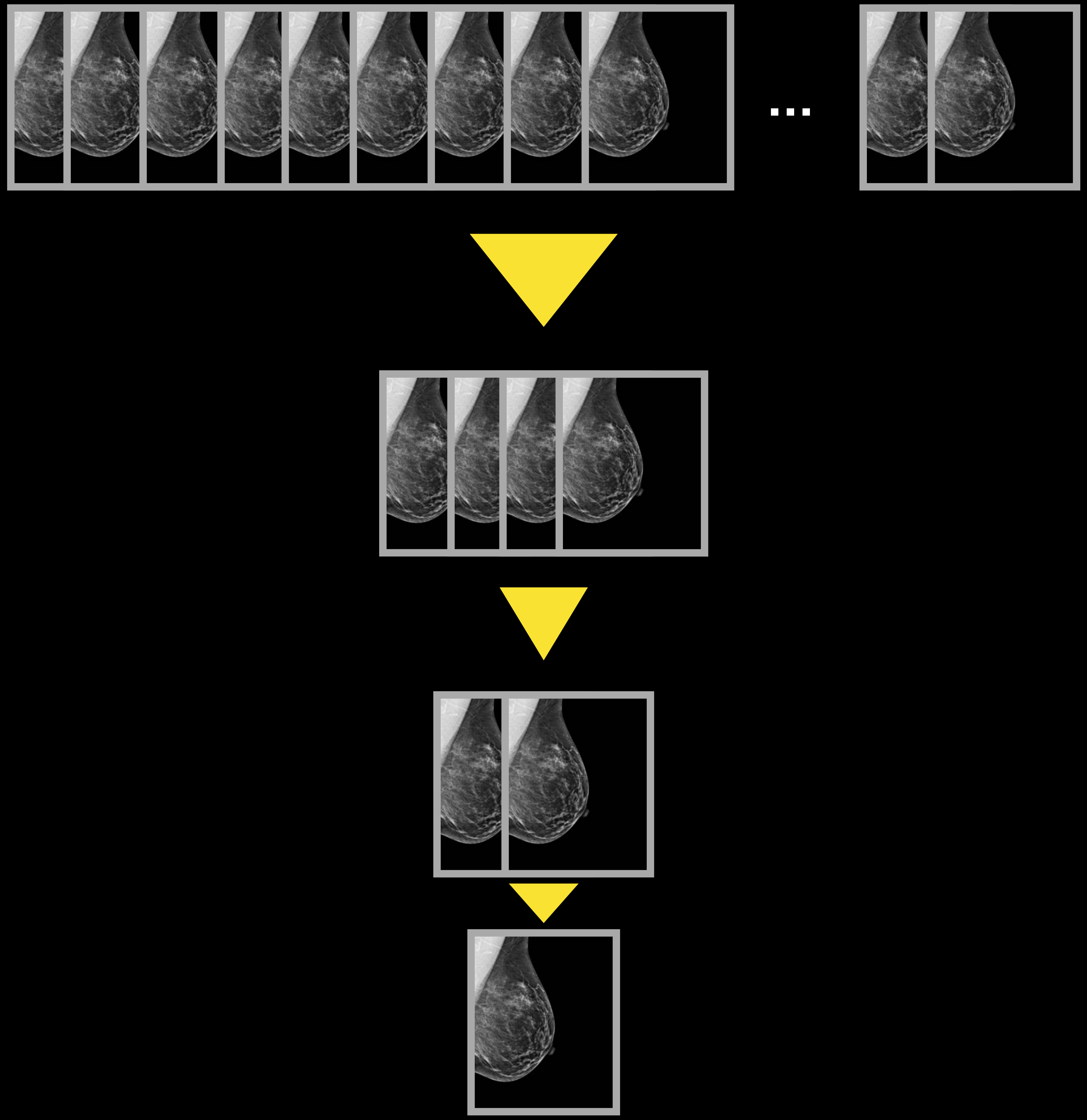
Agenda

- **Interpreting Mammograms**
  - Cancer Detection and Triage
- Assessing Breast Cancer Risk
- How to Mess Up
- How to Deploy

Triaging Mammograms



1. Routine Screening

   1000 Patients

2. Called back for Additional Imaging

   100 Patients

3. Biopsy

   20 Patients

4. Diagnosis

   6 Patients

Triaging Mammograms

- **>99%** of patients are **cancer-free**
- Can we use a cancer model to automatically **triage** patients as **cancer-free**?
  - Reduce False positives, improve efficiency.
- Overall Idea:
  - Train a cancer detection model and pick a **cancer-free** threshold
    - chosen by **min probability** of a **caught-cancer** on the dev set
  - Radiologists can **skip** reading mammograms bellow threshold

Triaging Mammograms

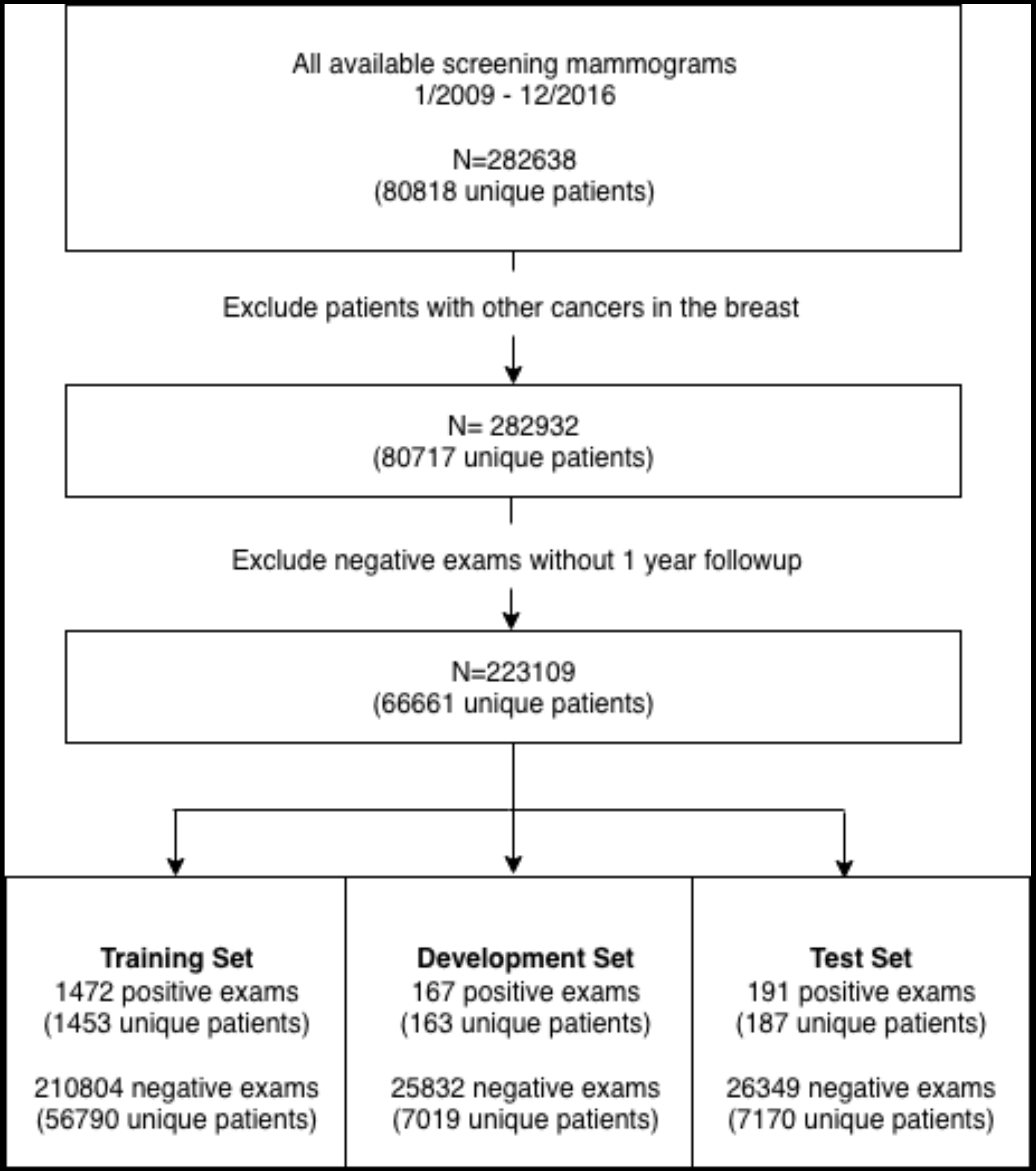
- The plan
  - **Dataset Collection**
  - Modeling
  - Analysis

Dataset Collection

- Consecutive Screening Mammograms
  - 2009-2016
- Outcomes from Radiology EHR, and Partners

5 Hospital Registry

- No exclusions based on race, implants etc.
- Split into Train/Dev/Test by Patient



Triaging Mammograms

- The plan
  - Dataset Collection
  - **Modeling**
    - General challenges in working with mammograms
    - Specific methods for this project
  - Analysis

Modeling: Is this just like ImageNet?

[Image of mammogram, removed for patient privacy]

Modeling: Is this just like ImageNet?

[Image of mammogram, removed for patient privacy]

Modeling: Is this just like ImageNet?

Many shared lessons, but important differences
in-size and nature of signal.

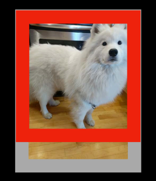
[Image of mammogram, removed for patient privacy]

3200 px

50 x 50px

2600 px

256 px



256 x 200px

256 px

Modeling: Is this just like ImageNet?

Many shared lessons, but important differences in-size and nature of signal.

[Image of mammogram, removed for patient privacy]

3200 px

50 x 50px

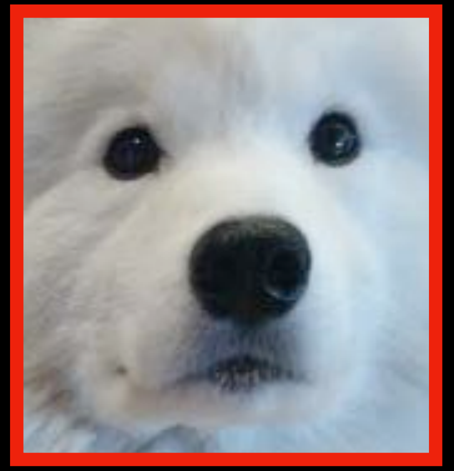
50 x 50px

2600 px

Context-dependent Cancer

REDACTED

Context-independent Dog



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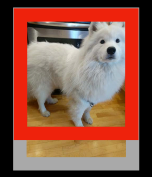

256 x 200px

256 px

Modeling: Challenges

- **Size of Object / Size of Image:**
  - Mammo: **~1%**
- **Class Balance:**
  - Mammo: **0.7%** Positive
  - **220,000** Exams, **<2,000** Cancers
- **Images per GPU:**
  - **3** Images (< 1 Mammogram)
  - **128** ImageNet Images
- Dataset Size
  - **12+** TB

The data is too small!

The data is too big!

Modeling: Key Choices

- How do we make the model actually **learn**?
  - **Initialization**
  - Optimization / Architecture Choice
- How to use the model?
  - Aggregation across images
  - Triage Threshold
  - Calibration

Modeling: Actual Choices

- How do we make the model learn?
  - Initialization
    - **ImageNet Init**
  - Optimization
    - Batch size: **24**
    - **2** steps on **4** GPUs for each optimizer step
    - Sample **balanced batches**
  - Architecture Choice
    - **ResNet-18**

