SIG Oncology – Fertility-Preserving Surgery in Gynecologic Oncology: A New Standard of Care (Didactic)

PROGRAM CHAIR
Nadeem Abu-Rustum, MD

PROGRAM CO-CHAIR
Audrey Tsunoda, MD

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Professional Education Information

Target Audience
This educational activity is developed to meet the needs of residents, fellows and new minimally invasive specialists in the field of gynecology.

Accreditation
AAGL is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The AAGL designates this live activity for a maximum of 3.75 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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This course provides a comprehensive overview of fertility-sparing surgical techniques in the management of select women with cervical, endometrial, and ovarian malignancies. Novel surgical techniques such as sentinel node mapping and radical trachelectomy will be presented in great detail. The lectures will also summarize the oncologic and reproductive outcomes of these novel approaches and describe future directions in surgical strategies and medical management.

**Learning Objectives:** At the conclusion of this activity, the clinician will be able to: 1) Identify opportunities in select cases to consider fertility-sparing approaches that were not otherwise possible; 2) apply new techniques learned to relevant pelvic surgery including sentinel node mapping; 3) summarize the current literature regarding the management of stage I uterine and cervical cancer in women who want to preserve fertility; 4) explain the theory and rational for fertility-sparing radical trachelectomy; 5) differentiate between types of ovarian neoplasia suitable for consideration of a fertility-sparing approach; and 6) compare different treatment strategies in the egg embryo freezing for women with cancer.

**Course Outline**

8:00  Welcome, Introductions and Course Overview  
N. Abu-Rustum

8:05  Fertility Sparing Surgery for Stage 1 Cervical Cancer: A New Standard of Care  
N. Abu-Rustum

8:45  Selection of Suitable Candidates for Uterine Preservation in Women with Endometrial Cancer  
N. Abu-Rustum

9:05  Ovarian Borderline Tumors: Who Are the Candidates for Fertility Sparing Surgery?  
N. Abu-Rustum

9:25  State-of-the-Art Oncofertility Services for the Cancer Patient  
N. Noyes

9:45  Fertility Preserving Surgery in Ovarian Cancer  
A. Tsunoda

10:05  Questions and Answers  
All Faculty

10:15  Break

10:30  Family Planning for BRCA Carriers  
N.D. Kauff

10:50  Update on Lynch Syndrome for the Gynecologist  
N.D. Kauff
11:10 Case Presentation #1 and Discussion All Faculty
11:30 Case Presentation #2 and Discussion All Faculty
11:50 Questions & Answers All Faculty
12:00 Course Evaluation/Adjourn
PLANNER DISCLOSURE
The following members of AAGL have been involved in the educational planning of this workshop and have no conflict of interest to disclose (in alphabetical order by last name).
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Viviane F. Connor
Consultant: Conceptus Incorporated
Kimberly A. Kho*
Frank D. Loffer, Executive Vice President/Medical Director, AAGL*
Linda Michels, Executive Director, AAGL*
M. Jonathan Solnik*
Johnny Yi*

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C.Y. Liu*
Javier F. Magrina*
Andrew I. Sokol*

FACULTY DISCLOSURE
The following have agreed to provide verbal disclosure of their relationships prior to their presentations. They have also agreed to support their presentations and clinical recommendations with the “best available evidence” from medical literature (in alphabetical order by last name).
Nadeem Abu-Rustum*
Audrey T. Tsunoda*
Noah D. Kauff
Consultant: Pfizer
Other: Expert Testimony: Pfizer
Nicole Noyes*

Asterisk (*) denotes no financial relationships to disclose.
Abdominal Radical Trachelectomy Cervical Cancer

Nadeem R. Abu-Rustum, M.D.
Memorial Sloan-Kettering Cancer Center, New York

Conflict of Interest Disclosure

Nadeem R. Abu-Rustum, M.D.
I have no financial relationships with a commercial entity producing health-care related products and/or services.

2013 NCCN Guidelines

Changes in Surgical Approach Stage I 2001-2013

Stage I Cervical Cancer
- Trachelectomy Vaginal 2001
- Abdominal 2004
- Conization 2005
- Nodal Assessment SLN 2003 Algorithm 2010

Stage IA1 No LVI

- Can be treated with Cone
- Review Pathology

Stage IA1 with LVI

SLN & Conization

“Less is more….”
Robert Browning
Stage IA2
Cancer invasion is 3-5 mm deep and < 7 mm wide

Stage IB1

- Radical Abdominal (Wertheim) Hysterectomy
- Radical Vaginal (Schauta) Hysterectomy
- Complete Bilateral Pelvic Lymphadenectomy +/- Paraaortic Lymph Node Sampling

History of Abdominal Trachelectomy

- Eugène Aburel Bogdan (1899-1975)
  - Bucharest, Romania. In 1931, pioneer of regional anesthesia first to describe blocking the lumbar plexus during early labor, followed by caudal epidural injection.
  - (Technique: Aburel, 1956)

- Franz Novak (Belgrade) did first case Oct. 27, 1950

First case Oct. 27, 1950
Proceedings: Extended abdominal extirpation of cervix and isthmus in early stages of cervix carcinoma (carcinoma in situ and microcarcinoma)


Treating with less than hysterectomy:

F. Novak 1952 (Belgrade)
E. Aburel 1956 (Bucharest)

30 years later - Vaginal Trachelectomy:
D. Dargent in France - First case April 1987.

Left Parametrial LN continuous with trachelectomy specimen

We recommend exercising caution when considering abbreviation of parametrectomy and based on our data we continue to include this procedure in our surgical algorithm for the majority of stage IB1 cervical cancers.
3 & 9 O'clock: 1cc superficial on each side

Cervical Injection Under Anesthesia
22GA Spinal Needle 2cc at 3 & 2cc at 9 O'clock

Most Common Drainage

23 yo IB1 adeno with LVI 3.5mm x 8mm wide neg margins
Radical Abdominal Trachelectomy for Cervical Cancer in Pediatric Patients  
2004  
6 & 8 Year old girls with vaginal bleeding and cervical mass =  
Stage IB1 Clear Cell Cancer
8 Year Old with Vaginal Bleeding & Polyp = Clear Cell Cancer

Abu-Rustum NR, et al. Gynecol Oncol 2005

Post Pediatric Abdominal Trachelectomy Neo-cervix

6 year old
New cervix 6 months postop

9 year old
New cervix 15 months postop

Blood Supply to Uterine Fundus

Gray's Anatomy

Uterine Perfusion via Ovarian Arteries Observed During Uterine Artery Embolization

