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# Sentinel Lymph Node Mapping in Endometrial Cancer: Our Initial Experience in a Resource Limited Setting

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## Rezumat

***Biopsia nodului santinelă în cancerul endometrial: experiența noastră inițială într-un context cu resurse limitate***

*Introducere:* Statusul limfonodal este unul dintre cei mai importnați factori de prognostic în cancerul endometrial, însă limfadenectomia sistematică este asociată cu morbiditate semnificativă. Biopsia nodului santinelă (NS) oferă o alternativă mai puțin invazivă la limfadenectomia sistematică, însă datele privind utilizarea acestei metode în absența verdelui de indocianină sunt limitate, mai ales în contexte cu resurse limitate.
*Metode:* Între noiembrie 2019 şi martie 2025, au fost incluse într-un studiu prospectiv 29 de paciente cu cancer endometrial în stadiul FIGO I-III. Pentru biopsia nodului santinelă s-a utilizat injectarea cervicală de albastru de metilen, cu sau fără technetiu-99m. Nodul santinelă a fost prelucrată conform protocolului de ultrastadializare. La pacientele cu boală cu risc înalt s-a realizat suplimentar limfadenectomie pelvină şi para-aortică completă. Au fost calculate ratele de detecție, sensibilitatea şi valoarea predictivă negativă (VPN).
*Rezultate:* Rata de detecție generală şi bilaterală a fost de 75% respectiv, 48% (pentru albastru de metilen: 72% / 44%; pentru metoda combinată: 100% / 75%). Metastaze limfonodulare au fost identificate la 9 dintre cele 29 de paciente (31%). Sensibilitatea la nivel de pacientă a fost de 71 %, cu VPN de 88%. Aplicarea algoritmului de completare a limfadenectomiei în hemipelvisul în care nu s-a detectat NS a crescut sensibilitatea la 86 %. Sensibilitatea şi VPN calculat pe hemipelvis unde s-a depistat NS au atins 100%. Invazia spațiului limfovascular şi invazia miometrială > 50% s-au asociat semnificativ cu prezența metastazelor limfonodulare ($p < 0.05$). Nu s-au înregistrat complicații legate de procedura de biopsie a NS.
*Concluzii:* Identificarea nodului santinelă utilizând albastru de metilen, cu sau fără asocierea cu radiocoloid, în combinație cu un algoritm de completare ce presupune limfadenectomie pe hemipelvisul cu identificare eşuată a nodului santinelă, permite o stadializare limfatică precisă chiar şi în absența metodei de detecție prin fluorescență.

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**Cuvinte cheie:** cancer endometrial; nod santinelă; albastru de metilen; limfadenectomie; context cu resurse limitate; stadializare nodală

## Abstract

*Background:* Nodal status is one of the most important prognostic factors in endometrial cancer (EC), but systematic lymphadenectomy is associated with significant morbidity. Sentinel lymph node (SLN) mapping offers a less invasive alternative. However, data are limited where indocyanine green is unavailable.

*Methods:* Between November 2019 and March 2025, 29 women with FIGO stage I–III EC were prospectively enrolled in this study. Cervical injection of methylene blue, with or without technetium-99m, was used for SLN mapping. Ultrastaging was performed routinely. In patients with high-risk disease, full pelvic and para-aortic lymphadenectomy was also performed. Detection rates, sensitivity, and negative predictive value (NPV) were calculated.

*Results:* Overall and bilateral detection rates were 75% and 48%, respectively (methylene blue: 72% / 44%; dual tracer: 100% / 75%). Nodal metastases were identified in 9 of 29 patients (31%). Patient-level sensitivity was 71%, with an NPV of 88%. Application of the side-specific completion algorithm increased sensitivity to 86%. Side-specific sensitivity and NPV reached 100%. Lymphovascular space invasion and > 50% myometrial invasion were significantly associated with nodal metastasis ($p<0.05$). No mapping-related complications were observed.

