# Breast Cancer
# Where we were, where we are, and where we're going.

By: Rhonda Wachsmuth, MD

When I was training, in the 80's, mastectomy and axillary lymph node dissection (modified radical mastectomy) was the mainstay of treatment for breast cancer. With the advent of chemotherapy, the debilitating Halstead radical mastectomy, with removal of pectoralis muscle and level III lymph nodes, no longer provided benefit over more limited surgery in most breast cancer patients. It was during this time that breast conservation in the treatment of breast cancer began to emerge with the NSABP B-06 study results, which confirmed no survival benefit to more aggressive surgical treatment. It was slow to be adopted in some areas, but eventually became the standard of care with mastectomy only recommended in a minority of situations. With breast conservation, we added whole breast radiation in order to achieve the same outcome as mastectomy.

The next significant advancement in surgical de-escalation was heralded by the NSABP B-32 study, which yielded paradigm-shifting data regarding axillary surgery. This study showed that sentinel lymph node biopsy, already established as a standard of care in melanoma, could be safely and effectively used in breast cancer in the absence of known axillary disease. Axillary lymph node dissection (ALND) was the most debilitating aspect of our surgical treatment at that time and was truly used for staging purposes more than for treatment. However, in cases of known axillary disease or a positive sentinel lymph node biopsy, we still performed ALND. This would change as well several years later when the ACOSOG Z0011 trial confirmed that ALND provided no survival benefit in cases of early stage breast cancer with 1-2 positive sentinel lymph nodes. Furthermore, around that time we also learned from the AMAROS trial that axillary radiation treats the axilla as well as surgical ALND and with fewer complications, particularly lymphedema of the arm. However, ALND was still used to treat patients who presented with lymph node positive disease.

While our surgical approach was undergoing this development, we were of course simultaneously making advancements in medical therapy. While it may seem obvious today, we were coming to understand that not all breast cancers are the same – some are more aggressive with an increased propensity to metastasize and subsequently kill our patients. We learned how to identify these more aggressive cancers and developed targeted chemotherapy, a critical advancement with major implications for surgical management. The ability to risk-stratify and treat patients preoperatively allowed us to de-escalate surgical treatment for many patients. Patients who prior to this would have required a mastectomy could now be down-staged and treated with more limited breast conserving surgery. In addition, we de-escalated axillary surgery: patients with limited lymph node disease who receive preoperative chemotherapy and subsequently demonstrate a clinical response in the lymph nodes are now treated with sentinel lymph node biopsy and, if there is no residual disease, no further axillary surgery is performed. These patients still receive regional lymph node radiation but there are ongoing studies to determine if this is truly necessary. Likewise, patients who demonstrate a pathologic complete response in the breast still receive whole breast radiation if breast conservation is performed and in some cases postmastectomy radiation if indicated based upon preoperative data; in the future this may be proven unnecessary and there are a number of trials evaluating this. Regarding radiation, we have been able to decrease the length of treatment, which has been six weeks historically, to three weeks in many cases, and even to one week or one intraoperative treatment in some patients. Furthermore, partial breast irradiation has been shown to be equally effective compared to whole breast irradiation in certain situations.

Moving beyond traditional surgical approaches, cryoablation of small early stage breast cancers is now being studied. Early data from the ICE3 clinical trial suggests that cyroablation is an effective alternative to surgery for small breast tumors with low-risk features in women over 60 years of age. Looking even further into the future, I suspect that we may ultimately be able to avoid surgery in patients who we can prove have had a pathologic complete response to chemotherapy.

Medical advancements have also continued and have been especially augmented by developments in the field of tumor genomics. We are now able to identify breast cancers that will not respond to specific adjuvant treatments and thereby spare patients the associated morbidity. In the past, these decisions were based upon tumor staging, resulting in the over- or undertreatment of many patients. For example, we are now able to identify patients with ductal carcinoma in situ who derive no benefit from radiation therapy and eliminate this step in treatment. Based on a tumor's genetic profile we can identify patients who will derive no benefit from cytotoxic chemotherapy and avoid this costly (both financially and in terms of morbidity) treatment. Lastly, the targeted chemotherapies that are now available equip us to treat tumors much more successfully, and ongoing research in this field promises increasing options in this area.

Unfortunately, the one aspect of care which has not been de-escalated is the financial toxicity of treatment. Rather, the financial burden on patients and our health care system as a whole has continued to soar. While we have certainly improved outcomes and come a long way from the debilitating origins of breast cancer treatment, cost remains a major stumbling block. In many cases finances can be an insurmountable barrier to treatment for our patients. Advances in this area will be key to diminishing inequities in breast cancer care.

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