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# Data-driven Decision Support to Improve Breast Cancer Diagnosis and Outcomes

Elizabeth Burnside, MD, MPH, MS

Departments:
Radiology
Population Health
Biostatistics and Medical Informatics
Industrial and Systems Engineering

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# Informatics & Breast Imaging

- General Overview
  - History/Motivation
- Methodological Considerations
  - Algorithms & metrics to measure performance
- Projects
  - Improving mammographic predictions
  - Improving image-guided core biopsy

# Motivation

- Information overload
  - Medical articles in pubmed-online
  - EHR information
  - Genetic risk factors
- Human decision making involves heuristics that may not scale up alone

# History

- Tools first conceived in:
  - Leeds Abdominal Pain System went operational in 1971

System = 91.8%
Physician = 79.6 %

- Barriers
  - Not integrated in clinical workflow
  - Errors

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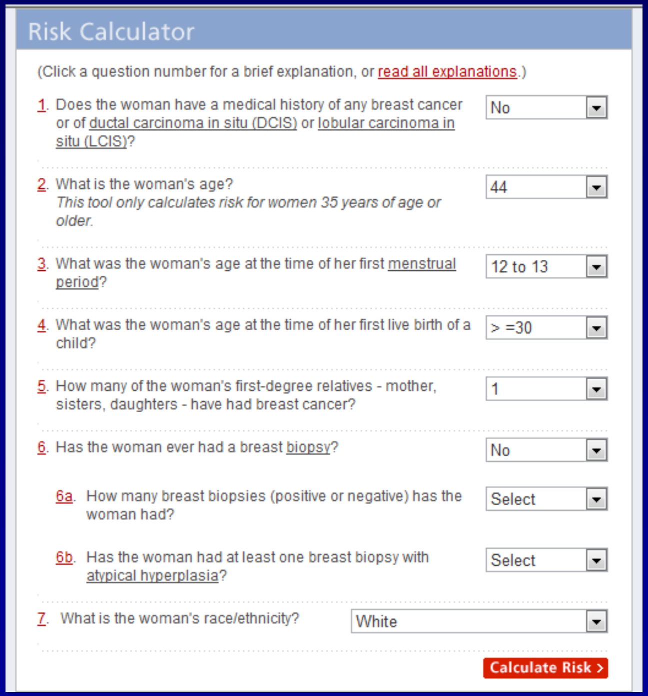
# The Gail Model


Risk Calculator

(Click a question number for a brief explanation, or read all explanations.)

1. Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS)? — No

2. What is the woman's age? *This tool only calculates risk for women 35 years of age or older.* — 44

3. What was the woman's age at the time of her first menstrual period? — 12 to 13

4. What was the woman's age at the time of her first live birth of a child? — > =30

5. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer? — 1

6. Has the woman ever had a breast biopsy? — No

6a. How many breast biopsies (positive or negative) has the woman had? — Select

6b. Has the woman had at least one breast biopsy with atypical hyperplasia? — Select

7. What is the woman's race/ethnicity? — White

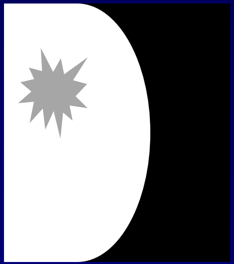
Calculate Risk >

- Uses data (BCDDP)
- Predicts Breast CA
  - Five year/lifetime risk

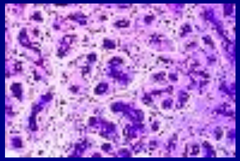
Low signal predictors

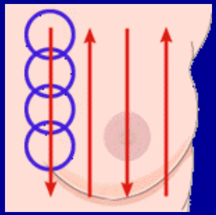
http://www.cancer.gov/bcrisktool/Default.aspx

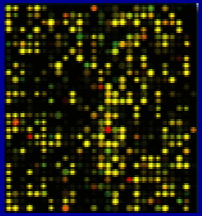
# Predictive Information



AGE





Breast Cancer

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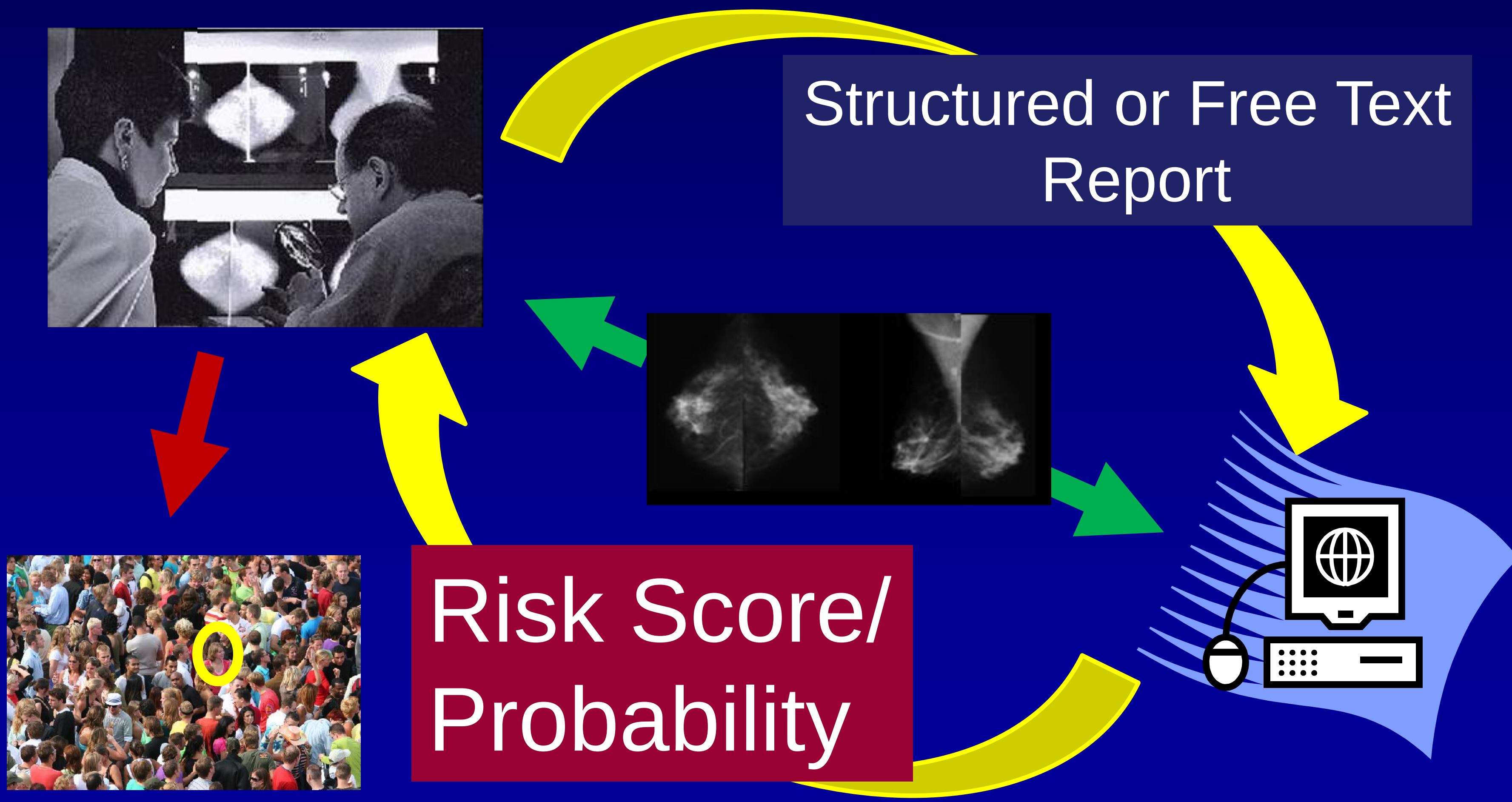
# Human Computer Interaction
# COMMUNICATION



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# The Mammography Risk Prediction Project

Elizabeth Burnside, MD, MPH, MS
C. David Page, PhD
Jude Shavlik, PhD
Charles Kahn, MD (MCW)

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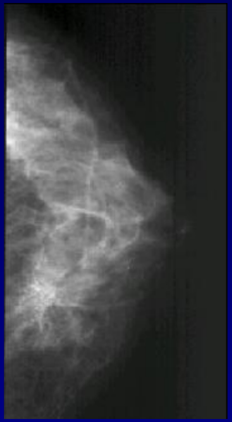
# Background-Opportunity



- 200,000 breast cancer diagnosed in US
- 20 million mammograms per year
  - False positives
    - Millions of diagnostic mammograms/US
    - Hundreds of thousands biopsies
  - False negative
    - 10-30% of breast cancers not detected on mammography
- Variability of practice impacts many women
- **Evidence-based decision support has the potential to drive substantial improvement**

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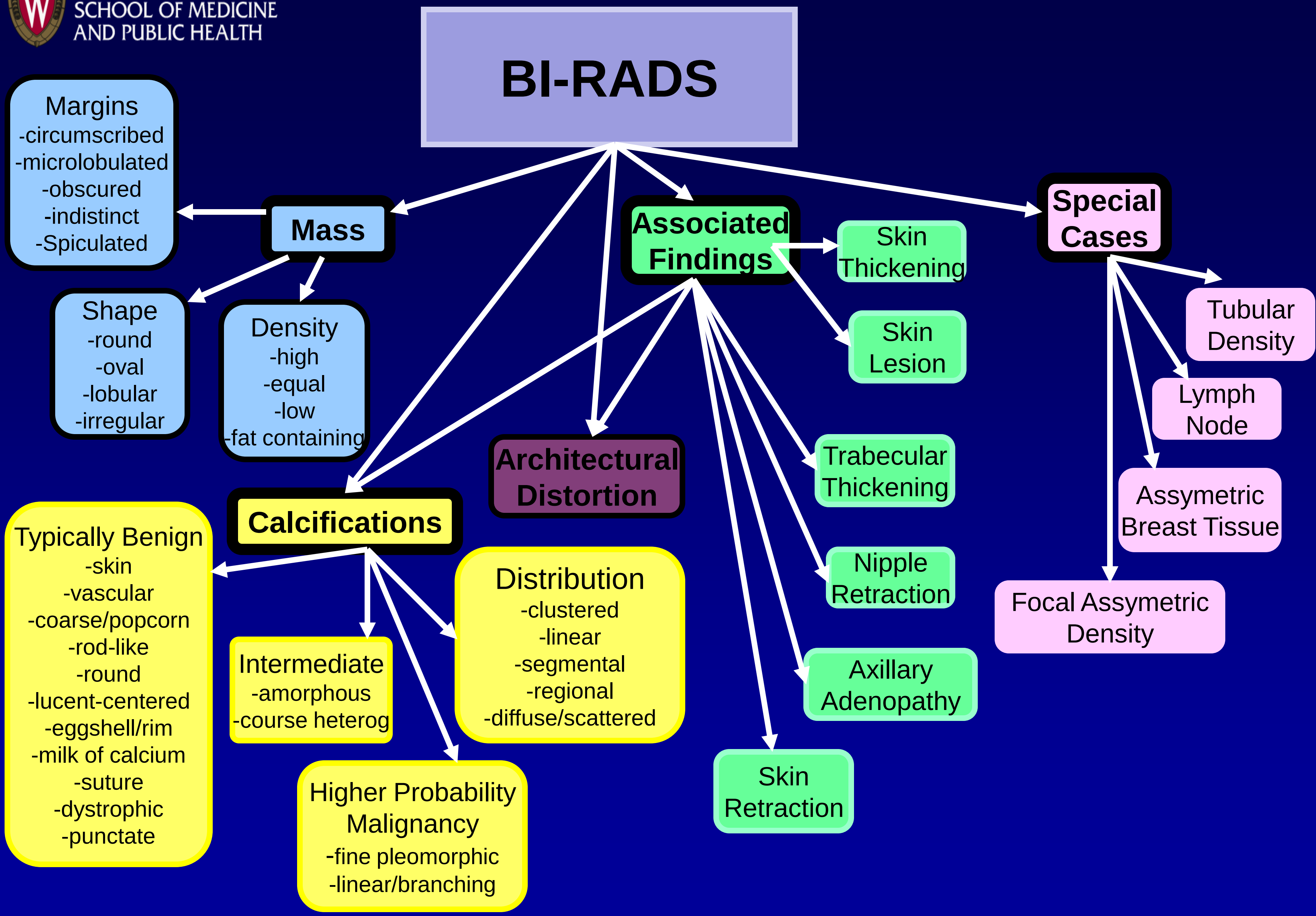