*Conclusions:* SLN mapping with methylene blue, with or without technetium, combined with a side-specific completion algorithm, enables reliable nodal staging even without fluorescence imaging.

**Keywords:** endometrial cancer, sentinel lymph node, methylene blue, lymphadenectomy, resource limited setting, nodal staging

## Introduction

Endometrial cancer (EC) has become a major global women's health concern, with 420 368 new cases estimated in 2022, making it the sixth most common malignant disease in women worldwide (1). GLOBOCAN 2020 data further underline its public health impact, recording approximately 417 000 diagnoses and 97 370 deaths - figures that continue to rise in parallel with trends in population ageing, obesity, and diabetes (2).

Accurate assessment of lymph node status is pivotal because nodal involvement upgrades the disease to FIGO stage IIIC and independently worsens survival. Contemporary series report lymph node metastases in 0.8-4.8% in low-risk and 17 % in high-risk early stage tumours (3-5). Detecting nodal spread by systematic lympha-denectomy refines prognosis and guides adjuvant radiotherapy or systemic treatment, but adds morbidity without a clear survival benefit (6).

The morbidity associated with comprehensive lymph node dissection is substantial. Up to one third of patients experience early or late sequelae such as lymphoceles, vascular injury or chronic lower extremity lymphoedema (7). The cumulative incidence of lower limb lymphoedema after pelvic± para-aortic dissection is 30-40 %, rising to 60 % when combined with adjuvant radiotherapy (7,8).

Sentinel lymph node (SLN) mapping offers a compromise: it yields the staging information needed to personalise adjuvant therapy while sparing most women a full lymph node dissection. A meta-analysis of 44 studies confirmed a pooled detection rate of 83% and a sensitivity of 91% for SLN mapping in detecting nodal metastasis (9). Crucially, SLN mapping reduces lymphoedema rates (2.0% vs 21.3% after pelvic lympha-denectomy) and abolishes lymphocele formation in some series (10). International guidelines therefore endorse SLN algorithms as the preferred nodal staging strategy in early stage EC (11,12).

Fluorescence with indocyanine green (ICG) achieves the highest bilateral detection and is recommended as the gold standard tracer for SLN mapping in endometrial cancer (12). Alternative low cost tracers, such as methylene blue used alone or combined with technetium-99m nanocolloid, are still employed in resource-constrained settings, but their overall and bilateral detection rates are generally lower.

The aim of our study was to evaluate the

performance of SLN mapping using methylene blue alone and in combination with technetium 99m. Primary endpoints were overall and bilateral detection rates. Secondary endpoints included sensitivity, negative predictive value (NPV), and identification of factors influencing these outcomes, with the goal of providing practical guidance for settings where ICG technology is not available.

## Methods

This prospective observational study was conducted between November 2019 and March 2025, at the First Obstetrics and Gynaecology Clinic of the Emergency Clinical County Hospital in Târgu Mureş, affiliated with the George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Târgu Mureş. Ethical approval was obtained from the institutional ethics committee (no.33680/13 December 2019), and all participants provided written informed consent before enrollment.

Eligible patients had a pathologically confirmed diagnosis of endometrial carcinoma, were in preoperative FIGO stage I-III (2018 classification), and were scheduled for surgical treatment. Preoperative evaluation included clinical gynaecological examination and imaging (ultrasound, CT, or MRI), performed by specialists in gynaecologic oncology and cancer surgery.

All patients underwent total hysterectomy with bilateral salpingo-oophorectomy, via an abdominal or laparoscopic approach. The uterus and any macroscopically suspicious lymph nodes were examined intraoperatively by frozen section. If the tumour showed < 50% myometrial invasion and was grade 1 or 2, pelvic and para-aortic lymphadenectomy was not performed. If > 50% myometrial invasion, grade 3 tumour, or FIGO stage II-III disease was detected on frozen section, pelvic and para-aortic lymphadenectomy was performed. In selected cases, if bilateral SLNs were identified, lymphadenectomy was omitted.