Injection of left ovarian artery shows substantial supply to uterine fundus that may cause UAE treatment to fail

Radical Abdominal Trachelectomy in Adult Patients

Danger Area for Vascular Injury
Lessons Learned from Frozen-Section

• We send trachelectomy for endocervical margin clearance
• Also send a shave margin from remaining uterus
• Send EMC for FS

Symmetrical & Functional Reconstruction

Resuspened the round ligaments – uterine antversion
Approximate parts of the peritoneum
5 weeks post operative

3 months later

7 weeks postop

4 months later

Grossly (+) endocervical margins IB1

Distance between tumor and internal cervical os on MRI versus ultimate surgical outcome

<table>
<thead>
<tr>
<th>Distance to Internal Os</th>
<th>Surgical Procedure</th>
<th>Fisher’s exact test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hyderectomy</td>
<td>Trachelectomy</td>
<td></td>
</tr>
<tr>
<td>0 – 5 mm</td>
<td>9 (100%)</td>
<td>7%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6 – 9 mm</td>
<td>3 (60%)</td>
<td>2 (40%)</td>
<td></td>
</tr>
<tr>
<td>≥ 10 mm</td>
<td>3 (6%)</td>
<td>45 (94%)</td>
<td></td>
</tr>
</tbody>
</table>

Lakhman Y. 2013

FIGURE 1

Expanding the Indications for Radical Trachelectomy: A Report on 29 Patients With Stage IB1 Tumors Measuring 2 to 4 Centimeters.

Wethington, Stephanie; Sonoda, Yukio; Park, Kay; Alektiar, Kaled; Tew, William; Chi, Dennis; Leitao, Mario; Jewell, Elizabeth; Barakat, Richard; Abu-Rustum, Nadeem


DOI: 10.1097/IGC.0b013e318296034e
A very special day at MSKCC
New York 2011

Thank You
SPARING FERTILITY IN YOUNG PATIENTS WITH ENDOMETRIAL CANCER

NADEEM ABU-RUSTUM
Memorial Sloan-Kettering Cancer Center

Introduction

Endometrial cancer is the most frequent gynecological neoplasia.

The 5 year survival rate is excellent. [In Spain: 84.3%]

FIGO stage is the independent variable that best shows the prognosis of this tumor.

Objective

To study if sparing fertility in selected cases of young women with endometrial cancer is:

- a safe therapeutic option.
- the reproductive outcome in these patients after treatment.

Patient’s Age
Spanish National Survey

Average age: 64 yo
Oldest: 93 yo
Youngest: 31 yo

Desv. típ. = 10.47
Media = 64
N = 965.00

Average age: 64 yo
Oldest: 93 yo
Youngest: 31 yo

Desv. típ. = 10.47
Media = 64
N = 965.00

Disclosure

I have no financial relationships to disclose.
11 % were premenopausal when diagnosed

In the literature this group of young women comprises between 1.5 - 14 % of all endometrial cancers.

Patient’s characteristics

<table>
<thead>
<tr>
<th>Specimen: Well Diff.</th>
<th>&lt; 45 yo N=24</th>
<th>&gt;45 yo N=1030</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplasia</td>
<td>62 %</td>
<td>41 %</td>
<td>0.09</td>
</tr>
<tr>
<td>Invasión &gt; 50 %</td>
<td>8.1 %</td>
<td>31.6</td>
<td>0.05</td>
</tr>
<tr>
<td>FIGO stage I</td>
<td>44 %</td>
<td>64 %</td>
<td>-</td>
</tr>
</tbody>
</table>

Patient’s characteristics

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<th>&gt;45 yo N=1030</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Malignancy</td>
<td>66 %</td>
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</tr>
<tr>
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</tr>
<tr>
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<td>44 %</td>
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</tr>
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</table>

Age < 45 yo Spanish National Survey 1999

Only 2.3 % of 1054 patients were under 45 yo.

Patient’s characteristics

<table>
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<th>&gt;45 yo N=1030</th>
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<td>44 %</td>
<td>64 %</td>
<td>-</td>
</tr>
</tbody>
</table>
**Synchronous ovarian tumors**

<table>
<thead>
<tr>
<th>Endometrial cancer &lt;45 yo</th>
<th>Synchronous ovarian tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gisth et al. (1995)</td>
<td>29 %</td>
</tr>
<tr>
<td>Evans-Metcalf et al. (1998)</td>
<td>11 %</td>
</tr>
<tr>
<td>Walsh et al. (2005)</td>
<td>25 %</td>
</tr>
</tbody>
</table>

4 % with Normal appearance

**In summary ...<45 years old**

- Infrequent Situation
- High percentage of nulliparity.
- Past medical history of infertility.
- Better differentiated tumors.
- Less myometrial invasion.
- Better survival rate.
- Significant risk of concomitant ovarian neoplasias.

**Questions**

- Is it possible to take a conservative approach when facing an endometrial cancer?
- In which cases?
- How do we treat these patients?
- What is their reproductive outcome?
- What are the risks they run?

**Patient Selection**

- Diagnosis of well differentiated carcinoma of endometrium (G1), by an expert gyn-pathologist.
- Only G1 tumors can be selected for conservative treatment.

Therefore, we will exclude all high risk variants of endometrial cancer.
Endometrial Carcinomas in Women Aged 40 Years and Younger: Tumors Associated With Loss of DNA Mismatch Repair Proteins Comprise a Distinct Clinicopathologic Subset

- DNA mismatch repair: MLH1, PMS2, MSH2, MSH6

Loss of DNA Mismatch Repair Proteins

- Tumors were of higher grade and associated with worse clinical outcomes.
- These tumors also showed lower estrogen receptor/progesterone receptor expression.
- They may not be appropriate candidates for conservative management.

PTEN (gen)

- PTEN (phosphatase and tensin homolog) is a protein codified by the PTEN gen, localize in Chromosome 10.
- PTEN, a tumor suppressor gene, is mutated in 30–55% of endometrial carcinomas.
- The most highly mutated tumor-suppressor gene in the post-p53 era.
- It is now becoming clear that PTEN plays a significant role not only in inducing cell cycle arrest and programming apoptosis, but also in other aspects of cell physiology.
  - Regulation of cell adhesion
  - Migration
  - Differentiation.

PTEN antagonizes PI3K activity and negatively regulates the Akt-mediated signaling pathway, which is involved in cell survival and proliferation.

