

Declaration of Financial Interests or Relationships

Wen Li:

I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.



University of California
San Francisco

Combination of MRI quantitative measures improves prediction of residual disease following neoadjuvant chemotherapy (NAC) for breast cancer in the I-SPY 2 TRIAL

Wen Li, PhD; David C. Newitt, PhD; Lisa J. Wilmes, PhD; Ella F. Jones, PhD; Jessica Gibbs, BS; Elizabeth Li, MS; Bo La Yun, MD; John Kornak, PhD; Bonnie Joe, MD PhD; Christina Yau, PhD; Laura J. Esserman, MD MBA; Nola M. Hylton, PhD

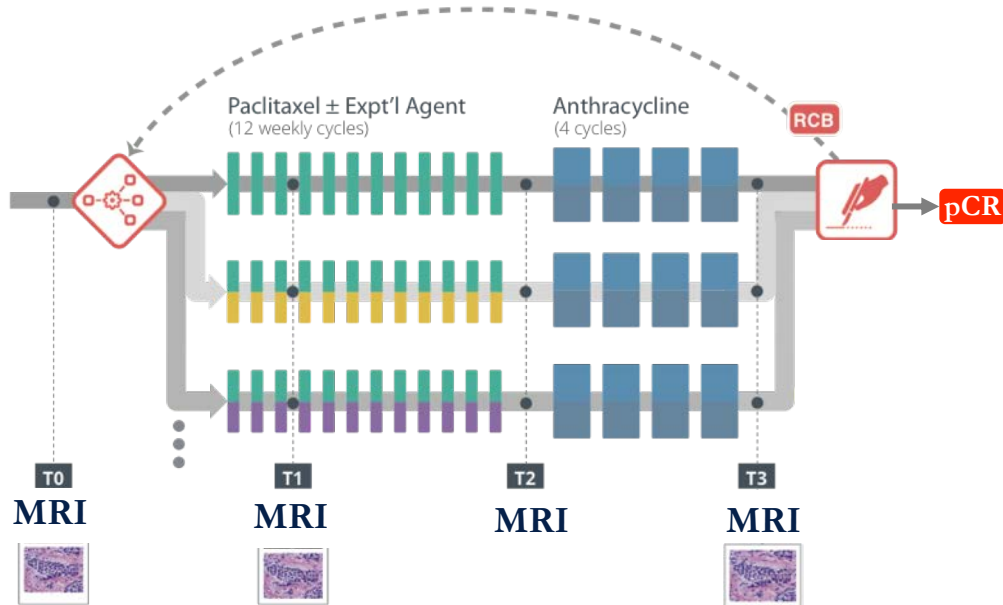
On behalf of the I-SPY 2 Consortium

Presenter: Wen Li, PhD

5/13/19

I-SPY 2

An adaptive phase II trial testing novel investigational agents for neoadjuvant therapy of breast cancer (compare novel + standard vs. standard)



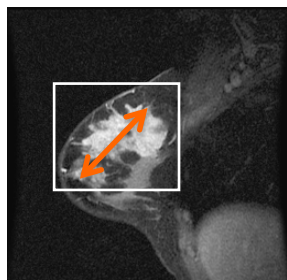
- Longitudinal MRIs were acquired during treatment
- Drugs graduate within subtypes defined by hormone receptor (HR) status, HER2 status, and MammaPrint score
- Pathologic complete response (pCR) is the primary endpoint
- Trial opened in March 2010; 25 sites participated; 18 sites currently open (>2600 patients enrolled)

Purpose

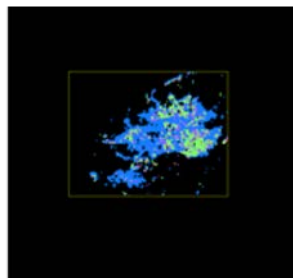
- To test if the combination of multiple MR measurements is superior to any measurement alone in the prediction of residual disease after neoadjuvant chemotherapy