# Breast Cancer Probability Based on BI-RADS Category

| | |
|---|---|
| BI-RADS 0: | Needs Additional Imaging |
| BI-RADS 1: | Negative |
| BI-RADS 2: | Benign |
| BI-RADS 3: | Probably Benign |
| BI-RADS 4: | Suspicious for malignancy |
| BI-RADS 5: | Highly suggestive of malignancy |

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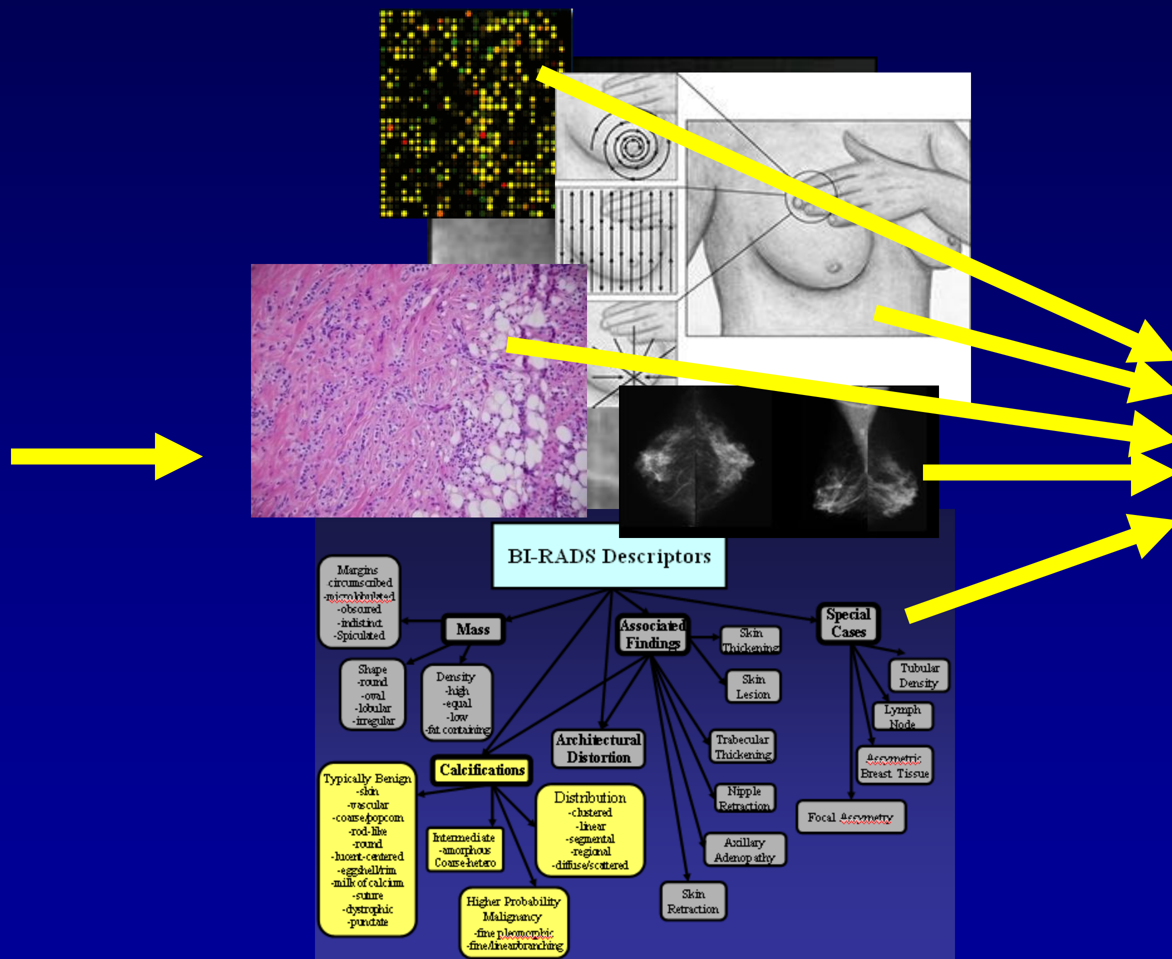
# Breast Cancer Predictors




**BI-RADS Category**

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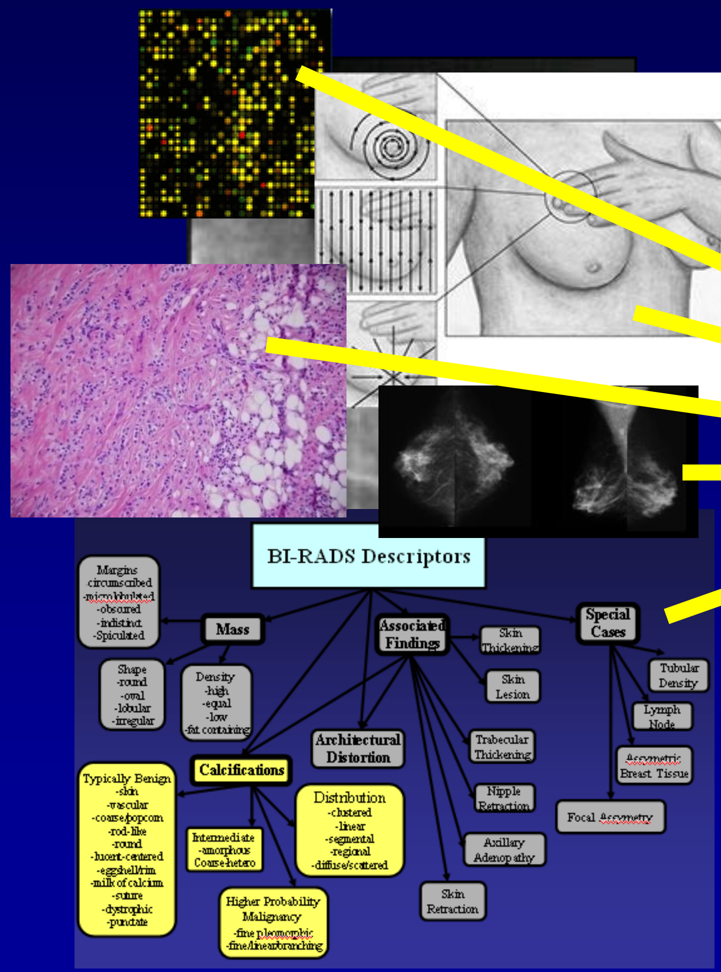
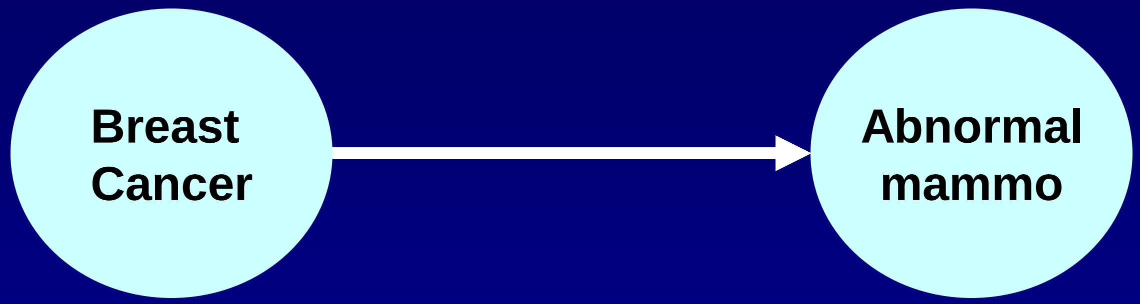
# Breast Cancer Predictors




**Risk**

**Detection** **Characterization** **Classification**

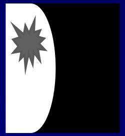
# Bayesian Networks

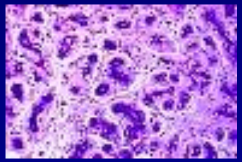


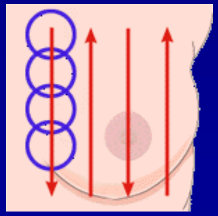
# What do we want to know?

We generally learn P(f|d)

Breast cancer



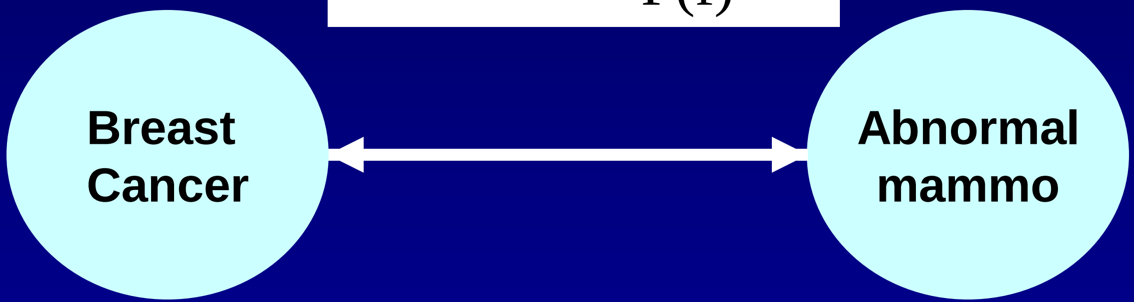




We generally want to know P(d|f)

# Bayesian Networks

$$P(d \mid f) = \frac{P(f \mid d)\, P(d)}{P(f)}$$




| Breast CA | Symbol | Prob |
|---|---|---|
| Yes | P(d) | 1.0% |
| No | P(d-) | 99.0% |

| Breast CA | mammo | Symbol | Prob |
|---|---|---|---|
| Yes | Yes | P(f\|d) | 90% |
| Yes | No | P(f-\|d) | 10% |
| No | Yes | P(f\|d-) | 10.1% |
| No | No | P(f-\|d-) | 89.9% |

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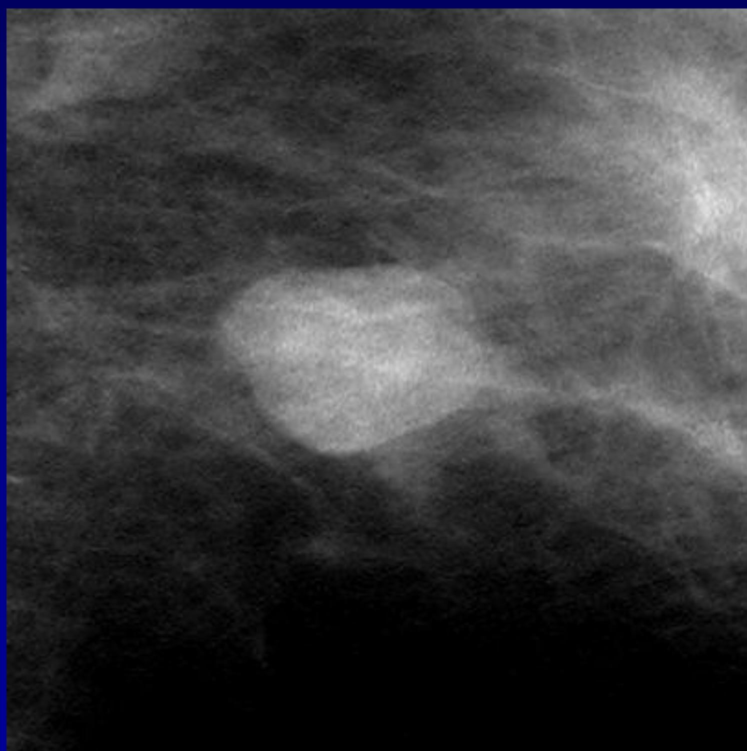
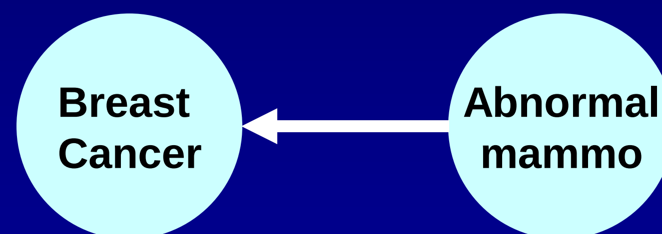
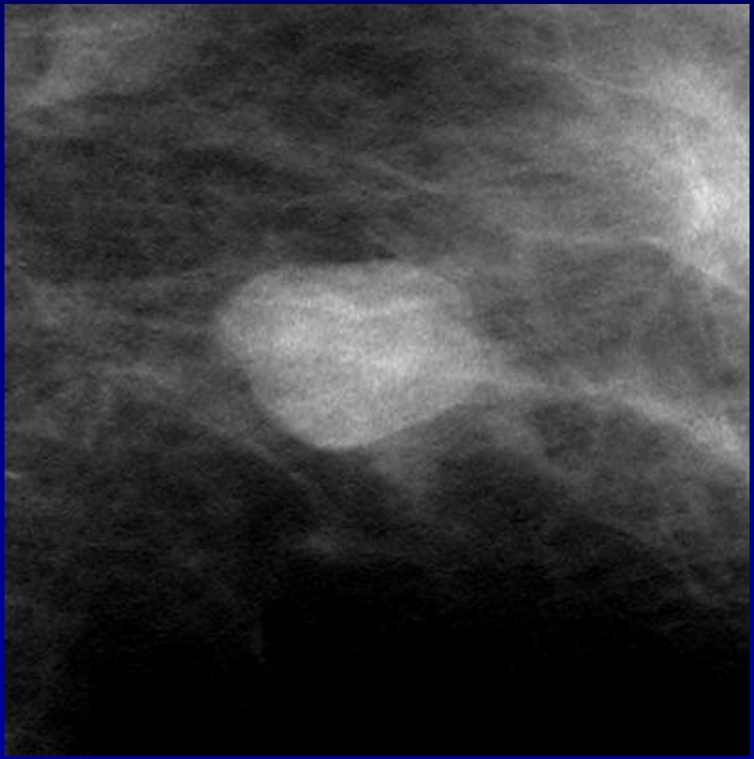
# Estimates

