Update on sentinel lymph node biopsy in gynecologic cancers

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Abstract

The sentinel lymph node biopsy (SLNB) holds the promise of more accurate staging of the primary tumor and fewer wound complications and lymphedema than associated with lymphadenectomy. Regional lymphadenectomy may no longer be a requirement in SLNB-negative patients if the SLN procedure is adequately validated in prospective clinical trials for gynecologic malignancies.

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Sentinel lymph node biopsy (SLNB) is one of the most important innovations in surgical oncology in the last 20 years. The SLN is defined as any lymph node that receives direct drainage from the tumor site and is identified by a procedure called lymphatic mapping. Lymphatic mapping is the injection of radiocolloid or vital blue dye in such a way as to access the microlymphatics draining the area around the primary tumor. The radiocolloid, blue dye, or both, are concentrated in the SLN and can be identified preoperatively or intraoperatively. The SLN is then subjected to special studies by the surgical pathologist to identify micrometastases that could be missed by routine processing. SLNB holds the promise of more accurate staging of the primary tumor and fewer wound complications and lymphedema associated with lymphadenectomy. Regional lymphadenectomy may no longer be a requirement in SLN-negative patients if the SLN procedure is adequately validated in prospective clinical trials.

SLNB has been incorporated into the standard care of patients with melanoma and breast cancer. Surgical specialists treating gynecologic, genitourinary, and gastrointestinal tumors have been investigating how to incorporate SLNB into the care of patients with primary tumors at these sites. In the case of gynecologic cancers, the greatest progress has been made in patients with vulvar cancer. Almost 400 published cases have been reported of SLNB followed by inguinal–femoral lymphadenectomy in case series of at least 20 cases. In this combined experience, the sensitivity of the SLN is 97.6% and the false-negative rate is 2.4% [1]. Based on this experience, two large multi-institutional trials were launched in 2000. Gynecologic Oncology Group (GOG) protocol 173 is still open and will determine the sensitivity, false-negative rate, and negative predictive value of SLNB in a large community-based setting [4]. Accrual has slowed in recent years, suggesting some GOG investigators might be performing SLNB alone on patients eligible for GOG 173.

The second trial has resulted in a landmark report in the Journal of Clinical Oncology by van der Zee et al. [3]. In this trial, patients underwent SLNB only, and if negative, were observed. With 2-year follow-up on more than 200 patients, the groin relapse rate in patients with unifocal disease was 2.3%. These data suggest that when performed by a skilled multidisciplinary team, the groin relapse rate for SLNB only is similar to the groin relapse rate of inguinal–femoral lymphadenectomy as currently performed. GOG 173 will hopefully be closed within a year, and further data will be available to assist gynecologic oncologists deciding how to incorporate SLNB into their practice [2].

The cervix has proven a more difficult target for the SLNB strategy. The cervix is a midline structure with complex lymphatic drainage patterns. More than 800 single-institution case series of more than 20 patients [5] as well as a multi-institutional trial from Germany of 600 patients [6] have been published. None of these patients were managed with SLNB alone. The retrospective studies demonstrated a higher false-negative rate among cervical cancer patients than vulvar cancer patients; however, Hauspy et al [7] have

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suggested that the definitions used by investigators may have overestimated false negatives in cervical cancer patients. In the large Germany study, the sensitivity for SLNs in patients with small tumors was slightly greater than 80%, the predetermined target; however, it was less than 80% for patients with tumors larger than 2 cm, leaving uncertainty about the role of SLNB in this population.

Several technical issues are still being worked out in patients with cervical cancer. Parametrial lymph nodes are difficult to identify in radical hysterectomy patients because they are very close to the primary tumor. Investigators have suggested several strategies for addressing this issue. Hauspy et al. [7] recommended removing the parametrium on all patients so as not to miss a parametrial SLN. This results in radical surgery in patients with a very low risk (perhaps 1–2%) of parametrial lymph node metastases. Rob et al. [8] suggested a technique for identification of parametrial SLNs and simple trachelectomy or cone biopsy if SLNs are negative.

There is great promise for SLNB in cervical cancer, especially in combination with fertility-sparing procedures; however, further development is still required.

Endometrial cancer is another gynecologic disease site that has been targeted for lymphatic mapping. The primary tumor is difficult to inject; therefore, cervix or fundal injections have been described. Hysteroscopic injections have been reported and appear to hold the greatest promise. There are no prospective studies of SLNB alone in patients with endometrial cancer. At present, SLNB for endometrial cancer should still be considered in the feasibility stage of development as described in an excellent recent review by Khoury-Collado and Abu-rustum [9].

Conflict of interest statement
The author has no conflicts of interest to declare.

References