Quantitative measures in DCE-MRI

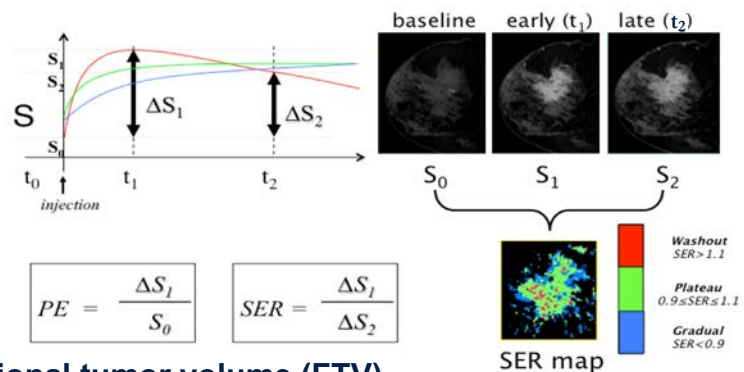
- **Longest diameter of disease (LD)**
 - measured by site radiologists
- **Functional tumor volume (FTV)**
 - region of interest (ROI) drawn manually on axial and sagittal projection images
 - Percent enhancement (PE) and signal enhancement ratio (SER) calculated at each voxel in the ROI
 - Voxels above thresholds for PE and SER are summed to give FTV



Longest diameter (LD)

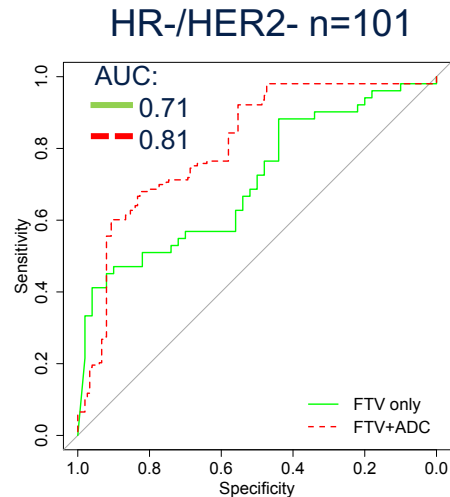
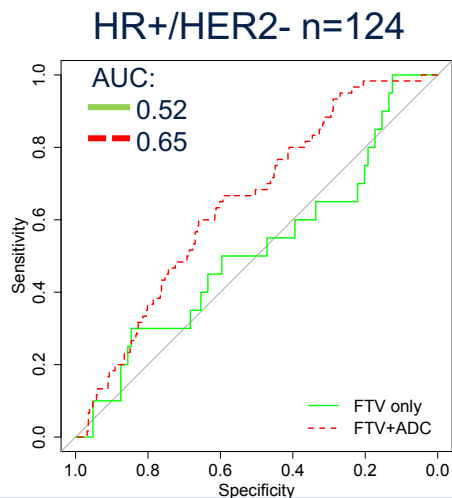


Functional tumor volume (FTV)



Quantitative measure in DWI

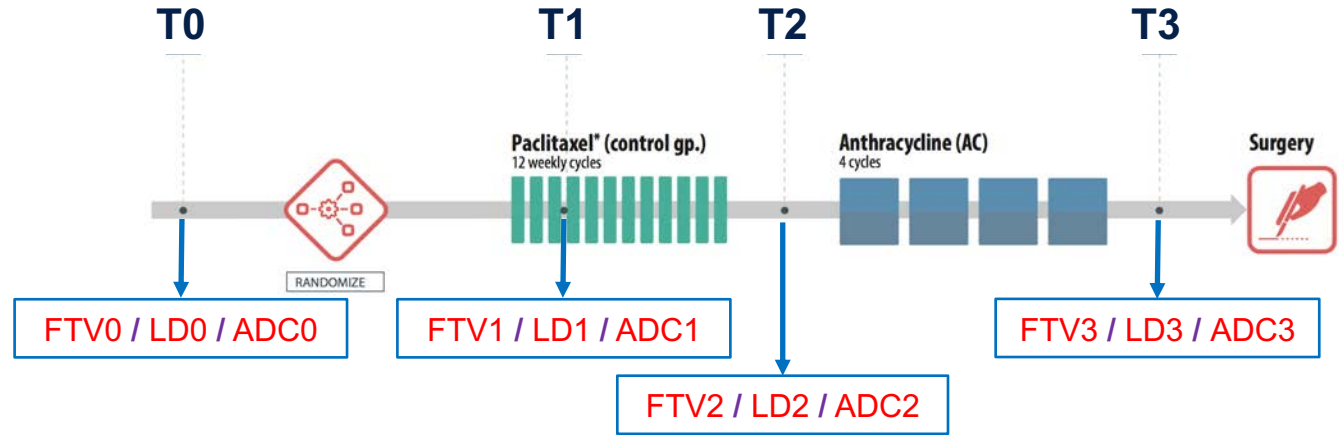
- **Tumor ADC** was measured from 2b DWI (b=0 and b=800)
 - Multi-slice ROI was manually delineated on the ADC map for the whole tumor
 - ACRIN 6698, a sub-study of I-SPY 2 showed that ADC at later treatment time points were predictive of pCR ($p=0.003$ after 12 week and $p=0.004$ at pre-surgery)*
 - Recently published study showed additive value of ADC to FTV in HR/HER2 subtype**



*Partridge et al. Radiology 2018

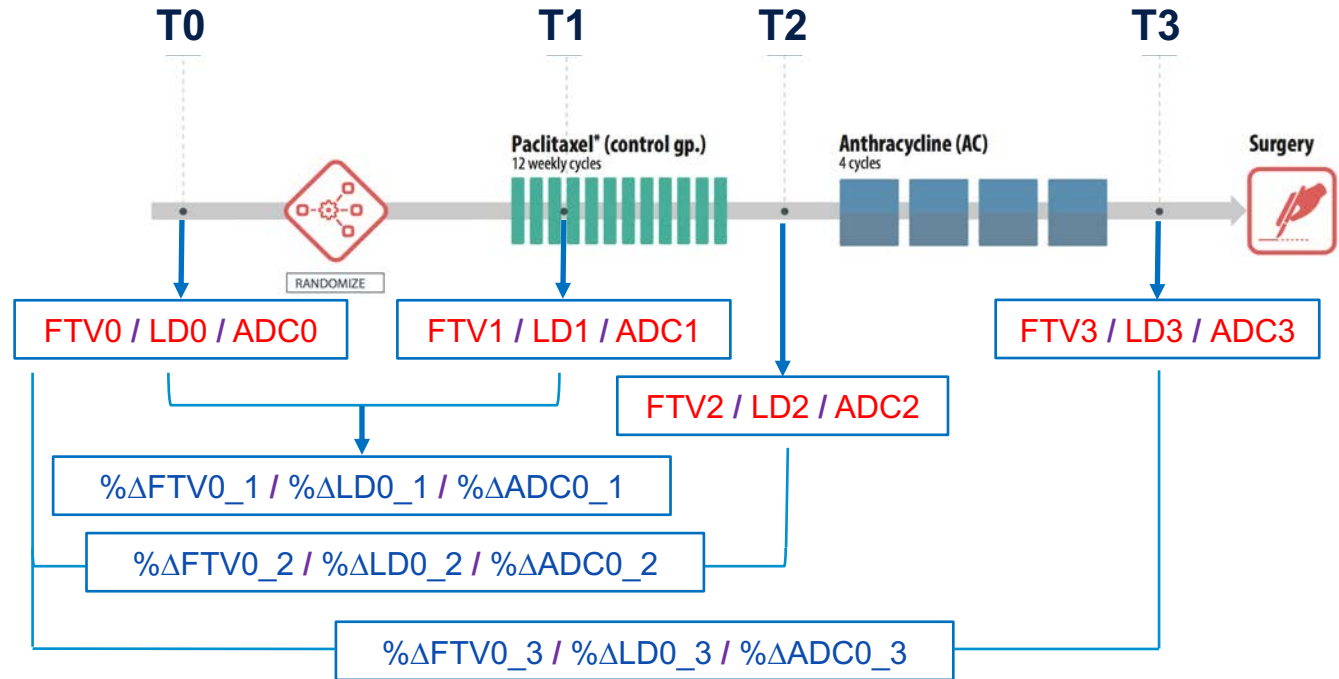
**Li et al. JMRI 2019

MR measurements

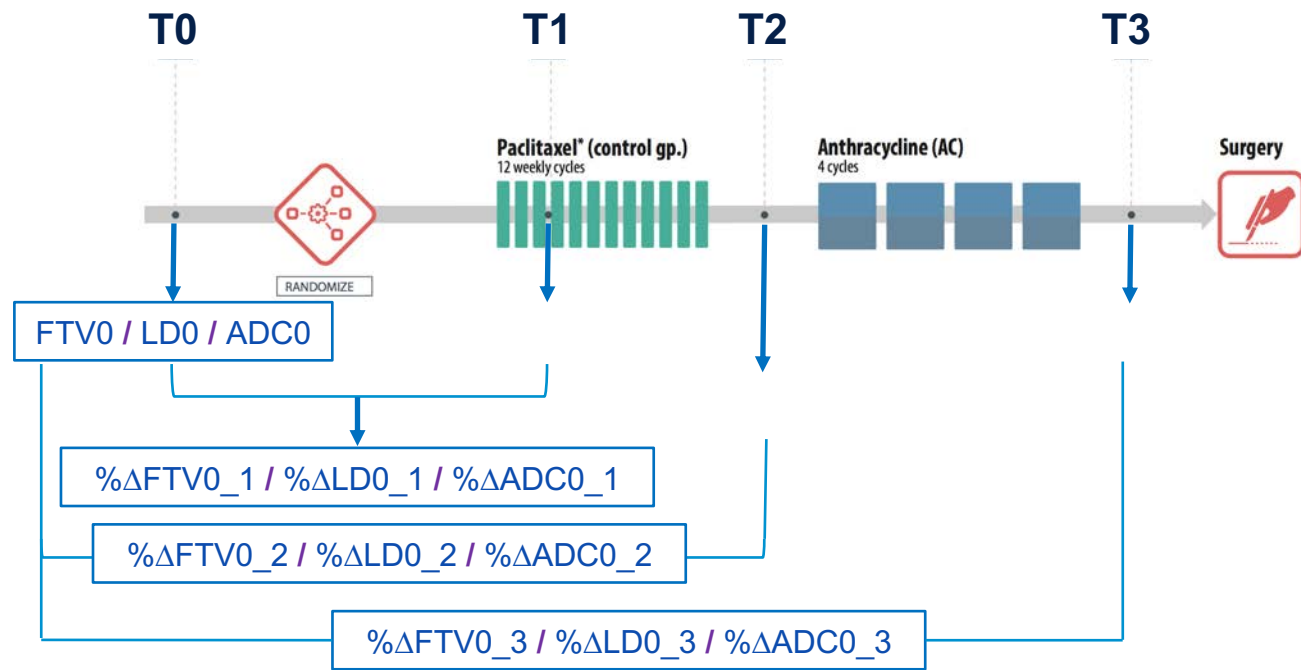


- Each patient had 3 MR measurements measured longitudinally over course of treatment
 1. *Functional tumor volume (FTV)*
 2. *Longest diameter (LD)*
 3. *Apparent diffusion coefficient (ADC)*

MR measurements



MR measurements in analysis



Statistic analysis

- ROC analysis of logistic regression model
- Optimized models = highest AUC (10-fold cross validation)
 - **FTV only:** $FTV0$, $\% \Delta FTV0_1$, $\% \Delta FTV0_2$, $\% \Delta FTV0_3$
 - **LD only:** $LD0$, $\% \Delta LD0_1$, $\% \Delta LD0_2$, $\% \Delta LD0_3$
 - **ADC only:** $ADC0$, $\% \Delta ADC0_1$, $\% \Delta ADC0_2$, $\% \Delta ADC0_3$
 - **Combined:** all variables above
- Full cohort and by subtype

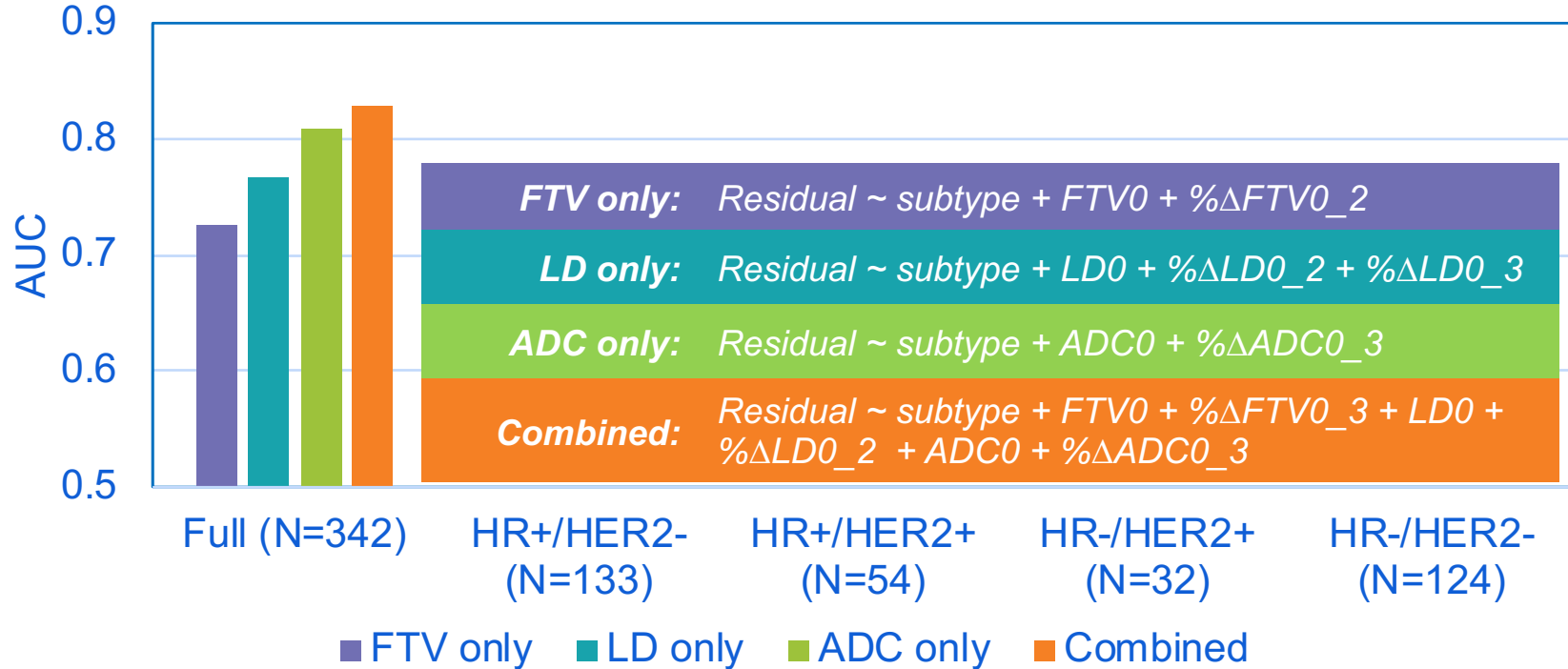
Results – Patients (N=342)

	RESIDUAL (N=207)	NO RESIDUAL (N=135)	P
Age (mean ± sd)	48 ± 10 y/o	48 ± 11 y/o	0.97
Subtype			<0.0001
HR+/HER2-	101 (76%)	32 (24%)	
HR+/HER2+	36 (67%)	18 (33%)	
HR-/HER2+	14 (44%)	18 (56%)	
HR-/HER2-	56 (46%)	67 (54%)	

