

# BREAST CANCER AND THE ROLE OF OOPHORECTOMY

Katharina Kieser

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Division of Gynecologic Oncology

QEII HSC



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# OBJECTIVES

- Review breast cancer
- Who is at risk for having breast cancer
- Role of oophorectomy to reduce the risk of having breast cancer
- Role of oophorectomy in the treatment for breast cancer



# EPIDEMIOLOGY

- Breast cancer affects 22,200 Canadian women annually
- Age standardized incidence rate: 106 / 100,000
- Most common cancer affecting Canadian women
- 2nd most common cancer death
- Median age
  - 25% in premenopausal
  - 50% in women age 50 -69



# PROBABILITY OF DEVELOPING OR DYING FROM CANCER

SITE	Lifetime probability of dying (1 in X)	Probability of developing cancer in the next 10 years (%)					
		30-39	40-49	50-59	60-69	70-79	80-89
BREAST	26.8	0.4	1.3	2.4	3.1	3.1	2.5
UTERINE	185.2	-	0.1	0.5	0.7	0.7	0.5
OVARY	90.9	-	0.1	0.3	0.4	0.5	0.4



# RISK FACTORS FOR BREAST CANCER

RISK FACTOR	RISK
<b>Family History</b>	
<i>First-Degree Relative</i>	
Premenopausal diagnosis	OR 3.0
Bilateral disease	OR 5.0
Premenopausal diagnosis and bilateral disease	OR 9.0
Postmenopausal diagnosis	OR 1.5
<i>Second-Degree Relative</i>	
Premenopausal diagnosis	OR 1.2
Postmenopausal diagnosis	No increased risk
<b>Germline Mutations</b>	
BRCA1/BRCA2	60%–80% lifetime risk
<b>Alcohol</b>	
<sup>3</sup> 10 drinks/wk	OR 1.6
<b>Oral Contraceptives</b>	
<i>Current Users</i>	OR 1.2
>10 yr after stopping	OR 1.0
<b>Hormone Replacement Therapy<sup>4</sup></b>	OR 1.1–1.4
<b>Reproductive Factors</b>	
Menarche before 16 yr	OR 1.2
Menopause after 50 yr	OR 1.5
Nulliparity	OR 2.0
Breast-feeding	4.3% decreased risk/yr



# PATHOLOGY

- Prognostic factors
  - Tumor size
  - Axillary node status
  - Histology
  - Tumor grade
  - Lymphovascular invasion
- Predictive factors
  - Estrogen receptor
  - Progesterone receptor
  - HER2



# 'STAGING'

- Early breast cancer
  - Local or locoregional disease
- Late breast cancer
  - Distant disease

