Biomedical Engineering for Global Health

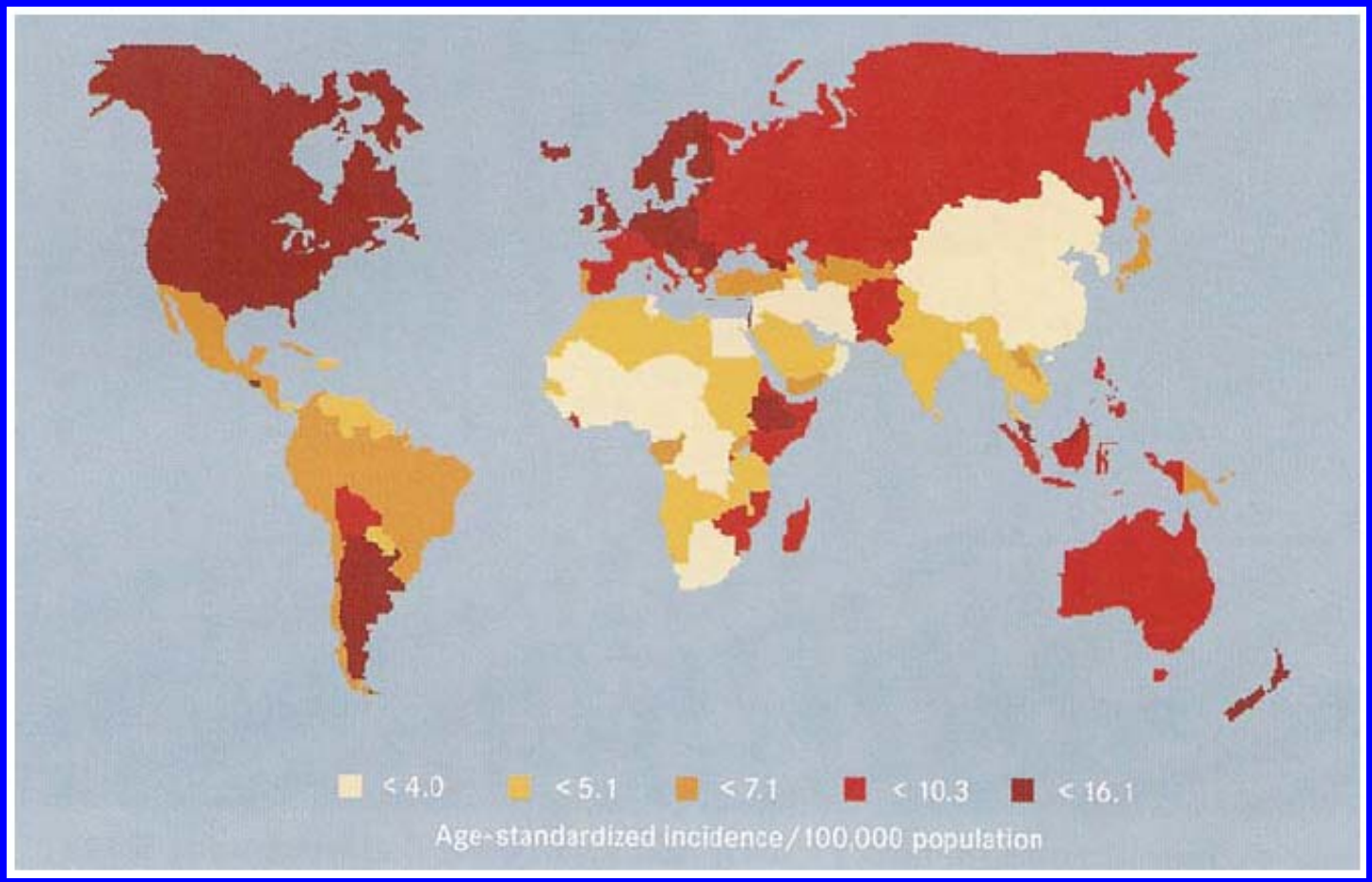
Lecture Fifteen

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

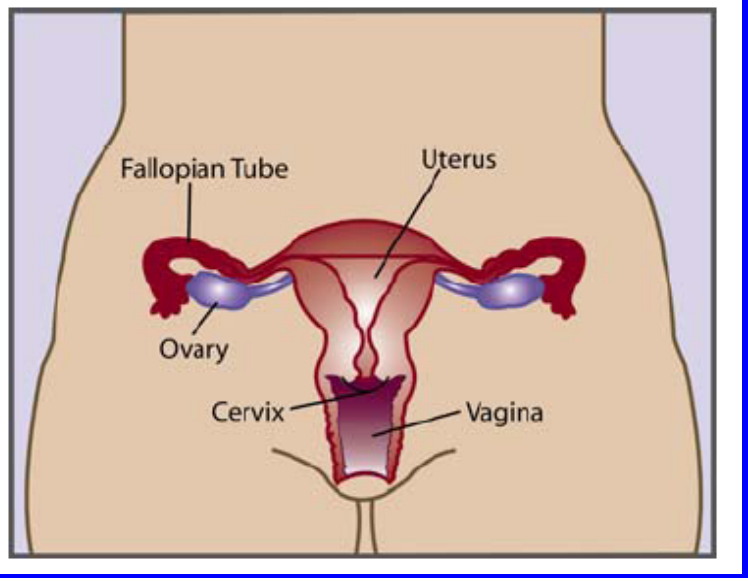


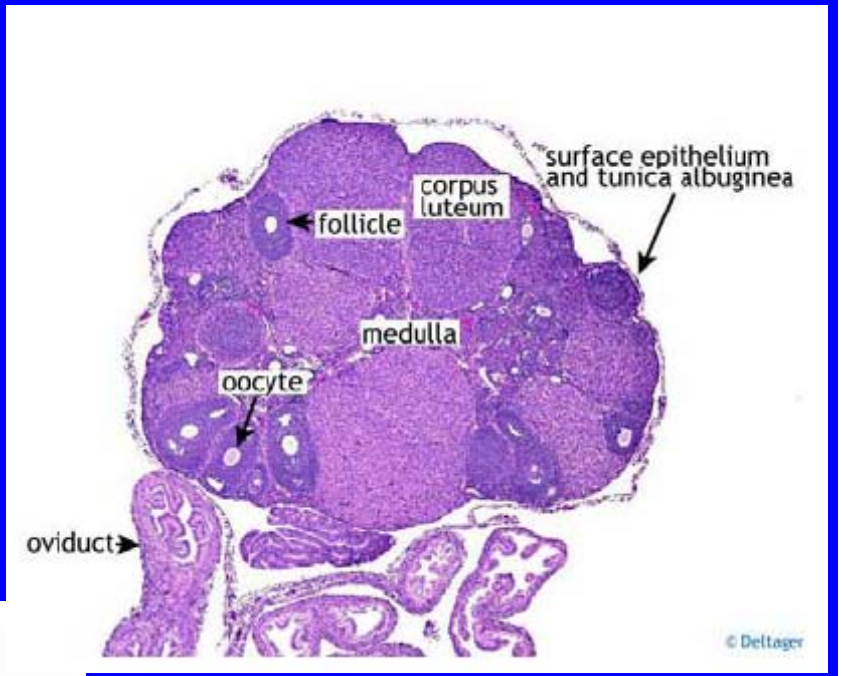