Modeling: Key Choices

- How do we make the model actually **learn**?
  - Initialization
  - Optimization / Architecture Choice
- How to use the model?
  - Aggregation across images
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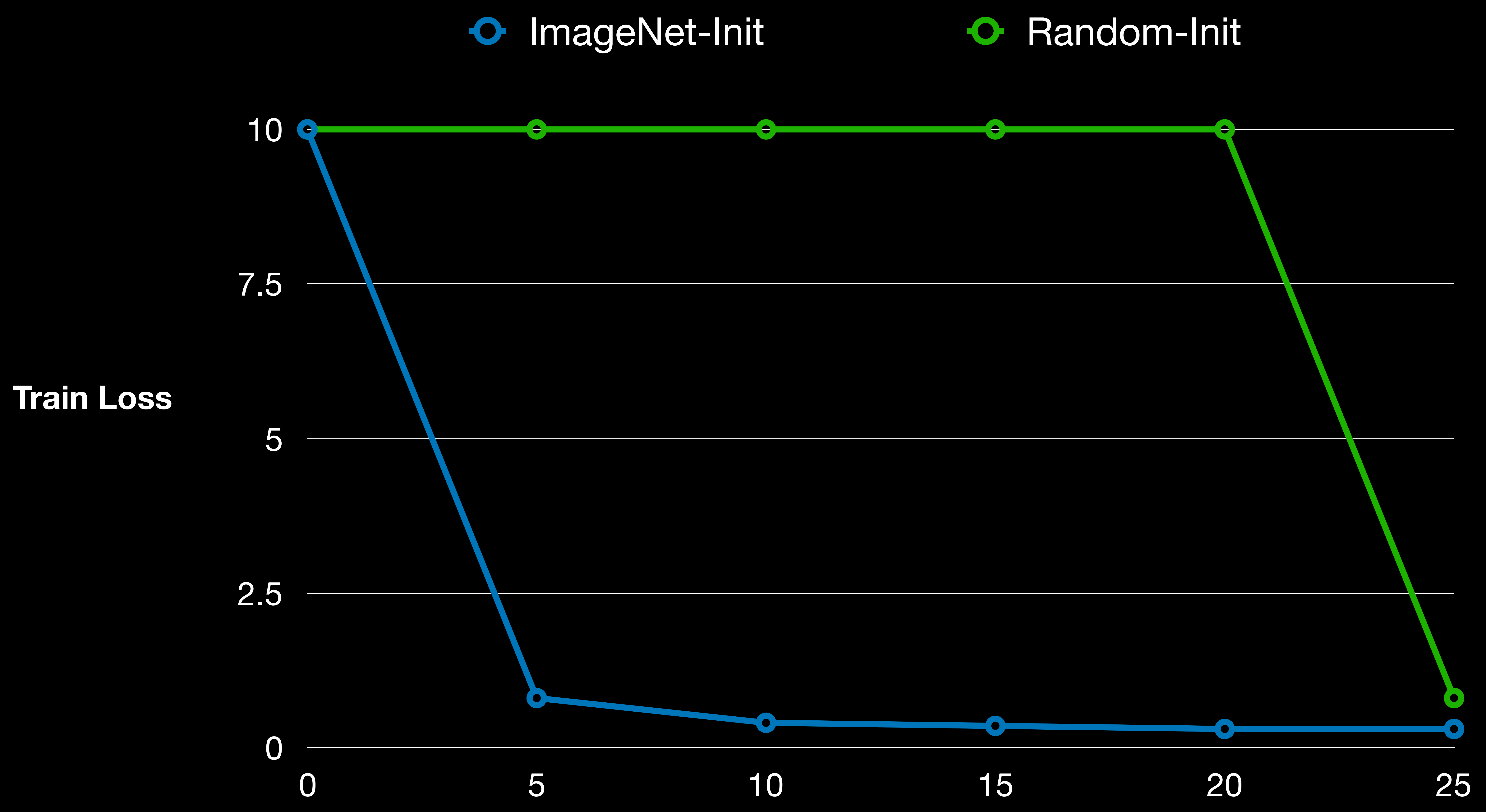
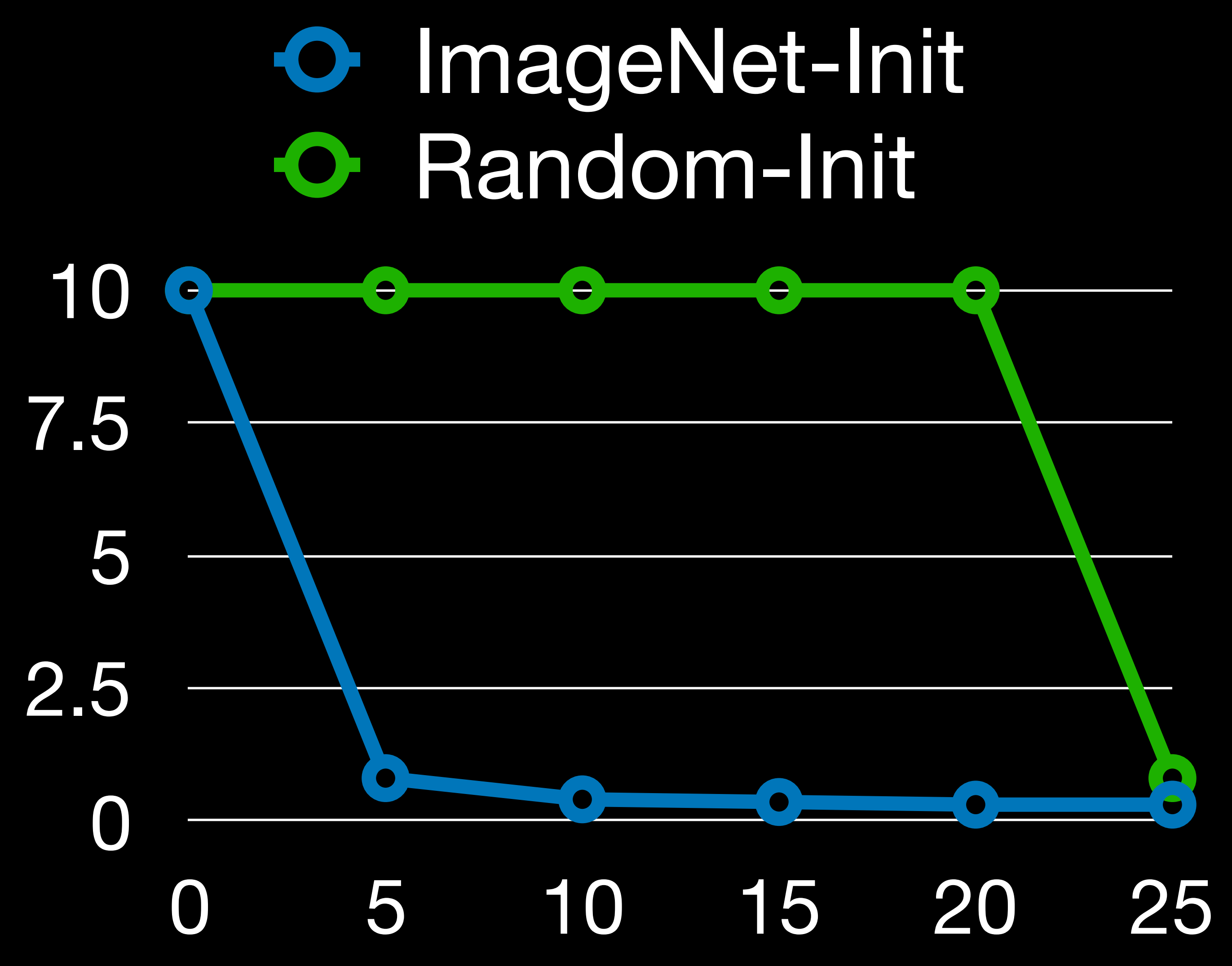
  - Calibration

Modeling: Initialization

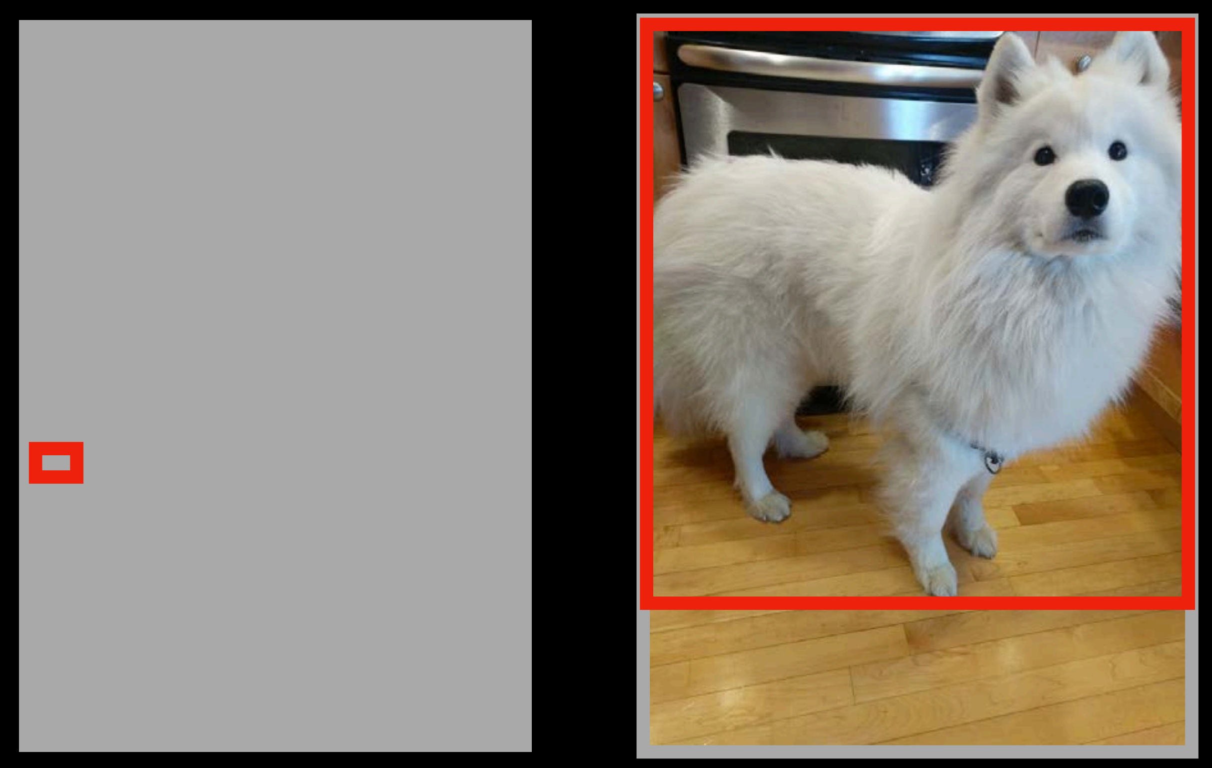


Modeling: Initialization



Empirical Observations

- ImageNet initialization learns immediately.
    - Transfer of particular filters?
        - Hard edges / shapes not shared
    - Transfer of BatchNorm Statistics
- Random initialization doesn't fit for many epochs until sudden cliff.
    - Unsteady BatchNorm statistics (3 per GPU)

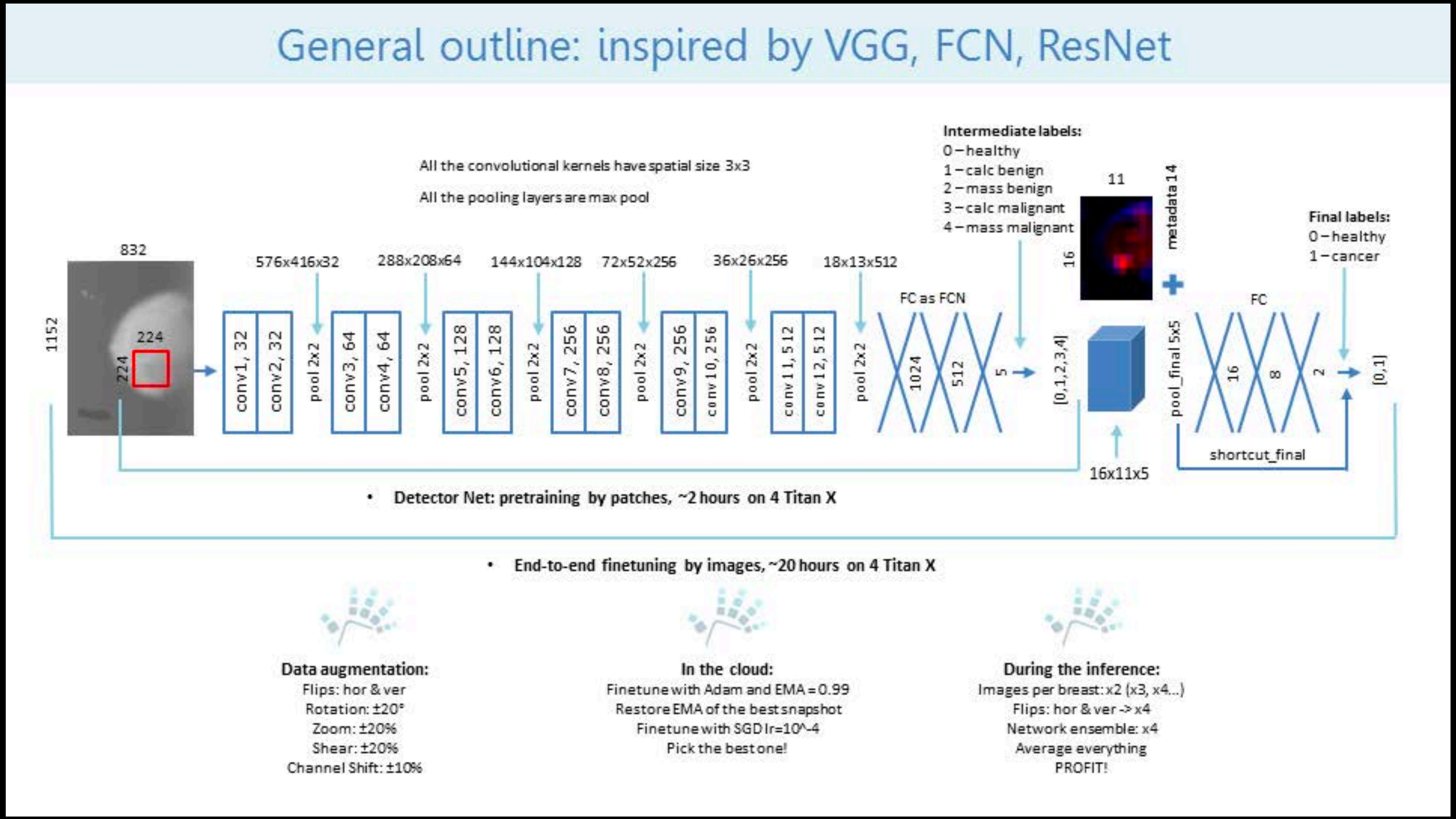


Modeling: Key Choices

- How do we make the model actually **learn**?
  - Initialization
  - **Optimization / Architecture Choice**
- How to use the model?
  - Aggregation across images
  - Triage Threshold
  - Calibration

Modeling: Common Approaches

- **Core problem:**
  - Low signal-to-noise ratio
- **Common Approach:**
  - Pre-Train at Patch level
    - High batch-size > 32
  - Fine-tune on full images
    - Low batch-size < 6



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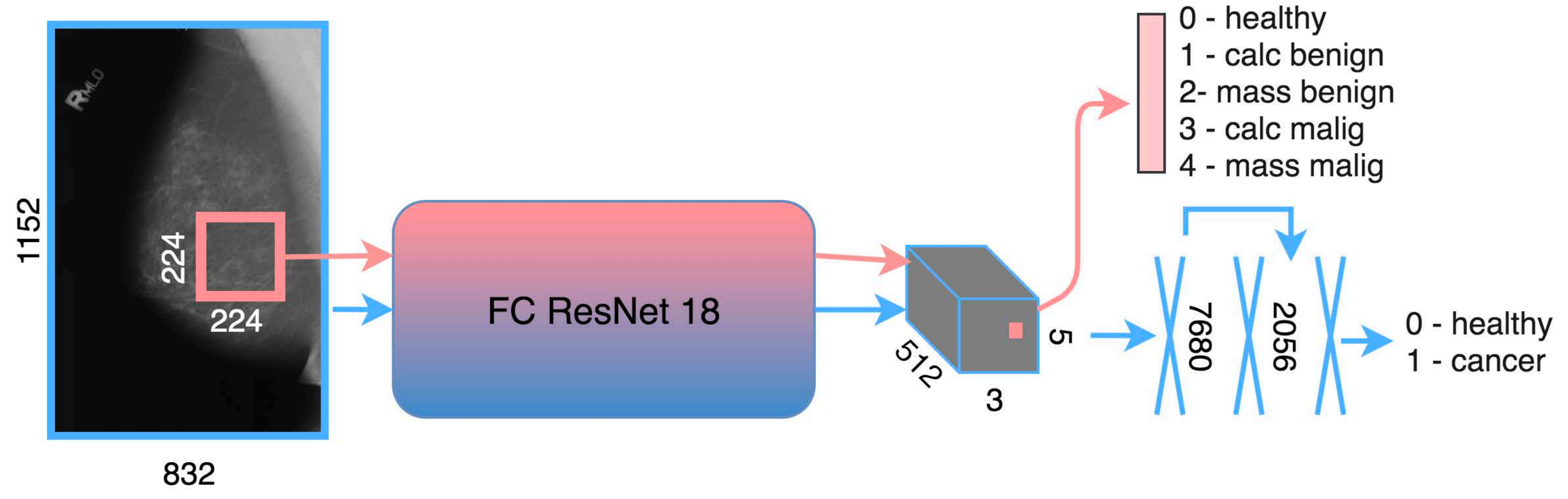

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Modeling: Base Architecture

- Many valid options:
  - VGG, ResNet, Wide-ResNet, DenseNet…
- Fully convolutional variants (like ResNet) are the easiest to transfer across resolutions.
  - Use ResNet-18 as base for speed/performance trade-off.

