



Is Sentinel Lymph Node Biopsy Alone an Insufficient Treatment in High-Risk Endometrial Cancer ?

Dr. İlker Kahramanoğlu
SBÜ Diyarbakır Gazi Yaşargil EAH
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1980s

SLN Mapping

Breast Cancer





1960s 1990s

28.11.2019



Vulvar Cancer



Melanoma



A composite background image featuring a space station in orbit, an astronaut working outside, and a large white '2010s' text overlay.

2010s

28.11.2019

A vertical timeline consisting of a dark blue line with three white circles and a starburst symbol at the bottom.

Cervical Cancer

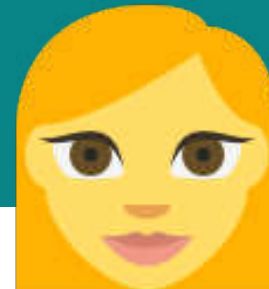
Low risk EC

High risk EC

1A

1B

2



3A

3B

3C

4A

4B





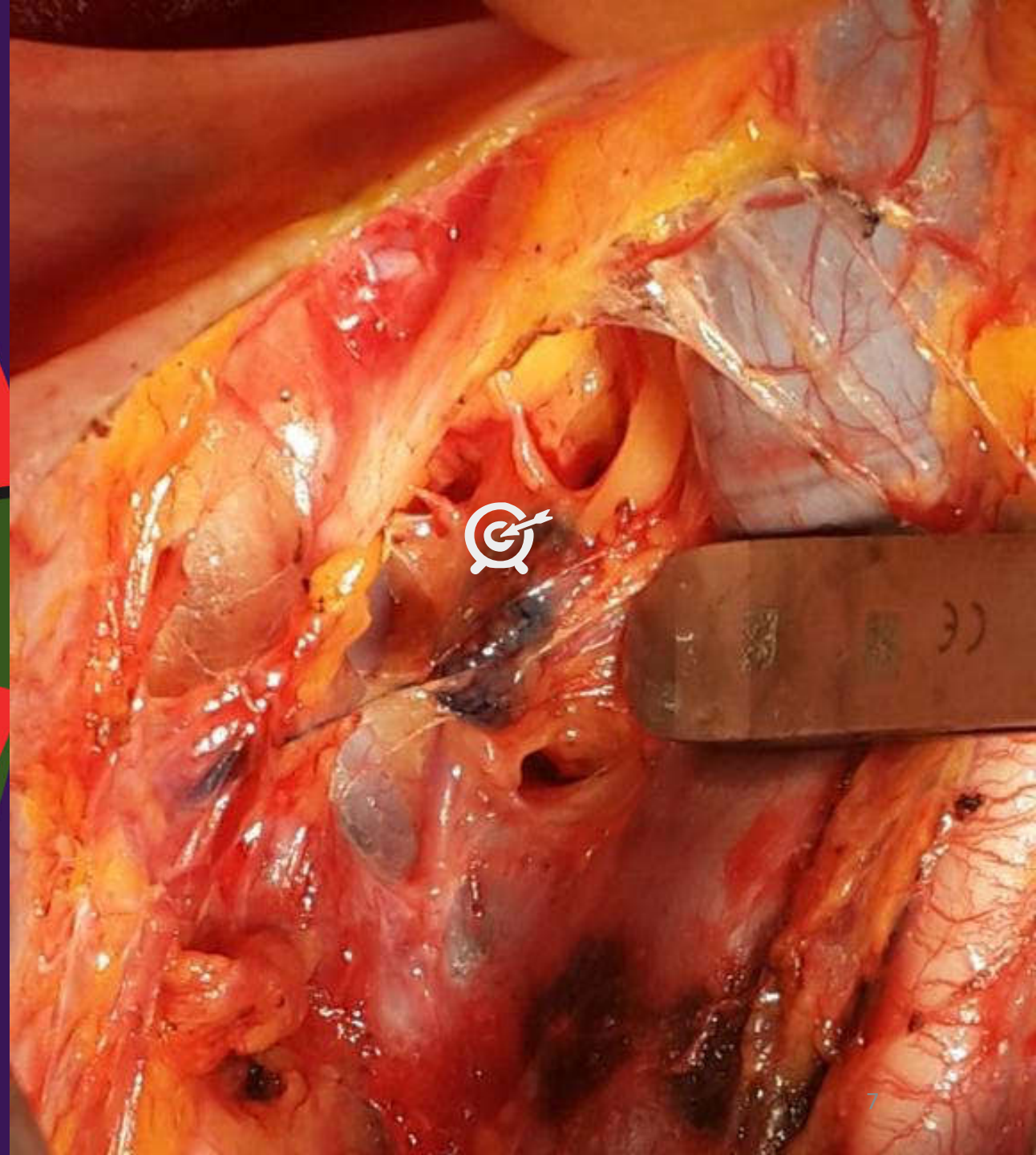
Benedetti Panici et al. 2008

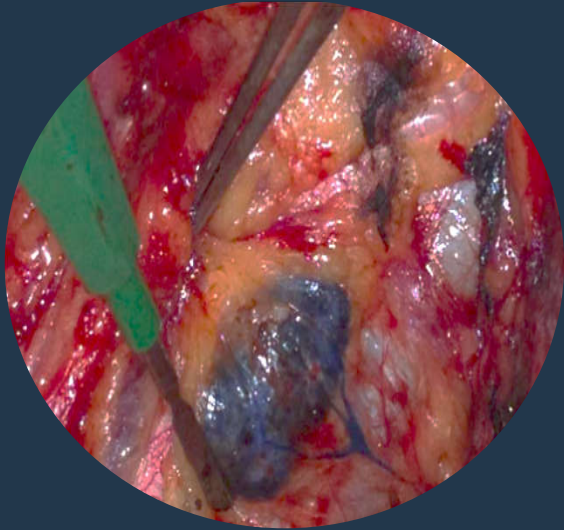


ASTEC 2009



28.11.2019



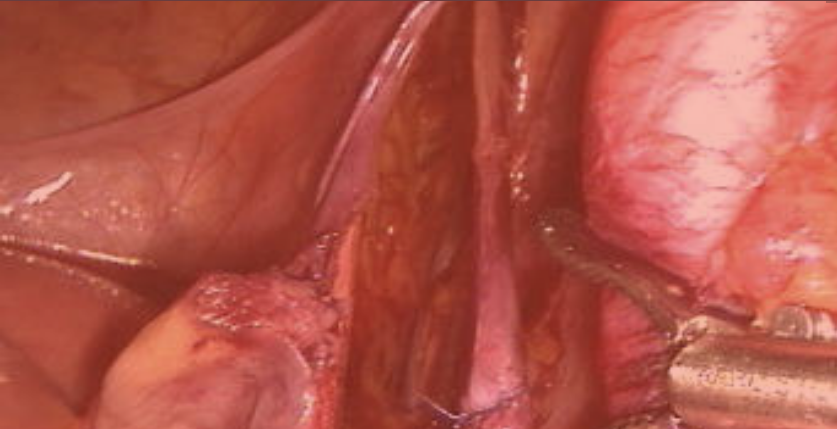
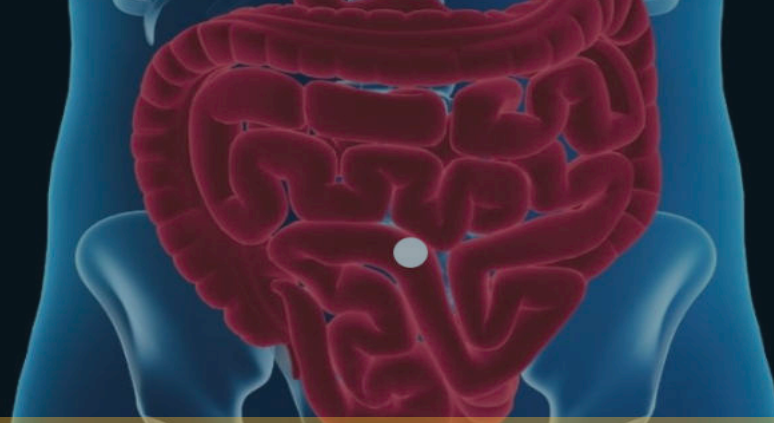


Is it good enough ?

