Inherited Breast and Ovarian Cancer: 20 Years of Progress and Future Directions

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Duke Cancer Institute / Duke University Health System
Disclosures

• I have nothing relevant to disclose.
Identification of **BRCA1** and **BRCA2**

**Research Articles**

**Linkage of Early-Onset Familial Breast Cancer to Chromosome 17q21**

Jeff M. Hall, Ming K. Lee, Beth Newman, Jan E. Morrow, Lee A. Anderson, Bing Huey, Mary-Claire King

Hall JM et al. Science Dec 1990

Newsweek: Dec 6, 1993

**A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene BRCA1**


Science: October 1994

Newsweek: Dec 6, 1993

**Identification of the breast cancer susceptibility gene BRCA2**


Nature: December 1995
Cancer Risk Estimates for *BRCA* Mutation Carriers
(Summary Analysis of 22 Studies)


![Graphs showing cumulative risk of breast and ovarian cancer for BRCA1 and BRCA2 mutation carriers across different age ranges.](image-url)
BRCA1-Linked Hereditary Breast and Ovarian Cancer

- Multiple cases of early onset breast cancer and/or ovarian cancer at any age
- Affects multiple generations
- Penetrance is not complete
Potential Risk-Reduction Strategies

– Breast
  • Intensive Surveillance (Mammogram, U/S, MRI)
  • Chemoprevention (Tamoxifen, Raloxifene, Aromatase Inhibitors)
  • Risk-Reducing Surgery (Mastectomy, Oophorectomy)

– Ovary
  • Chemoprevention (Oral Contraceptives)
  • Risk-Reducing Surgery (Salpingo-Oophorectomy, Salpingectomy)
Intensive Surveillance
# Mammogram Screening in BRCA Mutation Carriers

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Sensitivity</th>
<th>Invasive Cancer</th>
<th>Lymph Node Metastases</th>
</tr>
</thead>
</table>
MRI Breast Screening

Normal Mammogram
Performed at Time of MRI

MRI Detected
Occult Stage I Breast Cancer
### Prospective Studies of MRI Screening for Breast Cancer in Women with BRCA1/2 Mutations

<table>
<thead>
<tr>
<th></th>
<th>Dutch MRISC study, Kriege et al, 2004</th>
<th>Toronto, Canada, Warner et al, 2004</th>
<th>MARIBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of women</td>
<td>1909</td>
<td>236</td>
<td>649</td>
</tr>
<tr>
<td>No. of BRCA 1/2 carriers</td>
<td>354</td>
<td>236</td>
<td>120</td>
</tr>
<tr>
<td>MRI sensitivity (95% CI)</td>
<td>71.1%</td>
<td>77.3%</td>
<td>77%</td>
</tr>
<tr>
<td>MRI specificity</td>
<td>89.8%</td>
<td>95.4%</td>
<td>81%</td>
</tr>
<tr>
<td>Mammogram sensitivity</td>
<td>40%</td>
<td>36.4%</td>
<td>40%</td>
</tr>
<tr>
<td>Mammogram specificity</td>
<td>95%</td>
<td>99.8%</td>
<td>93%</td>
</tr>
</tbody>
</table>

Stage Shift – Breast MRI


- 1275 women with a BRCA1 or BRCA2 mutation
  - 445 women in MRI Trial; 830 in Comparison Group
  - Followed for mean of 3.2 yrs, cancer incidence estimated at 6 yrs

- DCIS or Stage I
  - 13.8% in MRI; 7.2% in Mammo (p=0.01)

- Stage II-IV
  - 1.9% in MRI; 6.6% in Mammo (p=0.02)
  - HR = 0.30 (95% CI 0.12 – 0.78, p=0.008)
Chemoprevention
Oral Contraceptives in BRCA Mutation Carriers: Ovarian Cancer Risk

  – Ever use of OC’s associated with a decreased risk of ovarian cancer (OR 0.57; 95%CI 0.47-0.70)
  – Increased duration of use associated with decreased risk (OR 0.95; 95%CI 0.93-0.97)

