 1973: Grade 1, 2, 3
    b. WHO / ISUP classification 2004: Low vs. high grade

6. Histology of non-invasive bladder cancer
    a. Papillary urothelial neoplasm of low malignant potential (PUNLMP)
    b. Ta bladder cancer
    c. Carcinoma in situ

7. Histology of invasive urothelial carcinoma[2]
    a. Lamina propria invasion, with understanding of T1 substaging based on muscularis mucosa invasion
    b. Muscularis propria invasion
    c. Lymphovascular invasion – identify and understand prognostic significance[3]

8. Histology of variants of urothelial carcinoma
    a. Squamous cell carcinoma
    b. Adenocarcinoma
    c. Squamous and glandular differentiation of urothelial carcinoma
    d. Micropapillary bladder cancer
    e. Small cell carcinoma
    f. Sarcomatoid carcinoma/carcinosarcoma
    g. Lymphoepithelial-like carcinoma
    h. Nested variant
    i. Others

2. Epidemiology of bladder cancer

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

1. Demonstrate sufficient knowledge and understanding of the incidence and prevalence of bladder cancer, including gender differences

2. Demonstrate a clear understanding of the risk factors associated with the development of bladder cancer

Contents:

1. Epidemiology of bladder cancer, including typical age of onset, as well as racial, gender and ethnic demographics[4,5]

2. Risk factors for bladder cancer[6-9]
    a. Smoking
    b. Industrial exposures
    c. Other risk factors (radiation, others)

3. Presenting signs and symptoms, with relative frequencies[10-14]

4. Genetic Epidemiology

3. Diagnosis and staging of bladder cancer

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

1. Be able to describe the indications and appropriate testing for evaluation of signs and symptoms associated with bladder cancer.

2. Be able to interpret diagnostic test results, including imaging studies and urinary markers, and understand the limitations of each.

3. Understand and be familiar with the updated staging classification of bladder tumors

4. Be able to interpret clinical and pathologic factors that determine risk stratification of non-muscle invasive and muscle-invasive disease.

Contents:

1. AUA Guidelines for workup of asymptomatic microscopic hematuria[10]

2. Efficacy of cystoscopy and voided urine cytology in different stages and grades of NMI bladder cancer (including false positive and false negative results)

3. Urinary markers including cytology, BTA, NMP22 and Uroyvision FISH tests, as well as emerging urinary markers[15-17]
    a. Biochemistry or molecular biology of each marker
    b. Diagnostic efficacy in different stages and grades of urothelial cancer

4. Impact of new cystoscopic technologies including fluorescent cystoscopy (Cysview™)[18,19] and narrow band imaging[20] for the detection and resection of NMI bladder cancer.

5. Indications for and evaluation of CT scan, CT Urography, MRI, bone scans, chest imaging and PET Scan in bladder cancer patients[21-23]

6. Indications for resection of tumor and re-resection of tumor after initial diagnosis

7. Indications for and efficacy of EUA (examination under anesthesia) and correlation with clinical and pathologic staging

4. Management of non-muscle invasive bladder cancer

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

1. Demonstrate knowledge and understanding of indications, management and complications associated with transurethral surgery of the bladder.

2. Master endoscopic surgical procedures required to evaluate the bladder for neoplasm, including cystoscopy, retrograde pyelography, ureteroscopy, bladder biopsy, urethral biopsy, and transurethral resection of tumors in the bladder.

3. Understand the role and method of repeat transurethral resection.

4. Understand the role and method of examination under anesthesia (EUA).

5. Understand the indications, contra-indications, and scheduling of intravesical therapy for non-muscle invasive bladder cancer.

6. Recognize the potential adverse side effects associated with a specific intravesical agent and the management of the adverse side effects.

7. Understand and describe anticipated results from the use of intravesical therapy, and be knowledgeable about the methods and frequency of the surveillance protocols.

8. Understand the importance of considering patient factors (i.e. competing causes of mortality) in treatment decisions

Contents:

a. Risk stratification of non-muscle invasive bladder cancer[24]

b. Indication for bladder biopsy[25]
    i. Directed versus random biopsies
    ii. Biopsy of the prostatic urethra
    iii. Biopsies of the tumor base

c. Surgical technique for transurethral resection of bladder tumors (TURBT)[26]
    i. Goals of resection
    ii. Factors influencing efficacy

iii. Perioperative management
iv. Risks and complications of TURBT and their management[27]
v. Selection of patients for 'staged TURBT' for appropriate clearance of tumors
vi. Interpretation of pathology report from TURBT and understanding of markers of adequate resection

d. Role of repeat TURBT[28]

e. Role of peri-operative chemotherapy[29]
i. Selection of appropriate chemotherapeutic agent
ii. Timing and appropriate dosing
iii. Relative and absolute contraindications
iv. Associated adverse effects

f. Immunotherapy (BCG +/- interferon) and chemotherapy (mitomycin C, others)[26,30-35]
i. Indications and efficacy in each stage/grade of disease
ii. Dose, concentration and dosing schedule of each agent
- Including maintenance therapy[36]
iii. Factors associated with improved efficacy (i.e. restriction of urinary volume)[37]
iv. Understanding of new technologies such as electromotive delivery of intravesical chemotherapy[38,39]
v. Risks and complications[40-42]
vi. Management of complications of therapy
vii. Appropriate strategies to adjust therapy to adverse effects to optimize duration of therapy (i.e. dose reduction with BCG).
viii. Timing of repeat cystoscopy and biopsy
ix. Special considerations
i. Immunosuppression
ii. Variant histology (i.e. micropapillary)[43]
x. Randomized comparative studies and meta-analyses

g. BCG Failure[44]
i. Differentiation between early and late failures (>12 months disease free interval) and its prognostic significance
ii. Differentiation in determination of response in Cis versus high grade T1 disease
iii. Differentiation between BCG refractory, BCG resistant, BCG intolerant and BCG relapsing disease and their significance
iv. Management of BCG Failure
1. Role of radical cystectomy
2. Role of second line intravesical therapy and inherent risks and limitations

h. Post-TURBT surveillance
i. Timing and frequency of cystoscopy
ii. Timing and frequency of upper tract imaging

i. Role of radical cystectomy in NMI bladder cancer.
    i. Patients with tumors too extensive for TURBT
    ii. Patients with NMI at high-risk for progression –i.e. identify adverse prognostic features in patients with high-grade T1 disease – associated CIS, LVI, tumor size/multifocality
    iii. Risk of understaging
    iv. Efficacy
    v. Risks and complications
    vi. Extent of node dissection with respect to stage of bladder cancer

j. Guidelines for management of non-muscle invasive bladder cancer[45,46]

5. Management of muscle-invasive bladder cancer

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

1. Demonstrate knowledge and understanding of indications, management and complications associated with radical cystectomy surgery of the bladder (intra-operative, post-operative and long-term). Be familiar with long-term outcomes following surgery, and prognostic variables associated with survival.

2. Demonstrate knowledge and understanding of indications, management and complications associated with partial cystectomy (intra-operative, postoperative and long-term). Be familiar with long-term outcomes following partial cystectomy, and prognostic variables associated with survival.

3. Master surgical procedures related to radical cystectomy for bladder cancer

    a. Understand the extent and limits of node dissection
    b. Understand the optimal methods of resection of the urinary bladder with specific reference to reducing positive margins and improving quality of life (i.e. neurovascular bundle preservation)

4. Demonstrate knowledge and understanding of indications, technique, management and complications of different types of urinary diversions

a. Ileal conduit urinary diversion
b. Orthotopic continent urinary diversion[47]
c. Cutaneous continent urinary diversion

5. Understand the indications, contra-indications, and scheduling of radiation therapy for bladder cancer. Be familiar with long-term outcomes following radiation, and prognostic variables associated with survival.

6. Recognize the potential adverse side effects associated with radiation therapy and the management of side effects.

7. Understand the role and outcomes for management of muscle-invasive bladder cancer with transurethral resection alone

8. Understand the importance of considering patient factors (i.e. competing causes of mortality) in treatment decisions

Contents:

1. Indication for radical cystectomy and partial cystectomy
    a. Role of pre-operative biopsies
    b. Biopsy of the prostatic urethra

2. Partial cystectomy[48]
    a. Goal of partial cystectomy
    b. Factors influencing efficacy
    c. Intraoperative assessment of margin status
    d. Perioperative management
    e. Risks and complications of partial cystectomy their management

3. Radical Cystectomy
    a. Goal of radical cystectomy
    b. Factors influencing efficacy
    c. Perioperative management
    d. Risks and complications of radical cystectomy and their management
    e. Long-term outcomes and prognostic variables associated with survival – clinicopathologic, molecular

4. Surgical technique for urinary diversions
    a. Goal of Urinary Diversions
    b. Factors influencing choice of diversion

c. Perioperative management
d. Risks and complications of urinary diversions and their management

5. Trimodal therapy for bladder cancer[49,50]
    a. Patient selection
        i. Appropriate staging
        ii. Random biopsies
    b. Multidisciplinary management
        iii. Concomitant chemotherapy
        iv. Doses and dose schedules for radiation
        v. Role of re-resection and possible interim re-biopsy
        vi. Role of salvage radical cystectomy
        vii. Cystoscopic surveillance post-radiation
    c. Expected outcomes
        i. Toxicity
            1. Early
            2. Late (including bladder dysfunction)
        ii. Rate of bladder preservation
        iii. Oncologic outcomes
        iv. Surgical management of NMI recurrences

6. Radiation for chemo-ineligible patients

7. Palliative radiation
    a. Indications
    b. Expected outcomes
    c. Dose and fractionation

8. Transurethral resection alone for muscle-invasive bladder cancer
    a. Indications
    b. Technique
    c. Outcomes

6. Chemotherapy for bladder cancer

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

1. Understand the indications, contra-indications, and scheduling of systemic chemotherapy for invasive bladder cancer.

2. Recognize the utility of systemic chemotherapy in the neoadjuvant and adjuvant setting and appropriate patient selection for each.

3. Understand the indications, contra-indications, and scheduling of systemic chemotherapy for metastatic bladder cancer.