Sentinel lymph node mapping was performed using two tracer methods: (1) intracervical injection of methylene blue alone, and (2) intracervical injection of methylene blue combined with technetium-99m radiocolloid. The mapping technique followed a previously published protocol of the authors for cervical cancer (13).

In cases using a radiotracer, lymphoscintigraphy was performed preoperatively, either on the day of surgery or the day before, in the Nuclear Medicine Department. The procedure was conducted according to guidelines of the European Association of Nuclear Medicine and national standards. It included radiotracer injection, acquisition of preoperative images, intraoperative lesion localisation using a gamma probe, and excision of the identified SLNs.

Periorificial injections of technetium-99m nanocolloidal albumin (Nano-HAS ROTOP Pharmaka GmbH, Dresden, Germany or NanoScan Medi-Radiopharma Ltd., Érd, Hungary) were administered in four quadrants of the cervix using a 20- or 22-gauge needle, avoiding necrotic areas. A dose of approximately 110 MBq in a total volume of 2 mL (0.5 mL per deposit) was used. Dynamic imaging (10 min, 1 min/frame) and static imaging (3-5 min, early and late) were performed from anterior, posterior, and lateral views at 15 and 60 minutes post-injection. Early images delineated lymphatic ducts and first-echelon nodes; late images distinguished SLNs from second-echelon nodes. Subsequently, SPECT acquisition was conducted to enhance contrast and spatial resolution and to provide a 3D anatomical reference, especially for parametrial or atypical SLN locations.

Immediately before surgery, after induction of general anaesthesia, 4 mL of methylene blue was injected into the cervix at the 3 and 9 o'clock positions (2 mL per side, ~1 cm depth) using a 26-gauge needle. SLNs were identified intraoperatively using the Europrobe 3.2 console (Eurorad, S.A., Eckbolsheim, France) for radiotracer detection and by visual inspection for blue-stained lymphatics. Nodes with markedly elevated radioactivity or blue staining were considered SLNs. When multiple nodes were detected, the most radioactive or the proximal, blue-stained node was designated as the SLN. Radiolabelled nodes were also verified ex vivo.

SLN localisation was recorded according to seven anatomical regions as defined by Cibula et al.: right and left external iliac, right and left interiliac (obturator), right and left common iliac, and presacral (14). The para-aortic region was additionally included.

All SLNs were submitted separately for histopathological examination. Ultrastaging was performed by gynaecologic oncology pathologists according to the institution's protocol. Each SLN was sectioned at 2 mm intervals, embedded in separate paraffin blocks, and cut into 4 μm sections using a microtome. Serial sectioning continued until block depletion. Hematoxylin and eosin staining was used in all cases, and immunohisto-

chemistry was additionally performed.

After the SLN biopsy full pelvic lymphadenectomy with paraaortic lymphadenectomy was carried out according to the stage and risk metrics of the disease as described above.

The detection rate was used to quantify the technical success of SLN mapping. The overall detection rate was considered the proportion of patients in whom at least one SLN was visualised and excised on either pelvic side, whereas the bilateral detection rate was the proportion in whom SLNs were retrieved from both hemipelvises. Diagnostic accuracy was evaluated on both a per patient and a per side basis. Sensitivity and negative predictive value (NPV) were calculated with reference to metastases in the non sentinel lymph nodes. A true-positive result required ≥1 metastatic SLN. A false-negative result required negative or absent SLNs with metastasis in a non-sentinel node. A true-negative result required tumour-free SLNs and non-sentinel nodes.

## Results

A total of 29 patients were included in the analysis, with a mean age of 61.1 ± 7.6 years (range 46-73 years). Patient data, tumour characteristics and type of surgery are shown in *Table 1*.

