Introduction: Chemotherapy and radiation treatment can cause significant changes in the gross and microscopic appearance of benign and malignant breast tissue. Because neoadjuvant chemotherapy is now being offered to a larger subset of breast cancer patients, pathologists are more frequently presented with breast specimens harboring such changes. These changes may interfere with recognition of microscopic residual tumor, particularly near margins and in lymph nodes, estimation of residual tumor size, and tumor staging. This lecture will review the spectrum of histologic alterations that can be seen in benign and malignant treated breast tissue and implications for grossing, diagnosis and staging.

Treatment Induced Changes in Breast Tissue

In Benign Tissue
- Lobular atrophy
- Lobular fibrosis
- Epithelial atypia (nucleocytomegaly, hyperchromasia)
- Stromal fibrosis

In Malignant Tissue
- Reduction in tumor bulk/cellularity (residual tumor may be grossly occult)
- Reduction in cytologic atypia (tumor cells acquire bland nuclear features)
- Acquisition of foamy/apocrine cytoplasm (tumor cells mimic histiocytes)
- Conversion to ductal morphology of lobular cancer

Potential Pitfalls in Evaluation of Treated Breast Cancer
- Under-recognition of residual tumor (false diagnosis of “no residual tumor”)  
- Under-estimate of residual tumor size
- Under-recognition of positive margin involvement
- Under-recognition of nodal involvement
- Misclassification of ductal carcinoma as lobular carcinoma
- Under-staging
- Over-diagnosis of treatment induced atypia in benign epithelium

Neoadjuvant Chemotherapy (NACT) Effects on the Breast

Candidates for NACT: Pre-operative chemotherapy (also known as primary therapy or neoadjuvant chemotherapy, NACT) was initially introduced for managing patients with locally advanced breast cancer and is now considered standard of care for such patients. NACT is now also being selectively offered to certain patients with large but operable breast cancer. Among patients with locally advanced cancer, the goal of NACT is to improve operability, to enhance local control, and to convert some patients from mastectomy to breast conserving therapy (also called “downstaging”). The same goals apply to patients with large but operable cancer. Additionally, by determining response to therapy (i.e. tumor shrinkage), one can potentially tailor future chemotherapy decisions for a given patient.

In the handful of randomized clinical trials to date, overall survival and disease free survival are the same in patients receiving NACT versus adjuvant chemotherapy. The advantages are that; more patients are able to undergo breast conserving surgery and more patients are found to be axillary node negative. Patients who have no pathologic evidence of residual tumor following NACT do have better disease-free survival and overall survival; this occurs in 6% to 19% of patients treated with NACT.
The key tasks in evaluating the breast excision specimen (lumpectomy or mastectomy) following NACT are:

- determining residual tumor size
- distinguishing treatment effect on benign breast from tumor
- detecting nodal metastases in the presence of treatment effect
- evaluating margin status for occult single tumor cells

**Defining Response to Chemotherapy**

The World Health Organization and International Union Against Cancer have defined criteria for evaluating response to systemic therapy in general:

- **Complete response (CR):** complete absence of detectable disease
- **Partial response (PR):** >50% reduction in maximal dimension of tumor
- **Progressive disease (PD):** increase in tumor size by more than 25%
- **Stable disease (SD):** no increase in tumor size more than 25%
- **No response (NR):** scenarios that do not fulfill any of the above criteria

Response can be evaluated clinically, in which case the nomenclature is prefixed by the letter “c”. For example, cCR indicates a complete disappearance of tumor by clinical exam. Response can also be evaluated pathologically at time of surgery. For example, pCR indicates that no residual tumor is found in the specimen. pPR indicates that the residual tumor found in the specimen is more than 50% smaller than the pre-treatment size. This nomenclature is predominantly used clinically. As long as the residual tumor size (or its absence) is indicated in surgical pathology reports, the pathologist need not incorporate this vocabulary into the pathology report.