RESULTS

- Before MPA
- PTEN-null cells
- Low phospho-Akt
- Higher risk of persistent or recurrent disease after MPA
Before MPA | After MPA

Anti-tumor effect of MPA may be mediated by dephosphorylation of akt.
Way of action of Progesterone in negative PgR.

Phospho-Akt

Diagnostic problems

The office biopsy or curettage might not be representative.
Hysteroscopic evaluation is mandatory in these cases.

Diagnostic problems

There are severe difficulties in obtaining a consistent diagnosis. Inter and intra observer differences up to 40%.
Difficulties in differentiating atypical hyperplasia and well differentiated carcinoma.

Atypical hyperplasia | Well differentiated carcinoma

Diagnostic problems

Evaluation of cervical invasion.

Evaluation of myometrial invasion

Myometrial invasion is very difficult to determine by biopsy, curettage or histeroscopy.

Absence of cervical or myometrial invasion

Only superficial tumor can be selected for conservative treatment.

Patient Selection

Absence of cervical or myometrial invasion

Only superficial tumor can be selected for conservative treatment.

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Patient Selection

Absence of cervical or myometrial invasion

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Diagnostic problems

Diagnostic problems

Diagnostic problems
Assessment of myometrial invasion


ULTRASOUND
CT SCAN
MRI

Assessment of myometrial invasion

MRI with Gadolinium:
- PPV between 85-91%
- PNV: much lower, 50%

Superficial invasion (arrow)
Deep myometrial invasion in the posterior myometrial wall

Selection Criteria: Summary

- Well differentiated carcinoma
- Tumor does not invade the myometrium.
- Absence of suspicious pelvic or paraaortic nodes.
- Absence of synchronous ovarian tumor.
- No contraindications for medical treatment.
- Patient understands and accepts that this is not a standard treatment.
- Patient shows her desire of adhesion to the follow up protocol.

Treatment

Taking advantage of this tumor hormonal sensitivity, most authors have used hormonal-based treatments.

Exceptionally, some authors have proposed a local surgical excision by hysteroscopy or repeated curettage as well as progesterone IUD as local treatment.

The near future?

Successful pregnancy after hysteroscopic removal of grade 1 endometrial carcinoma in a young woman with Lynch syndrome

(2006)

Endometrioid adenocarcinoma treated by hysteroscopic endomyometrial resection

(2007)
Step 1: Removal of the tumor
Step 2: Removal of the endometrium adjacent to the tumor
Step 3: Removal of the myometrium underlying the tumor

Medical Treatment

Hormonal treatments:
- Progestins
- LHRH agonists
- Antiestrogens
- Aromatase inhibitors

Medical Treatment

Progestins
- Produce a secretory differentiation.
- Inhibit oestrogens receptor function.
- Inhibit endometrial cells mitosis.
- Promote apoptosis.
- Some of them have an antiangiogenic effect.

Conservative Treatment: Endometrial Carcinoma

REVIEW

Average age: 32 yo

Conservative Treatment

Tumor excision with clear margins
Positive Lateral margins
Positive Deep margins
CLOSE FOLLOW-UP
HORMONAL THERAPY
HISTERECTOMY

Conservative Treatment: Progestins

Publications 1966-2008

<table>
<thead>
<tr>
<th>Progestins</th>
<th>N=161</th>
<th>N</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medroxyprogesterone acetate</td>
<td>93</td>
<td>57</td>
<td>300-600 mg/day</td>
</tr>
<tr>
<td>Medroxyprogesterone acetate</td>
<td>40</td>
<td>24</td>
<td>80-160 mg/day</td>
</tr>
<tr>
<td>17-OH Progesterone</td>
<td>6</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>GnRH analogs</td>
<td>5</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Hydroxyprogesterone Acetate</td>
<td>4</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Oxyprogesterone Caproate</td>
<td>3</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Nonsteroidal acetates</td>
<td>2</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Others/unknown</td>
<td>8</td>
<td>4</td>
<td>-</td>
</tr>
</tbody>
</table>
Conservative Treatment: Initial Response

N = 161 pt

74% (120/161) Responded to treatment

Average response time: 12 weeks (4-60)

Publications Review 1966-2008

FINDINGS AT HT N=60

Stage IA, grade 1 14
Stage IA, grade 1 12
Stage IB, grade 2 3
Stage IC grade 1-3 3
Stage II, grade 1 1
Stage III 6
Unstaged, grade 1 1
No Path report 17
Adenocarcinoma 1
Atypical hyperplasia 1
Atypical endometrium 1

Relapse

2º line of Progestins

N = 161

Relapse

40 p Average relapse time 20 months

Temporary Response 24% (41/161)
Absent Response 25% (41/161)

Response Rates

N = 161

(80/161) Lasting Complete Response 49%
(80/161) Temporary Response 24%
(80/161) Absence of Response 25%
Japan Gynecologic Cancer Study Group

Table 3. Response to MPA

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Initial Response</th>
<th>PgR</th>
<th>Pregnancy</th>
<th>Relapse Months</th>
<th>Site</th>
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<tbody>
<tr>
<td>#1</td>
<td>(2004) Yasuda et al</td>
<td>31</td>
<td>Yes</td>
<td>Primary POS</td>
<td>Relapse NEG</td>
<td>No</td>
</tr>
<tr>
<td>#2</td>
<td>(2005) Ota et al</td>
<td>34</td>
<td>Yes</td>
<td>NEG</td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>#3</td>
<td>(2005) Ferrandina et al</td>
<td>30</td>
<td>Yes</td>
<td>Primary POS</td>
<td>Relapse NEG</td>
<td>Yes</td>
</tr>
<tr>
<td>#4</td>
<td>(2005) Rubatt et al</td>
<td>40</td>
<td>Yes</td>
<td>N/A</td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>#5</td>
<td>(2007) Cormio et al</td>
<td>31</td>
<td>Yes</td>
<td>N/A</td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>#6</td>
<td>(2008) Corrado et al</td>
<td>36</td>
<td>Yes</td>
<td>N/A</td>
<td></td>
<td>No</td>
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<tr>
<td>#7</td>
<td>(2008) Kothari et al</td>
<td>24</td>
<td>No</td>
<td>N/A</td>
<td></td>
<td>No</td>
</tr>
</tbody>
</table>

Reproductive Outcome

- **80** women got pregnant after conservative treatment of endometrial cancer.
- **At least 80%** were nulliparous.
- **In 96%** of them the tumor was well differentiated.
- In the literature, there are **three cases** of residual carcinoma in the surgical specimen, 6, 8 and 22 months after the delivery.
- In another case, during a C/S, an ovarian carcinoma was found.
SIN TTO, SEIS MESES DESPUÉS

Approximately 50% of well differentiated tumors show a stable complete response to hormonal treatment.