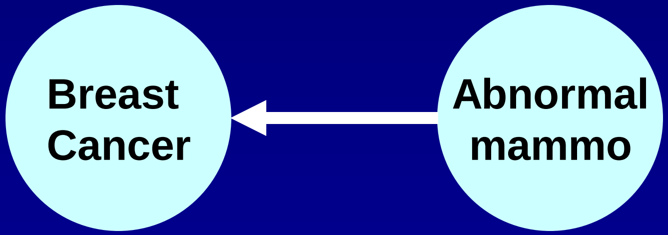




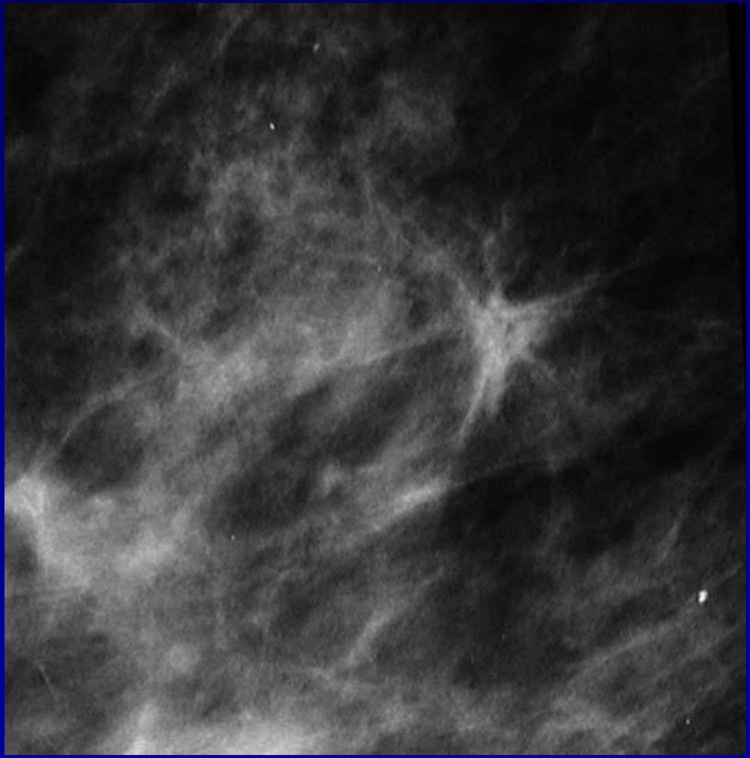
# Estimates

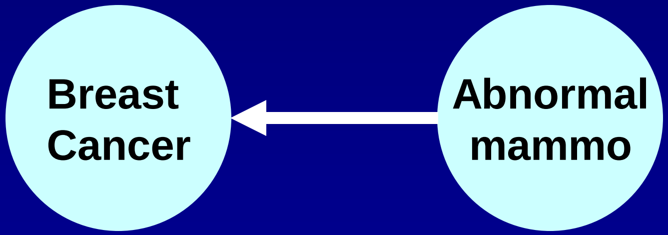


8.3%



# Estimates





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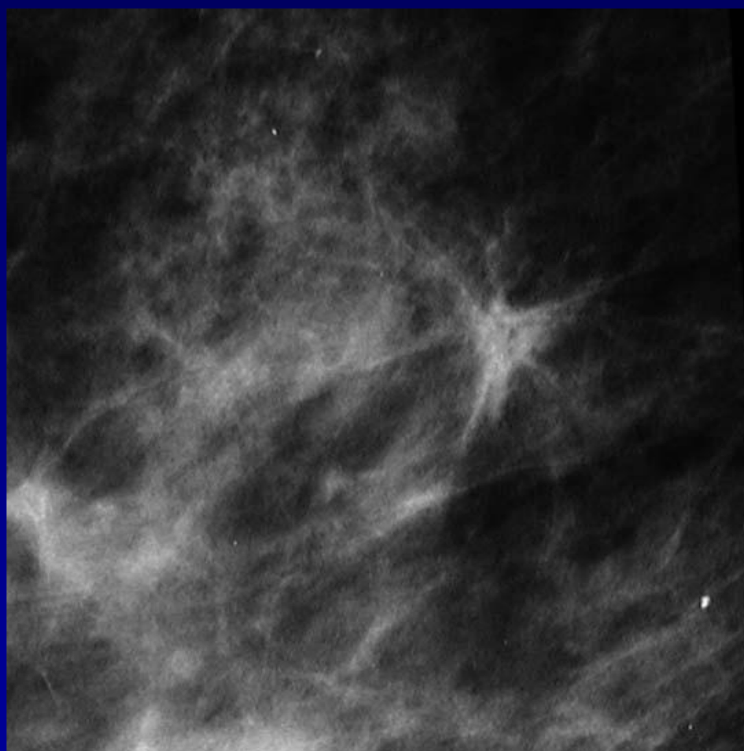
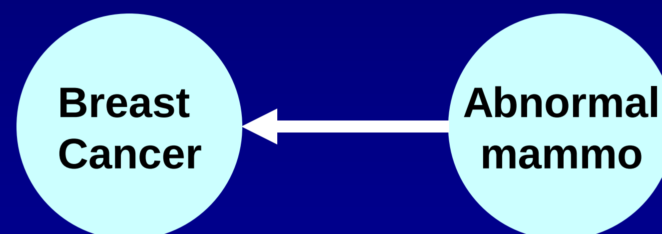
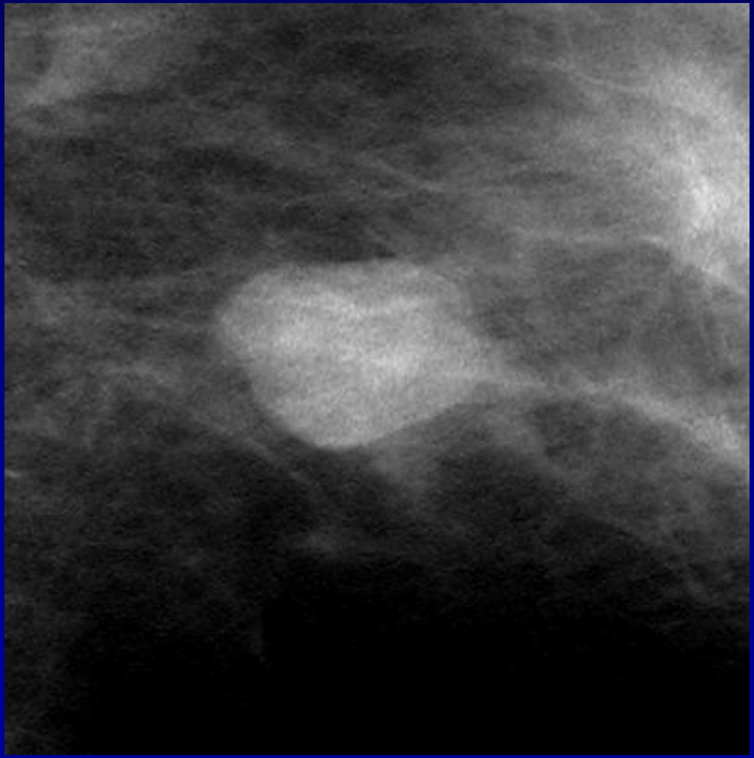
# Estimates