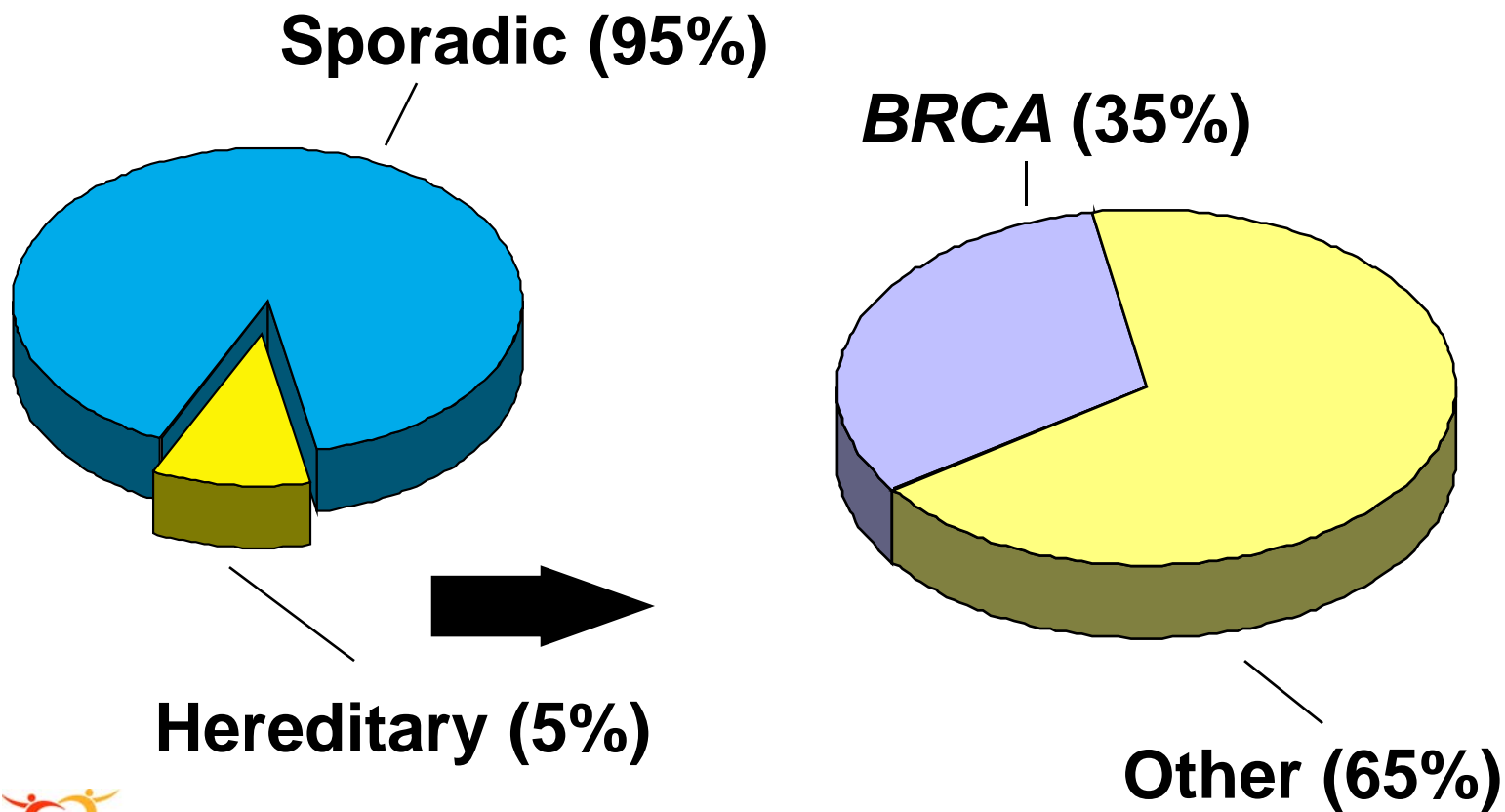


# BREAST CANCER SCREENING

- Asymptomatic women age 50-69
  - Biennial mammogram
  - Clinical breast exam
- Participation target = 70%
  - Increased participation
  - Atlantic Provinces have 22 - 53% participation



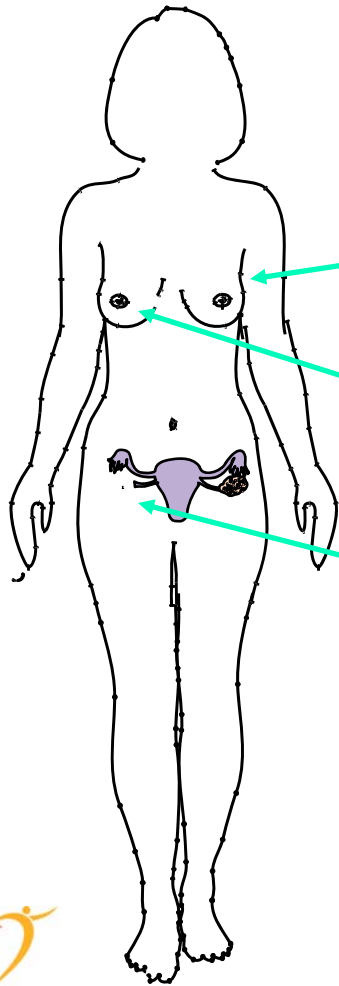
# ETIOLOGY OF BREAST CANCER



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# BRCA ASSOCIATED CANCERS: LIFETIME RISK



