# Processing and Reporting of Breast Specimens in the Neoadjuvant Setting

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**KEYWORDS**

• Breast cancer • Neoadjuvant • Pathology • Response to treatment • Residual disease • pCR • Sampling • Cellularity

**Key points**

- Post-neoadjuvant surgical breast cancer specimens are challenging. Systematic sampling of the correct area of the breast with correlation of gross and microscopic findings allows efficient and accurate reporting.
- Specimens should be clearly identified, as neoadjuvant, and the location and size of the tumor pretreatment must be known. Equipment to photograph or radiograph sliced specimens and create a map of the gross findings and the sections submitted is essential.
- Pathologic complete response (pCR), residual cancer burden (RCB), and yAJCC (American Joint Commission on Cancer) stage are recommended measures of residual disease.
- Patients with a pCR (ypT0/is ypN0 or ypT0ypN0) have an excellent prognosis regardless of breast cancer subtype and of the type of neoadjuvant systemic therapy received. RCB is prognostic overall, in breast cancer subtypes, and within stage groups.
- The processing approach and elements needed in the report for quantification of residual disease in the breast and lymph nodes will likely be the same regardless of the addition of other prognostic factors and irrespective of breast cancer subtype or type of treatment received.

## ABSTRACT

Standardization of quantification of residual disease in the breast and lymph nodes with routine pathologic macroscopic and microscopic evaluation leads to accurate and reproducible measures of response to neoadjuvant treatment. Multidisciplinary collaboration and correlation of clinical, imaging, gross and microscopic findings is essential. The processing approach to post-neoadjuvant breast cancer surgical specimens and the elements needed in the pathology report are the same regardless of breast cancer subtype or type of neoadjuvant treatment. The residual cancer burden incorporates response in the breast and in the lymph nodes into a score that can be combined with other emerging prognostic factors.

## NEOADJUVANT TREATMENT OF BREAST CANCER

Although many patients with breast cancer may be cured by surgery alone, adjuvant systemic chemotherapy, endocrine therapy, and/or anti-HER2 therapy reduce the risk of recurrence and mortality for selected patients. With more than 15 years of follow-up, we know that survival is the same whether the adjuvant chemotherapy is given before (neoadjuvant) or after surgery (adjuvant).[1] Systemic neoadjuvant treatment is increasingly

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used for locally advanced breast cancer, for downstaging tumors to facilitate breast-conserving surgery, and for early stage high-risk breast cancer. Systemic neoadjuvant treatment can be considered any time it is known before the surgery that the patient will require systemic (neo)adjuvant treatment. A discussion of the pros and cons of systemic neoadjuvant treatment and which patients might benefit the most from the different types of systemic neoadjuvant treatment are beyond the scope of this article. **Fig. 1** summarizes how neoadjuvant systemic treatment affects some aspects of the care of patients with breast cancer. When treatment is given before surgery, response to treatment can be evaluated. For individual patients with a poor response to neoadjuvant treatment there is an opportunity to change or add treatment after surgery. Neoadjuvant clinical trials are an opportunity to accelerate the development of new therapeutic agents and biomarkers. Clinical response to systemic neoadjuvant treatment does not correlate well with pathologic response. Accurate and reproducible pathologic evaluation of the post-neoadjuvant surgical breast cancer specimen is crucial.

## MULTIDISCIPLINARY COLLABORATION

Neoadjuvant treatment of breast cancer introduces challenges for each discipline involved.

