As increasing data become available regarding breast tumor biology, risk of systemic micrometastases in early stage disease, and survival equivalence for breast conservation versus mastectomy, it becomes tempting to conclude that surgical skill and technique are inconsequential to breast cancer outcome. The study on axillary recurrence reported by Wright et al. in the November issue of the Annals of Surgical Oncology is a sobering reminder that surgical expertise is indeed quite relevant for the prevention and management of breast cancer relapse.

Surgeons have struggled to define the optimal extent of regional nodal dissections in breast cancer patients since the beginning of the 20th century, when the Halstedian radical mastectomy was adopted as standard management for a disease that was previously assumed to be untreatable and universally fatal. This classic (and now largely obsolete) procedure described by Sir William Stuart Halsted included resection of the breast en bloc with the underlying pectoralis musculature and a level I-III axillary dissection. During this era it was commonplace for women to present with bulky chest wall and nodal disease. The successes achieved by the radical mastectomy were encouraging enough to motivate the development of even more aggressive surgical approaches, such as the inclusion of supraclavicular lymph node surgery or internal mammary lymph node dissection (as with the extended radical mastectomy). The therapeutic and conceptual goal was that radical extirpation of the nodal basins would preempt the mechanical, stepwise spread of disease before the establishment of distant organ involvement. Sadly, these disfiguring procedures failed to improve breast cancer outcome, and the concept of early detection as a means of improving outcome of breast cancer emerged.

The National Surgical Adjuvant Breast Project (NSABP) B-04 study provided proof that a paradigm shift regarding the role of surgery in breast cancer outcome was warranted. B-04 consisted of two parallel clinical trials designed to prospectively evaluate the impact of variations in locoregional management on breast cancer survival. One thousand seventy-nine patients with operable, clinically node-negative disease were randomized to radical mastectomy versus total mastectomy and locoregional irradiation, versus total mastectomy and no axillary treatment. Nearly 600 other women with clinically diseased axillae were randomized to either radical mastectomy or total mastectomy with axillary irradiation. Overall survival at 25 years was equivalent for the three study arms among the node-negative patients (19% to 26%), and this outcome was better than that observed for the two clinically positive study arms (14% for each arm). Axillary metastases were identified in 40% of the clinically node-negative patients who were randomized to radical mastectomy, and because the patients were matched by clinical stage, it is assumed that approximately 40% of the other two treatment arms were also node-positive.

Effective systemic therapy was not yet available for breast cancer during the 1971–1974 accrual years for this study, and these results therefore confirmed that in the absence of adjuvant medical therapy, breast cancer survival is not substantially influenced by surgical resection of axillary lymph nodes. Furthermore, because only 19% of the clinically node-negative patients required a delayed axillary lymphadenectomy for axillary relapse, it can be inferred that axillary failure is not an inevitable event for patients with clinically occult metastases. The
oncology community subsequently developed a strengthened appreciation for nodal status as a reflection of synchronously occurring distant micrometastatic tumor burden.

This landmark phase III clinical trial therefore set the stage for focusing attention on management of occult systemic disease in breast cancer patients. Additional randomized studies demonstrating the survival equivalence of breast conservation therapy in comparison with mastectomy strengthened the perception that surgery is of secondary importance in controlling the life-threatening sequelae of breast cancer. The pendulum of opinion thereby swung from one end of the spectrum to the other: from the belief that breast cancer requires aggressive attempts to eradicate any soft-tissue involvement on the chest wall that could be reasonably encompassed within a surgical field to the belief that breast cancer is largely a systemic disease at the time of detection.

The sentinel lymph node technology has prompted reconsideration of long-term control risks in the axillary nodal basin and is centralizing the pendulum of opinion regarding the importance of surgical technique in breast cancer management. Ironically, the oncology community has worked diligently to minimize the morbidity and disfigurement resulting from breast cancer surgery, and one consequence of our success is that we are now bracing ourselves to face increasing rates of axillary relapse, a form of disease failure that historically has been a rare event. Although past studies lead us to infer that regional control rates are not likely to plummet dramatically in the current era of sentinel lymph node biopsy, it is nonetheless appropriate to acknowledge the potential for alterations in patterns of disease failure, and we must be prepared to provide care accordingly. Hence, the accompanying study by Wright et al. is a valuable resource in defining the prognostic significance and management options for axillary nodal recurrence.

The M.D. Anderson Cancer Center surgical breast section expressed similar aims in its review of management strategies and associated outcome for 44 patients presenting with axillary recurrence as the initial site of treatment failure. In this high-volume tertiary referral center, axillary recurrences accounted for 1% of all breast cancers treated between 1982 and 1992. All recurrences in this series were clinically resectable at the time of relapse detection. Several cases were definitively diagnosed via percutaneous needle biopsy (as opposed to surgical resection of the metastatic lymph node), and overall there were 17 patients treated with systemic and radiation therapy only. The essential findings from this study were that (1) axillary recurrence represents (as would be expected) a marker of aggressive disease biology but that (2) prolonged disease-free survival can be achieved when multimodality treatment is delivered, including surgery, radiation, and systemic therapy. With a median follow-up of 70.8 months, this approach yielded regional control of disease in 94% of cases, and 65% were free of distant metastases. In comparison, regional control was obtained in 69% and 36% of cases managed with dual and single-modality therapy, respectively; distant disease-free survival was seen in only 44% and 36%, respectively. Wright et al. report an overall 10-year survival of 56%. All patients in this series underwent surgery; 60% received systemic therapy and 27% were irradiated regionally as well. These survival rates following multimodality therapy were therefore comparable to those at M.D. Anderson.

Wright et al. also made some important and provocative observations regarding the relationship between adequacy of surgical technique and risk of axillary failure. In some of the cases, the recurrence was located within an undissected axillary arch. Conceivably, application of the sentinel node technology might compensate for a surgeon who might otherwise have failed to clear this area in a standard axillary lymphadenectomy. On the other hand, as the practice of sentinel lymph node biopsy continues to expand, it is likely that fewer surgeons will be documenting their expertise and successful fulfillment of the lymphatic mapping learning curve by performing an initial series of sentinel node biopsies with a concomitant axillary lymphadenectomy. It is therefore also conceivable that inadequate surgical technique with the sentinel lymph node dissection might contribute to higher rates of axillary failure.

In summary, Wright et al. have confirmed several concepts that surgical oncologists have suspected for several decades, despite a growing emphasis on the systemic aspects of breast cancer management: (1) surgical technique is critical in optimizing locoregional outcome; (2) axillary failure is an adverse prognostic event, but aggressive treatment can save a substantial fraction of patients; and (3) surgical intervention is an essential component of the multimodality management approach once an axillary recurrence is detected. Although past clinical trials suggest that axillary failure in a clinically negative nodal basin is an uncommon event, its occurrence may reflect either an underlying aggressive tumor biology or an inadequate surgical technique. Whether sentinel lymph node biopsy will correct or exacerbate this recurrence risk remains to be determined, and it will ultimately depend on the surgical skill of surgeons performing these mapping procedures.