Image-Based Models for Predicting Advanced Breast Cancer Risk

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Objective

Investigate imaging features associated with risk of advanced breast cancer

- Motivation
  - Advanced cancer is associated with poorer survival
  - Hawai‘i has a high rate of advanced-stage breast cancer
  - Risk models for advanced breast cancer are limited and do not include imaging information.

- Hypothesis - AI can fully interrogate images for any signals of advanced cancer risk

SEER Staging

Surveillance, Epidemiology, and End Results (SEER) Summary Staging

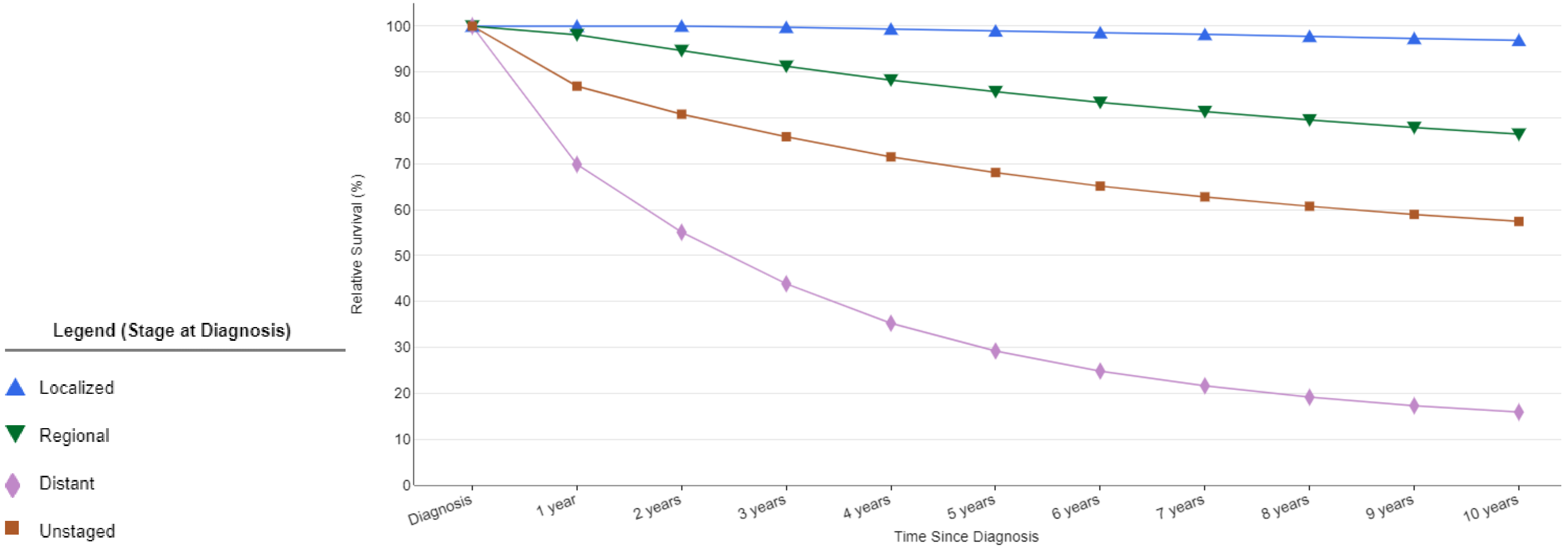
Code	Definition
0	*In situ*
1	Localized only
2	Regional by direct extension only
3	Regional lymph node involvement only
4	Regional by both direct extension and lymph node involvement
7	Distant site(s) involved

Stage	TNM
Stage 0	Tis, N0, M0
Stage IA	T1, N0, M0
Stage IB	T0, N1mi, M0
	T1, N1mi, M0
Stage IIA	T0, N1, M0
	T1, N1, M0
	T2, N0, M0
Stage IIB	T2, N1, M0
	T3, N0, M0
Stage IIIA	T0, N2, M0
	T1, N2, M0
	T2, N2, M0
	T3, N1, M0
	T3, N2, M0
Stage IIIB	T4, N0, M0
	T4, N1, M0
	T4, N2, M0
Stage IIIC	Any T, N3, M0
Stage IV	Any T, Any N, M1

Kalli, Sirishma, et al. "American joint committee on cancer's staging system for breast cancer: what the radiologist needs to know." Radiographics 38.7 (2018): 1921-1933.

