Current Perspectives on Lymphatic Mapping in Carcinomas of the Uterine Corpus and Cervix

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Key Words
Cervix cancer, endometrial cancer, sentinel lymph node, lymphatic mapping

ABSTRACT
Lymphatic mapping and sentinel node identification are rapidly becoming the standard of care in managing many malignancies. These procedures have allowed focused evaluation of relevant regional lymphatics, which has led not only to improved precision of nodal pathology, but also to treatment triage and the potential for reduced postoperative morbidity. Given its clinical potential, new cancer primary sites are being evaluated, including those of the female genital tract. Of these, carcinoma of the vulva seems the most appropriate; however, it is a rare malignancy and therefore large randomized treatment trials based on sentinel node triage are difficult to perform. Cancers of the uterus–cervix and corpus are more common. Because the physiologic lymphatic drainage from this organ is ambiguous, principle lymphatic basins are located in many different anatomic locales, making sentinel node identification precarious, yet highly relevant and informative. Current experience in carcinoma of the cervix suggests the concept is feasible. A consensus in corpus cancer has not been reached, although both sites are of keen interest with the increasing use of laparoscopy in surgical management. Prospective multi-institutional validation studies are underway. (JNCCN 2006;4:471–478)

Carcinomas arising within the uterus are separated into those located primarily within the uterine cervix and those located in the corpus. In 2006, more than 51,000 patients are expected to be diagnosed with either cervix or corpus uterine cancer.¹ Within the United States, improved access to screening has effectively reduced the annual incidence of cervix cancer; however, the occurrence of corpus cancer appears to be increasing. The reasons for this increase are not entirely understood, but may be partly caused by increasing rates of obesity, increased life expectancy, and exogenous hormone exposure. These 2 malignancies are among those most frequently diagnosed in women worldwide.

Despite their proximity within the primary organ, the 2 malignancies have divergent risk factors, clinicopathology, and treatment approaches. Consistent with primary tumors elsewhere, the histologic status of the regional lymph nodes is a major prognostic factor in these malignancies. Typically, this information is gathered during the primary extirpation procedure; however, if nodal metastases are suspected in cervix cancer, treatment intent will often be directed at histologic confirmation and primary chemoradiotherapy. In contrast, patients with endometrial cancer will often undergo primary resection of the uterus with attempted nodal resection or debulking. Adjuvant therapy is dependent on findings at exploration and frequently entails radiation, chemotherapy, or both. In each case, accurate evaluation of the regional lymphatics is critical for effective treatment.

Because of the ambiguous nature of lymphatic drainage, lymphatic mapping and sentinel node identification for malignancies involving the uterus are of increasing interest. Depending on tumor location, at-risk lymph node basins may include the parametria, obturator, internal and external iliac, common iliac, paraaortic, presacral, and superior rectal nodal/vascular basins.² Although nodal metastases are most frequently seen within the tributaries of the dominant lateral lymphatic trunk (terminating in the external iliac junctional node or “Leveuf et Godard” node), independent isolated metastatic disease has been identified in each of these sites.² Such ambiguity is challenging in sentinel node localization but helps identify less-frequently evaluated nodal basins reflecting anatomic variations in regional lymphatic drainage.

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This potential for improved precision highlights the virtue of mapping in these cases and has driven similar investigation in other tumor types, such as breast cancer, melanoma, and vulva cancer.4,6

This article presents the current status of investigation into lymphatic mapping for carcinomas within the uterine cervix and corpus and highlights the methodology and outcomes of pilot trials being conducted around the world.

Uterine Cervix Cancer

Although Papanicolaou testing has decreased the incidence of cervical cancer in the United States, an estimated 9710 new cases and 3700 deaths will occur in 2006.1 For women with seemingly early-stage cervical cancer, pelvic lymph node status remains among the most important prognostic factors for long-term survival. Unfortunately, modern imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI),7 and positron emission tomography (PET)8 do not detect small volume nodal disease well. Therefore, current standard of care for patients with early-stage cervical cancer remains radical hysterectomy and full pelvic lymph node dissection. Complete lymphadenectomy is performed in all patients, although the risk for pelvic lymph node metastasis for stage IB tumors is only 17.3%,9 meaning more than 80% of patients with negative lymph nodes will undergo lymphadenectomy with its potential morbidities, including lymphedema, lympho cysts, and urologic complications.10 Furthermore, more than 25% of women with stage IB cervical cancer who undergo radical hysterectomy also undergo postoperative radiotherapy.11 The risks for complications from multimodality therapy are greater than those of surgery or radiotherapy alone.12