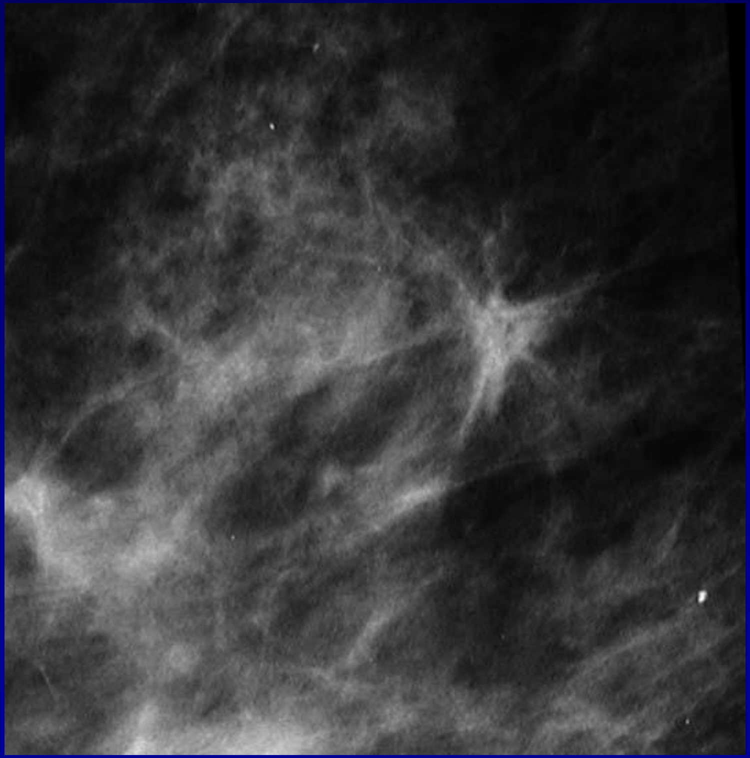
**8.3%**



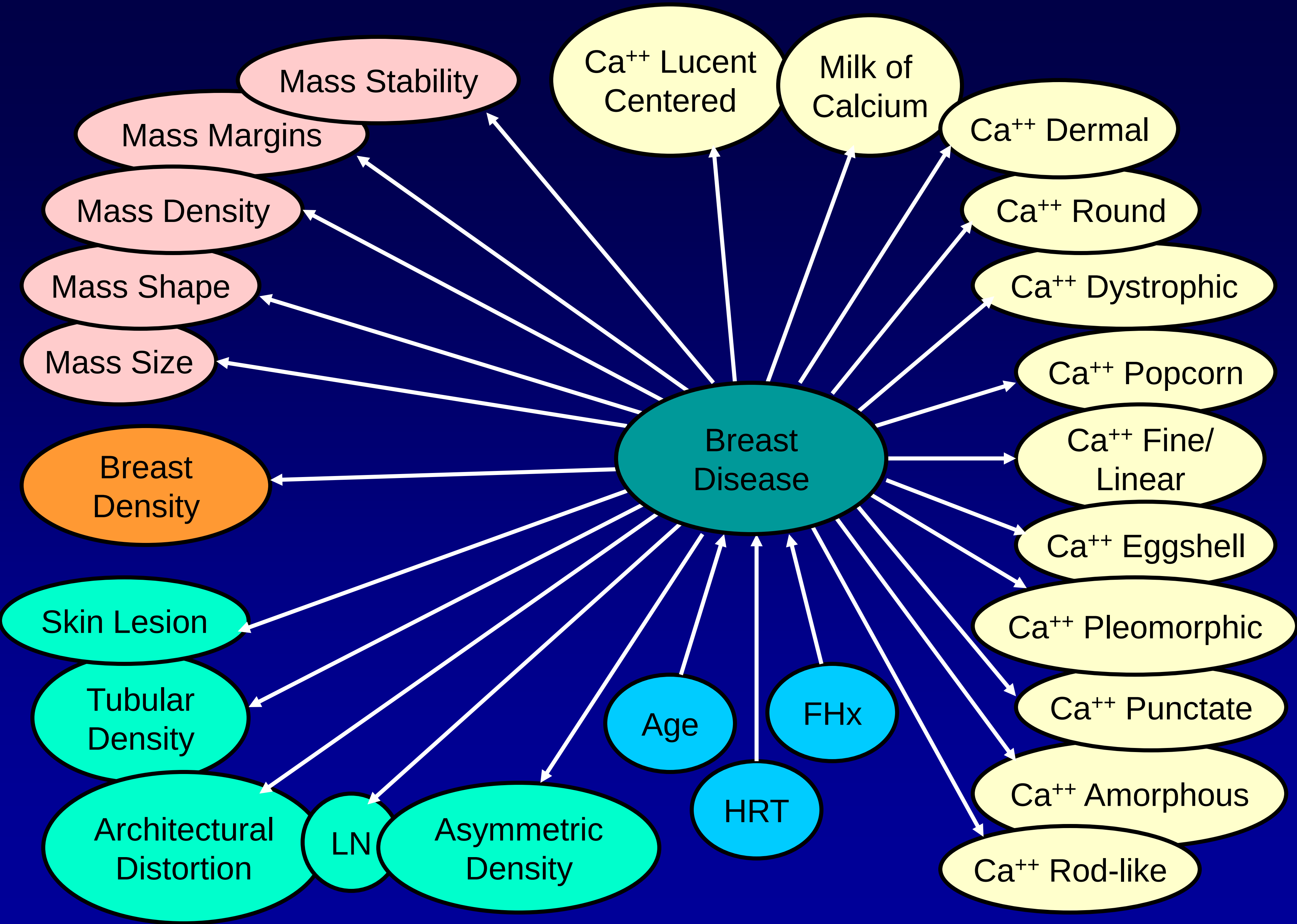
# Probability Estimates



**8.3%**

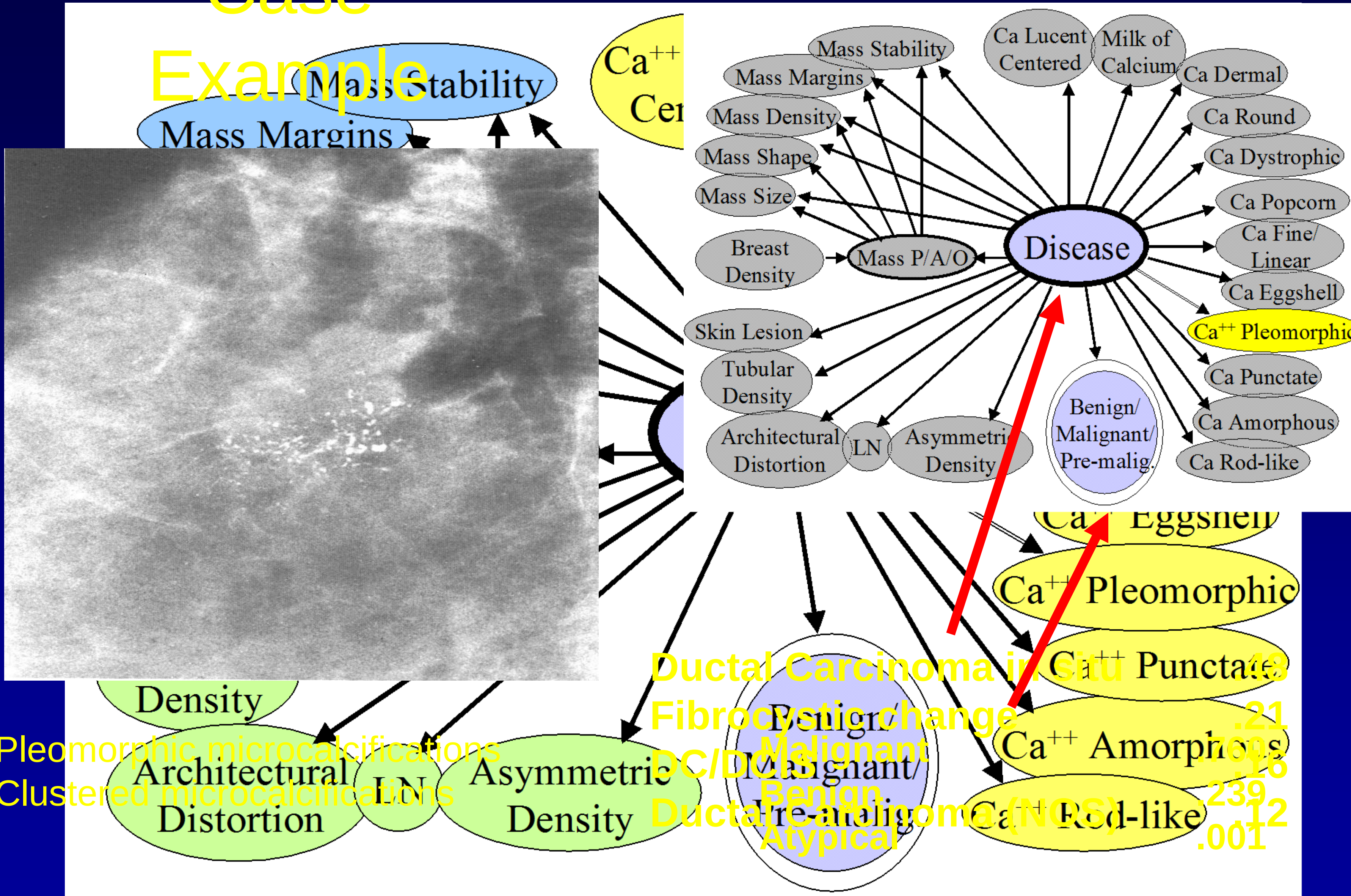


**8.3%**



Mass Stability
Mass Margins
Mass Density
Mass Shape
Mass Size
Breast Density
Skin Lesion
Tubular Density
Architectural Distortion
LN
Asymmetric Density
Age
HRT
FHx
Breast Disease
Ca++ Lucent Centered
Milk of Calcium
Ca++ Dermal
Ca++ Round
Ca++ Dystrophic
Ca++ Popcorn
Ca++ Fine/ Linear
Ca++ Eggshell
Ca++ Pleomorphic
Ca++ Punctate
Ca++ Amorphous
Ca++ Rod-like

# Case Example




Pleomorphic microcalcifications
Clustered microcalcifications

Ductal Carcinoma in Situ .48
Fibrocystic change .21
DC/DCIS .16
Ductal Carcinoma (NOS) .12

Malignant .760
Benign .239
Atypical .001

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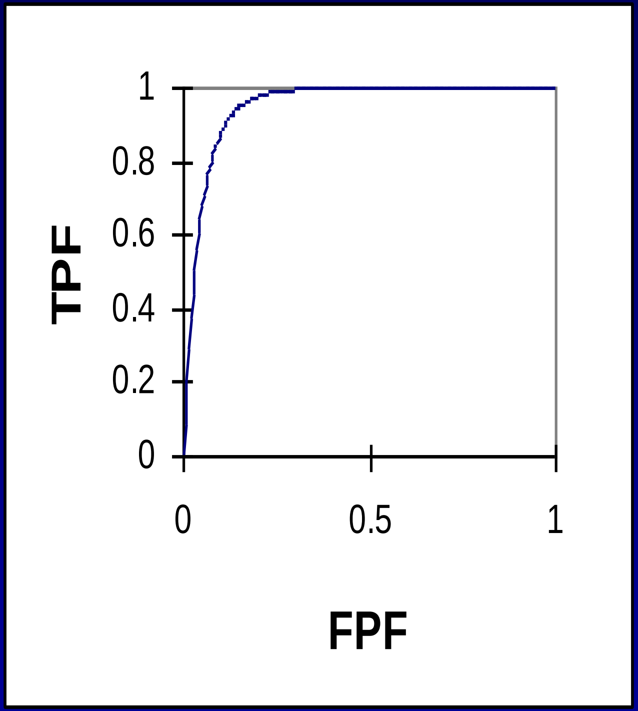
# Teaching cases

- 105 cases
- Created ROC curve
- Comparable to
  - Neural networks

Az = .953



# Training on Data

- Motivation
  - Accurate probabilities are critical
  - Some are not available in literature
  - Modeling the relevant patient population is possible with training

***Expert & Rule Based*** → ***Machine Learning***

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# Idea: Data Driven Decisions

| Patient Table |
| --- |
| Age |
| Personal Hx Breast CA |
| Family Hx Breast CA |
| ….. |

| Mammogram Table |
| --- |
| Mass shape |
| Mass margins |
| Mass density |
| Mass size |
| Mass stability |
| MicroCa$^{++}$ shape |
| MicroCa$^{++}$ distribution |
| BI-RADS category |
| ….. |

| Registry Table |
| --- |
| Patient ID |
| Margin status |
| Grade |
| Prior radiation |
| ….. |

| Biopsy Table |
| --- |
| Needle size |
| Number of samples |
| Post-proc appearance |
| Accurate clip position |
| ….. |

| Pathology Table |
| --- |
| Pathology Result |
| Concordance |
| Recommendation |
| ….. |

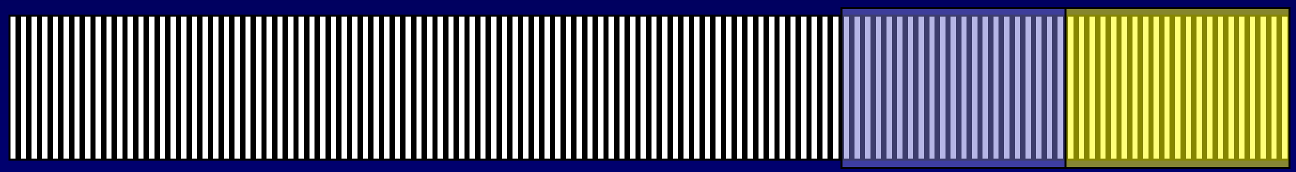
# Idea: Data Driven Decisions

| Patient | Abnormality | Date | Calc | Mass | Mass Size | location | B/M |
|---|---|---|---|---|---|---|---|
| P1 | 1 | 5/08 | N | Y | 3 mm | RUO | B |
| P1 | 2 | 5/10 | Y | Y | 5 mm | RUO | M |
| P1 | 3 | 5/10 | N | Y | 3 mm | LLI | B |
| P2 | 4 | 6/09 | N | Y | N/A | RLI | B |
| … | … | … | … | … | … | … | |

# Data

- Our dataset contains
  - 350 malignancies
  - 65,630 benign abnormalities
- Linked to cancer registry data
  - Outcomes (benign/malignant)

# Training the BN



**Training set**

**Tuning set**

**Test set**

- Standard Machine learning
  - Use known cases to train
  - Use the tuning set for optimal training
  - Performance based on hold out test set