Stage vs. Survival

Cancer diagnosed at later stages has significantly lower percent survival

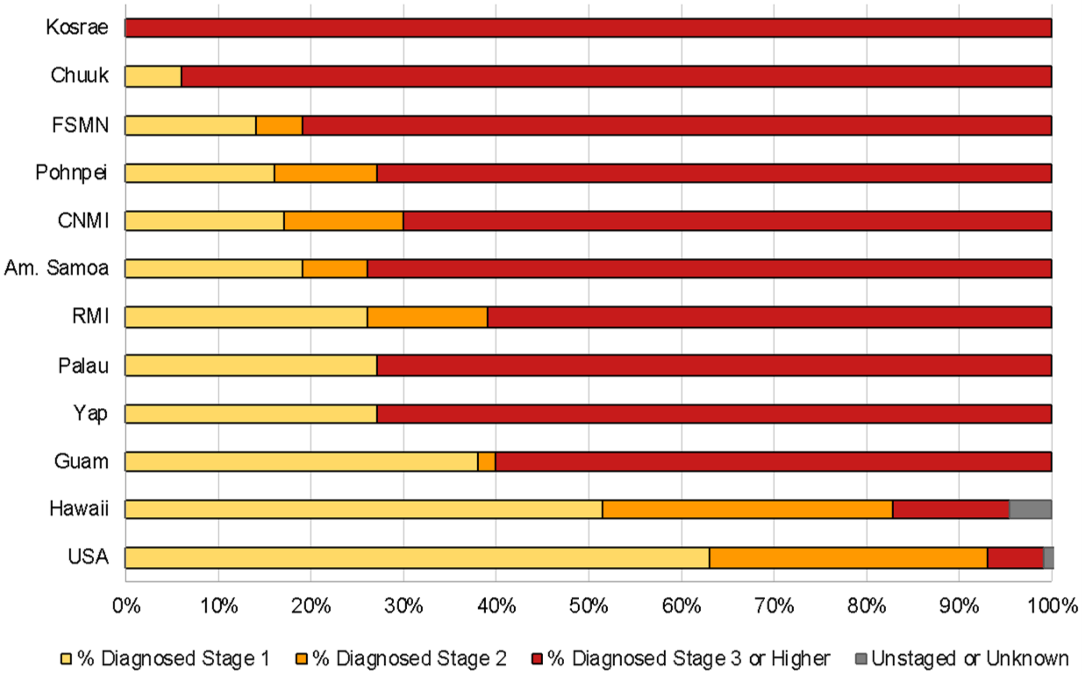


SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute; 2023 Apr 19. [cited 2023 Jun 4]. Available from: https://seer.cancer.gov/statistics-network/explorer/.

High Rate of Advanced-Stage Cancer in the Pacific

- Rates of advanced-stage cancer are high throughout the Pacific

- Despite a comprehensive screening program, Hawai‘i has higher rates of advanced-stage compared the to the continental US



SEER*Stat Database: Hawaii 1975-2017 and SEER Cancer Statistics Review 1975-2017)

Associations of Standard Risk Factors to Advanced Stage

- Risk factors with strong associations to advanced cancer:
  - Disease with atypia
  - Dense breasts
  - Obesity

Risk factors	Advanced prognostic stage II+[a]			
	Annual		Biennial	
	Premenopausal OR (95% CI)	Postmenopausal OR (95% CI)	Premenopausal OR (95% CI)	Postmenopausal OR (95% CI)
Age (in years) – linear term	0.98 (0.91, 1.06)	1.03 (1.00, 1.05)	1.01 (0.93, 1.11)	1.05 (1.02, 1.08)
Age (in years), quadratic term	0.99 (0.99, 1.00)	1.00 (1.00, 1.00)	1.00 (0.99, 1.00)	1.00 (1.00, 1.00)
Race and ethnicity				
Asian//Pacific Islander	0.79 (0.51, 1.24)	0.82 (0.60, 1.10)	0.66 (0.41, 1.09)	1.03 (0.79, 1.35)
Black, non-Hispanic	1.65 (1.16, 2.36)	1.94 (1.61, 2.35)	1.17 (0.75, 1.82)	1.53 (1.17, 1.99)
Hispanic	0.75 (0.41, 1.39)	1.33 (0.95, 1.87)	0.98 (0.59, 1.63)	0.84 (0.55, 1.28)
White, non-Hispanic	ref	ref	ref	ref
Other/Mixed	1.39 (0.65, 2.97)	1.28 (0.76, 2.14)	0.87 (0.36, 2.11)	1.11 (0.65, 1.91)
1st degree family history of breast cancer[b]				
Yes	1.61 (1.21, 2.13)	1.37 (1.16, 1.60)	1.44 (1.00, 2.07)	1.20 (0.95, 1.51)
No	ref	ref	ref	ref
History of breast biopsy				
No prior biopsy	ref	ref	ref	ref
Prior biopsy, benign diagnosis unknown	1.73 (1.25, 2.40)	1.58 (1.34, 1.87)	1.79 (1.23, 2.61)	1.60 (1.29, 1.97)
Non-proliferative	1.36 (0.85, 2.17)	1.64 (1.27, 2.11)	1.30 (0.66, 2.54)	1.24 (0.79, 1.95)
Proliferative without atypia	1.08 (0.48, 2.43)	1.65 (1.10, 2.47)	1.34 (0.43, 4.19)	1.24 (0.57, 2.67)
Proliferative with atypia	2.43 (0.60, 9.82)	2.18 (1.03, 4.60)	0.00 (0.00, Inf)	2.37 (0.59, 9.52)
BI-RADS breast density				
Almost entirely fat	0.41 (0.15, 1.14)	0.44 (0.31, 0.62)	0.40 (0.13, 1.25)	0.38 (0.24, 0.59)
Scattered fibroglandular densities	ref	ref	ref	ref
Heterogeneously dense	2.29 (1.64, 3.20)	1.82 (1.55, 2.13)	1.85 (1.27, 2.69)	1.61 (1.32, 1.97)
Extremely dense	2.64 (1.71, 4.06)	2.41 (1.78, 3.25)	2.44 (1.49, 3.99)	2.11 (1.45, 3.06)
Body mass index, kg/m^2				
Underweight (<18.5)	0.64 (0.19, 2.10)	1.32 (0.74, 2.36)	0.79 (0.25, 2.49)	1.20 (0.61, 2.38)
Normal (18.5-24.9)	ref	ref	ref	ref
Overweight (25.0-29.9)	1.31 (0.93, 1.85)	1.42 (1.14, 1.76)	1.72 (1.19, 2.49)	1.61 (1.22, 2.11)
Obese, grade I (30.0-34.9)	1.38 (0.88, 2.18)	1.72 (1.35, 2.20)	1.54 (0.97, 2.42)	2.07 (1.58, 2.71)
Obese, grade II/III (≥35.0)	1.83 (1.17, 2.86)	2.30 (1.80, 2.95)	1.40 (0.79, 2.48)	1.85 (1.30, 2.65)

