

1st Emirates Gynecological Oncology and MEMAGO 4th Annual Conference

11-12 October, 2019 | Rosewood Hotel, Abu Dhabi, UAE




Is there enough evidence to shift to
sentinel lymph node concept
in cervical cancer

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Division Of Gynocol Oncol 2019 October, AbuDhabi

Faculty Disclosure

X	No, nothing to disclose
	Yes, please specify:

High-risk factors for recurrence in early-stage cervical cancer after surgical management



Positive LNs
Parametrial involvement
Positive margins

Adjuvant Ch-Rt

Lymphadenectomy or lymphatic evaluation is standard procedure

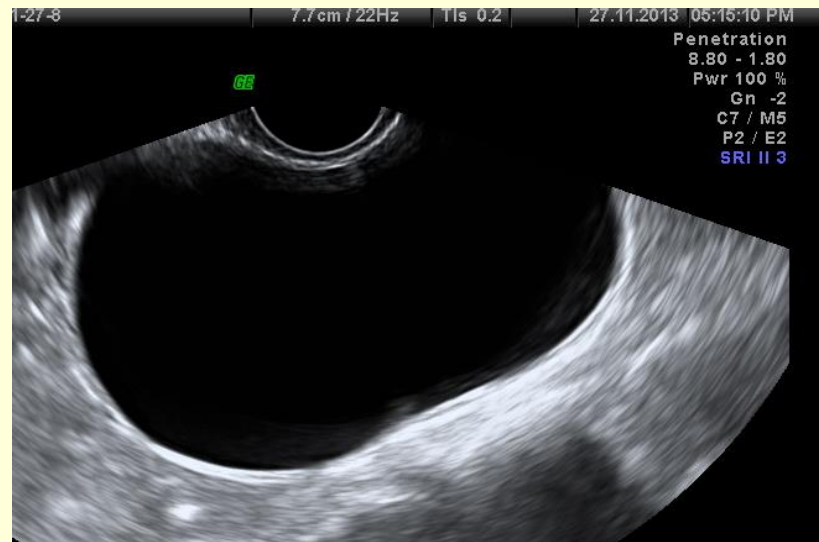
More than 80% of women with cervical cancer
have no metastatic lymph nodes (Ia2-IIa)



This group of women will not benefit from
lymphadenectomy, which is associated with
potentially significant morbidity.

increased risk.....

blood loss, neurovascular and ureteral injuries,
infections, lymphedema, lymphocyst and
venous thromboembolism



Can sentinel lymph node mapping(SLNM) be alternative to systematic LA ?

efficacy of mapping ?

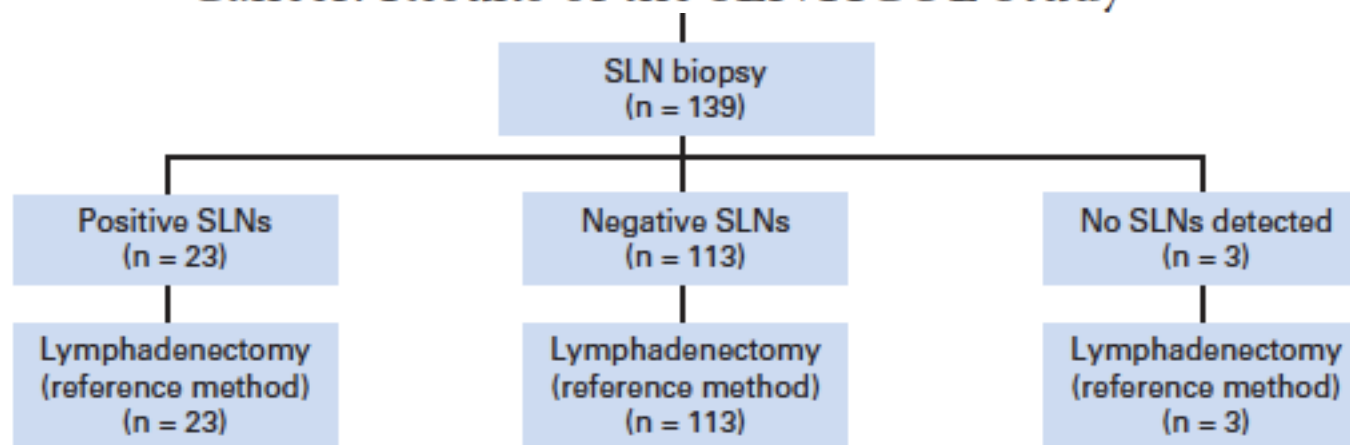
uncertainty of the data ?

concern for missing positive nodes ?

IA1(+LVSI)- IB1 SLNM with Tc99 and Blue dye, then LA

Bilateral Negative Sentinel Nodes Accurately Predict
Absence of Lymph Node Metastasis in Early Cervical
Cancer: Results of the SENTICOL Study

