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Breast cancer host immune and stromal biology

51P REPRODUCIBILITY OF ASSESSING IMMUNE INFILTRATION IN CORE BIOPSIES COMPARED TO PRIMARY BREAST TUMORS

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Introduction: Breast tumors are infiltrated with a diversity of immune cells based on histological and immunohistochemical (IHC) analysis as well as immune gene signature expression. Previous studies found that greater infiltration is associated with an increased benefit from preoperative chemotherapy; however, these studies evaluated tumor infiltrating lymphocytes (TIL) in core biopsies alone. The aims of this study were to examine the reproducibility of assessing the level and organization (tertiary lymphoid structures; TLS) of TIL between biopsies and primary tumors and to set a TIL density threshold for biopsies that accurately predicts significant immune infiltration in the primary tumor.

Methods: This retrospective study was performed on matched pairs of paraffin-embedded core biopsy and surgically excised primary tumor specimens from untreated HER2+ and triple negative breast cancer patients. Immune infiltration levels in the biopsy/tumor pairs (n = 65) were independently assessed on CD45 (pan leukocyte marker) and CD23 (follicular dendritic and germinal center B cell marker to denote TLS) IHC stained slides by two pathologists. Further analysis (n = 53) was performed by digital analysis software to quantify CD45 IHC or qRT-PCR to assess RNA expression of an eight gene TLS signature.

Table: 51P

Correlation biopsy / tumor	Spearman's rank correlation coefficient	95% CI
CD45 (% TIL/tumor area)	0.84	0.74–0.9
CD23 (# TLS/tumor area)	0.61	0.41–0.74
Digital analysis of CD45 (TIL/tumor area)	0.78	0.64–0.86
Immune signature	0.6	0.39–0.75

Results: Based on our analysis we set a threshold of ≥5% TIL in the biopsy as TIL positive and this was 100% effective for predicting ≥5% TIL in the primary tumor. Alternatively, <5% TIL in the biopsy only predicted TIL negative tumors half of the time.

Conclusion: This preliminary study suggests that analysis by trained pathologists is more reproducible for biopsy tumor pairs than current digital analysis algorithms and our gene expression signature. These data further indicate that TIL in the biopsy (≥5%) accurately identify TIL positive tumors. However, the presence of organized TLS is more problematic in the biopsy than the tumor.

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