Risk factors

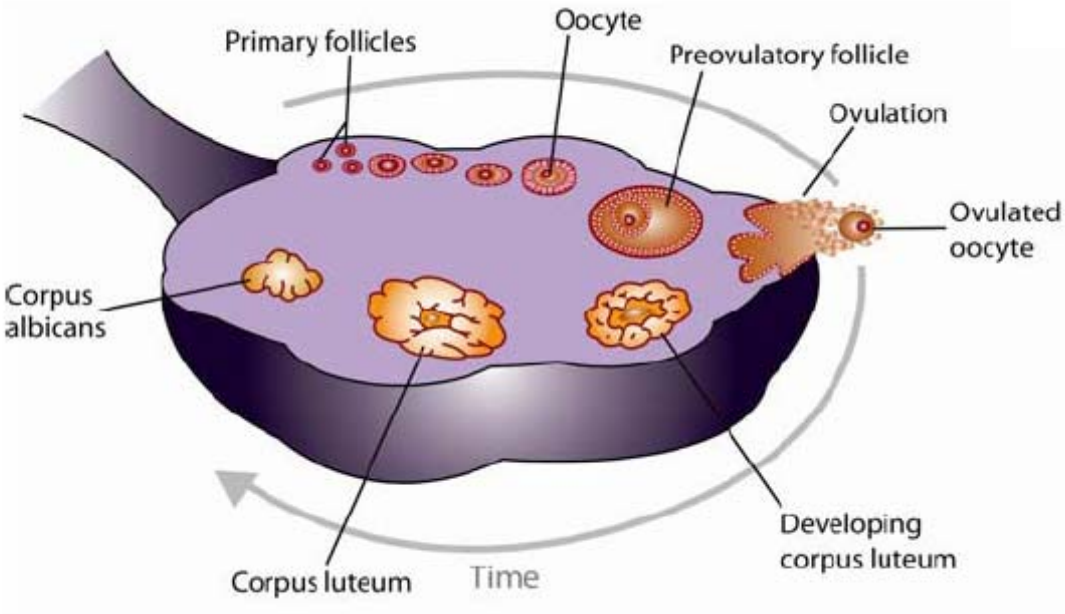
- Age
  - Most ovarian cancers develop after menopause
- Personal or family history of breast, ovarian, endometrial, prostate or colon cancer.
- Reproductive history

  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



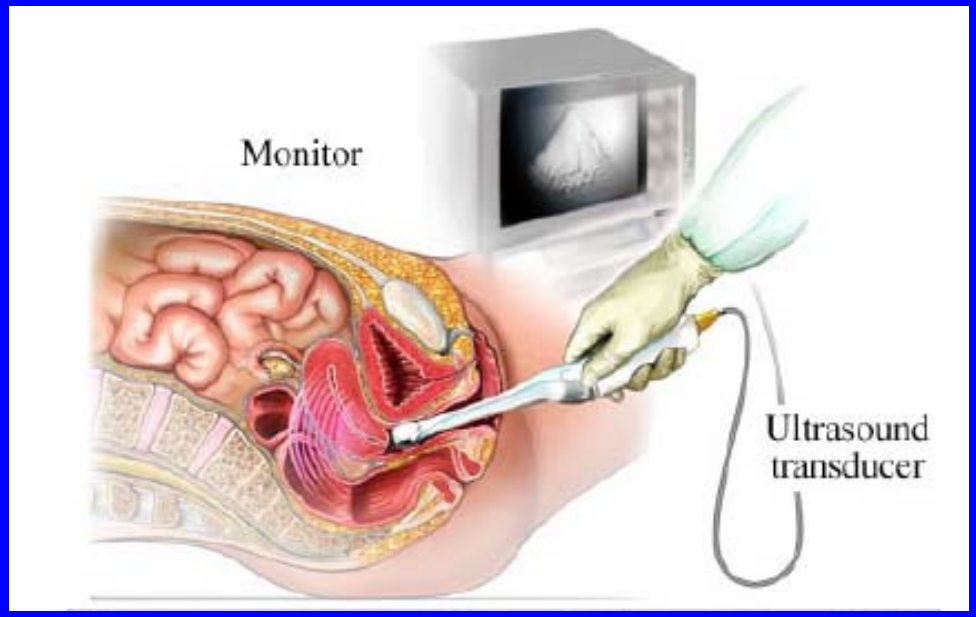




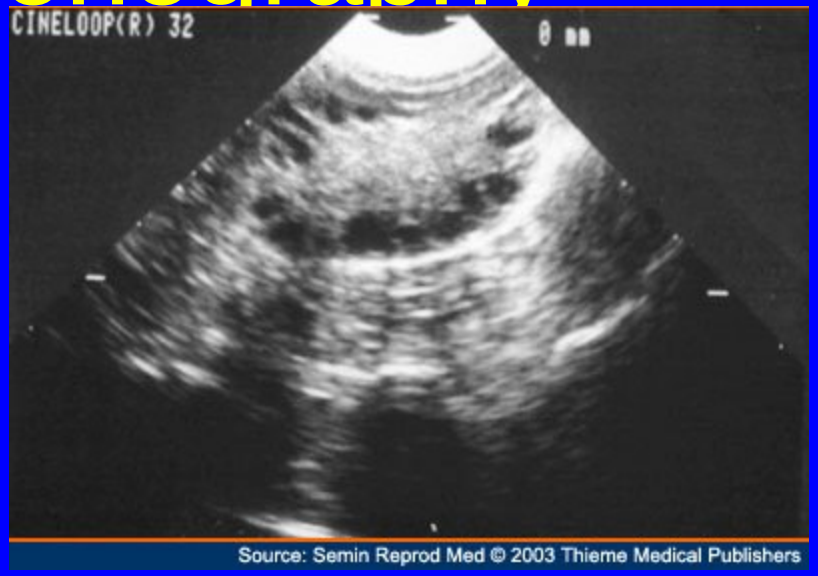
Screening of Ovarian Cancer

- Pelvic and rectal exam
- CA125 test
- Transvaginal sonography

Transvaginal Sonography



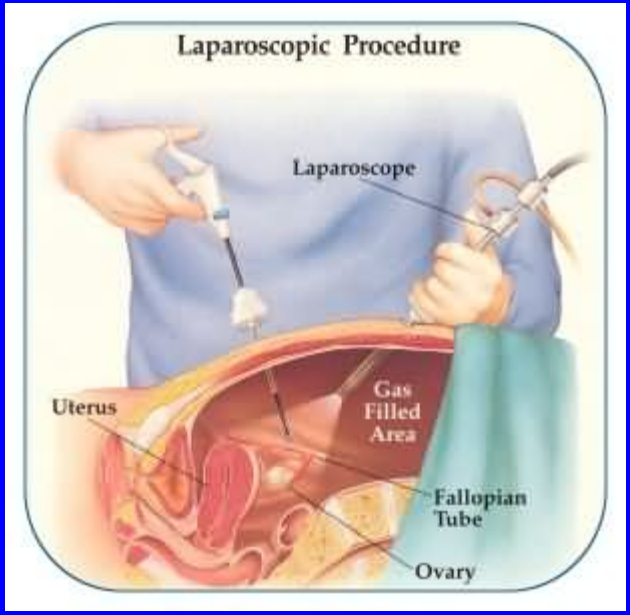
Nucleus Medical Art



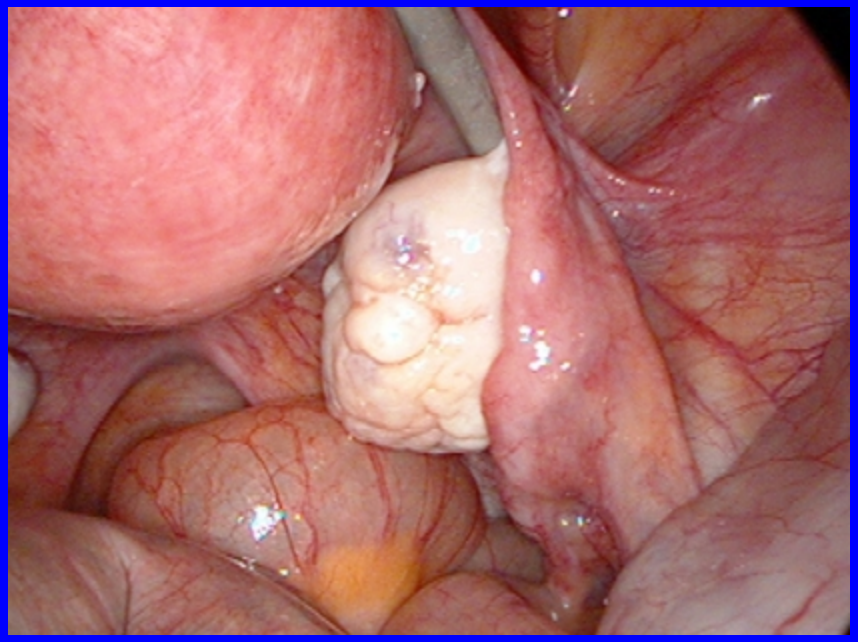
www.ivf-infertility.com.

