

# Biomedical Engineering for Global Health

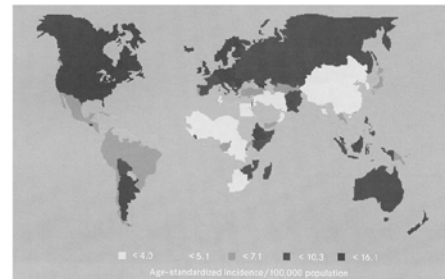
## Lecture Fifteen

# Bioengineering and Ovarian Cancer

## Statistics on Ovarian Cancer

- United States:
  - Incidence: 22,430
  - Mortality: 15,280
- Worldwide:
  - Incidence: 190,000
  - Mortality: 114,000

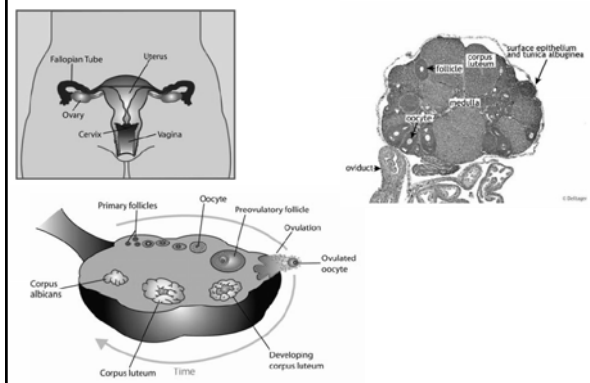
## Global Burden of Ovarian Cancer



## Risk factors

- Age
  - Most ovarian cancers develop after menopause
- Personal or family history of breast, ovarian, endometrial, prostate or colon cancer.
- Reproductive history
  - Increases with the more lifetime cycles of ovulation that a woman has undergone. Thus, women who have undergone hormonal treatment for infertility, never used birth control pills, and who never became pregnant are at higher risk for ovarian cancer

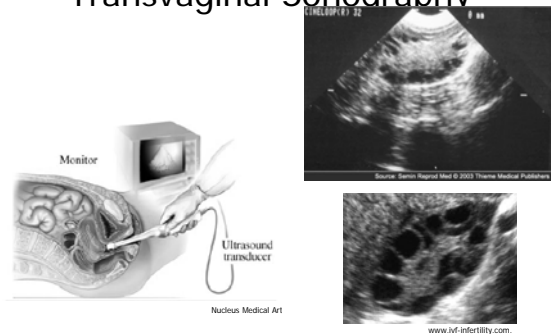
## Pathophysiology



## Screening of Ovarian Cancer

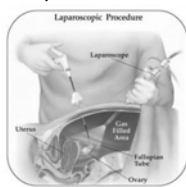
- Pelvic and rectal exam
- CA125 test
- Transvaginal sonography

## Transvaginal Sonography

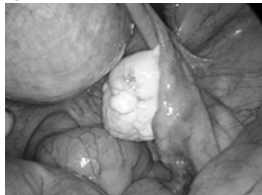


## Diagnostic Laparoscopy

Complication Rate = 0.5



Allon Health Center - Center for Women's Medicine



John P.A. George, M.D., Washington Hospital Center

## Detection and Treatment

- Screening
  - Pelvic exam
  - CA125 test
  - Transvaginal ultrasound
- Diagnosis
  - Diagnostic laparoscopy
- Treatment:
  - Surgery, radiation therapy, chemotherapy
- 5 year survival
  - Localized disease: 93% (20% diagnosed at this stage)

## Screening Scenarios

- Scenario #1:
  - Screen 1,000,000 women with CA125
    - $p = .0001$  (100 cancers)
    - $Se=35\%$ ,  $Sp=98.5\%$
    - Cost = \$30
  - Follow with laparoscopy
    - Complication rate = 1%
    - Cost=\$2,000
  - TP=35 FP=14,999 Complications=150
  - PPV =0.23% NPV = 99.99%
  - Cost per cancer found = \$1,716,200