Mapping Technique for Patients with Cervical Cancer

Intraoperative lymphatic mapping and sentinel lymph node detection in patients with cervical cancer can be performed either through laparotomy or laparoscopy. Vital blue dyes or gamma-emitting radiocolloid are typically used in this procedure. At M. D. Anderson Cancer Center, isosulfan blue (Lymphazurin 1%; U.S. Surgical, Co., Norwalk, CT) is intraoperatively injected peritumorally at the 12-, 3-, 6-, and 9-o’clock positions while avoiding direct tumor injection. If the patient has undergone a previous conization or loop electrosurgical excision procedure (LEEP), equal aliquots of blue dye are injected into the cervical stroma in 4 quadrants. Before, during, or after the injection, the pelvic peritoneum is incised to expose the retroperitoneal lymph channels and nodes. Uptake of the blue dye through the lymph channels and sentinel lymph nodes is easily visualized directly.

The other method for detecting sentinel nodes involves preoperative injection of radiocolloid with intraoperative identification using a handheld gamma counter. The radiocolloid injection must be performed at least 1 hour, but up to 24 hours, before surgery.13 For that reason, the injection does not typically occur in the operating room but rather in the nuclear medicine suite while the patient is awake, which can cause some discomfort. A preoperative lymphoscintigram is commonly performed at that time. The most frequently used radiocolloids include sulfur colloid,14 technicium-99m sulfur colloid,15 technicium-99m phytate,16 and colloidal albumin.17 We consider a radioactive node to be sentinel if it records ex vivo radiation levels at least tenfold above background levels on the gamma counter.

Many experts believe sentinel nodes are best detected through combined intraoperative lymphatic mapping using both blue dye and radiocolloid. Three investigators reported their experiences using both single and combined modalities. Using radiocolloid only, Malur et al.17 detected sentinel nodes in 76% of patients, or in 90% of women when blue dye was added to the radiocolloid. When Plante et al.14 performed their first 41 sentinel node procedures using blue dye only, they found a sentinel node in only 79%; however, when they performed preoperative lymphoscintigraphy and intraoperative mapping using a handheld gamma counter in addition to a blue dye injection, they reported a 93% detection rate for sentinel nodes. Rob et al.18 increased the side-specific detection rate from 71% to 93% by using radiocolloid and blue dye compared with blue dye alone. Although some of these improvements may be attributable to increasing experience with mapping techniques, we believe the intraoperative combined modality approach optimizes sentinel node detection.

Preoperative lymphoscintigrams are commonly obtained after radiocolloid injection to highlight localizing nodes. However, the merit of reviewing these preoperative images has been questioned. In a review of our experience with this “triple modality approach,” we found that preoperative lymphoscintigraphy added little benefit to sentinel node detection, but increased
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health care costs. For many reasons, preoperative lymphoscintigraphy probably does not improve sentinel node detection compared with intraoperative lymphatic mapping using blue dye and radiocolloid. The primary draining lymph node basins are all located in the pelvis or abdominal portion of the aorta and all patients with cervix cancer are presumed to have bilateral lymphatic drainage. Therefore, all at-risk lymphatic basins can be accessed through a single incision. Even aberrant drainage directly to the lymph node basins outside the pelvis would be well within the operative field. Thus, the results of preoperative lymphoscintigraphy would not influence the surgical approach or the incision type or site. The surgeon has an intraoperative view of the entire field of lymph nodes draining the primary lesion, and blue dye and radiocolloid can be followed using direct visualization and a handheld gamma counter. For that reason, we have made preoperative lymphoscintigraphy an optional study in patients enrolling in our mapping protocols for cervical cancer.

