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Diffusion-weighted magnetic resonance imaging for subtype-specific prediction of pathologic complete response in neoadjuvant chemotherapy.

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Background

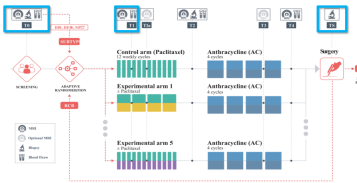
Apparent diffusion coefficient (ADC) presents a biomarker that is sensitive to tumor cellularity.

Diffusion-weighted magnetic resonance imaging (DW-MRI): non-invasive, quantitative imaging approach to retrieve ADC maps of tumor regions.

Objective: to evaluate predictive performance of percentile ADC metrics for pathologic complete response (pCR) in HER2-negative breast cancer undergoing standard neoadjuvant chemotherapy

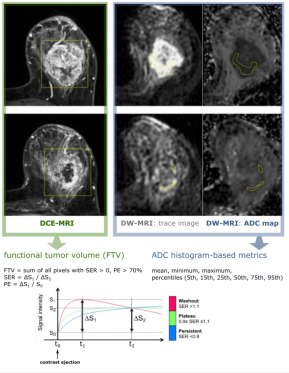
I-SPY 2: a multi-center trial for NAC

I-SPY 2: A multicenter, phase 2 trial using response-adaptive randomization within biomarker subtypes to evaluate novel agents as neoadjuvant therapy for high-risk breast cancer.

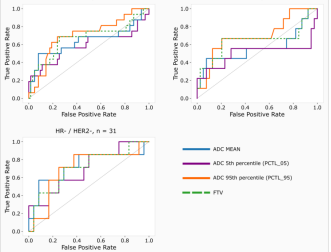


Quantitative Analysis of DCE and DWI-MRI

- **N = 79 female patients** with high-risk, stage II/III breast cancer, undergoing NAC with *Paclitaxel* (I-SPY 2 control patients of *Pembrolizumab* and *MK2206* arm)
  - 48 patients with HR+/HER2-
  - 31 patients with HR-/HER2-
- Two MR imaging timepoints:
  - **pre-treatment (T_0)**
  - after **three weeks (T_1)**
- Retrospective analysis of
  - **ADC metrics from DW-MRI** [1,2]
  - **FTV** from dynamic-contrast enhanced **(DCE) MRI**
  - **clinical outcome** (pCR+ responders vs. pCR- non-responders
- For every metric M: **%-change = 100 × (M_{T1} – M_{T0}) / M_{T0}**



Results: Predictive power of ADC-based metrics and FTV for pCR



Receiver operating characteristic (ROC) curves for ADC MEAN, 5th percentile, 95th percentile, and FTV for all controls, HR+/HER2- controls, and HR-/HER2- controls.

	ADC metrics retrieved from DW-MRI			DCE-MRI
	MEAN	PCTL_05	PCTL_95	FTV
all patients (n=79, pCR=20.3%)				
pCR (%-change) [Q1, Q3]	18.1 [3.9, 25.2]	18.6 [-5.7, 34.1]	19.4 [8.9, 21.5]	-58.8 [-80.6, -22.5]
non-pCR (%-change) [Q1, Q3]	10.4 [3.9, 16.1]	10.1 [0, 19.7]	7.3 [0.9, 13.7]	-28.2 [-54.2, -2.7]
AUC	0.64	0.59	0.7	0.67
95% CI	[0.47, 0.79]	[0.42, 0.74]	[0.56, 0.83]	[0.52, 0.82]
p-value	0.085	0.278	0.012 *	0.036 *
HR+/HER2- (n=48, pCR=18.8%)				
pCR (%-change) [Q1, Q3]	12.3 [1.8, 25.2]	18.2 [-8.2, 32.1]	20.5 [5.9, 24.7]	-57.7 [-73.8, 2.6]
non-pCR (%-change) [Q1, Q3]	9.4 [3.9, 15.8]	9.4 [1.5, 19.7]	7.5 [0.4, 11.2]	-28.2 [-50.2, -6.6]
AUC	0.56	0.5	0.69	0.64
95% CI	[0.35, 0.78]	[0.27, 0.76]	[0.5, 0.87]	[0.41, 0.85]
p-value	0.552	0.988	0.072	0.191
HR-/HER2-, 'triple-negative' (n=31, pCR=22.6%)				
pCR (%-change) [Q1, Q3]	20.5 [14.3, 22.9]	19.1 [11.6, 33.5]	18.6 [12.3, 20.2]	-59.9 [-88.2, -44.3]
pCR (%-change) [Q1, Q3]	11.4 [5, 16.2]	11.2 [-2.3, 18.9]	7 [1.5, 14.9]	-30.6 [-60.5, 1.6]
AUC	0.73	0.7	0.7	0.71
95% CI	[0.49, 0.94]	[0.49, 0.9]	[0.48, 0.9]	[0.51, 0.9]
p-value	0.065	0.119	0.108	0.098

Statistical analysis of ADC-based and FTV metrics for predicting treatment response at 3 weeks into NAC: %-change (calculated as median over respective population) for pCR (responders) and non-pCR (non-responders), AUC, and p-values. (: statistically significant, p < 0.05)**

- 16 out of 79 patients (20.3 %) reached pCR (residual cancer burden (RCB) index = 0)
  - 18.8 % pCR among HR+/HER2-
  - 22.5 % pCR among HR-/HER2-
- pCR patients show higher %-change regarding all metrics (ADC and FTV)
- %-change of 95th percentile ADC yielded the highest AUC
- %-change of FTV yielded second highest AUC
- Highest AUCs for %-change per **subtype-specific analysis**:
  - HR+/HER2- 95th percentile ADC
  - HR-/HER2- MEAN ADC

Conclusions

- Histogram **percentile ADC metrics have potential** to achieve better **predictive performance than mean tumor ADC at early treatment**, especially for HR+/HER2- cancer subtype
- **Additional studies are warranted** to increase the cohort size.

ADVOCATE'S PERSPECTIVE: Histogram percentile ADC metrics have the potential to achieve better predictive performance than mean tumor ADC at early treatment. Early prediction of responders and non-responders **will increase treatment optimization** by allowing responders to switch early to their next scheduled trial therapy while allowing non-responders to switch early to a different trial therapy thereby avoiding side effects from a therapy which is not working for them.

REFERENCES: [1] Li et al., Cancers 14 (18):4436, 2022; [2] Partridge et al., Radiology 289(3):618-27 (2018)

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