## Screening Scenarios

- Scenario #2:
  - Screen 1,000,000 women with transvaginal US
    - $P = .0001$  (100 cancers)
    - $Se=100\%$ ,  $Sp=96\%$
    - Cost = \$150
  - Follow with laparoscopy
    - Complication rate = 1%
    - Cost=\$2,000
  - TP=100 FP=39,996 Complications=401
  - PPV =0.25% NPV = 100%
  - Cost per cancer found = \$300,672

## Screening Scenarios

- Scenario #3:
  - Screen 1,000,000 women >age 50 with TVUS
    - P = .0005 (500 cancers)
    - Se=100%, Sp=96%
    - Cost = \$150
  - Follow with laparoscopy
    - Complication rate = 1%
    - Cost=\$2,000
- TP=500 FP=39,980 Complications=405
- PPV = 1.24% NPV = 100%
- Cost per cancer found = \$60,670

## Screening Scenarios

- Scenario #3 cont.:
  - Screen 1,000,000 women > age 50 with TVUS
    - P = .0005 (500 cancers)
    - Se=100%, Sp=??%
    - Cost = \$150
  - How high does Sp need to be for PPV to reach 25%?
    - Sp = 99.985%

## Does Ultrasound Screening Work?

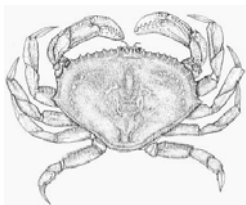
- Two studies of over 10,000 low-risk women:
  - The positive predictive value was only 2.6%
  - Ultrasound screening of 100,000 women over age 45 would:
    - Detect 40 cases of ovarian cancer,
    - Result in 5,398 false positives
    - Result in over 160 complications from diagnostic laparoscopy
  - Jacobs I. Screening for early ovarian cancer. Lancet; 2:171-172, 1988.

## Ongoing Clinical Trials

- United Kingdom
  - 200,000 postmenopausal women
    - CA 125 level plus transvaginal ultrasound examination
    - Transvaginal ultrasound alone
    - No screening
- United States:
  - 37,000 women (aged 55–74)
    - Annual CA 125 level and transvaginal ultrasound examination
    - No screening
- Europe:
  - 120,000 postmenopausal women
    - No screening,
    - Transvaginal ultrasound at intervals of 18 months
    - Transvaginal ultrasound at intervals of 3 years

[http://www.mja.com.au/public/issues/178\\_12\\_160603/and10666\\_fm.pdf](http://www.mja.com.au/public/issues/178_12_160603/and10666_fm.pdf)

## Ovarian Cancer



Risk factors  
Detection  
Treatment  
Challenges  
New technologies

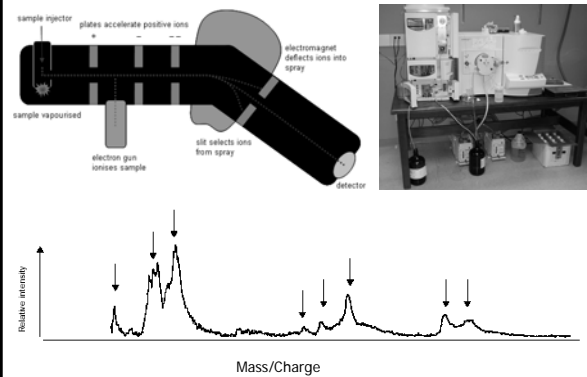
## Challenge

Better screening methods to detect early stages of ovarian cancer

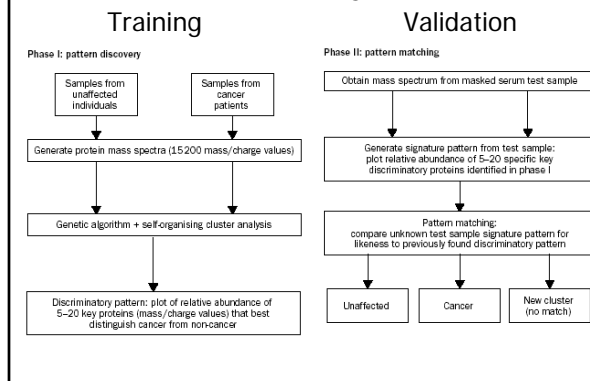
## Cancer Screening Exams

- Cellular/Morphological Markers
  - Pap smear
- Serum protein markers
  - PSA
  - CA125
- DNA markers
  - HPV DNA

