Comparison of in situ hybridization methods for the assessment of HER-2/neu gene amplification status in breast cancer using a tissue microarray

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**A B S T R A C T**

**Background:** This project compared HER-2/neu gene status in breast cancers, as demonstrated by FISH (fluorescent *in situ* hybridization) and CISH (chromogenic *in situ* hybridization) and using a tissue microarray (TMA). The study also aimed to show whether the TMA technique could be used in clinical diagnostics, rather than remain a scientific tool.

**Materials and methods:** A TMA was constructed using 121 breast cancer specimens, 6 cores from each specimen. Demonstration and assessment of HER-2/neu gene status was by FISH (Vysis Path) and CISH (DAKO Duo CISH).

**Results:** The 121 breast cancer specimens were divided into 3 groups by HER-2 status, as determined by immunohistochemistry. In the HER-2 negative group no amplification was observed in 36 out of 40 cases. 3 cases showed amplification by both methods and one by CISH alone. The equivocal HER-2 group showed no amplification in 30 out of 41 cases and amplification in 9 cases. One case was FISH negative CISH positive and one was discarded. In the HER-2 positive group, amplification was confirmed in 37 of the 40 cases by both methods. 3 cases were unsuitable for assessment.

**Conclusions:** This study indicated that CISH is a sensitive alternative to FISH in detecting HER2 gene amplification and may replace FISH in HER2 testing. Good agreement was observed between methods (98.5% – 119 out of 121 cases). Furthermore, as only 4 out of 121 cases were unsuitable for assessment (no signal or missing TMA cores) – it may be feasible to use TMA in diagnostics.

**Keywords:** Breast cancer, CISH (duo-CISH), FISH HER-2, Tissue microarray