Selecting carefully patients is crucial for obtaining a satisfactory oncological outcome.

Conclusions

Conclusions

DEPARTMENT OF GYNECOLOGIC ONCOLOGY

Conservative management in patients with EC is a therapeutic challenge.

25% of patients will suffer a relapse after a temporary response.

Once reproductive desires have been fulfilled, a standard surgical treatment must be considered.

Patients must know the risks that they run with these approach.

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Patients must know the risks that they run with these approach.

25% of patients will suffer a relapse after a temporary response.

Once reproductive desires have been fulfilled, a standard surgical treatment must be considered.

Patients must know the risks that they run with these approach.
Ovarian borderline tumors

Nadeem R. Abu-Rustum, MD
Memorial Sloan-Kettering Cancer Center
New York

Disclosure
I have no financial relationships to disclose.

Key Points
  - Low-grade serous (BRAF & KRAS mutations)
  - High-grade serous (Tumor Protein 53, p53 mutations)
- Serous LMP
- Mucinous LMP
- Favorable outcome
- Fertility consequences

Borderline tumors
- Synonyms:
  - Tumor of borderline malignancy
  - Tumor of low malignant potential (LMP)
  - Atypical proliferative tumor

Borderline tumors
- Borderline: Neither clinically benign nor malignant
  - Recurrence can occur, but death is uncommon

Borderline tumors
- Borderline: Neither clinically benign nor malignant
  - Recurrence is common, but death is uncommon
- Borderline: Neither morphologically benign nor malignant
  - Architectural complexity but without malignant cytologic features & NO invasion
Borderline tumors

- Serous BTs and seromucinous BTs are both pathologically "borderline" and clinically "borderline."

Gastrointestinal mucinous, endometrioid & transitional BTs are only pathologically "borderline."

- They are clinically BENIGN.

Serous LMP: Bilateral in 30%
If Micropapillary then Bilateral 75%
Serous LMP

Serous LMP: peritoneal evaluation

Accuracy of frozen-section diagnosis of ovarian borderline tumor

- N=120 frozen-section cases
- 12% reclassified as invasive cancer on final pathology
- Micropapillary serous FS: 43% cancer vs. 3% for non-micropapillary tumors
- Tumor size >8 cm: 22% cancer on final pathology vs. 3% in tumors ≤ 8 cm
- Endometrioid, and clear cell histology more likely to be cancer on final

Shih KK, Gaeg K, Socolow RA, Chen DS, Abu-Rustum NR, Barakat RR. (MSKCC) Gynecol Oncol 2011

If Borderline tumors at frozen-section

- When and why do you perform staging operations?
  - Detect extra ovarian surface disease
  - Usually for Serous and Seromucinous BT
- Concern that the diagnosis will be "upgraded" to carcinoma on permanent sections
- Micropapillary serous
Serous Carcinoma: Pathogenesis

Familial: Fimbria?
Sporadic: Cystadenoma
Serous Epithelium

Dysplasia

TP53 mutation

High Grade Serous Carcinoma

Borderline tumor (BT)

TP53 mutation

Low Grade Serous Carcinoma

BRAF & KRAS

Disease continuum of serous borderline & Low-grade serous ovarian cancer

- BRAF & KRAS: <1% of high-grade serous ovarian cancer
- P53: 96% of high-grade serous ovarian cancer
- In Serous Borderline & Low-Grade Serous Cancer
  - Mutation KRAS: 23%
  - Mutation BRAF: 35%


Low-grade serous carcinoma: pathogenesis

Ovarian LMP Tumors

- 10-15% of epithelial tumors
- Median age mid-40s
- Bilateral: 50% of serous tumors & 10% of mucinous
- Stage I: 70% of serous & 90% of mucinous
- Fertility-sparing surgery possible in majority of young patients
- 10-yr. survival ~90% for both tumor types

Risk factors for recurrence of ovarian borderline tumors

- N=266 patients.
- Median age was 43 years (range, 15–94 years).
- 68% had FIGO stage I disease and serous histology (74%).
- Only 23 (9%) patients developed recurrent disease.
- The median PFS was 10 years.

Risk factors for recurrence of ovarian serous borderline tumors

- Elevated preoperative CA-125
- Micropapillary histology
- Invasive implants
- Residual peritoneal disease

Evaluation of peritoneum & omentum much more important than lymph nodes

Shih K, Abu-Rustum NR (MSKCC) Gynecol Oncol 2011
Risk factors for recurrence of ovarian borderline tumors

Shih K, Abu-Rustum NR (MSKCC) Gynecol Oncol 2011

Role of adjuvant chemotherapy in stage II-IV serous ovarian borderline tumors

Shih K, Abu-Rustum NR (MSKCC) Gynecol Oncol 2010

Serous Borderline Tumors: 10-20 year Follow-up

- 70% Stage I
- 30% > Stage I
- 90-95% Non-Inv
- 5-10% Inv
- 56% No Rec
- 44% Recur
- 83% Inv**
- 17% Non-Inv

**75% of patients died
Serous Carcinoma: Pathogenesis

**Familial**
- Fimbria?
- BRCA1 mutation

**Sporadic**
- Dysplasia
- TP53 mutation

Cystadenoma
- Serous Epithelium
- KRAS
- BRAF

Borderline tumor (BT)
- Micropapillary BT

High Grade Serous Carcinoma
Low Grade Serous Carcinoma

Bilaterality common in Serous = Loss of Fertility

Significance of Micropapillary (MP) Architecture

Courtesy: Rob Soslow, MSKCC

Ovarian Preservation: Serous LMP

Image 1: Serous Carcinoma Pathogenesis Diagram

Image 2: Bilaterality in Serous Carcinoma

Image 3: Significance of Micropapillary Architecture

Image 4: Ovarian Preservation Image
Micropapillary Serous Tumor

- Papillae arise directly from the stromal cores in contrast to hierarchical branching seen in conventional serous borderline tumors.