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

Ovarian Cancer

Risk factors

Detection

Treatment

Challenges

New technologies

Challenge

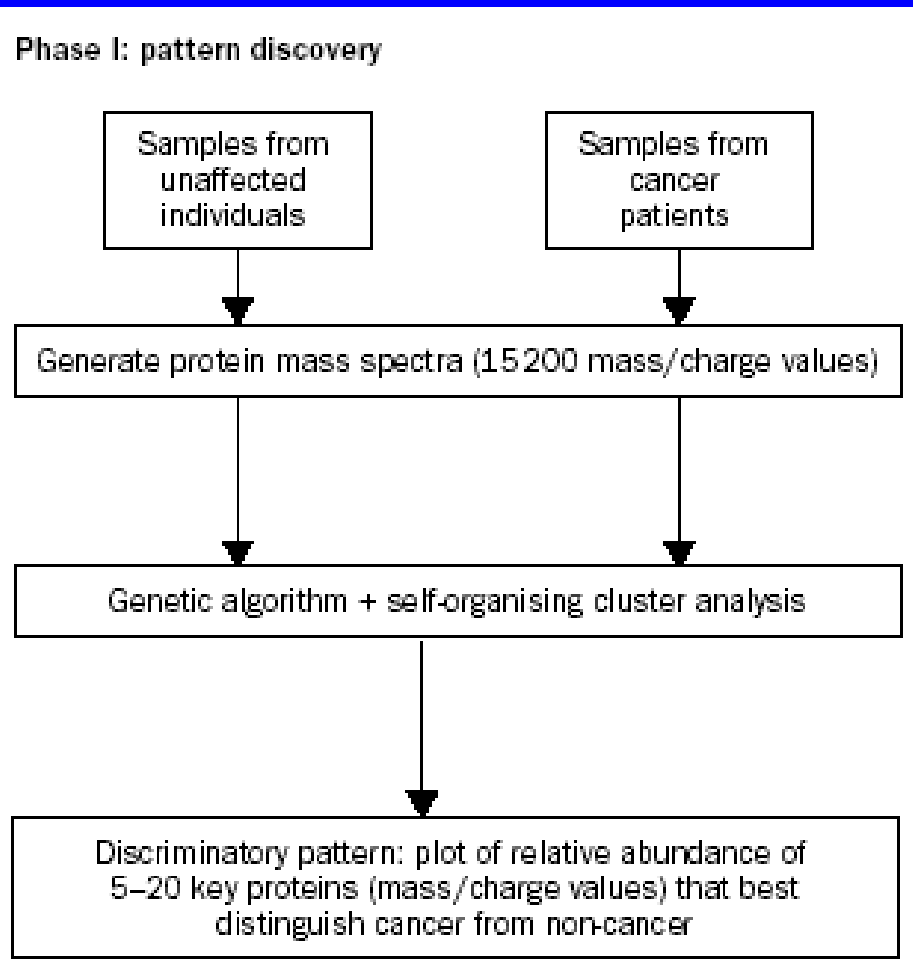
Better screening methods to detect early stages of ovarian cancer

