Staging and Treatment for GYN Cancers

2016-2017 FCDS Educational Webcast Series
Rescheduled from 1/19/2017

February 16, 2017
Steven Peace, CTR

CDC & Florida DOH

“We acknowledge the Centers for Disease Control and Prevention, for its support of the Florida Cancer Data System, and the printing and distribution of the materials for the 2016-2017 FCDS Webcast Series under cooperative agreement DP003872-03 awarded to the Florida Department of Health. The findings and conclusions in this series are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention”.

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Presentation Outline

- AJCC TNM Staging – NPCR Quick Reference
- Overview Major GYN Cancer Characteristics
- Anatomy of the Female Reproductive System
- GYN Cancer Staging – FIGO and AJCC TNM 7th ed.
- Site Specific Factors for GYN Cancers
- NCCN/FIGO Treatment Guidelines
- Text Documentation
- Questions

Manual Ordering Information

- COST: $64.95
- ISBN: 978-0-387-88440-0
- Required - Florida Mandate
  - FCDS will not purchase
  - Facility may purchase
  - Individual may purchase
- Also Required to Purchase 8th Edition in 2016-2017
  - https://cancerstaging.org
  - http://springer.com
  - 1-800-SPRINGER

Chapter Outline and Contents

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<td>Overview of factors affecting staging and outcome</td>
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|                      | o Metastatic sites |
| Rules for Classification | o Clinical  
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| Prognostic Features | Identification and discussion of non-anatomic prognostic factors |
| Definitions of TNM  | T: Primary tumor  
|                      | N: Regional lymph nodes  
|                      | M: Distant metastasis |
| Anatomic Stage Prognostic Groups |
| Prognostic Factors (SSFs) | a. Required for staging  
|                      | b. Clinically significant |
| Grade |
| Histopathologic Type |
| Bibliography |
| Staging Form |

AJCC Cancer Staging Manual, 7th ed. – Chapter 1, Table 1.10, p.14

TNM Staging – Points in Time

**Timing for Clinical Stage** – Date of Diagnosis up to the 1st treatment... in the Absence of Disease Progression or within first 4 months after Diagnosis

**Timing for Pathologic Stage** – Date of Diagnosis through definitive surgery... in the Absence of Disease Progression or within first 4 months after Diagnosis

**Timing for Post-Treatment Stage (Pathologic - yp)** – Pathologic Stage following treatment with neoadjuvant therapy(s) and definitive surgery (can include progression after neo-TX)

**Timing for Post-Treatment Stage (Clinical - yc)** – Clinical Stage following treatment with neoadjuvant therapy(s) and before definitive surgery or no definitive surgery (can include progression after neo-TX)

Source: NPCR AJCC TNM 7th ed. Quick Reference
**Clinical Stage – Pretreatment**

Clinical Stage (Pre-TX Stage) is the extent of disease defined by diagnostic study before information is available from surgical resection or initiation of neoadjuvant therapy, or within 4 months after date of diagnosis, whichever is shorter.

- Patient Medical History
- Physical Examination
- Diagnostic Imaging Studies
- Endoscopy
- Biopsy of primary tumor
- Biopsy of single node or sentinel nodes
- Biopsy of metastatic sites
- Exploratory Surgery
- Other relevant lab tests, biomarker tests, or examinations

**Lymph Node Bx or Resection**

A lymph node biopsy can be either clinical or pathologic. If the only assessment of the primary tumor is a clinical (cT) assessment, then a biopsy of a single lymph node or of a sentinel lymph node can also be included in the clinical (cN) stage. In this situation, there would have been no evaluation of the primary tumor that qualifies for the pT. This allows for the assignment of a clinical stage when a pathological stage is not applicable.

Generally a resection of the primary tumor that qualifies for the pT is required in order to assign the pN. If there is a resection that qualifies for the pathologic assessment of T (pT), then any microscopic evidence of regional node involvement is classified as pN. MUST have at least ONE node microscopically examined to assign a pN. This can be a FNA, biopsy or excision of a node as long as there is microscopic confirmation.
Pathologic Stage

Pathologic Stage includes any information obtained about the extent of cancer through completion of definitive surgery as part of the first course of treatment or identified within 4 months after the date of diagnosis, whichever is longer, as long as there is no systemic or radiation therapy initiated or the cancer has not clearly progressed during that timeframe.

Must meet chapter-specific criteria for surgical resection to assign

Includes all of the clinical stage information from clinical stage, plus
- Observations at time of surgical resection from operative report
- Pathologic Examination of surgically resected primary specimen
- Pathologic Examination of surgically resected regional lymph nodes
- Pathologic Examination of biopsy or resection of metastasis

Source: NPCR AJCC TNM 7th ed. Quick Reference

Pathologic Stage

Pathologic stage classification starts at moment of DIAGNOSIS.

Pathologic stage is defined by the same diagnostic studies used for clinical staging supplemented by findings from surgical resections and histologic examination of the surgically removed tissues.

Pathologic stage includes three equal pieces of information:
- All of the clinical classification information not disproven by the intra-operative or pathology findings.
- PLUS includes the operative findings during the resection not submitted to or disproven on pathology.
- PLUS includes the pathology report findings of the resected specimen.

Source: NPCR AJCC TNM 7th ed. Quick Reference
Pathologic Stage

If a biopsied tumor is not resected for any reason (e.g., when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

- To use the highest T and highest N to assign the pathologic stage, you have to have both microscopic confirmation of the highest T for a pT AND microscopic confirmation of the highest N for a pN.

- IMPORTANT: pT blank and pN3 is not enough for a pathologic stage so the pN will be used for the clinical stage.

Source: NPCR AJCC TNM 7th ed. Quick Reference

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Post-Treatment Stage

Documents measured response to initial (neoadjuvant) therapy(s)

- Complete Response
- Partial Response
- No Response
- Progression

May be clinical measurement only – yc

- Based on post-treatment imaging, physical examination, biopsy

More often it is post-treatment pathologic stage – yp

- Based on post-treatment surgical resection of primary site and regional nodes
- Must meet chapter-specific criteria for surgical resection

What about pre-treatment that consisted of less than 1 month of endocrine therapy – hormone therapy (prostate, breast, thyroid)?

