

## Actualities in breast cancer HER2 diagnostics

Determination of the HER2 status has become an inevitable step of routine pathological breast cancer diagnostics, not only having prognostic significance, but also being important in therapeutic decision making. HER2 positive breast cancer has poor prognosis, however monoclonal antibody trastuzumab is a new therapeutic approach to extend survival of these patients. HER2 determination is currently based on immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH). Both techniques demand high-level standardization in order to produce reliable results. Tissue microarrays (TMAs) can provide standard conditions for both IHC and FISH reactions.

Our aim was first to validate the reliability of our TMAs in breast cancer HER2 diagnostics for IHC and FISH examinations, then we compared and characterized six promising, commercially available anti-HER2 immunohistochemical antibodies (HercepTest, NCL-CB11, NCL-CBE1, NCL-CBE356, Pathway CB11, Pathway RM-4B5). Finally, from the collected data a reliable and cost-effective HER2 diagnostic algorithm was to be designed.

Validation of tissue microarrays was carried out on 174 invasive breast cancer cases by direct comparison of IHC on traditional large sections and on TMA slides, confronted with the corresponding FISH results. Taking FISH as the end point sensitivities, specificities, positive and negative predictive values and accuracies associated with the six anti-HER2 antibodies were determined based on immunohistochemical results of 199 breast cancer cases.

According to our results we can claim that our TMAs can be utilized reliably in breast cancer HER2 diagnostics. Summarizing our immunohistochemical experiences HercepTest has proved to be most appropriate for conducting HER2 immunohistochemistry, however a second reaction with a different antibody (NCL-CB11) is advised to be performed in order to increase the sensitivity of IHC. With the help of tissue microarrays fluorescence in situ hybridization may be conducted on all cases, thus the losing of FISH positive, but IHC negative cases can be minimized. In cases with strong protein expression lacking HER2 gene amplification, TMA based FISH results are to be confirmed on traditional large sections.