Contents:

1. Use of perioperative chemotherapy for high-risk, resectable, muscle-invasive disease (cT2-4aN0M0)
    a. Indications, Sequence and Timing of multi-modality management
    b. Pros and cons of neoadjuvant and adjuvant chemotherapy in comparison – be familiar with published randomized clinical trial data, as well as noted limitations of these studies[51-55]
    c. Expected outcomes
        i. Toxicity
            1. Acute
            2. Perioperative
            3. Long-term
        ii. Efficacy
        iii. Understand the rationale for radical cystectomy following neoadjuvant chemotherapy – i.e. be familiar with the data regarding the outcomes for patients who do not undergo cystectomy following chemotherapy

2. Use of chemotherapy for potentially resectable disease (i.e. cT4bNx or cTxN+ or oligometastatic disease)[56-58]
    a. Indications, Sequence and Timing of multi-modality management
    b. Identifying appropriate candidates for surgical consolidation
    c. Expected outcomes
        i. Toxicity
            1. Acute
            2. Perioperative
            3. Long-term
        ii. Efficacy
3. Chemotherapy for metastatic disease
    a. First line
    b. Second line

4. Standard Chemotherapy Regimens
    a. "Fit" patients (high performance status, adequate renal, etc.)
        i. Agents, Regimens, rationale for combination[25]

ii. Expected toxicity and management
iii. Efficacy benchmarks

b. "Unfit" patients (i.e. poor performance status, poor renal function, pre-existing neuropathy, pre-existing hearing loss, advanced age)
   i. Agents, Regimens, rationale for combination
   ii. Expected toxicity and management
   iii. Efficacy benchmarks

c. Small cell histology
   i. Agents, Regimens, rationale for combination[59]
   ii. Expected toxicity and management
   iii. Efficacy benchmarks
   iv. Consolidative surgery versus radiation therapy

Important publications

1. Sauter G, Algaba F, Amin M, et al: Tumours of the urinary system: non-invasive urothelial neoplasias, in Eble JN, Sauter G, Epstein Jl, et al (eds): WHO classification of classification of tumours of the urinary system and male genital organs. Lyon, IARCC Press, 2004

2. Sobin LH, Wittekind C: Urinary Bladder, International Union against Cancer (UICC):TNM: Classification of Malignant Tumors. New York, Wiley-Liss, 1997, pp 187-190

3. Streeper NM, Simons CM, Konety BR, et al: The significance of lymphovascular invasion in transurethral resection of bladder tumour and cystectomy specimens on the survival of patients with urothelial bladder cancer. BJU Int 103:475-9, 2009

4. Fleshner NE, Herr HW, Stewart AK, et al: The National Cancer Data Base report on bladder carcinoma. The American College of Surgeons Commission on Cancer and the American Cancer Society. Cancer 78:1505-13, 1996

5. Siegel R, Naishadham D, Jemal A: Cancer statistics, 2012. CA Cancer J Clin 62:10-29, 2012

6. Kaldor JM, Day NE, Kittelmann B, et al: Bladder tumours following chemotherapy and radiotherapy for ovarian cancer: a case-control study. Int J Cancer 63:1-6, 1995

7. Kantor AF, Hartge P, Hoover RN, et al: Urinary tract infection and risk of bladder cancer. Am J Epidemiol 119:510-5, 1984

8. Morrison AS: Advances in the etiology of urothelial cancer. Urol Clin North Am 11:557-66, 1984

9. Morrison AS, Cole P: Epidemiology of bladder cancer. Urol Clin North Am 3:13-29, 1976

10. Davis R, Jones JS, Barocas DA, et al: Diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adults: AUA guideline. J Urol 188:2473-81, 2012

11. Messing EM, Vaillancourt A: Hematuria screening for bladder cancer. J Occup Med 32:838-45, 1990

12. Messing EM, Young TB, Hunt VB, et al: Comparison of bladder cancer outcome in men undergoing hematuria home screening versus those with standard clinical presentations. Urology 45:387-96; discussion 396-7, 1995

13. Schwalb DM, Herr HW, Fair WR: The management of clinically unconfirmed positive urinary cytology. J Urol 150:1751-6, 1993

14. Varkarakis MJ, Gaeta J, Moore RH, et al: Superficial bladder tumor. Aspects of clinical progression. Urology 4:414-20, 1974

15. Grossman HB, Messing E, Soloway M, et al: Detection of bladder cancer using a point-of-care proteomic assay. JAMA 293:810-6, 2005

16. Grossman HB, Soloway M, Messing E, et al: Surveillance for recurrent bladder cancer using a point-of-care proteomic assay. JAMA 295:299-305, 2006

17. Fritsche HM, Burger M, Dietmaier W, et al: Multicolor FISH (UroVysion) facilitates follow-up of patients with high-grade urothelial carcinoma of the bladder. Am J Clin Pathol 134:597-603, 2010

18. Fradet Y, Grossman HB, Gomella L, et al: A comparison of hexaminolevulinate fluorescence cystoscopy and white light cystoscopy for the detection of carcinoma in situ in patients with bladder cancer: a phase III, multicenter study. J Urol 178:68-73; discussion 73, 2007

19. Grossman HB, Stenzl A, Fradet Y, et al: Long-term decrease in bladder cancer recurrence with hexaminolevulinate enabled fluorescence cystoscopy. J Urol 188:58-62, 2012

20. Naselli A, Introini C, Timossi L, et al: A randomized prospective trial to assess the impact of transurethral resection in narrow band imaging modality on non-muscle-invasive bladder cancer recurrence. Eur Urol 61:908-13, 2012

21. Husband JE, Olliff JF, Williams MP, et al: Bladder cancer: staging with CT and MR imaging. Radiology 173:435-40, 1989

22. Sager EM, Talle K, Fossa SD, et al: Contrast-enhanced computed tomography to show perivesical extension in bladder carcinoma. Acta Radiol 28:307-11, 1987

23. Vargas HA, Akin O, Schoder H, et al: Prospective evaluation of MRI, (1)(1)C-acetate PET/CT and contrast-enhanced CT for staging of bladder cancer. Eur J Radiol 81:4131-7, 2012

24. Sylvester RJ, van der Meijden AP, Oosterlinck W, et al: Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORTC risk tables: a combined analysis of 2596 patients from seven EORTC trials. Eur Urol 49:466-5; discussion 475-7, 2006

25. van der Meijden A, Oosterlinck W, Brausi M, et al: Significance of bladder biopsies in Ta,T1 bladder tumors: a report from the EORTC Genito-Urinary Tract Cancer Cooperative Group. EORTC-GU Group Superficial Bladder Committee. Eur Urol 35:267-71, 1999

26. Kulkarni GS, Hakenberg OW, Gschwend JE, et al: An updated critical analysis of the treatment strategy for newly diagnosed high-grade T1 (previously T1G3) bladder cancer. Eur Urol 57:60-70, 2010

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28. Herr HW: The value of a second transurethral resection in evaluating patients with bladder tumors. J Urol 162:74-6, 1999

29. von der Maase H, Sengelov L, Roberts JT, et al: Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patients with bladder cancer. J Clin Oncol 23:4602-8, 2005

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31. Morales A, Eidinger D, Bruce AW: Intracavitary Bacillus Calmette-Guerin in the treatment of superficial bladder tumors. J Urol 116:180-3, 1976

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Upper Tract Urothelial Carcinoma

1. Anatomy and pathology

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

6. Recognize and demonstrate an understanding of the normal anatomy and physiology of the upper collecting systems and ureters

7. Understand the relationship of the anatomy of the upper tract collecting system and ureters to surrounding organs, as pertains to gender-specific differences

8. Understand and identify the pathologic difference between normal urothelium and urothelial carcinoma

9. Identify the grade and stage of urothelial cancer

10. Understand and identify the different histologic variants of urothelial carcinoma

Contents:

9. Normal gross anatomy of the male and female upper urinary tracts, including surgical relationships to renal parenchyma, great vessels, adrenal gland, retroperitoneal musculature, pelvic floor, prostate, uterus, ovaries, ovarian blood supply, and vagina

10. Lymphatic drainage of the kidneys and ureters

11. Relationship of the kidneys and ureters to the neuroanatomy of the retroperitoneum

12. Histology of normal urothelium

13. Histology of urothelial carcinoma grading

    a. WHO / ISUP classification 1973: Grade 1, 2, 3
    b. WHO / ISUP classification 2004: Low vs. high grade

14. Histology of non-invasive urothelium
    a. Papillary urothelial neoplasm of low malignant potential (PUNLMP) and its virtual non-existence in the upper tracts
    b. Ta urothelial carcinoma
    c. Carcinoma in situ

15. Histology of invasive urothelial carcinoma
    a. Lamina propria invasion
    b. Muscularis propria invasion
    c. Lymphovascular invasion – identify and understand prognostic significance

16. Histology of variants of urothelial carcinoma
    a. Squamous and glandular differentiation of urothelial carcinoma
    b. Micropapillary cancer
    c. Small cell carcinoma
    d. Sarcomatoid carcinoma/carcinosarcoma
    e. Lymphoepithelial-like carcinoma
    f. Nested variant
    g. Pure non-urothelial histology (e.g. squamous or adenocarcinoma) are rare
    h. Collecting duct carcinoma may share embryologic origins with urothelial carcinoma

2. Epidemiology of upper tract urothelial carcinoma

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

3. Demonstrate sufficient knowledge and understanding of the incidence and prevalence of upper tract urothelial carcinoma

4. Demonstrate a clear understanding of the risk factors associated with the development of upper tract urothelial carcinoma

Contents:

5. Epidemiology of upper tract urothelial cancer, including typical age of onset, as well as racial, gender and ethnic demographics

6. Risk factors for upper tract urothelial cancer
    a. Bladder cancer history
    b. Smoking
    c. Industrial exposures
    d. Other risk factors (radiation, inflammation, Balkan nephropathy, aristolochic acid)

7. Presenting signs and symptoms

8. Familial / hereditary Epidemiology (esp. Lynch syndrome)

3. Diagnosis and staging of upper tract urothelial carcinoma

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

5. Be able to describe the indications and appropriate testing for evaluation of signs and symptoms associated with upper tract urothelial cancer.

6. Be able to interpret diagnostic test results, including imaging studies and urinary markers, and understand the limitations of each.

7. Understand and be familiar with the staging classification of upper tract urothelial tumors

8. Be able to interpret clinical and pathologic factors that determine risk stratification of high and low risk disease.

Contents:

8. AUA Guidelines for workup of asymptomatic microscopic hematuria

9. Efficacy of ureteroscopy, ureteral / renal washings, targeted and voided urine cytology in different stages and grades of upper tract urothelial cancer (including false positive and false negative results)

10. Role of urinary markers including cytology, BTA, NMP22 and Uroyvision FISH tests, as well as emerging urinary markers
    a. Biochemistry or molecular biology of each marker
    b. Diagnostic efficacy in different stages and grades of urothelial cancer

11. Indications for and evaluation of CT scan, CT Urography, MRI, bone scans, chest imaging and PET Scan in upper tract urothelial cancer patients

12. Understanding limitations of clinical staging (i.e. on imaging and biopsy) and role of clinical variables such as hydronephrosis, tumor grade, and cytology in improving accuracy of clinical staging.

4. Management of low grade / low stage upper tract urothelial cancer

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

9. Demonstrate knowledge and understanding of indications, management and complications associated with endoscopic management of upper tract urothelial carcinoma.