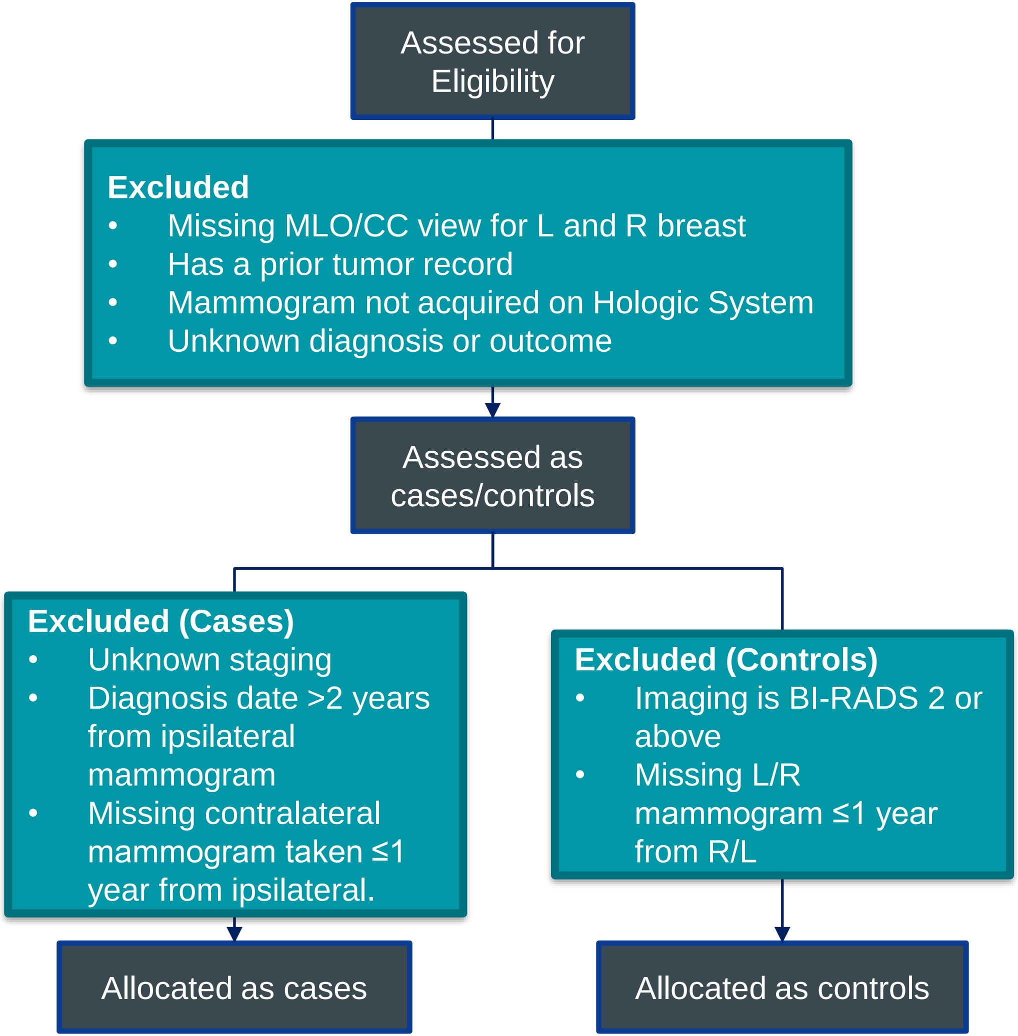
Kerlikowske K et al. Cumulative Advanced Breast Cancer Risk Prediction Model Developed in a Screening Mammography Population. JNCI : Journal of the National Cancer Institute. 2022;114(5):676-85.

Data

The data used in this study are sourced from the Hawaiʻi and Pacific Islands Mammography Registry (HIPIMR)

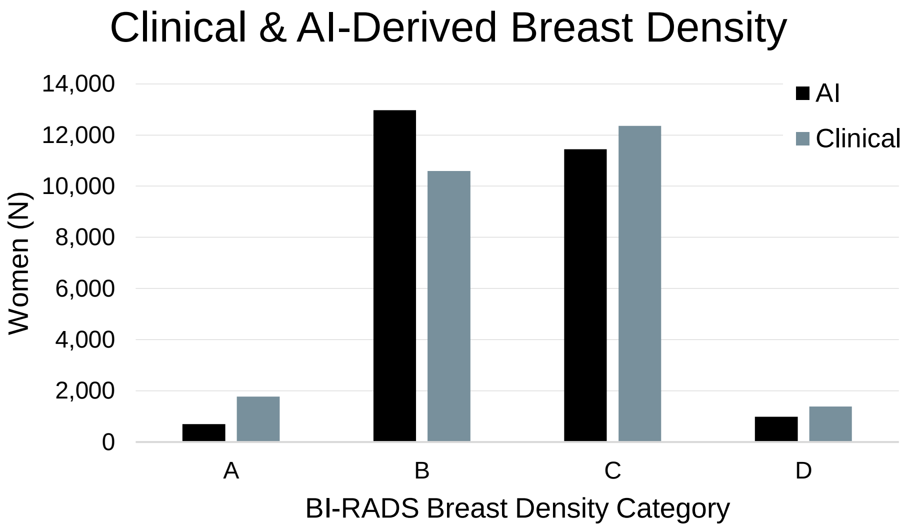
Inclusion

- In the registry before 8/31/22
- All 4 standard mammographic views or images
- Known staging, diagnosis, and outcome