Overall Success of Sentinel Node Detection

As interest in this field has grown, so has the number of individual institutions reporting feasibility experiences. Many of these trials have included small numbers of patients and report the authors’ technical learning curve. Therefore, meaningful conclusions are difficult to draw. However, a recent review summarizing the outcomes from 8 studies involving cohorts of more than 20 patients showed an overall rate of 89% for detecting at least 1 sentinel lymph node in a patient. Little difference in sentinel node detection was shown among studies that used blue dye only (88%), radiocolloid only (87%), and combined modalities (91%). Sentinel node identification may be decreased in patients with large tumors (≥4 cm) and locally advanced disease. Some investigators have reported decreased identification rates in patients with prior conization, but others have not found this relationship to be valid. The effects on successful identification of the sentinel node of benign gynecologic conditions, such as endometriosis or pelvic inflammatory disease, obstetrical trauma, or caesarean section, are not currently known.

Of the 649 patients reported in the 8 combined studies (Table 1), 138 (21%) had metastatic disease to the lymph nodes. The overall sensitivity of the sentinel lymph node for detecting metastatic disease in patients with cervical cancer is 91.3%. The overall false-negative rate, defined as positive lymph node metastasis in the lymphadenectomy specimen with no metastatic tumor in the identified sentinel node, was 8.7%. The overall negative predictive value for the combined studies was 97% (374 patients with true-negative sentinel nodes and 12 patients with false-negative sentinel lymph nodes).

Although false-negative rates less than 10% are routinely reported in sentinel lymph node biopsy in patients with cervical cancer, Marichole et al. reported a false-negative rate of 38%. Their study used blue dye only, frozen section analysis of sentinel nodes, and immunohistochemical analysis of nonsentinel lymph nodes. Use of frozen section analysis to manage melanoma and breast cancer has been abandoned because tissue is lost and small metastases are difficult to identify. In addition, immunohistochemical analysis of nonsentinel lymph nodes probably identified micrometastasis, defined as tumor metastasis less than 2 mm. This explains the high rate of false-negatives in this study. However, the clinical significance of these few metastatic cells (micrometastases) detected in the lymph nodes is unknown.

A French group also reported no false-negatives in their experience when using the same pathologic protocol described by Marichole et al. The main difference between the 2 studies was that the French group used the combined mapping technique rather than that of blue dye only used by Marichole et al.

Pathology Controversies for Sentinel Nodes

Although most investigators agree that ultrastaging of nonsentinel lymph nodes has limited usefulness, controversy remains regarding the necessity of microsectioning and immunohistologic staining of sentinel nodes. Levenback et al. resubmitted sentinel nodes from 31 patients with no metastasis found on routine hematoxylin and eosin (H&E) staining. For these specimens, serial step sectioning was performed, with no additional metastasis detected. Furthermore, another 10 patients with no metastasis on H&E staining underwent serial step sectioning and immunohistochemical analysis of sentinel nodes, with no additional metastasis found. Microstaging identified a micrometastasis in a contralateral sentinel node in one patient with a metastasis in a pelvic sentinel node found through H&E. These conclusions are supported by Niikura et al., who submitted all pathologically negative sentinel nodes found on H&E staining for immunohistochemistry, with no additional metastasis detected. Angioli
et al. also reported no additional metastasis found through immunohistochemistry on sentinel lymph nodes that showed no tumor on H&E. In contrast, Barranger et al. found 12 sentinel nodes with metastatic disease in 8 patients. Of these 12 nodes, 4 (33%) had grossly positive macroscopic disease, 5 (42%) were detected on H&E staining, and 3 (25%) were found on immunohistochemical staining. These results suggest the importance of microstaging of sentinel lymph nodes. None of these studies address the clinical significance of these micrometastases detected on immunohistochemistry.

### Endometrial Cancer

Endometrial cancer is the most common gynecologic cancer in the United States, with more than 41,200 estimated cases reported in 2006. It is also one of the most curable gynecologic cancers. Although no screening test is available, most patients present when the cancer is limited to the uterus. Early symptoms, particularly postmenopausal bleeding, lead to early detection, which is largely responsible for the relatively low disease-specific mortality (7310 estimated deaths from endometrial cancer in the United States in 2005).