enri Marret,



Detection rate(DR) **98%** Bilateral DR **77%**

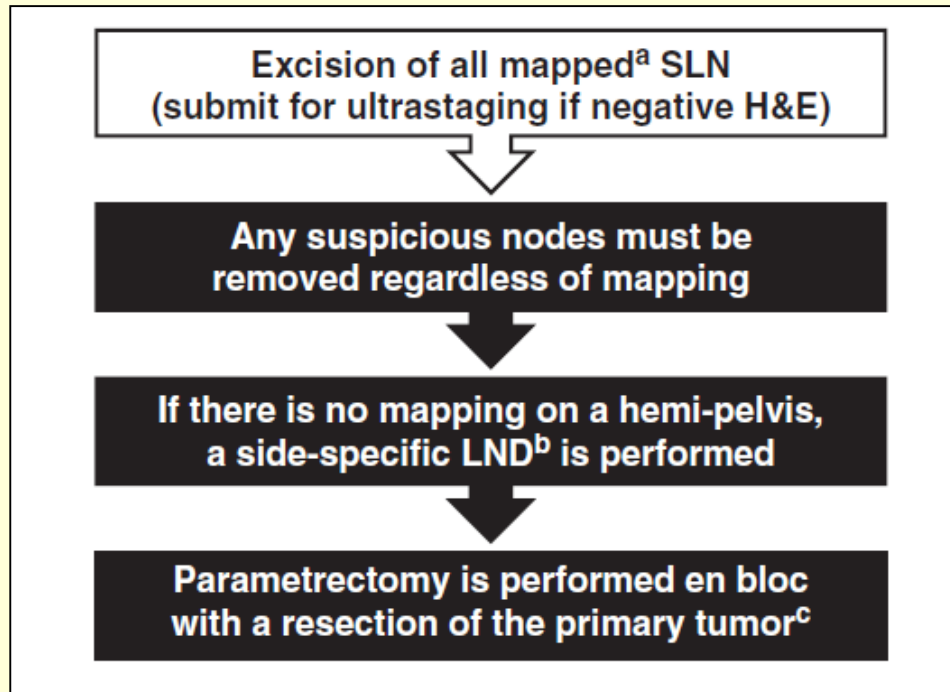
No false-negative

results were observed in whom SLN were identified **bilaterally**

Establishing a sentinel lymph node mapping algorithm for the treatment of early cervical cancer

Gynecologic Oncology 122 (2011) 275-280

Beatrice Cormier^a, John P. Diaz^b, Karin Shih^a, Rachael M. Sampson^c, Yukio Sonoda^a, Kay J. Park^d, Khaled Alektiar^e, Dennis S. Chi^a, Richard R. Barakat^a, Nadeem R. Abu-Rustum^{a,*}



n:122

All patient underwent SLNM followed complet LA

Detection rate	93%
Unilateral mapping	19%
Bilateral mapping	75%

SLNM correctly diagnosed 21 of 24 patients with nodal spread.
3 pts. had + non-SLN

2 pts had positive parametrial nodes(nodes removed en bloc with cervix
1 pts had unilaterally mapped

with optimal mapping

SLNM pracedure can implement instaed of systamatic LA.

The sentinel node procedure in early stage cervical cancer, taking the next step; a diagnostic review

C. Tax et al. / Gynecologic Oncology 139 (2015) 559–567

Casper Tax^{a,*}, Maroeska M. Rovers^{a,b}, Corine de Graaf^c, Petra L.M. Zusterzeel^c, Ruud L.M. Bekkers^c

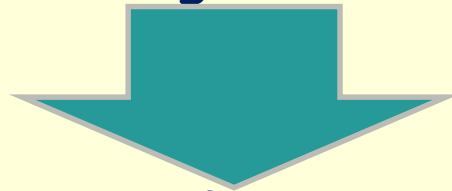
^a Radboud University Medical Centre, Radboudumc Institute for Health Sciences, Department of Operating Rooms, P.O. Box 9101, 6500 HB Nijmegen, the Netherlands

Ia1,Ib1,IIa(tumor size < 40mm)SLN mapping with dye tracer, isotop tracer, combined

The rate of metastatic node was 21% (710/3426 patients).

Overall SLN DR was 91%, Bilateral DR was 87% in pts with 2 cm tm

.....no suspicious pre-, and per-operative lymph nodes
.....have bilateral negative SLNs after ultra staging



FNR was 0.08% (1/1257 patients)

n:17 SLNs were detected bilaterally

All patients were undergone total PLA

A total of 573 pelvic LNs were examined by ultrastaging

With the ultrastaging of bilateral detected SLN

Sensitivity rate reaches 100% for the presence
of

both MAC and MIC in pelvic LNs.

They believe it is time to change the standard of care for women with early-stage cervical cancer to SLN biopsy only.



188 CC patients had SLNM followed by total pelvic LA

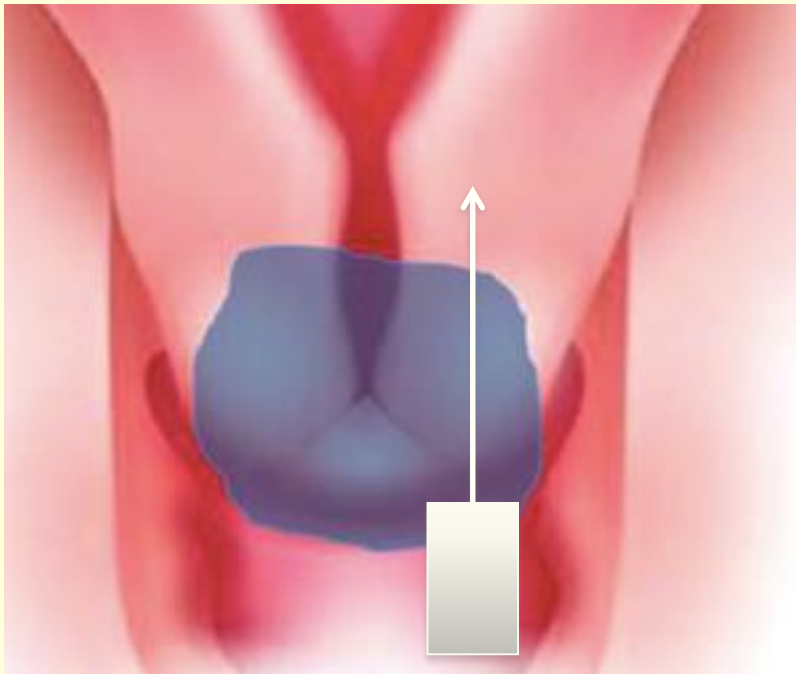
(SLNM with Tc99 and/or ICG, Bilateral DR 62%)