Breast cancer 50% - 85%

Second primary breast cancer 40% - 60%

Ovarian cancer 15%- 45%



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# BRCA1 & BRCA2 GENES

- Germline mutation
- Autosomal dominant inheritance
- Several hundred mutations
- Several generations in the affected families are at risk
- Inherited BRCA gene abnormalities have a high penetrance
- Penetrance vary according to the specific gene and locus that is mutated, and other genetic and environmental factors



# GUIDELINES FOR GENETIC CONSULTATION

- Dx with breast cancer < 35 yrs
- Dx with both breast cancer & ovarian cancer at any age
- Dx with B/L breast cancer with one diagnosis made <age 50
- Dx with ovarian cancer <age 50
- Ashkenazi Jewish or Icelandic ancestry
- Dx with breast cancer <50 and a relative on the same side of the family with ovarian cancer
- Male Dx with breast cancer
- Known familial mutation
- $\geq 2$  1st and /or 2nd degree relatives Dx with breast or ovarian cancer



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<http://www.iwk.nshealth.ca/genetics/index.cfm>

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# TESTING FOR BRCA MUTATIONS

- Blood test
- Usually need affected person to initiate testing
  - If mutation is found then other family members can be tested
- + family history set for 10% detection rate



# PATIENTS AT RISK FOR BREAST CANCER

- 1) Enhanced surveillance
- 2) Behavioral modification
- 3) Chemoprevention
- 4) Prophylactic mastectomy &/or oophorectomy



# PROPHYLACTIC SURGERY

- Reduces risk of breast cancer by 50%
- Reduces risk of ovarian cancer by 100% but....
  - 3-17% incidental 'ovarian' cancer
    - Of those - 40% primary fallopian tube
  - <2% subsequent 1° peritoneal



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Brose MS et al :J Natl Cancer Inst 2002  
Leeper K et al :Gynecol Oncol 2002  
Paley PJ et al :Gynecol Oncol 2001  
Colgan TJ et al :Gynecol Oncol 2002

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# PROPHYLACTIC SURGERY

- H + BSO
- Expert pathologist



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# CASE #1

- 30yo F
- + family history of breast cancer
  - Mother & maternal uncle
- Genetic consult
- + BRCA2
- Discussion re mastectomy & H+BSO
- H+BSO first



# PREMENOPAUSAL BREAST CANCER TREATMENT

- Surgery
- Adjuvant radiotherapy
- Adjuvant chemotherapy
- SERM
- Aromatase Inhibitors
- Ovarian ablation



# MEDICAL TREATMENT FOR PREMENOPAUSAL BREAST CANCER

- Adjuvant chemotherapy
  - CMF, CAF, CEF, TAC
- SERM
  - Tamoxifen
- Aromatase Inhibitors
  - Arimidex / Letrozole
  - Nonsteroidal aromatase inhibitor
  - Stops peripheral conversion of androstenedione to estrone
  - 80% reduction in estradiol
- Ovarian ablation

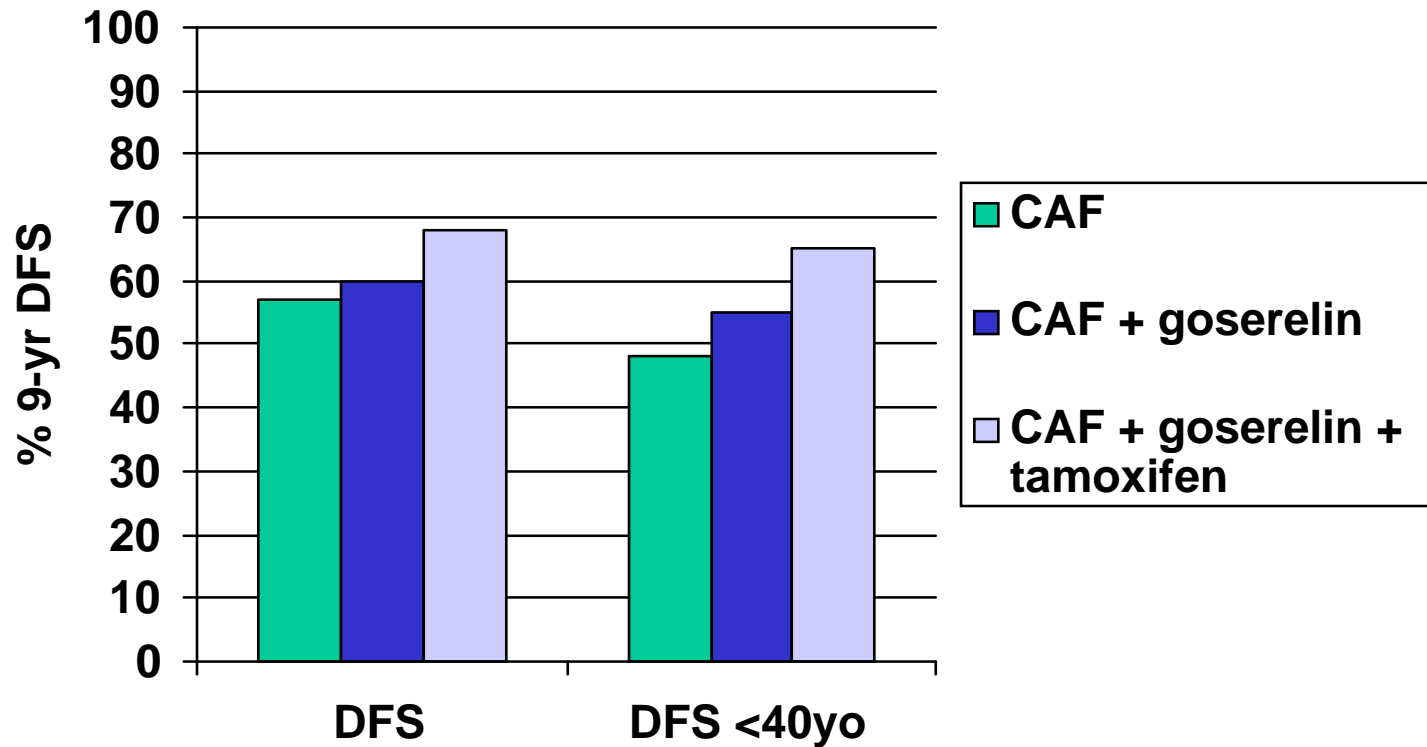


# PREMENOPAUSAL BREAST CANCER TREATMENT

- Adjuvant chemotherapy
  - 27% relative risk reduction for death
- Tamoxifen (ER+)
  - 32% relative risk reduction for death
- Arimidex (ER+)
  - requires ovarian ablation
- Ovarian ablation
  - equal to chemotherapy for ER+
  - <10% response in ER-
  - 2yr duration of treatment



# TREATMENT OF EARLY BREAST CANCER



# AMENORRHEA POST CHEMOTHERAPY

Chemotherapy	% Pt with amenorrhea	
	Age 30-39	Age ≥40
CMF	30-40	80-95
CAF	10-25	80-90
CEF	48	87



# OVARIAN ABLATION

- Medical
  - Chemotherapy
  - LHRH analogues
- Surgical
- Radiation
  - Long term toxicities
  - >13% menses



# SURGICAL OVARIAN ABLATION

## PRO

- Permanent
- ‘Cheap’

## CON

- Permanent
- Surgical risks
- May ‘find’ metastatic disease
- Not reversible



# SURGICAL ISSUES

- Metastatic disease
- Laparotomy vs laparoscopy
- Oophorectomy vs Salpingoophorectomy +/- hysterectomy
- General surgical risks



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Lancet 339:1–15, 1992.

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# COST OF OVARIAN ABLATION

Drug	Dose	Cost/Dose	3mo Cost	2yr Cost
Goserelin LA (Zoladex)	10.8mg	1639.56	1639.56 327.91	13,116.48 <b>2623.30</b>
Leuprolide (Lupron)	11.25mg	1501.94	1501.94 300.39	12,015.52 2403.10
Anastrozole (Arimidex)	1mg	6.99	629.10 125.82	5032.80 <b>1006.56</b>
Tamoxifen	20mg	0.75	67.50 13.50	540.00 <b>108.00</b>



BSO OR time + hospital stay = 2h@\$1000/h + 1d@\$1500/d  
= **\$3500.00**

## CASE #2

- 41yo G2P1A1
- Diagnosed with metastatic breast cancer 5 months ago
- Had CMF followed by tamoxifen
- Progression of disease
- Switch to anastrozole
- Consult for BSO
- Goserelin



## CASE #3

- 36yo G2P2
- Diagnosed with early ER+ breast cancer
- Offered Goserelin & consult for BSO
- BSO



# CONCLUSIONS

- H+BSO for women with proven BRCA mutations
  - Expert pathologist
- BSO for women with early hormone sensitive breast cancer
  - Risk of surgery vs patient out of pocket cost



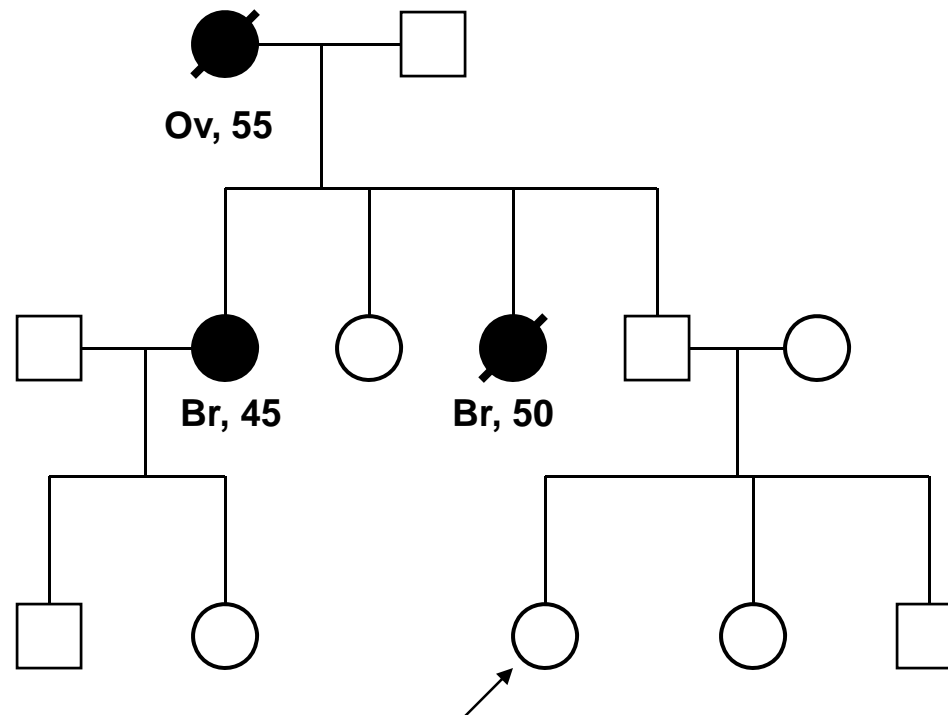
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TIFF (Uncompressed) decompressor  
are needed to see this picture.

# Testing for BRCA mutations

- Tests:
  - Molecular sequencing
    - You can sequence the whole gene but this is expensive, time consuming & you don't know whether the abnormality is functionally significant
  - Protein truncation
    - The protein is run on a gel with the normal to see whether it is the same size & shape
  - PCR
    - Used in different ways but you can amplify known portions of the sequence & run it on gel to see whether it is the same as normal (DNR/RNA)
  - FISH
    - use a labeled sequence to anneal to the specimen to see whether it binds to the site of abnormality
  - Heteroduplex analysis
  - SSCP, CSGE, ASP assay
  
- Hospital based: 14-16 months
- Myriad Genetics: 1-2 months



# Pedigree



Does this family history warrant genetic testing?  
How should this be done? Who? What test? What  
counseling?