If SLN can replace...

All needed





Why **SLND** over PPLND ?

Morbidity



Cost





28.11.2019



GOG-244 (The LeG Study) Abstract

Carlson J et al.

Leg volume change

N= 734 with EC

>10%

34%

>15%

19%

>20%

11%

Paraaortic Lymphadenectomy



x 2

30-days morbidity

SLN Mapping in Low Risk EC



National
Comprehensive
Cancer
Network®

NCCN Clinical Practice Guidelines in Oncology

NCCN Guidelines™



Society of Gynecologic Oncology

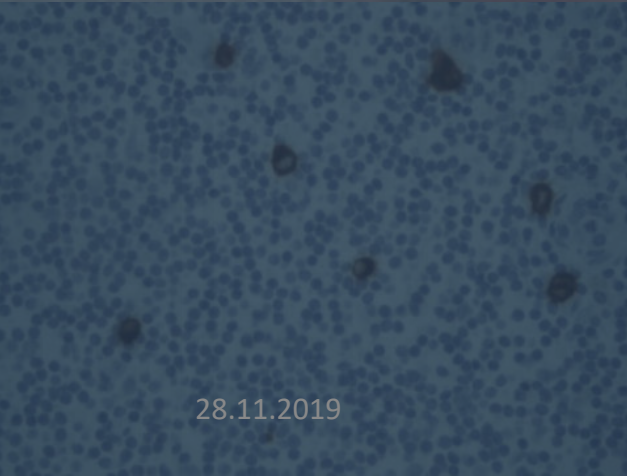




Why **SLND** over PPLND ?

Detection





Micrometastasis
Stage IIIC1



Stage IA
?

