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Daniel Shao
Case Western Reserve University

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Nuclear Shape of ER+ Breast Tumor Whole Slide Images Predict Recurrence and Survival

Daniel Shao
Mentored by Dr. Anant Madabhushi, Dr. Cheng Lu
Case Western Reserve University
Center for Computational Imaging and Personalized Diagnostics

Breast Cancer Prognosis

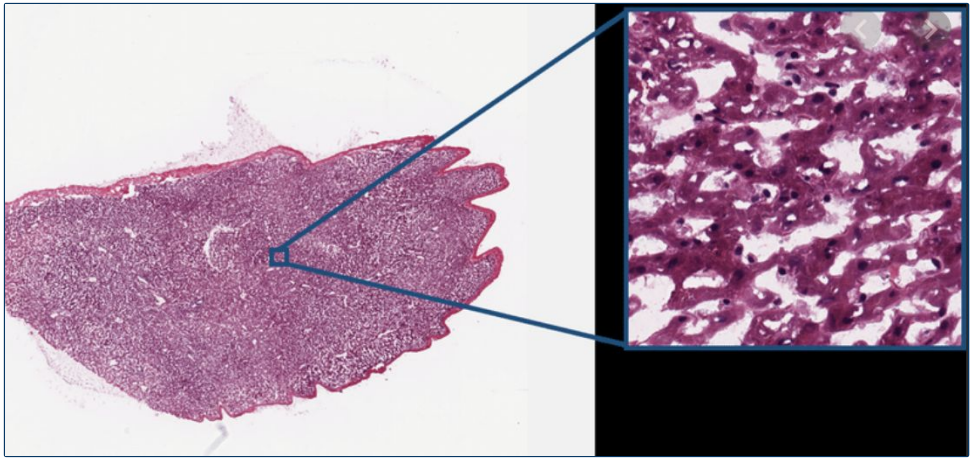
Surgical removal

How aggressive is the tumor?

- Lymph Node Involvement
- Receptor status
- Tumor Pathology

Quantitative Analysis

- Computer-analyzed features
- Machine Learning



Motivation

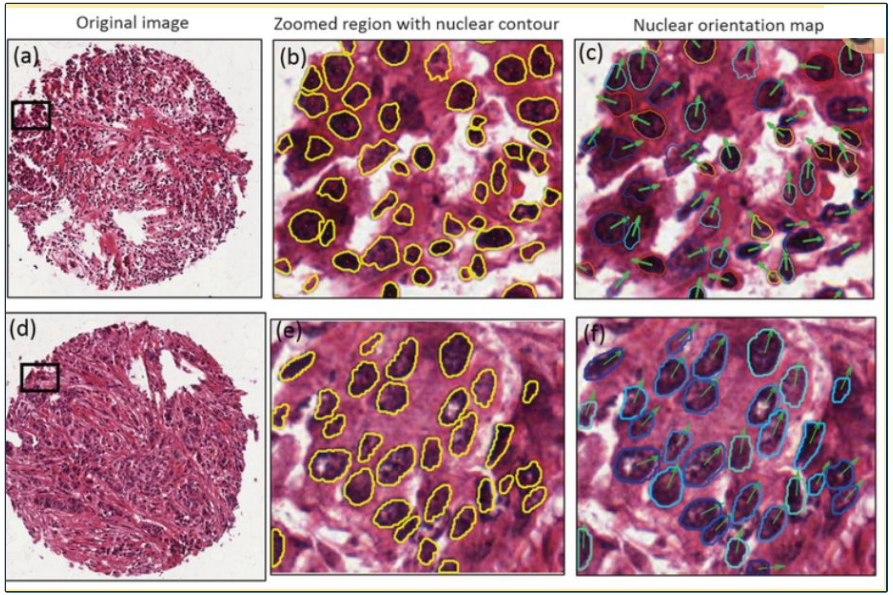
Challenges of Machine Learning approach:

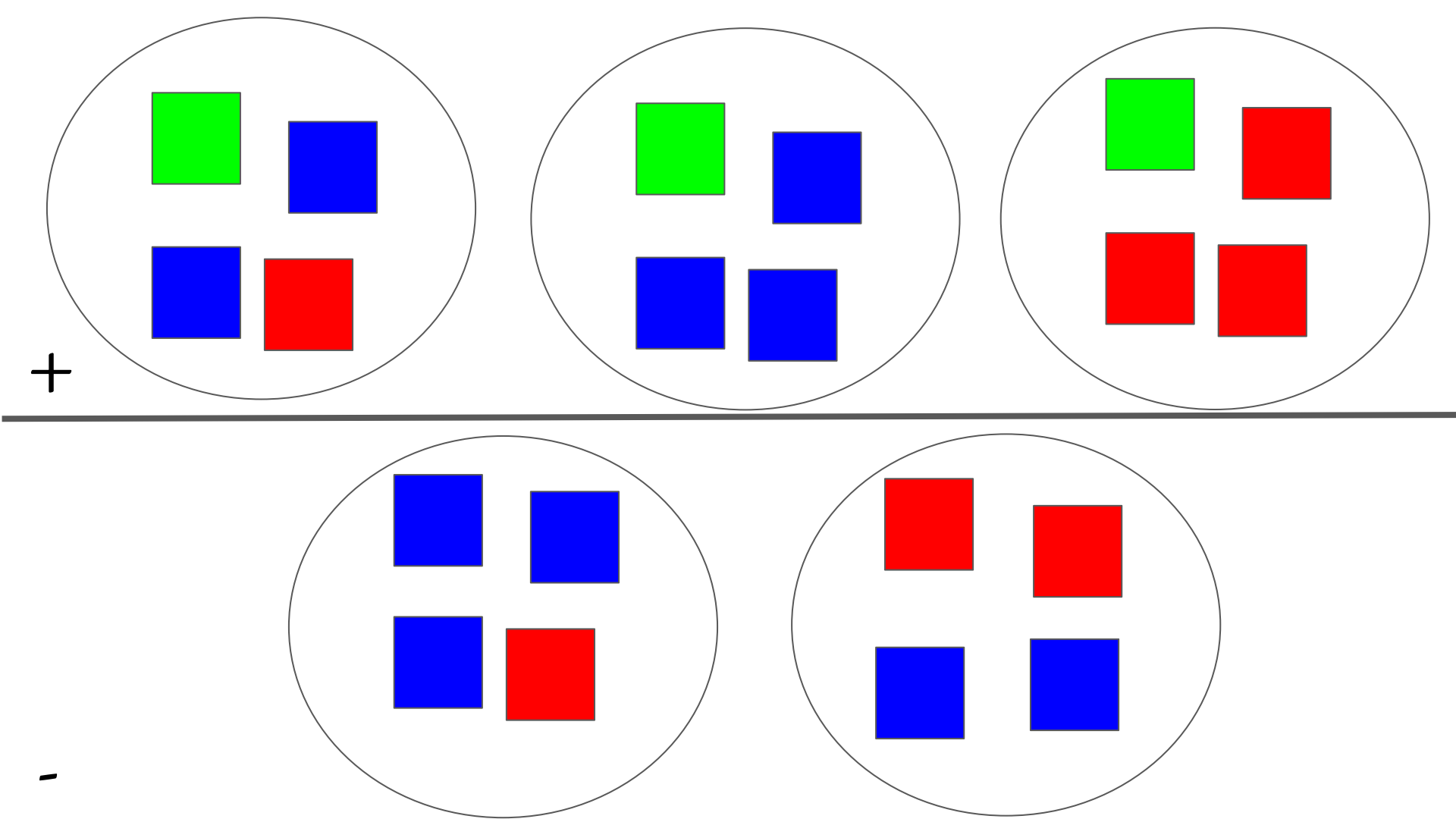
- Region of interest
- Feature relevance

Is Multiple Instance Learning appropriate?

- finds most indicative region on image

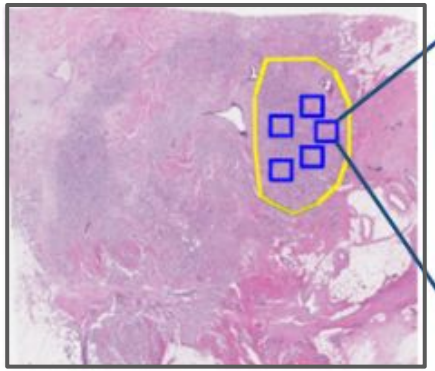
How prognostic is nuclear shape?