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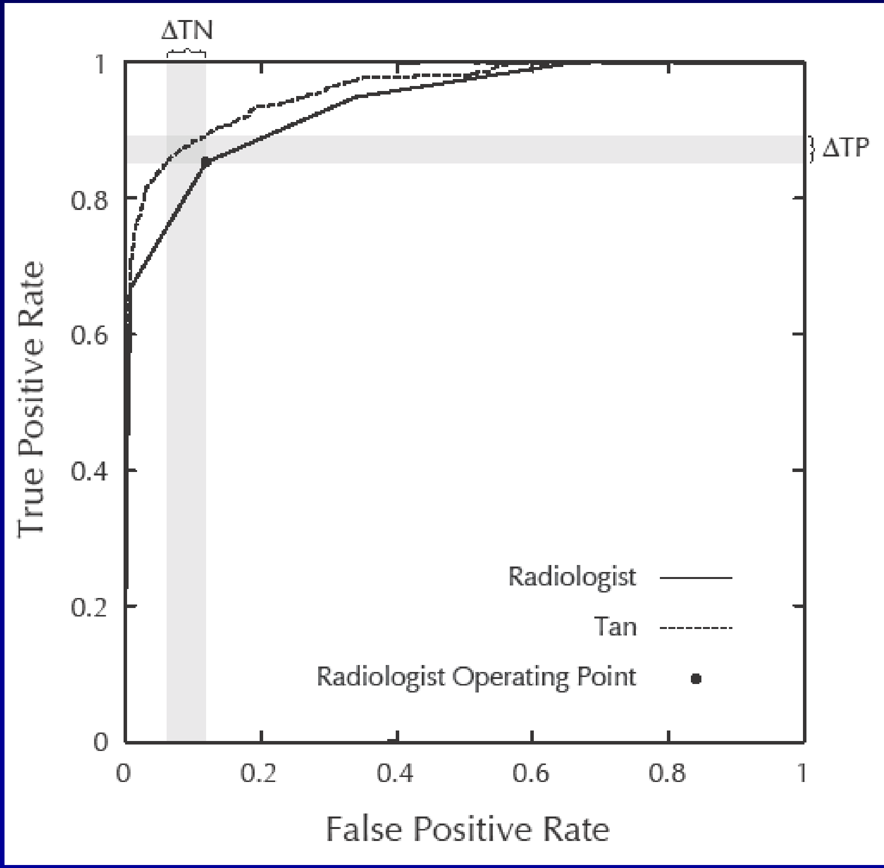
# Performance




- AUC 0.960 *vs*. 0.939
  - $P < 0.002$
- Sensitivity
  - 90.0% *vs*. 85.3%
  - $P < 0.001$
- Specificity
  - 93.9% *vs*. 88.1%
  - $P < 0.001$

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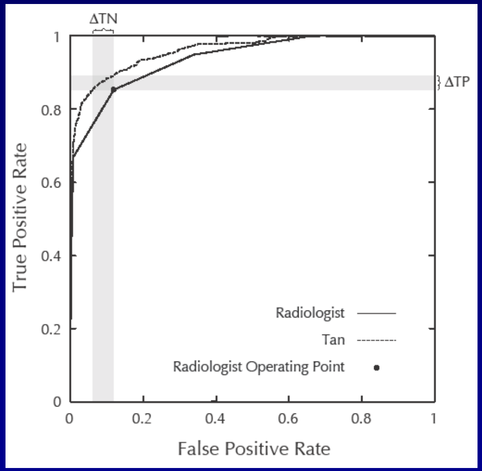
# What does that mean?

- At a specificity of 90%

  **38 conversions FN → TP**

- At a sensitivity of 85%

  **4226 conversions FP → TN**



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# Ultimately Decision Support Aids the Physician

- Output of the system is
  - Advisory
  - Utilized in the clinical context
  - System performance alone is not the point
  - Performance/Physician performance is the key to improvement of care

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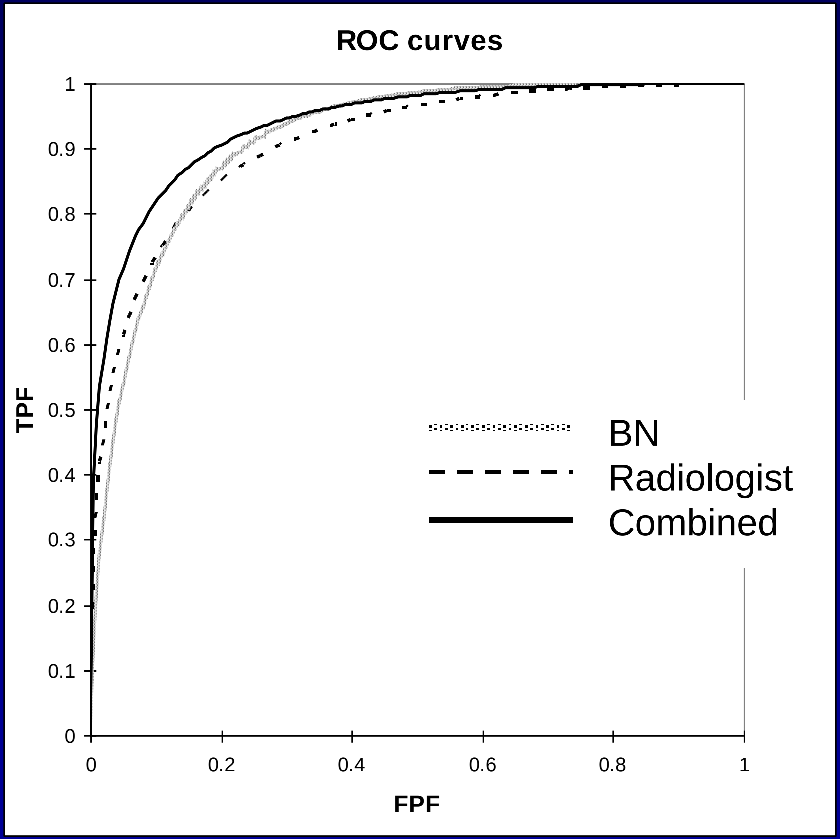
# Collaborative Experiment




Radiologist

.916

Bayes Net

.919

Combined

.948

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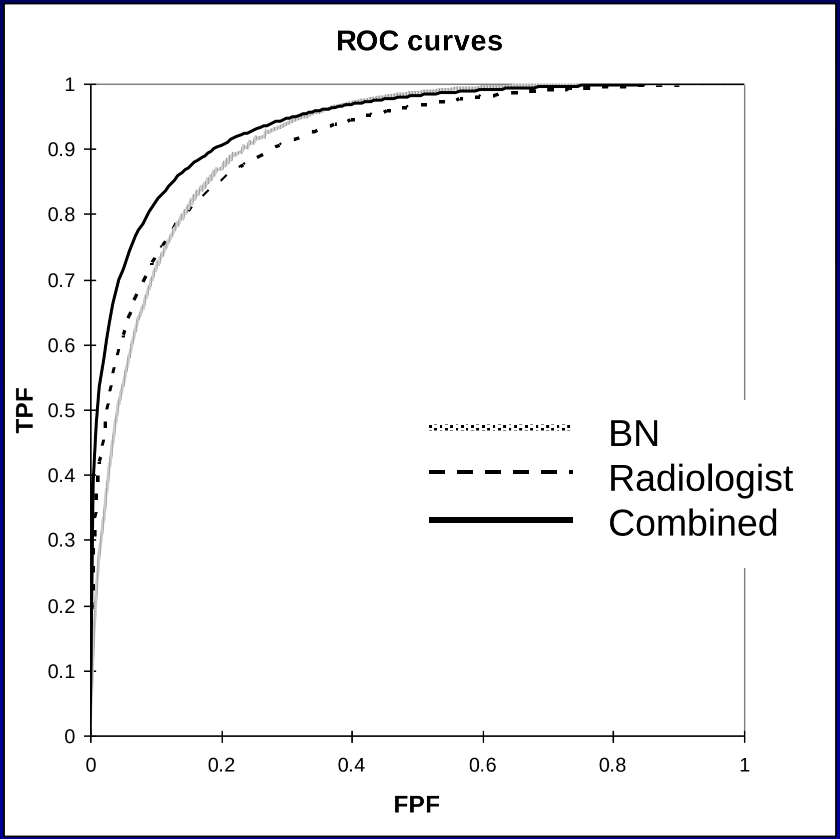
# Results




Radiologist
.916

Bayes Net
.919

p=.03

Combined
.948

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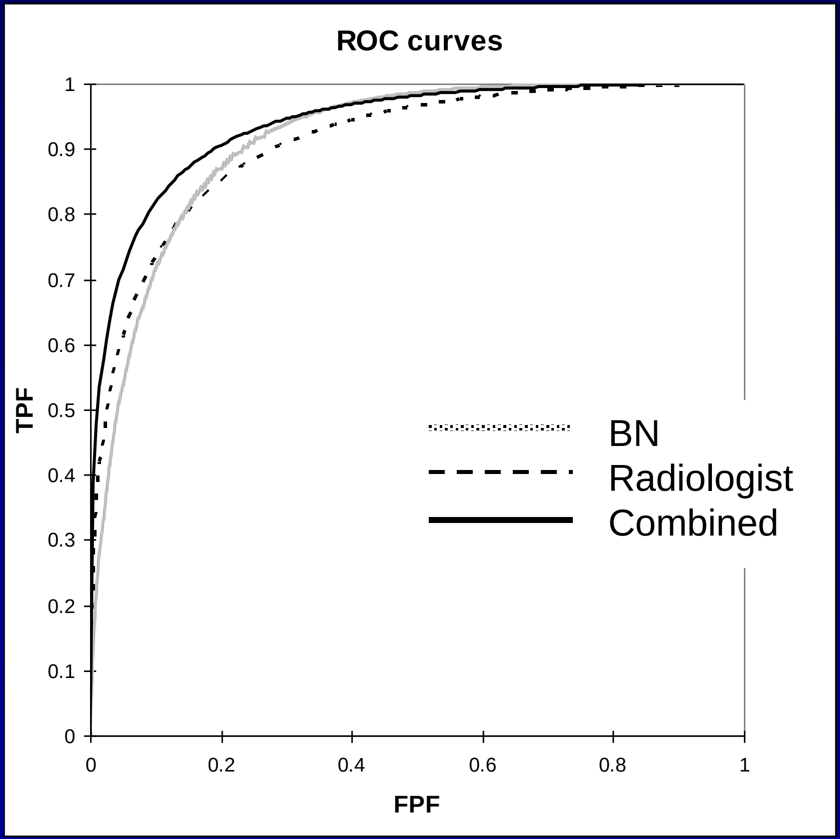
# Results