  – Ever use of OC’s associated with a decreased risk of ovarian cancer (OR 0.58; 95%CI 0.46-0.73)
Oral Contraceptives in *BRCA* Mutation Carriers: Breast Cancer Risk

  - Case-Control: No increased risk of breast ca in *BRCA1* or *BRCA2* (*BRCA1*: OR 1.08, p=0.25; *BRCA2* OR 1.03, p=0.79)
  - Cohort: Increased breast ca risk in *BRCA1* mutation carriers (*BRCA1* OR 0.1.48; 95%CI 1.14-1.92)

  - Ever use of OC’s associated with a non-significant increased risk (OR 1.21; 95%CI 0.93-1.58)
Risk-Reducing Surgery
Oophorectomy for the Prevention of Ovarian Cancer

- Liber AM. Arch Path 1950
  - Described a family of five sisters and their mother, all with histologically confirmed papillary adenocarcinoma of the ovary.
  - Recommended that family members should undergo frequent gynecologic screening and that prophylactic oophorectomy should be considered.
Risk-Reducing Oophorectomy


“The value of oophorectomy in mutation carriers has not yet been proven, however, and there are concerns that the benefit may be less than intuitively expected….

…….peritoneal papillary serous carcinoma indistinguishable from ovarian cancer occurs in some women following oophorectomy. Studies that better define how often this occurs also are needed to establish more firmly the value of prophylactic oophorectomy”
Risk-Reducing Salpingo-Oophorectomy
MSKCC Prospective Series

- 265 women with BRCA mutations

**EXCLUSIONS:**
- 63 bilateral salpingo-oophorectomy before testing
- 25 younger than 35 years old at time of testing
- 4 lost to follow-up

- Inception Cohort of 173

Risk counseling and BRCA testing

Salpingo-oophorectomy

Surveillance
Risk-Reducing Salpingo-Oophorectomy


# Risk-Reducing Salpingo-Oophorectomy

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N (RRSO)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kauff, et al. NEJM 2002</td>
<td>Prospective</td>
<td>98</td>
<td>0.15 (0.02-1.31)</td>
</tr>
<tr>
<td>Rebbeck, et al. NEJM 2002</td>
<td>Retrospective</td>
<td>259</td>
<td>0.04 (0.01-0.16)</td>
</tr>
<tr>
<td>Rutter, et al. JNCI 2003</td>
<td>Retrospective</td>
<td>251</td>
<td>0.29 (0.12-0.73)</td>
</tr>
<tr>
<td>Finch, et al. JAMA 2006</td>
<td>Combined</td>
<td>1045</td>
<td>0.20 (0.07-0.58)</td>
</tr>
<tr>
<td>Kauff, et al. JCO 2008</td>
<td>Prospective</td>
<td>509</td>
<td>0.12 (0.03-0.41)</td>
</tr>
<tr>
<td>Domchek, et al. JAMA 2010</td>
<td>Combined</td>
<td>939</td>
<td>0.14 (0.04-0.59)</td>
</tr>
</tbody>
</table>

(Kauff ND - Principal Author). Obstet Gynecol 2009

HR = 0.04 (95% CI: 0.01-0.16) (95% CI: 0.33-0.84)
Mutations in **BRCA1** and **BRCA2** Cause Distinct Cancer Susceptibility Syndromes

- **Breast Cancer**
  - **BRCA1**: 10-24% ER positive
  - **BRCA2**: 65-79% ER positive

- **Ovarian Cancer**
  - **BRCA1**: 34-46% risk (to age 70)
  - **BRCA2**: 10-27% risk (to age 70)
## Risk of *BRCA*-associated Breast Cancer following RRSO

<table>
<thead>
<tr>
<th></th>
<th>RRSO</th>
<th>Surveillance</th>
<th></th>
<th></th>
<th></th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Cancers</td>
<td>N</td>
<td>Cancers</td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td><em>BRCA1 &amp; BRCA2</em></td>
<td>303</td>
<td>19</td>
<td>294</td>
<td>28</td>
<td>0.53</td>
<td>0.29 – 0.96</td>
</tr>
<tr>
<td><em>BRCA1</em></td>
<td>190</td>
<td>15</td>
<td>178</td>
<td>19</td>
<td>0.61</td>
<td>0.30 – 1.22</td>
</tr>
<tr>
<td><em>BRCA2</em></td>
<td>113</td>
<td>4</td>
<td>116</td>
<td>9</td>
<td>0.28</td>
<td>0.08 – 0.92</td>
</tr>
</tbody>
</table>
### Impact of RRSO on ER-positive vs. ER-negative Breast Cancer