NPV 99.3 FNR 3.6%

Gloria Salvo Pedro T. Ramirez, Charles F. Levenback, Mark F. Munsell, Elizabeth D. Euscher, Pamela T. Soliman, and Michael Frumovitz
MD Anderson cancer center Gynecol Oncol, 2017

n: 350 all patients had SLNM , then Systematic LA

	< 2 cm	2- <4 cm	≥4 cm	
Bilateral detection rate	79%	83%	76%	p 0.460
FNR(at bilateral detect)	0,9%	0,9%	0,0%	P 0.999



SLNM with blue dye and Tc99

Dostalek L, Gynecol Oncol 2018

OPEN

Sentinel Lymph Nodes Mapping in Cervical Cancer a Comprehensive Review


Yasser Diab, MBBS, FRANZCOG, MD

**182 → 24
study**

Received July 26, 2016. Accepted for publication August 8, 2016.

(*Int J Gynecol Cancer* 2016;00: 00–00)

Conclusions: The review takes us to the strong conclusion that sentinel lymph node mapping is an ideal technique for detection of sentinel lymph nodes in cervical cancer patients with excellent detection rates and high sensitivity. The review also takes us to the supposition that a routine clinical evaluation of sentinel lymph nodes is feasible and a real-time florescence mapping with indocyanine green dye gives better statistically significant overall and bilateral detection than methylene blue.

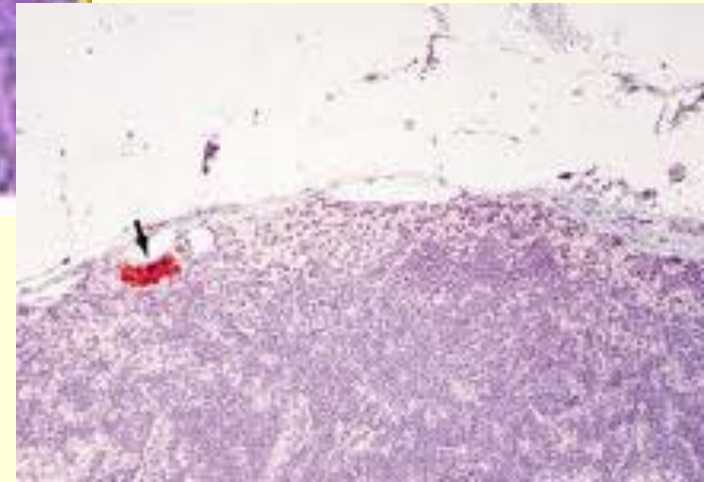
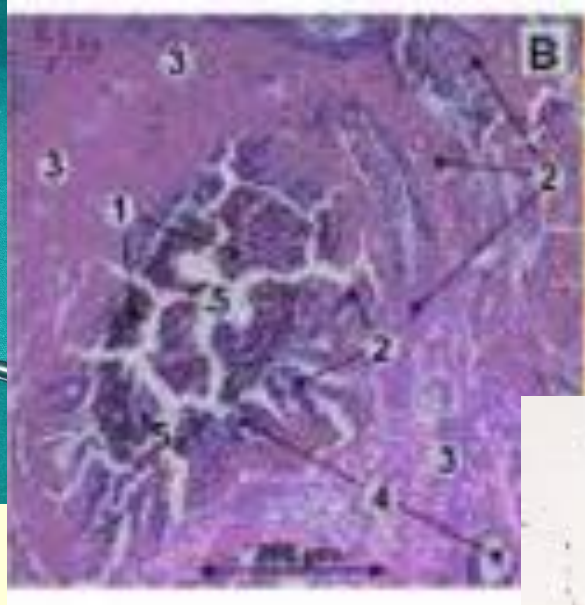
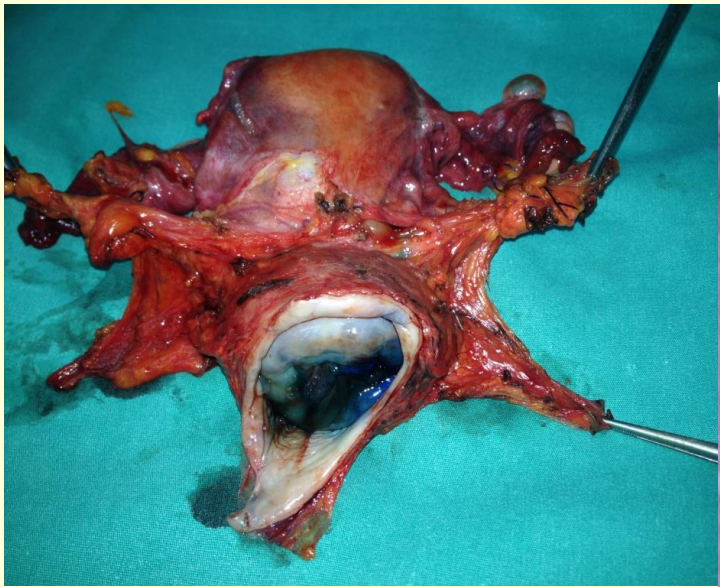


Additionally with SLNM

Preliminary data from the SENTICOL -2 randomized study (NCT01639820, www.clinicaltrials.gov) showed a 20% reduction in early lymphovascular morbidity, and 13% reduction in early neurological complications in patients undergoing SLN procedure only versus SLN plus pelvic LND.

15 % more + node was detected with SLNM compared to Systematic LA

Most of them are MM and ITC which may not be detected by standard H&E



What about prognostic significance of MM and ITC

The rate of micrometastases within metastatic nodes of patient having cervical cancer



10-22%

Cibula D et al *Gynecologic Oncology* 124 (2012) 496-501

Horn LC et al *Gynecologic Oncology* 111 (2008) 276-281

The Prognostic Effect the Nodal Micrometastases

Multivariate analysis of prognostic factors regarding overall survival

	RR	95%-CI	<i>p</i> -value
Pelvic lymph node involvement			
None (pN0)	Reference		
Micrometastases (pN1mic)	2.5	1.5-4.0	0.0002
Macrometastases (pN1)	3.4	2.4-4.7	<0.0001

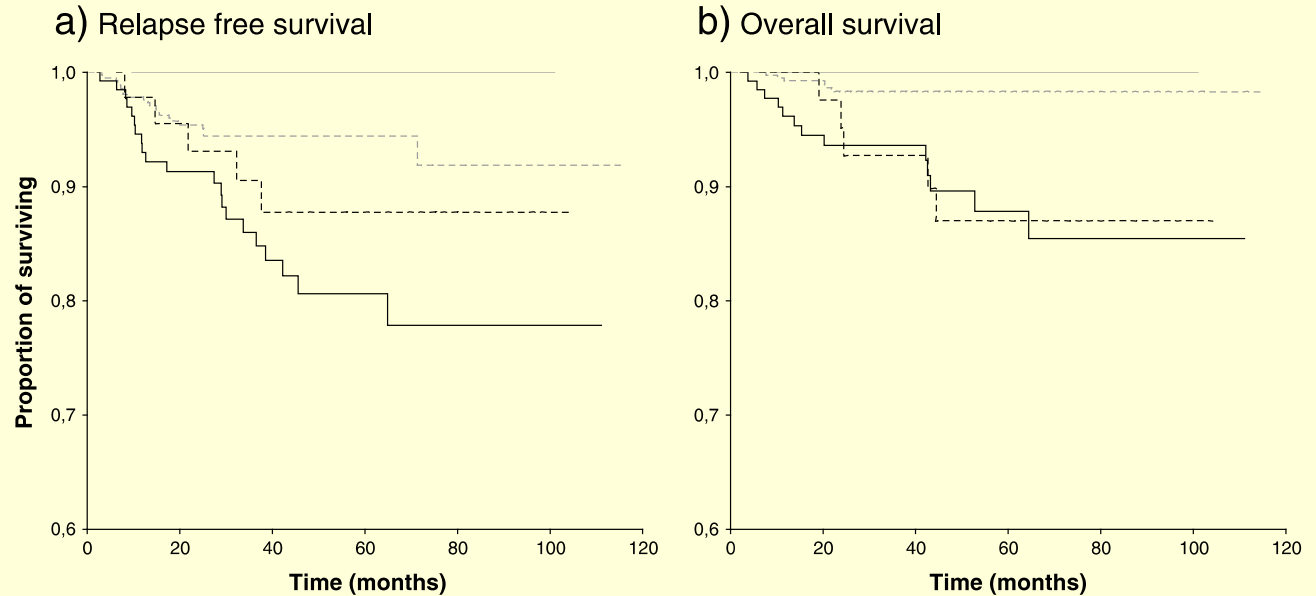
Horn LC et al *Gynecologic Oncology* 111 (2008) 276-281

Prognostic significance of low volume disease (micrometastases and ITC) detected in sentinel nodes (SN) of patients with early stages cervical cancer.

A total of 645 patients from 8 centers

LN status: SN ultrastaging	
Negative	N = 456 (70.7%)
Macrometastasis	N = 95 (14.7%)
Micrometastasis	N = 65 (10.1%)
ITC	N = 29 (4.5%)
LN status: non-sentinel nodes (nSN)	
Positive	N = 89 (13.8%)
LN status: final status (SN ultrastaging and pelvic nSN)	
Macrometastasis	N = 136 (21.1%)
Micrometastasis	N = 46 (7.1%)
ITC	N = 25 (3.9%)
Negative	N = 438 (67.9%)

Cibula D et al Gynecologic Oncology 124 (2012) 496-501



Mutual comparison of categories (p values):

	Negative	ITC	Micro-met.
Macro-met	0.001*	<0.001*	0.258
Micro-met.	0.128	0.008*	
ITC	0.201		

- ITC
- - - Negative
- Micro-metastases
- . - . Macro-metastases

Mutual comparison of categories (p values):

	Negative	ITC	Micro-met.
Macro-met.	<0.001*	0.009	0.886
Micro-met.	<0.001*	0.036	
ITC	0.549		



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journal homepage: www.elsevier.com/locate/ijgo



CLINICAL ARTICLE

Lymph node micrometastases in initial stage cervical cancer and tumoral recurrence

Leandro F. Colturato ^{a,*}, Roney C. Signorini Filho ^b, Raquel C.M. Fernandes ^c,
Luiz H. Gebrim ^{d,e}, Antônio H. Oliani ^a



Low-volume lymphatic metastasis is an important risk factor for tumor recurrence (OR=11.73, 95% CI: 1.57-87.8, p=0.017)

These pts should be considered eligible for adjuvant chemo-radiation

Additionally, MIC/ITCs were significantly associated with deep stromal invasion (p=0.046)

Impact of micrometastasis or isolated tumor cells on recurrence and survival in patients with early cervical cancer: SENTICOL Trial

Int J Gynecol Cancer 2019;29:447–452.

Benedetta Guani,¹ Maxence Dorez,² Laurent Magaud,³ Annie Buenerd,⁴ Fabrice Lecuru,⁵
Patrice Mathevet^{1,6}

ultrastaging resulted in 12.4% increase in detection rate in SLN positivity

The median follow-up was 36 (range 1-69) months

13 (9%) recurrences in 139 patients.

Among patients with SLN positive for micrometastases, only one had a recurrence. No recurrences occurred in any of the patients with SLN positive for isolated tumor cells.

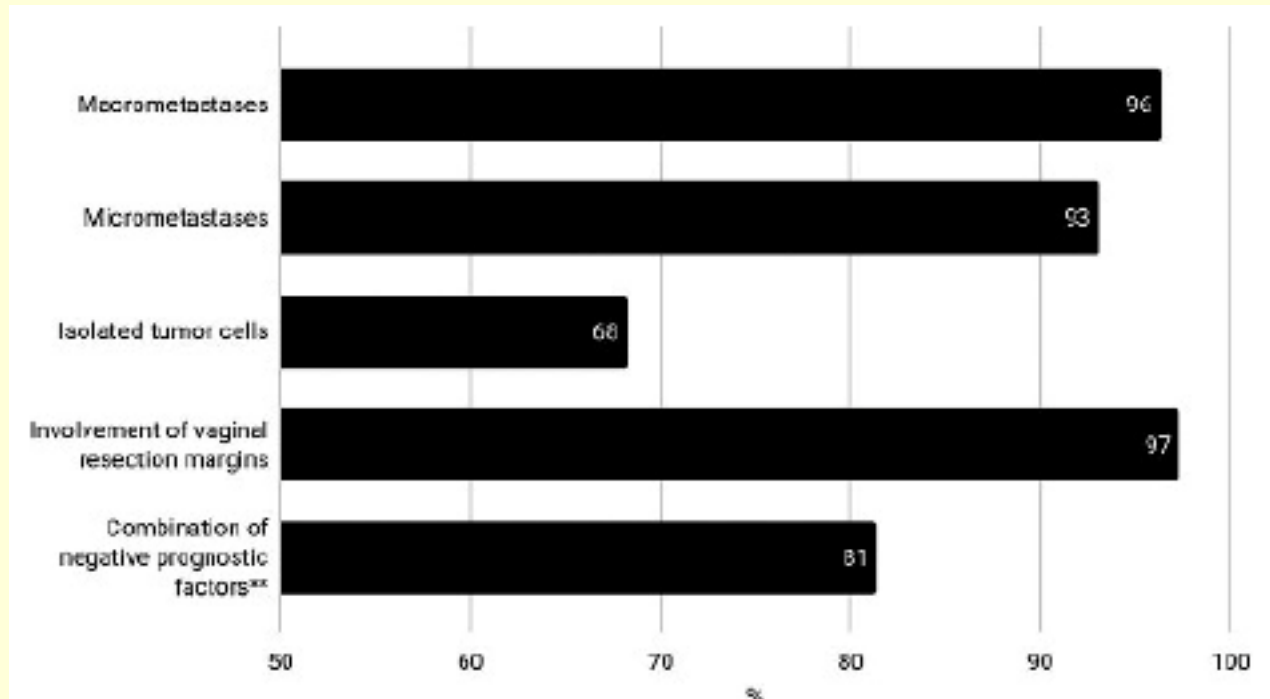
Conclusion Evidence of micrometastasis or isolated tumor cells in the SLN of untreated patients with early cervical cancer in the SENTICOL1 trial did not impact progression-free survival.