Preoperative Risk Stratification

Low Risk

Endometrioid
IA, G 1-2

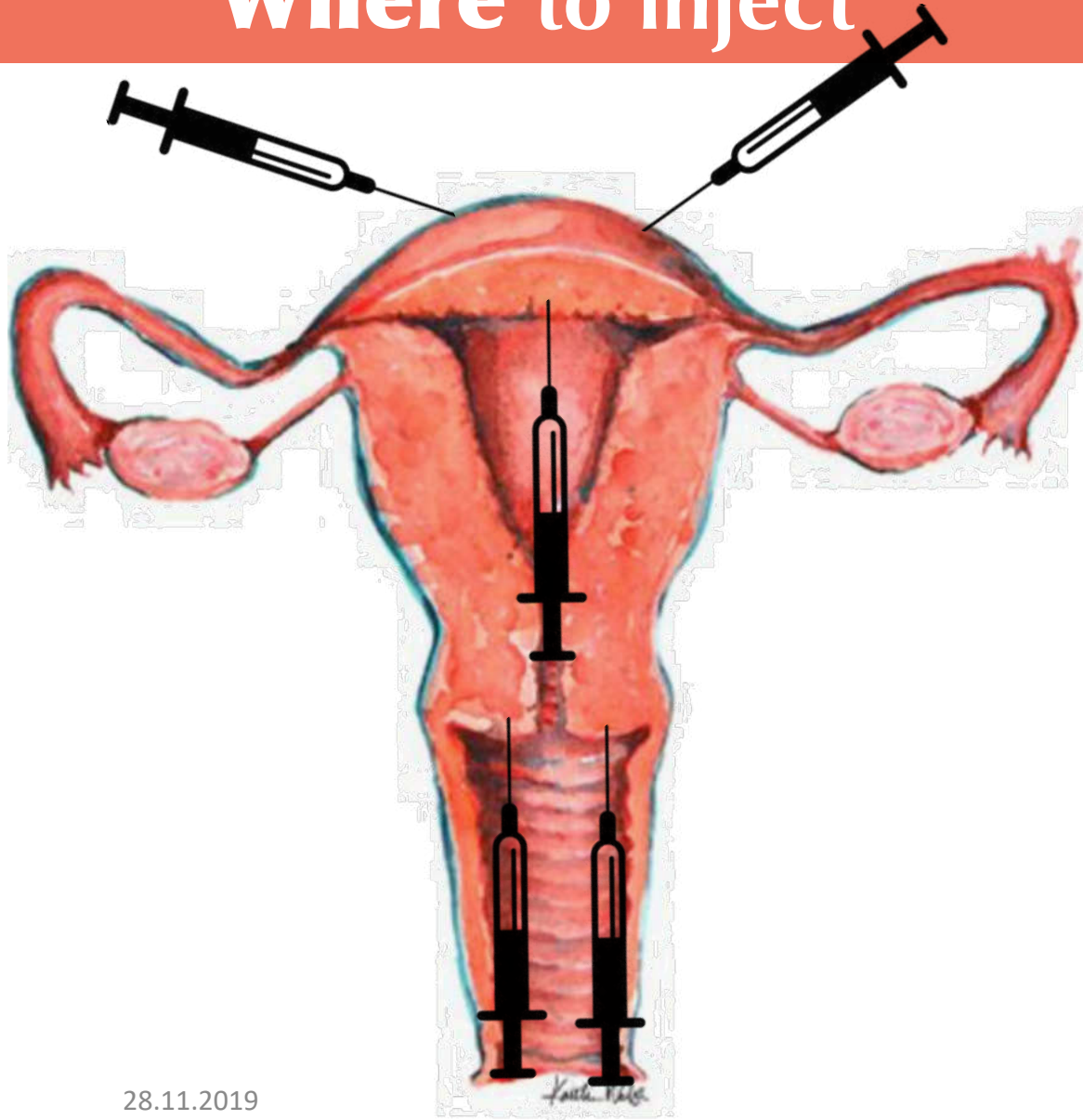
Intermediate

Endometrioid
IA, G3
IB, G2

High Risk

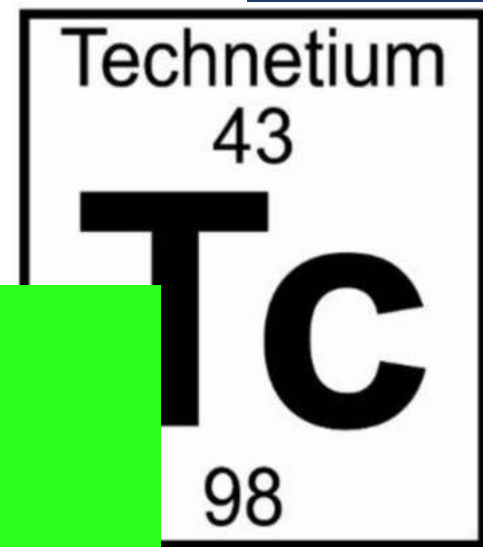
Endometrioid IB, G3
Non-endometrioid
Stage 2 or more
Large tumor

Where to inject



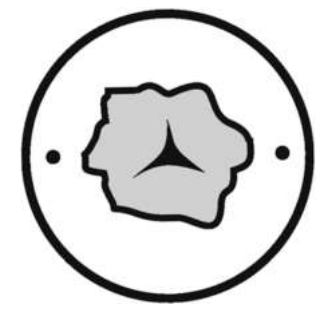
28.11.2019

What to inject



16

Finding SLNs



Near-infrared fluorescence for detection of sentinel lymph nodes in women with cervical and uterine cancers (FILM): a randomised, phase 3, multicentre, non-inferiority trial