Data Demographics

- Data exported as of 08/31/22
  - 240,000 images
  - 26,000 women
    - 195 diagnosed with advanced-stage breast cancer

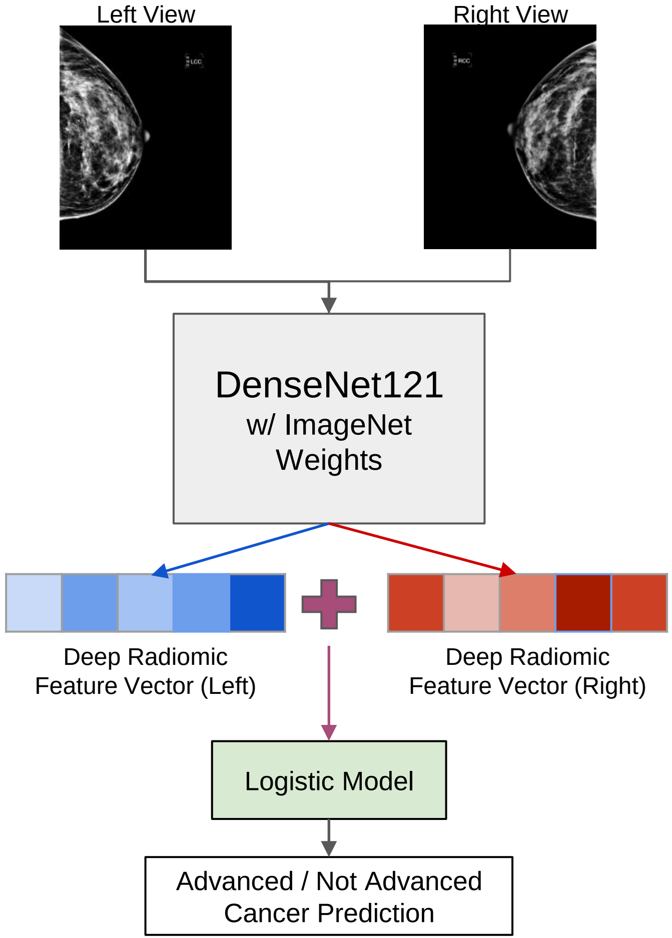


- AI-derived labels are sourced from NYU breast density algorithm

Wu N. et. Al Breast Density Classification with Deep Convolutional Neural Networks. 2018 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP); 2018 2018-04-01: IEEE.

Image-based Modeling Approach

- Imaging/deep radiomic feature extractor
  - Base architecture
    - DenseNet121
    - Pretrained ImageNet
    - Weights locked
- Logistic models take in both L and R views