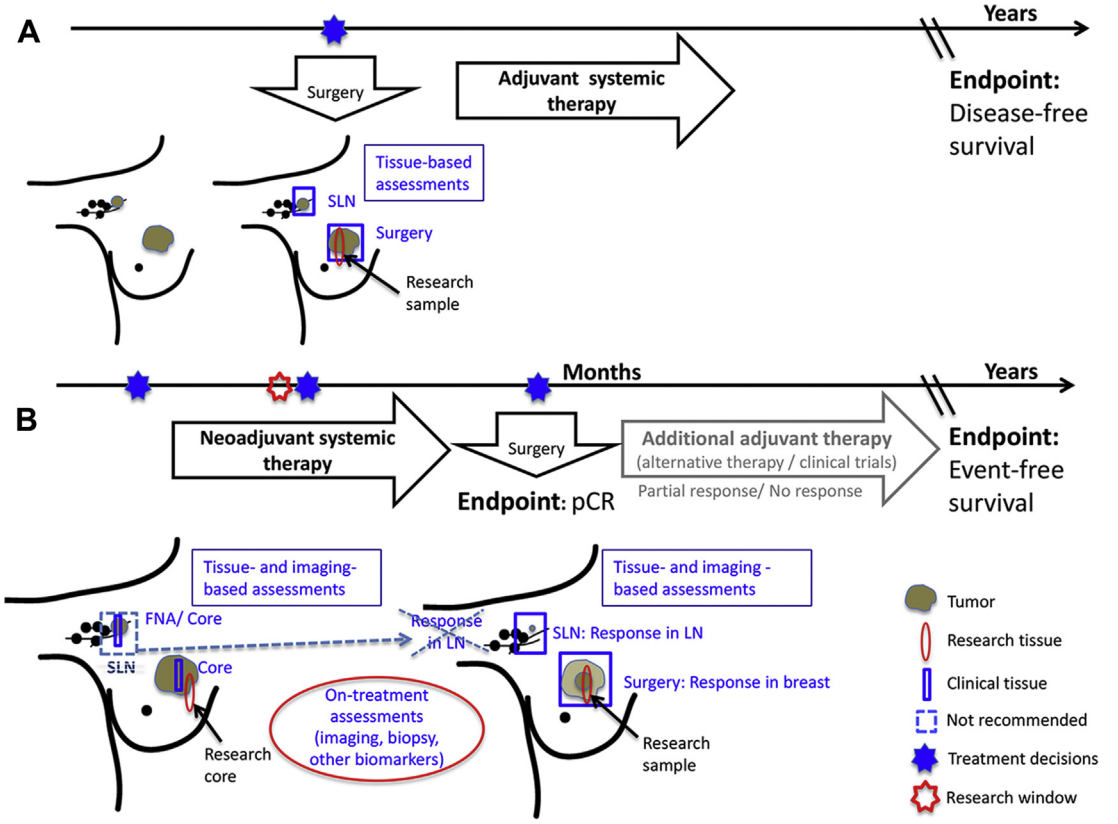


*Fig. 1.* Clinical and research tissue sampling and indicators of treatment effectiveness in the traditional setting (*A*) and in the neoadjuvant setting (*B*). In the setting of *adjuvant therapy* (*A*), the pathologist has the opportunity to evaluate the lymph nodes and the primary tumor unaltered by systemic therapy. The first available endpoint for clinical trials of adjuvant systemic therapy is generally disease-free survival after a many years. In contrast, in the setting of *neoadjuvant systemic therapy* (*B*), stage (tumor size and lymph node status) is determined by physical examination and imaging. Tumor grade and type as well as ER, PR, HER2, Ki67, and multigene assays are performed on a representative core needle biopsy sample. Research samples can be obtained at different time points. The surgical specimen provides the opportunity to evaluate the response to therapy in both the lymph node and the breast. If pretreatment SLN biopsy was performed, the opportunity to evaluate the response in the lymph nodes is lost. For patients with residual disease, there is an opportunity for additional therapy or to change to an alternative therapy after months rather than years. pCR provides a short-term, after months rather than years, endpoint for clinical trials. FNA, fine needle aspiration; LN, lymph node; SLN, sentinel lymph node. Note that disease-free survival and/or event-free survival (EFS) are the preferred survival endpoints (the FDA recommended EFS).