Cancer Screening Exams

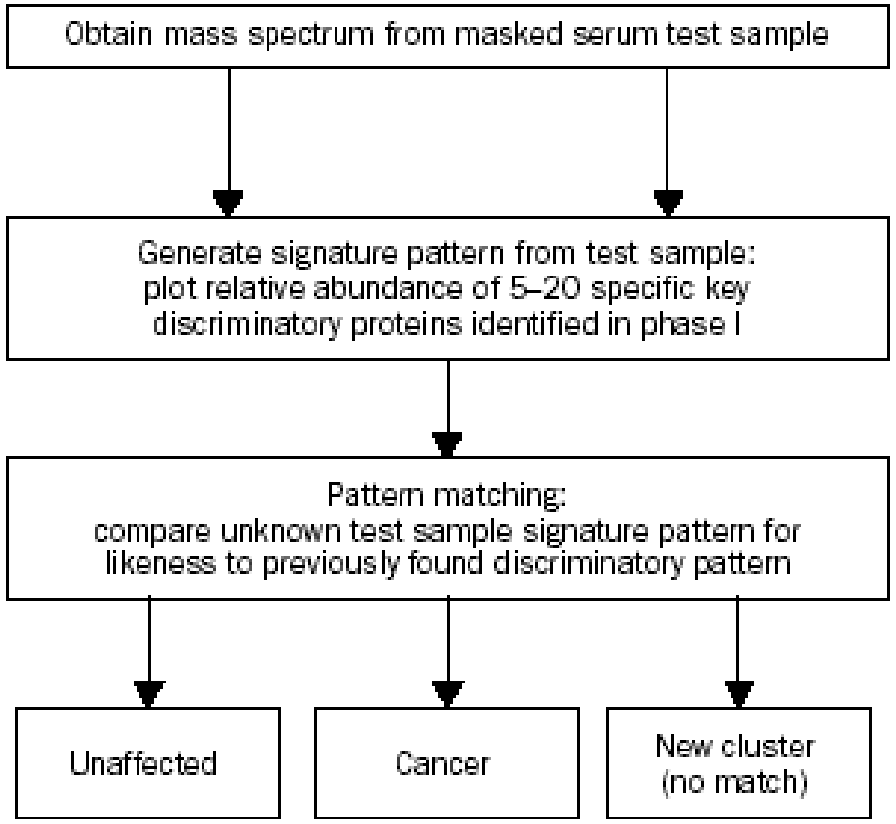
- Cellular/Morphological Markers
  - Pap smear
- Serum protein markers
  - PSA
  - CA125
- DNA markers
  - HPV DNA

Data Analysis

Training

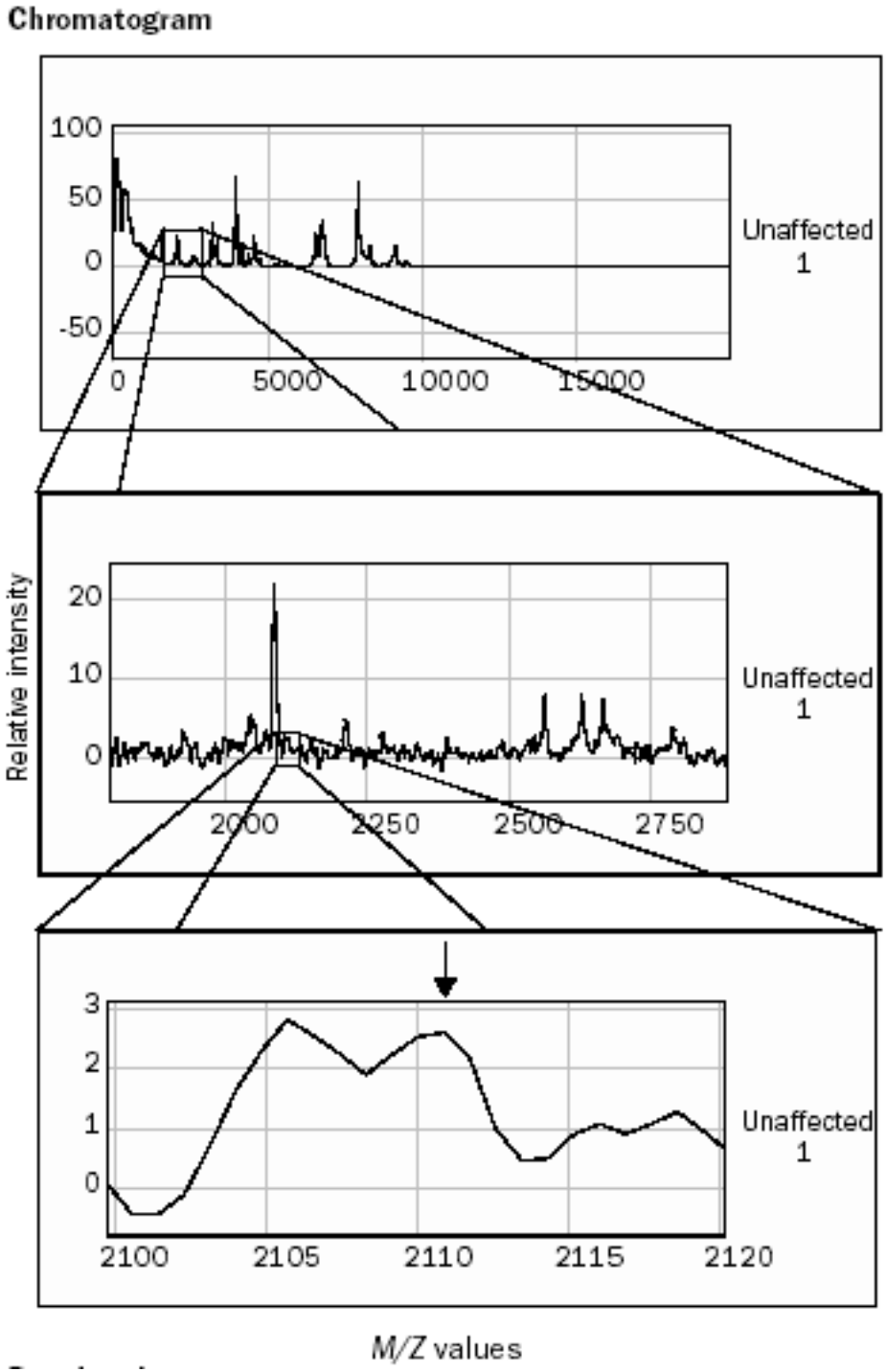


Validation



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