According to the 2018 FIGO staging system, 15 patients (52%) were classified as stage IA, 12 patients (41%) as stage IB, one patient (3%) as stage II, and one patient (3%) as stage IIIB. Histopathology was dominated by endometrioid adenocarcinoma (24/29, 83%), with mixed histology in 2 patients (7%), while serous adenocarcinoma, clear cell carcinoma and dedifferentiated carcinoma were each identified in one patient (3% each). Tumour grade was mainly Grade 2 (16/29, 55%), with Grade 3 in 7 patients (24%) and Grade 1 in 6 patients (21%). The average maximum tumour diameter was 39.1 ± 29.3 mm (range, 0-134 mm). Myometrial invasion was less than 50% in 16 patients (55%) and greater than 50% in 13 patients (45%). Lymphovascular space invasion (LVSI) was identified in 11 patients (38%).

Laparoscopic surgery (total hysterectomy with bilateral salpingo-oophorectomy (BSO)) was performed in 13 patients (45%), with right pelvic lymphadenectomy added in one patient due to failiure of SLN mapping on that side. Abdominal surgery was chosen for 15 patients (52%), most frequently including pelvic and para-aortic lymphadenectomy (11 patients, 38%). Para-aortic lymphadenectomy was omitted in two cases because intraoperative frozen section showed < 50% myometrial invasion, and in one case due to advanced age and poor physical condition.

**Table 1.** Patient data, tumour characteristics and type of surgery

| Number of Patients | 29 |
|---|---|
| Age | Mean: 61.1 ± 7.6 years (range: 46–73) |
| Preoperative Stage | |
| IA | 15 (51.7%) |
| IB | 12 (41.4%) |
| II | 1 (3.4%) |
| IIIB | 1 (3.4%) |
| Histological Type | |
| Endometrioid adenocarcinoma | 24 (82.8%) |
| Serous adenocarcinoma | 1 (3.4%) |
| Clear cell carcinoma | 1 (3.4%) |
| Dedifferentiated carcinoma | 1 (3.4%) |
| Mixt types | 2 (6.9%) |
| Tumour Grade (FIGO) | |
| Grade 1 | 6 (20.7%) |
| Grade 2 | 16 (55.2%) |
| Grade 3 | 7 (24.1%) |
| Largest Tumour Diameter | Mean: 39.1 ± 29.3 mm (range: 0–134) |
| Myometrial Invasion | |
| <50% | 16 (55.2%) |
| >50% | 13 (44.8%) |
| LVSI | |
| Positive | 11 (37.9%) |
| Negative | 18 (62.1%) |
| Type of Surgery | |
| Laparoscopic hysterectomy + BSO | 13 (44.8%) |
| Laparoscopic hysterectomy + BSO + pelvic lymphadenectomy | 1 (3.4%) |
| Abdominal hysterectomy + BSO + pelvic & para-aortic lymphadenectomy | 11 (37.9%) |
| Abdominal hysterectomy + BSO + pelvic lymphadenectomy | 3 (10.3%) |
| Abdominal hysterectomy + BSO | 1 (3.4%) |

BSO: bilateral salpingo-oophorectomy

The SLN mapping, as shown in *Table 2*, was performed using Methylene Blue alone in 25 patients and in combination with technetium-99m radiocolloid in 4 patients. The overall detection rate, where the SLN was identified at least on one side of the pelvis, was 75%, with a bilateral detection rate of 48%. Detection rates using only blue dye were 72% overall with 44% bilateral, while the combined technique achieved 100% overall with 75% bilateral detection.

The mean number of SLNs retrieved was 1.03 ± 1.20 (range: 0-5). Most SLNs were found in the interiliac (obturator) region (56%), followed by the external iliac area (39%). Paracaval and parametrial regions each accounted for one SLN (3% each).

Among the 29 patients, at least 1 SLN was

**Table 2.** SLN mapping

| | |
|---|---|
| Tracer Method | |
| Methylene Blue only | 25 (86%) |
| Combined with Tc99 radiocolloid | 4 (14%) |
| Detection Rate | |
| Overall | 22/29 (76%) |
| Bilateral | 14/29 (48%) |
| Blue Dye Only | |
| Overall | 18/25 (72%) |
| Bilateral | 11/25 (44%) |
| Combined Technique | |
| Overall | 4/4 (100%) |
| Bilateral | 3/4 (75%) |
| Mean SLNs Retrieved | 1.03 ± 1.20 (range: 0–5) |
| Locations of SLNs | |
| External iliac | 14/36 (39%) |
| Interiliac (Obturator) | 20/36 (56%) |
| Paracaval | 1/36 (3%) |
| Parametrial | 1/36 (3%) |

identified in 22. SLN metastases were found in 5 of these 22 patients (23%), whereas the remaining 17 patients (77%), had histologically negative SLN as shown in *Fig. 1.* Completion lymphadenectomy of non sentinel nodes was undertaken in 8 of the 17 patients whose SLNs were negative. Occult metastases in non sentinel nodes were discovered in 2 of these 8 patients, representing false negative cases, while the other 6 showed no additional nodal disease and were classified as true negatives. The remaining 9 patients with negative SLN did not undergo additional nodal dissection, as no indication was present based on guideline recommendations, and were therefore excluded from the accuracy analysis. After this exclusion, 13 patients were evaluable, including 5 true positives, 6 true negatives and 2 false negatives, as detailed in *Table 3.* On this basis the patient specific sensitivity was 71 % and the negative predictive value was 75 %. Among the 2 false negative cases 1 had a contralateral pelvic lymph node metastasis without SLN identification on that side, and 1 had an isolated para-aortic metastasis without metastatic lymph nodes in the pelvis. Under the algorithm that mandates a completion lymphadenectomy whenever no sentinel node is identified in a hemipelvis, overall sensitivity rose to 86%.

If a side-specific analysis is performed, 21 hemipelvises can be identified where complete lymphadenectomy was performed alongside SLN mapping. Metastatic SLNs were identified in 7 hemipelvises. In the remaining 14 hemipelvises with negative SLN, no additional metastatic nodes were identified. This resulted in a side-specific sensitivity and NPV of 100%, demonstrating that the SLN method accurately determined the lymph node status of each lymphatic basin where mapping was successful.

Factors influencing detection rate, nodal spread and sensitivity are presented in *Table 4.* Mapping of both pelvic basins was most successful when the combined blue dye plus radioisotope technique was employed, reaching 75 % versus 44 % with blue dye alone. Tumours with superficial (< 50%) myometrial invasion achieved bilateral detection in 9/16 cases (56%), whereas invasion > 50% dropped this to 5/13 (38%). A comparable gradient