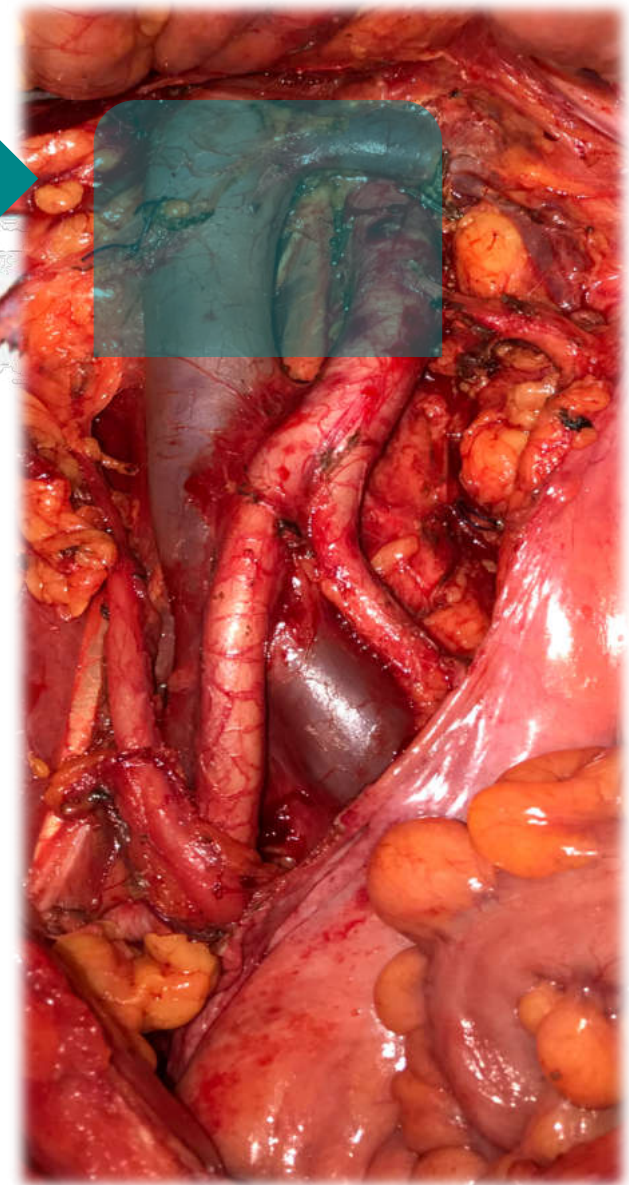
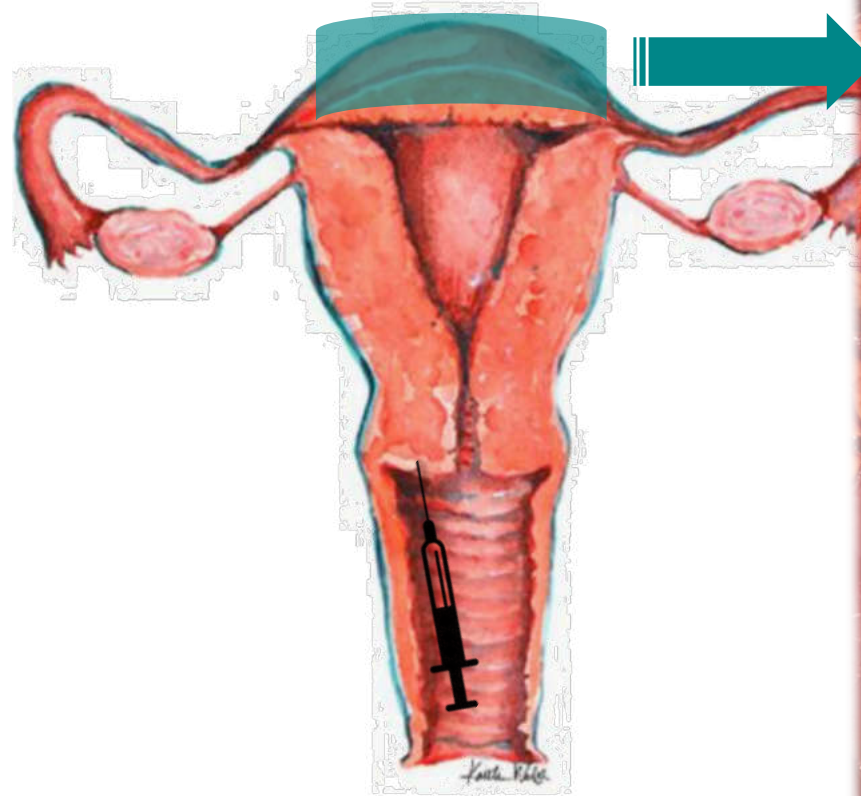
