Dr. Cody presents a very thorough review of the use of sentinel lymphadenectomy in breast cancer. The article raises key issues related to a procedure that is becoming more widespread and may indeed replace axillary dissection for the staging of breast cancer.

The sentinel node concept is based on the assumption that if a tumor spreads through the lymphatics, the lymph node that first drains the primary tumor, ie, the sentinel lymph node, will be the node most likely to harbor metastases. It follows that if the sentinel node is free of metastases, there is a high likelihood that the rest of the regional nodal basin will be negative.

This work provided a model for the investigation of the sentinel node concept in other cancers, particularly breast cancer. Many groups have now published their series of sentinel lymphadenectomy in breast cancer, using modified techniques and either dye, a radiopharmaceutical, or a combination of both as the lymphagogue of choice.

The author's Table 1 summarizes the identification, sensitivity, false-negative, and accuracy rates of the procedure cited in published series. The authors of all of these series achieved excellent results with their particular technique and validated these results by an immediate complete axillary lymph node dissection. As Dr. Cody emphasizes, it is apparent that, regardless of the agent used, the three different approaches are quite comparable.

**Issues Raised by Memorial Sloan-Kettering Pilot Study**

Dr. Cody advocates the use of both radiopharmaceutical and blue dye, and he describes a pilot study conducted at Memorial Sloan-Kettering Cancer Center in which all patients underwent lymphoscintigraphy and injection of blue dye followed by radioguided surgery with a handheld gamma probe.[2] We will discuss three issues raised by the results of this pilot study.

First, while lymphoscintigraphy was positive in the axilla in only 75% of cases, the radioisotope allowed the detection of the sentinel node alone in 88% of cases. As mentioned in this article, it is interesting that a negative lymphoscintigram does not preclude successful radiolocalization of the sentinel node at surgery. Possible reasons for this phenomenon include the following: either gamma camera imaging or positioning of the patient in nuclear medicine was not optimal; image timing was miscalculated; or soft tissue, skin, and air between the hot sentinel node and camera caused excess scatter and loss of signal that became detectable only by the handheld gamma probe. These are some of the reasons why the role of preoperative lymphoscintigraphy as a routine procedure remains unclear among those who advocate radioguided sentinel lymphadenectomy.

Second, it seems artificial to isolate the sentinel node identification rate for each method when, in fact, no patient received either agent alone. Perhaps lymphatic uptake of blue dye is inhibited after the breast has been injected with a large volume of saline and radiopharmaceutical. Finally, we question the inclusion of intradermal injection of radiopharmaceutical as a recommended option in the treatment algorithm, given that Cody's group did not validate this technique with a complete axillary dissection in their initial study. To date, there are few data supporting the intradermal injection of radiopharmaceutical. This approach needs to be formally evaluated.

At the John Wayne Cancer Institute, we have been proponents of the use of blue dye alone, while others profess the advantages of radioisotope injection and localization with a handheld gamma probe, either alone or together with dye. The debate will continue, especially as newer agents emerge for detecting the sentinel node. If a high level of accuracy is achieved with any number of different techniques, the controversy will become moot.

The success and accuracy of the chosen technique require validation within each contributing group.
of the multidisciplinary team. The practicing surgeon also should be comfortable and familiar with the technique.

Selection of Patients
We agree entirely with Dr. Cody's outline of cases selected for sentinel lymphadenectomy. At the John Wayne Cancer Institute, we currently include patients with high-grade or extensive ductal carcinoma in situ (DCIS) in a separate experimental protocol. It is likely that the detection of axillary metastases will increase with the use of sentinel lymphadenectomy. Recent data show a 4.6% incidence of axillary metastases in DCIS, which is much higher than the historical incidence of roughly 1%. We can theorize that scrutiny of a single sentinel node using immunohistochemistry may be easier than searching the primary tumor for an area of microinvasion; if metastases are identified, microinvasion may be assumed.

Internal Mammary Drainage Detected by Lymphoscintigraphy
Most of the specific clinical issues raised in the article can be answered only by multicenter clinical trials, such as those presented in the author's Table 5. Internal mammary drainage detected by lymphoscintigraphy has rekindled the debate on managing the internal mammary nodes in breast cancer. Our practice is to obtain a lymphoscintigram in patients with primary tumors in the medial hemisphere and then offer standard axillary sentinel lymphadenectomy using blue dye. The majority of lesions drain to the axilla, with an occasional lesion draining solely to the internal mammary chain. In the latter case, the blue sentinel node will still occasionally be found in the axilla, but, if not identified, we would perform a complete axillary lymph node dissection. We have attempted sentinel lymphadenectomy of internal mammary nodes in a small number of patients but have not pursued the procedure to any great degree. If this procedure could be refined, identification of patients with internal mammary node positivity with minimal surgery would help determine prognosis and adjuvant systemic therapy. Obviously, further investigation into the management of internal mammary node drainage is warranted.

Importance of Adequate Training
Sentinel lymphadenectomy for breast cancer, by virtue of its less invasive nature, will become commonplace and will be practiced by surgeons who may or may not scientifically assess their results. We stress that, presently, this remains an experimental procedure, and that surgeons should complete an axillary lymph node dissection to determine their success at their particular institution. Furthermore, completion of the trials outlined by Dr. Cody must be supported.

In a recently completed multicenter trial using radioisotope alone, surgeons were trained in the technique with five cases and then entered patients into the study. The 11 surgeons who enrolled patients in the study had a widely discrepant technical success rate in identifying the hot spot. This result shows that a proper learning phase is required by all surgeons who are interested in using sentinel node lymphadenectomy, especially those who wish to participate in the available trials. When completed, these trials will hopefully provide answers to the questions posed by Dr. Cody that all clinicians are struggling with in the management of patients who have undergone sentinel lymphadenectomy for breast cancer.

References: