Axillary lymph node surgery remains an integral component of breast cancer treatment. Node status provides key prognostic information that is used to direct adjuvant systemic therapy (1). Removal of the nodes may also improve local control, although the preponderance of data shows no survival advantage with node dissection itself (2).

Until recently, surgery required full axillary lymph node dissection (ALND). However, recovery from ALND is painful, and the procedure carries the risk of permanent lymphedema. In the early 1990s, it was hypothesized that colloidal material injected into the breast would drain to the same first node(s) as the cancer (3,4). The commonly used agents are radiolabeled sulfur colloid alone or in combination with a blue dye (isosulfan blue or methylene blue), which are detected by a hand-held gamma probe or by visual identification of blue-stained nodes. Early confirmatory studies proved that this procedure, termed “sentinel lymph node biopsy” (SLNB) for those first nodes “standing guard” in the axilla, was accurate in that sentinel node was positive in all but a few women who had any positive nodes on subsequent ALND (5,6). It was therefore felt that a negative SLNB could make ALND unnecessary.

In 1999, two National Cancer Institute (NCI)–sponsored trials (National Surgical Adjuvant Breast and Bowel Project [NSABP] B-32 and American College of Surgeons Oncology Group [ACOSOG] Z-0010) opened to fully define the accuracy of SLNB and to determine if omission of ALND in patients with a negative SLNB would affect survival. Although the NCI considered SLNB investigational, its obvious advantages in tolerability and morbidity led to its increasing use outside the clinical trials. Indeed, a study of practice at five NCI-designated centers showed that SLNB was used in place of ALND even before the trials started. These centers entered few women on the randomized NSABP study (7).

In this issue of the Journal, Chen et al. (8) identify a similar pattern of increasing use of SLNB in a national population sample of 491,000 women with stage I and II disease who were treated between 1998 and 2005. In 1998, 27% of the women who received SLNB without ALND, and this proportion increased to 65% in 2005. The authors did not report how many of these women entered the NCI-sponsored trials, but the 7500 women with SLNB on the trials could account for at most 3% of women receiving SLNB in this population study. Therefore, the frequency reported by Chen et al. (8) represents the use of SLNB as standard care.

New treatments and technologies are regularly promoted to physicians and the public with the promise of improved outcome and lower morbidity. The demand for new approaches outpaces the ability to conduct definitive studies to prove efficacy and safety. For new drugs, the requirements for Food and Drug Administration approval and the high cost and fear of toxicity mostly limit use until trials are completed. However, new surgical and radiation techniques are largely free of regulatory oversight and often are cost neutral with current therapies. This situation can lead to their use before definitive evidence is available.

Oncologists justified the early adoption of SLNB by arguing that ALND is primarily a staging procedure that has no therapeutic value in women with negative nodes. Thus, the only question was whether SLNB accurately defined node status. Based on these arguments, the National Comprehensive Cancer Network (NCCN) incorporated SLNB into its guidelines as an alternative to ALND in 1998 (as a category IIb recommendation—no high-level evidence). Chen et al. (8) demonstrate that other surgeons also rapidly adopted SLNB. Initially performed primarily at teaching hospitals in 1998, the procedure rapidly spread to all classes of hospitals.

Whether “early adoption” of SLNB represented good judgment or a rush to judgment remains unclear. “Early adoption” of new drugs before clinical trial data are available is generally not accepted. Yet the same oncologists at NCI-designated cancer centers who design and promote these drug trials largely eschewed the randomized NSABP trial of SLNB and even questioned whether it was necessary and would be completed (7). The sponsors of the NSABP trial criticized the failure of these oncologists to participate in the trial in this Journal (9). In hindsight, SLNB has proven accurate and safe and is accepted as standard care (5,10). The clinical trials filled and are providing important data on SLNB while we await final outcome analysis.

Does a happy ending vindicate early adopters? What risk of harm is tolerated? What are patients told? As one of those early adopters, I still believe that approach was reasonable in the case of SLNB. However, one does not need to look beyond breast cancer to understand the need for caution. High-dose chemotherapy with bone marrow rescue, widely touted as an advance by “early adopters,” was proven dangerous and ineffective only after substantial human and financial loss.

Another early adoption dilemma is brewing in breast cancer. Accelerated partial breast irradiation (APBI), in which the current standard of 6 weeks of radiation to the whole breast is replaced with only 5 days of radiation limited to the area of the lumpectomy, has intuitive advantages and market value. It is increasingly offered to patients.
as a standard option despite the absence of any long-term follow-up data, while there is an ongoing NCI-sponsored randomized trial (NSABP B-39). However, caution is warranted, with recent meta-analyses showing a survival advantage for women who have effective local control with whole breast radiation (11). Are such early adopters of APBI prescient or rushing to judgment? Certainly new treatments should be adopted when proven effective. However, the burden of proof rests with the early adopters, and patients must be fully informed of the limitations of knowledge, whatever the presumed advantage of therapy.

The analysis of Chen et al. (8) includes another disturbing observation. There were statistically significant disparities in the application of SLNB between racial and ethnic groups as well as disparities related to socioeconomic and health insurance status. These disparities were seen even after controlling for geography and hospital type. Such disparities are seen in all aspects of cancer care. Given America’s track record of disparate care, I suppose we should not be surprised that racial and ethnic minorities were disproportionately deprived of another medical advance. However, this observation is profoundly disappointing and sobering. It is yet another call for us to redouble efforts to identify and correct the root causes of disparities.

Chen et al. (8) also noted differences in use of SLNB related to age. Unfortunately, they did not account for the proportion of women who had no axillary surgery. Previous studies have shown that older women are more likely to have no axillary surgery (7,12). Therefore, the findings of Chen et al. (8) with respect to age may well be explained by failure to account for this group. Similarly, Chen et al. (8) reported the use of SLNB only for the aggregate of women treated with mastectomy and breast-conserving surgery (BCS), although most users of SLNB initially limited its use to women treated by BCS. Guidelines such as those of the NCCN provided only for SLNB with BCS. I would especially have liked to see the data related to disparities reported for women undergoing BCS only.

Finally, this study highlights the critical importance of cancer registry efforts. Maintaining data on cancer care was one of the key recommendations of the National Cancer Policy Board in its 1999 review of the quality of cancer care (13). Cancer registry efforts are under increasing scrutiny at hospitals because of budgetary constraints. The National Cancer Data Base (NCDB) of the Commission on Cancer is the only source with the granularity and timeliness of treatment data sufficient to conduct this study. The study by Chen et al. (8) provides the oncology community notice that their support of cancer registry operations including the NCDB should be renewed and strengthened.

References