This is Not Neoadjuvant Tx... even though it begins before surgery

Source: NPCR AJCC TNM 7th ed. Quick Reference
AJCC 8th edition – Order Info

- COST: $119.99
- ISBN: 978-3-319-40617-6

- 1429 pages
- 512 Illustrations
- 187 color Illustrations

- Required - Florida Mandate
  - FCDS will not purchase
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- https://cancerstaging.org
- http://springer.com
- 1-800-SPRINGER

Presentation Outline

- Cervix, Vagina, Vulva – In Situ and HPV-Related Neoplasms
  - Reporting Requirements - CIN III, VAIN III, VIN III, AIN III and SIN III
- Cervix, Vagina, Vulva – Invasive Cancers (SCC, melanoma)

- Corpus Uteri – Epithelial (adenocarcinoma)
- Corpus Uteri – Mesenchymal (pure sarcoma)
- Corpus Uteri – Mixed Tumors (adeno-sarcoma)

- Ovary/Fallopian Tube – Epithelial and Stromal Tumors
- Ovary/Fallopian Tube – Borderline Malignancy
- Ovary/Fallopian Tube – Germ Cell Tumors

- Female Primary Peritoneal Malignancy
Female Reproductive System

Lesser Omentum

Source: http://teachmeanatomy.info

Female Reproductive System

Peritoneal Cavity

Sacrum

Source: http://www.anatomypic.com
Female Reproductive System

Source: http://www.cea1.com/femaleanatomy

Female Reproductive System

Source: http://www.novartis.com
Female Reproductive System

Source: http://www.cancer.org

Overview – Cervix, Vagina, Vulva

- Causes & Risk Factors
- Signs and Symptoms
- PAP and HPV Testing
- WHO Classification

- Stage - FIGO/AJCC TNM 7th ed.
- Site-Specific Factors – stage/prognosis/tx
- NCCN/FIGO Treatment Guidelines
Causes and Risk Factors

Environmental
- HPV Infection
- Chlamydia Co-Infection
- HIV Immunosuppression
- Do Not Get Screened
- Oral Contraceptive Use
- Smoking Cigarettes

Genetic
- 80% in women > 50yrs
- Personal History
- DES Exposure
- Family History

Cervical Cancer Screening

April 2014 the FDA Approved the First HPV DNA Test for Primary Cervical Cancer Screening for women age 25+ that examines 14 high-risk strains of HPV

Test developed by Roche called “cobas”

Clinical Trials suggest “cobas” is better for screening than pap test because it can identify women at risk for pre-cancerous lesions earlier than pap smear

May eventually replace pap smear
Signs and Symptoms

- Tumor Mass
- Wart-like bump
- Abnormal color
- Abnormal texture
- Itching or Burning
- Unusual vaginal discharge
- Bleeding between periods
- Bleeding after menopause
- Bleeding or pain during sex

http://www.inovio.com

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Signs and Symptoms

<table>
<thead>
<tr>
<th>Gynecologic Cancer Symptoms</th>
<th>Cervical Cancer</th>
<th>Ovarian Cancer</th>
<th>Uterine Cancer</th>
<th>Vaginal Cancer</th>
<th>Vulvar Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal vaginal bleeding or discharge</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td></td>
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<tr>
<td>Pelvic pain or pressure</td>
<td></td>
<td>✗</td>
<td></td>
<td>✗</td>
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<tr>
<td>Abdominal or back pain</td>
<td></td>
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<td>✗</td>
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<tr>
<td>Bloating</td>
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<td>✗</td>
</tr>
</tbody>
</table>

http://www.cdc.gov/cancer/gynecologic/images/GYN_Symptoms
PAP and HPV Testing

- >6 Million Women in U.S. have HPV Infection – at risk
- >33% of Women Eligible for Screen are NOT Screened
- Routine Screening detects most cancers pre-invasive
- PAP and HPV DNA Screening are for “Prevention”
- PAP Screening detects >90% of cancers
- HPV DNA Screening may replace PAP Screen
- Annual PAP No Longer Routine
- Post-Menopausal Risk
- Other GYN cancers and HPV – vulva, vagina, anus

Source: American Cancer Society

HPV > Neoplasia > Cancer

HPV Vaccine for Prevention of HPV not Treatment

Source: http://www.clinicalepigeneticsjournal.com/1868-7083-4-13-1.jpg
Other Characteristics

- **Reportable** Non-invasive carcinoma
  - Anus - AIN III
  - Vulva - VIN III
  - Vaginal - VAIN III

- **Not Reportable** Non-invasive carcinoma
  - Cervix - CIS (carcinoma in-situ)
  - Cervix - CIN III

WHO Histologic Classification

- Squamous cell carcinoma
- Adenocarcinoma
- Adenosquamous carcinoma
- Malignant Melanoma
Overview – Corpus Uteri

- Causes & Risk Factors
- Signs and Symptoms
- WHO Classification

- Stage - FIGO/AJCC TNM 7th ed.
- Site-Specific Factors – stage/prognosis/tx
- NCCN/FIGO Treatment Guidelines

Causes and Risk Factors

Environmental
- Oral Contraceptive Use
- Obesity and Diabetes
- Early age at menarche
- Late menopause
- Null parity – NO Children
- Hormone Manipulation
  - Estrogen Replacement
  - Tamoxifen Therapy
- Recurrent Bladder Infections
- History of Radiation Therapy

Genetic
- Older age (> 55 years)
- Race – Uterine Sarcoma
- Retinoblastoma Gene
- Lynch syndrome

Signs and Symptoms

- Unusual vaginal discharge
- Bleeding between periods
- Bleeding after menopause
- Bleeding or pain during sex
- Pelvic pain
- Pain during intercourse
- Pain or difficulty when emptying the bladder

Source: American Cancer Society

WHO Histologic Classification

- Carcinoma and Carcinosarcoma
  - 8000-8790, 8980-8981, 9700-9701

- Adenosarcoma
  - 8380

- Sarcoma (pure sarcoma)
  - 8890-8898, 8930-8931
Other Characteristics

- ICD-O-3 term “stromal endometriosis” [8931/3] – This Condition IS Reportable

Source: http://fertilitydocs.com/gif/endodiag.gif

Overview – Ovary, Fallopian Tube & Primary Peritoneal Neoplasms

- Causes & Risk Factors
- Signs and Symptoms
- WHO Classification

- Stage - FIGO/AJCC TNM 7th ed.
- Site-Specific Factors – stage/prognosis/tx
- NCCN/FIGO Treatment Guidelines
Causes and Risk Factors

Environmental
- Hormone manipulation
  - Estrogen Replacement
  - Fertility Drug – Clomid
- Obesity
- Oophorectomy reduces risk of ovarian and fallopian tube cancer but may increase risk for primary peritoneal cancer after prophylactic salpingooophorectomy

Genetic
- Age > 40
- Family history
- BRCA1 and BRCA2
- Lynch syndrome
- HNPCC syndrome (hereditary non-polyposis colorectal cancer)
- Fallopian Tube - NCCN suggested that these cancers may be the origin of some ovarian and primary peritoneal cancers

Source: 2014 Cancer Facts & Figures - American Cancer Society

Signs and Symptoms

- Pelvic mass detected on abdominal/pelvic exam
- Ascites – malignant fluid in the peritoneal cavity
  - Causes abdominal distention and bloating
- Pelvic or abdominal pain
- Difficulty eating or feeling full quickly – early satiety
- Urinary symptoms (urgency or frequency) without other obvious source of malignancy