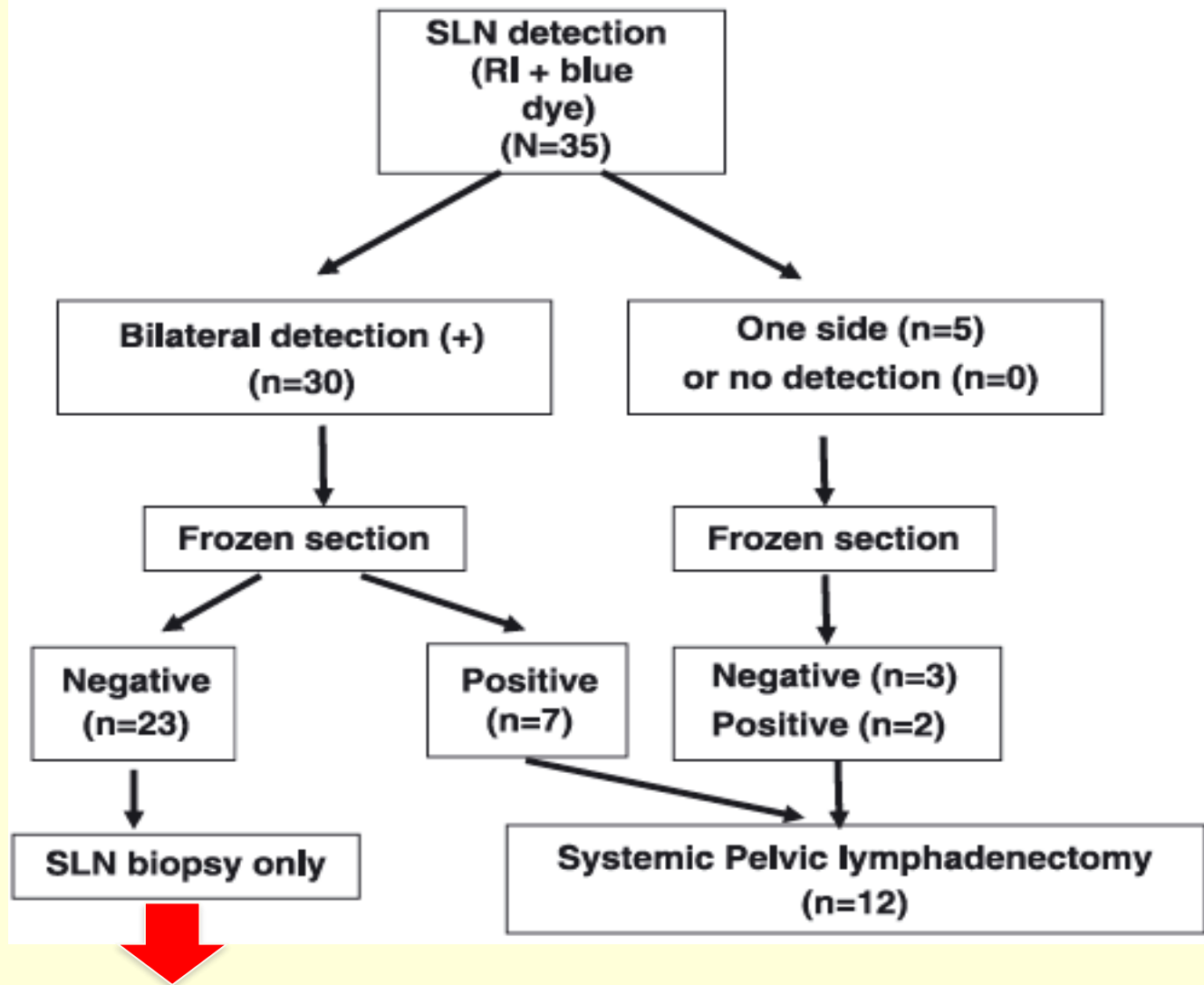
ESGO Survey on Current Practice in the Management of Cervical Cancer

Lukas Dostalek, MD, Elisabeth Åvall-Lundqvist, MD,† Carien L. Creutzberg, MD,‡
Dina Kurdiani, MD,§ Jordi Ponce, MD,|| Iva Dostalkova, PhD,¶ and David Cibula, MD**

Questioner results from 1445 members and 566 responses

Answers related to adjuvant treatment





9/23 received adj therapy

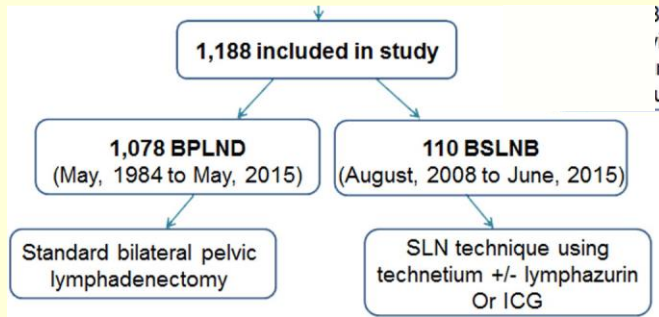
No recurrence in 49 months(Median Follow-up)

Can sentinel lymph node biopsy replace pelvic lymphadenectomy for early cervical cancer?

Genevieve K. Lennox^a, Allan Covens^{a,b,*}

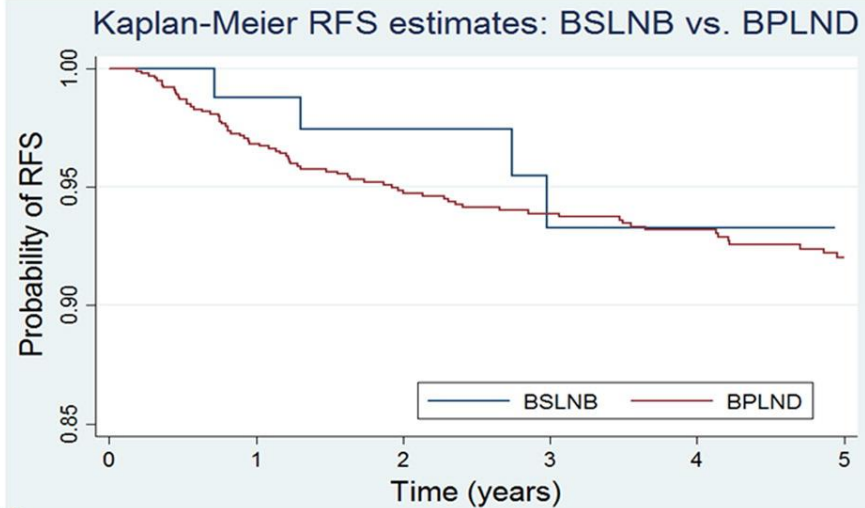
Gynecologic Oncology xxx (2016) xxx-xxx

^a Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Toronto, M700-610 University Avenue, Toronto, ON M5G 2M9, Canada
^b Division of Gynecologic Oncology, T2051 Odette Cancer Centre, University of Toronto, 2075 Bayview Avenue, Toronto, ON M4N 3M5, Canada



Morbidity in BSLNB versus BPLND groups.