**Efficacy of NACT**

The NSABP-B18 trial is one of the largest prospective randomized trials to evaluate NACT in breast cancer. 608 patients were randomized to receive a pre-operative course of four cycles of AC (doxorubicin and cyclophosphamide) and 626 patients were randomized to receive post-operative treatment by the same chemotherapy. Patients were followed for 9 years. Overall, 80% of tumors showed at least a clinical partial response and clinical complete response in 36%; among these with cCR, 38% had pCR. 13% had both cCR and pCR while 7% had pCR without cCR. Lymph node metastases were also fewer in the NACT group compared to standard post-operative adjuvant treatment. From a clinical management perspective, more patients were able to undergo lumpectomy following NACT, a benefit that extended to patients whose tumors were initially clinically measured >5 cm. Overall survival and disease free survival was no different, however, between pre and post-operatively treated patients. Among neoadjuvant treated patients, better overall survival and disease free survival occurred in those with both a clinical and pathologic complete response. Poor nuclear grade in pre-treatment biopsy was associated with pCR (26% achieve pCR) versus good nuclear grade (14%). A recent meta-analysis of the handful of well-designed clinical trials confirmed this finding that overall survival is the same as standard adjuvant therapy. The main benefit is conversion to breast conservation in a subset of patients as well as identifying non-responders to chemotherapy.

**Gross Pathologic Changes Following NACT**

Stromal fibrosis and a wound-healing type of response are common changes in breast tumors that respond to NACT. This can sometimes, but not always be appreciated grossly.

If a pathologic complete response occurs, the gross appearance may be either unremarkable or fibrotic at the site of the original tumor bed. If microscopic residual tumor exists, there might not be any gross finding other than fibrosis. We have encountered cases of apparent complete clinical response in which there no gross findings but occult tumor cells were widely scattered throughout the breast.
Sampling Recommendations for NACT breast specimens

Gross estimation of residual tumor size can be misleading because of stromal fibrosis. Both overestimates and underestimates of residual tumor size can occur, therefore, careful correlation with findings on histologic slides is important. Reconstruction of tumor size based on slide findings is more accurate in our experience (see below).

It is important to know the pre-chemotherapy estimate of tumor size. Tissue from across at least that dimension should be sampled from the mastectomy regardless of whether gross pathology is present or not. For example, if the pre-chemotherapy tumor was 5 cm but the gross residual tumor is 2 cm, tissue should be sampled from at least 5 cm surrounding the center of the residual mass. In fact, because clinical/radiologic size estimates can be under-estimates, we would extend the sampling to beyond a 5 cm size just in case microscopic tumor was present beyond the clinically estimated boundaries. Heavy sampling of margins is also advised, regardless of whether the gross appearance is suspicious or not.

Measuring Residual Tumor Following NACT

Tumors do not necessarily shrink concentrically from the outside inwardly or vice versa; tumor regression can be patchy and irregular. Residual tumor may be present in one of several patterns:

- A dominant mass (usually grossly visible)
- Scattered nodules amongst altered stroma (usually grossly visible)
- Occult microscopic foci scattered amongst altered stroma (not grossly visible)
- Rare scattered single cells (not grossly visible).

This variability causes difficulty not only in measuring residual tumor size, but also in missing occult tumor cells.

Until the recent 7th edition of the AJCC Staging System, there were no standardized methods of pathologically measuring residual tumor following NACT. It is not a straightforward task because of the various distribution patterns that can be seen. Relying on radiologic size is not always accurate. Both under and overestimation can occur. For example, if a 5 cm radiologic mass is reduced to a hyalinized, relatively acellular tumor bed which contains two microscopic foci of occult tumor cell clusters measuring 0.2 cm each but separated by 3 cm, how should residual tumor size be interpreted. Is this a 3 cm tumor? Or is this microscopic residual tumor foci, measuring up to 0.2 cm each? (an interpretation that could be substantiated if the intervening 3 cm contains normal proliferative changes without any evidence of stromal changes of tumor regression). The clinical significance of the difference in these interpretations is unknown.

AJCC Definition of residual tumor size: AJCC now states that the single largest mass of residual invasive cancer should be measured and used for ypT staging. The background fibrotic tumor bed (granulation tissue, fibrosis, organizing hemorrhage) should not be counted. If there are scattered nests of tumor cells rather than a “mass”, AJCC states that the “largest contiguous area of invasive carcinoma” should be measured.

Recommendation: We follow the new AJCC rules, however in many scenarios it is not clear how to apply them.

Scenario 1: If there are multiple discrete foci of residual invasive cancer, we base AJCC ypT on the largest discrete focus, but we also document in our report the total span of all invasive foci.