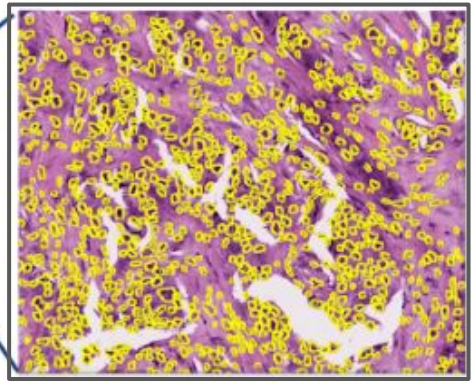


Design

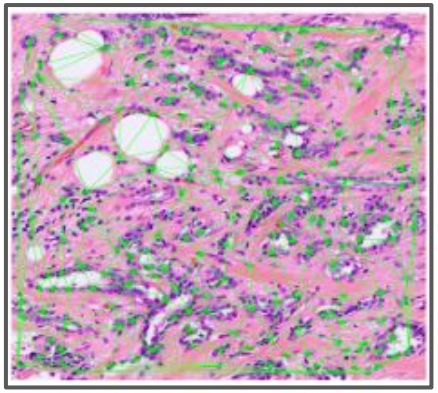
Five 2000x2000 patches from tumor regions of WSI



→ Nuclear Segmentation →



Feature extraction of 120 nuclear features →



Feature Selection

↓

Model Training

↓

Evaluation

Simplifying Multiple Instances

Intuition: get one feature vector per patient

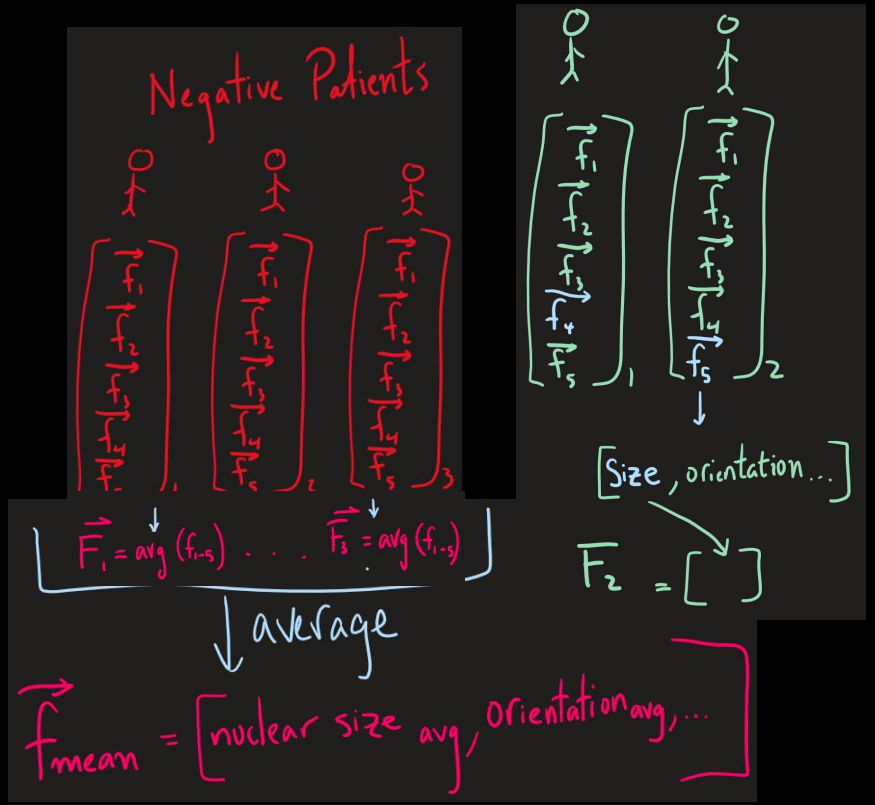
Negative patients: all patches are informative

Positive patients: most different patch

Computation:

Construct vector F of feature values for each patient

- Negative patients: mean feature of all patches
- Positive patients: Most distant patch from mean of negatives