Gynecologic Cancer Symptoms

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<td>⬤</td>
<td>⬤</td>
</tr>
</tbody>
</table>

http://www.cdc.gov/cancer/gynecologic/images/GYN_Symptoms
WHO Histologic Classification

- **Ovarian Epithelial**
  - Serous cystadenocarcinoma
  - Mucinous cystadenocarcinoma
  - Endometrioid adenocarcinoma
  - Clear cell cystadenocarcinoma

- **Ovarian Germ Cell Tumors**
  - Dysgerminoma
  - Embryonal carcinoma
  - Choriocarcinoma
  - Teratoma – malignant reportable

- **Borderline Malignant Neoplasm**

Source: [http://www.clearityfoundation.org/images]
Borderline Neoplasm of Ovary

- 1973 – 1989 Not Reportable ICD-O
- 2001 – Not Reportable ICD-O-3
- ??? ??? ICD-O-4

Source: http://www.nccn.org/ovary
Other Characteristics

- Epithelial Neoplasms – Ovary/Peritoneum
  - Bulky Disease at First Presentation
  - Common Sites for Seeding
    - Peritoneum
    - Diaphragm
    - Liver Surface
  - Pulmonary Involvement Common
  - Pleural Involvement Common
  - Elevated CA-125 Common

Other Characteristics

- Historical Assessment

- Classified as Ovarian in Origin
  - Serous Tumors with Ovarian Involvement
  - Mucinous Tumors with Ovarian Involvement

- Current Evaluation Criteria – evolving

- Improvements in Imaging and IHC/FISH expected to reduce misclassification
Other Characteristics

- Serous Tumors forming 6mm mass in ovary should be considered ovarian primaries.

- Serous Tumors forming multiple small ovarian masses should be considered peritoneal if the disease is mainly extra-ovarian.

- Mucinous neoplasms metastatic to ovary are often misclassified as ovarian primaries.

Staging GYN Cancers

Federation Internationale de Gynecologie et d'Obstetrique (FIGO)
FIGO and AJCC TNM 7th ed.

FIGO and AJCC TNM criteria for stage are nearly identical.

<table>
<thead>
<tr>
<th>FIGO</th>
<th>TNM</th>
<th>CS Ext</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>IA2</td>
<td>1A2</td>
<td>112</td>
</tr>
<tr>
<td>IIIB</td>
<td>2B</td>
<td>220</td>
</tr>
<tr>
<td>IIIC</td>
<td>3C</td>
<td>330</td>
</tr>
<tr>
<td>IIIC1</td>
<td>3C1</td>
<td>331</td>
</tr>
<tr>
<td>IVA</td>
<td>4A</td>
<td>410</td>
</tr>
</tbody>
</table>

SS2000 has not been updated to current FIGO criteria.

Use the FIGO stage stated in the medical record.

When both FIGO Stage (or AJCC Stage) and TNM detail are available, record the more specific T, N, M Category Code with detail in preference to a statement of FIGO stage.

AJCC TNM Chapter & Name

- Chapter 33 – Vulva
- Chapter 34 – Vagina
- Chapter 35 – Cervix Uteri
- Chapter 36 – Corpus Uteri
- Chapter 37 – Ovary AND Primary Peritoneal Carcinoma
- Chapter 38 – Fallopian Tube
- Chapter 39 – Gestational Trophoblastic Tumors
FIGO and AJCC TNM

<table>
<thead>
<tr>
<th>Stage</th>
<th>FIGO</th>
<th>TNM</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor limited to one ovary. Capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings</td>
<td>T1a</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor limited to both ovaries, capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings</td>
<td>T2a</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor limited to any of the following: capsule ruptured, tumor on ovarian surface. Malignant cells in ascites or peritoneal washings</td>
<td>T3a</td>
</tr>
<tr>
<td>T4</td>
<td>Any T</td>
<td>Any N</td>
</tr>
</tbody>
</table>

Regional Lymph Node Metastasis
- N0: Regional lymph nodes cannot be assessed
- N1: Regional lymph node metastasis
- N2: Regional lymph node metastasis

Distant Metastasis
- M0: No distant metastasis
- M1: Distant metastasis (excludes peritoneal metastasis)

Note: Liver capsule metastasis is T3a (Stage III); liver parenchymal metastasis, M1/Stage IV. Pleural effusion must have positive cytology for M1/Stage IV.

TNM – FIGO – CS Data Collection

<table>
<thead>
<tr>
<th>Stage</th>
<th>FIGO</th>
<th>TNM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1a</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T1b</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IC</td>
<td>T1c</td>
<td>N0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T2a</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T2b</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IC</td>
<td>T2c</td>
<td>N0</td>
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<tr>
<td>Stage III</td>
<td>T3</td>
<td>N0</td>
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<tr>
<td>Stage IIA</td>
<td>T3a</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T3b</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IIC</td>
<td>T3c</td>
<td>N0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
</tr>
</tbody>
</table>

Note: For histologic grade and histopathologic type, see AJCC staging manual.
SS2000 last updated in 2000
SS2000 is NOT consistent with 2010 FIGO Stage

Regional Stages
A. Direct extension
B. To regional lymph nodes
C. Combination of A and B

Therefore, FIGO Stage noted in SS2000 may not meet same criteria as FIGO 2010

DO NOT USE 2010 FIGO to assign SS2000
DO Apply SS2000 Anatomic Stage Criteria as Described in the SS2000 Manual
**Uterine Carcinoma – FIGO/AJCC TNM**

### Staging-Endometrial Carcinoma

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th>FIGO Stages</th>
<th>Surgical-Pathologic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>IA</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td>Carcinoma in situ (precursor)</td>
</tr>
<tr>
<td>T1b</td>
<td>IA</td>
<td>Tumor confined to corpus uteri</td>
</tr>
<tr>
<td>T1c</td>
<td>IB</td>
<td>Tumor limited to endometrium or invades cervical stroma</td>
</tr>
<tr>
<td>T1d</td>
<td>IB</td>
<td>Tumor invades one-half or more of the myometrium</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumor invades stromal connective tissue of the cervix but does not extend beyond the lower 1/3 of the cervix</td>
</tr>
<tr>
<td>T3a</td>
<td>IA</td>
<td>Tumor invades serosa and/ or adnexa (direct extension or metastasis)</td>
</tr>
<tr>
<td>T3b</td>
<td>IB</td>
<td>Vaginal involvement (direct extension or metastasis)</td>
</tr>
<tr>
<td>T3c</td>
<td>IB</td>
<td>or perineal involvement</td>
</tr>
<tr>
<td>T4</td>
<td>IV</td>
<td>Metastases to pelvic and/or para-aortic lymph nodes (or metastases to pelvic or para-aortic nodes, and/or distant metastases)</td>
</tr>
</tbody>
</table>

### Distant Metastasis (M) | FIGO Stages | Surgical-Pathologic Findings |
<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>IVA</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>M2</td>
<td>IIB</td>
<td>Regional lymph node metastasis to regional lymph nodes or to pelvic lymph nodes without positive pelvic lymph nodes</td>
</tr>
<tr>
<td>M3</td>
<td>III</td>
<td>Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes</td>
</tr>
</tbody>
</table>

### Regional Lymph Nodes (N) | FIGO Stages | Surgical-Pathologic Findings |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td></td>
<td>No evidence of regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>IIA</td>
<td>Regional lymph node metastasis</td>
</tr>
<tr>
<td>N2</td>
<td>IIB</td>
<td>Regional lymph node metastasis</td>
</tr>
</tbody>
</table>

**Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original and primary source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer Science and Business Media LLC (SBM). For complete information and data supporting the staging tables, visit [www.springer.com](http://www.springer.com). Any citation or quotation of this material must be credited to the AJCC as its primary source. The inclusion of this information herein does not authorize any reuse of further distribution without the express written permission of Springer SBM, on behalf of the AJCC.**


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**Uterine Sarcoma – FIGO/AJCC TNM**

### Staging-Uterine Sarcoma

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th>FIGO Stages</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>IA</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Tumor limited to the uterus</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumor extends beyond the uterus, within the pelvis</td>
</tr>
<tr>
<td>T3a</td>
<td>IA</td>
<td>Tumor involves other pelvic organs</td>
</tr>
<tr>
<td>T3b</td>
<td>IB</td>
<td>Tumor infiltrates abdominal tissues (not just protruding into the abdomen)</td>
</tr>
<tr>
<td>T3c</td>
<td>IB</td>
<td>One site more than one site</td>
</tr>
</tbody>
</table>

**Note:** Sarcomas of the uterine corpus and ovary/pelvis in association with ovaropelvic endometriosis should be classified as independent primary tumors.

<table>
<thead>
<tr>
<th>Distant Metastasis (M)</th>
<th>FIGO Stages</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>IVA</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M2</td>
<td>IIB</td>
<td>Distant metastasis (excluding adnexal, pelvic, and abdominal tissues)</td>
</tr>
</tbody>
</table>

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Staging Ovary – FIGO/AJCC TNM

<table>
<thead>
<tr>
<th>Schema Name</th>
<th>2014 FCDS Required</th>
<th>Additional CoC Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>AdnexaUterineOther</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Cervix</td>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>CorpusAdenosarcoma</td>
<td>2</td>
<td>1,3,4,5,6</td>
</tr>
<tr>
<td>CorpusCarcinoma</td>
<td>2</td>
<td>1,3,4,5,6</td>
</tr>
<tr>
<td>CorpusSarcoma</td>
<td>2</td>
<td>1,3,4,5,6</td>
</tr>
<tr>
<td>FallopianTube</td>
<td>None</td>
<td>1,4,5,6,7</td>
</tr>
<tr>
<td>GenitalFemaleOther</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>MerkelCellVulva</td>
<td>3,11</td>
<td>1,16,17,18,22</td>
</tr>
<tr>
<td>Ovary</td>
<td>None</td>
<td>1,2,3</td>
</tr>
<tr>
<td>PeritoneumFemaleGen</td>
<td>25</td>
<td>1,2,3</td>
</tr>
<tr>
<td>Placenta</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Vagina</td>
<td>None</td>
<td>1,2,3,4,5,6,7</td>
</tr>
<tr>
<td>Vulva</td>
<td>11</td>
<td>10</td>
</tr>
</tbody>
</table>
NCCN/FIGO Treatment Guidelines
Cervix, Vulva, Vagina

Choosing the Most Appropriate Type of Surgery
Based on Clinical Stage

Any Histology

NCCN Guidelines – Cervical Cancer – Version 1.2017
Surgery: Cervix, Vulva, Vagina

**Principles of Surgery: Surgical Staging**

- Valvar cancer is staged using the American Joint Committee on Cancer (AJCC) and the International Federation of Gynecology and Obstetrics (FIGO) staging systems (Table 3).15
- Staging involves complete surgical resection of the primary valvar tumor(s) with at least 1-cm margins and either a unilateral or bilateral inguinal lymphadenectomy, or an SLN biopsy in select patients. Inguinal lymphadenectomy removes the LNs superficial to the inguinal ligament, within the proximal femoral triangle, and deep to the crural fascia.
- SLN status is the most important determinant of survival.9
- Historically, an elective resection of the valvar tumor and complete bilateral inguinoaxillary lymphadenectomy (removal of superficial inguinal and deep femoral nodes) was performed, but this approach was associated with significant morbidity.10
- The current standard involves resection of the valvar tumor and LNs through separate incisions.10
- The choice of valvar tumor resection technique depends on the size and extent of the primary lesion and may include radical local excision and modified radical vulvectomy.
- The depth of the resection is similar for both radical local excision and radical vulvectomy (ie, to the uterovaginal diaphragm).11
- There are no prospective trials comparing the resection techniques above. retrospective data suggest there is no difference in recurrence outcome between radical local excision compared with radical vulvectomy.
- For a primary valvar tumor that is <4 cm, located 2 cm or more from the valvar midline and in the setting of clinically negative inguinoaxillary LNs, a unilateral inguinoaxillary lymphadenectomy or SLN biopsy is appropriate (see Principles of Surgery: Inguinal Sentinel Lymph Node Biopsy).16
- For a primary valvar tumor located within 2 cm from or crossing the valvar midline, a bilateral inguinoaxillary lymphadenectomy17 or SLN biopsy is recommended.
- Some patients are not candidates for lymphadenectomy including those with stage IA disease due to a <1% risk of lymphatic metastases.11
- For patients with stage IB-III disease, inguinal lymphadenectomy is recommended due to a risk of >40% of lymphatic metastases.10
- A negative unilateral lymphadenectomy is associated with a <3% risk of contralateral metastases.12
- In the setting of positive LN disease after unilateral lymphadenectomy, contralateral lymphadenectomy or radiation of the contralateral groin is recommended. Any nodes that are grossly enlarged or suspicious for metastases during the unilateral lymphadenectomy should be frozen section pathology in order to tailor the extent and bilaterality of the LN dissection.
- Those with locally advanced disease may benefit from neoadjuvant radiation with concurrent platinum-based radiosensitizing chemotherapy. If a complete response is not achieved, surgical resection of the residual disease is recommended in patients with resectable disease who are appropriate surgical candidates.11
- The management of bulky inguinoaxillary LNs in the setting of an unresectable or T3 primary valvar lesion is unclear. It is reasonable to consider either 1) primary cytoreductive surgery of the bulky LNs followed by platinum-based chemosensitizing radiation to the bilateral groins and primary valvar tumor, or 2) platinum-based chemosensitizing radiation to the bilateral groins and primary valvar tumor alone.15