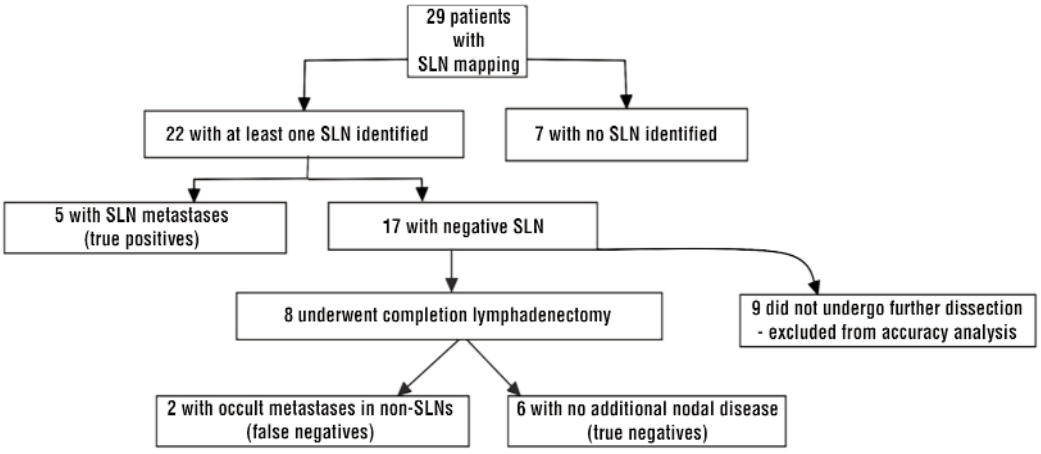


**Figure 1.** Patient specific analysis of the acuracy of the SLN method

**Table 3.** Sensitivity and negative predictive value

| Analysis level | True Positive | False Positive | False Negative | True Negative | Sensitivity | NPV |
|---|---|---|---|---|---|---|
| Patient-specific[1] | 5 | 0 | 2 | 6 | 71 % | 75 % |
| Patient-specific algorithm[2] | 6 | 0 | 1 | 6 | 86% | 86% |
| Side-specific[3] | 7 | 0 | 0 | 14 | 100 % | 100 % |

[1]Counts each patient once; positive if any SLN is metastatic, negative only if all nodes are tumor-free.
[2]Algorithm: completion lymphadenectomy whenever no SLN is identified in a hemi-pelvis
[3]Assesses each hemi-pelvis independently; a side counts as positive only if metastasis is found on that side

appeared in relation to LVSI: bilateral mapping occurred in 10/18 LVSI negative cases (56%) but in only 4/11 (36%) LVSI positive tumours. Surgical approach had modest impact - open surgery yielded bilateral detection in 8/15 patients (53%) compared with 6/14 (43%) for laparoscopy. None of these contrasts reached statistical significance (all $p > 0.05$), yet the numerical trends favour the combined technique and low risk pathology.

The accuracy of the SLN algorithm was highest in low risk cancers. Sensitivity was perfect (100%) in the three hallmark low risk settings: LVSI negative tumours (2/2 nodes identified), myometrial invasion < 50 % (2/2), and FIGO Grade 1 disease (1/1). Sensitivity fell to 3/7 (43%) in LVSI positive lesions, 3/7 (43%) when myometrial invasion exceeded 50%, and 0/2 (0%) in Grade 3 tumours. While p values remained above the 0.05 threshold, the marked decline underscores the difficulty of accurate mapping in biologically aggressive cancers.

Statistically significant differences were confined to the probability of metastatic spread. LVSI positivity was associated with nodal metastasis in 7/11 patients (64%), compared with 2/18 (11%) when LVSI was absent ($p \approx 0.01$). Deep myometrial invasion (> 50%) likewise carried metastasis in 7/13 cases (54%) versus 2/16 (13%) with superficial invasion ($p \approx 0.041$). Other factors - including tracer choice, surgical route, tumour grade, and cervical stromal invasion - showed no significant influence on nodal spread, detection success, or sensitivity within this 29 patient series.

## Discussions

Blue dye alone - whether isosulfan or methylene blue - has the weakest performance for SLN mapping in endometrial cancer. Early series documented overall detection rates of only 44 – 80 %, with successful bilateral pelvic