Modeling: Building Batches

- **Build Balanced Batches:**
  - Avoid model forgetting
- Bigger batches means **less noisy stochastic gradients**

$$w := w - \eta \nabla Q(w) = w - \eta \sum_{i=1}^{n} \nabla Q_i(w)/n,$$

  - Makes 2-stage training unnecessary.
- Trade-off: the bigger the batches, the slower the training

bs	tr acc	dev acc	dev auc	test acc	test auc
PACNN					
2	73.98%	72.32%	0.80	70.61%	0.74
4	85.84%	81.19%	0.89	77.33%	0.83
10	85.25%	80.64%	0.89	77.60%	0.83
16	84.79%	79.72%	0.89	77.47%	0.84
ResNet18 on image size 832 × 1152					
2	65.09%	67.60%	0.71	68.28%	0.63
4	77.74%	74.62%	0.82	71.58%	0.75
10	85.34%	79.29%	0.87	79.16%	0.83
16	82.44%	79.53%	0.89	74.67%	0.82

Old Experiments on Film Mammography Dataset

Modeling: Key Choices

- How do we make the model actually **learn**?
  - Initialization
  - Optimization / Architecture Choice
- **How to use the model?**
  - Aggregation across images
  - Triage Threshold
  - Calibration

Modeling: Actual Choices

- How do we make the model learn?
  - Initialization
    - **ImageNet Init**
  - Optimization
    - Batch size: **24**
    - **2** steps on **4** GPUs for each optimizer step
    - Sample **balanced batches** with **data augmentation**
  - Architecture Choice
    - **ResNet-18**

Modeling: Actual Choices (Continued)

- Overall Setup:
  - Train Independently per Image
    - From each image, predict cancer in that breast
  - Get prediction for whole mammogram exam by taking max across Images
  - At each Dev Epoch, evaluate ability of model to Triage
  - **Use the model that can do Triage best on the development set.**

Not necessarily the highest AUC

Modeling: How to actually Triage?

- **Goal:**
  - Don’t miss a single cancer the radiologist would have caught.
- **Solution:**
  - Rank radiologist true positives by model-assigned probability
  - Return min probability of radiologist true positive in development set.

Modeling: How to calibrate?

- **Goal:**
    - Want model assigned probabilities to correspond to real probability of cancer.
        - Why is this a problem?
            - Model trained artificial incidence of 50% for optimization reasons.
- **Solution:**
    - Platt's Method:
        - Learn sigmoid to scale and shift probabilities to real incidence on the development set.

Triaging Mammograms

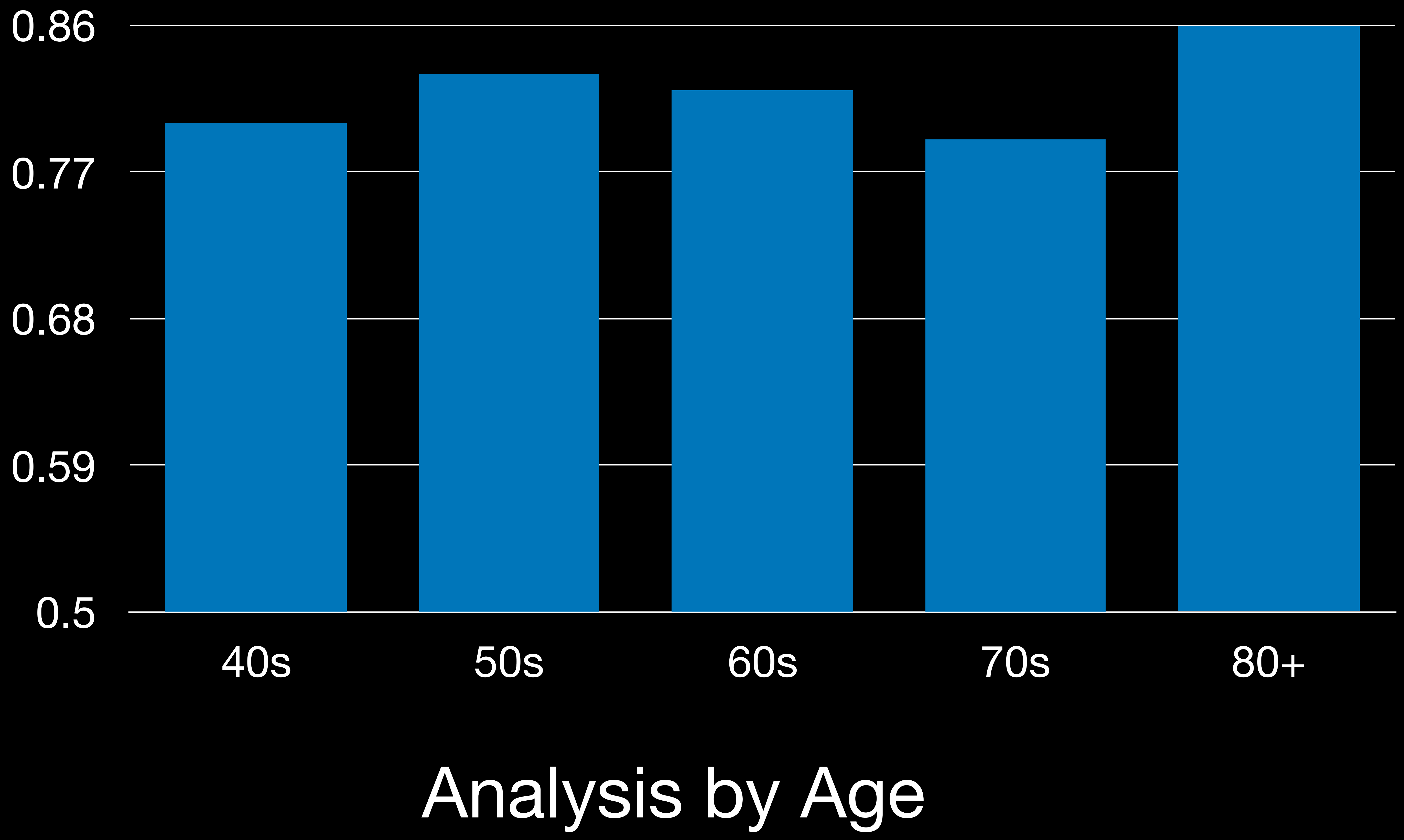
- The plan
  - Dataset Collection
  - Modeling
  - **Analysis**

Analysis: Objectives

- Is the model discriminative across all populations?
    - Subgroup Analysis by **Race**, **Age**, **Density**
- How does model relate to radiologist assessments?
- Simulate actual use of Triage on the Test Set

