# MRI models by response predictive subtype for predicting pathologic complete response

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#### BACKGROUND

- MRI predictive modeling is a key component of the pre-RCB (Predicted Residual Cancer Burden) clinical workflow for re-directing "excellent responders" to skip AC (anthracycline) and proceed to surgery early in I-SPY 2 TRIAL
- Drug allocation by the new response-predictive subtype (RPS) could lead to a higher pathologic complete response (pCR) rate than allocation based on HR/HER2 subtype1

The purpose of this study is to optimize MRI prediction model based on RPS

## **OMIT AC OPTION IN I-SPY 2**



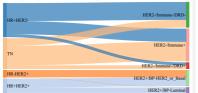
- Patients with excellent response at T2 (inter-regimen) have the option to skip AC and undergo surgery early
- Functional tumor volume (FTV) measured from dynamic-contrast enhanced (DCE) MRI is a standard imaging marker for predicting response to neoadjuvant chemotherapy (NAC)2
- MRI prediction model can be built using FTV variables ➤ Baseline FTV
- > Percent change of FTV at T1 and at T2
- Performances of MRI models vary by cancer subtype

## Methods - MRI models by subtype

Subtype-specific MRI prediction models were performed by

- · Receptor subtype defined by HR/HER2 status
- RPS defined by immune, DNA repair deficiency (DRD), HER2. BluePrint (Agendia)

#### Sankey diagram of receptor subtype and RPS



#### Distribution of RPS within receptor subtypes

- HR+/HFR2- n=336 HR-/HFR2+ n=74 > 53% HER2-/Immune-/DRD-

  - > 39% HFR2-/Immune+ > 9% HER2-/Immune-/DRD+
- HR+/HER2+ n=141 > 62% HER2+/BP-HER2 or Basal
- > 38% HER2+/BP-Luminal
- > 97% HER2+/BP-HER2 or Basal > 3% HFR2+/BP-Luminal Triple negative n=303
  - > 63% HER2-/Immune-/DRD-> 25% HFR2-/Immune+
- > 12% HER2-/Immune-/DRD+

## Statistical analysis

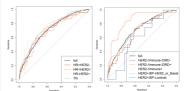
- Logistic regression model of predicting pCR
- · Best models were chosen by achieving the highest AUC
- · Models were optimized using data from the full cohort of 854 patients or within subtype-defined cohort

## Results - MRI models by subtype

Summary of subtype-specific MRI models

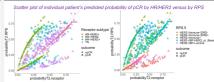
Cohort	N	pCR rate	AUC	FTV predictors included		
				Baseline FTV	Percent change T1	Percent change T2
Full	854	301 (35%)	0.71	✓	✓	✓
HR+/HER2-	336	65 (19%)	0.71			✓
HR+/HER2+	141	54 (38%)	0.68		1	
HR-/HER2+	74	49 (66%)	0.73			✓
Triple negative	303	133 (46%)	0.74	✓		✓
HER2-/Immune-/DRD-	252	26 (10%)	0.68			✓
HER2-/Immune-/DRD+	65	27 (42%)	0.84		✓	✓
HER2-/Immune+	322	145 (45%)	0.71	1		1
HER2+/BP-HER2_or_Basal	159	95 (60%)	0.71	✓		✓
HER2+/BP-Luminal	56	8 (14%)	0.59			✓

Receiver operating characteristic curve of MRI models optimized by receptor subtype (left) and by RPS (right)



- When MRI model was optimized by receptor subtype, best models achieved AUC in range of 0.68 - 0.74
- When MRI model was optimized by RPS subtype, best models achieved AUC in range of 0.59 - 0.84

### Results - Individual patient prediction



AUCs if patients were predicted by RPS-specific MRI model All patients: from 0.77 to 80

HR+/HFR2-: from 0.71 to 0.82

HR+/HFR2+: from 0.68 to 0.77 HR-/HFR2+: from 0.73 to 0.69

## TN: from 0.75 to 0.76 CONCLUSIONS

- · Wider range of performances were observed when MRI models were optimized by RPS compared to models optimized by receptor subtype
- · Improved predictive performance was observed using RPS-specified MRI model in HR+ breast cancer
- RPS-specific MRI models will be implemented in treatment re-direction algorithms in the ongoing I-SPY 2.2 TRIAL

#### Advocate statement

Predicting patients' probability of pCR by RPS can improve the effectiveness of MRI in measuring treatment response. Early prediction of responders will increase treatment optimization by giving responders the option of omitting AC chemotherapy and going to directly to surgery after their first treatment regimen avoiding the side and late effects of AC and likely improving their quality of life.

#### ACKNOWLEDGEMENTS:

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1 Wolf et al. Cancer Cell. 2022; 2 Hylton et al. Radiology. 2012