Contemporary management of this disease involves removing the uterus, fallopian tubes, and ovaries and assessing the lymphatic basins. Rare histologic subtypes (e.g., clear cell, serous) will also undergo intraperitoneal spread assessment in the absence of gross disease. Early anatomic work evaluating the lymphatic drainage of the uterus clearly identified a complex uterine lymphatic lattice servicing the nodes residing in the pelvic and paraortic areas. Although clinicopathologic studies of metastatic nodal involvement clearly suggest an ordered pattern of spread, isolated disease can occur in any of these basins. For instance, paraortic metastases in the absence of pelvic node metastases occurred in less than 3% of cases reported by Creasman et al. on behalf of the Gynecologic Oncology Group.

### Endometrial Cancer as a Target for Lymphatic Mapping

Endometrial cancer is a difficult target for lymphatic mapping as applied in other tumor sites. The primary
tumor is not easily seen, imaged, or palpated using standard clinical tools. Intuitively, peritumoral injection of dye or radionuclide should provide the most accurate data on key lymphatics. However, uterine tumors may be diffuse in the endometrial cavity, deeply invasive and diffuse despite a small intracavitary focus, and multifocal. Recognizing these challenges, several investigators have used various injection techniques to pilot uterine sentinel node mapping.

### Lymphatic Mapping Studies in Patients with Endometrial Cancer

Table 2 outlines the clinical trials evaluating uterine lymphatic node mapping. Most experience is limited to small cohorts and single-institution experiences with various techniques and tools. Early experience primarily involved direct uterine injection with blue dye at laparotomy. This quickly evolved to include cervical injection combined with laparoscopy, similar to the method used in cervix cancer mapping. Most recently, hysteroscopic injection of tracers has been attempted. Consistent with observations made in cervix and vulvar cancer mapping, the combination of dye and radionuclide seems to provide the best opportunity to identify a sentinel node. Nonetheless, each technique has its own challenges and benefits.

Burke et al. described intraoperative injection of isosulfan blue into the subserosal myometrium at 3 sites: the midline of the fundus, 2 cm anteriorly, and 2 cm posteriorly. These sites were chosen to mimic a fundal endometrial cancer. Dye uptake was seen in the lymphatic channels and lymph nodes within 10 minutes. Blue-stained nodes were identified, the location recorded, and the nodes sent to pathology as separate specimens. A selective pelvic and para-aortic lymphadenectomy was then performed. Blue dye was deposited in lymph nodes in 10 of 15 patients. Blue nodes were found in the pelvic and para-aortic areas. Blue nodes were not found between the bifurcation of the aorta and the origin of the inferior mesenteric artery. This finding confirms anatomist observations that lymphatic drainage of the uterus follows 2 paths: along the uterine vessels to the pelvis and along the gonadal vessels to the para-aortics at the level of the renal vessels. Four patients had positive lymph nodes and 2 had positive blue-stained nodes. One patient with bulky nodes experienced no dye uptake and 1 patient experienced micrometastasis to an unstained node in the obturator space.

Echt et al. described attempts at sentinel node identification in patients with endometrial cancer. Patent blue dye was injected into the uterine fundus at a depth of approximately half the thickness of the

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Injection Site</th>
<th>SN Detection</th>
<th>Evaluation Procedure</th>
<th>SN Total/ SN Positive (%)</th>
<th>Sensitivity (%)</th>
<th>FNR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burke et al. (1996)</td>
<td>15</td>
<td>Uterus</td>
<td>67%</td>
<td>Laparotomy</td>
<td>31/2</td>
<td>50</td>
<td>50</td>
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<td>Echt et al. (1999)</td>
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<td>Laparotomy</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>Holub et al. (2002)</td>
<td>13</td>
<td>Uterus</td>
<td>62%</td>
<td>Laparoscopy</td>
<td>16/2</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Pelosi et al. (2002)</td>
<td>11</td>
<td>Uterus</td>
<td>100%</td>
<td>Laparoscopy</td>
<td>17/3</td>
<td>100</td>
<td>0</td>
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<tr>
<td>Gargiulo et al. (2003)</td>
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<td>17/3</td>
<td>100</td>
<td>0</td>
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<tr>
<td>Lelievre et al. (2004)</td>
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<td>Laparoscopy</td>
<td>33/3</td>
<td>100</td>
<td>0</td>
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<tr>
<td>Holub et al. (2004)</td>
<td>25</td>
<td>Cervix</td>
<td>84%</td>
<td>Laparoscopy</td>
<td>53/2</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Barranger (2004)</td>
<td>17</td>
<td>Cervix</td>
<td>100%</td>
<td>Laparoscopy</td>
<td>42/10</td>
<td>100</td>
<td>0</td>
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<td>Fersis et al. (2004)</td>
<td>10</td>
<td>Hysteroscopy (8 successful)</td>
<td>88%</td>
<td>Laparotomy</td>
<td>9/2</td>
<td>100</td>
<td>0</td>
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<tr>
<td>Niiikura et al. (2004)</td>
<td>28</td>
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<td>82%</td>
<td>Laparotomy</td>
<td>71/1</td>
<td>100</td>
<td>0</td>
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<tr>
<td>Rasagliesi et al. (2004)</td>
<td>18</td>
<td>Hysteroscopy (17 successful)</td>
<td>100%</td>
<td>Laparotomy</td>
<td>45/NS</td>
<td>100</td>
<td>0</td>
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<tr>
<td>Maccauro et al. (2005)</td>
<td>26</td>
<td>Hysteroscopy</td>
<td>100%</td>
<td>NS</td>
<td>B + L*</td>
<td>65/4</td>
<td>100</td>
</tr>
</tbody>
</table>