Significance of Micropapillary (MP) Architecture

- Associated with invasive implants
  - More aggressive because of invasive implants
  - Recur more frequently
- More bilateral (70% vs. 20%)
- More involve surface (60% vs. 30%)

Implant Terminology

- Ovarian borderline tumor + peritoneal disease = borderline tumor with implants
- Ovarian carcinoma + peritoneal disease = metastatic ovarian carcinoma

Implant Terminology

- Ovarian borderline tumor + noninvasive peritoneal disease = borderline tumor with noninvasive implants
- Ovarian borderline tumor + invasive peritoneal disease = low grade serous carcinoma
**Significance of Implant Type**

Non-invasive implant 10 year survival: 95%

Invasive implant 10 year survival: 33-50%

Stage III Low-grade serous ca 10 yr survival: 25-50%

---

**Impact of Implants Serous LMP**

<table>
<thead>
<tr>
<th>Recurrence Non-Invasive</th>
<th>Recurrence Invasive</th>
</tr>
</thead>
<tbody>
<tr>
<td>18%</td>
<td>36%</td>
</tr>
</tbody>
</table>

Evaluation of peritoneum & omentum much more important than lymph nodes

---

**Impact of Implants Serous LMP**

<table>
<thead>
<tr>
<th>Death Non-Invasive</th>
<th>Death Invasive</th>
</tr>
</thead>
<tbody>
<tr>
<td>6%</td>
<td>25%</td>
</tr>
</tbody>
</table>

Evaluation of peritoneum & omentum much more important than lymph nodes

---

**Implant Assessment**

- Fat invasion
  - Yes
  - ?Invasive
  - Non-invasive

- Cytologic atypia
  - Yes
  - Carcinoma
  - Micropapillary
  - No

Fat or muscle invasion: invasive implant

---

No invasion AND no diffuse high-grade cytologic atypia or micropapillary architecture:
non-invasive epithelial implant

---

Courtesy of Rob Soslow, MSKCC
Lymph Nodes

- 30% of stage III SBTs have involved LNs
- **NO** Prognostic implication
- Differential diagnosis:
  - Carcinoma
  - Nodular aggregates > 1mm
  - Benign Mullerian inclusions (endosalpingiosis)
  - Mesothelial hyperplasia


Therapy of LMP & Low-Grade Serous Carcinoma

**Surgery is the main treatment**

- Hormonal therapy (90% or SBT are ER+)
- Cytotoxic chemotherapy
- 4% complete response to platinum and taxol*
- Targeted therapy
  - MEK inhibitors for invasive implants/low grade serous carcinoma


Serous Carcinoma: Pathogenesis

- **Familial**
  - Fimbriae?
- **Sporadic**
  - Cystadenoma Serous Epithelium

**Chemo Response**

- High Grade Serous Carcinoma: 80%
- Low Grade Serous Carcinoma: 4%

Disease continuum of serous borderline & Low-grade serous ovarian cancer

In Serous Borderline & Low-Grade Serous Cancer:

- Mutation KRAS: 23%
- Mutation BRAF: 35%

**BRAF mutation:**
- Associated with improved outcome
- Early-stage at presentation
- Serous borderline histology
- Prevents progression to more aggressive disease
- Rare in patients who need chemotherapy


Behavior of Serous Borderline Tumors

- Well staged Ovary-confined SBT (with or without MP) = Benign
- Unstaged SBT+MP = uncertain malignant potential
- SBT with non-invasive implants = slow malignant potential
- SBT with invasive implants = carcinoma

Mucinous Borderline Ovarian Tumors

1. **Gastrointestinal (85%)**
   - Unilateral Large – very large
   - Does not present with implants
2. **Endocervical or Seromucinous (15%)**
   - Bilateral: 20-30%
   - May present with implants
3. **Metastasis from GI primary**
Mucinous Borderline: Pathogenesis

- Rule out GI Primary
- Sporadic
- Cystadenoma
- Gastrointestinal Mucinous BT
- KRAS mutation
- Endometriosis
- Serous Mucinous BT
- ARID1A mutation in 33%
- Endocervical Mucinous BT

Seromucinous Borderline Tumors (15% of Mucinous LMP)

- Synonyms
  - Endocervical-type mucinous borderline tumor
  - Mixed epithelial borderline tumor
- “True” borderline tumor, like serous borderline tumor

Seromucinous Borderline
Seromucinous Borderline Tumors

- Similarities with serous borderline tumor
- Assessment of micropapillary architecture
- Association with implants
- Possibility of malignant behavior (rare!)


Seromucinous Borderline Tumors

- Differences with serous borderline tumor
- Association with “Precursor” Endometriosis
- Malignant potential is lower

Mucinous Borderline: Pathogenesis

- Rule out GI Primary
- Cystadenoma
  - KRAS
  - Gastrointestinal Mucinous BT
- Mucinous BT
  - Endometriosis
  - ARID1A mutation in 33%
- Endocervical Mucinous BT
- Seromucinous BT

Seromucinous BT:
Evidence Supporting Relation to Endometrioid Neoplasia

- Lack or paucity of WT1 staining
- Presence of ARID1A mutation in approximately 1/3 of cases

Gastrointestinal Mucinous Borderline Tumors

- **Problems with accurate diagnosis**
  - Large, unilateral, heterogeneous tumors
  - Does NOT present with implants
  - Many metastases to the ovary have a "borderline appearance"
    - Low-grade appendiceal mucinous neoplasms
    - Pancreatobiliary carcinoma
    - Endocervical adenocarcinoma

Intestinal-Type Mucinous Tumors: Features Favoring Metastasis

- Bilateral disease
- Surface involvement
- Destructive stromal invasion
- Nodular growth pattern
- Signet ring cells
- Vascular invasion


Classic Mucinous Borderline Tumor

Mucinous BT

Mucinous borderline tumors very large technically limits ovarian preservation

Mucinous BT
• Intestinal type virtually always limited to ovary & behaves benign
• Data on endocervical seromucinous type are limited, but benign behavior common
• Mucinous PMP almost invariably derived from GI tract, usually appendix

Algorithm for distinguishing primary vs. metastatic mucinous carcinoma (and borderline tumors)
• Bilateral mucinous carcinomas = metastatic
• Unilateral mucinous ca & <12 cm = metastatic
• Unilateral mucinous ca & >12 cm = primary ovarian

Metastatic carcinoma may look benign or “borderline”
• Pseudomyxoma-associated tumors are notorious
• Metastatic pancreatobiliary carcinomas frequently mimic the appearance of primary ovarian tumors

Summary
• Serous BT Prognosis depends on surgery, stage, implant type, and micropapillary architecture
• Tumors with NON-invasive implants may recur as invasive implants/Low-grade serous carcinoma
• Borderline tumors with invasive implants are similar to Low-grade serous carcinoma

“Ovarian cancer” is distinct disease entities: Genotype

<table>
<thead>
<tr>
<th></th>
<th>Response to platinum taxane</th>
<th>p53</th>
<th>KRAS</th>
<th>BRAF</th>
<th>PIK3CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Grade Serous</td>
<td>80%</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Low-Grade Serous</td>
<td>4%</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Mucinous</td>
<td>-</td>
<td>KRAS+++</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endometrioid</td>
<td>-</td>
<td>+</td>
<td>++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear cell</td>
<td>-</td>
<td>-</td>
<td>+++</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Low-grade serous carcinomas are clinically, biologically and morphologically distinct from High-Grade serous carcinoma.