Useful M/Z:

534

989

2111

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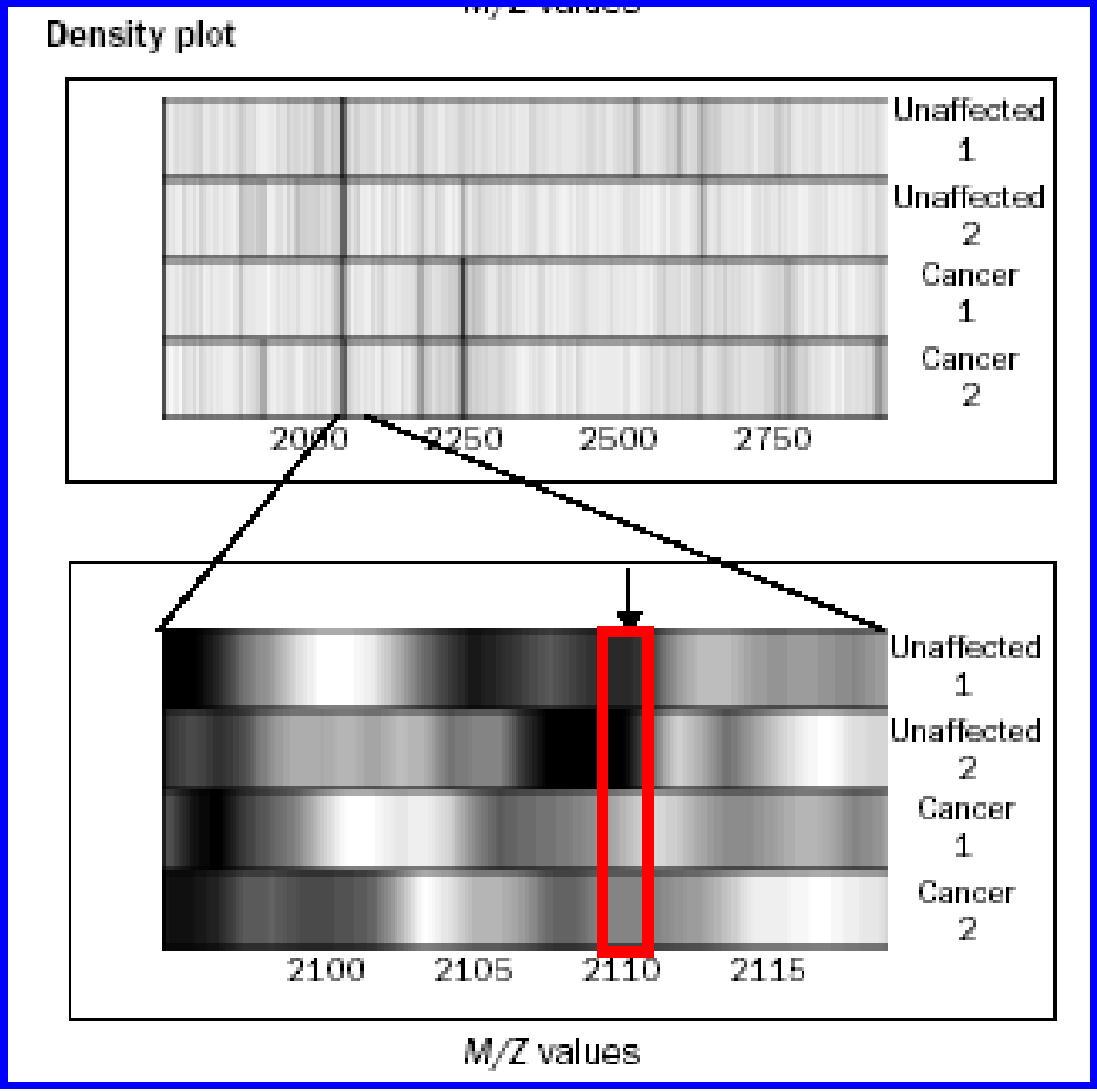
2465