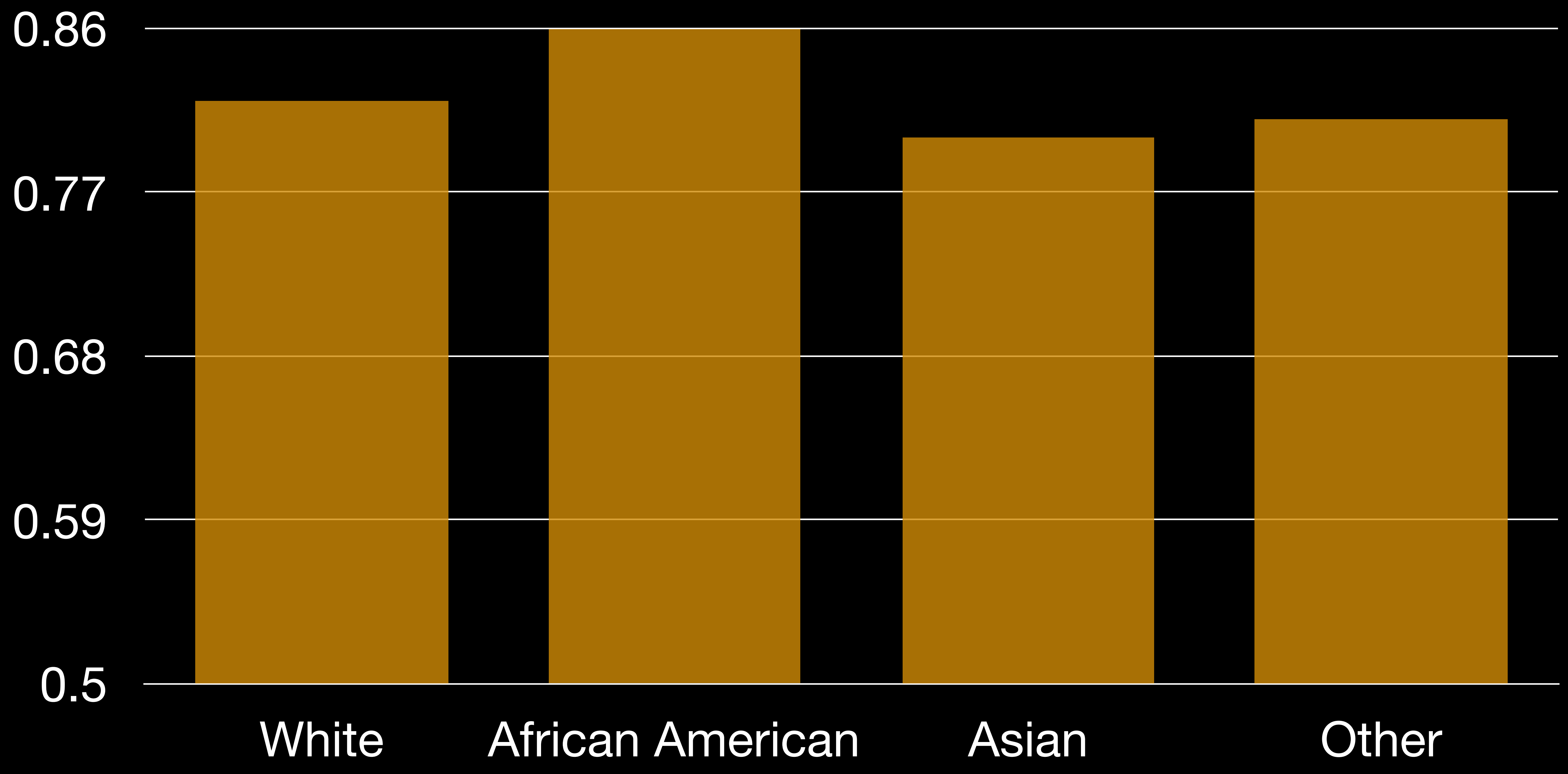
Analysis: **Model AUC**

Overall AUC: **0.82 (95%CI .80, .85)**



Analysis: Model AUC

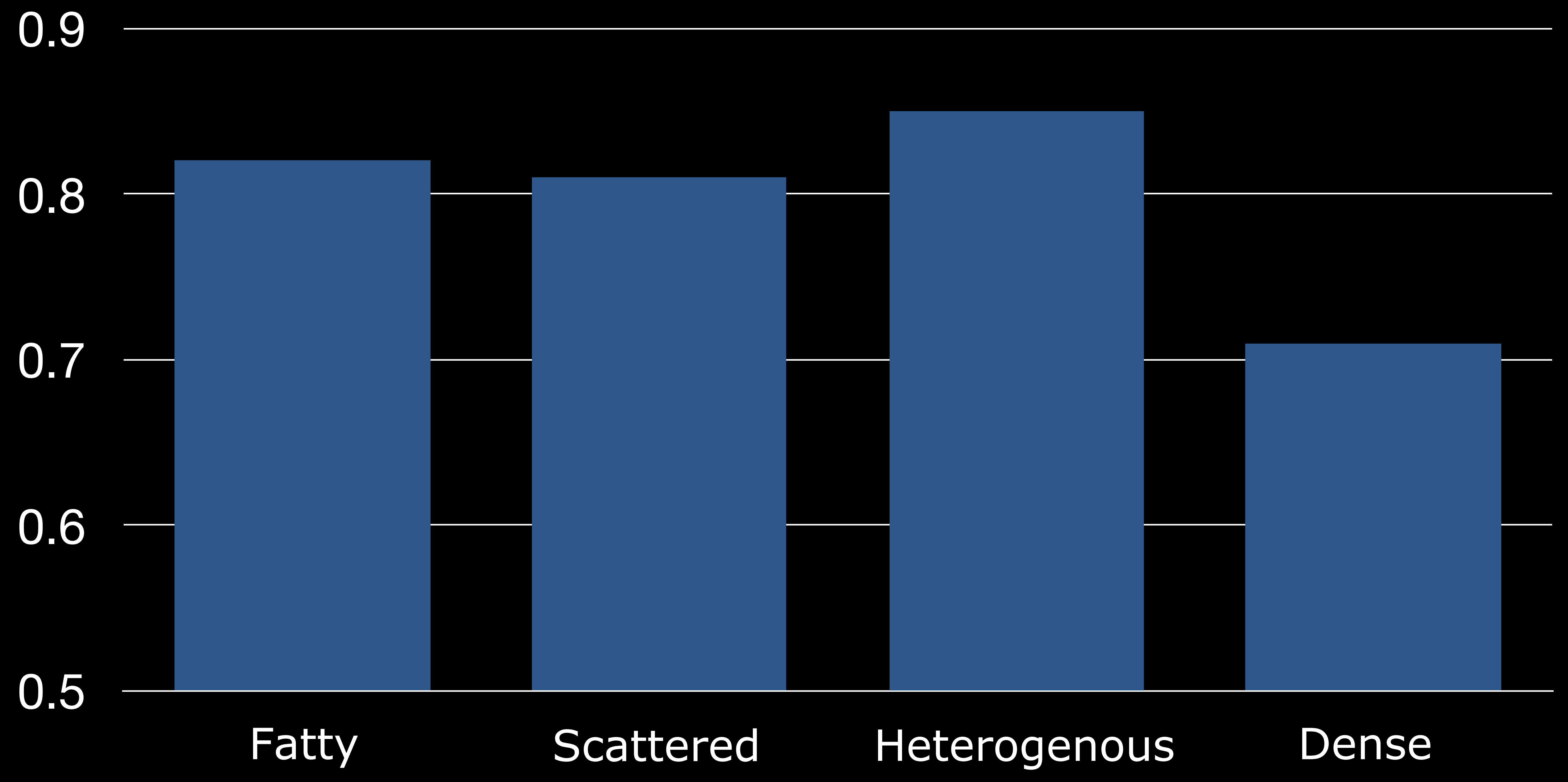
Overall AUC: **0.82 (95%CI .80, .85)**



Analysis by Race

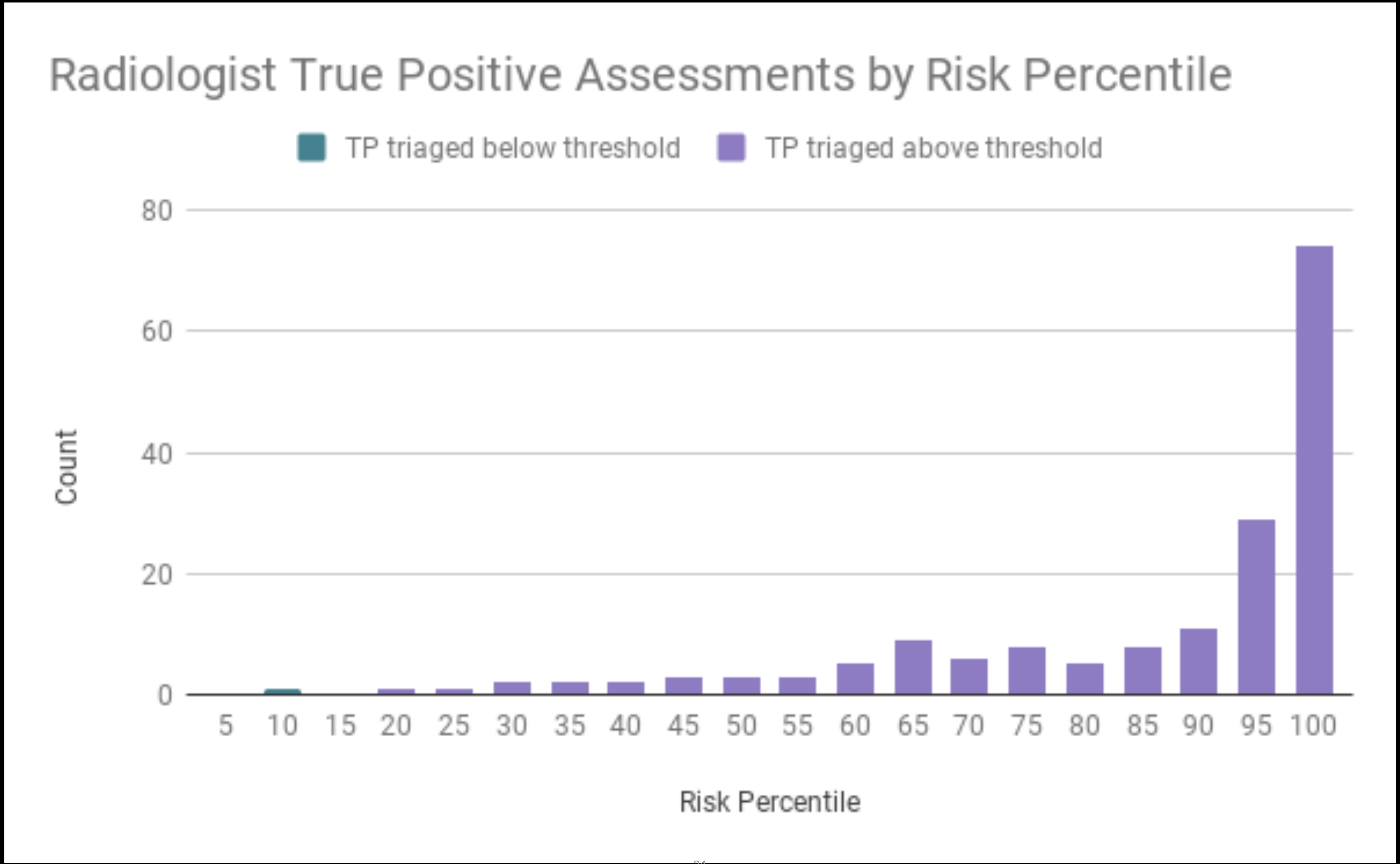
Analysis: Model AUC

Overall AUC: **0.82 (95%CI .80, .85)**

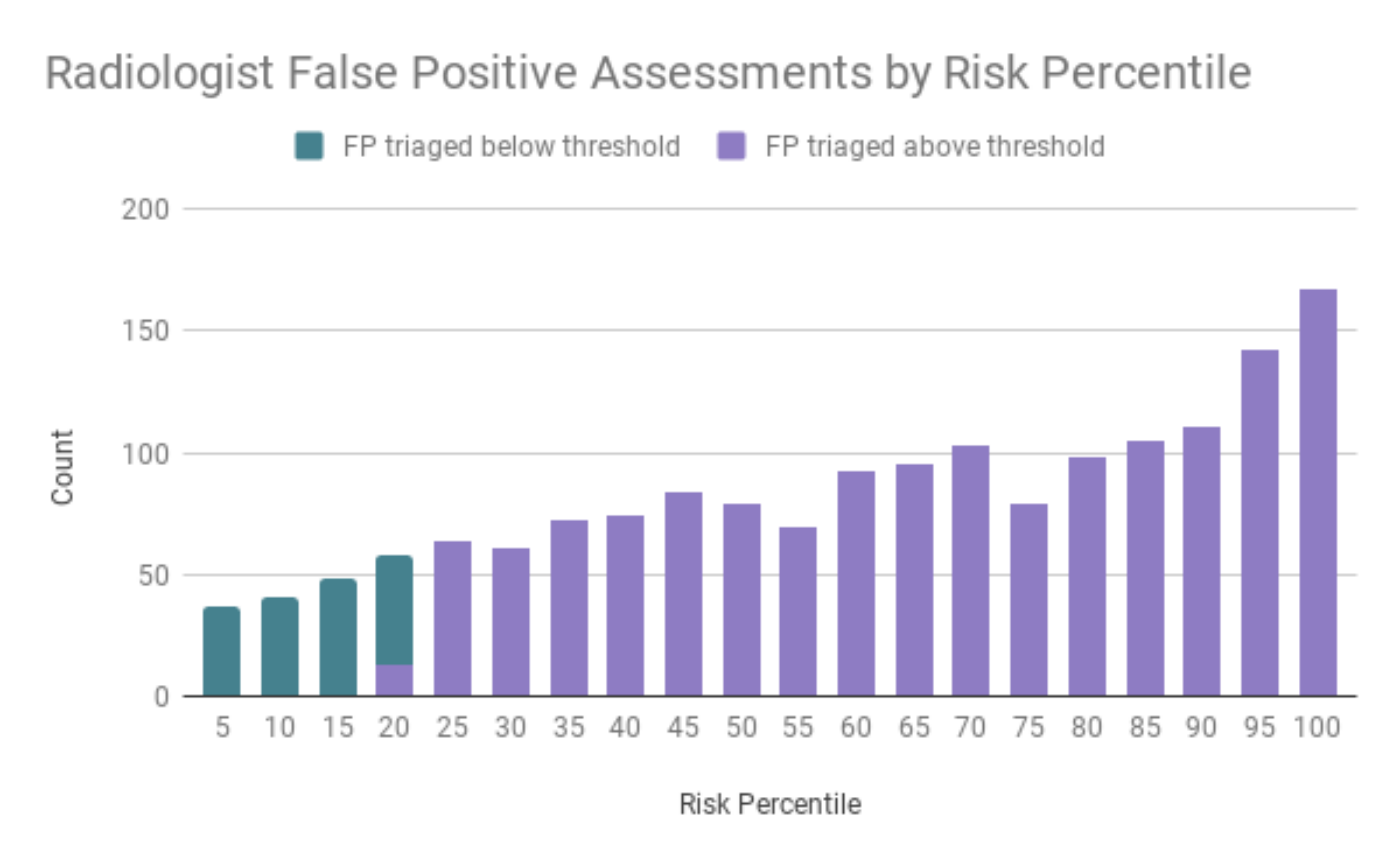


Analysis by Density

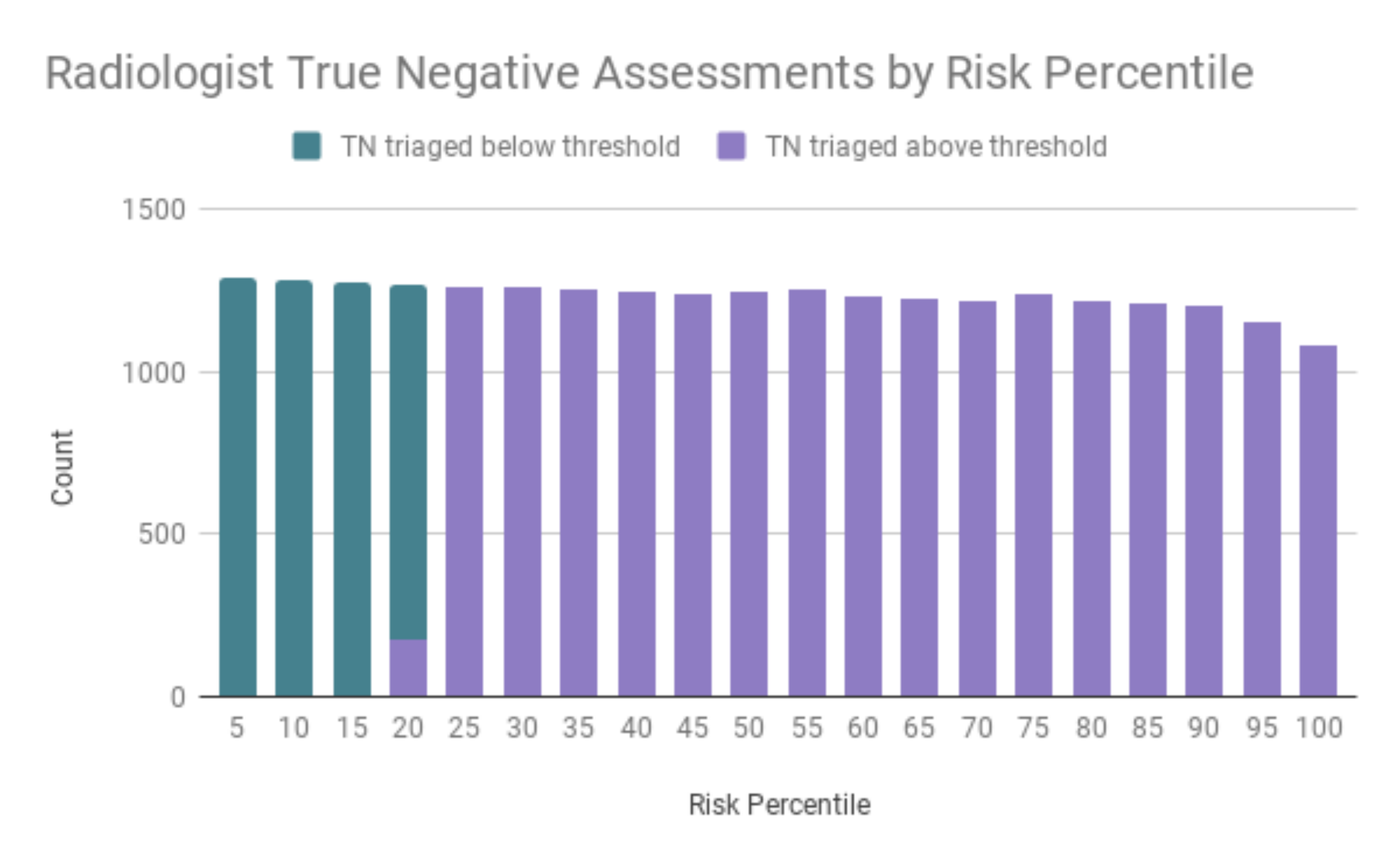
Analysis: Comparison to radiologists



Analysis: Comparison to radiologists



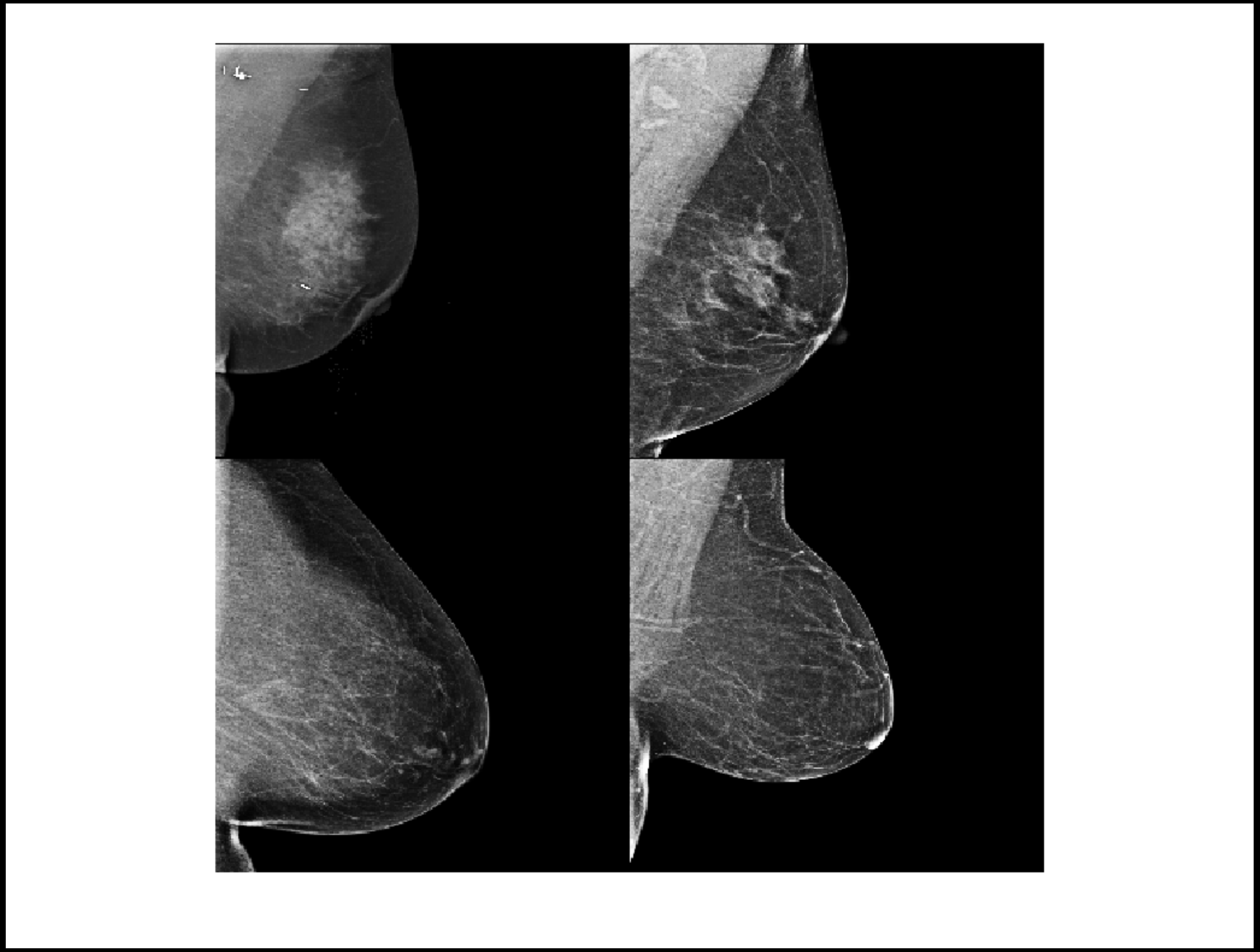