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**Principles of Evaluation and Surgical Staging**

**Table 1: Resection of Cervical Cancer as Primary Therapy**

<table>
<thead>
<tr>
<th>Comparison of Hysterectomy Types</th>
<th>Comparison of Tachurectomy Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple/Supraabdominal Hysterectomy Type A**</td>
<td>Modified Radical Hysterectomy Type B**</td>
</tr>
<tr>
<td>Indication</td>
<td>Stage IA-1</td>
</tr>
<tr>
<td>Intact</td>
<td>Curative for microinvasion</td>
</tr>
<tr>
<td>Ulcer</td>
<td>Removed</td>
</tr>
<tr>
<td>Ovaries</td>
<td>Optional removal</td>
</tr>
<tr>
<td>Cervix</td>
<td>Removed</td>
</tr>
<tr>
<td>Vaginal margin</td>
<td>None</td>
</tr>
<tr>
<td>Urethra</td>
<td>Not mobilized</td>
</tr>
<tr>
<td>Carcinomatous ligaments</td>
<td>Resected at uterine and cervix</td>
</tr>
<tr>
<td>Ureteral ligaments</td>
<td>Divided at cervical border</td>
</tr>
<tr>
<td>Bladder</td>
<td>Mobilized to base of cervix</td>
</tr>
<tr>
<td>Rectum</td>
<td>Not mobilized</td>
</tr>
<tr>
<td>Surgical approach</td>
<td>Laparotomy or laparoscopy</td>
</tr>
</tbody>
</table>

Radiation Therapy Cervix, Vulva, Vagina

- External radiation therapy with high-energy beam
- Intracavitary radiation therapy
  - Low-dose brachytherapy
  - High-dose brachytherapy
- Interstitial radiation therapy
  - Needles containing radioactive material are placed directly into the cancer and surrounding tissue(s)
- Combinations of above

http://radonc.ucla.edu/Gyn-CTDosimetry

Chemo and Immuno Therapy Cervix, Vulva, Vagina

**Early Stage Chemotherapy/Immunotherapy Options**
Fluorouracil (5FU) - Topical Chemotherapy applied directly to skin
Imiquimod - Topical Immunotherapy applied directly to effected skin

**Targeted Therapies** – Cetuximab, Erlotinib or Pazopanib + or – Chemo

NCCN Guidelines – Cervical Cancer – Version 1.2017
NCCN/FIGO Treatment Guidelines
Corpus Uteri – Endometrium

CANCER
IT’S PERSONAL
THE RIGHT PATIENT. THE RIGHT TREATMENT.

Uterine Neoplasm Histology Groupings

Endometrial Carcinoma
Primary Treatment

INITIAL CLINICAL FINDINGS

ADDITIONAL WORKUP

PRIMARY TREATMENT

THBSO\(^\text{a}\) and surgical staging\(^{\text{a,b,c,d}}\)

Radical hysterectomy and bilateral salpingo-oophorectomy (THBSO)\(^\text{a}\) and surgical staging\(^{\text{a,b,c,d}}\)

Adjuvant treatment for surgically staged\(^{\text{a,b,c}}\)

- Stage I (See ENDO-4)
- Stage II (See ENDO-5)
- Stage III (See ENDO-6)

Incompletely staged → See (ENDO-7)

Not suitable for primary surgery

Medically operable

EBRT + brachytherapy: 75-80 Gy to point A/paracervical dose\(^{\text{c,d}}\) (category 2B)

EBRT + systemic therapy\(^{\text{g}}\)

Surgical resection, if rendered operable

EBRT + brachytherapy\(^{\text{g}}\)

Surgical resection, if rendered operable (EBRT + brachytherapy\(^{\text{g}}\) if still inoperable)

*See (ENDO-1) for clarification of uterine neoplasms.
*See Histology and Pathologic Evaluation (ENDO-8).


Endometrial Carcinoma
Primary Surgery

THBSO: Total hysterectomy + bilateral salpingo-oophorectomy
RH: Radical hysterecetomy

Pathologic assessment to include:
- Uterus
- Ratio of depth of myometrial/stromal invasion to myometrial thickness
- Cervical stromal or glandular involvement
- Tumor size
- Tumor location (fundus vs. lower uterine segment/cervix)
- Histologic subtype with grade
- Lymphovascular space invasion
- Universal testing of endometrial tumors for mismatch repair (MMR) gene
- Fallopian tubes/ovaries
- Peritoneal cytology\(^{\text{j}}\)
- Nodes (when resected)
- Level of nodal involvement (ie, pelvic, common iliac, para-aortic)
- Universal testing of endometrial carcinomas for mismatch repair (MMR) gene
- Testing should be done on the final hysterectomy specimen (can be done on presurgical biopsy if hysterectomy not performed)
- MLH1 loss should be further evaluated for promoter methylation to assess epigenetic process.
- Genetic counseling and testing for all other MMR abnormalities
- Genetic counseling and testing for patients without MMR abnormalities, but who have a significant family history of endometrial and/or colorectal cancer (See Lynch syndrome/HRPCC in the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal)


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Endometrial Carcinoma Primary Surgery & Surgical Staging

**PRINCIPLES OF EVALUATION AND SURGICAL STAGING**

**Principles of Surgical Staging for Endometrial Cancer**

- Total hysterectomy, bilateral salpingo-oophorectomy (THBSO), and lymph node assessment is the primary treatment of apparent uterine-confined endometrial carcinoma, unless patients desire (and are candidates for) fertility-sparing options (see ENDO.C). Select patients with metastatic endometrial carcinoma are also candidates for hysterectomy. (See Hysterectomy and Pathologic Evaluation [ENDO.B]).
- Endometrial carcinoma should be removed en bloc to optimize outcomes; intraperitoneal morbidity or tumor fragmentation should be avoided.
- THBSO and lymph node assessment may be performed by any surgical route (eg, laparoscopic, robotic, vaginal, abdominal), although the standard in those with apparent uterine-confined disease is to perform the procedure via a minimally invasive approach. Randomized trials, a Cochrane Database Systematic Review, and population-based surgical studies support that minimally invasive techniques are preferred in this setting due to a lower rate of surgical site infection, transfusion, venous thromboembolism, decreased hospital stay and lower cost of care, without compromise in oncologic outcomes.4-10
- The lymph node assessment includes evaluation of the nodal basins that drain the uterus, and often comprises a pelvic nodal dissection with or without aortic nodal dissection. This continues to be an important aspect of surgical staging in women with uterine-confined endometrial carcinoma, as the procedure provides important prognostic information that may alter treatment decisions.
- Pelvic lymph nodes from the external iliac, internal iliac, obturator, and common iliac nodes are frequently removed for staging purposes.
- Para-aortic nodal evaluation from the infrarenal to the hilar regions may also be utilized for staging in women with high-risk tumors such as deeply invasive lesions, high-grade histology, and tumors of serous carcinoma, clear cell carcinoma, or carcinosarcoma.
- Sentinel lymph node (SLN) mapping may be considered in select patients. (See pages 2-4 of ENDO.C)
- Excision of suspicious or enlarged lymph nodes in the pelvic or aortic regions is important to exclude nodal metastasis.
- Some patients may not be candidates for lymph node dissection.
- Visual evaluation of the peritoneal, diaphragmatic, and serosal surfaces with biopsy of any suspicious lesions is important to exclude extraperitoneal disease.
- Some patients may not be candidates for lymph node dissection.
- While peritoneal cytology does not impact staging, FIGO and AJCC nonetheless recommend that surgeons continue to obtain this during the THBSO.
- Omental biopsy is commonly performed in those with serous carcinoma, clear cell carcinoma, or carcinosarcoma histologies.