10. Master endoscopic surgical procedures required to evaluate and treat the ureter and upper tract collecting system for neoplasm, including cystoscopy, retrograde pyelography, ureteroscopy, and percutaneous nephroscopic treatments.

11. Understand the indications, contraindications, scheduling, and risks of using intravesical agents in the upper tracts.

12. Understand and describe anticipated results from the use of intravesical therapy in the upper tracts, and be knowledgeable about the methods and frequency of the surveillance protocols.

13. Understand the importance of considering patient factors (i.e. competing causes of mortality) in treatment decisions

Contents:

a. Risk stratification of upper tract urothelial cancers

b. Indication for upper tract biopsy
    i. Directed biopsies using conventional biopsy tools
    ii. Directed biopsies using stone baskets
    iii. Directed biopsies using backloading biopsy tools
    iv. Biopsies of the tumor base

c. Surgical technique for endoscopic treatment of upper tract urothelial carcinoma
    i. Goals of resection / ablation
    ii. Factors influencing efficacy
    iii. Understanding of obtaining appropriate access to the upper tract
        1. Use of access sheaths
        2. Flexible ureteroscopy
        3. Semirigid ureteroscopy
        4. Appropriateness of dilation of ureteral orifices / strictures
        5. Percutaneous nephroscopic access
    iv. Energy modalities uses for tumor ablation
        1. Electrocautery
        2. LASER energy
            a. Holmium:YAG
            b. Neodynium:YAG
    v. Perioperative management
    vi. Risks and complications of endoscopic management
    vii. Selection of patients for “staged” upper tract tumor endoscopic management for appropriate clearance of tumors
    viii. Interpretation of pathology report and understanding of markers of adequate resection / ablation

d. Role of repeat endoscopic surveillance / tumor ablation

e. Post-endoscopic treatment surveillance
    i. Timing and frequency of ureteroscopy and upper tract imaging
    ii. Timing and frequency of lower tract endoscopy

f. Role of nephroureterectomy for management of low grade upper tract urothelial cancer.
    i. Patients with tumors too extensive for endoscopic management
    ii. Patients with tumors at high-risk for progression –i.e. identify adverse prognostic features in patients upper tract disease – large size, multifocality, challenging location, associated hydronephrosis, high grade cytology.
    iii. Risk of understaging
    iv. Efficacy – risk of incomplete endoscopic ablation
    v. Risks and complications

5. Management of high grade / high stage upper tract urothelial carcinoma

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

9. Demonstrate knowledge and understanding of indications, management and complications associated with nephroureterectomy. Be familiar with long-term outcomes following surgery, and prognostic variables associated with survival.

10. Demonstrate knowledge and understanding of indications, management and complications associated with segmental and distal ureterectomy (intra-operative, postoperative and long-term). Be familiar with long-term outcomes following ureterectomy, and prognostic variables associated with survival and recurrence.

11. Master surgical procedures related to nephroureterectomy and distal ureterectomy

    a. Understand the role, extent, and limits of node dissection – extrapolation of rationale from bladder cancer data, awareness of existing data in upper tract disease, recognition of impact of limitations in preoperative staging
    b. Understand the optimal methods of resection of the kidney and ureter

12. Demonstrate knowledge and understanding of indications, technique, management, complications and limitation of different types of bladder cuff management

    a. intravesical
    b. extravesical
    c. endoscopic

13. Demonstrate knowledge and understanding of available prospective randomized trial data for administration of intravesical chemotherapy in order to reduce risks of bladder recurrence.

14. Understand the importance of considering patient factors (i.e. competing causes of mortality) in treatment decisions

Contents:

9. Indication for nephroureterectomy and distal ureterectomy
    d. Role of pre-operative biopsies
    e. Role of pre-operative cytology
    f. Role of tumor location, size, and multifocality

10. Distal ureterectomy
    f. Goal of distal ureterectomy
    g. Factors influencing efficacy
    h. Intraoperative assessment of margin status
    i. Perioperative management
    j. Risks and complications and their management

11. Nephroureterectomy
    f. Goal of nephroureterectomy
    g. Factors influencing efficacy
    h. Perioperative management
    i. Risks and complications of nephroureterectomy and their management
    j. Long-term outcomes and prognostic variables associated with survival – clinicopathologic, molecular
    k. Role of intravesical chemotherapy to prevent bladder tumor recurrence

12. Surgical technique for nephroureterectomy and distal ureterectomy
    e. Open surgery
        i. Single incision approach
        ii. Two incision approach
    f. Laparoscopic surgery
        i. Transperitoneal approach
        ii. Retroperitoneoscopic approach
        iii. Robotic assistance
    g. Bladder cuff management
        i. intravesical
        ii. extravesical
        iii. endoscopic

6. Chemotherapy for upper tract urothelial carcinoma

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

4. Understand the indications, contra-indications, scheduling, and limitations of available data for systemic chemotherapy for high risk upper tract urothelial carcinoma.

5. Recognize the utility of systemic chemotherapy in the neoadjuvant and adjuvant setting and appropriate patient selection for each.

6. Understand the indications, contra-indications, and scheduling of systemic chemotherapy for metastatic urothelial upper tract cancer.

Contents:

5. Use of perioperative chemotherapy for resectable, high-risk upper tract urothelial carcinoma
    a. Indications, Sequence and Timing of multi-modality management
    b. Pros and cons of neoadjuvant and adjuvant chemotherapy – extrapolation of bladder cancer data, understand expected reduction in renal function following nephroureterectomy and implications on receipt of cisplatin-based adjuvant chemotherapy
    c. Expected outcomes
        i. Toxicity
            1. Acute
            2. Perioperative
            3. Long-term
        ii. Efficacy
        iii. Extrapolation of data from muscle-invasive bladder cancer cohorts
6. Use of chemotherapy for potentially unresectable disease (i.e. cT4bNx or cTxN+ or oligometastatic disease)
    a. Indications, Sequence and Timing of multi-modality management
    b. Identifying appropriate candidates for surgical consolidation after initial chemotherapy for advanced disease
    c. Expected outcomes
        i. Toxicity
            1. Acute
            2. Perioperative
            3. Long-term
        ii. Efficacy
7. Chemotherapy for metastatic disease

a. First line
b. Second line

8. Standard Chemotherapy Regimens
    a. "Fit" patients (high performance status, adequate renal, etc.)
        i. Agents, Regimens, rationale for combination
        ii. Expected toxicity and management
        iii. Efficacy benchmarks
    b. "Unfit" patients (i.e. poor performance status, poor renal function, pre-existing neuropathy, pre-existing hearing loss, advanced age)
        i. Agents, Regimens, rationale for combination
        ii. Expected toxicity and management
        iii. Efficacy benchmarks
    c. Small cell histology
        i. Agents, Regimens, rationale for combination
        ii. Expected toxicity and management
        iii. Efficacy benchmarks

RENAL PARENCHYMAL MASSES

Objectives:

Upon completion of this unit, the urologic oncology fellow will have mastered the pertinent epidemiology, anatomy, pathology, evaluation, and management of renal parenchymal masses.

I: Histology, pathology, epidemiology of renal masses

Unit Objectives:

Upon completion of this unit the urologic oncology fellow will understand:

1. The various types of benign and malignant masses that arise within the renal parenchyma
2. The pathologic features that are significant in renal cell carcinoma
3. The epidemiology of renal masses
4. Etiologic factors for renal masses, including genetic aberrations, immunologic factors, and environmental factors

Contents

1. WHO Classification of renal masses, benign and malignant
2. Epidemiology of renal masses - incidence and prevalence of each type of renal mass
3. Etiology
    a. Environmental factors
    b. Genetic factors
    c. Patient factors – i.e. HTN, obesity, smoking
4. Pathologic features that predict outcome for renal cell carcinoma (RCC)
    a. Stage
    b. Grade
    c. Vascular invasion
    d. Fat invasion
    e. Collecting system involvement
    f. Tumor size
    g. Tumor necrosis
    h. Histology
        i. Clear cell
            1. Differentiate and explain significance of solid conventional RCC versus cystic RCC
        ii. Papillary
        iii. Chromophobe
        iv. Other
        v. Benign renal tumor pathology- angiomyolipoma, oncocytoma
    i. Sarcomatoid features
    j. Additional pathology, including immunostaining for molecular factors

II: Renal Mass Presentation, Diagnosis, Evaluation

Unit Objectives:

Upon completion of this unit, the urologic oncology fellow will have accomplished:

1. Understand the signs, symptoms, and presentation of renal masses
2. Elucidate the critical points in the diagnosis and evaluation of renal masses

Contents

1. Symptoms/signs of renal masses, benign and malignant
    a. Classic triad: flank pain, hematuria, mass
    b. Symptoms associated with metastatic RCC
    c. Clinical features (including frequent multi-organ system manifestations) associated with renal tumor syndromes and genetic testing for suspected syndromes – understanding of the genes and, when known, subsequent molecular pathways associated with various genetic RCC/renal tumor syndromes, specifically:
        i. VHL
        ii. TS
        iii. BHD
        iv. Familial papillary RCC
        v. HLRCC
2. Current frequency and clinical significance of an incidentally discovered renal mass versus symptomatic renal mass
3. History and physical examination
4. Imaging studies for diagnosis and staging of renal masses
    a. Relative value, uses and indications for abdominal imaging modalities including:
        i. CT
        ii. MRI
        iii. Ultrasound
    b. Indications and appropriate use of staging studies
        i. Chest x-ray
        ii. CT
        iii. Bone scan
        iv. Head CT/MRI
        v. PET
5. Biopsy of renal masses
    a. Indications for renal mass biopsy
    b. Data pertaining to accuracy of renal mass biopsy
6. Recognition of features suggestive of primary renal tumors versus secondary tumors/metastasis to the kidney
7. Laboratory studies for the newly diagnosed renal mass, including studies for paraneoplastic syndromes and studies that aid in prognostication

III. Staging and Prognosis

Unit objectives

Upon completion of this unit the urologic oncology fellow should understand the current and relevant historic staging systems for RCC, the prognosis based on stage, and prognostic models for RCC.

Contents

1. AJCC/UICC staging, current system
    a. Outcome data
2. Robson staging
3. Clinical data on size of renal mass as it pertains to pathology, chance of metastasis, and oncologic outcomes
4. Established prognostic models integrating multiple clinicopathologic features
5. Models and standards for evaluation and follow up after treatment of benign and malignant renal masses
    a. Follow up for benign renal lesions after resection
    b. Stratification of risk and follow up for localized RCC
    c. Stratification of risk and follow up for metastatic RCC

IV: Management of Localized RCC

Unit Objectives

Discuss options for management and comparative outcomes for each modality of managing incidental small renal masses, including impact on renal function, cancer-specific mortality, and all-cause mortality. Discuss management of larger renal tumors, including locally-advanced disease and venous tumor thrombus. Demonstrate intimate understanding of surgical anatomy of the kidney.