Scenario 2: If there is residual invasive cancer but instead of a discrete focus it is present as microscopic cells or clusters distributed in a low cellularity across a large span, we base AJCC ypT on the total span of the invasive cancer. We also give a subjective description of the cellularity (i.e. scant cellularity, low cellularity, high cellularity) to distinguish a 4 cm focus of highly cellular residual cancer from a 4 cm focus of scant residual cancer cells embedded in organizing fibrosis.
Histologic Changes Following NACT

Changes can be seen in the tumor architecture and cytology, the stroma, and the architecture of the terminal duct lobular unit (TDLU).

In Benign Tissue
- Lobular atrophy
- Lobular fibrosis
- Epithelial atypia (nucleocytomegaly, hyperchromasia)
- Stromal fibrosis

In Malignant Tissue
- Reduction in tumor bulk/cellularity (residual tumor may be grossly occult)
- Reduction in cytologic atypia (tumor cells acquire bland nuclear features)
- Acquisition of foamy/apocrine cytoplasm (tumor cells mimic histiocytes)
- Acquisition of lobular “morphology” in ductal carcinoma

Histiocytoid changes:
Cytoplasmic eosinophilia, dense or glassy cytoplasm, and rounded tumor cell shape can occur, often resulting in a histiocyte-like appearance. Rare, scattered single tumor cells with such changes can be difficult to distinguish from histiocytes. The presence of nuclear atypia or mitoses is helpful; in some cases, when a margin is involved, keratin immunohistochemistry may be useful. Clustering of a few tumor cells together to form a small tight ball may give a multinucleated appearance that also can mimic histiocytes. Clinical significance of these changes is unknown. The importance is to be aware of occult tumor cells mimicking histiocytes near surgical margins.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Treated tumor cell mimicking histiocytes</th>
<th>Histiocyte</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>larger than histiocyte</td>
<td>small</td>
</tr>
<tr>
<td>Cytoplasmic contents</td>
<td>mucin, large vacuoles</td>
<td>hemosiderin</td>
</tr>
<tr>
<td>Nuclear pleomorphism</td>
<td>present</td>
<td>absent</td>
</tr>
<tr>
<td>Multinucleation</td>
<td>can be present</td>
<td>usually absent</td>
</tr>
<tr>
<td>Hyperchromasia</td>
<td>present</td>
<td>absent</td>
</tr>
<tr>
<td>Mitoses</td>
<td>can be present</td>
<td>absent</td>
</tr>
<tr>
<td>Keratin staining</td>
<td>positive</td>
<td>negative</td>
</tr>
</tbody>
</table>

Cytoplasmic vacuolation of tumor cells:
Optically clear cytoplasmic vacuoles sometimes may be seen in tumor cells. Rarely, it is possible to mistake cells with prominent clear vacuoles as myoepithelium. When such tumor cells are arranged in small glandular or tubular architecture and display minimal atypia, it is possible to mistake the tumor for benign breast epithelium. We have even encountered rare cases of mimicry in which residual tumor cells are distributed in sclerosing adenosis-like pattern and also have cytoplasmic vacuoles. Such appearance can easily be misinterpreted as benign proliferative disease. When diagnostic doubt is raised, immunohistochemical myoid markers can distinguish vacuolated tumor cells from myoepithelial cells.
**Recommendation:** If the pre-treatment tumor was HER2 positive by immunohistochemistry, HER2 can be used to distinguish residual treated tumor cells from benign mimics (histiocytes, normal epithelium). This is especially useful when evaluating margins or cells with crush artifact.

**Evaluating tumor type following NACT**

Because of the cumulative changes to the cytoplasm, nuclei, architecture, and distribution of residual tumor cells following NACT, it may be difficult to assess histologic tumor type. The pre-treatment breast biopsy is the most informative specimen for assessing tumor type. The histiocytoid changes to tumor cells and the isolated single cell distribution pattern, for example, in some residual tumors may mimic lobular or even pleomorphic lobular differentiation even though the pre-treatment core biopsy shows clear cut ductal differentiation. In the NSABP B18 trial, most of the cases were classified as carcinoma NOS following NACT.

**Recommendation:** Comparing the histologic subtype of the pre-treatment tumor to the post-treatment tumor is good practice, since the two should be concordant. If the post-treatment tumor shows lobular differentiation, but the pre-treatment tumor is ductal, the change may be an artifact of treatment rather than real. E-cadherin/p120 immunohistochemistry is advised if there is a discrepancy.