## Proteomics: Mass Spectrometer

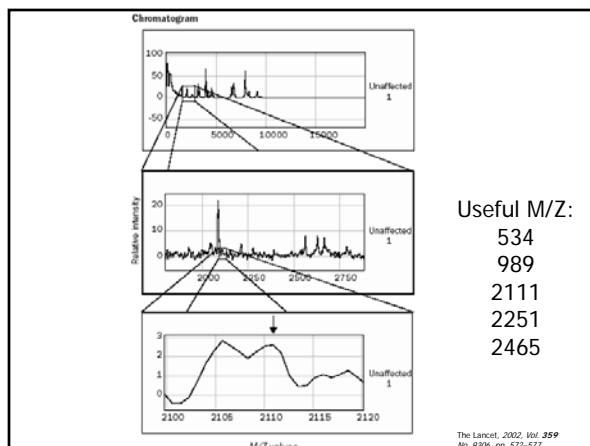


## Data Analysis

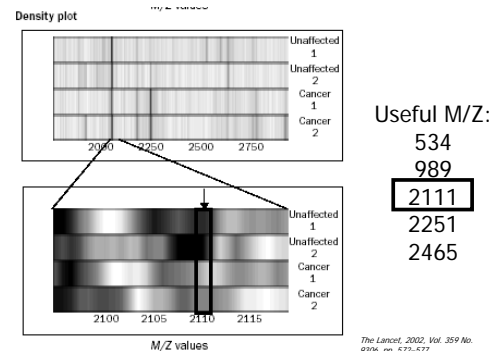


## OvaCheck

- Quest Diagnostics and LabCorp:
  - Will analyze blood samples sent by doctors, rather than sell test kits to doctors and hospitals
  - Tests performed at a central location do not require F.D.A. approval
  - Cost: \$100-\$200



## Comparative Analysis



Lance Liotta, lead author:

"The most important next goal is validating the promise of these results in large, multi-institutional trials."

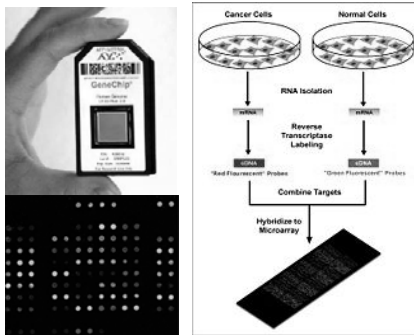


*Bioinformatics (Oxford, England), 2004 Mar 22; 20(5): 777-85.*

## Response

- Dr. Eleftherios P. Diamandis, head of clinical biochem at Mount Sinai Hospital in Toronto.
  - "If you don't know what you're measuring, it's a dangerous black-box technology... They are rushing into something and it could be a disaster."
- Dr. Nicole Urban, head of gynecologic cancer research at the Fred Hutchinson Cancer Research Center in Seattle.
  - "Certainly there's no published work that would make me tell a woman she should get this test."
- Dr. Beth Karlan, director of gynecologic oncology at Cedars-Sinai Medical Center
  - "Before you mass-market to the uninformed, fearful population, it should be peer-reviewed,"
  - When asked whether she would recommend her patients not get tested, she said: "It doesn't matter what I recommend. They are going to do it anyway."

## DNA Microarray



## New screening technologies

- New screening technologies
  - Proteomics
  - DNA microarrays
  - Optical technologies