Contents

1. Anatomy
    a. Surface anatomy and landmarks for surgery
    b. Incisions and approaches
    c. Vascular anatomy of the kidney, great vessels and lymphatics
    d. General abdominal and retroperitoneal anatomy
2. Recognition and management of benign or likely indolent renal masses
    a. Cystic neoplasms
        i. Bosniak classification (I, II, IIF, III, IV)
        ii. Features suggestive of benign/malignant
        iii. Indications for intervention and modalities of treatment

iv. Outcome

b. AML
    i. Indications for treatment and modalities of therapy
c. Small solid renal masses
    i. Data pertaining to size and incidence of metastasis
    ii. Size and histology
    iii. Management options for the small renal mass (fellows' understanding of the interaction of competing causes of morbidity/mortality for patients with a small renal mass is critical to decision-making regarding management)
        1. Active surveillance
            a. Protocols for surveillance
            b. Role of biopsy
            c. Published outcomes to date – renal tumor growth rate during observation, tumor progression, mortality
            d. Indications for treatment in patients on active surveillance
        2. Ablation – RFA and cryotherapy; percutaneous and laparoscopic
            a. Outcome data
            b. Mechanisms and biology of tissue interaction
            c. Recommended follow-up after ablation + definition of tumor recurrence after ablation
        3. Open and minimally invasive nephron sparing surgery
            a. Importance of and outcomes for NSS – renal function outcomes, oncologic efficacy, potential overall health benefit
            b. Implications of, use of, and ways to minimize impact of ischemia in NSS
            c. Complication rates and management
            d. Technique, approaches – open, laparoscopic, robotic-assisted
            e. Factors for selection of appropriate candidates, such as tumor complexity (including various published classification systems for quantifying tumor complexity) and preoperative renal function
            f. Rationale for elective NSS including data pertaining to overall survival, renal preservation, quality of life – randomized trial data + observational (retrospective) analyses
d. Larger renal masses
    i. Indications for surgery
    ii. Surgical approaches, including minimally invasive and open
    iii. Lymphadenectomy- templates, landing zones, management of complications specific to LND (i.e. chylous ascites)
    iv. Management of the adrenal gland during radical nephrectomy
    v. Surgery for tumor thrombus- preoperative evaluation of patient, surgical technique for various levels of tumor thrombus, and outcomes

vi. Management of complications

e. Adjuvant/neoadjuvant therapy for renal cancer
   i. Currently available agents and most common side effects of these agents
   ii. Knowledge of clinical trials which have evaluated adjuvant therapy in RCC
   iii. Understanding of published data to date and ongoing clinical trials evaluating the impact of neoadjuvant therapy on primary renal tumors as well as on perioperative outcomes/complications
f. Management of bilateral renal masses
   i. Synchronous and metachronous
   ii. Consideration of familial tumor syndromes and impact upon management (i.e. indications for medical genetics referral)
g. Management of renal masses in special patients
   i. Chronic kidney disease (CKD)
   ii. End-stage renal disease (ESRD) / Dialysis
   iii. Transplant
   iv. Genetic syndromes

V: Management of Metastatic RCC

Unit objectives:

Understand the history of management of metastatic RCC. Have a working knowledge of the various patient risk classification systems for metastatic RCC. Define the role of surgery in the setting of metastatic RCC. Understand mechanism of action, uses, adverse effects, and outcomes of various systemic therapy options for metastatic RCC.

Contents

1. Historical data pertaining to outcomes after surgical management of metastatic RCC
2. Patient risk classifications associated with prognosis/survival for patients with metastatic RCC (i.e. MSKCC/Motzer criteria, Heng criteria)
3. Cytoreductive nephrectomy in metastatic RCC
   a. Indications, patient selection criteria
   b. Extent and approach to surgery, LND, adrenal, contiguous organ involvement, tumor thrombus, etc.
   c. Outcomes and data (including randomized trial outcome data) pertaining to cytoreductive nephrectomy in the immunotherapy era
   d. Cytoreductive nephrectomy and targeted therapy - timing of surgery and peri-procedural management of medications (including knowledge of ongoing clinical trials investigating the optimal timing of surgery vs systemic therapy with targeted agents)
4. Systemic therapy

a. Mechanisms of resistance to cytotoxic chemotherapy
    i. Data on response to cytotoxic therapy
    ii. MDR gene, glutathione reductase, etc
    iii. Recent trial data
b. Immunotherapy
    i. Historical data with interferon, interleukins, tumor vaccines
    ii. Current data regarding high-dose interleukin-2
    iii. Indications for current use, selection of appropriate candidates
    iv. Complications, oncologic efficacy
    v. Rationale for new modalities, such as dendritic-cell based and other personalized immunotherapies
c. Targeted therapies - including anti-VEGF agents, TKIs, mTOR inhibitors, other agents
    i. Indications (i.e. tumor histology, patient risk classification) for various targeted therapies
    ii. Complications/adverse events associated with specific different targeted agents (it is critical that fellows develop an understanding of the side effect profile associated with the targeted agents for RCC)
    iii. Oncologic efficacy of targeted therapies
    iv. Current and recent trial data
    v. Indicators of response
    vi. Mechanism of action/molecular pathways affected by approved agents
    vii. Surgery pre and post- targeted therapy – safety/efficacy

5. Radiotherapy for bone and brain metastasis
6. Metastasectomy
    a. Indications and selection of appropriate candidates
    b. Relevant data regarding oncologic outcomes
    c. Understanding of integration within multimodal treatment approach

Testicular Cancer

I. Anatomy, pathology, and epidemiology of testicular cancer

Learner Objectives

Upon completion of this unit, the urologic oncology fellow should understand:

1) Normal anatomy of the testis and surrounding structures
2) Normal anatomy of the retroperitoneum and patterns of lymph node metastasis in testicular cancer
3) Normal histology of the testis and epididymis
4) Classification and histology of germ cell and non-germ cell tumors of the testis
5) Incidence, demographics, and risk factors for testicular cancer

Contents

1) Normal gross anatomy of the testis, epididymis, and spermatic cord
2) Normal gross anatomy of the retroperitoneum, including location and anatomic relationships of the sympathetic chain, postganglionic fibers, and hypogastric plexus
    a. Physiology of normal antegrade ejaculation
3) Lymphatic drainage of the testis
4) Normal and malignant histology of the testis
    a. Normal testis
    b. Orchitis
    c. Seminoma
    d. Spermatocytic seminoma
    e. Embryonal cell
    f. Choriocarcinoma
    g. Yolk sac
    h. Teratoma

i. Intratubular germ cell neoplasia
j. Leydig cell tumors
k. Sertoli cell tumors
l. Rhabdomyoscarcoma

5) Testicular cancer staging
   a. TNM staging for primary testis tumor
   b. Clinical staging
   c. IGCCCG risk groups

6) Extragonadal primary germ cell tumor sites[1]

7) Annual incidence of testicular cancer and distribution across tumor types,[2] as well as temporal trends in incidence

8) Age of onset and risk factors associated with the development of testicular cancer, including cryptorchidism

9) Genetic epidemiology[3]

II. Diagnosis and staging of testicular cancer

Learner Objectives:

Upon completion of this unit, the urologic oncology fellow should understand:

1) The indications and workup for evaluation of a testicular mass

2) Appropriate interpretation of scrotal ultrasound and tumor marker results

3) Staging evaluation, classification, and initial management of a testis tumor

4) Risk group stratification and prognosis in a patient with a newly diagnosed testis tumor

Contents:

1) Clinical presentation and testicular ultrasound interpretation

2) The role of serum tumor markers in diagnosis, prognosis, and management

a. Tumor marker half-lives and causes of false elevation
b. Identifying NSGCT by presence of AFP elevation

3) Role of sperm banking[4]

4) Surgical technique for radical orchiectomy

5) Indications for biopsy of contralateral testicle[5-8]
   a. Suspicious ultrasound
   b. Cryptorchid testis
   c. Atrophy

6) Role of testis-sparing surgery[9,10]

7) Post-diagnostic imaging, including indications for brain imaging

8) Define staging classification system, post-orchiectomy risk stratification, and prognosis by tumor type and risk category[11]
   a. i.e. no poor-risk seminoma

III. **Surgical considerations in the management of testicular cancer**

Learner Objectives:

Upon completion of this unit, the urologic oncology fellow should understand:

1) Indications for retroperitoneal lymph node dissection (RPLND)

2) Principles of RPLND

3) Postoperative management of patients following RPLND

4) Management of intraoperative complications

5) Recognition and management of post-operative complications

Contents:

1) Boundaries of RPLND, full bilateral template, and modified RPLND templates
    a. Nerve-sparing technique
    b. Rates of preservation of ejaculation
    c. Approach for stage I NSGCT vs. post-chemotherapy setting

2) RPLND technique, including "split and roll" and ligation of lumbar vessels
    a. Potential indications for resecting adjacent organs
    b. Management of vascular, bowel, or other organ injury

3) Prevention and management of complications[12,13]
    a. Chylous ascites
    b. Pulmonary complications, impact of bleomycin
    c. Wound infection
    d. Small bowel obstruction
    e. Loss of antegrade ejactulation

III. Management of pure seminoma

Learner Objectives:

Upon completion of this unit, the urologic oncology fellow should understand:

1) Primary treatment options according to stage

2) The relative risks and benefits to the disparate management strategies for stage I seminoma- cancer outcomes versus treatment-related toxicities

3) Risk of recurrence according to stage and treatment, strategies for post-treatment surveillance

4) Indications for chemotherapy in stage II/III seminoma and chemotherapeutic regimens

5) Management of the patient with a residual retroperitoneal mass following chemotherapy

Contents:

1) Surveillance versus single-agent carboplatin versus radiotherapy for stage I seminoma[14-16]
    a. Advantages and disadvantages of each, risk of recurrence, overtreatment, and short- and long-term complications of therapy
    b. Surveillance schedule[17,18]
    c. Principles of radiotherapy, dosing, field, timing
        i. Impact of prior scrotal surgery on RT delivery

d. Risk of recurrence over time
e. Long-term risks related to radiation and chemotherapy

2) Management of Stage IS seminoma
    a. Surveillance protocol following radiation
    b. Rates of relapse in comparison to those in patients with stage IA/B disease treated with radiation

3) Management of stage II and stage III seminoma
    a. Radiotherapy in stage IIA and IIB, treatment field in comparison with stage I, surveillance strategies
        i. Dosing, fields, timing of radiotherapy
    b. Selection of chemotherapy regimen in IIC and III[19,20]
        i. Good vs. intermediate risk
    c. Post-chemotherapy management: role of tumor size, PET imaging[21,22]
        i. Timing of PET scan
        ii. Indications for RPLND, radiotherapy
        iii. Second-line chemotherapy (TIP, VIP)[23-25]

IV. Management of nonseminoma

Learner Objectives:

Upon completion of this unit, the urologic oncology fellow should understand:

1) Primary treatment options for NSGCT, according to stage

2) The relative risks and benefits to the disparate management strategies for stage I NSGCT

3) Risk of recurrence according to stage and treatment, strategies for post-treatment surveillance in patients with NSGCT

4) Role and risks of post-chemotherapy RPLND

5) Chemotherapeutic regimens utilized in the management of NSGCT according to stage as well as salvage strategies in patients with advanced metastatic disease

Contents:

1) Surveillance versus primary chemotherapy versus RPLND for stage I NSGCT
    a. Surveillance: schedule and risk of recurrence[26,27]

        i. Role of surveillance in T2 disease
    b. Management of relapse after surveillance
    c. Role and timing of RPLND, rates and location of relapse[28]
        i. Surveillance imaging following RPLND in comparison with primary surveillance or chemotherapy
    d. Primary chemotherapy in stage IB, regimens, and risks[29-31]
        i. Long term complications of chemotherapy[32,33]
        ii. Rates of recurrence
        iii. Randomized trial of RPLND vs. BEP x 1[34]
    e. Overall cure rate

2) Surveillance schedule following surgery for pN0 disease

3) Management of pN+ disease following RPLND
    a. Distinction between pN1, pN2, and pN3 disease
        i. Rates of cure with RPLND alone for pN1 disease[35]
    b. Chemotherapy regimens and number of cycles

4) Management of stage IS NSGCT
    a. Chemotherapy regimens and number of cycles
    b. Role of postchemotherapy RPLND

5) Management of stage IIA and IIB NSGCT
    a. Positive vs. negative markers[36]
    b. RPLND vs. chemotherapy in setting of negative markers[37]
    c. Management after primary chemotherapy[38]
    d. Role of chemotherapy following primary RPLND[39]

6) Post-chemotherapy RPLND
    a. Probability of necrosis, teratoma, or viable tumor
    b. Management according to pathology and chemotherapy regimens
    c. Management of extra-retroperitoneal sites of disease
        i. i.e. knowledge of rates of concordance/discordance in histology between retroperitoneum and extra-retroperitoneal disease

7) Management of advanced metastatic NSGCT
    a. Risk stratification groupings
    b. Good risk: primary chemotherapy regimens
    c. Intermediate risk (stage IIIB): chemotherapy regimens
        i. Post-chemotherapy management
    d. Poor risk (stage IIIC): chemotherapy regimens
        i. Post-chemotherapy management

8) Salvage chemotherapy, stem cell rescue for metastatic tumors[40-42]
    a. Pathologic distribution (necrosis, teratoma, viable tumor) in retroperitoneum at RPLND after salvage chemotherapy
    b. Role of “desperation” RPLND

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Penile Cancer

1. Epidemiology

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

5. Demonstrate knowledge and understanding of the incidence and prevalence of penile cancer
6. Demonstrate an understanding of the risk factors associated with the development of the disease
7. Demonstrate a knowledge and understanding of the natural history of penile cancer.

Contents

1. Incidence of penile cancer, including geographic and racial variations, and age distribution in incidence
2. Risk factors associated with the development of penile cancer (phimosis, infant circumcision, poor hygiene, chronic infections, HPV (association with specific subtypes 16, 18), and tobacco products)
3. Predisposing conditions, including condyloma acuminata, balanitis xerotica obliterans, and leukoplakia
4. Natural history, recurrence, and metastatic patterns of penile cancer
5. Implication(s) of population-level HPV vaccination on the epidemiology of penile cancer

2. Anatomy and Pathology

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

1. Recognize and demonstrate an understanding of the normal anatomy and physiology of the penis, as well as the inguinal and pelvic lymph nodes. Display this knowledge during clinical evaluation and surgery.
2. Understand the specific surgical relationship(s) of the anatomy of the penis with the surrounding organs.

3. Understand and identify the pathologic difference between normal epithelium and penile carcinoma, with particular attention to histologic features suggestive of tumor grade and tumor stage.
4. Formulate a differential diagnosis for the patient with a penile lesion

Contents

1. Anatomy of the penis, including layers and corpora.
2. Anatomy of the inguinal region, including lymphatics (with special attention to nodal regions and drainage patterns of the penis), blood vessels, nerves and muscles
3. Anatomy of the pelvic region, including the pelvic organs and lymph nodes
4. Pathology of penile lesions
    a. Benign Lesions
    b. Premalignant Cutaneous Lesions
    c. Viral-Related Dermatologic Lesions
    d. Buschke-Lowenstein Tumor (Verrucous Carcinoma, Giant Condyloma Acuminatum)
    e. Squamous Cell Carcinoma
    f. Nonsquamous Malignancy (Basal Cell Carcinoma, Melanoma, Sarcoma, Paget's Disease)
5. Pathology of nodal involvement

3. Clinical Diagnosis and Staging

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

9. Recognize the signs and symptoms associated with penile cancer, and differentiate them from the presentation of benign penile conditions.

10. Be able to describe the indications and appropriate tests for further evaluation of a penile lesion.

11. Be able to interpret relative diagnostic test results, including imaging and laboratory studies, in the diagnostic evaluation of a suspected or known penile cancer.

12. Be knowledgeable about the current staging for penile cancer, including of the primary tumor and locoregional lymph nodes

13. Be fluent in contemporary risk-stratification paradigms to facilitate efficient and effective therapy for penile cancer, including understanding the risk of lymph node involvement and the consequent indications for inguinal lymphadenectomy.

Contents

1. Variable presentation of the primary tumor
    a. May present as erythema, induration, or verrucoid growth
    b. May present as an ulcerated and destructive lesion
2. Role of penile biopsy in diagnosis
3. Role of penile MRI for clinical staging purposes
4. Role of excisional biopsy/partial penectomy in diagnosis
    a. Understand technique of partial penectomy/penile preservation
    b. Understand morbidity of partial penectomy/penile preservation
5. Variable presentation of the inguinal nodes
    a. Differentiate between infection and tumor involvement
    b. Variable risk of lymph node metastases by primary tumor type (sarcomatoid carcinoma > SCC > Condylomatous tumor), as well as by primary tumor stage, grade, and presence of lymphovascular invasion
    c. Role of antibiotics in nodal evaluation
6. Understand role and limitations of radiographic and laboratory staging
    a. Evaluation of inguinal and pelvic lymph nodes – CT, MRI
        i. Potential use of PET-CT
        ii. Potential use of lymphotropic nanoparticle-enhanced MRI
    b. Role for chest imaging

c. Role for laboratory evaluation – i.e. serum calcium

7. Understand the indication(s) for nodal staging
    a. Physical examination of inguinal nodes
    b. Importance of timing of presentation with lymph node enlargement – at diagnosis versus delayed
    c. Role of antibiotic therapy
    d. Role of fine needle aspiration
    e. Role of sentinel node biopsy
    f. Inguinal lymph node dissection
        i. Nodal drainage (unilateral vs. bilateral)
        ii. Depth of dissection (superficial vs. deep)
    g. Pelvic lymph node dissection (indications)
8. Be familiar with most recent AJCC TNM staging classification

4. Treatment of the primary tumor in penile cancer

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

15. Demonstrate knowledge and understanding of indications, management, and complications associated with topical therapies for penile cancer.
16. Demonstrate knowledge and understanding of indications, management, and complications associated with partial penectomy for penile cancer.
17. Demonstrate knowledge and understanding of indications, management, and complications associated with total penectomy for penile cancer.
18. Demonstrate knowledge and understanding of indications, management, and complications associated with radiotherapy to the primary lesion for penile cancer.

Contents

1. Role of topical therapies for penile cancer
    a. Indication(s)
    b. Specific agents
    c. Efficacy

    d. Safety
2. Laser therapy for penile tumors
    a. Indication(s)
    b. Differential depth of penetration/tissue destruction of various lasers [Nd:YAG, KTP, and CO_2]
    c. Morbidity
    d. Outcomes
3. Mohs micrographic surgery
    a. Indication(s)
    b. Technique
    c. Morbidity
    d. Efficacy/recurrence rates
4. Conservative (penile-sparing) surgical excision of a penile tumor
    a. Indication(s)
    b. Technique
    c. Morbidity
    d. Efficacy
5. Partial penectomy
    a. Indication(s)
    b. Technique
    c. Morbidity
    d. Efficacy
6. Total penectomy
    a. Indication(s)
    b. Technique, including perineal urethrostomy
    c. Morbidity
    d. Efficacy
7. Radiation therapy
    a. Indication(s) for management of a primary penile tumor
    b. Technique [external beam vs. brachytherapy]
    c. Morbidity

d. Efficacy

5. Management of inguinal/pelvic lymph nodes in patients with squamous cell carcinoma of the penis

Learner Objectives:

Upon completion of the unit, the urologic oncology fellow should:

1. Demonstrate knowledge and understanding of the indications, technique, and complications associated with inguinal lymphadenectomy.
    a. Understand the extent and limits of node dissection.
    b. Understand the optimal methods (pre-, intra-, and postoperatively) of minimizing complication risk with lymphadenectomy.
2. Understand indications for pelvic lymph node dissection in penile cancer

Contents

1. Definitions of "low risk" versus "high risk" penile cancers with regards to lymph node involvement
    a. Grade of primary tumor
    b. Stage of primary tumor
    c. Presence of lymphovascular invasion in primary tumor
    d. Physical examination of inguinal regions
2. Demonstrate knowledge of the indication(s) for antibiotic therapy and indication(s) for nodal biopsy/FNA to evaluate lymph node enlargement
3. Understand the role of Dynamic Sentinel Node Biopsy
    a. Rationale
    b. Technique
    c. Results
4. Understand the role of inguinal lymphadenectomy in patients without clinical evidence of inguinal lymphadenopathy
    a. Indications for superficial and deep dissection
    b. Technique and templates
    c. Techniques to reduce morbidity

5. Demonstrate knowledge of the therapeutic efficacy of lymphadenectomy in patients with clinical lymphadenopathy, and the morbidity associated with the procedure (both modified and radical ilioinguinal lymphadenectomy), including:
    a. Role of unilateral inguinal lymphadenectomy in patients who present with late unilateral palpable lymphadenopathy
    b. Role of pelvic lymphadenectomy in patients with high-volume locoregional lymphadenopathy (i.e. fixed inguinal nodal mass, presence of pelvic lymphadenopathy)
    c. Role of reconstruction after inguinal node dissection
        i. Indications
        ii. Technique, morbidity
        iii. Use of tissue flaps including sartorius muscle and rectus abdominus, skin grafts
6. Demonstrate knowledge of protocols for inguinal surveillance after lymph node dissection
7. Understand the role of radiation therapy in the management of inguinal lymph node involvement of penile cancer
    a. Indications for radiation therapy as primary management of inguinal lymphadenopathy
    b. Role for radiation in combination with surgical lymphadenectomy – neoadjuvant/adjuvant
    c. Dose/portals
    d. Morbidity and efficacy of therapy

6. Management of advanced locoregional and/or metastatic penile cancer

Learner Objectives:
Upon completion of the unit, the urologic oncology fellow should:

7. Understand the indications, contra-indications, and scheduling of systemic chemotherapy for penile cancer, including the most frequently utilized chemotherapeutic agents, with the expected side effect profiles.

