



## **Update on Recommendations for Immunohistochemical Testing of Hormone Receptor Status in Breast Cancer**

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Breast cancer is the most frequent form of cancer in women worldwide.<sup>1</sup> Numerous risk factors have been associated with the development of breast cancer including advanced age, personal and family history, reproductive history, and lifestyle factors. Varying histological subtypes of breast cancer have been described, including ductal and lobular carcinomas, each of which may demonstrate both in situ and invasive components. While the inheritance of susceptibility genes is the cause of breast cancer in approximately 12% of patients, most breast cancers occur sporadically and are not associated with inherited genetic mutations. Mutations of *BRCA1/2* genes are found in approximately 3% of breast cancers.<sup>2</sup>

In addition to histological subtype, tumor size, and nodal status, numerous prognostic and predictive markers help guide the clinical management of breast cancer patients. Estrogen receptor (ER) and progesterone receptor (PgR) status, which are currently determined mainly by immunohistochemistry, are two of the most important markers.

Per the most recent guideline recommendations by the College of American Pathologists (CAP) and American Society of Clinical Oncology (ASCO), ER and PgR status should be determined on all invasive breast cancers and breast cancer recurrences.<sup>3</sup> ER receptor status is one of the most important biomarkers for breast cancer due to the efficacy of estrogen ablation in ER-positive breast cancers. This distinction is critical, as ER negative patients do not normally benefit from estrogen ablation therapy. Although PgR status is typically determined alongside ER status, its exact role in patient care is less well defined.

Careful consideration and standardization of tissue handling is essential when collecting specimens that may be examined for ER and PgR status. Given the efficacy of adjuvant hormonal therapy in receptor positive disease, efforts must be made to limit false negative testing. During tissue acquisition, numerous pre-analytical variables need to be considered. Included in these variables is the time from interruption of the blood supply to tumor excision (warm ischemia time) as well as the time from excision to tissue fixation (cold ischemia time). Since ER and PgR molecules are labile and demonstrate decreased activity after the interruption of blood flow, decreasing the warm and cold ischemia times is essential.<sup>3</sup> Additional recommendations include fixation for a minimum of six hours and maximum of 72 hours, and use of an adequate volume of 10% neutral buffered formalin (NBF).<sup>3,4</sup> Ten percent NBF should be the only fixative utilized in the collection of breast tissue specimens.<sup>3,5</sup>

In conclusion, ER and PgR status should be established in all invasive and recurrent breast cancers. To reduce the possibility of false negative testing, special attention must be paid in specimen handling to limit the degradation of these biomarkers and ensure accurate reporting.

## References

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