*(BRCA1/BRCA2 Combined – Adjusted for Mutation Type)*

<table>
<thead>
<tr>
<th></th>
<th>ER-positive</th>
<th></th>
<th>ER-Negative</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Events</td>
<td>HR (95% CI)</td>
<td>P Events</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>RRSO</td>
<td>300</td>
<td>0.22 (0.05-1.05)</td>
<td>0.058</td>
<td>1.10 (0.48-2.51)</td>
</tr>
<tr>
<td>No RRSO</td>
<td>284</td>
<td></td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

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**Kauff ND, Domchek SM....Offit K, Rebbeck TR et al. J Clin Oncol 2008**
What can study of individuals with inherited malignancies teach us about tumor biology in general?
Ovarian Tumorigenesis – 2002

• Risk factors
  – Nulliparity
  – Early Menarche
  – Late Menopause
  – Talc

• Protective Factors
  – Pregnancy
  – Lactation
  – Oral Contraceptive Use

Drapkin and Hecht, *Women’s Oncol Rev* 2002
Dysplasia – Carcinoma Sequence
## Prevalence of Occult Cancer in Women with Mutations in \textit{BRCA1} or \textit{BRCA2}

<table>
<thead>
<tr>
<th>Study</th>
<th>Pts (n)</th>
<th>Occult Cancers</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebbeck, et al. 2005</td>
<td>259</td>
<td>6</td>
<td>2.3%</td>
</tr>
<tr>
<td>Kauff, et al. 2002</td>
<td>98</td>
<td>3</td>
<td>3.1%</td>
</tr>
<tr>
<td>Leeper, et al. 2002</td>
<td>17</td>
<td>4</td>
<td>23.5%</td>
</tr>
<tr>
<td>Lu, et al. 2000</td>
<td>22</td>
<td>4</td>
<td>18.2%</td>
</tr>
<tr>
<td>Powell, et al. 2005</td>
<td>67</td>
<td>7</td>
<td>10.4%</td>
</tr>
<tr>
<td>Olivier, et al. 2005</td>
<td>65</td>
<td>5</td>
<td>7.7%</td>
</tr>
<tr>
<td>Finch, et al. 2006</td>
<td>490</td>
<td>11</td>
<td>2.2%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>918</td>
<td>40</td>
<td>4.4%</td>
</tr>
</tbody>
</table>
Precursor Lesions in Pelvic Serous Cancer

Karst el al. J Oncol 2010
What is the Role of Risk-Reducing Salpingectomy?
Hormonal Effects on the Fallopian Tube and Ovarian Inclusion Cysts and Ovarian Cancer

1. R21CA181923-01 (Kauff ND, Pike M – Co-PIs)
   - To determine the effect of different endogenous estrogen-progesterone circumstances on cell proliferation, apoptosis, and expression of ER and PR receptors in the fallopian tube fimbria and mullerian-type CICs in women undergoing an RRSO.

<table>
<thead>
<tr>
<th>Follicular Phase</th>
<th>Luteal Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.98%</td>
<td>0.34%</td>
</tr>
<tr>
<td>1.62%</td>
<td>0.29%</td>
</tr>
<tr>
<td>1.56%</td>
<td>0.17%</td>
</tr>
<tr>
<td>1.06%</td>
<td>0.00%</td>
</tr>
<tr>
<td>0.92%</td>
<td></td>
</tr>
</tbody>
</table>
Is it Reasonable to Remove Just the Fallopian Tubes for Risk-Reduction?

• We do not know the latency period from time of genetic changes in the fallopian tube to development of invasive pelvic serous cancer.

• We do not know what proportion of pelvic serous cancers will be prevented by this approach.

