



**THE SOCIETY OF GYNECOLOGIC ONCOLOGY OF CANADA (GOC)
POSITION STATEMENT JULY 2017
*SENTINEL LYMPH NODE (SLN) MAPPING IN ENDOMETRIAL AND CERVICAL CANCER***

SUMMARY STATEMENT

SLN mapping rests on the premise that cancer spreads through the lymphatic system in an orderly sequence. If metastases are not found in the SLN (the first node in the anatomical sequence), they are unlikely to be present in the other nodes in the same lymph node basin. By targeting the nodes most likely to contain metastases, the SLN procedure reduces the number of lymph nodes that need to be removed, thus sparing patients the potential morbidity associated with systematic lymphadenectomy, while providing the pathologist with the most significant lymph node in the draining basin.

For this reason, SLN mapping is now the standard of care in melanoma, breast, and vulvar cancer. SLN is used widely in cervical cancer, when supported by a treatment algorithm^{1,2} and the data is similarly supporting its use in endometrial cancer.

Based on the current body of evidence, The Society of Gynecologic Oncology of Canada (GOC) recommends SLN mapping as part of the staging strategy for patients with cervical cancer, as well as for endometrial cancer patients for whom lymph node assessment is being considered.

CONTEXT

The role of lymphadenectomy in the surgical staging of apparent early-stage endometrial cancer has been debated in the literature for more than 10 years. Not only does the procedure incur extra costs and morbidity, but 2 randomized controlled trials have failed to show a survival advantage to routine lymphadenectomy in a low-risk population.^{3,4} At the same time, a small proportion of patients with apparent early-stage disease do harbour lymph node metastases,⁵ and this information is critical in guiding adjuvant treatment decisions.

Due to the morbidity associated with lymphadenectomy, gynecologic oncologists have proposed limiting the procedure to those patients at highest risk of metastases. Identifying such patients before surgery can be a challenge, however. Imaging or intraoperative palpation to identify lymph node metastasis is unreliable,⁵ preoperative tumor grade does not always reflect the actual grade of disease on final pathology,⁶⁻⁸ and imaging for depth of myometrial invasion has inconsistent sensitivity and specificity.⁹ Evaluation of uterine risk factors intra-operatively through frozen section does help identify low-risk patients,¹⁰ but financial and logistical constraints preclude the widespread use of this strategy at most Canadian centres.

As experts continue to debate the value of lymphadenectomy, SLN is emerging as an alternative, less invasive strategy that may reliably detect lymphatic spread.¹¹ In a recent meta-analysis, SLN mapping in endometrial cancer yielded pooled detection rates at 81%, with a sensitivity at 96%.¹² These results are similar to those reported in melanoma and breast cancer, in which SLN mapping is considered the standard of care.

Although American^{1,13} and European¹⁴ guidelines and position statements consider SLN mapping a suitable approach to surgical staging of cervical and endometrial cancer, many Canadian centers do not have access to the required equipment and infrastructure.

In November 2016, a GOC working group convened to discuss SLN mapping. Based on the evidence demonstrating clinical value, the group concluded: “If there is an indication to obtain information about lymph node status in endometrial or cervical cancer, SLN provides that information with less morbidity compared to lymphadenectomy and with no significant deleterious impact on outcomes.”

SLN MAPPING PROTOCOL

The following sections highlight important considerations in the SLN procedure. These points are discussed in greater detail in a 2015 GOC review¹¹ and in a recent meta-analysis of 4915 women who underwent SLN mapping for endometrial cancer.¹²

Technique

Sentinel lymph node mapping has been reported with different dyes (technetium 99, methylene blue, lymphazurin, patent blue dye, indocyanine green). Historically, studies combining blue dye and technetium 99 have yielded the best detection rates, although cost and inconvenience have led technetium to fall out of favour. Early reports suggest even higher bilateral detection rates with near-infrared imaging (NIR) and indocyanine green (ICG) dye¹⁵, though this technique remains costly.

For cervical cancer, submucosal injection takes place directly in the cervix at the 3 and 9 o’clock positions. Injection sites studied for endometrial cancer include sub-serosal and intra-myometrial, but cervical injection (submucosal and deep towards the lower uterine segment at the 3 and 9 o’clock positions) seems to yield the best detection rates and is more practical.

Ultrastaging

Once a sentinel lymph node is identified, it should be subjected to ultrastaging, a process that includes serial sectioning and immunohistochemistry (IHC) staining for cytokeratin. SLNs are considered positive if they contain macrometastases (defined as tumor clusters > 2 mm), micrometastases (tumor clusters < 2mm and > 0.2 mm).¹² The significance of isolated tumor cells (tumor clusters < 0.2 mm) is unclear and warrants further research.

The ultrastaging procedure results in “upstaging” (revision to a higher cancer stage) in about 5% of cases, and identifies about 40% of all lymph node metastases—metastases that would not have been detected otherwise—including micrometastases and isolated tumor cells.^{12,14} While management of low-volume metastases remains controversial, identifying them can help researchers determine the best post-operative approach for such cases.

Algorithm

The US National Comprehensive Cancer Network (NCCN) Guidelines’ surgical algorithm calls for a side-specific lymphadenectomy in the event of failed SLN mapping in one hemi-pelvis, and removal of all suspicious lymph nodes irrespective of mapping.¹ Applying this algorithm reduces the false negative rate to less than 5%.^{16,17} While this algorithm is widely accepted in cervical cancer, where the indication for lymph node assessment is generally agreed upon, some have been critical of performing side-specific lymphadenectomy after failed SLN mapping in low-risk endometrial cancer cases. An alternative strategy would be to remove SLNs (if found) but omit lymphadenectomy.¹⁸

Clinical experience

SLN mapping should be performed by trained specialists at centres that have experience with lymph node dissections and pathological expertise in ultrastaging. Such expertise is required to locate SLNs and minimize false-negative results. The learning curve in surgeons already skilled in pelvic lymphadenectomy has been reported to be 30 cases or less^{19, 20}. GOC advises that clinicians document their results until their detection rates approach 80% and their false negative rates fall below 5%.

Patient selection

SLN mapping is a reasonable alternative for patients with endometrial grade 1 endometrioid adenocarcinoma in which pelvic lymph node assessment is being considered. For high-risk cases, the decision to perform completion lymphadenectomy remains at the attending surgeon's discretion based on individualized patient characteristics and tumor risk criteria.²¹

SLN mapping is an accurate method for determining lymph node metastatic status in cervical cancer patients undergoing surgical treatment, and the oncologic safety of omitting complete pelvic lymphadenectomy following successful SLN mapping is being examined in randomized trials.

CONCLUSION

Sentinel lymph node technique has the potential to improve identification of women with lymph node metastasis while minimizing the morbidity and burden of extensive lymphadenectomy. While this continues to be an area of active research, GOC considers that SLN is a technique which significantly contributes to clinical care for many women with endometrial and cervical cancer and that its availability and implementation should be improved across the country.

On behalf of The Society of Gynecologic Oncology of Canada,



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MISSION

The Society of Gynecologic Oncology of Canada is a non-profit organization consisting of physicians, nurses, scientists and other health care professionals specializing in gynecologic oncology. Its purpose is to improve the care of women with or at risk of gynecologic cancer by raising standards of practice, encouraging ongoing research, promoting innovation in prevention, care and discovery, and advancing awareness. GOC also seeks to disseminate knowledge to practitioners, patients and the general public on gynecologic cancer as well as cooperate with other organizations committed to women's health care, oncology, and related fields.