Re: Breast Cancer Gene Microarrays Pass Muster

We were pleased to see the recent News article about breast cancer gene microarrays (1). This discussion of a recent article published in the New England Journal of Medicine (NEJM) (2) concludes that “biology may trump anatomy” regarding the
importance of genomic analysis in the prognosis of patients with early-stage breast cancer. It also points out that the NEJM article strongly suggests that knowing the molecular biology of a breast tumor may be more important than knowing “traditional” factors, such as size, grade, and lymph node status.

The News article is not accurate, however, in labeling one of the genomic prognostic tests evaluated in the NEJM article as “Oncotype DX™.” The Oncotype DX assay is performed in the reference laboratory of Genomic Health, Inc, in Redwood City, CA. Oncotype DX was developed by performing eight clinical studies in more than 2600 patients (3–6). The Oncotype DX assay uses a standardized quantitative reverse transcriptase–polymerase chain reaction (RT–PCR) assay, a technology that is considered to be the gold standard for measuring gene expression (7). Controls and calibrators are routinely used for each reagent and for each step to ensure precision and reproducibility.

The NEJM article examined five genomic classifiers, including one that yielded a “recurrence score” that was derived from the same 21 genes used in the Oncotype DX assay. However, the authors of that article did not, as the News article implied, use the standardized quantitative RT–PCR assay as performed by Genomic Health, Inc. Although the same genes were analyzed, the authors used DNA microarrays that were qualified for research use only and not for clinical testing to measure gene expression and did not include appropriate controls. Furthermore, the information derived from the gene expression analysis was limited by the fact that the authors of the NEJM article chose to categorize patients in two groups, yielding groups with a high or a low likelihood of recurrence. That is, the authors did not examine the quantitative and continuous measure of risk that is provided by the Genomic Health Oncotype DX assay.

Although these distinctions concerning the specifics of assay methods and performance may seem small to some readers, there is abundant prior evidence that methods matter and that attention to standardization and quality control is critical to bringing diagnostic tests to clinical practice and to improving the quality of treatment decisions.

References