Parameter ^a	BSLNB	BPLND	p value
	N (%)	N (%)	
Intra-operative complications	5 (4.6)	66 (6.1)	0.67
Intra-operative blood loss (mL)	100 (0–300)	500 (30–5500)	<0.001
Surgical time (hours)	2.0 (0.8–3.5)	2.8 (1–9)	<0.001
Blood transfusion	0 (0)	246 (23.1)	<0.001
Length of stay (days)	0 (0–1)	6 (0–65)	<0.001
Time to normal residual urine (days)	5 (0–12)	6 (0–120)	0.13
Short-term morbidity	5 (4.6)	55 (5.1)	1.0
Post-operative infection (%)	0 (0)	115 (10.7)	<0.001



No. at risk	0	1	2	3	4	5
BSLNB	110	78	64	43	34	9
BPLND	1078	917	813	715	612	485

Conclusion

A negative BSLNB is not associated with a difference in RFS compared to a negative BPLND.

experience of Cerrahpaşa Gynecologic Oncology Department

Istanbul University-Cerrahpaşa

No FNR in Pet-CT negative group

The Combination of Preoperative Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography and Sentinel Lymph Node Mapping in the Surgical Management of Endometrioid Endometrial Cancer

Tugan Bese, MD, Veysel Sal, MD,* Fuat Demirkiran, MD,* Ilker Kahramanoglu, MD,*
Nedim Tokgozoglu, MD,* Sennur Ilvan, MD,† Ovgu Aydin, MD,† Metin Hallac, MD,‡
Betul Vatankulu, MD,‡ Gokhan Demirayak, MD,§ Hasan Turan, MD,* and Macit Arvas, MD*
(Am J Clin Oncol 2016;39:516–521)*

Cervical Cancer unpublished Data

47 pts mapped with LA(I) and 21 without LA(II)
Bilateral DR 69%(I) 8((17%) + nodes , all sentinel nodes(I)
3 recurrences (11- 52 months), all out side retroperitoneal
area

We suggest....

SLNM can be implemented to management of early st. CC

Cervical Cancer, Version 2.2015

Featured Updates to the NCCN Guidelines

PRINCIPLES OF EVALUATION AND SURGICAL STAGING†

Sentinel Lymph Node Mapping for Cervical Cancer:

- SLN mapping as part of the surgical management of select stage I cervical cancer is considered in gynecologic oncology practices worldwide. While this technique has been used in tumors up to 4 cm in size, the best detection rates and mapping results are in tumors less than 2 cm.⁹⁻¹² This simple technique utilizes a direct cervical injection with dye or radiocolloid Technetium-99 (99Tc) into the cervix, usually at 2 or 4 points as shown in Figure 1 (below). The SLNs are identified at the time of surgery with direct visualization of colored dye, a fluorescent camera if indocyanine green (ICG) was used, or a gamma probe if 99Tc was used. SLNs following a cervical injection are commonly located medial to the external iliac vessels, ventral to the hypogastric vessels, or in the superior part of the obturator space (Figure 2). SLNs usually undergo ultrastaging by pathologists, which allows for higher detection of micrometastasis that may alter postoperative management.^{2,13}

Figure 1: Options of SLN Cervical Injection Sites†

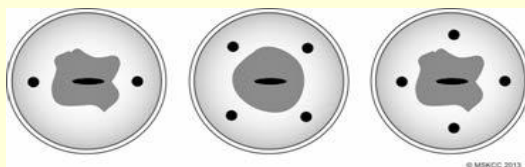
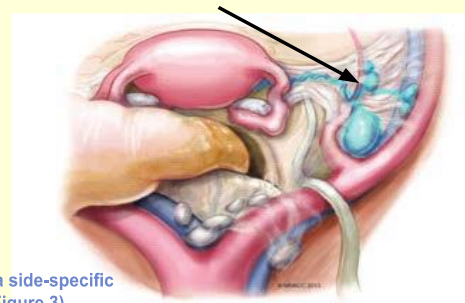


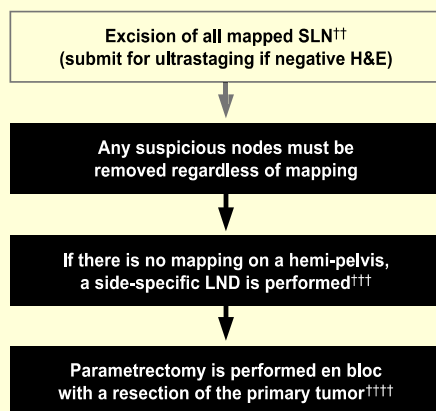
Figure 2: SLNs (blue, arrow) After Cervical Injection Are Commonly Located Medial to the External Iliac, Ventral to the Hypogastric, or in the Superior Part of the Obturator Space†



PRINCIPLES OF EVALUATION AND SURGICAL STAGING WHEN SLN MAPPING IS USED†

The key to a successful SLN mapping (category 2B) is the adherence to the SLN algorithm, which requires the performance of a side-specific nodal dissection in cases of failed mapping and removal of any suspicious or grossly enlarged nodes regardless of mapping (Figure 3)

Figure 3: Surgical/SLN Mapping Algorithm for Early-Stage Cervical Cancer†



SENTICOL III: an international validation study of sentinel node biopsy in early cervical cancer. A GINECO, ENGOT, GCIG and multicenter study

Lecuru FR, et al. *Int J Gynecol Cancer* 2019;

Fabrice P Lecuru,¹ Mary McCormack,² Peter Hillemanns,³ Amelia Anota,⁴ Mario Leitao,⁵

• Squamous or adenocarcinoma of the cervix,
• Stage Ia1 with lymphovascular emboli, Ia2, Ib1 and IIa1,

Patients with bilateral detection without macroscopic suspicious node and negative frozen section on SLN (pNO)

Randomisation
1 : 1

Arm A (experimental) :

hysterectomy or trachelectomy.