8. Recognize the potential utility of a multimodal treatment approach to patients with penile cancer and locoregional lymph node involvement, including surgical resection +

systemic chemotherapy with or without concurrent radiotherapy in the neoadjuvant and adjuvant settings

9. Understand the role for palliative therapy in advanced penile cancer

Contents

1. Standard chemotherapy regimens for penile cancer (squamous cell carcinoma)
    a. Agents/rationale for combination
    b. Expected toxicity and management
    c. Efficacy
2. Use of chemotherapy +/- radiotherapy in patients with locoregional lymph node involvement treated with surgical resection
    a. Indications, sequence, and timing (neoadjuvant, adjuvant) of multi-modality management
    b. Outcomes
        i) Toxicity
            -Acute
            -Perioperative
            -Long-term
        ii) Oncologic efficacy
3. Use of Chemotherapy for Systemic Disease
4. Palliative options for patients with locally-advanced and metastatic penile cancer
    a. Surgery – rationale (prevent devastating local complications)
    b. Radiation
    c. Chemotherapy

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Prostate Cancer Core Curriculum

1. Epidemiology and Natural History

Learner Objectives

Upon completion of this unit, the urologic oncology fellow will be able to:

1. Understand impact of age, race, and geographic location on prostate cancer incidence and natural history
2. Understand the influence of androgens and specifically the interaction of testosterone, dihydrotestosterone, and the androgen receptor on the development of prostate cancer
3. Be familiar with dietary and other exogenous factors influencing prostate cancer incidence.
4. Understand the data from chemoprevention trials with 5-alpha reductase inhibitors and anti-oxidant supplements.
5. Know the natural history of treated and untreated prostate cancer

Contents

1. Incidence and prevalence of disease[1, 2]
2. Risk factors for development of prostate cancer
    a. Age[3]
    b. Race and ethnicity [3]
    c. Geography
    d. Family History[4]
    e. Molecular Genetics[5]
    f. Dietary factors, obesity, medications and inflammation
    g. Role of testosterone, DHT, 5-alpha reductase, androgen receptor
3. Chemo/dietary prevention of prostate cancer
    a. Prostate Cancer Prevention Trial (Finasteride)[6] – findings of trial and subsequent controversy
    b. REDUCE Trial (Dutasteride)[7]
    c. Antioxidants and Dietary Interventions (Selenium, Vitamin E, Vitamin C)[8, 9]
    d. Complementary and alternative medicine
4. Natural history of prostate cancer[10, 11] – treated and untreated
    a. Prognosis based on risk factors and phase of disease
    b. Factors influencing mortality from prostate cancer, including competing causes of death

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2. Pathogenesis, Molecular Biology, Pathology of Prostate Cancer

Learner Objectives

At the end of this unit, the urologic oncology fellow should:

1. Know the prevailing theories for prostate carcinogenesis
2. Be capable of recognizing the basic histologic patterns of HGPIN, ASAP, and prostate cancer of varying Gleason scores
3. Understand the clinical implications of HGPIN and ASAP, and be able to provide recommendations for subsequent patient management in these cases
4. Understand the Gleason scoring system

Contents

1. Role of inflammation and oxidative stress[1, 2]
2. Role of androgen receptor signaling
3. Anatomy and Pathology[3, 4]
    a. Normal anatomy, sites of disease, and implications for diagnosis
    b. Histology
    c. High-grade PIN
        i. Microscopic characteristics
        ii. Risk association with future biopsies/cancer
        iii. Management
    d. ASAP
        i. Microscopic characteristics
        ii. Risk association with future biopsies/cancer
        iii. Management
    e. Cancer
        i. Gleason scoring system
            1. Microscopic characteristics
            2. Grading of primary, secondary and tertiary patterns
            3. How grade affects prognosis[5]
            4. Changes in grading system over time[6]
        ii. Absence of basal cell layer in cancer
        iii. Histologic variants
        iv. Clinical impact of biopsy findings, such as peri-neural invasion, number and percent of cores involved, Gleason score[7]
        v. Pathologic evaluation of radical prostatectomy specimens, and clinical significance of findings such as positive surgical margins, extraprostatic extension, seminal vesicle invasion, and lymph node involvement

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Chapter 96: Pathology of Prostatic Neoplasia

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Chapter 4: Anatomy and Pathology of Prostate Cancer

4A: Anatomy of the Prostate and the Pathology of Prostate Cancer Peter A. Humphrey

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3. Early Detection/Diagnosis and Evaluation/Staging/Risk Stratification and Prognostication

Learner Objectives

At the end of this unit, the urologic oncology fellow should:

1. Understand role of PSA and PSA adjuncts as screening tests for prostate cancer
2. Understand the important screening studies and early detection guidelines from AUA, NCCN and USPSTF
3. Understand the impact of DRE findings on clinical evaluation for cancer
4. Know the proper transrectal ultrasound technique for prostate biopsy

5. Know the zonal anatomy of the prostate and its implications in location of biopsy needle placement
6. Be familiar with the complications associated with prostate needle biopsy, and the efforts to prevent/limit these complications
7. Know the AJCC clinical staging system for prostate cancer
8. Understand the role of predictive nomograms (e.g. Kattan) and predictive tables (e.g. Partin tables) as well as risk-group classification systems (e.g., D'Amico)
9. Know the indications for obtaining radiographic imaging (i.e. bone scan, cross-sectional imaging) in patients with newly-diagnosed prostate cancer

Contents

1. Early Detection
    a. Biology of PSA and development of PSA as a screening tool[1, 2]
        i. Biologic characteristics, function, serum half-life
        ii. Historical and current thinking on cut-off values: PCPT suggests there is no 'normal' PSA value[3-5]
        iii. PSA isoforms, and their role in diagnostic patient evaluation
    b. Improving on the test characteristics of PSA
        i. Age-adjusted PSA[6]
        ii. PSA velocity/doubling time, with knowledge of the controversy surrounding these parameters [7-10]
        iii. PSA density[11]
        iv. Free PSA[12]
        v. DRE[2]
    c. Other markers
        i. PCA-3
        ii. TMPRSS2:ERG rearrangement
    d. Predictive models
    e. Screening studies
        i. Catalona[2]
        ii. Tyrol[13]
        iii. PLCO[14]
        iv. ERSPC[15]
        v. Goteborg[16]
    f. The role of shared decision making in screening decisions
    g. Expected benefits and harms of screening for the individual; number needed to screen/treat and how that compares to screening for other diseases; sub-populations likely to benefit most and least from screening
    h. Change in incidence, stage at diagnosis and mortality since the introduction of PSA based screening[17, 18]
    i. Screening recommendations and guidelines – AUA, NCCN, American Cancer Society, CUA, USPSTF
2. Diagnosis

a. Appropriate interpretation and management of PSA values – often appropriate to repeat an outlying value; not appropriate to treat asymptomatic men with elevated PSA with antibiotics
b. Biopsy equipment, technique, complications
    i. Antibiotic prophylaxis (AUA guideline)
    ii. Use of anesthetics
    iii. Use of extended biopsy template (at least 8-12 cores), laterally directed[19]
c. Predictive models for biopsy candidates[20, 21]
d. Criteria for repeat biopsy
e. Role of imaging in biopsy decisions and targeting[22]
    i. MRI
    ii. Ultrasound and associated technologies
    iii. Elastography
f. Saturation biopsy
g. Trans-perineal mapping biopsy in patients considering focal therapy

3. Staging
    a. AJCC staging system
        i. Clinical TNM system
        ii. Pathologic TNM system
    b. Role of imaging
        i. Not typically considered in tumor staging
        ii. Yield of imaging in localized prostate cancer, including guidelines (i.e. NCCN) for avoiding unnecessary imaging in low-risk disease and obtaining appropriate studies per patient risk classification
        iii. Imaging modalities and specific indications for:
            1. Bone scan
            2. CT
            3. MRI
                a. Role of endorectal coil vs. 3T magnet
                b. Use of spectroscopy
            4. Choline PET
            5. Sodium Fluoride PET
4. Risk Stratification, Prognostication
    a. Pre-treatment look-up tables, nomograms, and other prognostic tools to predict pathologic results of surgery, response to therapy, or survival[23]
        i. Partin look-up tables[24]
        ii. Kattan nomogram[25]
        iii. D'Amico classification
        iv. Neural networks
        v. NCCN classification
        vi. CAPRA score[26]
        vii. Epstein criteria for prediction of indolent disease

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USPSTF Prostate Cancer Screening Recommendation Statement
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AUA Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis

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Chapter 98 - Prostate Cancer Tumor Markers

Chapter 99 - Early Detection, Diagnosis, and Staging of Prostate Cancer

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- 6A: Early Detection of Prostate Cancer
- 6B: Screening for Prostate Cancer

Chapter 7: Prostate Needle Biopsy Techniques and Interpretation

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Chapter 10: Imaging in Prostate Cancer

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4. Management of Localized, Locally Advanced and Locally Recurrent Disease; Survivorship

Learner Objectives

Upon completion of this unit, the urologic oncology fellow should:

1. Understand the appropriate patient selection for active surveillance and be familiar with the existing protocols for patient follow-up on active surveillance, including the need for repeat biopsy.
2. Know the advantages and disadvantages of the different radical prostatectomy approaches (i.e. open, laparoscopic, and robotic-assisted), including indications for pelvic lymph node dissection (PLND), and be familiar with the surgical techniques associated with these procedures.
3. Know the short and long-term complications associated with radical prostatectomy.
4. Understand the implications of PSA recurrence and/or persistence after prostatectomy.
5. Know the management strategies for adverse pathology findings at radical prostatectomy – positive margins, extracapsular extension, seminal vesicle invasion and/or positive lymph nodes.
6. Understand patient selection for external beam radiation and interstitial brachytherapy, and the definitions of success or failure of these therapies.
7. Know possible complications following radiation therapy.
8. Know the possible role of prostate cryotherapy in the treatment of localized disease and understand the side-effects and oncologic outcomes of this treatment.
9. Be aware of ablative techniques currently being studied.
10. Know the impact of each treatment on quality of life, sexual function, urinary function, and bowel function, and the management of adverse outcomes.