• Deferring oophorectomy will negate the benefit conferred by RRSO against breast cancer.
What is the Role of Hysterectomy?
What is the Role of Hysterectomy?

Weighing Surgeries in Light of a Breast Cancer Gene

By JILL WERMAN HARRIS

October 7, 2013 2:13 pm

When Tracy Dunbrook, a bioethicist in Sherman, Conn., tested positive for the BRCA gene mutation, she was told she had a 40 to 60 percent chance of developing ovarian cancer in her lifetime. Doctors advised her to have her ovaries removed.

She considered going further and having a hysterectomy, in which her uterus would be removed, but in the end opted for the standard of care: a procedure known as risk-reducing salpingo-oophorectomy (RRSO), removal of her ovaries and fallopian tubes. Five years later, she was given a diagnosis of Stage 3 uterine cancer.

“I couldn’t believe it,” she said, “I thought, this is the dirtiest trick.”
Methods

• 1083 BRCA+ women from 9 centers who underwent RRSO with their uterus left in situ
  – Deleterious BRCA1 or BRCA2 mutation
  – Enrolled on a prospective follow-up study (MSKCC/Penn/PROSE)
  – Unaffected with gynecologic cancer at start of follow-up
  – Prospectively followed from the latest of ascertainment, receipt of genetic testing results or RRSO
  – Censoring occurred at hysterectomy, new gyn cancer, last f/u, or death
## Results: Median F/U – 5.1 yrs

<table>
<thead>
<tr>
<th></th>
<th>Expected</th>
<th>Observed</th>
<th>O:E Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All corpus cancers</td>
<td>4.30</td>
<td>8</td>
<td>1.9 (0.8-3.7)</td>
<td>0.09</td>
</tr>
<tr>
<td>Endometrioid carcinoma</td>
<td>3.62</td>
<td>2</td>
<td>0.6 (0.1-2.0)</td>
<td>0.88</td>
</tr>
<tr>
<td>Serous/serous-like carcinoma</td>
<td>0.34</td>
<td>5</td>
<td>14.8 (4.8-34.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>0.14</td>
<td>1</td>
<td>7.1 (0.2-39.4)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Shu CA, Pike MC…Kauff ND. JAMA Oncology 2016
### Table 2. Observed and Expected Rates for Serous and/or Serous-like Endometrial Cancer in BRCA Mutation Carriers

<table>
<thead>
<tr>
<th>Category of Analysis</th>
<th>Expected No. of Cases</th>
<th>Observed No. of Cases</th>
<th>O:E Ratio (95% CI)</th>
<th>P Value</th>
<th>Follow-up, Woman-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRCA1+ (n = 627)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>BRCA2+ (n = 453)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior breast cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n = 727)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (n = 356)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamoxifen exposurea</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Yes (n = 273)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (n = 655)</td>
<td></td>
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</tbody>
</table>

Original Investigation

**Uterine Cancer After Risk-Reducing Salpingo-oophorectomy Without Hysterectomy in Women With BRCA Mutations**

Catherine A. Shu, MD; Malcolm C. Pike, PhD; Anjali R. Jotwani, BS; Tara M. Friebel, MPH; Robert A. Soslow, MD; Douglas A. Levine, MD; Katherine L. Nathanson, MD; Jason A. Konner, MD; Angela G. Arnold, MS; Faina Bogomolnyi, BS; Fanny Dao, MS; Narciso Olvera, BA; Elizabeth K. Bancroft, RN, PhD; Deborah J. Goldefrank, MD; Zsofia K. Stadler, MD; Mark E. Robson, MD; Carol L. Brown, MD; Mario M. Leitao Jr, MD; Nadeem R. Abu-Rustum, MD; Carol A. Aghajanian, MD; Joanne L. Blum, MD, PhD; Susan L. Neuhausen, PhD; Judy E. Garber, MD, MPH; Mary B. Daly, MD, PhD; Claudine Isaacs, MDCM; Rosalind A. Eeles, PhD; Patricia A. Ganz, MD; Richard R. Barakat, MD, Kenneth Offit, MD, MPH; Susan M. Domchek, MD; Timothy R. Rebbeck, PhD; Noah D. Kauff, MD
BRCA1 Immunohistochemistry