Analysis: Comparison to radiologists

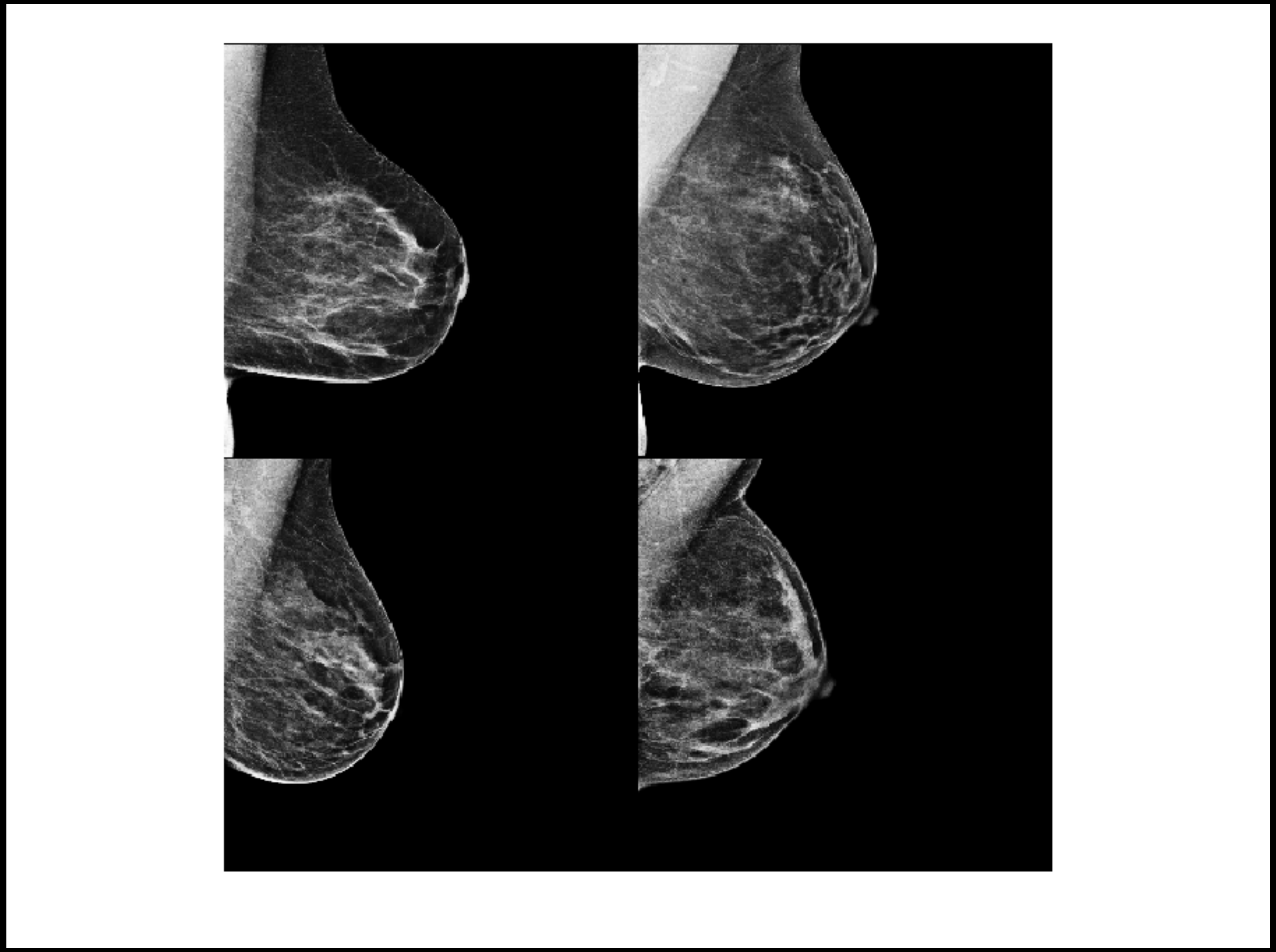


Analysis: Simulating Impact

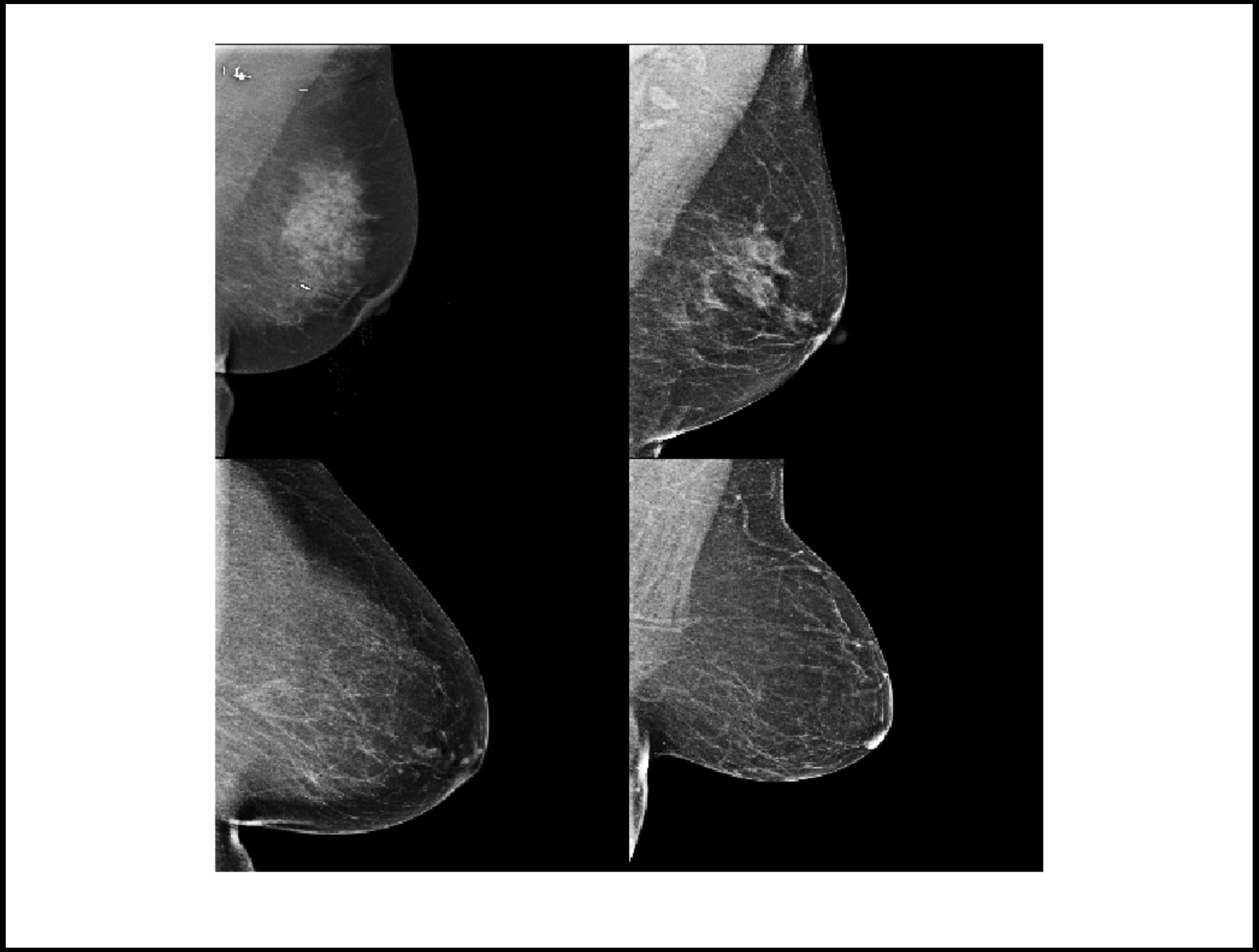
Setting	Sensitivity (95% CI)	Specificity (95% CI)	% Mammograms Read (95% CI)
Original Interpreting Radiologist	90.6% (86.7, 94.8)	93.0% (92.7, 93.3)	100% (100, 100)
Original Interpreting Radiologist + Triage	**90.1% (86.1, 94.5)**	**93.7% (93.0, 94.4)**	**80.7% (80.0, 81.5)**

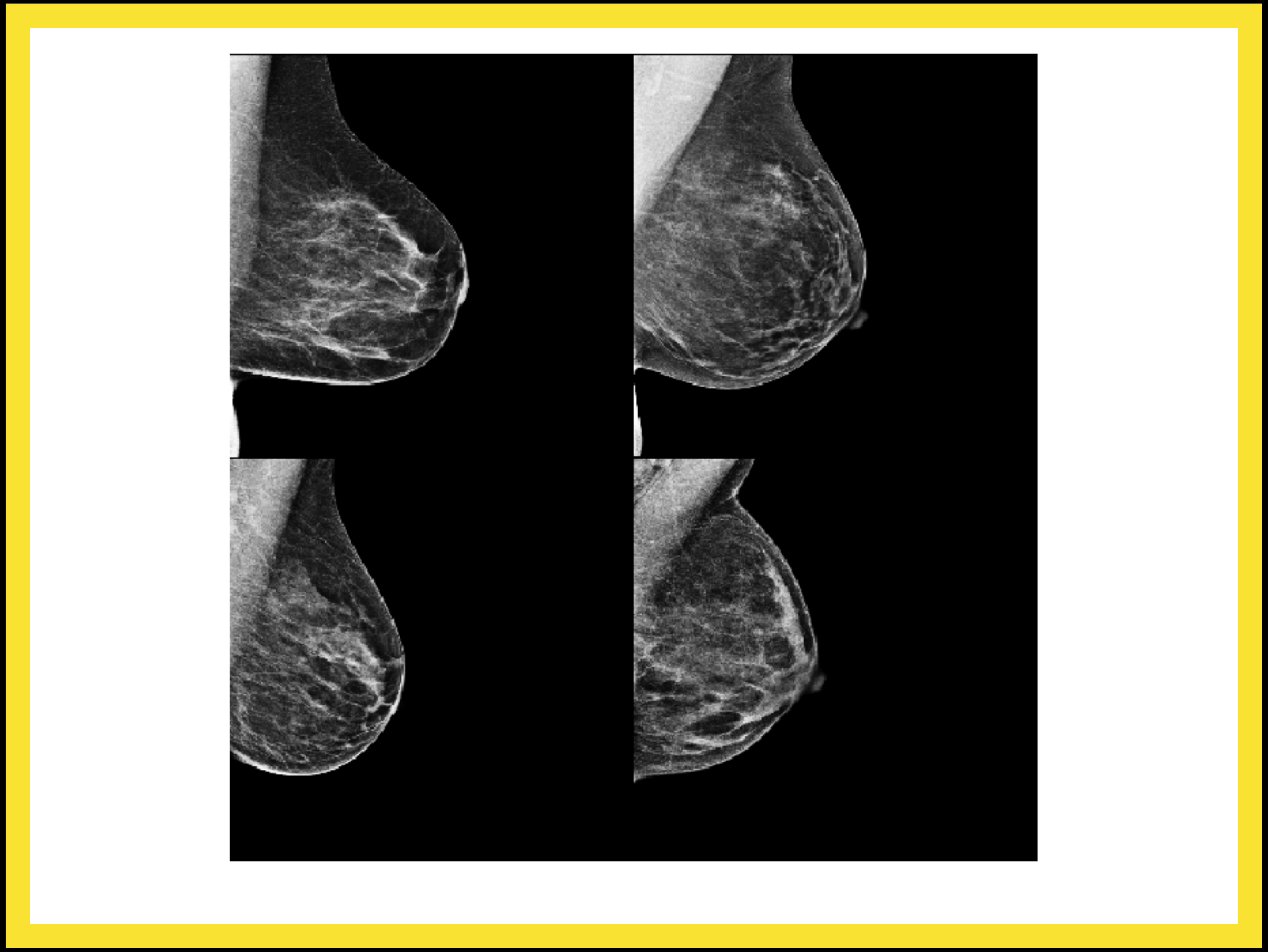
Example: Which were triaged?





Example: Which were triaged as cancer-free?





