

SABCS 2009 Abstract #6021

Molecular Characterization of Breast Cancer Core Biopsy Specimens by Gene Expression Analysis Using Standardized Quantitative RT-PCR.

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Background: Core biopsies (CBx) are increasingly the initial diagnostic procedure of choice for breast masses. Clinical studies of the 21 gene assay, which was optimized for small amounts of fixed paraffin-embedded tumor tissue, have been performed on core biopsies in the neoadjuvant setting (Gianni et al, JCO 2005 and Chang et al, Br Cancer Res Treat 2008). We report here the results of pathology review and quantitative RT-PCR analysis of a large number of CBx in clinical practice.

Methods: Cases included all Oncotype DX tests reported by the Genomic Health laboratory from July 15, 2005 through May 31, 2009. Pathology review of H and E stained sections, manual microdissection, RNA quantification, and quantitative RT-PCR analysis for each gene were performed according to the pre-specified eligibility criteria and methods used in the NSABP and Kaiser Permanente clinical validation studies. Descriptive analysis was performed on de-identified data with IRB approval. **Results:** There were 103,863 submissions to the clinical laboratory, of which 11,757 (11.3%) were identified on pathology review as CBx. The initial submission success rate was 94.3% on all cases, and was slightly lower in the CBx (91.6%) than in surgical resections (SRx) (95.7%). The most common reason for initial failure was insufficient tumor or no tumor found in 5.6% of CBx and 3.0% of SRx. Insufficient RNA (<275 ng) was found in 2.6% of CBx and 0.3% of SRx. Other causes of failure, such as RT-PCR process failures, were uncommon. In 80% of cases of initial failure another specimen was submitted by the site; the success rate on the resubmissions was 80% for both initial CBx and initial SRx. Thus, the overall success rate was >97%. As expected, the rate of manual microdissection to remove non-tumor elements was higher in SRx than CBx (33.0 vs 3.9% of cases). In addition, the total yield of RNA, on average, was greater in SRx than CBx (4.2 µg vs 2.5 µg). The average Recurrence Score (RS) in CBx and SRx was similar - RS mean (±SD) = 18.9 (±12.4) in CBx and 19.7 (±11.3) in SRx. A wide range of RS was observed in CBx. The proportion of tumors with RS <18, 18 - 30, and ≥ 31 was 58.8%, 28.6%, and 12.6% in CBx and 52.3%, 35.6%, and 12.1% in SRx. The distributions of quantitative ER, PR, and HER2 in CBx were also similar to SRx.

Conclusions: This large study indicates that quantitative RT-PCR analysis can be successfully performed on breast cancer core biopsies. Rigorous pathology review prior to gene expression analysis to identify cases with insufficient or no tumor is required to ensure the quality of gene expression analysis.

Sunday, December 13, 2009 7:00 AM