

## Correspondence



# Sentinel lymph node detection in endometrial cancer: make injection site the difference?

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► See the letter “Sentinel lymph node detection in endometrial cancer: hysteroscopic peritumoral versus cervical injection” in volume 27, e11.

### Correspondence to

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### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

### Reply to Alessandro Buda:

We thank Dr. Buda et al., for their interest in our paper [1]. Buda et al. question the utility of hysteroscopic injection for sentinel node mapping in endometrial cancer. In the present letter, Buda et al. reclaimed the opinion of Professor Abu-Rustum, supporting the safety of cervical injection for uterine lymphatic mapping [2].

As aforementioned in our expert opinion paper, we stated that cervical injection is an effective technique for detection of the most representative lymphatic ways of the uterus. Obviously, as demonstrated by several studies on this issue, cervical injection is a safe procedure, especially in those patients affected by low-risk diseases [3-7]. In particular, Abu-Rustum and colleagues [8] from the Memorial Sloan-Kettering Cancer Center developed and incorporated an algorithm in order to reduce false-negative rate of surgical sentinel lymph node mapping. With application of this algorithm (which includes: peritoneal staging, excision of all suspicious nodes regardless of mapping; and side specific lymph node dissection in case of absent mapping on one hemipelvis) the rate of false-negative dropped to 2%, being 15% in patients undergoing just excision of mapped nodes [8,9].

However, we have to take in account that the lymphatic drainage of the uterus is complex and not only achieved from the para-cervical tissues [2,10]. As reported by Frumovitz et al. [2], it is well known that there are two major routes of lymphatic drainage for the uterus. The main one follows the uterine vessels through the parametrium (the one identified through cervical injection) and another way follows the ovarian vessels to nodal basins into the para-aortic area (this one may be identified using corporal or deep cervical injection techniques). Taking into account this latter way of drainage is paramount for endometrial cancer management. In fact, it is estimated that more than 90% of patients had tumor located in the upper uterine corpus [2,11]. For these reasons, the use of an intracorporeal injection technique may theoretically improve the detection of the first nodes draining the tumor. Interestingly, a previous investigation of our study group, evaluating the detection rate of sentinel nodes

using hysteroscopic tracer's injection, suggested that more than 50% of patients had sentinel nodes in the para-aortic area ( $\pm$ pelvis); while, only 44% had sentinel nodes limited to the pelvis [12]. Additionally, we have to take into account that endometrial cancer (especially in high-risk cases) is not just a pelvic confined disease. In fact, as demonstrated by several investigations, awareness of tumor spread into the para-aortic area may improve patients' outcomes [13-15]. In 2008, Mariani et al. [16], observed that about 67% of patients with lymphatic dissemination had metastases in the para-aortic area. Similarly, the same study group in a prospective study [17] confirmed these results, thus suggesting that about 12% of endometrial cancer patients had tumor's spread in the para-aortic nodes. Furthermore, they observed that the rate of positive para-aortic nodes is 51% and 3% in case of positive and negative pelvic nodes, respectively [17]. Moreover, Todo et al. [18], in an interesting study on stage IIIC1 patients who had pelvic and para-aortic node dissection, suggested the rate of para-aortic node metastases to be probably underestimated. They observed that more than 70% of patients with stage IIIC1 endometrial cancer had undiagnosed macro- and micro-metastases in aortic lymph nodes [18]. Therefore, it's easy to understand the importance of assessing the status of para-aortic area in endometrial cancer patients.

A recent review published on behalf of the Communities of Practice Group of the Society of Gynecologic Oncology of Canada on the role of sentinel node mapping in endometrial cancer reviewed the current evidence comparing cervical and intracorporeal (i.e., myometrial [subserosal] and peritumoral) injection techniques [19]. The overall detection rate of sentinel nodes after cervical injection ranged from 62% to 100%, being 73% to 95% after corporeal injection. All studies including more than 100 endometrial cancer patients had an overall detection rates greater than 80% [19].

In conclusion, cervical and perilesional tracers' injection techniques may be two promising procedures for sentinel node mapping. In a setting in which hysteroscopic skills are lacking, cervical injection should be the preferred way to sentinel node identification. In experienced hands, intraoperative hysteroscopy with indocyanine green injection required few minutes (generally less than 10 minutes). However, this shouldn't be considered as a waste of time, since it potentially allows to identify few patients harboring para-aortic node metastases. For these patients, the correct identification of positive para-aortic nodes may improve their curative chances. Further prospective studies are needed in order to assess the role of sentinel node biopsy in endometrial cancer. Hence, further randomized studies comparing different injection techniques are warranted.