Next Step: Clinical Implementation

Agenda

- Interpreting Mammograms
  - Cancer Detection and Triage
- **Assessing Breast Cancer Risk**
- How to Mess up
- How to Deploy

Classical Risk Models: BCSC

Age

Family History

Prior Breast Procedure

Breast Density

Risk

AUC: **0.631**

AUC: 0.607 without Density

William E. Barlow, Emily White, Rachel Ballard-Barbash, Pamela M. Vacek, Linda Titus-Ernstoff, Patricia A. Carney, Jeffrey A. Tice, Diana S. M. Buist, Berta M. Geller, Robert Rosenberg, Bonnie C. Yankaskas, Karla Kerlikowske, "Prospective Breast Cancer Risk Prediction Model for Women Undergoing Screening Mammography," *Journal of the National Cancer Institute,* Vol. 98, No. 17, September 6, 2006. pp. 1204-14.

Assessing Breast Cancer Risk

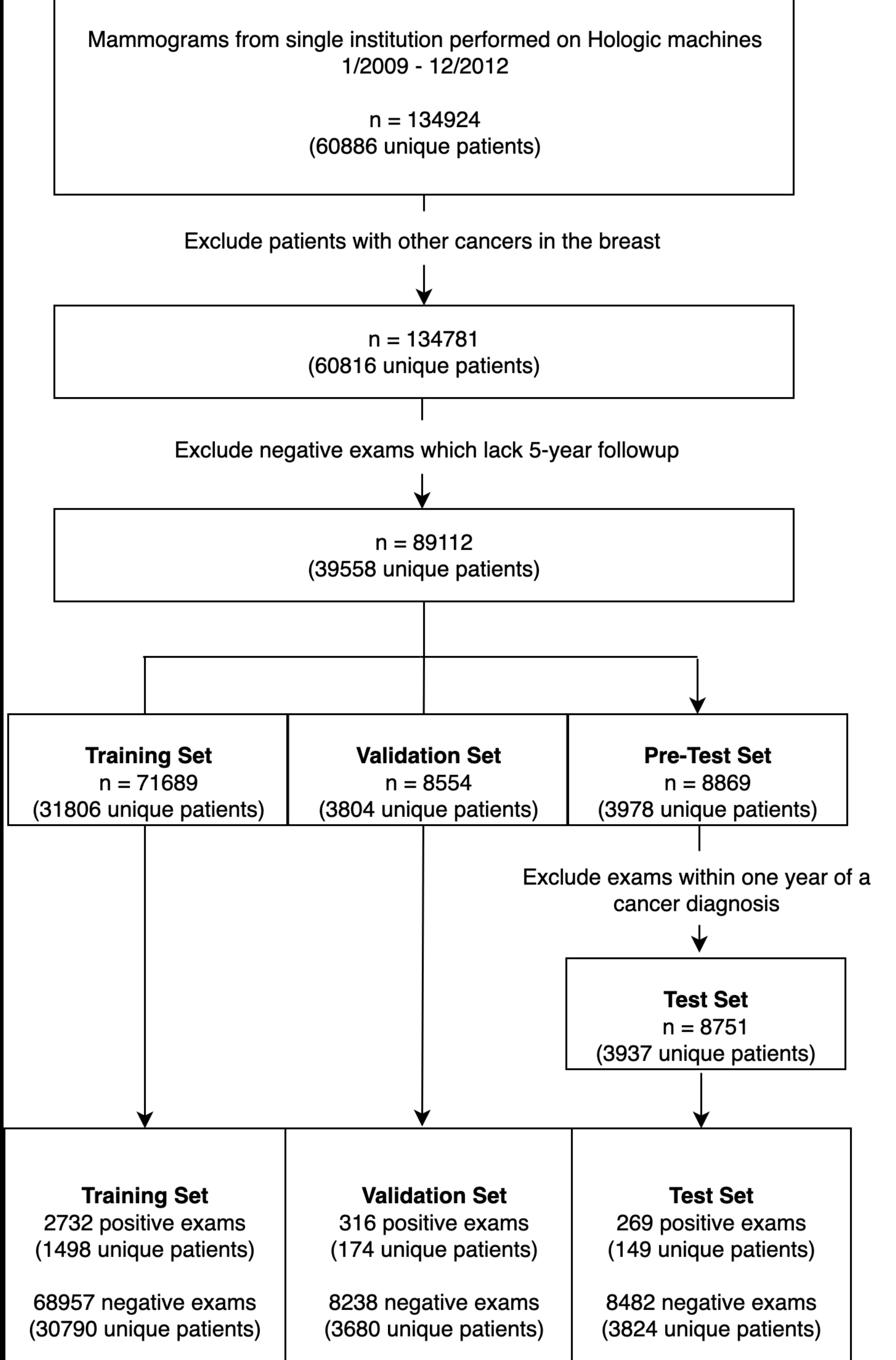
- The plan
  - **Dataset Collection**
  - Modeling
  - Analysis

Dataset Collection

- Consecutive Screening Mammograms
  - 2009-2012
- Outcomes from Radiology EHR, and Partners

5 Hospital Registry

- No exclusions based on race, implants etc.
- Exclude for followup for negatives
- Split into Train/Dev/Test by Patient



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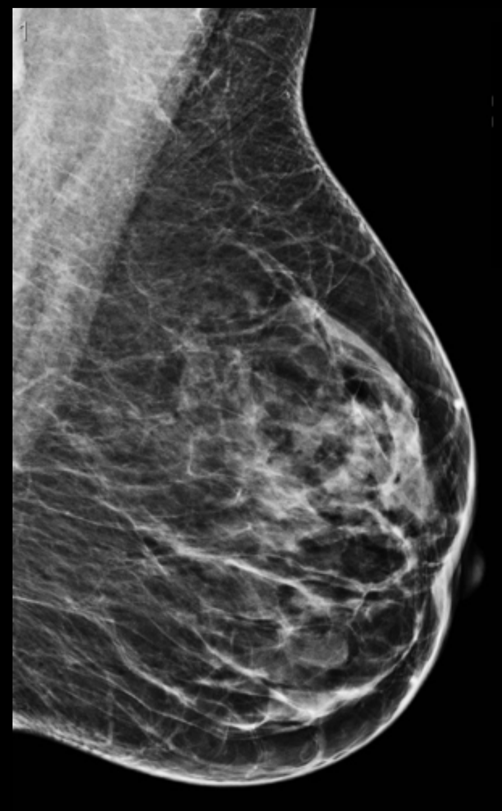
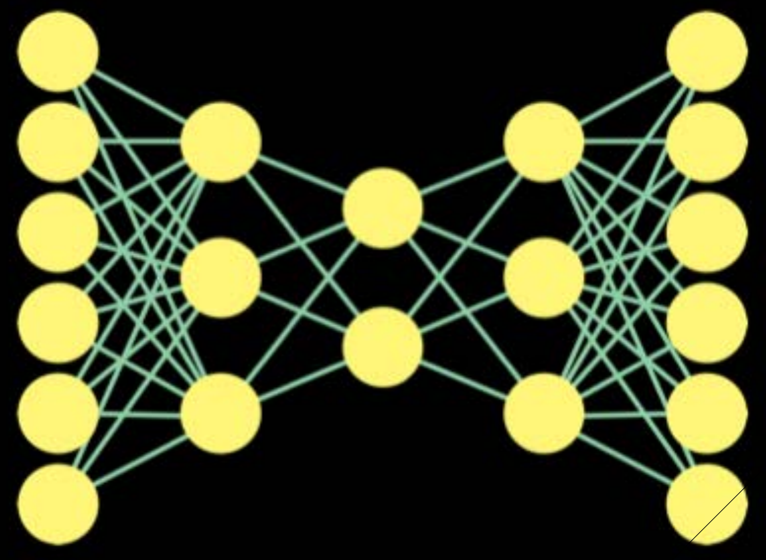
Modeling

- **ImageOnly**: Same model setup as for Triage
- **Image+RF :** ImageOnly + traditional Risk Factors at last layer trained jointly

Analysis: Objectives

- Is the model discriminative across all populations?
    - Subgroup Analysis by **Race**, **Menopause Status, Family History**
- How does this relate to classical approaches?





5 Year Breast Cancer Risk

Training Set:

Patients: 30,790
Exams: 71,689

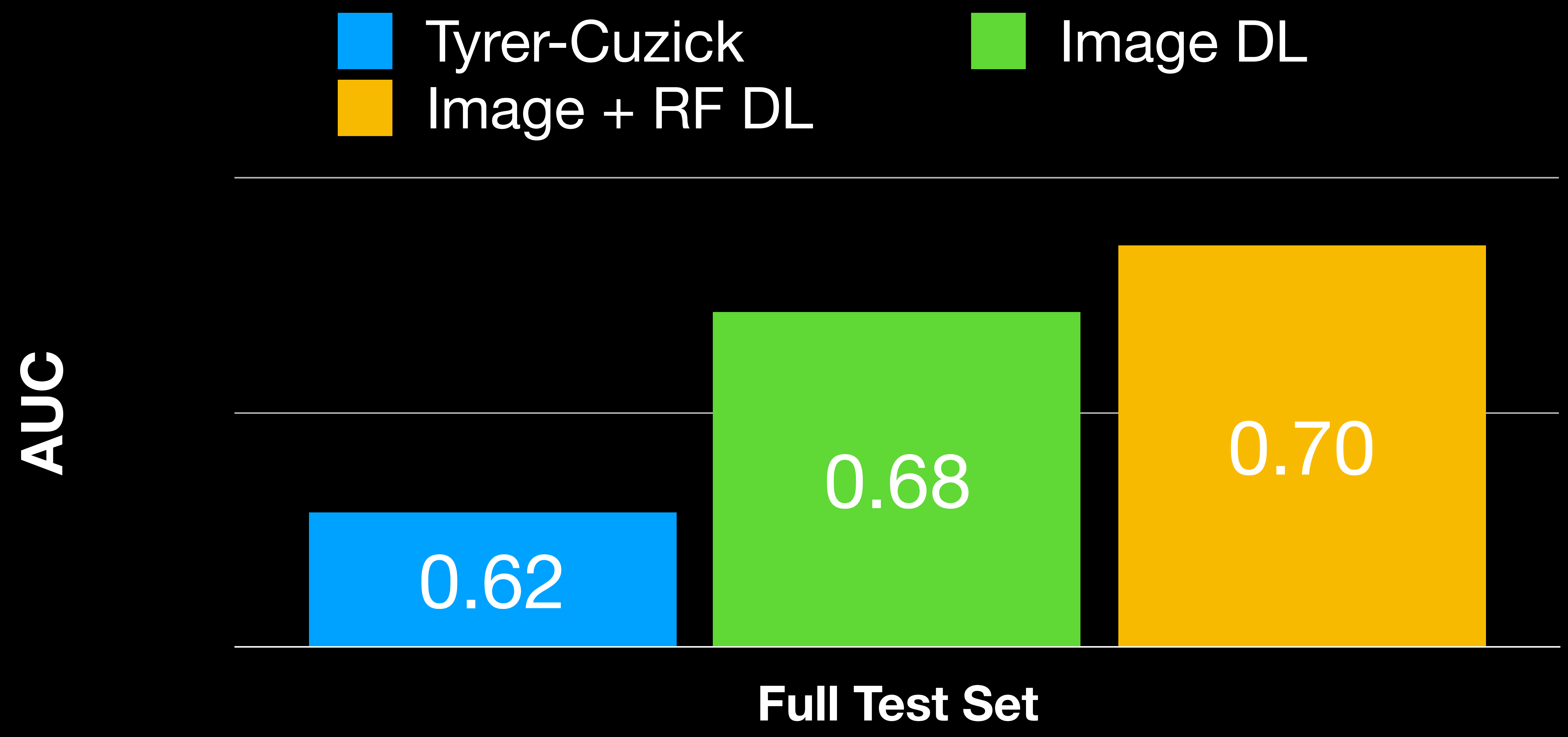
No Exclusions

Testing Set:

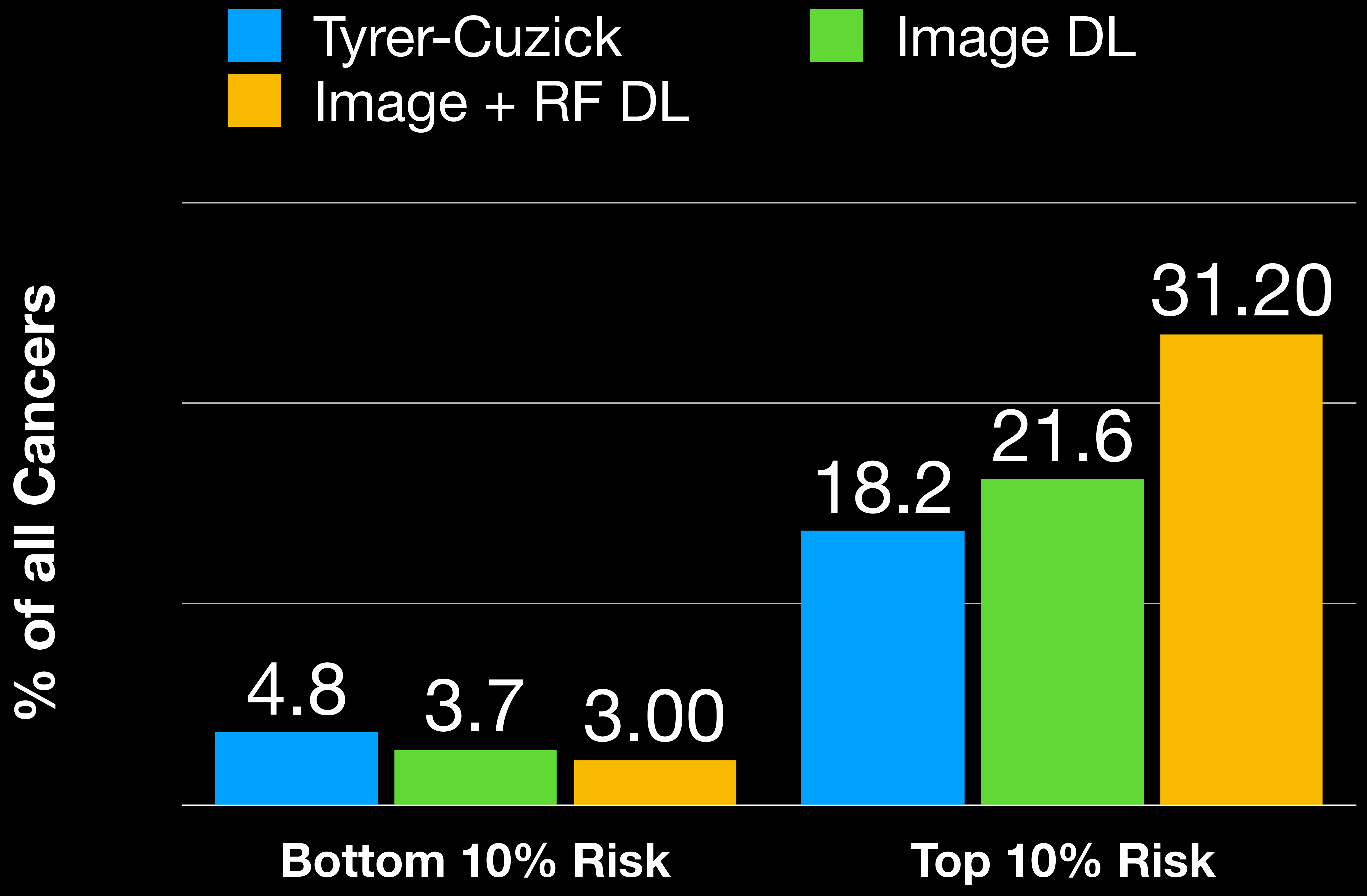
Patients: 3,937
Exams: 8,751

Exclude Cancers within 1 Year of mammogram

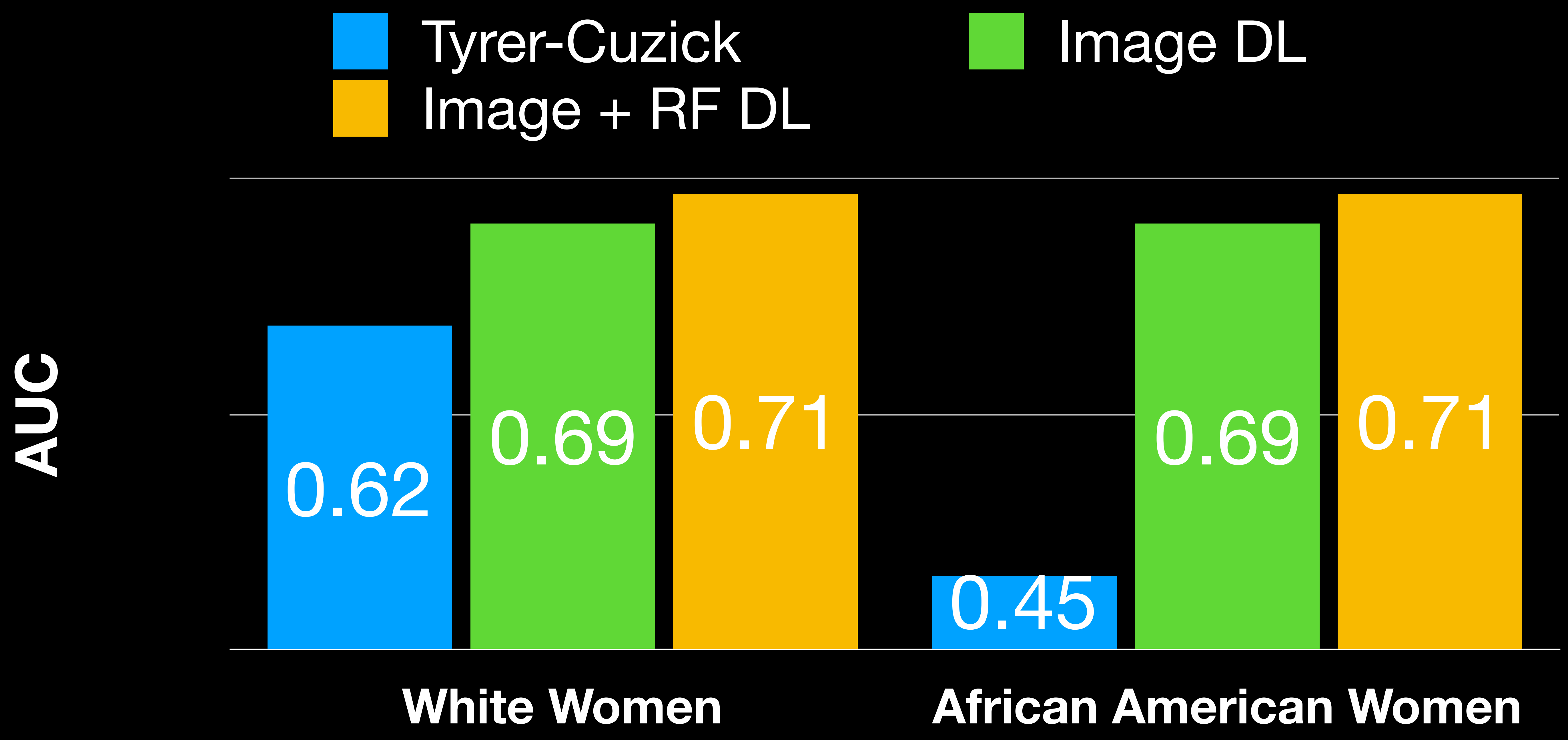
Performance



Performance



Performance



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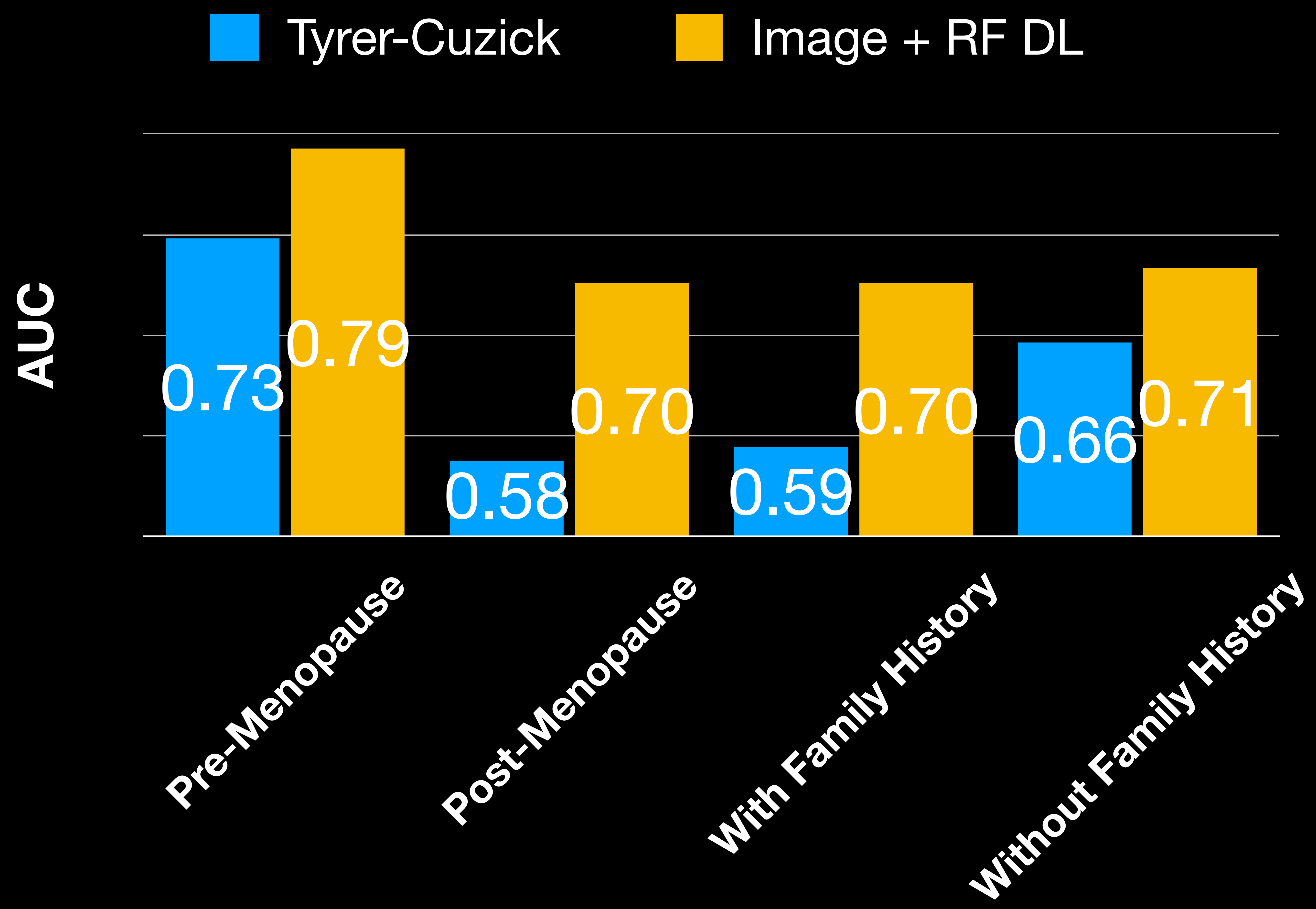

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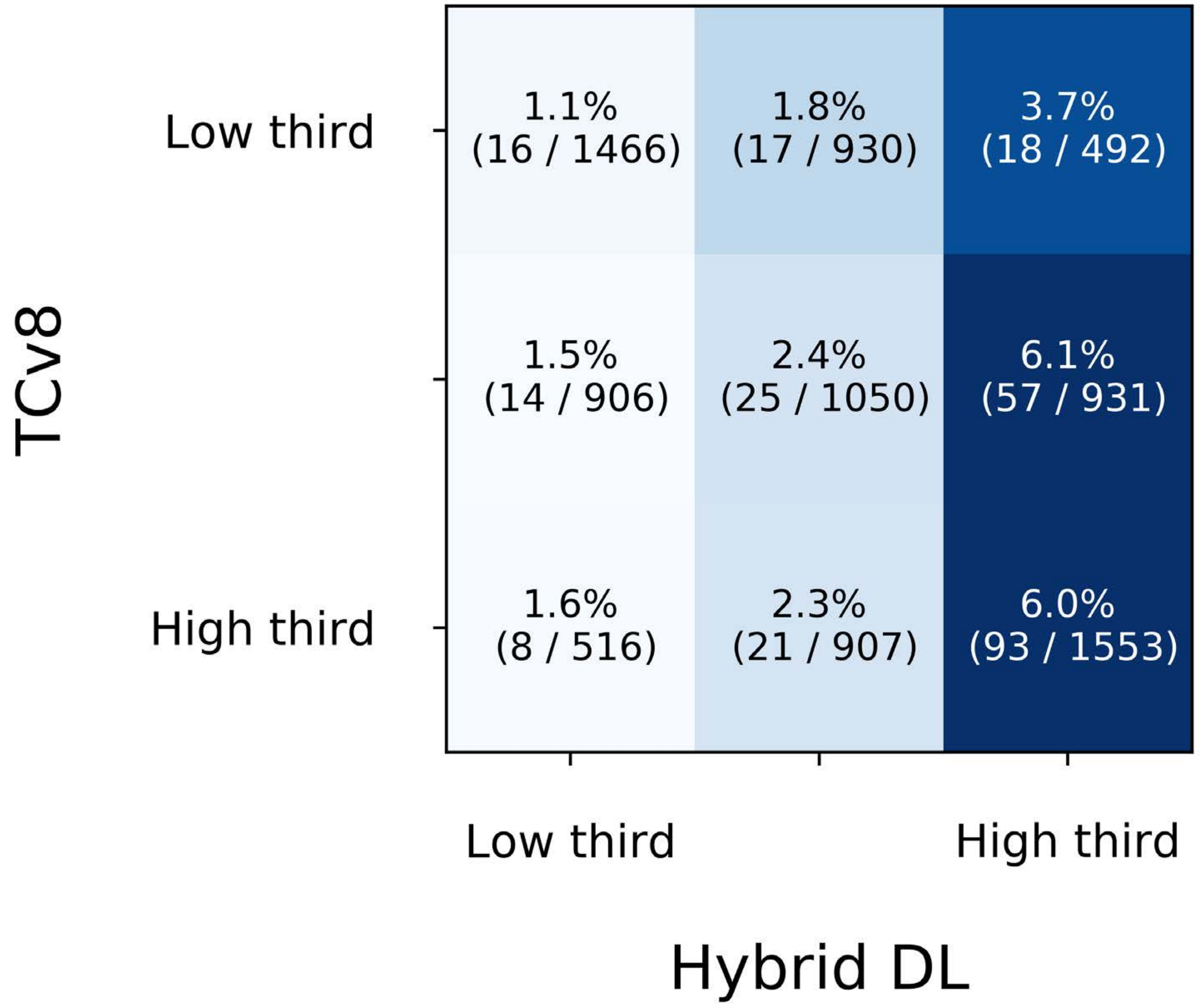