---

**PRINCIPLES OF EVALUATION AND SURGICAL STAGING WHEN SLN MAPPING IS USED**

- The role of SLN mapping in endometrial carcinoma is under evaluation. Prospective and retrospective studies demonstrate that compared to systemic lymphadenectomy, SLN mapping with ultrastaging may increase the detection of lymph node metastasis with low false-negative rates in women with apparent uterine-confined disease.10-22 To date, no randomized trials evaluating this technique in endometrial carcinoma have been conducted. If SLN mapping is considered, the expertise of the surgeon and attention to technical detail is critical. The use of SLN mapping in high-risk histologies (serous carcinoma, clear cell carcinoma, or carcinosarcoma) should be undertaken with particular caution.
- A cervical injection with dye has emerged as a useful and validated technique for identification of lymph nodes that are at high risk for metastases.3-5, SLN in patients with early-stage endometrial cancer.10-14
- The combination of a superficial (1-3 mm) and deep (1-2 cm) cervical injection leads to dye delivery to the main layers of lymphatic collateral origins in the cervix and corpus, namely the superficial subserosal, intermediate stromal, and deep submucosal lymphatic sites of origin (Figure 1 on ENDO.C: 3 of 5).
- Injection into the uterine cervix provides excellent dye penetration to the region of the uterine vessels and main uterine lymphatic trunks that condense in the parametria and appear in the broad ligament leading to pelvic and occasionally para-aortic sentinel nodes.
- The uterine body lymphatic trunks commonly cross over the obliterated umbilical artery with the most common location of pelvic SLN being medial to the external iliac, ventral to the hypogastric, or in the superior part of the obturator region (Figure 2 on ENDO.C: 3 of 5).
- A less common location is usually seen when the lymphatic trunks do not crossed over the obliterated umbilical and move cephalad following the mesorector; in these cases, the SLN is usually seen in the common iliac presacral region (Figure 3 on ENDO.C: 3 of 5).
- The radiolabeled colloid most commonly injected into the cervix is technetium-99m Ethylentol; colored dyes are available in a variety of forms (isocyanate blue 1% and methyl blue 1%, Patent Blue 2.5% sodium).
- Indocyanine green (ICG) recently emerged as a useful imaging dye that requires near infrared camera for localization, provides a very high SLN detection rate, and is commonly used in many practices at the present time.19
- Low volume nodal metastasis to SLN detected only by enhanced pathologic ultrastaging is another potential value to staging with SLN.10,20-22
- Key points to a successful SLN mapping is the adherence to the SLN algorithm, which requires the performance of a side-specific nodal dissection in cases of failed mapping and removal of any suspicious or grossly enlarged nodes regardless of mapping (Figure 4 on ENDO.C: 4 of 5).
Endometrial Carcinoma Primary Surgery & Surgical Staging

PRINCIPLES OF EVALUATION AND SURGICAL STAGING WHEN SLN MAPPING IS USED

Peritoneal & serosal evaluation & washings

Retropertioneal evaluation
- Excision of all mapped SLN with ultrastaging
- Any suspicious nodes must be removed regardless of mapping

If there is no mapping on a hemi-pelvis, a side-specific LND is performed
- Para-aortic LND done at attending discretion

Endometrial Carcinoma Post-Surgical Adjuvant TX

All staging in guideline is based on updated 2010 FIGO staging. (See ST.1)

ADVERSE RISK FACTORS

CLINICAL FINDINGS
- Stage IA (<50% myometrial invasion)
- Stage IB (≥50% myometrial invasion)

Surgically staged: Stage I

Adverse risk factors not present
- G1
- G2
- G3

HISTOLOGIC GRADE/ADJUVANT TREATMENT*:

G1
- Observe or Vaginal brachytherapy
- Observe or Vaginal brachytherapy and/or EBRT (category 2B for EBRT)

G2
- Observe or Vaginal brachytherapy and/or EBRT
- Vaginal brachytherapy and/or EBRT (category 2B for EBRT)

G3
- Observe or Vaginal brachytherapy and/or EBRT
- EBRT and/or vaginal brachytherapy + systemic therapy^{d}

*The degree of surgical staging to assess disease status depends on intraoperative findings. Multidisciplinary expertise is recommended.
Endometrial Carcinoma Post-Surgical Adjuvant TX

All staging in guideline is based on updated 2019 FIGO staging. (See ST.3)


Treatment for Carcinosarcoma, Serous, or Clear Cell AdenoCA

Endometrial Carcinoma Radiation Therapy

**PRINCIPLES OF RADIATION THERAPY FOR UTERINE NEOPLASMS**

- RT is directed at sites of known or suspected tumor involvement, and may include external beam RT (EBRT) and/or brachytherapy. Diagnostic imaging is often used to assess locoregional extent and to rule out distant metastases before administration of RT. In general, EBRT is directed to the pelvis with or without the para-aortic region. Brachytherapy can be delivered: 1) to an intact uterus, either preoperatively or definitively; or 2) more commonly, to the vagina after hysterectomy. For the purposes of these guidelines, whole abdominal radiotherapy is not considered to be tumor-directed RT.

- Pelvic radiotherapy should target the gross disease (if present), the lower common iliacs, external iliacs, internal iliacs, parametria, upper vaginal/para-vaginal tissue, and presacral lymph nodes (in patients with cervical involvement). Extended field radiotherapy should include the pelvic volume and also target the entire common iliac chain and para-aortic lymph node region. The upper border of the extended field depends on the clinical situation and should at least be to the level of the renal vessels. External-beam doses for microscopic disease should be 45 to 50 Gy. Multiple conformal fields based on CT treatment planning should be utilized.

- Initiate brachytherapy as soon as the vaginal cuff is healed, preferably no later than 12 weeks after surgery. Brachytherapy doses for definitive therapy are individualized based on the clinical situation. For preoperative therapy in patients with gross stage IB disease, in general, a total dose of 75 to 80 Gy low-dose-rate equivalent to the tumor volume is recommended. For vaginal brachytherapy, the dose should be prescribed to the vaginal surface or at a depth of 0.5 cm from the vaginal surface; the dose depends on the use of EBRT.

- The target for vaginal brachytherapy after hysterectomy should be limited to the upper two-thirds of the vagina.

- For high-dose-rate brachytherapy, when used as a boost to EBRT, doses of 4 to 6 Gy x 2 to 3 fractions prescribed to the vaginal mucosa are commonly used.

- For high-dose-rate vaginal brachytherapy alone, commonly used regimens include 7 Gy x 3 prescribed at a depth of 0.5 cm from the vaginal surface or 6 Gy x 5 fractions prescribed to the vaginal surface.

- Evidence supports the use of combined-modality radiation and chemotherapy as adjuvant treatment for patients with extrarectal disease.1

- Palliative EBRT should be individualized to disease extent and patient performance status. Various dose/refraction schemes can be considered. A common approach is 30 Gy in 19 fractions.

Endometrial Carcinoma Systemic Therapies

**SYSTEMIC THERAPY FOR RECURRENT, METASTATIC, OR HIGH-RISK DISEASE**

(STRONGLY ENCOURAGE PARTICIPATION IN CLINICAL TRIALS)

**CHEMOTHERAPY REGIMENS**

- Multi-agent chemotherapy regimens preferred; if tolerated:
  - Carboplatin/paclitaxel
  - Carboplatin/doxorubicin
  - Carboplatin/doxorubicin/paclitaxel
  - Paclitaxel

- Single agents:
  - Carboplatin
  - Doxorubicin
  - Paclitaxel

- Hormone therapy:
  - Megestrol tamoxifen (alternating)
  - Progestational agents
  - Aromatase inhibitors
  - Tamoxifen
Uterine Sarcoma
Primary Treatment

NCCN Guidelines – Uterine Neoplasms Version 1.2017

Uterine Sarcoma
Post Clinical & Surgical Evaluation

NCCN Guidelines – Uterine Neoplasms Version 1.2017
Uterine Sarcoma: Post Clinical & Surgical Evaluation

**Pathologic Findings/Histologic Grade**

- High grade ESS
- U/S utMS

**Stage I**
- Observe or Consider systemic therapy (category 2B)*

**Stage II, III**
- Observe or Consider systemic therapy* and/or Consider EBRT†

**Stage IVA, IVB**
- Systemic therapy* and/or EBRT† and/or palliative EBRT‡

---

**Uterine Sarcoma – Radiation**

**Principles of Radiation Therapy for Uterine Neoplasms**

- RT is directed at sites of known or suspected tumor involvement, and may include external beam RT (EBRT) and/or brachytherapy.
- Diagnostic imaging is often used to assess locoregional extent and to rule out distant metastases before administration of RT. In general, EBRT is directed to the pelvis with or without the para-aortic region. Brachytherapy can be delivered to an intact uterus, either preoperatively or definitively; or 2) more commonly, to the vagina after hysterectomy.
- For the purposes of these guidelines, whole abdominal radiotherapy is not considered to be tumor-directed RT.
- Pelvic radiotherapy should target the gross disease (if present), the lower common iliac, external iliac, internal iliac, parametrial, upper vaginal/para-vaginal tissue, and presacral lymph nodes (in patients with pelvic involvement).
- Extended field radiotherapy should include the pelvic volume and also target the entire common iliac chain and para-aortic lymph node region. The upper border of the extended field depends on the clinical situation but should be at least at the level of the renal vessels. External-beam doses for microscopic disease should be 45 to 50 Gy. Multiple conformal fields based on CT treatment planning should be utilized.
- Initiate brachytherapy as soon as the vaginal cuff is healed, preferably no later than 12 weeks after surgery. Brachytherapy doses for definitive therapy are individualized based on the clinical situation. For preoperative therapy in patients with gross stage IIIb diseases, in general, a total dose of 75 to 86 Gy low-dose-rate equivalent to the tumor volume is recommended. For vaginal brachytherapy, the dose should be prescribed to the vaginal surface or at a depth of 0.5 cm from the vaginal surface; the dose depends on the use of EBRT.
- The target for vaginal brachytherapy after hysterectomy should be limited to the upper two-thirds of the vagina.
- For high-dose-rate brachytherapy, when used as a boost to EBRT, doses of 4 to 6 Gy x 2 to 3 fractions prescribed to the vaginal mucosa are commonly used.
- For high-dose-rate vaginal brachytherapy alone, commonly used regimens include 7 Gy x 3 prescribed at a depth of 0.5 cm from the vaginal surface or 6 Gy x 5 fractions prescribed to the vaginal surface.
- Evidence supports the use of combined modality radiation and chemotherapy as adjuvant treatment for patients with extraregional disease.5
- Palliative EBRT should be individualized to disease extent and patient performance status. Various dose/fractionation schemes can be considered. A common approach is 30 Gy in 18 fractions.
SYSTEMIC THERAPY FOR UTERINE SARCOMA
(Clinical trials strongly recommended)

Combination regimens:
- Docetaxel/gemcitabine
  (preferred for leiomyosarcoma)
- Doxorubicin/ifosfamide
- Doxorubicin/dacarbazine
- Gemcitabine/docetaxel
- Gemcitabine/vinorelbine

Single-agent options:
- Dacarbazine
- Doxorubicin
- Epirubicin
- Eribulin (category 2B)
- Gemcitabine
- Ifosfamide
- Liposomal doxorubicin
- Pazopanib
- Temsirolimus
- Trabectedin
- Vinorelbine (category 2B)
- Docetaxel (category 3)

HORMONE THERAPY
(For Low-grade ESS or Hormone-Receptor Positive (ER/PR) uLMS):
- Medroxyprogesterone acetate
  (category 2B for ER/PR positive uLMS)
- Megestrol acetate
  (category 2B for ER/PR positive uLMS)
- Aromatase inhibitors
- GnRH analogs
  (category 2B for low-grade ESS and
  ER/PR positive uLMS)

NCCN Guidelines – Uterine Neoplasms - Version 1.2017

NCCN/FIGO Treatment Guidelines
Ovary / Fallopian Tube / Primary Peritoneum
PRINCIPLES OF SURGERY (1 of 4)¹

Newly diagnosed invasive epithelial ovarian cancer apparently confined to an ovary or to the pelvis

In general, every effort should be made during a primary cytoreduction procedure to achieve maximum cytoreduction of all pelvic disease and to evaluate for occult disease in the upper abdomen or retroperitoneum.