Radiologist

.916

Bayes Net

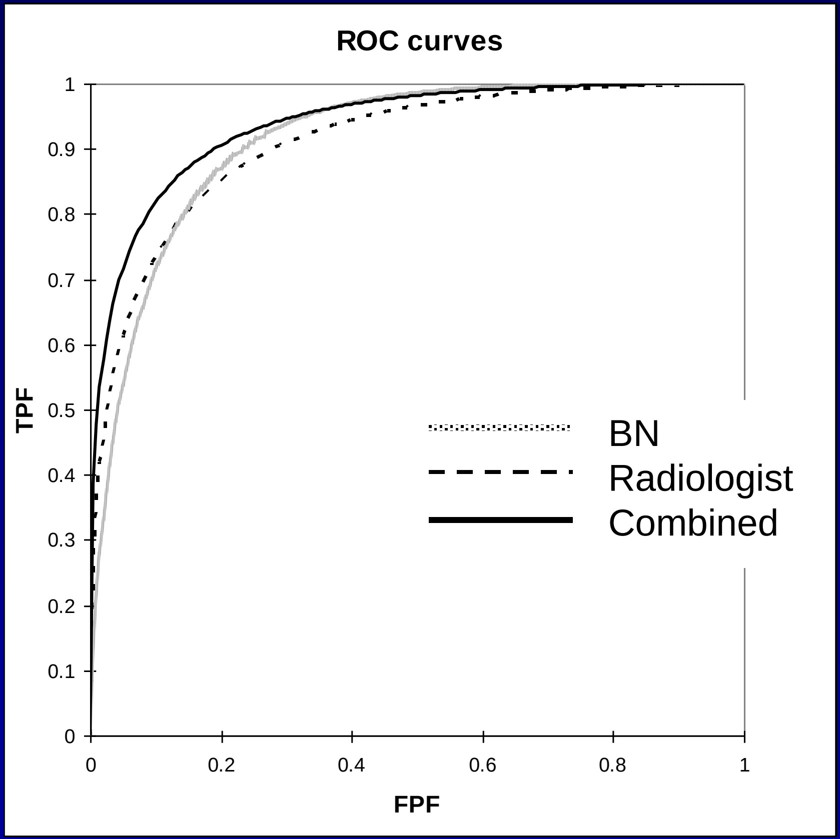
.919

p=.065

Combined

.948

# Results




Radiologist

.916

p=.99

Bayes Net

.919

Combined

.948

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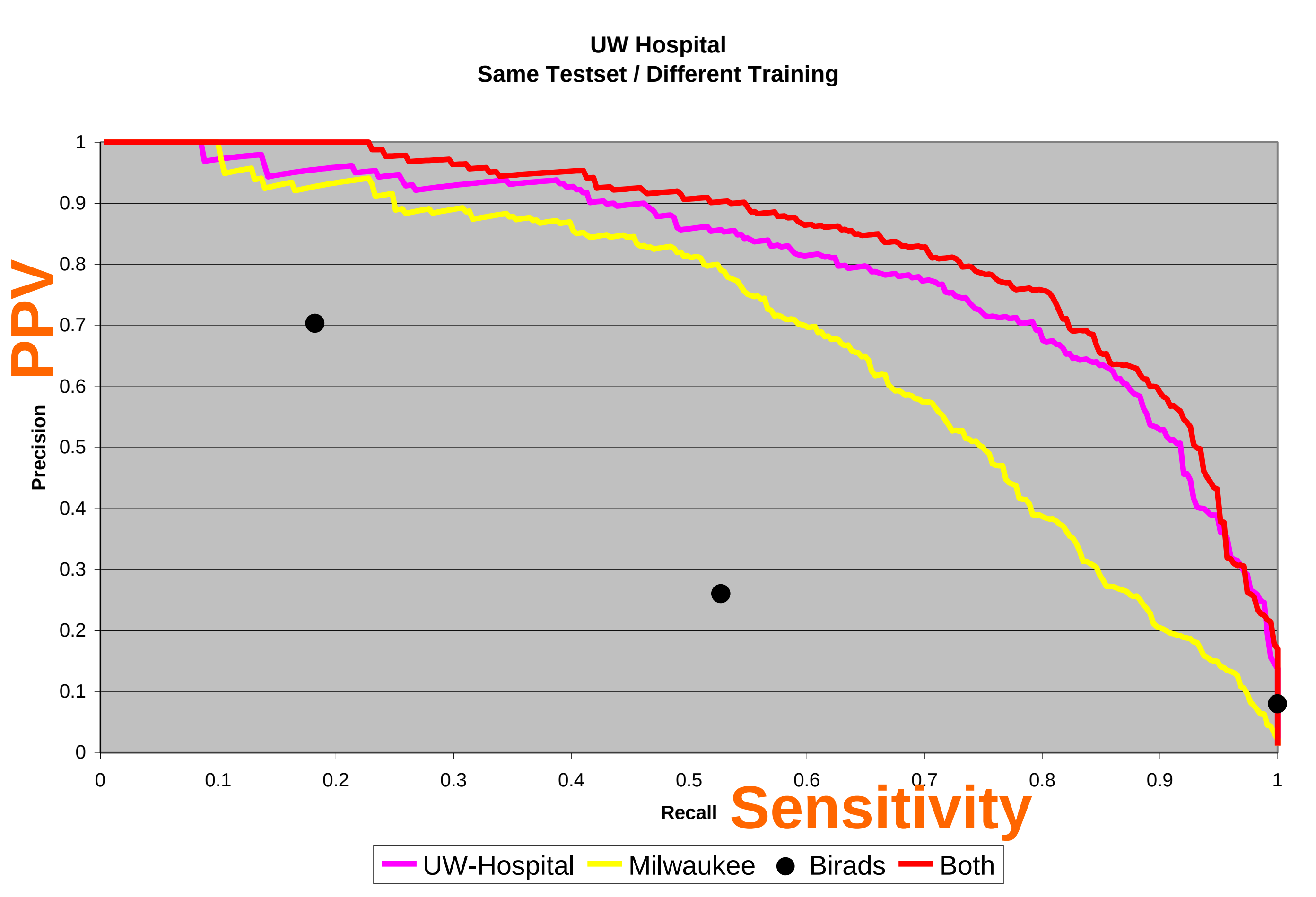
# Precision Recall Curves



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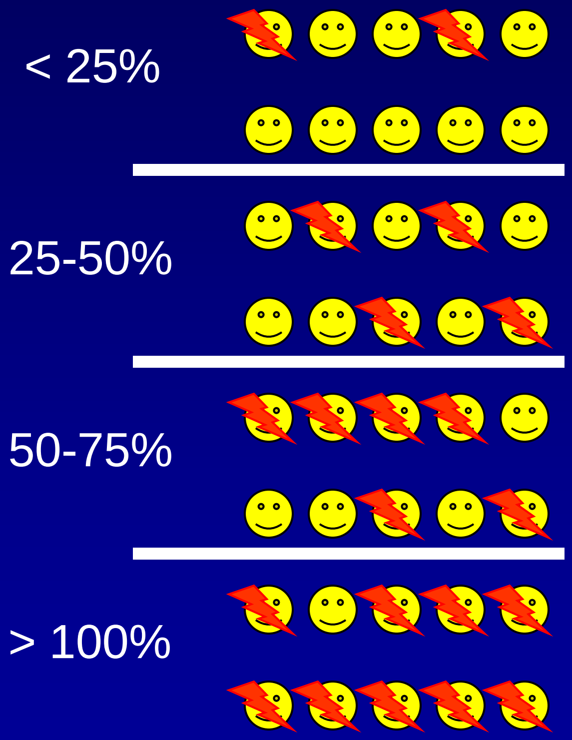
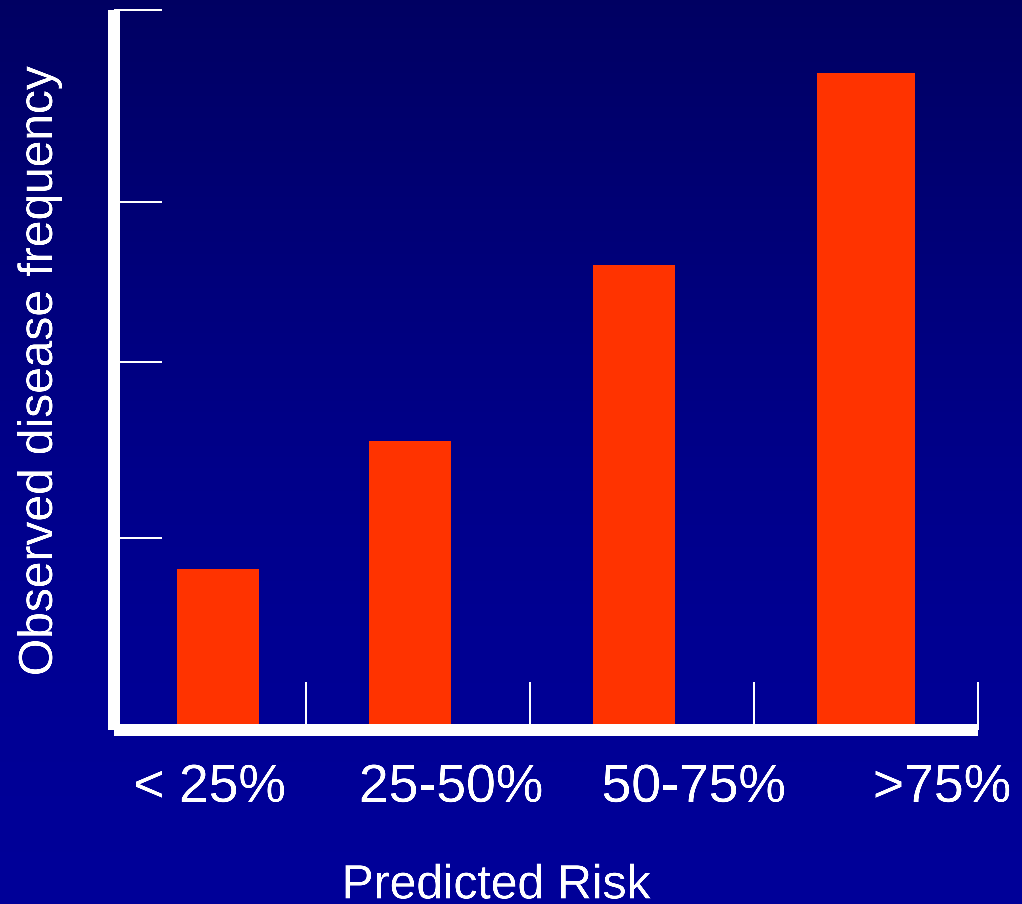
# Calibration Curves



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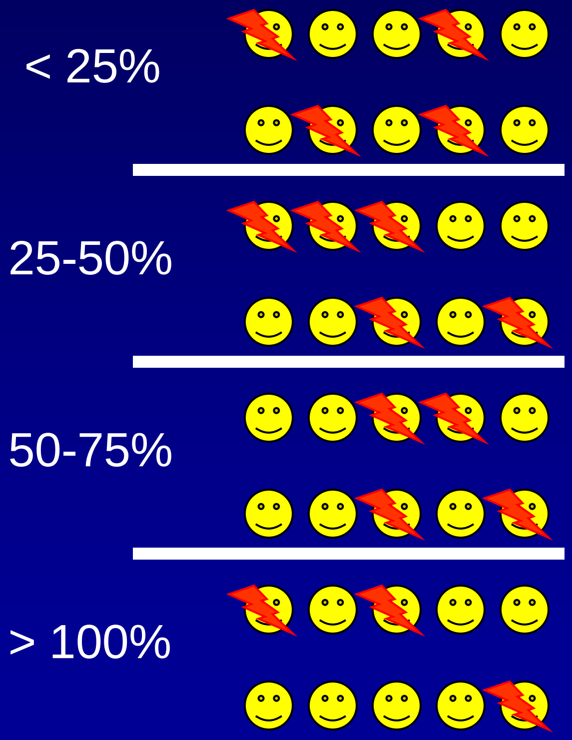


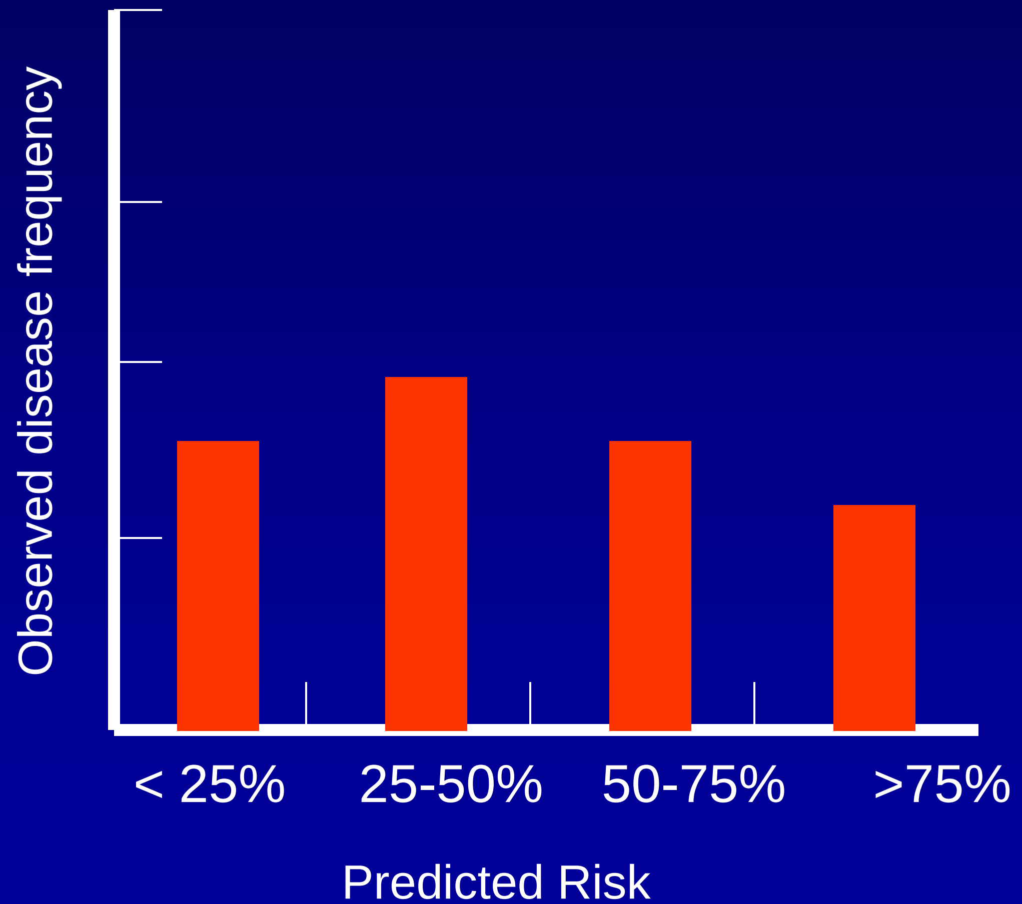

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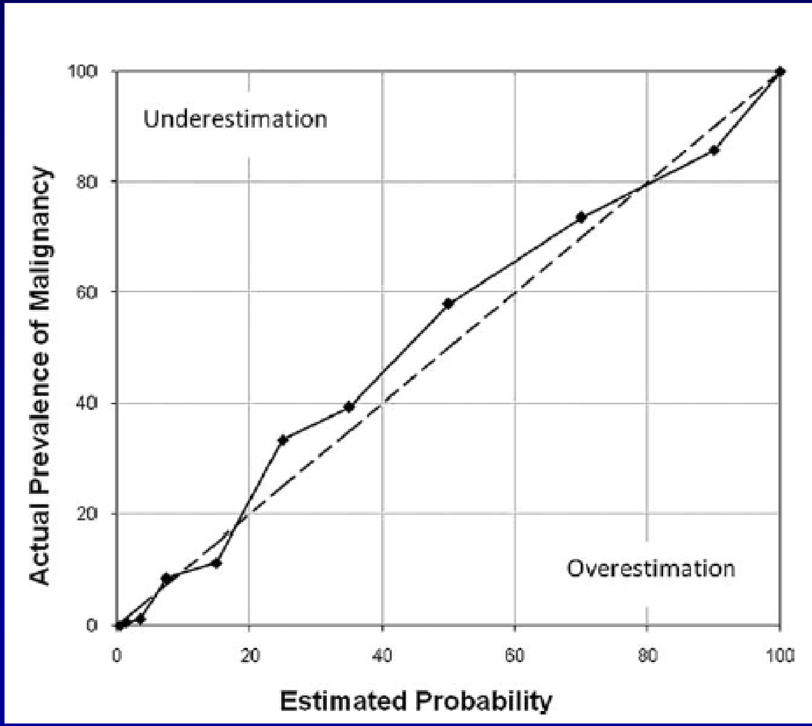
# Calibration