Many LG serous ca might represent progression from SBT and SBT with micropapillary features.

They rarely progress to a high-grade neoplasm.

For mucinous ovarian neoplasms always rule out a metastasis from other GI primary.

Acknowledgement
Robert Soslow, MD
STATE-OF-THE-ART ONCOFERTILITY SERVICES FOR THE CANCER PATIENT

Nicole Noyes MD
Professor
NYU Fertility Center
NYU School of Medicine
New York, New York

I have no financial relationships to disclose.

At the conclusion of this activity, the participant will be able to list and compare oncofertility services currently available to reproductive-age women newly diagnosed with malignancy.

ONCOFERTILITY
WHO ARE THE PATIENTS?

Cancer by Site – US Female – 2013
Fertility Preservation

- >700,000 cases annually: 10% in reproductive age
- Survival often associated with ovarian compromise

Probability of Menopause During 1st Year after Breast Cancer Diagnosis

Stem Cell/Bone Marrow Transplantation
Associated with Ovarian Failure

- Marrow Ablation/Transplantation
  - Chemotherapy
  - High-dose alkylating agent
  - Irradiation

Ovarian Failure following BMT
Sanders, 1996 99%
Teinturier, 1998 72%
Thibaud, 1998 80%
Meirow, 1999 79%
Grigg, 2000 100%

2006 ASCO Guideline Summary

American Society of Clinical Oncology Recommendations on Fertility Preservation in Cancer Patients

FP is an important, if not necessary, consideration when planning cancer treatment in reproductive-age patients

WOMEN ARE WAITING TO HAVE CHILDREN

U.S. Census Data

Births by Age Group
- Under 20 yrs
- 20-24 yrs
- 25-29 yrs
- 30-34 yrs
- 35-39 yrs
- 40-44 yrs (highest since 1969)


More women are being diagnosed with cancer who have not yet completed family

DIMINISHING OVARIAN RESERVE

- 20-week gestation: 6.7 x 10^6 oocytes
- No further germ cell proliferation
- Progressive atresia begins

Birth: 1.3 x 10^6 oocytes
- Oocytes arrested at prophase 1 as primordial or primary oocytes

Puberty: 300,000 (15%) oocytes
- Monthly cohort of follicles initiate growth and development
- One "ovulates" others become atretic

Age 30: 240,000 (~12%) oocytes
Age 40: 60,000 (~3%) oocytes
- Accelerated atresia

Coincident is a ↓ in quality of oocytes

A woman’s purpose
(without brain and/or choices)

Reproductive System Design Flaws:
1. Most fertile when too young
2. Only fertile for ~1/3 of expected lifespan

Cancer/Fertility Venn Diagram

- CANCER DIAGNOSIS AND SURVIVAL
- NO OR LOW # CHILDREN
- FERTILITY DESIRE OR UNSURE
ONCOFERTILITY
WHAT ARE THE OPTIONS?

Considerations for Fertility Preservation

- Patient age / ovarian reserve (FSH, AMH, AFC)
- Patient health and desires
- Presence of partner
  - Willingness to use donor gametes
  - Disposition of gametes/embryos stored
  - Ethical challenges
  - Posthumous rights (only 3 states with legislation: ND, Utah, CO)
- Clinic practices
- Government regulation
- Most important
  - Do what’s in the best interest of the patient

Embryo Freezing
Standard of Care
Supernumerary Livebirth Embryo Data

Oocyte Cryopreservation - History

- First human pregnancy was reported in 1986
- Early results disappointing
  - Low oocyte survival, fertilization and pregnancy rates
- Why oocytes difficult to freeze—
  - Large cell size (100 micrometers)
  - Ice crystal formation
  - Aqueous: High water content (80%)
  - Chromosomal arrangement (spindle)
**Oocyte Cryopreservation Breakthroughs**

- Fine-tuning dehydration protocols through modifications in cryoprotectant combinations, concentrations and exposure times
- Fertilization by Intracytoplasmic Sperm Injection (ICSI) - 1995
  - Circumvents zona pellucida hardening that may occur during freezing process
- Development of novel “cryotools”

**History Human Oocyte Cryopreservation Worldwide Literature-Reported Live Births**

- Over 500 oocyte cryopreservation babies born with no apparent increase in congenital anomalies
- No apparent increase in birth anomalies

**Cumulative Oocyte Preservation Outcome Data**

**Four RCTs Fresh vs. vitrified oocytes**

**Experimental Designation Lifted October 2012**

**Mature oocyte cryopreservation: a guideline**
3. In Vitro Maturation of Immature Oocytes

**Considered Experimental**

- Retrieval of immature oocytes after no or limited gonadotropin stimulation, then bank mature oocytes
- **Advantages**
  - If stimulation used, shorter duration
  - Lower risk of ovarian hyperstimulation
- **Disadvantages**
  - Relatively low success rates with low birth numbers
  - Like ovarian stimulation, ideal to begin at start of menses

<table>
<thead>
<tr>
<th>NYU Fertility Center Non-Cancer Thaw Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oocytes From Women &lt;Age 43</strong></td>
</tr>
<tr>
<td>n = 102: 31 donor + 71 autologous</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Donor</th>
<th>Autologous 25 - 34 y (n = 31)</th>
<th>Autologous 35 - 40 y (n = 42)</th>
<th>Autologous 41 - 42 y (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (y)</td>
<td>29</td>
<td>32</td>
<td>38</td>
<td>42</td>
</tr>
<tr>
<td>No. MI thawed</td>
<td>11</td>
<td>16</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>No. emb transferred</td>
<td>1.9</td>
<td>2</td>
<td>1.8</td>
<td>2.5</td>
</tr>
<tr>
<td>Pregnant n (%)</td>
<td>23(74%)</td>
<td>8(42%)</td>
<td>15(36%)</td>
<td>4(40%)</td>
</tr>
<tr>
<td>Spont abortion</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Ongoing/Delivered</td>
<td>17(55%)</td>
<td>8(42%)</td>
<td>13(31%)</td>
<td>2(8%)</td>
</tr>
</tbody>
</table>

Excludes PGD/PGS and “Sandy” cycles and ≥43 y oocytes. *1 baby from refrozen embryos.