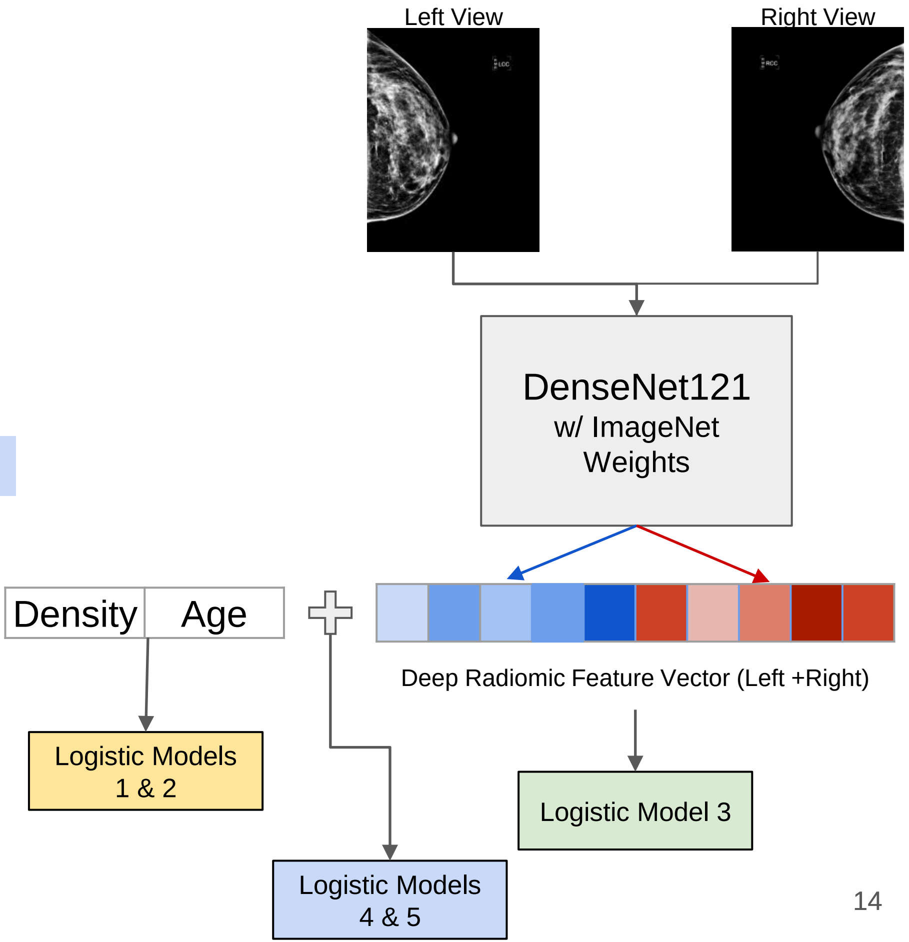


Logistic Models

We built 5 logistic models

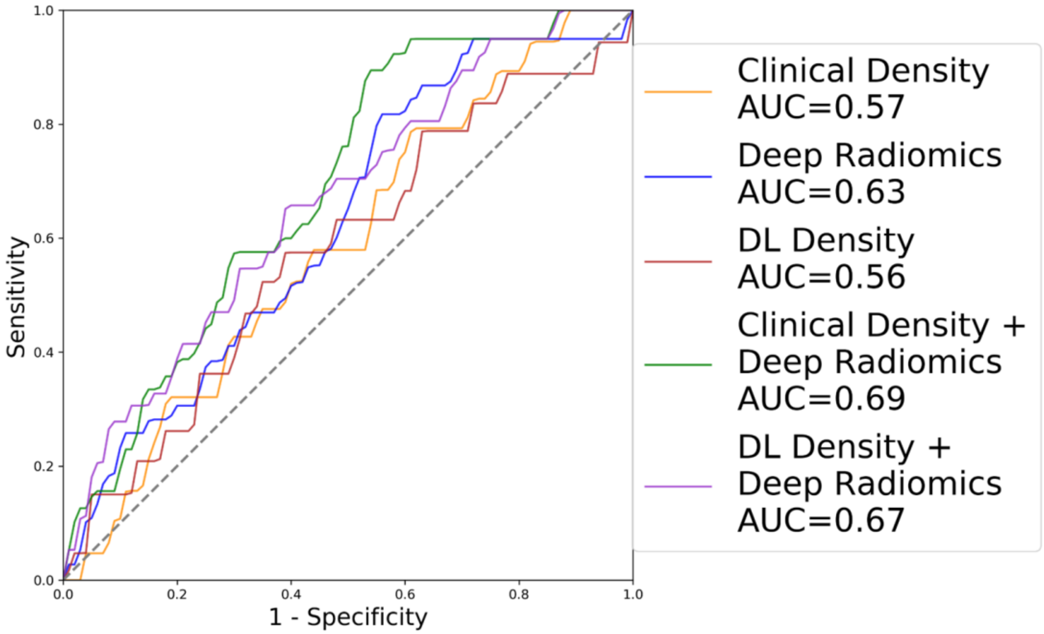
1. Clinical density only model
2. AI-derived density only model
3. Image feature only model
4. Combined clinical density and image features
5. Combined dl density and image features

All models which include density were age adjusted



Logistic Model Performance

- Image features perform better than density only models
- Combined models performed best
  - Imaging contains signals of risk unique to density



Conclusion

- Imaging contains predictive information related to risk of advanced cancer
  - Information is unique to breast density
- Such models can be used to identify high risk women and intervene appropriately

Caveats:

- Not all common risk factors were available
- Small number of cancers with category D density
  - So we combined C and D when computing odds ratios
- Small number of advanced cancer cases

Mahalo nui loa!

SHEPHERD RESEARCH LAB

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