- On entering the abdomen, aspiration of ascites or peritoneal lavage should be performed for peritoneal cytologic examinations.
- All peritoneal surfaces should be visualized, and any peritoneal surface or adhesion suspicious for harboring metastasis should be selectively excised or biopsied. In the absence of any suspicious areas, random peritoneal biopsies should be taken from the pelvis, paracolic gutter, and undersurfaces of the diaphragm (diaphragm scraping for Papanicolaou stain is an acceptable alternative).
- BSO and hysterectomy should be performed with every effort to keep an encapsulated mass intact during removal.
- For selected patients desiring to preserve fertility, U/SO may be considered.
- Omentectomy should be performed.
- Para-aortic lymph node dissection should be performed by stripping the nodal tissue from the vena cava and the aorta bilaterally to at least the level of the inferior mesenteric artery and preferably to the level of the renal vessels.
- The preferred method of dissecting pelvic lymph nodes is bilateral removal of lymph nodes overlaying and anterolateral to the common iliac vessels, overlaying and medial to the external iliac vessel, overlaying and medial to the hypogastric vessels, and from the obturator fossa at a minimum anterior to the obturator nerve.²

Newly diagnosed invasive epithelial ovarian cancer involving the pelvis and upper abdomen

In general, every effort should be made during a primary cytoreduction procedure to achieve maximum cytoreduction of all abdominal, pelvic, and retroperitoneal disease. Residual disease <1 cm defines optimal cytoreduction; however, maximal effort should be made to remove all gross disease since this offers superior survival outcomes.

- Aspiration of ascites (if present) should be performed for peritoneal cytologic examinations. All involved omentum should be removed.
- Suspicious and/or enlarged nodes should be resected, if possible.
- Those patients with tumor nodules outside the pelvis 5 cm (proximal stage III) should have bilateral pelvic and para-aortic lymph node dissection as previously described.
- Procedures that may be considered for optimal surgical cytoreduction (in all stages) include bowel resection and/or appendectomy, stripping of the diaphragm or other peritoneal surfaces, splenectomy, partial cystectomy and/or uterineectomy, partial hepatectomy, partial gastrectomy, cholecystectomy, and/or distal pancreatectomy.

Select patients with low-volume residual disease after surgical cytoreduction for invasive epithelial ovarian or peritoneal cancer are potential candidates for IP therapy. In these patients, consideration should be given to placement of IP catheter with initial surgery.


PRINCIPLES OF SURGERY (2 of 4)¹

Interval cytoreduction after neoadjuvant chemotherapy of invasive epithelial ovarian cancer

As with a primary cytoreduction procedure, every effort should be made to achieve maximum cytoreduction during an interval cytoreduction procedure. Maximal effort should be made to remove all gross disease in the abdomen, pelvis, and retroperitoneum.

- Interval cytoreductive surgery should be performed after 54 cycles of neoadjuvant chemotherapy for women with a response to chemotherapy or stable disease. Alternate timing of surgery has not been prospectively evaluated but may be considered based on individual patient-centered factors.
- All peritoneal surfaces should be visualized, and any peritoneal surface or adhesion suspicious for harboring metastasis should be selectively excised or biopsied.
- An omentectomy should be performed.
- Suspicious and/or enlarged nodes should be resected, if possible. Removal of lymph nodes noted to have potential metastasis at the time of initial diagnosis should be considered, even if not currently suspicious or enlarged.
- Procedures that may be considered for optimal surgical cytoreduction include bowel resection and/or appendectomy, stripping of the diaphragm or other peritoneal surfaces, splenectomy, partial cystectomy and/or uterineectomy, partial hepatectomy, partial gastrectomy, cholecystectomy, and/or distal pancreatectomy.

Risk-Reducing Salpingo-Oophorectomy (RSO) Protocol

- Perform operative laparoscopy.
- Survey upper abdomen, bowel surfaces, omentum, appendix (if present), and pelvic organs.
- Biopsy any abnormal peritoneal findings.
- Obtain pelvic washing for cytology (50 cc normal saline instilled and aspirated immediately).
- Perform total BSO, removing 2 cm of proximal ovarian vasculature/pedicle, all tube up to the cornu, and all peritoneum surrounding the ovaries and tubes, especially peritoneum underlying areas of adhesion between tube and ovary and the pelvic sidewall.¹
- Engage in minimal instrument handling of the tubes and ovaries to avoid traumatic exfoliation of cells.⁴
- Engage in minimal instrument handling of the tubes and ovaries to avoid traumatic exfoliation of cells.⁴
- Place ovaries and tubes should be placed in an endbag for retrieval from the pelvis.
- Ovaries and tubes should be processed according to SEE-FIM protocol.²
- If occult malignancy or ATIC is identified, provide referral to gynecologic oncologist.
- The prevention benefits of salpingectomy alone are not yet proven. If considered, the Fallopian tube from the fimbria to its insertion into the uterus should be removed. In addition, the Fallopian tube should be processed and assessed as described above. The concern for risk-reducing salpingectomy alone is that women are still at risk for developing ovarian cancer.


Breast and Ovarian

See NCCN Guidelines for Genetic/Genomic High-Risk Assessment: Breast and Ovarian.
Ovary, Fallopian Tube, & Primary Peritoneum Surgery

**Primary Surgery**
- Radical pelvic dissection
- Bowel resection
- Diaphragm or other peritoneal surface stripping
- Omentectomy
- Splenectomy
- Partial hepatectomy
- Cholecystectomy
- Partial cystectomy
- Ureteronocystomy
- Distal pancreatectomy

**Ancillary/Palliative Surgery**
- Paracentesis
- Thoracentesis/pleurodesis
- Ureteral stents
- Nephrostomy
- Surgical relief or intestinal obstruction
- Gastrostomy tube
- Vascular access device
- Indwelling peritoneal or pleural catheter
- Intestinal stents
- Video-assisted thoracoscopy

Ovary, Fallopian Tube & Primary Peritoneum Treatment by FIGO Stage & Grade


Ovary, Fallopian Tube & Primary Peritoneum Primary/Adjuvant Chemotherapy

Ovary, Fallopian Tube & Primary Peritoneum
Primary/Adjuvant Chemotherapy


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Ovary, Fallopian Tube & Primary Peritoneum
Chemotherapy for Recurrence


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Germ Cell & Sex Cord Stromal Tumor

Surgery followed by Chemotherapy

Additional Resources

- FIGO Staging Classifications for GYN Cancers, FIGO, 2012
- 2013 WHO Classification of Tumours of Female Reproductive Organs, World Health Organization, Lyon, France, 2013
- NCI Physician Data Query for Healthcare Professionals
- CDC Information about GYN Cancers
- American Cancer Society
- SEER Training for Cancer Registry Professionals
- NCRA Informational Abstracts (Text Documentation)
- NCCN Evidence Based Treatment Guidelines, NCCN, 2017
Questions

http://www.cdc.gov/cancer/gynecologic