A = Carcinosarcoma, B = High grade – serous/undiff, C = Serous, D = Leiomyosarcoma
High grade – serous/undiff (B): BRCA1 185delAG
Limitations

- Limited number of cases
- Possible misclassification of rare uterine cancer subtypes in SEER
- Possible confounding by history of breast cancer and tamoxifen exposure
Therapeutic Implications of BRCA Deficiency
### Studies Demonstrating Improved Survival in BRCA-Associated Ovarian Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N (Stage III-IV)</th>
<th>Stage III-IV Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubin, et al. NEJM 1996</td>
<td>Retrospective Case-Control</td>
<td>53 (43)</td>
<td>Median Survival 77 v 29 m (p&lt;0.001)</td>
</tr>
<tr>
<td>Boyd, et al. JAMA 2000</td>
<td>Single Institution Series</td>
<td>88 (81)</td>
<td>HR for Survival 0.75 (p=0.03)</td>
</tr>
<tr>
<td>Ben David, et al. JCO 2002</td>
<td>Prospective, Population Based</td>
<td>234</td>
<td>Median Survival 51 v 33 m (p&lt;0.05)</td>
</tr>
<tr>
<td>Cass, et al. Cancer 2003</td>
<td>Single Institution Series</td>
<td>34</td>
<td>Disease Free Interval 49 v 19 m (p=0.16)</td>
</tr>
<tr>
<td>Chetrit, et al. JCO 2008*</td>
<td>Prospective, Population Based</td>
<td>213</td>
<td>HR for Survival 0.72 (95% CI: 0.58-0.91)</td>
</tr>
</tbody>
</table>

* Update of 2002 Report
Olaparib as Maintenance Therapy – BRCA(+)
**BRCA-associated Ovarian CA – Overall Survival**

![Graph showing overall survival comparison between Olaparib and Placebo groups.](image)

<table>
<thead>
<tr>
<th></th>
<th>Olaparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths/total patients (%)</td>
<td>47/74 (64%)</td>
<td>48/62 (77%)</td>
</tr>
<tr>
<td>Median OS, months (95% CI)</td>
<td>34.9 (29.2–54.6)</td>
<td>30.2 (23.1–40.7)</td>
</tr>
<tr>
<td>HR 0.62 (95% CI 0.41–0.94); nominal p=0.025</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Does the Etiology for BRCA (HR) Dysfunction Matter?
Structure and Binding Partners of BRCA1

Orr and Savage in Biochemistry, Genetics and Molecular Biology 2015
Table 3: Multivariate Overall Survival*

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95%CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at dx (in 10yr int)</td>
<td>1·32 (1·02 - 1·71)</td>
<td>0·035</td>
</tr>
<tr>
<td>BRCA 1 vs. BRCA (-)</td>
<td>0·70 (0·36 - 1·38)</td>
<td>0·31</td>
</tr>
<tr>
<td>BRCA 2 vs. BRCA (-)</td>
<td>0·20 (0·06 - 0·65)</td>
<td>0·007</td>
</tr>
<tr>
<td>Optimal vs. Suboptimal</td>
<td>0·60 (0·36 - 1·00)</td>
<td>0·050</td>
</tr>
</tbody>
</table>

Differential Survival Between $BRCA1$- and $BRCA2$-Associated Ovarian Ca – TCGA

$BRCA1^+$ vs. $BRCA$-WT
HR=0.76 (95% CI: 0.43-1.35)

$BRCA2^+$ vs. $BRCA$-WT
HR=0.33 (95% CI: 0.16-0.69)

Yang et al. JAMA 2011; 306:1557-65
TCGA Data – Differential Outcome Between BRCA-mutated and BRCA-wildtype
Niraparib vs Placebo - Maintenance

BRCA Mutant: 21.0 months vs 5.5 months

BRCA WT; HR deficient: 12.9 months vs 3.8 months

BRCA WT; HR proficient: 9.3 months vs 3.9 months

Homologous Recombination

Is It Time to Stratify for *BRCA* Mutation Status in Therapeutic Trials in Ovarian Cancer?

