Correlation between MRI background parenchymal enhancement and serum estradiol in premenopausal patients on neoadjuvant endocrine therapy for breast cancer

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BACKGROUND

Background parenchymal enhancement (BPE)

- BPE is the contrast enhancement of **normal fibroglandular tissue** on dynamic contrast-enhanced breast MRI.
- BPE fluctuates with the menstrual cycle, lactation, and pregnancy, suggesting **hormonal dependence.** However, there is insufficient evidence demonstrating a clear association between BPE and estradiol levels.
- BPE is suppressed during neoadjuvant chemotherapy and endocrine therapy (NET) (***Figure1***). In hormone receptor-positive (HR+) cancer, our prior study found that **lack of BPE suppression was associated with inferior treatment response** to neoadjuvant chemotherapy.

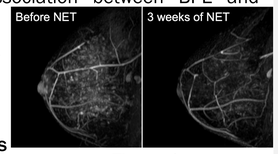


Figure 1.
A case of 40- year-old women with BPE suppression during NET

PURPOSE

1) To evaluate the correlation between BPE and serum estradiol levels in treatment-naïve premenopausal patients with HR+ breast cancer
2) To assess the association between BPE suppression and serum estradiol suppression during neoadjuvant endocrine therapy (NET).

METHODS – INCLUSION CRITERIA

- Premenopausal women with breast cancer enrolled in the I-SPY 2 TRIAL's Endocrine Optimization Protocol (EOP) sub-study testing new endocrine agents between 2021-23
- EOP eligibility: patients with stage 2/3, MammaPrint(MP) Low-risk (index 0 to 1), HR+/HER2-negative cancer. Patients with MP High1 (index -0.57 to 0) tumors were eligible if clinically node negative
- Patients with serial serum estradiol levels before and during NET
- Patients with BPE values obtained from DCE MRI before and during NET scanned as part of EOP trial

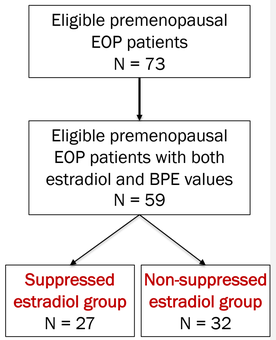


Figure 2. Cohort diagram

METHODS – DATA

Serum estradiol

- Tested through monthly local blood draws
- Serum estradiol levels prior to any treatment, including ovarian function suppression, was considered ***treatment-naïve estradiol***
- Cohort was divided into two groups:
  - Suppressed estradiol group:
    Mean estradiol level after first cycle of NET (<10 pg/mL)
  - Non-suppressed estradiol group:
    Mean estradiol level after first cycle of NET (≥10 pg/mL)

Background parenchymal enhancement (BPE)

- Fully automated measurement on contralateral breast
- Two timepoints at pre-treatment (before medication) and pre-surgery

RESULTS – STUDY COHORTS

- Among 73 eligible premenopausal EOP patients, 59 had both estradiol levels and BPE measurements: suppressed estradiol group, 27; non-suppressed estradiol group, 32 (***Figure 2***).
- Treatment-naïve estradiol levels were available for 33 of the 59 patients.

Table 1. Demographic and clinical characteristics

	All eligible patients (n=59)	Suppressed estradiol group (n=27)	Non-suppressed estradiol group (n=32)	p-value
Age	45 [41, 49]	44 [40.5, 47]	45.5 [41.8, 51.3]	0.17
Race	41 White (69.5%) 7 Asian (11.9%) 11 Unknown (18.6%)	18 White (66.7%) 3 Asian (11.1%) 6 Unknown (22.2%)	24 White (75%) 4 Asian (12.5%) 4 Unknown (12.5%)	0.43
Disease extent (cm)	4.0 [3.0, 6.6]	4.0 [3.15, 7.65]	3.5 [2.63, 4.25]	0.13
Node status	Negative (55.9%) Positive (44.1%)	Negative (59.3%) Positive (40.7%)	Negative (53.1%) Positive (46.9%)	0.83
Treatment arms	8 AM (14%) 11 AM + Abemaciclib (19%) 13 AM + Letrozole (22%) 12 Z-endoxifen (20%) 7 Lasofoxifene (12%) 8 SOC by AI (14%)	3 AM (11%) 6AM + Abemaciclib (22%) 11 AM + Letrozole (40%) 1 Z-endoxifen (3%) 0 Lasofoxifene 6 SOC by AI (22%)	5 AM (16%) 5 AM + Abemaciclib (16%) 2 AM + Letrozole (6%) 11 Z-endoxifen (34%) 7 Lasofoxifene (22%) 2 SOC by AI (6%)	$< 10^{-4}$

Note: AM = amcenestrant, AI = aromatase inhibitor
*Wilcoxon rank-sum test, Chi-squared test, or Fisher's exact test was used depending on the data type.

RESULTS – DATA ANALYSIS

Serum estradiol levels before and during NET

The median treatment-naïve estradiol level [1st, 3rd quartile] was 106 [42, 250] pg/mL.

Treatment naive estradiol levels were available for 8 patients who started ovarian function suppression (OFS) prior to C1D1 and 25 patients who started OFS either at C1D1 or C2D1.

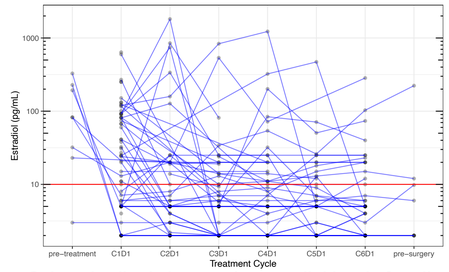


Figure 3. Longitudinal changes in estradiol levels for all patients
Y-axis is displayed in log(10) scale

Treatment-naïve estradiol and baseline BPE

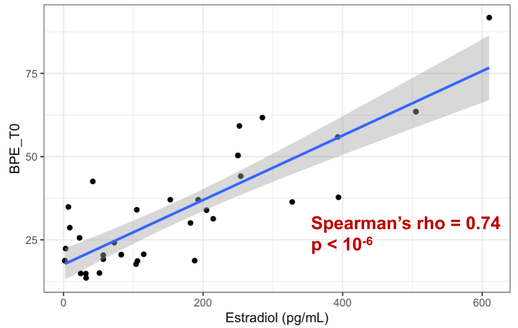


Figure 4. Treatment-naïve estradiol and baseline BPE levels
Positive correlation was observed with ρ = 0.74 ($p < 10^{-6}$)

BPE reduction during NET

Table 2. BPE change in estradiol suppressed and non-suppressed groups

Estradiol suppression during NET	N	BPE change Median %ΔBPE (IQR)	p-value
Suppressed group (<10 pg/mL)	27	-42.7% [-54.3, -21.8]	-
Non-suppressed group (≥10 pg/mL)	32	-15.0 % [-40.6, 6.85]	0.002

Patients with suppressed estradiol on NET show greater BPE reduction.

Note: %ΔBPE = ((pre-surgery BPE − baseline BPE)/baseline BPE) × 100.

*Wilcoxon rank-sum test

CONCLUSIONS

- BPE showed a positive correlation with serum estradiol levels in treatment-naïve premenopausal patients with HR+/HER2- breast cancer.
- Suppression of on-treatment estradiol was associated with greater BPE suppression following neoadjuvant endocrine therapy (NET).
- Our findings suggest that BPE could serve as an indicator of estradiol levels during NET, complementing other MRI biomarkers such as functional tumor volume.
- Together, these imaging biomarkers may capture both non-malignant and tumor-specific biological processes, potentially enhancing predictive performance of treatment response.

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