Contents

1. Management of localized disease
    a. Patient comorbidity and life expectancy assessment[1]
    b. Assessment of baseline function and quality of life, patient preferences and priorities[2, 3]
    c. Active Surveillance[4-7]
        i. Indications and patient selection (NCCN criteria and Epstein criteria)
        ii. Cohort studies demonstrating outcomes
        iii. Methods for surveillance and triggers for initiating treatment

d. Radiation Therapy[8, 9]
    i. Patient selection for radiation, including life expectancy and disease characteristics, prostate size, symptoms, comorbid conditions and patient preferences
    ii. Modalities for radiation therapy, including brachytherapy and external beam radiation therapy, using intensity modulation and image-guidance, as well as proton beam therapy, and be familiar with existing data which have evaluated relative comparative efficacy of these approaches
    iii. Basics of radiation therapy technique, including appropriate dose, appropriate use of hormone therapy
    iv. Expectations for PSA response and definitions for biochemical recurrence after radiation
    v. Oncologic outcomes
    vi. Short and long-term complications of radiotherapy
e. Surgery
    i. Patient selection, including life expectancy and disease characteristics, surgical risk, comorbid conditions and patient preferences
    ii. Impact of approach (open, robotic and laparoscopic surgery) on patient reported outcomes, cancer control, complications, cost, and access[10-15]
        1. Understanding of the differences between single surgeon/single center reported outcomes versus population-based dataset analyses
    iii. Impact of surgeon and facility experience on outcomes[16-18]
    iv. Indications for pelvic lymph node dissection
    v. Nerve-sparing techniques
    vi. Preoperative and post-operative care
    vii. Perioperative complications
    viii. Late complications (incontinence, erectile dysfunction and bladder neck contracture)
    ix. Long-term oncologic outcomes[19-21]
    x. Pathologic predictors of recurrence (Gleason grade, positive margins, seminal vesicle invasion, volume of tumor, extracapsular extension, and positive pelvic lymph nodes)[22] and familiarity with post-treatment predictive tools
f. Comparative effectiveness and harms of treatments[23]
    i. Optimal management for localized prostate cancer is unknown, and likely varies by specific scenario (disease characteristics, patient characteristics)
    ii. Surgery vs. observation trials[24, 25]
    iii. Observational studies[15, 26, 27]
g. Emerging modalities
    i. Ablation therapies
        1. Cryotherapy
            a. Patient selection
            b. Treatment methods and technique
            c. Treatment complications and side-effects
            d. Short-term oncologic outcomes
        2. HIFU – not FDA approved in US
    ii. Focal therapy

2. Management of locally advanced disease
    a. Case selection and evaluation of candidates
    b. Role of surgery[28, 29]
        i. Risk stratification methods
        ii. Impact after radical prostatectomy of positive margins, positive seminal vesicles and/or positive lymph nodes
        iii. Radiographic staging studies (CT, bone scan, MRI)
    c. Role of hormone therapy in conjunction with radiation therapy[30, 31]
3. Management of locally recurrent disease and the role of adjuvant treatment
    a. Case selection and evaluation of candidates for adjuvant and local salvage treatment
    b. Salvage surgery and salvage cryotherapy after radiation
    c. Adjuvant and salvage radiation therapy[32, 33]
4. Survivorship
    a. Impact of different treatments on quality of life[27, 34]
    b. Management of common complications of local therapies, including stress urinary incontinence, erectile dysfunction, bladder neck contracture, radiation cystitis, urethral stricture, depression.

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Chapter 101 - Expectant Management of Prostate Cancer

Chapter 102 - Radical Retropubic and Perineal Prostatectomy

Chapter 103 - Laparoscopic and Robotic-Assisted Laparoscopic Radical Prostatectomy and Pelvic Lymphadenectomy

Chapter 104 - Radiation Therapy for Prostate Cancer

Chapter 105 - Cryotherapy for Prostate Cancer

Chapter 106 - High-Intensity Focused Ultrasound for the Treatment of Prostate Cancer

Chapter 107 - Treatment of Locally Advanced Prostate Cancer

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Chapter 11: Treatment of Early Stage Prostate Cancer

11A: Quality of Life after Treatment for Early Stage Prostate Cancer

11B: Active Surveillance for Prostate Cancer: Rationale, Methods, and Results

11C: PLND: Indications for and Technique of Pelvic Lymph Node Dissection

11D: Radical Prostatectomy for Clinical Stage T1 and T2 Prostate Cancer

11E: Treatment of Early Stage Prostate Cancer: Laparoscopic Radical Prostatectomy

11F: Robotic-Assisted Laparoscopic Prostectomy

11G: Brachytherapy Alone and with External Beam Radiotherapy for Localized Prostate Cancer

11H: Other Interventions for the Treatment of Localized Prostate Cancer (Cryo, Hifu)

Chapter 12: Management of High Risk Prostate Cancer

12A: Combined Hormone Therapy and Radiation Therapy for High-Risk Prostate Cancer

12B: Surgical Management of Clinical T3 (cT3) and Node Positive (pN+) Adenocarcinoma

Chapter 13: Treatment of Locally Recurrent Prostate Cancer

13A: Recurrence Following Radiotherapy: Definitions, Prognosis, and Management

13B: Salvage Radical Prostatectomy for Recurrence Prostate Cancer after Radiation Therapy

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5. Management of Advanced Prostate Cancer

Learner Objectives

Upon completion of this unit the urologic oncology fellow should:

1. Know the molecular biology of the androgen axis and the physiological impact of hormonal interventions.
2. Know the mechanism of action for each form of androgen deprivation therapy.
3. Recognize complications associated with androgen deprivation therapy and possible therapeutic interventions.
4. Understand controversies surrounding the timing and methods of androgen deprivation therapy administration.
5. Know possible secondary hormonal manipulations for androgen independent prostate cancer.
6. Understand the role of chemotherapy in castrate-resistant disease.
7. Understand the mechanism, benefits and side effects of each of the FDA-approved and emerging therapies for metastatic prostate cancer.
8. Know risk factors associated with biochemical relapse after primary treatment.
9. Be familiar with definitions of biochemical recurrence after radical prostatectomy and radiation therapy.

Contents

1. Initial management of advanced prostate cancer: metastatic disease, lymph node positive disease and recurrence after primary therapy[1]
    a. Case selection and evaluation of candidates for systemic therapy
    b. Interpretation of CT, bone scan, and other radiographic imaging
    c. Biologic significance of androgen receptor signaling in advanced prostate cancer
    d. Hormone therapy
        i. LHRH agonist
        ii. Orchiectomy
        iii. LHRH antagonist

iv. Health maintenance for men on androgen deprivation therapy – i.e. bone health interventions

e. Androgen receptor blockers
f. Combined androgen blockade
g. Intermittent versus continuous LHRH therapy
h. Secondary hormonal interventions
i. Prevention or management of side effects: hot flashes, osteoporosis, weight gain, cognitive loss, metabolic syndrome
    i. Role of Calcium/Vitamin D and bisphosphonates

2. Biochemical persistence/recurrence after primary therapy
    a. Defining recurrence after surgery (i.e. different published definintions of biochemical recurrence/guideline recommendations) and after radiation (i.e. Phoenix criteria)
    b. Natural history of biochemical recurrence
    c. Predictors of progression to metastatic disease in patients with biochemical recurrence
3. Management of castrate-resistant prostate cancer
    a. Definition of CRPC, natural history, and controversies in sequencing of therapies
    b. Chemotherapy
        i. Familiarity with trials showing effect of Docetaxel on survival and Mitoxantrone on palliation[2, 3]
        ii. Cabazitaxel for progression after docetaxel
    c. Immunotherapy[4]
        i. Sipuleucel-T
            1. Theorized mechanism, administration, side effects and monitoring
            2. Trial data showing overall survival advantage vs. placebo
        ii. PROSTVAC – off the shelf vaccine[5]
    d. Novel hormonal therapies
        i. Abiraterone
            1. Mechanism, co-administration with prednisone, side effects and monitoring
            2. Trial data showing overall survival advantage vs. placebo in post-chemo[6] and pre-chemo settings[7]
        ii. Enzalutamide
            1. Mechanism, side effects and monitoring
            2. Trial data showing overall survival advantage vs. placebo in post-chemo setting[8]; pre-chemo trial pending
    e. Other novel therapies
        i. Denosumab
            1. Mechanism, side-effects and monitoring
            2. Trial data showing improvement in skeletal-related events vs. bisphosphonates in men with bone metastases[9], and bone-metastasis-free survival in men with CRPC[10]
        ii. Radium 223
    f. Role of clinical trials
    g. Sequencing of available treatments

Bibliography

Guidelines

AUA Guideline for the Management of Clinically Localized Prostate Cancer

NCCN Clinical Practice Guideline on Prostate (Management)

Campbell-Walsh Urology, 10th Edition – Ed., Wein

Chapter 108 - Clinical State of the Rising PSA Value after Definitive Local Therapy: A Practical Approach

Chapter 109 - Hormone Therapy for Prostate Cancer

Chapter 110 - Treatment of Castration-Resistant Prostate Cancer

Comprehensive Textbook of Genitourinary Oncology, 4th Edition – Ed., Scardino

Chapter 3: Androgen Receptor Signaling in Castrate Resistant Prostate Cancer

Chapter 14: Advanced Prostate Cancer

14A: Biology of Bone Metastases in Men with Prostate Cancer

14B: Initial Management of Metastatic Prostate Cancer

14C: Second Line Treatment: Going Beyond Hormones

14D: Management of Castration-Resistant Prostate Cancer

AUA Updates

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SUO Curriculum - Other Malignancies

1. Adrenal Tumors

A. Adrenal Gland: Anatomy/Physiology

Unit Objectives:

Upon completion of this unit, the urologic oncology fellow will demonstrate an understanding of the anatomy and physiology of the adrenal gland

Contents:

1. Histopathology of the adrenal gland
    a. Medulla
        i. Embryological origin
    b. Cortex
        i. Embryological origin
        ii. Knowledge of three zones, with hormones produced by each
2. Vascular anatomy of the adrenal glands
    a. Differences between right and left adrenal gland
    b. Relevant surgical anatomy as it relates to:
        i. Bleeding complications
        ii. Approach to functional tumors (i.e. pheochromocytoma)
        iii. Partial versus radical adrenalectomy
3. Surgical relationships to adjacent structures
4. Adrenal Physiology
    a. Cortex
        i. Hormones produced – regulation, activity
    b. Medulla
        i. Catecholamines produced
        ii. Regulation and pathways of catecholamine production
        iii. Actions of the catecholamines
    c. Syndromes/Diseases associated with adrenal tumors
        i. Cortisol excess
            1. Differential diagnosis + diagnostic evaluation
            2. Treatment principles
        ii. Aldosterone excess
            1. Differential diagnosis + diagnostic evaluation
            2. Treatment principles
        iii. Pheochromocytoma

1. Diagnostic evaluation
2. Treatment principles

B. Epidemiology

Unit Objectives:

Upon completion of this section the urologic oncology fellow should be able to describe the incidence and risk factors for the different types of adrenal tumors

Contents:

1. Epidemiology of tumors of the adrenal glands
    a. Age of onset
    b. Male to female ratio
    c. Ethnic and racial factors
2. Etiology of tumors of the adrenal glands
    a. Familial/genetic syndromes associated with adrenal tumors
    b. Exposure risks and other causes

C. Diagnostic Evaluation of Adrenal Tumors

Unit Objectives:

Upon completion of this section the urologic oncology fellow should be able to describe the diagnostic evaluation and outcomes following treatment of adrenal tumors

Contents:

1. Recognize the symptoms and physical exam findings of:
    a. Cortisol excess
    b. Pheochromocytoma
    c. Aldosterone excess
    d. Adrenocortical carcinoma
2. Appropriate imaging evaluation (i.e. CT, MRI, ultrasound, MIBG, FDG-PET, venous sampling) for adrenal tumors
    a. Understand the importance of quantitating intracellular lipid content for the radiologic characterization of adrenal tumors
    b. Understand/identify specific radiographic characteristics of:
        i. Adenomas – lipid rich (70%) vs lipid poor (30%)
            1. Identify lipid poor adenomas on CT washout
        ii. Pheochromocytomas
            1. Role of MRI, MIBG, FDG-PET (esp for mets)
        iii. Myelolipomas
        iv. Adrenocortical carcinoma
        v. Adrenal cysts
        vi. Metastases

3. Understand the evaluation of incidentally discovered adrenal masses
    a. Understand proper radiologic + biochemical functional evaluation of the "adrenal incidentaloma"
    b. Recognize the frequency of potentially surgical lesions among incidentally detected adrenal tumors
4. Understand the staging and clinicopathologic prognostic factors associated with adrenocortical carcinoma
    a. Recognizing known correlation of adrenal tumor size with risk of malignancy
    b. Understanding indications for excision of an adrenal lesion based on tumor size/growth rate
5. Understanding management of the adrenal gland during radical nephrectomy for renal cell carcinoma – i.e. indications for concurrent adrenalectomy
6. Understanding indications for resection of metastases to the adrenal gland

D. Surgical Management of Adrenal Tumors

Unit Objectives: Upon completion of this section, the urologic oncology fellow will:

1. Demonstrate knowledge of surgical indications for adrenal tumors
2. Demonstrate an understanding of the preoperative, intraoperative, and postoperative management of adrenal tumors
3. Understand the complications associated with adrenal surgery

Contents:

1. Indications, limitations, and risks of biopsy of an adrenal mass
2. Indications for adrenal surgery in the setting of
    a. Cortisol excess
    b. Aldosterone excess
    c. Pheochromocytoma
3. Options for adrenal resection
    a. Partial adrenalectomy
    b. Radical adrenalectomy
    c. Bilateral adrenalectomy
4. Surgical approaches to the adrenal gland
    a. Open (thoracoabdominal, transperitoneal, retroperitoneal)
    b. Minimally invasive (transperitoneal and retroperitoneal, laparoscopic and robotic-assisted)
5. Peri-operative management of pheochromocytomas
    a. Alpha receptor blockade
    b. Hydration
    c. Experienced anesthesiologist
    d. Appropriate vasoactive agents
6. Understand potential complications following surgery

E. Medical Management of Adrenal Tumors

Unit Objectives:

Upon completion of this section the urologic oncology fellow will be able to describe the medical management of benign functional adrenal tumors as well as chemotherapy options for metastatic pheochromocytoma and adrenocortical carcinoma

Contents:

1. Describe medical management of cortisol excess
2. Describe medical management of aldosterone excess
3. Describe medical management of pheochromocytoma in perioperative period as well as chemotherapy options in the metastatic setting
4. Describe chemotherapy options for advanced or metastatic adrenocortical carcinoma.

2. Urethral Carcinoma

A. Anatomy/Pathology

Unit Objectives:

Upon completion of this unit, the urologic oncology fellow should be able to describe normal urethral anatomy and the histopathology of urethral carcinomas.

Contents:

1. Normal anatomy of the male and female urethra – gross, histologic
2. Surgical relationships of the male and female urethra to surrounding structures
    a. Vagina
    b. Bladder
    c. Corpora cavernosum
    d. Prostate
3. Lymphatic Drainage of the urethra
    a. Male
    b. Female
    c. Based on location within the urethra (i.e. distal vs proximal)
4. Epithelial lining histology based on region of urethra
5. Tumor histopathology
        i. Squamous cell carcinoma
        ii. Urothelial carcinoma
        iii. Adenocarcinoma
        iv. Sarcoma

B. Epidemiology

Unit Objectives:

Upon completion of this unit, the urologic oncology fellow should understand the epidemiology, etiology, and risk factors for the development of urethral carcinoma.

Contents:

1. Describe the epidemiology of urethral cancers including
    a. Male to female ratio
    b. Age
    c. Racial or ethnic factors
2. Describe risk factors for the development of urethral carcinoma.
    a. Smoking
    b. Industrial exposures
    c. Infectious agents
    d. Stricture disease
    e. Previous urothelial carcinoma (i.e. of the bladder)
3. Describe prognostic factors for urethral tumors, including prediction of loco-regional + distant metastases
    a. Stage
    b. Grade
    c. Histology
    d. Location within the urethra

C. Diagnosis and Staging

Upon completion of this unit, the urologic oncology fellow should understand how to diagnose and stage urethral carcinoma.

Contents:

1. Presentation
    a. Hematuria
    b. Frequency and urgency
    c. Dysuria
    d. Obstruction
2. Diagnosis
    a. Physical exam
        i. Inguinal lymphadenopathy
        ii. Palpable lesion in the urethra
    b. Cystourethroscopy
    c. Imaging:
        i. CT scan
        ii. MRI
        iii. Bone scan
        iv. Ultrasound
3. Staging - TNM
4. Grading

D. Management

Unit Objectives:

Upon completion the urologic oncology fellow should be able to describe the management of urethral carcinoma, including surgical and multimodal treatment options

Contents:

1. Indications for biopsy of the urethra
2. Surgical technique for transurethral resection of a urethral tumor
3. Surgical technique for urethrectomy: partial vs. total
    a. Reconstruction techniques
4. Cystectomy with urethrectomy
    a. Indications
    b. Technique
    c. Options for reconstruction
5. Indications for inguinal lymph node dissection with urethral cancers
6. Chemotherapy and Radiotherapy for Urethral Cancer
    a. Describe the indications for chemotherapy and radiotherapy as a primary treatment for urethral cancer.
    b. Describe the indications for chemotherapy and radiotherapy for the treatment of urethral cancer in the following settings:

        a. Neoadjuvant
        b. Urethral sparing
        c. Adjuvant
        d. Locally advanced and unresectable urethral cancer

    e. Metastatic urethral cancer

3. Paratesticular Tumors

A. Anatomy/Pathology

Unit Objectives:

Upon completion of this unit the urologic oncology fellow will understand the anatomy of the testicle and paratesticular structures as well as relevant pathology of the most common paratesticular tumors

Contents:

1. Normal gross anatomy of the testicle and paratesticular structures including

a. Testicle
b. Tunica albuginea
c. Epididymis
d. Vas deferens
e. Spermatic cord

2. Describe the various benign and malignant tumors which affect the paratesticular structures
    a. Adenomatoid tumor
    b. Lipoma of the cord
    c. Cysts
    d. Spermatoceles
    e. Sarcomas
        i. Rhabdomyosarcomas
        ii. Leiomyosarcomas
        iii. Liposarcomas
        iv. Malignant fibrous histiocytomas

B. Diagnosis

Unit Objectives:

Upon completion of this section the urologic oncology fellow will be able to describe the diagnostic evaluation of a suspected paratesticular tumor.

Contents:

1. Physical exam
    a. Fixed versus mobile
    b. Transillumination
    c. Overlying skin involvement
    d. Regional lymph node involvement
2. Radiologic studies
    a. Scrotal ultrasound
    b. CT scan – chest/abdomen/pelvis
    c. MRI
3. Diagnostic strategies
    a. (Open) biopsy through inguinal incision
    b. Needle biopsy
    c. Radical inguinal orchiectomy

C. Management:

Objectives:

1. Discuss the surgical approach to a paratesticular tumor.
2. Discuss indications for multimodal management, including referrals for neoadjuvant/adjuvant chemotherapy and radiotherapy

Contents:

1. Inguinal approach to paratesticular tumors
    a. Wide local excision (vs. radical orchiectomy)
    b. Re-excision
        i. Indications
        ii. Intent
    c. Complications

2. Indications for retroperitoneal lymph node dissection

3. Multimodal treatment of paratesticular tumors
    a. Indications – histology, grade, margin status
    b. Use of chemotherapy
    c. Use of radiation therapy

4. Genitourinary Sarcomas

A. Epidemiology/Incidence

Objectives:

1. Discuss the incidence and epidemiology of the various genitourinary sarcomas.
2. Understand the implications of tumor location on management and prognosis for sarcomas

Contents:

1. Histology and associated biology of common genitourinary sarcomas
    a. Liposarcoma
    b. Rhabdomyosarcoma
    c. Leiomyosarcoma
    d. Carcinosarcoma

2. Locations
    a. Kidney
    b. Prostate
    c. Bladder
    d. Spermatic cord/paratesticular
    e. Testicular
    f. Retroperitoneal
3. Epidemiology
    a. Age/sex
    b. Racial
    c. Association of location with histology

B. Diagnosis

Unit Objective:

After completion of this section the urologic oncology fellow will be able to demonstrate and understanding the signs, symptoms, and diagnostic evaluation associated of genitourinary sarcomas

Contents:

1. Symptoms based on region of origin:
    a. Kidney
    b. Spermatic cord and paratesticular
    c. Bladder
    d. Prostate
    e. Testicle
    f. Retroperitoneal
2. Physical exam findings based on region of origin
3. Imaging evaluation
    a. Ultrasound
    b. CT scan
    c. MRI

C. Management and Prognosis

Objectives:

After completion of this unit the urologic oncology fellow will be able to discuss management for the various types of GU sarcomas, and will be familiar with the prognosis based on location and type.

Contents:

1. Surgical Management – wide local excision with negative surgical margins = critical. May require adjacent organ resection depending on location
    i. Spermatic cord/paratesticular – radical orchiectomy
    ii. Retroperitoneal - nephrectomy, ureteral resection, bowel/vascular resection
    iii. Pelvic – partial/radical cystectomy, prostatectomy
2. Multimodal Management
    a. Chemotherapy – understanding integration of pre/post resection chemotherapy, indications
    b. Radiotherapy – understanding role of pre/intra/postoperative radiation therapy, indications
3. Prognosis
    a. Related to site of origin
    b. Related to histologic type
    c. Related to grade, stage, and margin status