Assessing Tumor Percentage: A Possible Solution in Evaluating HER2 Copy Number (HER2CN) Data Generated by Molecular Inversion Probe (MIP) Technology on Formalin-Fixed Paraffin-Embedded (FFPE) Sections of Breast Cancer (BC) With Low Tumor Cellularity

Alexis Bousamra, MD, Hui Chen, Rajyalakshmi Luthra, Xinyan Lu, Gary Lu, Rajesh Singh, Ronald Abraham, MS, MHA, Shumaila Virani, Melissa Robinson, MBA, CG(ASCP), Bal Mukund Mishra Dr, Aysegul Sahin, MD, FASCP, MD Anderson Cancer Center

MIP technology has successfully produced quantitative HER2 copy number (HER2CN) data. Studies have shown high concordance between this emerging technology and conventional methods such as fluorescence in situ hybridization (FISH) and immunohistochemistry (IHC). OncoScan, the device behind MIP technology, appraises tumor percentage in the form of percent aberrant cells (%AC). However, inability to assess tumor heterogeneity, extensive stroma within the tumor, and prominent in situ carcinoma component constitute scenarios where %AC cannot be generated. We hypothesized that, when %AC is not generated, estimating tumor percentage on the designated slide circumvents this limitation of MIP with resultant accurate HER2CN data. We selected 27 invasive breast cancers (BCs; 17 with, 8 without, 2 equivocal for HER2 amplification by FISH) from the archives of our institution. For each tumor, 5 μm sections were cut from a representative formalin-fixed paraffin-embedded (FFPE) block and subjected to IHC, FISH, and MIP. In all 27 BCs, two breast pathologists estimated tumor percentage (%T) on H&E-stained slides. When OncoScan generates %AC, the resultant HER2CN(CNA) is the actual HER2CN(CNT). When %AC isn’t produced, CNA represents the average of both CNT and HER2CN within surrounding breast parenchyma (assumed to be diploid). In the latter scenario, CNT is calculated as: CNT = (CNA − (1 − %T) × 2)%T. Comparing HER2 overexpression (IHC) and CNA (MIP) in all cases resulted in 7 being the cut-off HER2CN(MIP) for distinguishing BCs with 3+ HER2 score from BCs with 0, 1+, or 2+ HER2 scores (P = .00076). In 13 of 27 BCs, %AC was generated. In 13 of the remaining 14 BCs without %AC, calculated CNT showed significant correlation with HER2CN by FISH (P = .0008), while CNA did not (P = .075). Our findings show that, when MIP arrays cannot assess the percentage of invasive tumor cells within the designated tumor area, a tumor percent estimate on the representative H&E slide is an important step in overcoming the limitations of this technology and establishing actual HER2CN by MIP(CNT).