Encouraging worldwide adoption of sentinel lymph node biopsies for gynecologic malignancies

Michael Frumovitz,¹ Alessandro Buda²

¹Gynecologic Oncology,
University of Texas MD
Anderson Cancer Center,
Houston, Texas, USA

²Department Obstetrics
and Gynecology, Azienda
Ospedaliera San Gerardo,
Monza, Italy

Correspondence to

Dr Michael Frumovitz,
Gynecologic Oncology,
University of Texas MD
Anderson Cancer Center,
Houston, Texas, USA;
mfrumovitz@mdanderson.org

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The sentinel node concept has been evolving over the last 40 years since Dr Ramon Cabanas first published on the model in 1977.¹ His original technique required cannulization of the dorsal lymphatics of the penis for direct injection of radiopaque dyes in order to perform a lymphangiogram to detect the general location of sentinel nodes in the groin. Since those original reports, the sentinel node technique has evolved significantly. We no longer cut down to find lymphatic channels for direct injection of mapping substances, but now inject into the tissue surrounding the tumor and allow for passive absorption of mapping substances into the lymphatic system. Mapping substances have evolved from radiopaque iodine to radiocolloids, blue dyes, and most recently indocyanine green. We no longer only obtain imaging, such as plain film or lymphoscintigram, to guide us to a general anatomic area, but now have means for direct visualization of the actual sentinel node or nodes, reducing the number of nodes removed and thereby short- and long-term morbidities.

Lymphatic mapping and sentinel lymph node (SLN) biopsy have long been the standard of care for patients with melanoma and breast cancer. The GONingen International Study on Sentinel nodes in Vulvar cancer (GROINSS-V) and the Gynecologic Oncology Group (GOG173) studies established lymphatic mapping and SLN biopsy alone as standard of care in the treatment of women with vulvar cancers.^{2,3} There is increasing evidence from validation studies for lymphatic mapping and SLN biopsy in cervical and uterine cancers, and there is mounting data supporting its safety in managing women with those cancers. The SENTICOL I (Ganglion Sentinelle dans le Cancer du Col) study showed that for women with early stage cervical cancer, SLN biopsy has a sensitivity of 96% for detection of metastatic disease to lymph nodes when following recommended guidelines for performing complete lymphadenectomy in unmapped hemi-pelvises, with a negative predictive value of 98%.⁴ SENTICOL III is a phase III trial that will evaluate disease-free survival for SLN biopsy only compared with complete pelvic lymphadenectomy in women with early stage cervical cancer, and should

complete accrual in early 2021.⁵ Validation studies in patients with uterine cancer have also shown high sensitivity and negative predictive value.^{6,7} The National Comprehensive Cancer Network (NCCN) guidelines include SLN biopsy only as an acceptable therapeutic approach to women with these malignancies,^{8,9} and the Society of Gynecologic Oncology has declared that the technique is a “reasonable staging strategy”, endorsing the procedure as a good option for women with uterine cancer.¹⁰

In this special issue of the *International Journal of Gynecological Cancer*, we focus on the most current research in the sentinel node concept as it applies to gynecologic malignancies.

The goal of this special issue is to encourage greater uptake of the technique into clinical practice by addressing two commonly cited reasons for resisting adoption. First, we present the most up-to-date data for lymphatic mapping and SLN biopsy in gynecologic cancers. One major reason often cited for not implementing these techniques into clinical practice is lack of data and we hope the manuscripts presented in this issue will add to the accumulating research supporting its use. Second, lack of availability of technology is another reason gynecologic oncologists offer for not performing the procedure.¹¹ Although many of the publications in this issue focus on the latest “high tech” equipment and procedures such as indocyanine green and near infrared imaging, one step nucleic acid amplification, and SPECT/CT, other manuscripts present data from studies utilizing blue dye and/or technetium-99, mapping substances available at most medical centers around the world. There is a misconception that blue dye and/or technetium-99 radiocolloid are inadequate for performing lymphatic mapping in women with gynecologic cancers. This is not true. Although SLN detection rates may be higher with indocyanine green than with blue dye,¹² the validity of the technique is equivalent for both tracers. In other words, if a sentinel node is detected, regardless of mapping substance, the surgeon can feel assured that the sentinel node represents the disease status of all the lymph nodes in the basin. Thus, even when blue dye is the only

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mapping substance available, we would still encourage gynecologic oncologists to perform mapping and SLN biopsy as there will be a great benefit in those 40–60% of patients in whom a sentinel node is identified. Finally, we cannot understate the importance of working closely with pathologists to assure that they understand the importance of ultrastaging and immunohistochemistry in their processing of the sentinel nodes. The great promise of sentinel node biopsies is not only in decreasing operative morbidity by abandoning complete lymphadenectomy, but also in increasing detection of metastatic disease by identification of micrometastases and isolated tumor cells.

Another important aspect explored in this special issue is the importance of the technical and anatomical details of the SLN technique. We cannot overstate the importance of mastering the learning curve before incorporating the SLN algorithm into routine practice. We strongly recommend performing 25–30 cases of lymphatic mapping and SLN biopsy followed by complete lymphadenectomy to assure that the surgeon is correctly identifying and removing the sentinel node. The educational videos in this issue can help surgeons achieve proficiency by showing the main technical and anatomical aspects to follow for implementation of lymphatic mapping and SLN biopsy for your patients. In addition, the videos depict useful tips to reduce the risks of “failed mapping” and to better identify the true sentinel nodes.

Ongoing research will hopefully establish a universally accepted, standardized approach for lymphatic mapping in order to improve the accuracy of the technique and to allow for high quality comparison of published data. This will allow the gynecologic oncology community to answer questions such as what the importance is of isolated tumor cells or the necessity for completion lymphadenectomy in patients with positive sentinel nodes.

Twitter Michael Frumovitz @frumovitz

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