**Grading residual tumor following NACT**

Because of the potential cytologic and architectural changes in tumor following NACT, it is reasonable to raise several questions about traditional tumor grading if applied to the residual tumor:

1.) does NACT cause a significant change before and after treatment?

2.) is the post treatment grade clinically valuable (i.e. does it predict survival)?

3.) should a grade be included formally in the surgical pathology report.

Available data with which to address these questions is limited. Frierson et al showed in a small study that pre and post treatment grades did not significantly differ but Sharkey et al found changes in about a third of patients. Both studies had small numbers of patients. Chollet et al tested Scarff-Bloom-Richardson grading as well as various combinations of grade with tumor size and lymph node status in post-treatment specimens; none of the variables showed any statistically significant relationship with overall survival, though disease-free survival was related to lymph node status and a modified combination of tumor size + grade. The best responders to NACT are those with poorly differentiated tumors where as the low grade tumors tend not to respond as well to NACT. This may confound the results when looking at outcome of post-treatment grading. Larger scale studies are required with long follow up.

**Recommendation:** Our current practice is to note that traditional SBR grading may not carry the same clinical significance in the NACT patient; with this caveat, we do provide a post-treatment tumor grade.

**Surgical margin evaluation following NACT**

Evaluating margins can be treacherous because single histiocytoid tumor cells may not be seen at low power. Occult tumor cells are likely to be hidden in granulation type tissue, a key visual clue at low power. The extent of occult tumor that is underestimated can be easily appreciated on a keratin stain. HER2 immunostaining is another option if the pre-treatment tumor was HER2 positive.

**Hormone receptor status following NACT**

Status of estrogen receptor (ER), progesterone receptor (PR), and Her2/neu is best determined on the surgical biopsy obtained prior to NACT because the mastectomy/lumpectomy specimen may not contain any or sufficient residual tumor for testing. The status of these biomarkers may be altered following a course of NACT but is usually concordant with pre-treatment status. The literature contains only few studies of pre and post NACT comparison of biomarker status. For ER and PR status, studies have reported changes in around 10% of cases but some studies document changes in up to a third of cases; most commonly, ER status changes from positive to negative. Her2 status appears to be more stable throughout NACT. Concordance between pre and post NACT Her2 status ranges from 65% to 100%.
FISH testing appears more stable than immunohistochemical testing for Her2, with concordance of 87% and higher reported.

**Changes in Benign Breast following NACT**

*Terminal Duct-Lobular Unit (TDLU) sclerosis / atrophy*

Sclerosis of the non-tumorous TDLU basement membrane can be extensive and the appearance may mimic age-related atrophic changes. TDLU sclerosis can be patchy and focal throughout the specimen. About two-thirds of neoadjuvant treated patients will exhibit some degree of TDLU sclerosis as will about half of adjuvant treated patients. This change can often be a clue that the patient has received NACT and is helpful to know about because the clinical history of NACT may not always be available to the pathologist at the time of slide review. In particular, the finding of TDLU sclerosis in a premenopausal patient should raise the possibility of NACT.

*TDLU epithelial atypia*

Changes in the epithelium of non-neoplastic TDLU acini following NACT can result in nuclear pyknosis or nuclear atypia. Again, these changes are neither common nor evenly distributed within a particular specimen (i.e. changes can be focal or patchy). Nuclear atypia is usually accompanied by overall enlarged cells (nucleocytomegaly). These changes are not as well reported in the literature as those following radiation treatment.

*Inflammation / duct ectasia*

Varying degrees of duct ectasia involving the benign breast may be evident. The ducts may be dilated and contain a mixture of histiocytes and proteinaceous debris. Histiocytes may be concentrically aggregated around the duct wall with varying amounts of chronic inflammatory infiltrates. Some specimens contain prominent bands of chronic inflammation surrounding ducts and TDLUs. These changes are not necessarily present near sites of residual tumor or original tumor bed. Larger aggregates of histiocytes within fibrotic stroma, often near sites of residual tumor can be seen. These aggregates may span several millimeters and are presumably sites that once contained tumor cells.