- Hosemer-Lemishow goodness of fit

Ayer, T., et al., *Breast cancer risk estimation with artificial neural networks revisited: discrimination and calibration.* Cancer, 2010. **116**(14): p. 3310-21.

# Idea: Data Driven Decisions

| **Patient Table** |
|---|
| Age |
| Personal Hx Breast CA |
| Family Hx Breast CA |
| ….. |

| **Mammogram Table** |
|---|
| Mass shape |
| Mass margins |
| Mass density |
| Mass size |
| Mass stability |
| MicroCa$^{++}$ shape |
| MicroCa$^{++}$ distribution |
| BI-RADS category |
| ….. |

| **Registry Table** |
|---|
| Patient ID |
| Margin status |
| Grade |
| Prior radiation |
| ….. |

| **Biopsy Table** |
|---|
| Needle size |
| Number of samples |
| Post-proc appearance |
| Accurate clip position |
| ….. |

| **Pathology Table** |
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| P2 | 4 | 6/09 | N | Y | N/A | RLI | B |
| … | … | … | … | … | … | … | |

Not independent and identically distributed (IID)

# Algorithmic Opportunities

- Inductive logic programming (ILP)
- Statistical Relational Learning (SRL)
- Natural Language Processing (NLP)

# Algorithmic Opportunities

- Inductive logic programming (ILP)
- Statistical Relational Learning (SRL)
- Natural Language Processing (NLP)

# ILP

Abnormality A in
Mammogram M for
Biopsy B in
Patient P

Is malignant if:

Malignant (A) IF
- A has mass present
- A has stability increasing
- P has family history of breast cancer
- B has atypia

# How does it work?

- Learn if-then rules that will become features in a predictive model
  - Inductive logic programming (ILP) to learn the rules
  - Integrated search strategy for constructing and selecting rules for classifcation algorithm

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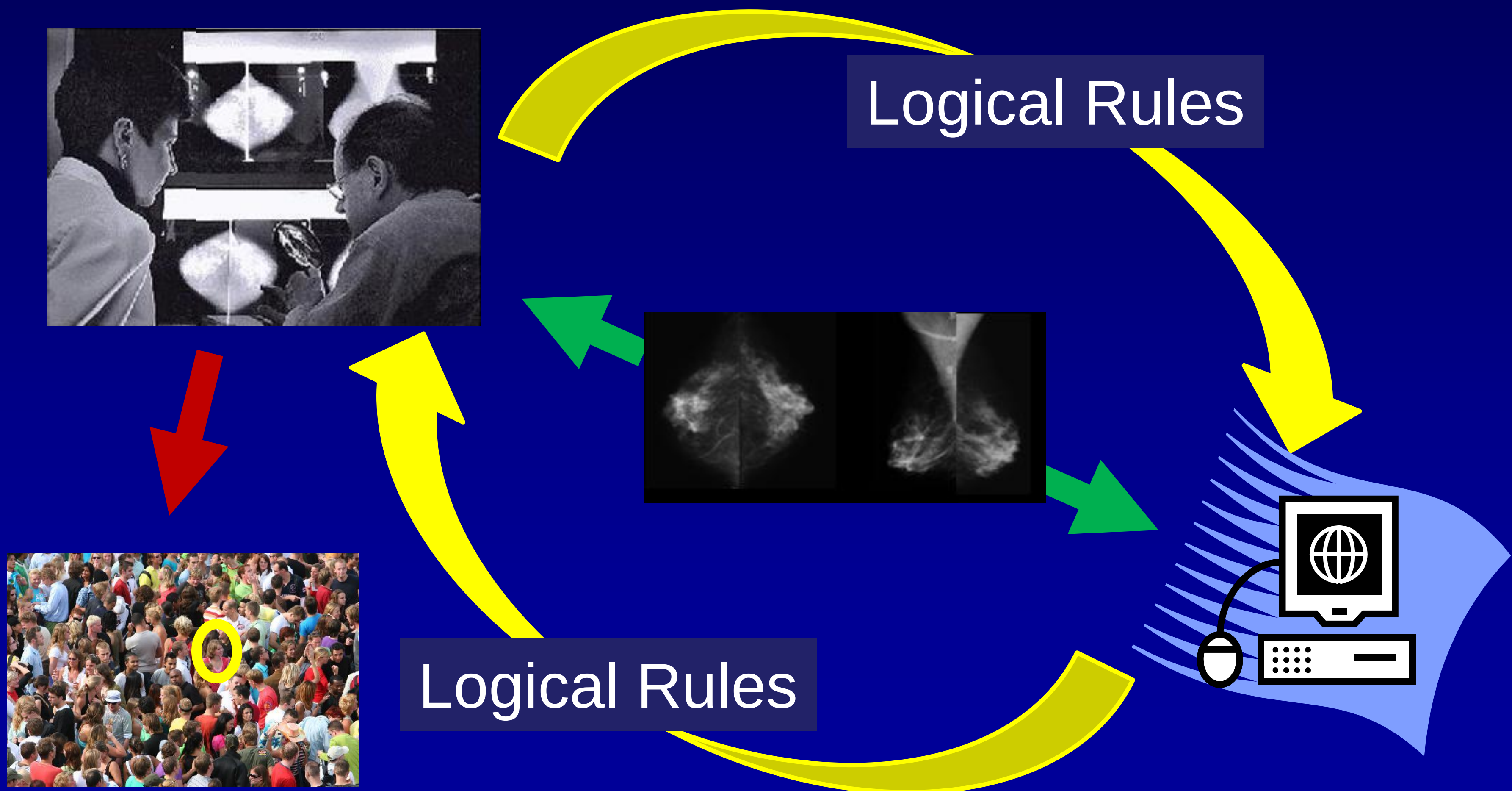
# Human Computer Interaction
# COMMUNICATION



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# The Breast Biopsy Project

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Heather Neuman, MD, MS
Andreas Friedl, MD
C. David Page, PhD
Jude Shavlik, PhD

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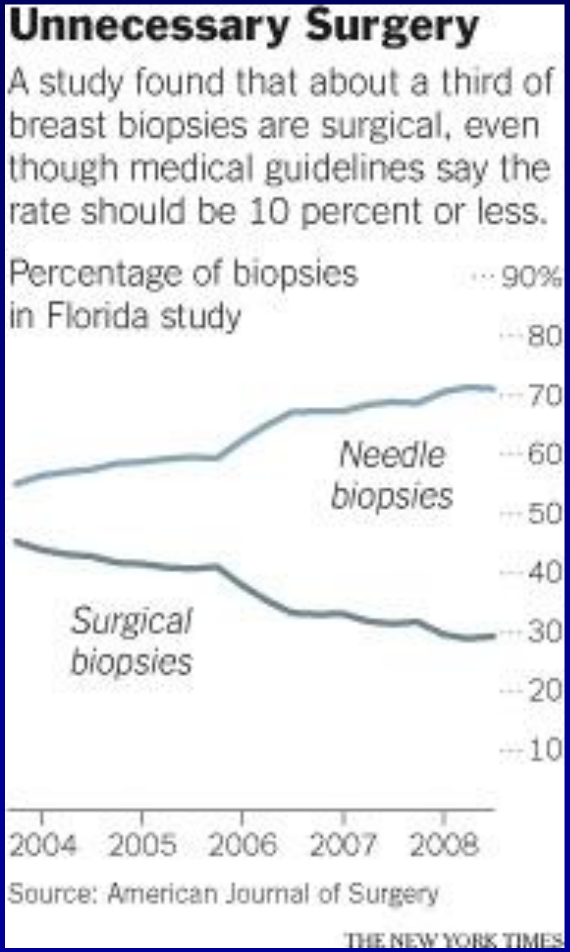
# Image-guided Breast Biopsy

- **Excisional biopsy for diagnosis of findings on mammography is overutilized**




Grobmyer, SR et al. Am J Surg. 2011 Feb 2.
**Utilization of minimally invasive breast biopsy for the evaluation of suspicious breast lesions.**

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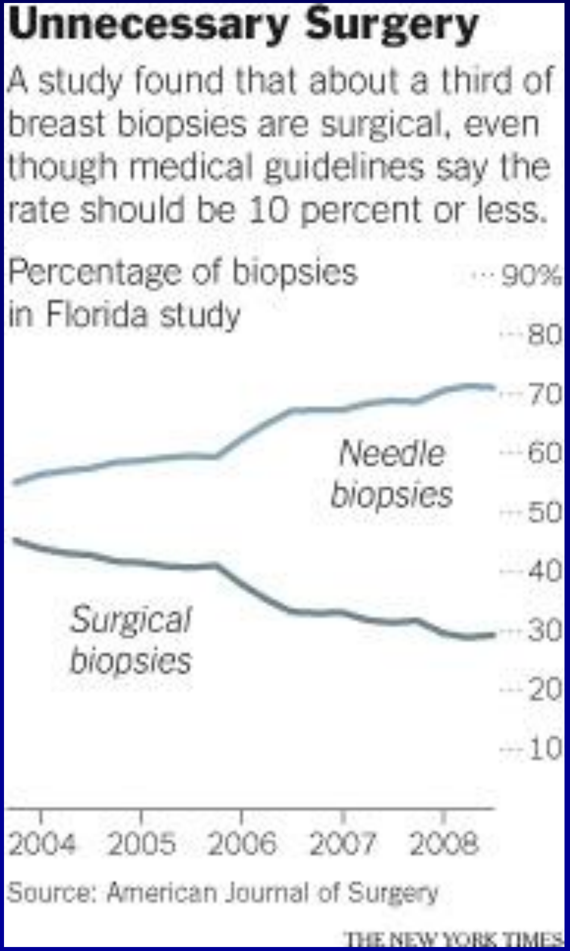
# Image-guided Breast Biopsy

- **Core biopsy not perfect**
  - 10% of benign core biopsies are non-definitive
  - 10-15% of these are upgraded to cancer at excisional biopsy

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# Breast Biopsy

- Biopsy: single most costly component of a breast cancer screening program

- Annual breast biopsy utilization in 2010

62.6/10,000 women

➢ 700,000 women

~35,000-105,000 non-definitive

# Breast Biopsy at UW

- 5 year experience at UW
  - 1228 consecutive image-guided core biopsies
    - 890 benign
    - 94 were deemed non-definitive
    - 15 were upgraded to malignancy
- Hypothesis: ILP rules from the data and from physicians could improve the accuracy of upgrade prediction

# Biopsy data

- Example rule:

Upgrade (A) IF

concordance (A, d),

biopsyProcedure (A, US_core) and

pathDx (A, benign_breast_tissue)

