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Editorial
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How to Choose the Site of Injection for Sentinel Lymph Node Mapping for Endometrial Cancer

*Nai-Ming Cheng[1,2], I-San Chan[1,5], Ying-Chu Shih[1,2], Peng-Hui Wang[1,2,3,4] and Yi-Jen Chen[1,2,3,4]**

[1]Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taiwan

[2]Department of Obstetrics and Gynecology, National Yang Ming Chiao Tung University, Taiwan

[3]Institute of Clinical Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taiwan

[4]Department of Obstetrics and Gynecology, Institute of Clinical Medicine, School of Medicine, National Yang Ming University, Taiwan

[5]Department of Medical Research, China Medical University Hospital, Taiwan

Editorial

Sentinel lymph node mapping and dissection has become an emerging method during staging surgery for endometrial cancer. Traditionally, complete pelvic lymph node dissection is performed during staging surgery for endometrial cancer. However, the use of this method in the early stage of the disease is debatable, due to the fact that the rate of lymph node metastasis in early-stage disease is relatively low. Additionally, complete lymph node dissection can potentially increase the rate of various complications, such as lymphedema. Instead, sentinel lymph node dissection identifies and removes only the lymph node that directly drains the tumor. This technique should be considered in patients with apparent uterine-confined endometrial cancer [1].

Lymphatic drainage of the uterus is considered to the following two routes [2,3]{Frumovitz, 2014 #33}{Frumovitz, 2014 #33}. One of the routes is the "cervical route", which travels through the uterine vessels, parametrium, and retroperitoneal pelvic area. The other route is the "ovarian route", which travels through the ovarian ligament, gonadal vessels, and para-aortic area. According to the latest National Comprehensive Cancer Network guidelines for Endometrial Carcinoma (Version 3. 2021), the standard site of tracer injection was in the deep and superficial cervix at positions of 3 o'clock and 9 o'clock. This cervical injection is considered to map the cervical route of lymphatic drainage.

However, the optimal *site* of tracer injection remains to be determined.

Several recent 5-years studies (Table 1) have demonstrated that tracer injections not involving the cervix provide comparable performance regarding the overall sentinel lymph node detection rate [4-6]. Most importantly, there is also an significant increase in the para-aortic lymph node detection rate if a tracer is injected in a site other than the cervix [5,6], or at least a trend of an increase in the rate [4]. Although it is not clearly understood, the increase in the pelvic lymph node detection rate is thought to be related to increased mapping of ovarian route lymphatic drainage [3]. In addition to the latest evidence that has been previously mentioned, there are numerous studies that have examined alternative sites of injection. These studies included fundal myometrium injection [3], hysteroscopic peritumor injection [7,8],ultrasound-guided transvaginal myometrium injection [9], and subserosal injection on the round ligament and uterus isthmus around the cervix [10,11]. Although direct comparisons to cervical injections were not conducted in these studies, some of them also proposed an improvement of para-aortic lymph node mapping [3,9].

A previous study has demonstrated that para-aortic lymph node involvement occurs in approximately 7% to 8% of endometrial cancer patients and in approximately 50% of patients with positive pelvic nodes [12]. They also concluded that the factors associated with para-aortic lymph node dissemination include advanced stage, high histological grade, deep myometrial invasion, cervical involvement, lymphovascular space involvement, and the presence of pelvic lymph node metastases [12]. The increase in the rate of para-aortic lymph mapping (as a result of uterine tracer injection) may be useful in patients with this disease.

In summary, we aim to draw attention to the site of injection regarding sentinel lymph node mapping in endometrial cancer. This focus is of paramount importance in an era emphasizing

Correspondence:
Yi-Jen Chen, Department of Obstetrics and Gynecology, Institute of Clinical Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 11217, Taiwan, Tel: (886)-2-2875-7566; Fax: (886)-2-2773-2778; E-mail: chenyj@vghtpe.gov.tw

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Table 1: Latest randomized control trial and meta-analysis comparing different site of injection to standard cervical injection.

Author Published year	Study type	Injection Site	Overall DR[a]	Para-aortic DR[a]
Gezer, 2020	RCT, n=81	Cervix	80%	2.5%
		Endometrium	85%	**41.5% (p<0.001)**
Ditto, 2020	RCT, n=165	Cervix	96.4%	19.5%
		Peri-tumor, hysteroscopic	86.3%	29% (p=0.18)
Smith, 2017	Meta-analysis, 55 studies, n=4915	Cervix, 35 studies	80.2%	6.7%
		Uterine, 24 studies	77.6%	**26.8% (p=0.001)**

[a]Detection Rate (DR): defined as the number of at least one SLN detected divided by SLN mapping procedure performed. Para-aortic (PA) DR defined as the number of at least one SLN in para-aortic area detected divided by SLN mapping procedure performed

precision medicine. Further studies are required to determine whether the cervix should remain as the optimal site of injection.

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