ASO Author Reflections: Molecular Testing in Breast Cancer: Is Core Biopsy Equivalent to Surgical Specimen?

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PAST

In the past two decades, gene-expression signatures, performed on surgical specimens, have transformed the treatment of breast cancer. Molecular testing adds prognostic and predictive information in patients with hormone receptor-positive, HER2-negative early-stage breast cancer. Notably, the 21-gene recurrence score (OncotypeDx) has allowed for improved selection of patients who would benefit from adjuvant chemotherapy and those who can safely forgo chemotherapy.1 Molecular testing, performed on core needle biopsies, has increased in recent years, especially during the COVID-19 pandemic, in the neoadjuvant setting for optimal selection of neoadjuvant systemic therapy.2,3 Despite this shift in clinical practice, correlation of the 21-gene recurrence score between paired core needle biopsy and surgical specimens has not been fully explored, raising questions about the equivalence of gene expression profiling in these paired samples.

PRESENT

In our study, we selected gene expression data, from two publicly available datasets, for paired core needle biopsies and surgical specimens taken from patients with hormone-receptor positive, HER2-negative, early-stage breast cancer (n = 80 patients). We evaluated the differences and correlation in the levels of expression levels of the genes included in the 21-gene recurrence score. We also estimated the recurrence score (also known as microarray-recurrence score) and evaluated the agreement between the two sample types.4

Overall, we found a high correlation in gene expression levels between the core needle biopsy and the surgical specimen, with only minor differences (median difference in gene expressions of the 21-gene approximated zero), demonstrating that both sample types provide similar information.4 Furthermore, the concordance rate of the microarray-based 21-gene recurrence score categories was at least 82%, which is similar to the observed concordance rate of anatomopathological evaluation of hormone receptors and HER2 in paired core needle biopsy and surgical specimens.5 This provides additional information on the similarities between the diagnostic and surgical tissue samples. However, gene expression did not show absolute concordance, reflecting the presence of some heterogeneity that needs to be considered when making clinical recommendations for systemic therapy.

FUTURE

Although we found no significant differences in gene expression between the core needle biopsy and surgical specimens, several factors may be involved in the variability of the specimens: the intrinsic tumor heterogeneity, differences in the sampling methods, tissue handling, analytical intra- or interassay variability, and intra- or interobserver interpretation. Therefore, careful handling and standardization of breast tissue specimen processing is critical. This is especially true for the molecular profiling based only in core needle biopsies, since this limited sample may be the only cancer tissue available, particularly in patients achieving a complete pathological response after neoadjuvant systemic therapy. Finally, our study, showing agreement of gene expression signature between the two sample types, needs to be confirmed and validated.
in future studies using testing paired samples with the commercially available molecular platforms before their routine use in clinical practice can be endorsed.

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