**Table 4.** Factors influencing detection rate, nodal spread and sensitivity

| Factor | Unilateral Detection | p | Bilateral Detection | p | LN Metastasis | p | SLN Sensitivity | p |
|---|---|---|---|---|---|---|---|---|
| SLN Detection Method | | | | | | | | |
| Methylene-Blue dye only | 18/25 (72%) | 0.546 | 11/25 (44%) | 0.329 | 9/25 (36%) | n/a | 5/7 (71%) | n/a |
| Combined technique | 4/4 (100%) | | 3/4 (75%) | | 0/4 (0%) | | n/a | |
| Myometrial Invasion | | | | | | | | |
| <50% | 12/16 (75%) | 1.0 | 9/16 (56%) | 0.34 | 2/16 (13%) | 0.04 | 2/2 (100%) | 0.444 |
| >50% | 10/13 (77%) | | 5/13 (38%) | | 7/13 (54%) | | 3/7 (43%) | |
| LVSI | | | | | | | | |
| Negative | 14/18 (78%) | 1.0 | 10/18 (56%) | 0.315 | 2/18 (11%) | 0.01 | 2/2 (100%) | 0.444 |
| Positive | 8/11 (73%) | | 4/11 (36%) | | 7/11 (64%) | | 3/7 (43%) | |
| Surgery Type | | | | | | | | |
| Laparoscopic | 10/14 (71%) | 0.68 | 6/14 (43%) | 0.57 | 2/14 (14%) | 0.28 | 1/2 (50%) | 1.0 |
| Open | 12/15 (80%) | | 8/15 (53%) | | 7/15 (47%) | | 4/7 (57%) | |
| FIGO Grade | | | | | | | | |
| Grade 1 | 5/6 (83%) | 0.607 | 4/6 (67%) | 0.411 | 1/6 (17%) | 0.63 | 1/1 (100%) | 0.165 |
| Grade 2 | 11/16 (69%) | | 6/16 (38%) | | 6/16 (38%) | | 4/6 (66%) | |
| Grade 3 | 6/7 (86%) | | 4/7 (57%) | | 2/7 (29%) | | 0/2 (0%) | |
| Cervical Stromal Invasion | | | | | | | | |
| Present | 5/6 (83%) | 1.0 | 3/6 (50%) | 1.0 | 2/6 (33%) | 1.0 | 1/2 (50%) | 1.0 |
| Absent | 17/23 (74%) | | 11/23 (48%) | | 7/23 (30%) | | 4/7 (57%) | |

mapping in just 31 – 50 % of patients (15,16). Gien et al. (2005), for example, achieved a 44 % detection rate with hysteroscopic isosulfan blue injection (16). Even the more effective cervical injection identified at least one SLN in only 62 % of cases in a 2013 multicentre study. Sensitivity was likewise sub optimal: 60 % when blue dye was used without a backup lymphadenectomy algorithm. Implementing a side-specific completion dissection (for unmapped hemipelvises) improved sensitivity to 86% (17).

Adding a radiocolloid to blue dye markedly improves performance. In the SENTI ENDO trial (Ballester et al., 2011) intracervical technetium 99m with blue dye yielded an 89 % overall detection rate, although bilateral detection remained low at 69%. Sensitivity was 84 %, reaching 100 % on side specific analysis (18).

ICG has emerged as the tracer of choice afterwards. Across multiple studies ICG consistently outperforms both blue dye and radiocolloid. Multiple studies have shown that ICG consistently outperforms both blue dye and radiocolloid. The FILM randomised trial (2018) reported an overall detection rate of 96% and a bilateral detection rate of 78% with ICG, compared to 74% and 31%, respectively, with blue dye(19). Buda et al. (2015) reported 100% overall and 88% bilateral detection with ICG, while blue dye achieved 84% and 50% (20). In the FIRES trial (Rossi et al., 2017), ICG mapping followed by systematic lymphadenectomy yielded a sensitivity of 97.2% and a negative predictive value of 99.6% (21). A 2017 meta-analysis by Lin et al. reported pooled overall detection at 93% and sensitivity between 87% and 95% (9).

Although our study could not employ ICG, the detection rates and sensitivity (71%) achieved with blue dye alone (72% overall, 44% bilateral) and in combination with radiocolloid (100% overall, 75% bilateral) are similar to those reported in the literature. When we applied a side specific algorithm - full lymphadenectomy on the mapped side in cases of failed detection - overall sensitivity increased to 86%. The only metastasis that would have been missed was a solitary para aortic node, which underscores the unresolved question of para aortic SLN mapping.

Large databases confirm that isolated para aortic metastases are uncommon but clinically relevant. In the National Cancer Database analysis by Nasioudis and Holcomb, 1.6% of 14,398 presumed low-risk stage I cases had isolated para-aortic involvement (22). A systematic review by Torrent et al. found a 1-3% rate of isolated para aortic positivity after a negative pelvic SLN in early stage disease (23). For high risk histologies (clear cel carinoma and carcinosarcoma) a rate of 5.8% was reported (24). In the case of uterine serous carcinoma the reported incidence was as high as 12% (25). Reflecting these data, the NCCN guidelines prefer pelvic SLN mapping for presumed uterine confined disease and leave para aortic dissection to the surgeon's discretion when pelvic SLNs are positive or in high risk tumours (11). The guidelines developed by the European Society of Gynaecological Oncology likewise accept SLN mapping as an alternative to systematic lymphadenectomy in stage I–II disease, recommending side-specific completion lymphadenectomy if mapping fails and reserving para-aortic staging for node-positive or selected high-risk cases (12).