## REFERENCES

1. Bogani G, Ditto A, Martinelli F, Signorelli M, Perotto S, Lorusso D, et al. A critical assessment on the role of sentinel node mapping in endometrial cancer. *J Gynecol Oncol* 2015;26:252-4.  
[PUBMED](#) | [CROSSREF](#)
2. Frumovitz M, Coleman RC, Soliman PT, Ramirez PT, Levenback CF. A case for caution in the pursuit of the sentinel node in women with endometrial carcinoma. *Gynecol Oncol* 2014;132:275-9.  
[PUBMED](#) | [CROSSREF](#)
3. Jewell EL, Huang JJ, Abu-Rustum NR, Gardner GJ, Brown CL, Sonoda Y, et al. Detection of sentinel lymph nodes in minimally invasive surgery using indocyanine green and near-infrared fluorescence imaging for uterine and cervical malignancies. *Gynecol Oncol* 2014;133:274-7.  
[PUBMED](#) | [CROSSREF](#)

4. Abu-Rustum NR. Sentinel lymph node mapping for endometrial cancer: a modern approach to surgical staging. *J Natl Compr Canc Netw* 2014;12:288-97.  
[PUBMED](#)
5. Cibula D, Oonk MH, Abu-Rustum NR. Sentinel lymph node biopsy in the management of gynecologic cancer. *Curr Opin Obstet Gynecol* 2015;27:66-72.  
[PUBMED](#) | [CROSSREF](#)
6. Darin MC, Gómez-Hidalgo NR, Westin SN, Soliman PT, Escobar PF, Frumovitz M, et al. Role of indocyanine green (ICG) in sentinel node mapping in gynecologic cancer: Is fluorescence imaging the new standard? *J Minim Invasive Gynecol* 2015 Oct 27 [Epub].  
[PUBMED](#) | [CROSSREF](#)
7. Signorelli M, Crivellaro C, Buda A, Guerra L, Fruscio R, Elisei F, et al. Staging of high-risk endometrial cancer with PET/CT and sentinel lymph node mapping. *Clin Nucl Med* 2015;40:780-5.  
[PUBMED](#) | [CROSSREF](#)
8. Barlin JN, Khoury-Collado F, Kim CH, Leitao MM, Chi DS, Sonoda Y, et al. The importance of applying a sentinel lymph node mapping algorithm in endometrial cancer staging: beyond removal of blue nodes. *Gynecol Oncol* 2012;125:531-5.  
[PUBMED](#) | [CROSSREF](#)
9. Leitao MM, Khoury-Collado F, Gardner G, Sonoda Y, Brown CL, Alektiar KM, et al. Impact of incorporating an algorithm that utilizes sentinel lymph node mapping during minimally invasive procedures on the detection of stage IIIC endometrial cancer. *Gynecol Oncol* 2013;129:38-41.  
[PUBMED](#) | [CROSSREF](#)
10. Plentl AA, Friedman EA. Lymphatic system of the female genitalia: the morphologic basis of oncologic diagnosis and therapy. Philadelphia: Saunders; 1971.
11. Westin SN, Lacour RA, Urbauer DL, Luthra R, Bodurka DC, Lu KH, et al. Carcinoma of the lower uterine segment: a newly described association with Lynch syndrome. *J Clin Oncol* 2008;26:5965-71.  
[PUBMED](#) | [CROSSREF](#)
12. Solima E, Martinelli F, Ditto A, Maccauro M, Carcangiu M, Mariani L, et al. Diagnostic accuracy of sentinel node in endometrial cancer by using hysteroscopic injection of radiolabeled tracer. *Gynecol Oncol* 2012;126:419-23.  
[PUBMED](#) | [CROSSREF](#)
13. AlHilli MM, Podratz KC, Dowdy SC, Bakkum-Gamez JN, Weaver AL, McGree ME, et al. Risk-scoring system for the individualized prediction of lymphatic dissemination in patients with endometrioid endometrial cancer. *Gynecol Oncol* 2013;131:103-8.  
[PUBMED](#) | [CROSSREF](#)
14. Bogani G, Dowdy SC, Cliby WA, Ghezzi F, Rossetti D, Mariani A. Role of pelvic and para-aortic lymphadenectomy in endometrial cancer: current evidence. *J Obstet Gynaecol Res* 2014;40:301-11.  
[PUBMED](#) | [CROSSREF](#)
15. AlHilli MM, Mariani A. Preoperative selection of endometrial cancer patients at low risk for lymph node metastases: useful criteria for enrollment in clinical trials. *J Gynecol Oncol* 2014;25:267-9.  
[PUBMED](#) | [CROSSREF](#)
16. Mariani A, Dowdy SC, Cliby WA, Gostout BS, Jones MB, Wilson TO, et al. Prospective assessment of lymphatic dissemination in endometrial cancer: a paradigm shift in surgical staging. *Gynecol Oncol* 2008;109:11-8.  
[PUBMED](#) | [CROSSREF](#)
17. Kumar S, Podratz KC, Bakkum-Gamez JN, Dowdy SC, Weaver AL, McGree ME, et al. Prospective assessment of the prevalence of pelvic, paraaortic and high paraaortic lymph node metastasis in endometrial cancer. *Gynecol Oncol* 2014;132:38-43.  
[PUBMED](#) | [CROSSREF](#)
18. Todo Y, Suzuki Y, Azuma M, Hatanaka Y, Konno Y, Watari H, et al. Ultrastaging of para-aortic lymph nodes in stage IIIC1 endometrial cancer: a preliminary report. *Gynecol Oncol* 2012;127:532-7.  
[PUBMED](#) | [CROSSREF](#)
19. Cormier B, Rozenholc AT, Gotlieb W, Plante M, Giede C; Communities of Practice (CoP) Group of Society of Gynecologic Oncology of Canada (GOC). Sentinel lymph node procedure in endometrial cancer: a systematic review and proposal for standardization of future research. *Gynecol Oncol* 2015;138:478-85.  
[PUBMED](#) | [CROSSREF](#)