In Vitro Maturation of Immature Oocytes

**Considered Experimental**

- No ovarian stimulation
- Minimal delay in treatment
- No partner needed
- Only option in prepubertal girls
- Possibility to cryopreserve thousands of oocytes

**Disadvantages**
- Requires surgical removal of ovarian tissue and 2nd surgery to replace
  - Autologous transplantation – human births
  - Maturation of oocytes in vitro – no human births
- Relatively few successes at this time

In Vitro Maturation of Immature Oocytes

**Considered Experimental**

<table>
<thead>
<tr>
<th></th>
<th>No Priming (n = 100)</th>
<th>NCG alone (10,000 IU) (n = 100)</th>
<th>FSH alone (150 IU/day x 5 days) (n = 100)</th>
<th>FSH + NCG (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>33.1</td>
<td>33.1</td>
<td>33.6</td>
<td>33.2</td>
</tr>
<tr>
<td># Oocytes</td>
<td>5.3</td>
<td>5.3</td>
<td>4.8</td>
<td>5.4</td>
</tr>
<tr>
<td>MI at retrieval</td>
<td>0</td>
<td>5.7%</td>
<td>0</td>
<td>20.3%</td>
</tr>
<tr>
<td>Clin Preg Rate/ET</td>
<td>15.3%</td>
<td>7.6%</td>
<td>17.3%</td>
<td>29.9%</td>
</tr>
<tr>
<td>Implantation Rate</td>
<td>9.2%</td>
<td>4%</td>
<td>10.6%</td>
<td>16.4%</td>
</tr>
</tbody>
</table>
Summary of 14 Births from Orthotopic Transplants

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>AGE at TRENTO</th>
<th>SURGICAL METHOD</th>
<th>REIMPLANTATION</th>
<th>PREGNANCY</th>
<th>REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hodgkin</td>
<td>25</td>
<td>Biopsy</td>
<td>Orthotopic</td>
<td>Spontaneous live birth</td>
<td>Donnez, 2004</td>
</tr>
<tr>
<td>Neuroendocrine</td>
<td>19</td>
<td>Biopsy</td>
<td>Orthotopic</td>
<td>Spontaneous live birth</td>
<td>Donnez, 2011</td>
</tr>
<tr>
<td>Hodgkin</td>
<td>20</td>
<td>Biopsy</td>
<td>Orthotopic</td>
<td>IVF after reimplantation, live birth</td>
<td>Donnez, 2011</td>
</tr>
<tr>
<td>Hodgkin</td>
<td>24</td>
<td>USO</td>
<td>Ortho and</td>
<td>2 spontaneous live births</td>
<td>Donnez, 2011</td>
</tr>
<tr>
<td>Neuroendocrine</td>
<td>27</td>
<td>USO</td>
<td>Orthotopic</td>
<td>IVF after reimplantation</td>
<td>Donnez, 2011</td>
</tr>
<tr>
<td>Hodgkin</td>
<td>36</td>
<td>Biopsy</td>
<td>Orthotopic</td>
<td>IVF after reimplantation, live birth</td>
<td>Donnez, 2011</td>
</tr>
<tr>
<td>Premature</td>
<td>24</td>
<td>Biopsy</td>
<td>Orthotopic</td>
<td>Live birth</td>
<td>Silver, 2008</td>
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<tr>
<td>Testicular</td>
<td>20</td>
<td>USO</td>
<td>Orthotopic</td>
<td>Spontaneous live birth</td>
<td>Roux, 2010</td>
</tr>
</tbody>
</table>

5. Ovariotomy

Ovarian Protection During Radiotherapy

− Moving the ovary away from the irradiation field
− Usually laterally and superiorly ~ 14 cm
− Ovaries can move back so surgery should occur as close to radiation treatment as possible
− Preserves ovarian function in 60% of patients
− Ovaries do not need to be moved back for spontaneous pregnancy or IVF
− GYN cancer: 32% pregnancy rate

6. Whole Ovary Transplantation

Considered experimental

Duration and subsequent function limited, mostly due to ischemia resulting from thrombosis. Micorsurgical techniques have led to improved survival.

References:
Fertility Preserving Surgery in Ovarian Cancer
Audrey Tsunoda, MD, PhD
Gynecologic Oncology Department – Barretos Cancer Hospital

Washington DC, November 11th, 2013

Disclosures
I have no financial relationships to disclose.

Learning Objectives
- To define Fertility Preserving Surgery in Ovarian Cancer
- Indications of FPS in epithelial ovarian cancer
- Indications of FPS in germ cell ovarian tumors
- To review the surgical technique for minimally invasive staging procedures in ovarian cancer

Ovarian cancer
- 22,000 new cases/year in the USA
- Most cases are diagnosed in advanced stages (70%)
- Stage I overall survival: 84% to 94%
- 3% to 17% in women aged <40yo


Ovarian Sparing Surgery in Ovarian Cancer
- Preservation of the uterus and the contralateral ovary
- Comprehensive staging procedure
  - USO – no indication of contralateral manipulation/biopsy
  - Peritoneal washings and biopsies
  - Omentectomy
  - Paraortic and pelvic lymphadenectomy
  - Appendectomy (mucinous)
Indications of FPS in EOC

- Desire to preserve fertility
- EOC Stage IA or IC
- No difference between OS and DFS
- 30% of upstaging after adequate surgery
- 10%-25% node positive in apparently stage I disease


doctor reference:
Wright. Cancer. 2009 Sep 15;115(18):4118

PFS in EOC overall survival

- SEER data
- Stage IA

PFS in EOC overall survival

- SEER data
- Stage IC

PFS in EOC overall survival

Table 4. Five-Year Survival Stratified by Stage and Ovarian or Uterine Preservation

<table>
<thead>
<tr>
<th>Group</th>
<th>Ovarian Oophorectomy</th>
<th>Ovarian Preservation</th>
<th>Hysterectomy</th>
<th>Uterine Preservation</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>81 (54)</td>
<td>94 (40)</td>
<td>91 (20)</td>
<td>92 (60)</td>
</tr>
<tr>
<td>95% CI, %</td>
<td>88-85</td>
<td>91-95</td>
<td>90-93</td>
<td>90-94</td>
</tr>
<tr>
<td>Stage IA</td>
<td>7.9% Survival, %</td>
<td>95 (67)</td>
<td>93 (120)</td>
<td>95 (42)</td>
</tr>
<tr>
<td>95% CI, %</td>
<td>91-96</td>
<td>91-97</td>
<td>90-95</td>
<td>90-95</td>
</tr>
<tr>
<td>Stage IC</td>
<td>6.1% Survival, %</td>
<td>89 (60)</td>
<td>87 (193)</td>
<td>88 (125)</td>
</tr>
<tr>
<td>95% CI, %</td>
<td>78-86</td>
<td>77-89</td>
<td>76-89</td>
<td>79-83</td>
</tr>
</tbody>
</table>

EOC with poor prognosis histology

- Rare cases
- Clear cell tumors are stage I in 56% of the cases
- A rare histology as clear cell tumor seems to have a poorer prognosis, but there is no sufficient evidence regarding fertility preservation
- Cases should be individualized

doctor reference:
**EOC with poor prognosis histology**

**Why FPS in germ cell ovarian tumors?**
- Young patients without complete childbearing
- Strong desire to preserve fertility
- No impairment in DFS or OS, regardless of stage
- 87% of regular menstrual function after FPS plus platinum based chemo

**Pure dysgerminomas**
- Complete surgical staging is indicated even for stage IA
- Relapses related to incomplete staging
- No relapses after complete staging
- Fertility sparing strongly recommended for young patients

**Comprehensive Laparoscopic Surgical Staging in ovarian cancer**

**Patient positioning**
Fertility Preserving Surgery in Ovarian Cancer

Trocar placement

- Umbilical 11mm
- Left lower quadrant 5mm
- Right lower quadrant 5mm
- Hypogastric 5mm

Salpingoophorectomy

- Recommended: tubal removal
- Avoid rupture or perforation during manipulation
- Video

Contralateral approach

- Less than 2% of grossly normal ovaries have metastasis
- Avoid contralateral biopsy
- Contralateral manipulation may impair fertility
- Video

Omentectomy

- Omentectomy video
Paraortic lymphadenectomy

- Paraortic video

Pelvic lymphadenectomy

- Pelvic video

Take home messages

- Comprehensive staging
- Consider FPS in Ia/Ic EOC and all germ cell tumors
  - Clear cell tumors and other poor prognosis histologies should be individualized
- No impairment of OS or DFS with FPS
- Laparoscopy/minimally invasive techniques are welcome in this setting!

Where are we from?

Barretos arena
Barretos Cancer Hospital

Gynecologic Oncology Dept - BCH
Only cancer patients from the Brazilian Public Health Care System

- Starting: Jan 2008
- Multidisciplinary team
  - Standardized treatment regimens
- New cases: 750/year
- Beds:
  - Surgical: 5
  - Clinical: 2
  - ICU: 1/month

Multidisciplinary team

BCH Laparoscopy and Gynecologic Oncology Dept 2011-2012

- Inpatient surgery: 420/yr
- Outpatient surgery: 600/yr
  - Prevention dept: 350/yr
- Mean hospital stay: 1.3d

Number of cases 406

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>406</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time interval</td>
<td>Jan2011 – Dec2012</td>
</tr>
<tr>
<td>BMI (mean)</td>
<td>28.9</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1 case</td>
</tr>
<tr>
<td>Blood loss (median)</td>
<td>52cc</td>
</tr>
<tr>
<td>Complications</td>
<td>16 (3.9%)</td>
</tr>
<tr>
<td>Conversion to laparotomy</td>
<td>9 (2.2%)</td>
</tr>
</tbody>
</table>
  - vascular lesion
  - technical issue |
| Trocar insertion | 2 |
| Vascular lesions | 8 |
| Intestinal lesions | 3 |
| Urinary tract lesions | 3 |
Thank you!

References


NCCN guidelines 2.2013


Governor Arnold Schwarzenegger signed into law **AB 1195** (eff. 7/1/06) requiring local CME providers, such as the AAGL, to assist in enhancing the cultural and linguistic competency of California's physicians (researchers and doctors without patient contact are exempt). This mandate follows the federal Civil Rights Act of 1964, Executive Order 13166 (2000) and the Dymally-Alatorre Bilingual Services Act (1973), all of which recognize, as confirmed by the US Census Bureau, that substantial numbers of patients possess limited English proficiency (LEP).

**California Business & Professions Code §2190.1(c)(3)** requires a review and explanation of the laws identified above so as to fulfill AAGL’s obligations pursuant to California law. Additional guidance is provided by the Institute for Medical Quality at [http://www.imq.org](http://www.imq.org).

**Title VI of the Civil Rights Act of 1964** prohibits recipients of federal financial assistance from discriminating against or otherwise excluding individuals on the basis of race, color, or national origin in any of their activities. In 1974, the US Supreme Court recognized LEP individuals as potential victims of national origin discrimination. In all situations, federal agencies are required to assess the number or proportion of LEP individuals in the eligible service population, the frequency with which they come into contact with the program, the importance of the services, and the resources available to the recipient, including the mix of oral and written language services. Additional details may be found in the Department of Justice Policy Guidance Document: Enforcement of Title VI of the Civil Rights Act of 1964 [http://www.usdoj.gov/crt/cor/pubs.htm](http://www.usdoj.gov/crt/cor/pubs.htm).

**Executive Order 13166, “Improving Access to Services for Persons with Limited English Proficiency”,** signed by the President on August 11, 2000 [http://www.usdoj.gov/crt/cor/13166.htm](http://www.usdoj.gov/crt/cor/13166.htm) was the genesis of the Guidance Document mentioned above. The Executive Order requires all federal agencies, including those which provide federal financial assistance, to examine the services they provide, identify any need for services to LEP individuals, and develop and implement a system to provide those services so LEP persons can have meaningful access.

**Dymally-Alatorre Bilingual Services Act** (California Government Code §7290 et seq.) requires every California state agency which either provides information to, or has contact with, the public to provide bilingual interpreters as well as translated materials explaining those services whenever the local agency serves LEP members of a group whose numbers exceed 5% of the general population.

If you add staff to assist with LEP patients, confirm their translation skills, not just their language skills. A 2007 Northern California study from Sutter Health confirmed that being bilingual does not guarantee competence as a medical interpreter. [http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2078538](http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2078538).