Abbreviations: B, blue dye; FNR, false-negative rate; L, radionuclide with lymphoscintigraphy; NS, not stated; SN, sentinel nodes. Radionuclide injection performed sequentially before blue dye.
myometrium. The authors did not identify any sentinel nodes in 8 patients.

Holub et al.\textsuperscript{47} described a laparoscopic-assisted technique for lymphatic mapping in patients with endometrial cancer. Using a 5-mm laparoscopic puncture needle, the authors intraoperatively injected a 8 patients with blue dye in the same locations described by Burke et al.\textsuperscript{37} Blue nodes were found in the obturator, internal iliac, and common iliac sites in 11 lymph nodes in 5 patients. In 2002, Holub et al.\textsuperscript{43} expanded the experience and reported on 2 techniques for lymphatic mapping in endometrial cancer. In this study, 13 patients underwent subserosal injection as described in the first report and 12 patients underwent subserosal and cervical injections. The combined injection technique increased the rate of observation of blue-stained lymph nodes to 83.3% compared with 61.5% in the subserosal injection–only group. The authors suggest that the combined approach is superior.

Pelosi et al.\textsuperscript{40} reporting on 11 patients with early endometrial cancer, modified the approach by injecting both dye and radionuclide into the cervix and identifying blue and radioactive nodes at laparoscopy. The authors identified 3 sentinel nodes that were positive for micrometastases.

This technique of cervix instillation of contrast agents was reported in 4 other studies, with similar results.\textsuperscript{41–43,48} Holub et al.\textsuperscript{43} reported on the largest series in which 25 patients underwent blue dye–only injection of the cervix followed by laparoscopic-assisted vaginal hysterectomy and bilateral salpingo-oophorectomy after predominantly pelvic lymph node dissection. In this series, 53 sentinel nodes were identified in 21 patients (84%). Bilateral sentinel nodes were identified in 17 patients with 2 of 2 sentinel nodes positive for metastatic disease. No false-negative sentinel nodes were identified.

Although this technique is not directly related to the primary tumor location, a 100% rate of sentinel node detection occurred in the trials using cervix injection of combined blue dye and radionuclide. No false-negative sentinel nodes were identified in this limited experience, and often the only metastatic sites were the sentinel nodes themselves. Importantly, most of these trials did not routinely evaluate the infrarenal para-aortic nodes. This technique outlined the nodal distribution, showing the dominant trunks servicing the cervix and lower uterine segment. Although fundal lesions draining through the ovarian vessel lymphatics may be theoretically underevaluated, a low risk for missing an isolated para-aortic node in these selected patients is anticipated given the natural history of disease. This experience seems to mimic that of evaluating patients with cervix cancer.

Investigators recently attempted perilesional injection through hysteroscopy.\textsuperscript{31,44–46} This technique, although the most promising for direct tumoral evaluation, is controversial because malignant cytology has been frequently identified after diagnostic and operative hysteroscopic procedures. In general, 4 to 5 injections with either radiocolloid or blue dye or both are made around the tumor location. Three studies used a combination of agents, with 2 attempting sequential injection. In these latter series, some patients experienced vagal episodes during injection. Because dye spillage after injection can eliminate cavity visualization, radionuclide injection should occur first. The depth of injection is usually approximately half of the myometrial thickness; a rich vascular network with subsequent uptake of dye or radionuclide may explain the infrequent vagal episodes experienced.