**Axillary lymph node changes following NACT**

Stromal fibrosis may be seen within axillary lymph nodes following NACT. Usually this occurs in nodes containing metastatic tumor (75% of positive nodes had a stromal response in the NSABP B18 study) and the fibrosis surrounds the metastatic tumor cells. Nodal fibrosis can be used as a visual clue to the presence of metastasis but it certainly can occur in the absence of metastatic cells (12% of cases in the NSABP B18 study); the clinical significance of this is unknown.

The 7th edition AJCC states that post-treatment lymph nodes should be ypN staged using the same criteria as in a non-treated patient. Thus, it is possible for residual small clusters of tumor cells to be present but, if the clusters are smaller than 200 in number or smaller than 0.2 millimeter, the node is staged as ypN0i+. The one caveat is that AJCC advises that any fibrotic stroma accompanying the tumor cells should be incorporated into the measurement. Thus, a 0.4 millimeter fibrotic deposit containing a few isolated tumor cells will be ypN1.

**Radiation Treatment Effects in the Breast**

**Scope of the Issue**

Breast conservation therapy (BCT) is now considered standard of care for early stage primary breast cancer. The National Cancer Institute position on BCT is based on multiple long term randomized clinical
trials demonstrating similar overall survival in early stage patients treated by lumpectomy plus radiation versus mastectomy. The role of radiation in BCT is to improve local-regional control (reduce local-regional recurrence).

Recurrence following BCT ranges from 5% to 22%. Most recurrences are detected within 2 years by post treatment surveillance mammography, however, a number of other etiologies can produce abnormal mammograms or palpable lumps post-treatment. Approximately 10% of BCT patients will develop a new mass, new calcifications, or an abnormal mammogram that requires biopsy. About half of these lesions are recurrent tumor; the other half are benign findings including fat necrosis or scar. Any of these biopsies may harbor radiation induced changes in the breast epithelium, regardless of benign or malignant status. These radiation-induced changes can be misinterpreted as atypia or malignancy. Distinguishing benign lesions from recurrent tumor in the setting of radiation effect may be challenging – or impossible in rare cases—but a few features help guide the distinction.

**Radiation-induced changes in benign breast**

Both the architecture (terminal duct-lobular unit, TDLU) and the cytology of the normal breast can be altered by radiation. The predominant changes occur at the level of the TDLU. Most notable at low power is an atrophic appearance of the TDLU. The basement membrane surrounding the acini is thickened and hyalinized/collagenized as is the intralobular stroma. The acinar epithelium appears atrophic; the cells are fewer in number per acini and smaller in size. These features resemble post-menopausal lobular atrophy. At high power, cytologic atypia can be seen in the acinar epithelium: enlarged hyperchromatic nuclei, small nucleoli, eosinophilic cytoplasm, or finely vacuolated cytoplasm. Atypia can also affect the larger ducts. Importantly, the cytologic atypia is not accompanied by any evidence of loss of polarity, proliferation, mitoses or necrosis. In addition to epithelial changes, the myoepithelial layer may become quite pronounced, with clear cytoplasm. Stromal changes may be appreciated. Nuclear enlargement, nuclear atypia, stellate or irregular nuclear contours and prominent nucleoli, can be seen in stromal fibroblasts. Vascular changes are not common; in Schnitt’s study only one quarter of specimens were affected. They noted vascular findings of myointimal proliferation, mural hyalinization and prominent capillary endothelial cells.

**Architectural changes in TDLU**
- atrophic TDLU (small size, fewer acinar epithelium)
- thick, hyalinized TDLU basement membrane
- hyalinized intralobular stroma

**Cytologic changes in TDLU**
- enlarged hyperchromatic nuclei
- prominent nucleoli
- eosinophilic cytoplasm
- finely vacuolated cytoplasm
- prominent myoepithelium (abundant clear cytoplasm)

This constellation of changes does not equally affect all radiated patients; in Schnitt et al’s study, about 30% of patients showed mild changes and the remainder showed more striking changes. The extent and degree of changes can be variable within a given specimen. For example, some TDLU could harbor only a few atypical cells while others may be completely involved by atypia. Finally, the extent/degree of changes do not appear related to the radiation dosage. More severe stromal changes such as fat necrosis and stromal fibroblast atypia may focally occur in the vicinity of tissue targeted for external boost doses.

**Duration of changes following radiation**

Radiation induced changes do not appear to regress over time. Moore et al studied 117 patients who had undergone radiation therapy and subsequent breast biopsy/excision up to 229 months later. The degree
of radiation changes was not altered by the amount of time elapsed between exposure and subsequent biopsy.