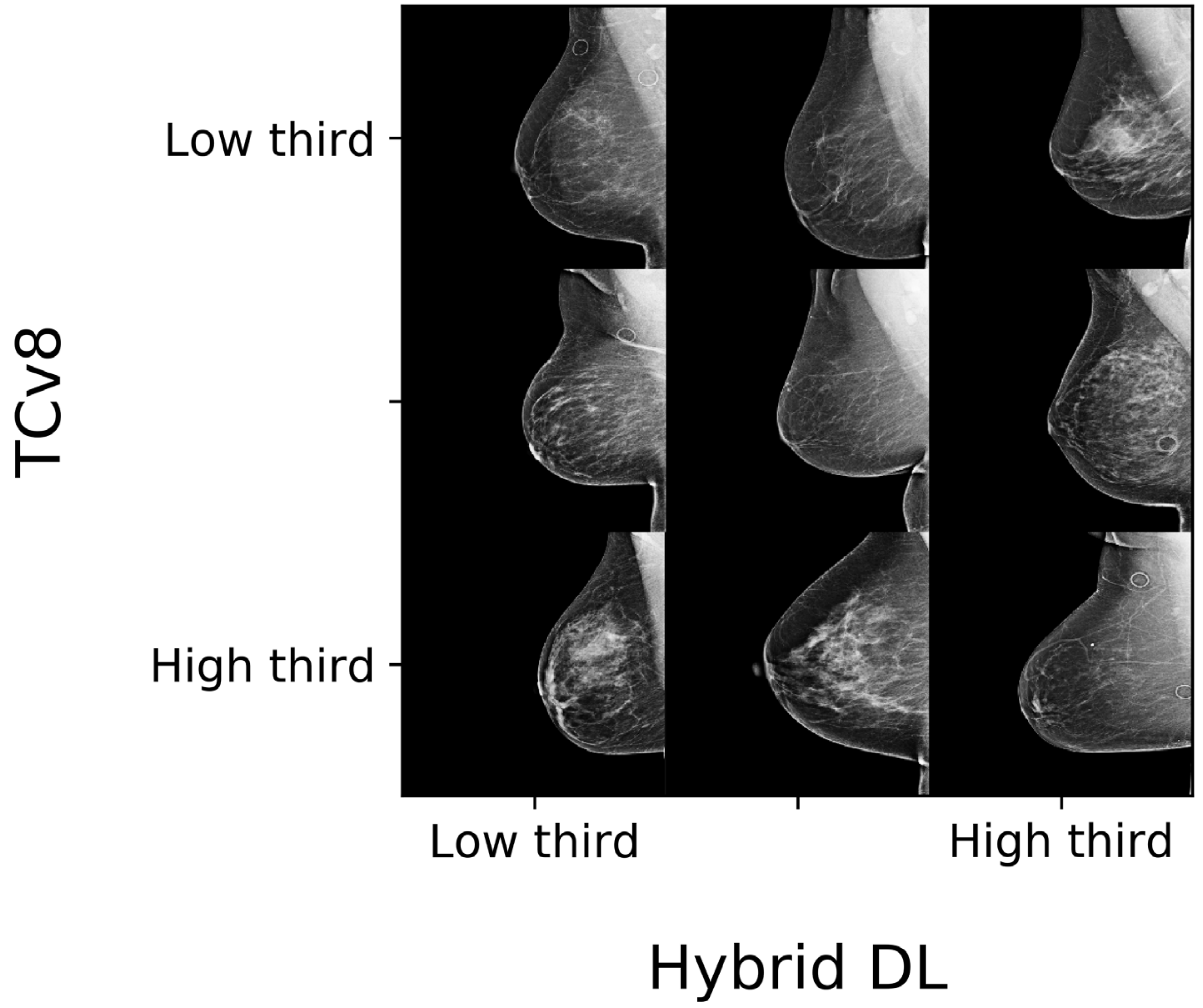

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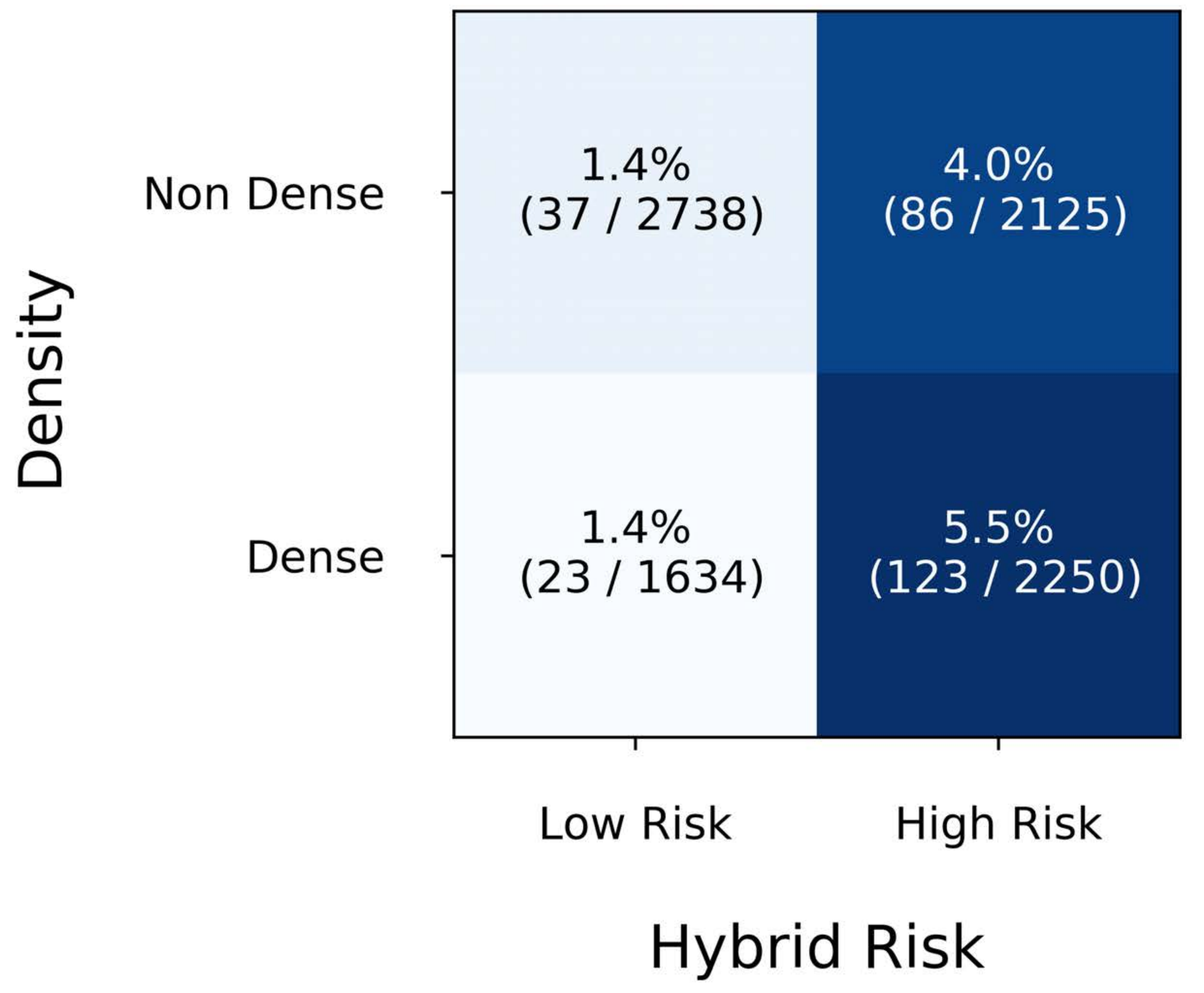
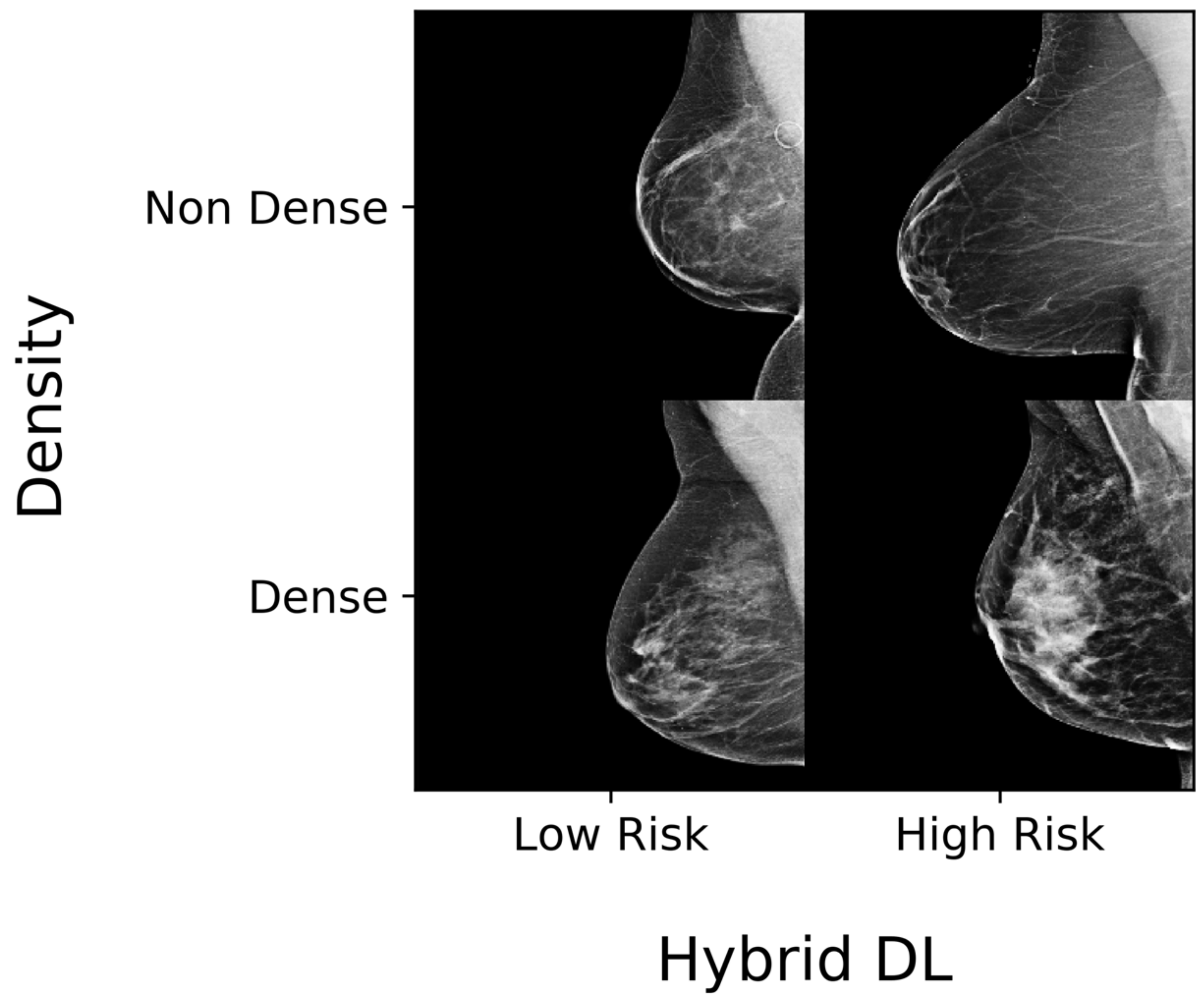
Performance





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Next Step: Clinical Implementation

Agenda

- Interpreting Mammograms
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  - Assessing Breast Density
- Assessing Breast Cancer Risk
- **How to Mess Up**
- How to Deploy

How to Mess Up

- The many ways this can go wrong:
  - **Dataset Collection**
  - Modeling
  - Analysis

How to Mess Up: **Dataset Collection**

- Enriched Datasets contain nasty biases
    - **Story**: Emotional Rollercoaster in Shanghai
        - Dataset with all Cancers collected first.
        - Negatives collected consecutively from 2009-2016
- Use old images (Film mammography) or datasets with huge tumors.
- Use a dataset without tumor registry linking.
- Is your dataset reflective of your actual use-case?

How to Mess Up: **Modeling**

- Assume the model will be Mammography Machine invariant
    - Now exploring conditional-adversarial training…

How to Mess Up: **Analysis**

- Only Test your model on White women and exclude *inconvenient* cases
    - Common standard in classical risk models; can’t assume model will transfer.
- Assume ***reader study = clinical implementation***

Agenda

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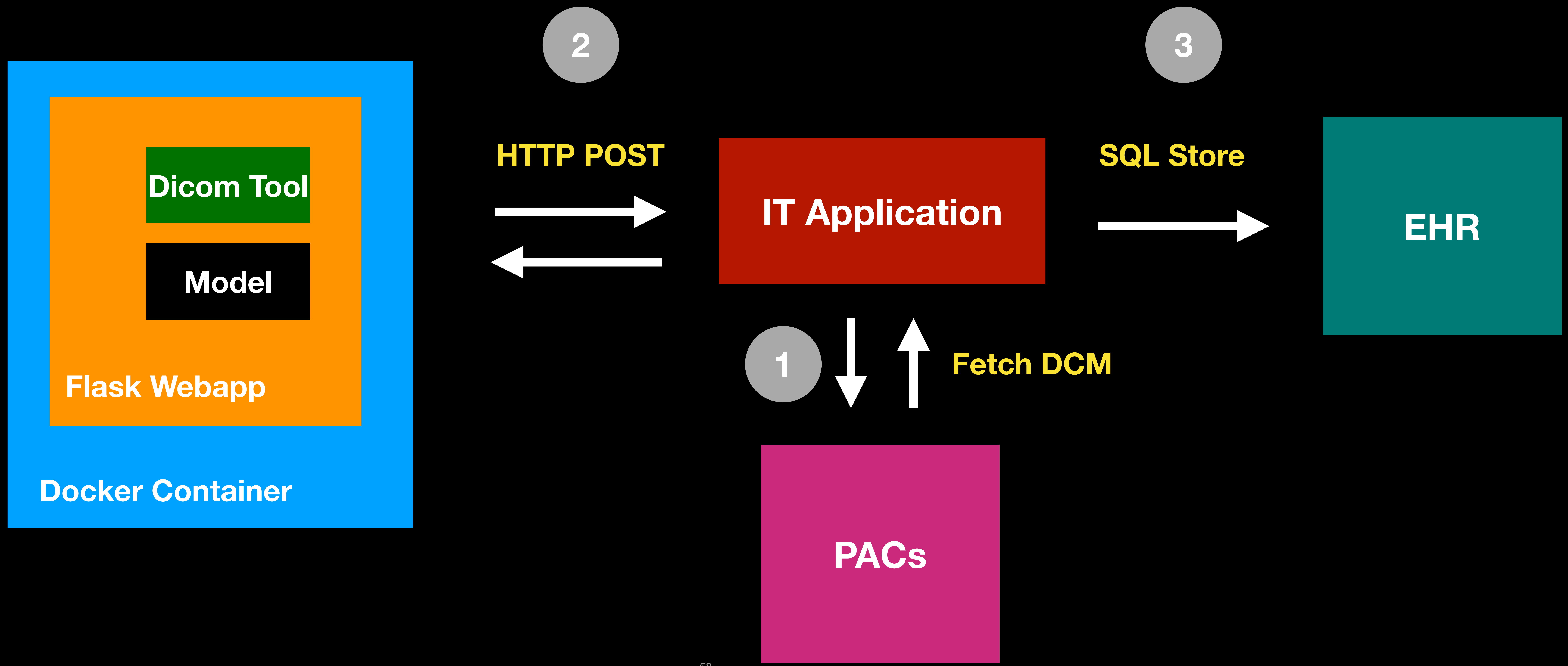
- **How to Deploy**

How to Deploy?



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