Superior Performance of Bayesian Networks in Predicting the Risk of Invasive Vs. In-Situ Breast Cancer in Older Women

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Introduction

Breast Anatomy

- Breast profile:
  - A ducts
  - B lobules
  - C dilated section of duct to hold milk
  - D nipple
  - E fat
  - F pectoralis major muscle
  - G chest wall/rib cage

Enlargement:
- A normal duct cells
- B basement membrane
- C lumen (center of duct)

Breast Cancer Progression

- Normal duct
- Atypical ductal hyperplasia
- Ductal carcinoma in situ (DCIS)
- Invasive ductal carcinoma

Mammography

- Susicious
- Aggressive Use
  - To prove the benign etiology of micro-califications
  - Result in PVP of 20%
  - Annually 700,000 biopsies
  - Estimated overspending in biopsies: $250M

Biopsy

- Sensitivity:
  - by Age
    - <40 → 54%
    - 40-49 → 77%
    - 50-65 → 87%
    - >65 → 81%

- by Breast Density
  - Younger women =68%
  - Older women =85%

Motivation

Why Invasive vs. DCIS?

- Each requires different types of treatment
- DCIS is a non-invasive malignant condition with a favorable diagnosis
- DCIS will not cause mortality or morbidity for many years, if ever
- Risk factors partially differ

If Prob(Invasive|Old) is small:

- Tolerate low PPV
- Manage with short-term follow-up

Why Age Stratification?

- Life expectancy difference in older and younger women
- Over diagnosis which does not correspond to reduced mortality
- Breast cancer less aggressive in older women
- Invasive procedures more risky in older women
- Resources could be better spent on more serious co-morbidities

Data & Methods

Structure of Data & Processing

- Cross-Validation
  - Multi-Networked Mammography Database System
  - Validation of the Network with leave-one-out in the Stratified Data

Data in Detail

- Data Summary
  - ROC Older vs. Younger
    - Age range: 27 to 97 with
    - Mean 59.7 and standard deviation 13.4
    - 1475 Diagnostic Mammograms → 1270 Patients
    - 1259 patients with single mammogram
    - 81 patients with two mammograms
    - 5 patients with three mammograms
    - 1063 cases invasive vs. 412 DCIS
    - Age range: 27 to 97 with
    - Mean 59.7 and standard deviation 13.4

Results & Conclusion

- Develop a risk prediction model for prospective differentiation of DCIS versus invasive breast cancer
- Measure model performance

- Evaluation of the Model
  - Validation of the Model
    - ROC & PR Curves, Statistical Testing
    - Sequential Decision Making in the Context Of Breast Cancer Screening
    - Clinical Implications
  - Age 50-64
  - Age 65+

- Improvement in False Negative Rates
  - Improvement in AUC = 0.043
  - Improvement in AUC = 0.063
  - With p-value = 0.112
  - With p-value = 0.041

Conclusion

- Mammography is not perfect and performs better in older women.
- There is a need for discriminating between invasive and DCIS to better manage the breast disease in the context of age and other comorbidities
- An age-based risk prediction model for assessing performance difference in discriminating invasive vs. DCIS is necessary
- Such a model would enable physicians to make more informed decisions
- Demonstration of performance difference and varying risk factors in different age cohorts justifies personalized treatment/management of invasive disease when biopsy decision is made.