**Changes detected by fine needle aspiration cytology**

Fine needle aspiration cytology of benign breast tissue with radiation-induced changes shows sparse cellularity, presumably due to atrophic changes. Cytologic atypia can be notable: nuclear enlargement, increased nuclear:cytoplasmic ratio; prominent nucleoli. The presence of myoepithelium is important to recognizing the tissue as benign. Equally important is sparse or low cellularity of the sampling and preserved cell cohesion. Necrosis is not seen in radiation atypia. Cystic lesions following radiation and surgery, which typically represent seromas, may occasionally be lined by atypical squamous metaplastic cells that can be detected on cytologic evaluation of the cyst contents.

**Distinguishing radiation-induced changes from carcinoma**

Local recurrence may occur in a small subset of patients; recurrent tumor typically resembles the primary tumor and rarely shows radiation effect. Nevertheless, cytologic atypia in benign TDLU and ducts exposed to radiation can mimic in-situ carcinoma. Studies by Schnitt et al, Girling et al, and Moore et al cite the following features of benign radiation atypia that distinguish it from carcinoma:

- no cellular proliferation
- no mitoses
- no TDLU distension
- preserved cell polarity
- preserved cell cohesion
- no necrosis

It is helpful to compare the morphology of in-situ carcinoma in the pre-radiation specimen to any suspicious findings in the post-radiation specimen. In-situ tumor tends to maintain similar morphology before and after radiation. Involvement of the TDLU by LCIS or DCIS results in distention of the TDLU rather than atrophy, as is seen in benign TDLU post-radiation. Loss of polarity, loss of cell cohesion, mitoses, and necrosis are helpful features that distinguish DCIS in lobules from radiation atypia. Involvement of larger ducts by cytologic atypia can be difficult to interpret. Although the features listed above can be helpful, it is not always possible to be definitive in evaluating cytologic atypia.

**Radiation induced malignancy in the breast**

- **Angiosarcoma of the breast** is a long recognized complication that may follow treatment of breast cancer; it may arise in one of several contexts. The angiosarcoma described originally by Stewart and Treves is thought to result from lymphedema following radical mastectomy and axillary dissection. These tumors usually involve the arm rather than the chest wall/breast. As more patients are now being treated with conservative surgery and radiation, a slightly different profile of post-treatment angiosarcoma has emerged in the literature: post-radiation angiosarcoma.

- **Post-radiation** angiosarcomas are almost always cutaneous based, though some parenchymal based tumors have been reported. Cutaneous angiosarcomas arise in the radiation field of treated patients (and are referred to as cutaneous post-radiation angiosarcoma of the breast). As opposed to the long interval of time between surgery and development of Stewart-Treves angiosarcoma (around 10 years), the latency period for cutaneous post-radiation angiosarcoma is short (around 5 years, some within 3 years). The tumors present as erythematous patches, plaques or nodules. Histologically they are confined to the dermis of the breast except in a few cases of parenchymal based angiosarcoma. Growth patterns range from the typical irregular vasoformative pattern of angiosarcoma to a sieve-like pattern to a solid pattern. Tumor cells may have epithelioid features and the majority show grade 3 nuclei. This tumor is aggressive: local recurrence is high and metastases are common. Median time to death is around 3 years. Fortunately, the overall incidence of angiosarcoma following radiation is extremely low. In one study of over 18,000 patients at risk, only 9 cases of angiosarcoma were documented, though others have reported incidences up to 1%.
Recurrent high grade carcinoma may mimic angiosarcoma. This is usually not a diagnostic challenge. Rarely, though, a patient’s original tumor may be a metaplastic carcinoma and the post-treatment biopsy may contain spindle cell pattern tumor that could either represent recurrent metaplastic carcinoma or angiosarcoma. Immunohistochemistry can be helpful; angiosarcoma should express a vascular marker such as CD31, CD34, or factor VIII and should not express keratin.

REFERENCES

Radiation Treatment and Breast Conservation, Current Reviews


Radiation induced Pathologic Changes in the Breast


Post-Treatment Sarcoma


Neoadjuvant chemotherapy (NACT), Current Reviews


NACT induced Pathologic Changes in the Breast


**Tumor Grade following NACT**


**Biomarkers following NACT**


**Axillary Nodes following NACT**