Noah D. Kauff, Clinical Genetics Service, Department of Medicine, and Gynecology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY

Kauff ND. J Clin Oncol 2008; 26:9-10
How Do We Expand Access to Genetic Services?
Why Do We Need to Expand Access to Genetic Services?

- Should Have Genetic Risk Evaluation – NCCN 2016

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Estimated Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer ≤ 45</td>
<td>26,400</td>
</tr>
<tr>
<td>Triple Negative Breast Cancer dx’d between 45 and 60</td>
<td>12,500</td>
</tr>
<tr>
<td>Ovarian Cancer – any age (high-grade epithelial)</td>
<td>15,600</td>
</tr>
<tr>
<td>Colorectal Cancer &lt;70</td>
<td>52,980</td>
</tr>
<tr>
<td>Endometrial Cancer &lt;50</td>
<td>10,800</td>
</tr>
</tbody>
</table>

Total: 118,280
Genetic Risk Assessment in Oncology: Current Model

New Diagnosis of Cancer
Evaluation by a Genetic Counselor
Molecular Genetic Testing
Discussion of Results
Cascade Testing

Curation of Family Hx
Pretest Education

Days to Months
By Telephone
I have been informed that graduate medical trainees (residents and fellows) and qualified non-physician practitioners specifically including physician assistants and nurse practitioners may be involved in my surgical procedure pre-operatively, intra-operatively, and post-operatively.

I also have been informed that (1) my attending physician will be physically present during the key and critical portions of my procedure; and (2) during other portions of my procedure, he/she may be involved in another procedure which is expected to overlap in part with my procedure. I have been informed that if my attending physician is not physically present during a non的关键 and non-critical portion of the procedure, he/she will be immediately available to return to the procedure if the need arises, or will arrange for another designated, attending level physician to be immediately available to assist if needed (as is unavoidable for any reason).

I certify that I have read this consent form (Pages 1 and 2), or it was read to me, and that I fully understand the information on both front and back that I have had the opportunity to ask questions, and the answers and additional information provided have met with my satisfaction.

Signature of Patient or Legally Authorized Representative

Date
Time

Relationship to Patient (if other than patient)

I certify that the Patient or Legally Authorized Representative has answered “yes” to all of the following questions:

a) Did your attending physician or his/her designee explain the procedure to you?

b) Have all your questions about the procedure been answered?

M.D.

MM/WW (Attending physician or designee)

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*Order of consent for non-physician: 1. Guardian or appointed pursuant to Article 5, 834A of the RCGA, subject to the exercise of authority by Health Care Agent as designated in the Durable Power of Attorney for Health Care, 2. Attending Physician of the patient, 3. Minimum age of 18. This document has been executed on 10/15/2023. The patient has signed, indicated his understanding of, and agreed to the contents of the consent form. A copy of the signed consent form has been given to the patient and all parties involved. This document is not to be altered in any way. It is the responsibility of the patient to ensure that all parties involved have read and understood this consent form.
Number of Cancer Genetic Counselors in US

- NSCG Website May 2016
  - Genetic Counselors who indicated they see cancer genetics patients (most not exclusively): 672
  - Each GC in U.S. would need to see 176 new cancer patients annually just to keep up with these 5 NCCN recommendations
Genetic Risk Assessment in Oncology: Future Model

- New Diagnosis of Cancer
- Streamlined Genetic Education
- Pathology Directed Testing
- Assisted Family Hx Curation
- Review by Clinical Genetics
- Results Discussion
- Cancer Genetics
- Results Discussion Primary Oncologist
- Cascade Testing
Where Do We Go From Here?

• Can we better identify which individuals at inherited risk will benefit from incremental risk-reduction?

• Can knowledge of biology allow us to make improvements in gynecologic cancer screening and chemoprevention to allow these to become viable alternatives to risk-reduction surgery?

• Will therapeutics targeting inherited susceptibility allow us to shoot for cure rather than control of advanced ovarian cancer?

• Can we develop sustainable models for providing responsible genetic risk assessment at a population level?
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