❖ *HR+ tumors were more likely to have residual disease*

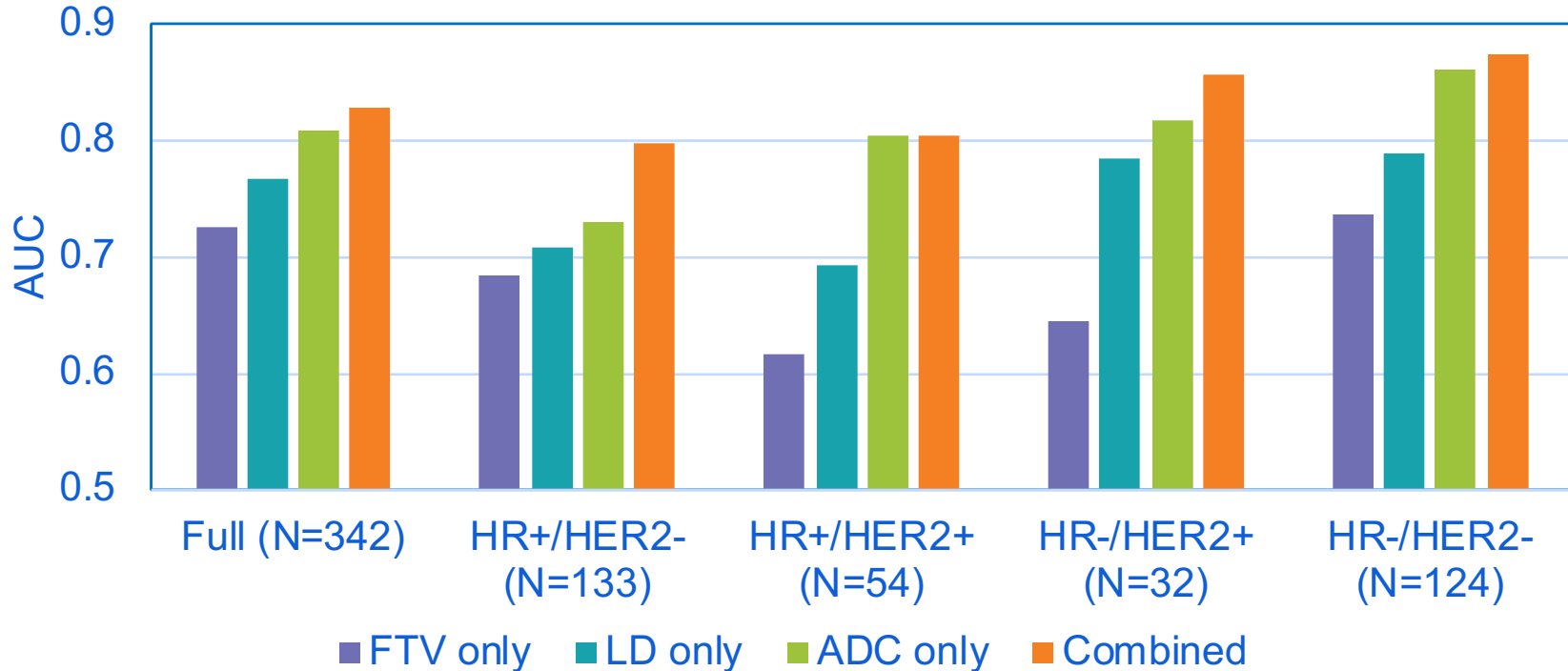
Results – AUCs in the full cohort

- Combined models achieved highest AUCs



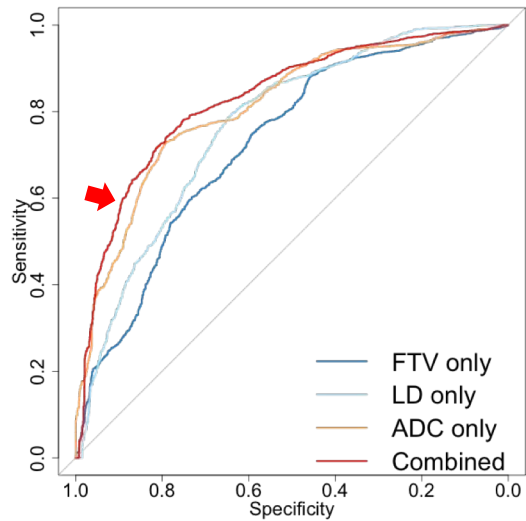
Results – AUCs by subtype

- Combined models achieved highest AUCs



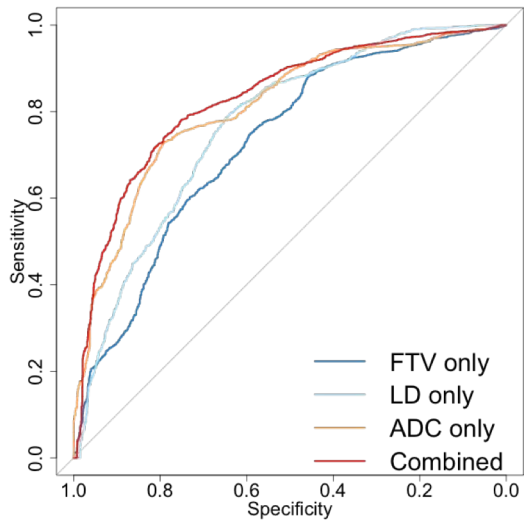
ROC curves

Full N=342

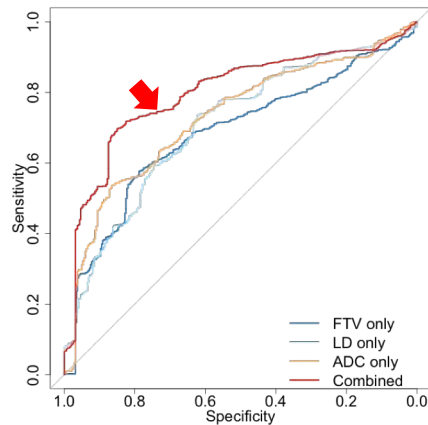


ROC curves

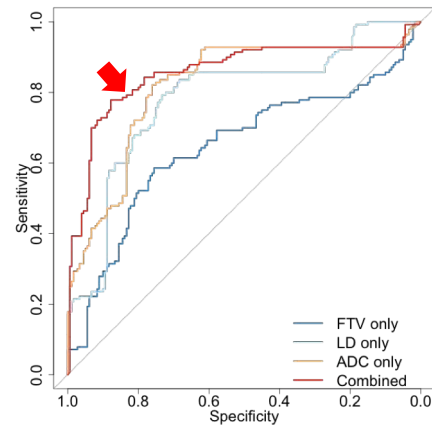
Full N=342



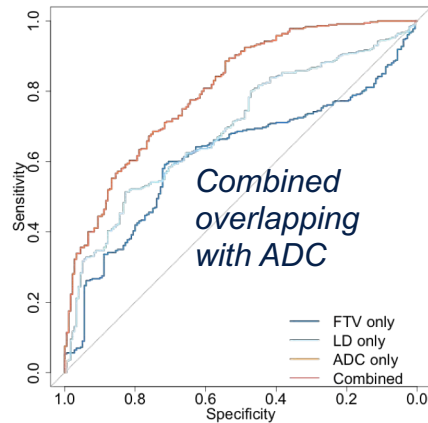
HR+/HER2- N=133



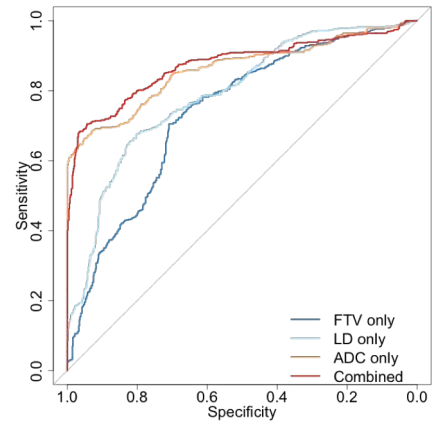
HR-/HER2+ N=32



HR+/HER2+ N=54



HR-/HER2- N=123



Discussion (limitations)

- MRI exams were performed using different systems (i.e. different manufacturers, field strength, breast coils)
- While DCE-MRI was under high standard QA/QC, DWI was acquired with limited QA/QC
- Patients received different chemotherapy regimens as randomized by I-SPY 2 TRIAL (multi-center treatment trial)
- Small number of patients may limit the ability to analyze by HR/HER2 subgroups

Conclusion

- Combining FTV/LD/ADC achieved higher AUC than individual measurements in the prediction of residual disease for patients with locally advanced breast cancer undergoing neoadjuvant chemotherapy
- The improvement was greatest in HR+/HER2- and HR-/HER2+ cancer subtypes

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