The Lancet, *2002, Vol.* ***359*** *No. 9306, pp. 572–577*

Comparative Analysis



Useful M/Z:

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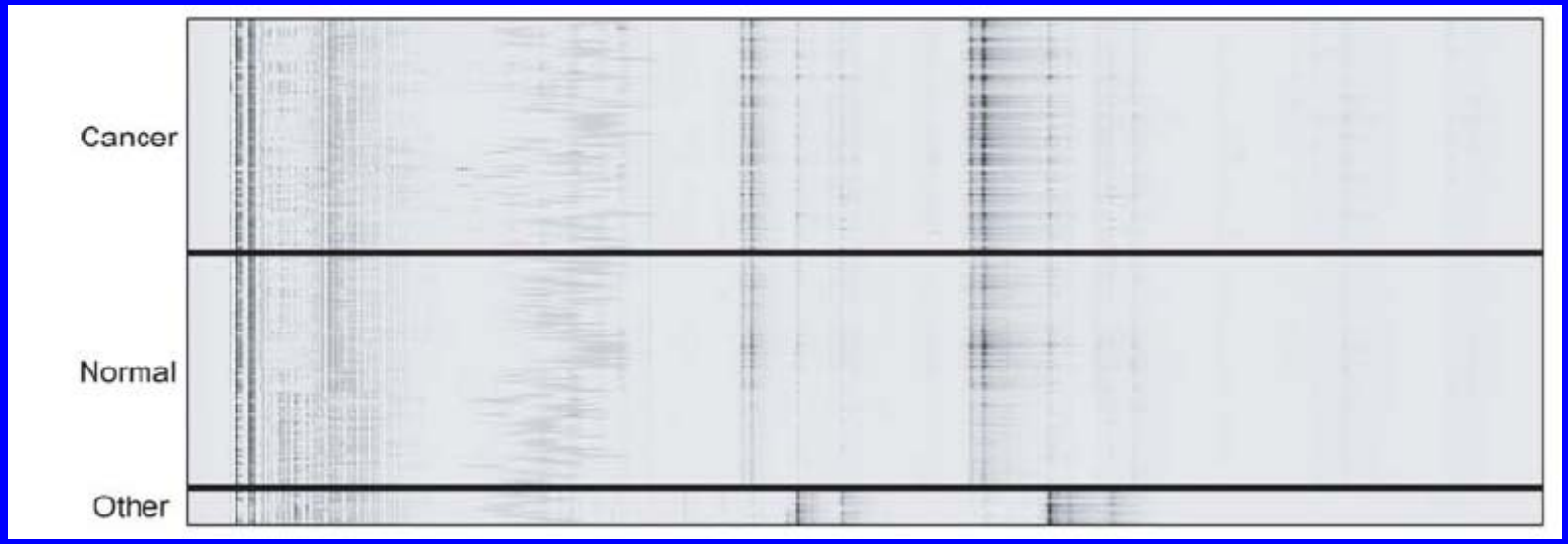
The Lancet, 2002, Vol. 359 No. 9306, pp. 572–577

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."

New screening technologies

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