

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

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 (T₀)
after three weeks (T₁)

- Retrospective analysis of

ADC metrics from DW-MRI [1,2]

FTV from dynamic-contrast enhanced (DCE) MRI

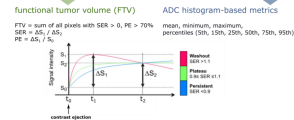
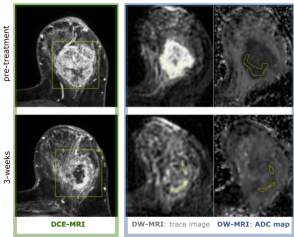
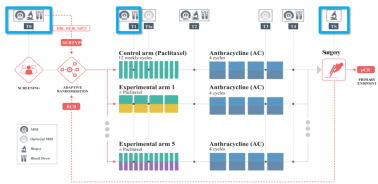
clinical outcome

(pCR+ responders vs. pCR- non-responders)

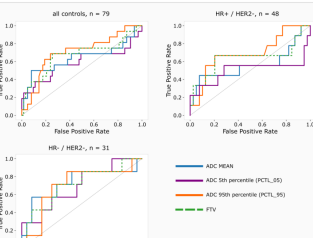
- For every metric M: **%-change** = $100 \times (M_{T1} - M_{T0}) / M_{T0}$

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.



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.

- 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

ADC metrics retrieved from DW-MRI		DCE-MRI	
MEAN	95th	FTV	
all patients (n=79, pCR=20.3%)			
pCR (%-change)	18.8	18.4	-23.8
[95% CI]	[5.9, 29.2]	[5.7, 34.1]	[8.9, 21.5]
non-pCR (%-change)	10.4	10.1	-28.2
[95% CI]	[3.8, 16.1]	[0, 19.3]	[14.2, -2.7]
AUC	0.64	0.59	0.7
95% CI	[0.47, 0.76]	[0.42, 0.74]	[0.56, 0.83]
p-value	0.001	0.078	0.006 **
HR+/HER2- (n=48, pCR=18.8%)			
pCR (%-change)	12.3	18.2	-20.5
[95% CI]	[1.6, 25.2]	[4.2, 32.1]	[9.9, 24.7]
non-pCR (%-change)	9.4	9.4	-28.2
[95% CI]	[3.9, 15.8]	[1.5, 18.7]	[4.0, 11.2]
AUC	0.58	0.5	0.69
95% CI	[0.35, 0.78]	[0.27, 0.76]	[0.15, 0.87]
p-value	0.552	0.968	0.075
HR-/HER2- (n=31, pCR=22.6%)			
pCR (%-change)	22.5	18.1	-18.8
[95% CI]	[14.3, 22.6]	[11.6, 33.5]	[12.3, 20.2]
non-pCR (%-change)	11.4	11.2	-30.6
[95% CI]	[5, 16.2]	[2.3, 18.8]	[1.5, 14.8]
AUC	0.73	0.7	0.71
95% CI	[0.49, 0.94]	[0.49, 0.9]	[0.48, 0.9]
p-value	0.005	0.008	0.001

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)

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 286(3):618-27 (2018)
ACKNOWLEDGEMENTS: NIH grants R01 CA232075, U01 CA232477, R01 CA232478, R01 CA232479, R01 CA232480, R01 CA232481, R01 CA232482, R01 CA232483, R01 CA232484, R01 CA232485, R01 CA232486, R01 CA232487, R01 CA232488, R01 CA232489, R01 CA232490, R01 CA232491, R01 CA232492, R01 CA232493, R01 CA232494, R01 CA232495, R01 CA232496, R01 CA232497, R01 CA232498, R01 CA232499, R01 CA232500, R01 CA232501, R01 CA232502, R01 CA232503, R01 CA232504, R01 CA232505, R01 CA232506, R01 CA232507, R01 CA232508, R01 CA232509, R01 CA232510, R01 CA232511, R01 CA232512, R01 CA232513, R01 CA232514, R01 CA232515, R01 CA232516, R01 CA232517, R01 CA232518, R01 CA232519, R01 CA232520, R01 CA232521, R01 CA232522, R01 CA232523, R01 CA232524, R01 CA232525, R01 CA232526, R01 CA232527, R01 CA232528, R01 CA232529, R01 CA232530, R01 CA232531, R01 CA232532, R01 CA232533, R01 CA232534, R01 CA232535, R01 CA232536, R01 CA232537, R01 CA232538, R01 CA232539, R01 CA232540, R01 CA232541, R01 CA232542, R01 CA232543, R01 CA232544, R01 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