- Incorporate physician and machine rules into a Bayesian Network

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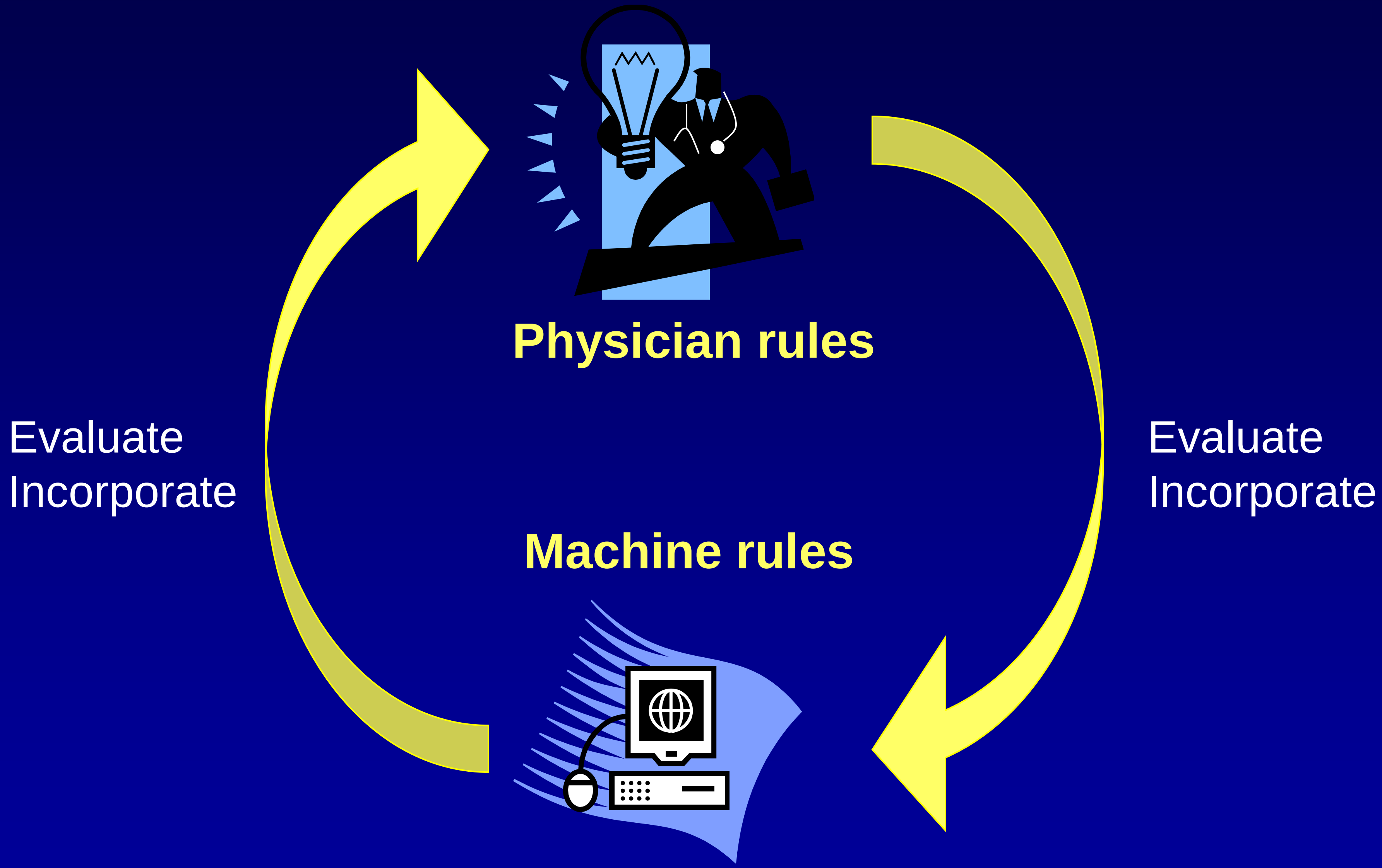

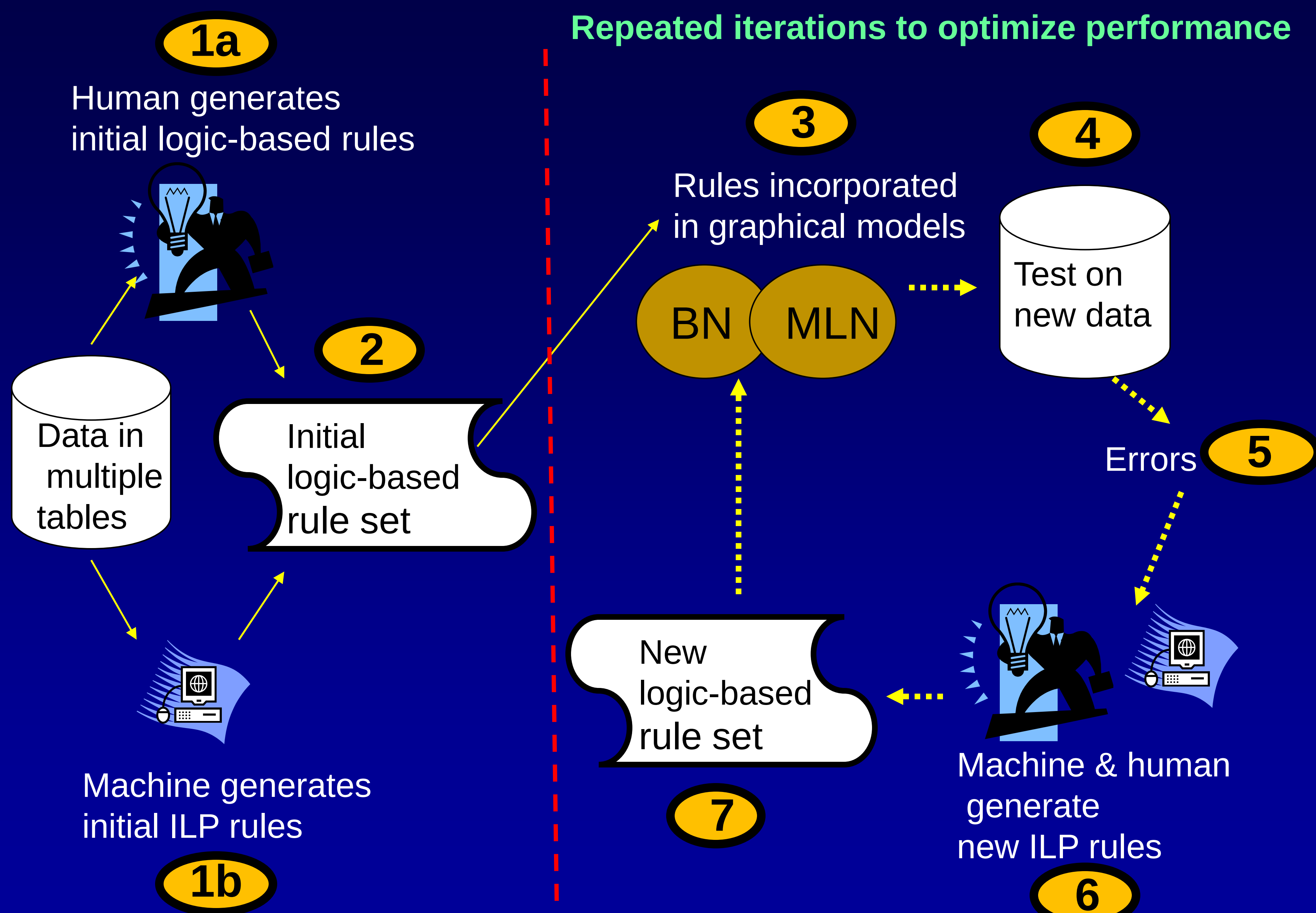
Repeated iterations to optimize performance
1a
Human generates
initial logic-based rules
Data in
multiple
tables
2
Initial
logic-based
rule set
1b
Machine generates
initial ILP rules
3
Rules incorporated
in graphical models
BN
MLN
4
Test on
new data
Errors
5
Machine & human
generate
new ILP rules
6
New
logic-based
rule set
7

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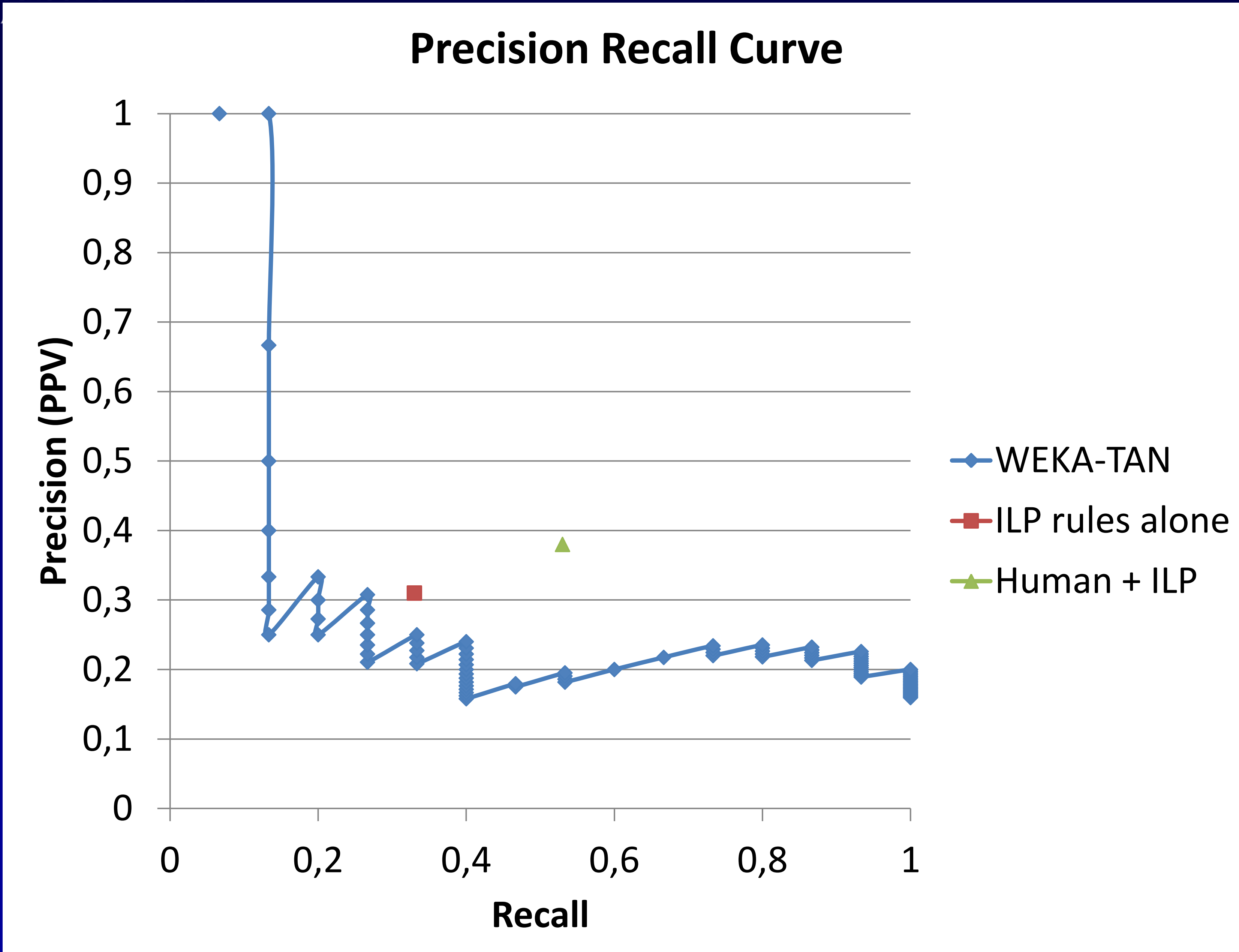

# PPV Improvement

| | Baseline | BN with rules |
|---|---|---|
| Benign biopsy | 890 | 890 |
| Non-definitive biopsy | 94 | 75 |
| Excision avoided | 0 | 19 |
| Malignant excision | 15 | 15* |
| Benign excision | 79 | 60 |
| PPV | 16.0% | 20.0% |

***No cancers missed***

# Potential for Translation

- Translate these decision support algorithms to the clinic to improve care
- Improve evidence-based decisions
- Encourage shared decision-making

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# Questions?


FIG. 1. Bayes' theorem in practice.