Does baseline mammographic and peri-tumoural density influence the response of breast cancer to NACT?

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Introduction

We aimed to assess the influence of baseline contralateral mammographic density (MD) and peri-tumoural density on the response of breast cancer and its sub-types to neoadjuvant chemotherapy (NACT).

Methods

Contralateral MD was retrospectively assessed using the BIRADS classification and a visual analogue scale (VAS) by two breast radiologists blinded to treatment outcomes.

Those women for whom raw FFDM images were available for analysis had contralateral volumetric breast density measured using VOLPARA software.

Two radiologists classified the immediate peri-tumoural tissues as either fatty, mixed or dense. Fatty was defined as >75% of the tumour margin being fatty while dense was >75% of the margin having dense tissue abutting the tumour. The remaining cases were called mixed.

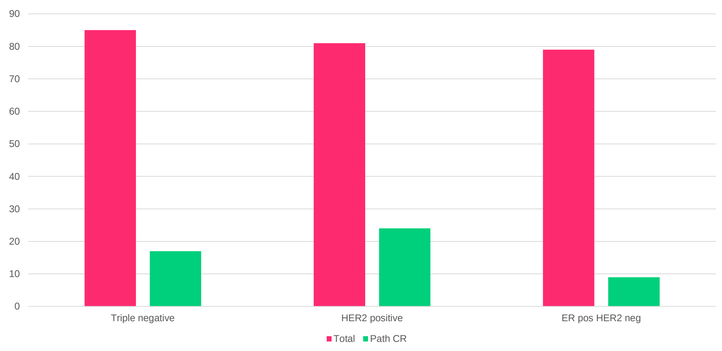
Associations between MD and rates of pathological complete response (PCR) were assessed for the whole cohort and immuno-histochemical subtypes using ROC analysis.

Results

243 women having 248 tumours

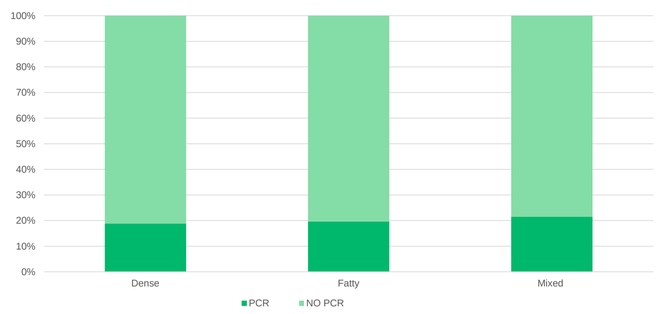
20% of tumours had a pathological complete response (PCR).

Figure 1 shows the distribution of subtypes in the population (red) and the PCR rates in each group (green).



Peritumoural Density

Figure 2: Association between the density around tumours and PCR following NACT.



No statistically significant associations were found for the whole cohort for any individual subtype.

MD and PCR by ROC analysis

Table 1: Area Under the Curve (AUC) for association between PCR and MD as measured by VAS and Volpara software. Results are shown for the whole cohort and for the HER2 positive subgroup.

		AUC	P-value
Whole cohort	VAS	0.536	0.264
	Volpara	0.607	0.076
HER2 positive	VAS	0.624	**0.013**
	Volpara	0.665	0.077

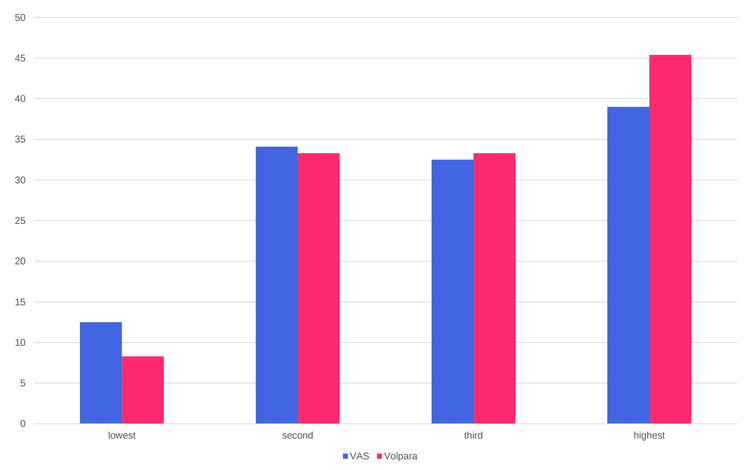
For the whole cohort a weak association between MD and PCR was not significant whether assessed by VAS or Volpara.

For HER2 positive patients MD as assessed by VAS did show a significant association with the rate of PCR. Volpara assessed MD showed the same trend but fell short of significance.

No significant association was found in triple negative tumours and the number of PCR's in ER positive HER2 negative women was to small for meaningful analysis.

MD quartiles in HER2 positives

Figure 3: PCR rates in HER2 positive women presented in quartiles of density as measured by VAS (blue) and Volpara (red) in the opposite breast at baseline prior to NACT.



Women with very fatty breast have a very low rate of PCR compared to women with higher breast densities. Women with moderately and very dense breast have similar PCR rates.

PCR by BIRADS: HER2 positives

Table 2: Frequency of PCR and no pCR by breast density in HER2 positive patients. Categories were combined as few patients were A or D.

	Path CR	No PCR	Total
Fatty (AB)	18(22.5%)	62(77.5%)	80
Dense (CD)	30(36.6%)	52(63.4%)	82

There is a trend suggesting that people with fatty breasts are only 0.6 times as likely to have a path CR. The 95% CI of the relative risk is 0.374 to 1.011.

Discussion

Objective, reproducible, timely and economical markers which can predict suboptimal response to neoadjuvant chemotherapy are needed so that potentially more efficacious strategies can be explored.

We have found that low baseline contralateral MD in women receiving NACT is associated with a low pCR rate in HER2 positive patients but not in other breast cancer subgroups.

The only significant association was seen when MD was assessed using VAS. The other density methods (BRIADS and Volpara) showed non-significant trends with the least dense groups showing the lowest PCR rate.

The relationship between MD and pCR rate in HER2 positive patients appears to be based on the presence or absence of any MD rather than the amount of density present, as the 3 upper quartiles of MD have similar rates of pCR.

Our findings are consistent with studies showing that peritumoural adipose tissue can promote tumour chemoresistance[1,2]. *In vitro* studies show adipocytes promoting resistance to trastuzumab to which most of our HER2 patients have been treated [3,4].

This is a single centre study with small numbers but if confirmed in other cohorts, this finding might have important therapeutic implications.

Conclusion

We have found that low baseline contralateral MD in women receiving NACT is associated with a low PCR rate in HER2 positive patients but not in other breast cancer subgroups.

References

1. Carraro A, et al. Cancer Sci. 2017 Dec; 108(12): 2393-404.
2. Yeh WL, et al. Stem Cell Res Ther. 2017 Jul 27; 8(1): 177.
3. Griner SE, et al. Curr Pharm Person Med. 2013 Mar 1; 11(1):31-41.
4. Duong MN, et al. Breast Cancer Res. 2015 Apr 24;17:57.