Training and Evaluation

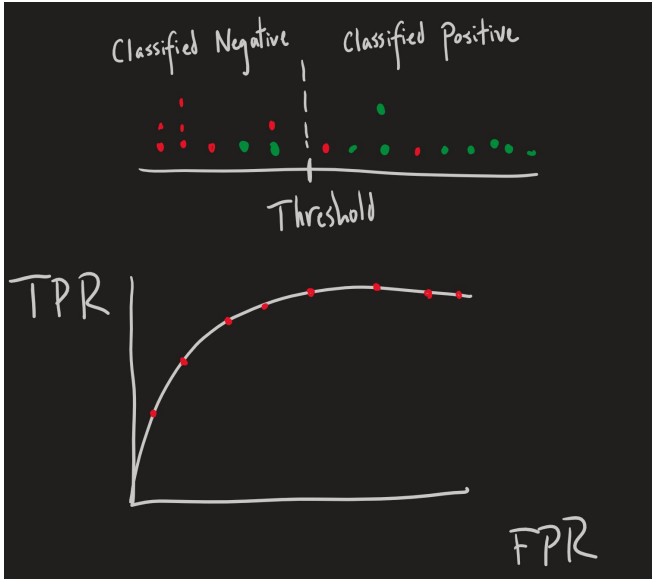
Evaluation

Construct Receiver Operating Curve

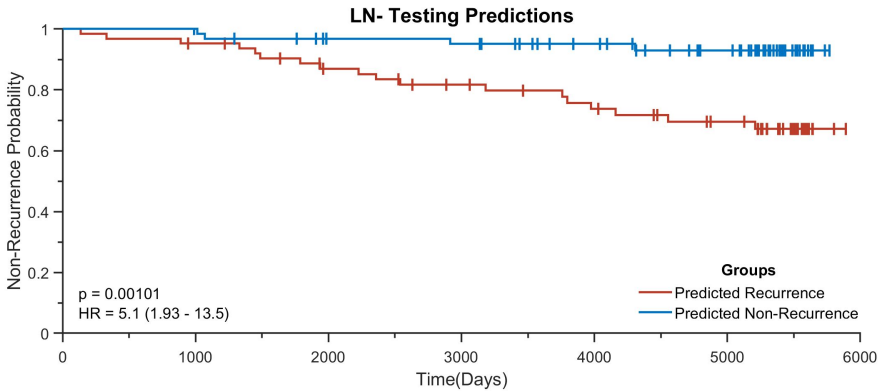
Threshold = unique feature values in F

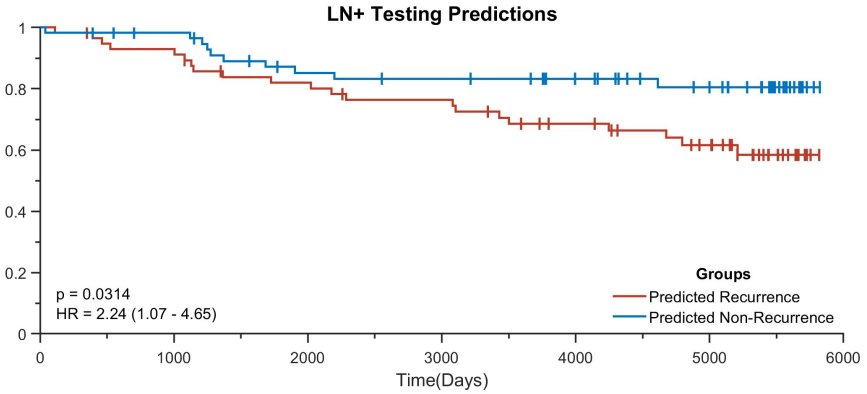
for each threshold, get coordinate (TPR, FPR)

construct line from coordinates and compute area under curve



Kaplan-Meier survival analysis





LN Status of Train/Test set	Multivariate Hazard Ratio (95% Confidence Interval), p-value
LN-	HR=4.64 (1.32 – 16.3) p=0.017
LN+	HR=2.36 (1.09 – 5.11) p=0.029

HER2 status, PR status, tumor grade, size, age

Discussion

- Multiple Instance Learning appropriate
- Nuclear shape an independent prognostic
- Nuclear size, orientation, texture, and contour most discriminative
- Lymph node negative survival better correlated to nuclear shape

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