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# Introduction: Locally Advanced Breast Cancer

This is the most exciting time in the history of breast cancer research and treatment. Advances occurring in all disciplines of breast cancer care have had the positive effect of improving survival and decreasing treatment side effects. For example, screening and public educational efforts have significantly decreased the percentage of breast cancer cases that present with locally advanced or metastatic disease. For those who do present with locally advanced breast cancer, advances in surgical therapies have helped minimize treatment-related morbidity and improved the quality of life for survivors. With respect to systemic therapies, new cytotoxic chemotherapies, new dose scheduling, and the introduction of aromatase inhibitors have helped minimize the risk of death from subsequent development of metastatic disease. The understanding of breast cancer biology is also rapidly changing, which has led to new therapeutics directed against selective molecular targets, such as the HER2/neu receptor. Finally, radiation treatments, which have been an integral component of breast cancer management for over 6 decades, have evolved. As a packet, these advances have made a real difference for breast cancer patients. Specifically, breast cancer death rates in the United States and the United Kingdom have shown a precipitous and consistent decline over the past decade.[1]

Despite this background, there is still room for improvement. Over 40,000 women in the United States are predicted to die of breast cancer each year.[1] Many of the patients who eventually die originally presented with lymph node-positive disease and/or locally advanced breast cancer. In countries without mammographic screening programs, the percentage of patients diagnosed with locally advanced breast cancer and the percentage of patients dying of disease are even more of a pressing issue.

It is imperative that radiation oncologists and other specialists remain aware of the number of changes developing in the understanding of locally advanced breast cancer and that locally advanced breast cancer is a potentially curable disease. Moreover, each new systemic treatment advance that increases the chance of eradicating micrometastases makes the role of radiation for locally advanced breast cancer even more critical. For example, patients treated for locally advanced breast cancer before the development of effective systemic treatments would often die of metastatic disease. Such patients received little benefit from radiation achieving eradication of persistent foci of local-regional disease after surgery. In contrast, with effective systemic treatment, failure of eradication of persistent local-regional disease has been shown to increase the risk of subsequent distant failures. Using systemic therapy, radiation benefits can translate into improved survival and cure rates.[2]

This issue of *Seminars in Radiation Oncology* provides the reader with a broad overview of the current status of locally advanced breast cancer. Newman updates the epidemiology of locally advanced breast cancer and highlights how disparities in health care can influence the incidence of this disease and its treatment success. Huber et al review how the evolving understanding of breast cancer biology is leading to an improved classification of breast cancer. Locally advanced breast cancer represents a spectrum of different biological diseases that have distinct patterns of presentation, molecular phenotypes, treatment responses to various agents, and prognoses. It is imperative that the radiation oncology community become familiar with the new molecular lexicon of breast cancer classifications and incorporate molecular features into their therapeutic thought processes.

The optimal management of locally advanced breast cancer requires multidisciplinary care. As highlighted by Specht and Gralow, neoadjuvant chemotherapy is now considered the standard of care for these patients. This treatment is associated with high response rates, which can convert inoperable disease to an operable status and can allow for some patients to be treated with breast conservation. With the move to sequence chemotherapy before surgery, accurate pretreatment assessment of disease is critical. Whitman and Strom review the importance of a clear delineation of local-regional disease status with appropriate diagnostic imaging and examination before embarking on a course of neoadjuvant chemotherapy. Of particular value is the use of ultrasound with fine-needle aspiration to evaluate the extent and location of regional adenopathy. The documentation of disease in lymph nodes before neoadjuvant chemotherapy can frequently change clinical staging and affect subsequent local-regional treatment decisions.

One major potential advantage that neoadjuvant chemotherapy offers for selected patients with favorable disease response is the opportunity of treating with breast-conserva-

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tion therapy. Breast conservation after neoadjuvant chemotherapy requires close multidisciplinary coordination and careful selection criteria to achieve optimal results. In this issue, Alm El-Din and Taghian review the published outcome data regarding breast conservation after neoadjuvant chemotherapy and help describe appropriate selection criteria for consideration of this treatment approach.

Radiation treatments also play an important role as adjuvant therapy for patients treated with mastectomy. Postmastectomy radiation has been found to contribute to the survival of patients with locally advanced disease, and, as systemic treatments improve, the benefits of local-regional therapies on survival increase. Jagsi and Pierce review the role of radiation after mastectomy and also discuss the published data regarding the use of postmastectomy radiation in patients treated with neoadjuvant chemotherapy.

With survival probabilities increasing, it is critical that the long-term risks of normal tissue injuries associated with radiation be minimized. Data from the Early Breast Cancer Trialists' Collaborative Group meta-analysis clearly show that radiation can be associated with an increased risk of death from cardiovascular disease.[2] Modern treatment techniques are available to minimize and potentially overcome this risk. Furthermore, 3-dimensional image-guided radiation treatment planning can help ensure that the adequate dose is delivered to important targets, which should help to improve the efficacy of treatment. Moran and Haffty review modern radiation treatment techniques to highlight some of these advances.

Finally, inflammatory breast cancer remains the most aggressive and malignant subcategory of locally advanced disease. Inflammatory breast cancer has unique clinical presentations, biological features, and natural histories. Woodward and Cristofanilli highlight these unique features, discuss optimal therapeutic approaches, and review future directions of research.

Advances in the management of locally advanced breast cancer have significantly improved the outcome for patients, and radiation treatments for this disease continue to complement the benefits of surgery and systemic therapy. The numerous advances in physics, imaging, and computer technologies have permitted radiation treatments to be much more precise, which has the real potential to overcome many of the limitations of the past. In addition, radiation oncologists need to continue contributing to the understanding of breast cancer biology and remain educated about the continuing advances in other subspecialties. It is with this aim that we dedicate this issue of *Seminars in Radiation Oncology*.

Thomas A. Buchholz, MD, FACR
*Guest Editor*

## References

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