Niikura et al.\textsuperscript{33} reported the largest experience of hysteroscopic lymphatic mapping in 28 patients with early-stage uterine cancer. The investigators mixed blue dye and radionuclide for efficient intrauterine injection, identifying sentinel nodes in 82% of the patient cohort. They suggested that tumors with deeper myometrial invasion were less likely to have a represented sentinel node. The authors identified sentinel nodes in 21 of 22 patients with superficially invasive tumors (<50% myometrial invasion), compared with 2 of 6 patients with deep invasion ($P = .003$). Fifteen patients had sentinel nodes in both pelvic and para-aortic locations, 5 patients had pelvic locations only, and 3 patients had para-aortic sites only, which was an unprecedented finding. The high rate of sentinel node localization in the para-aortic region highlights the need to evaluate these areas at surgical staging. Only 1 patient of 23 with identified sentinel nodes had metastases. The authors concluded that the technique may be useful in identifying sentinel nodes in early-stage endometrial cancer.

Maccauro et al.\textsuperscript{46} recently reported a similar experience in 26 patients undergoing hysteroscopic lymphatic mapping. Two patients experienced transient vagal episodes during the procedure, which was, nonetheless, completed in all patients. The authors sequentially administered radionuclide followed by
blue dye and evaluated the nodal distribution through lymphoscintigraphy immediately after the procedure. Sentinel nodes were identified in all patients at hysterectomy, including 4 (15%) with metastatic disease. Of the intraoperatively identified sentinel nodes, 21% were retrieved from the paraortic basins. All nodal metastases occurred in sentinel nodes identified as radioactive. Only 10 (38%) patients had blue-stained nodes. The authors were also careful to keep the intrauterine pressure around 40 mm Hg, and they identified only 1 instance of positive transrubal cytology. This corroborates the observations of Baker and Adamson, who documented that intrauterine pressures necessary for uterine distension were lower than 40 mm Hg and far lower than the pressures typically associated with tubal spillage (> 70 mm Hg).

This technique improves on those relying on injection into the uterine fundus or cervix without visualization of the tumor, and also provides a preoperative lymphoscintigram that can help in planning. This technique helps identify the most cephalad sentinel node and may help determine the length of the incision necessary to reach it. Conversely, a follow-up procedure is required and, in some cases, a 2-day sequence. Further experience will help determine reproducibility, tolerance, and safety.

Acceptance of this technology would mandate substantial modification to current clinical standard. However, a crucial benchmark before that acceptance is reached is an adequate false-negative rate. Although the rate may vary appropriately by primary site and according to the standards of adjuvant care, it must be acceptable to patients and physicians. Validation trials are necessarily large because they are designed on the basis of node-positive patients. For example, in the Gynecologic Oncology Group trial evaluating sentinel node biopsy in vulvar cancer, cohorts of node-positive women are serially accrued with probability-based stopping rules between cohorts. In this study, as many as 120 node-positive women will be accrued if early stopping rules (based on false-negative determinations) are not met. Strategic clinical design in carefully selected patients is needed as interest and experience in lymphatic mapping expands.

**Conclusions**

Lymphatic mapping in several gynecologic tumor sites is being evaluated with early success. Although the model is more closely followed in cancers of the vulva, the ambiguous drainage from the uterus may make primary tumors of the cervix and endometrium even more suited to directed lymphatic evaluation through sentinel node mapping. Because several basins may individually or collectively be at risk, potential sites must be carefully evaluated. Given the general overall safety of pelvic and paraortic dissections, the benefits of directed and limited sampling through sentinel node mapping must be quantified and tested in a multi-institutional setting. Currently, false-negative rates can approach 10%, which is likely too high for general acceptance of the techniques. Newer technologies, however, should help improve identification of sentinel nodes radiographically, intraoperatively, and pathologically, thereby decreasing false-negative rates. We believe that lymphatic mapping and sentinel lymph node biopsy will become standard care in treating cervical and endometrial cancers.

**References**