Several prospective studies suggest strategies to improve para aortic detection. Ruiz et al achived para aortic SLN identification in 59% of patients by dual cervical + fundal injection of ICG (26). Torrent et al. combined cervical and fundal ICG injection with technetium-99m and preoperative SPECT/CT, achieving a 66.7% para-aortic detection rate (23). In contrast, pure cervical injection detects para aortic SLNs in only 2-6% of cases and rarely reaches the upper para aortic field (27-29).

Predictors of nodal metastasis include LVSI positivity, > 50 % myometrial invasion, grade 3 tumours, non endometrioid histology and cervical stromal involvement. The presence of any single high risk uterine factor raises nodal positivity to roughly 10-25%, while two or more factors raise it above 30% (5). In our cohort, LVSI and deep myometrial invasion correlated with markedly higher nodal involvement. Conversely, when none of these risk factors were present, bilateral SLN detection rates were high and every metastasis was accurately localised, indicating that SLN mapping alone is sufficient for low risk patients. In this group, SLN mapping offers the greatest advantage: although only up to 3% harbour nodal metastases that would otherwise go undetected, the technique identifies these cases while sparing the remaining 97% from the morbidity associated with a full lymphadenectomy.

For high risk disease we advocate the optimal tracer (ICG when available) and, where feasible, dual site injection to maximise para aortic detection. Until high detection rate and sensitivity is reliably achieved, comprehensive pelvic ± para aortic lymphadenectomy remains a reasonable option in this subgroup as suggested by the actual guidelines (11,12). Finally, the learning curve for

consistent bilateral mapping appears to plateau after ~40 cases; our 29 patient series represents the initial phase of this experience (30).

A key strength of this series is its demonstration that meaningful sentinel lymph node staging is feasible even in the absence of the preferred near-infrared ICG platform. We obtained reasonably high detection rates and high sensitivity using blue dye alone. These data provide a realistic performance benchmark for low-resource centres and underscore the value of a strict side-specific completion algorithm to minimise false negative results.

The study's principal limitations mirror its pragmatic design. First, the absence of ICG prevents a direct comparison with the current gold standard and limits generalisability to centres that routinely employ fluorescence guidance. Second, the small cohort size constrains the precision of our point estimates and precludes robust subgroup analyses, particularly in high risk histologies. Third, the series captures the institutional learning curve; continued accrual and technical refinement may further improve bilateral detection and para aortic mapping rates.

## Conclusion

Our findings reaffirm that SLN mapping is a practical and clinically meaningful staging strategy for endometrial cancer, even in resource limited settings where only blue dye is available. When a strict side specific completion algorithm is applied, blue dye alone achieves a sensitivity that approaches that of more sophisticated techniques. Consequently, the method offers its greatest benefit to patients with low risk uterine disease: SLN mapping reliably identifies the small proportion (~2 – 3%) with occult nodal metastases while sparing the large majority from the morbidity of full lymphadenectomy.

For high risk histologies, the current data support a more cautious approach. Until SLN mapping consistently reaches high para aortic detection and near perfect sensitivity, comprehensive pelvic ± para aortic lymphadenectomy remains a reasonable option. Ultimately, wider adoption of ICG and hybrid tracers promises to raise detection rates further, narrow the false negative margin, and extend the advantages of SLN staging to all risk groups.

### *Conflicts of Interest and Source of Funding*

The authors declare no conflict of interest. This study did not receive any kind of financial aid or funding from the institution or the authors.

### *Ethics Approval*

The present study was approved by the institution's ethics committee (no.33680/13 December 2019).

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