Arm B (reference) :

Pelvic Lymphadenectomy + hysterectomy or trachelectomy

DFS, RFS, QOL, OS

Excision of all mapped^a SLN
(submit for ultrastaging if negative H&E)

Any suspicious nodes must be removed regardless of mapping

If there is no mapping on a hemi-pelvis, a side-specific LND^b is performed

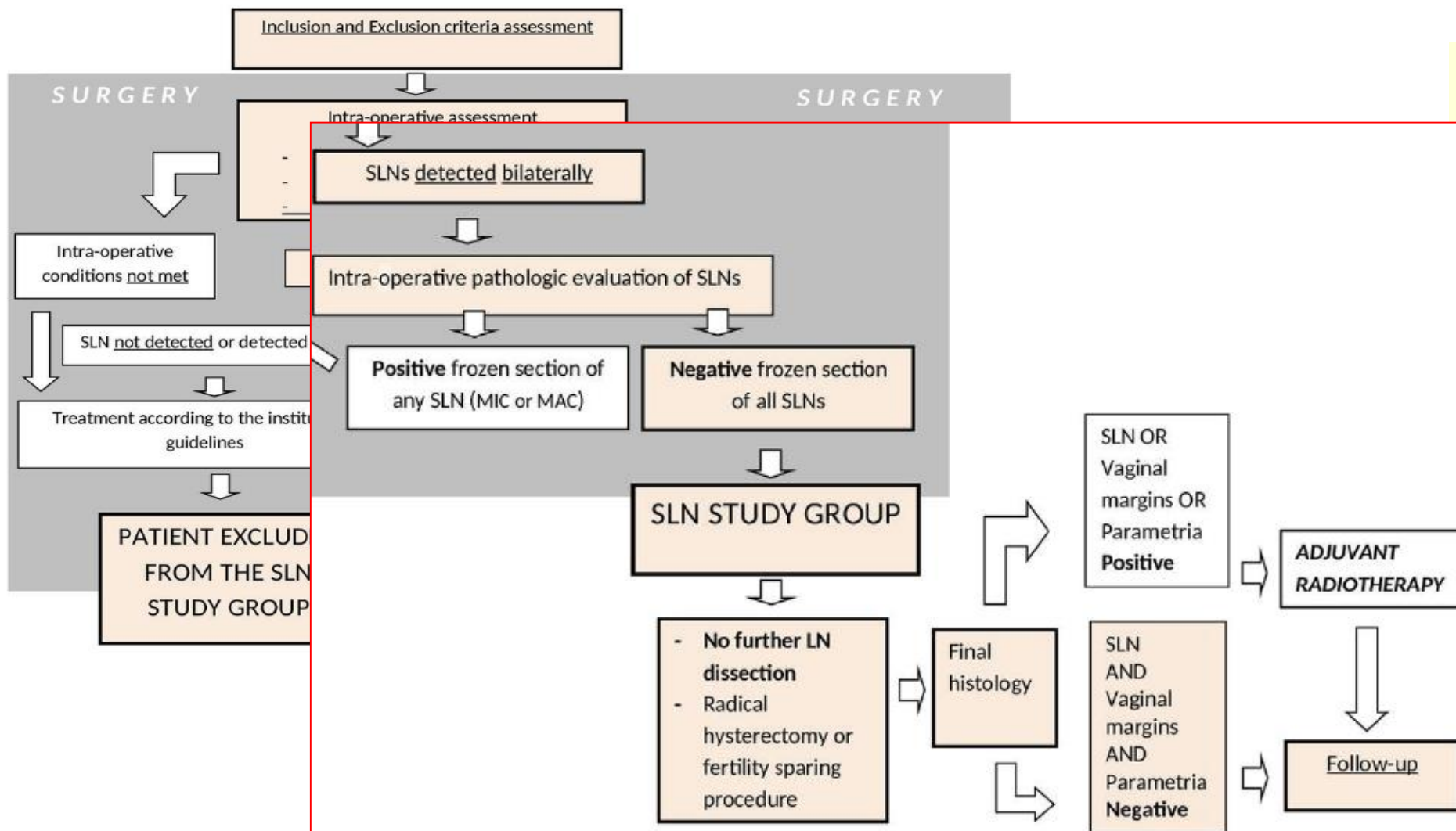
Parametrectomy is performed en bloc with a resection of the primary tumor^c

Followed in a separate cohort to record treatment and outcomes

It was approved by the ethics committee and competent authority in France in late 2017

A prospective multicenter trial on sentinel lymph node biopsy in patients with early-stage cervical cancer (SENTIX)

Cibula D. et al. *Int J Gynecol Cancer* 2019;29:212–215.



Summary

SLN Algorithm is a standard of care in many practices.

It is a reasonable strategy for Stage IA1 with LVSI, IA2, and IB1,B2 cervical cancer.

Every gynecologic oncology clinic must begin to consider it.

Thank you

In this context, the results by Cormier et al., who reported a single-side SLN failure rate of approximately 15% of cases, led to inclusion in the National Comprehensive Cancer Network (NCCN) guidelines of the recommendation to perform contralateral sidespecific LND in cases of unilateral SLN mapping.

Preliminary data from the SENTICOL -2 randomized study (NCT01639820, www.clinicaltrials.gov) showed a 20% reduction in early lymphovascular morbidity, and 13% reduction in early neurological complications in patients undergoing SLN procedure only versus SLN plus pelvic LND.