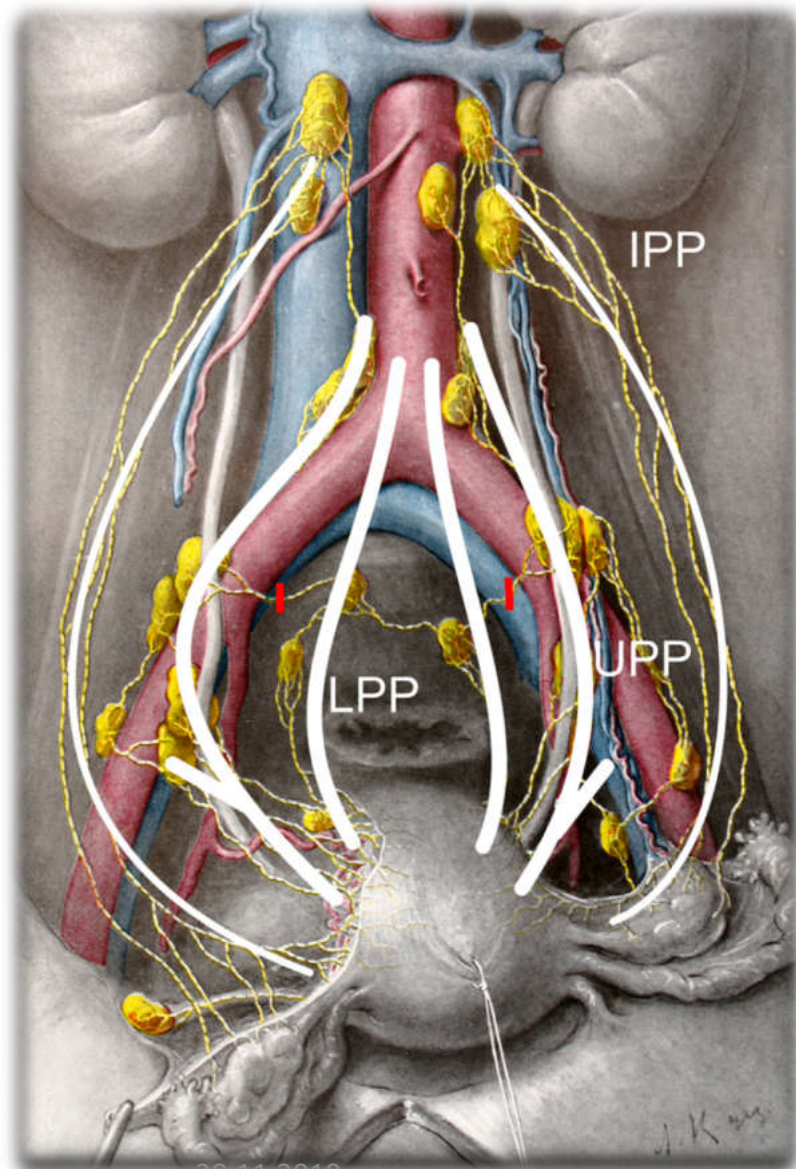
Lancet Oncol 2018;

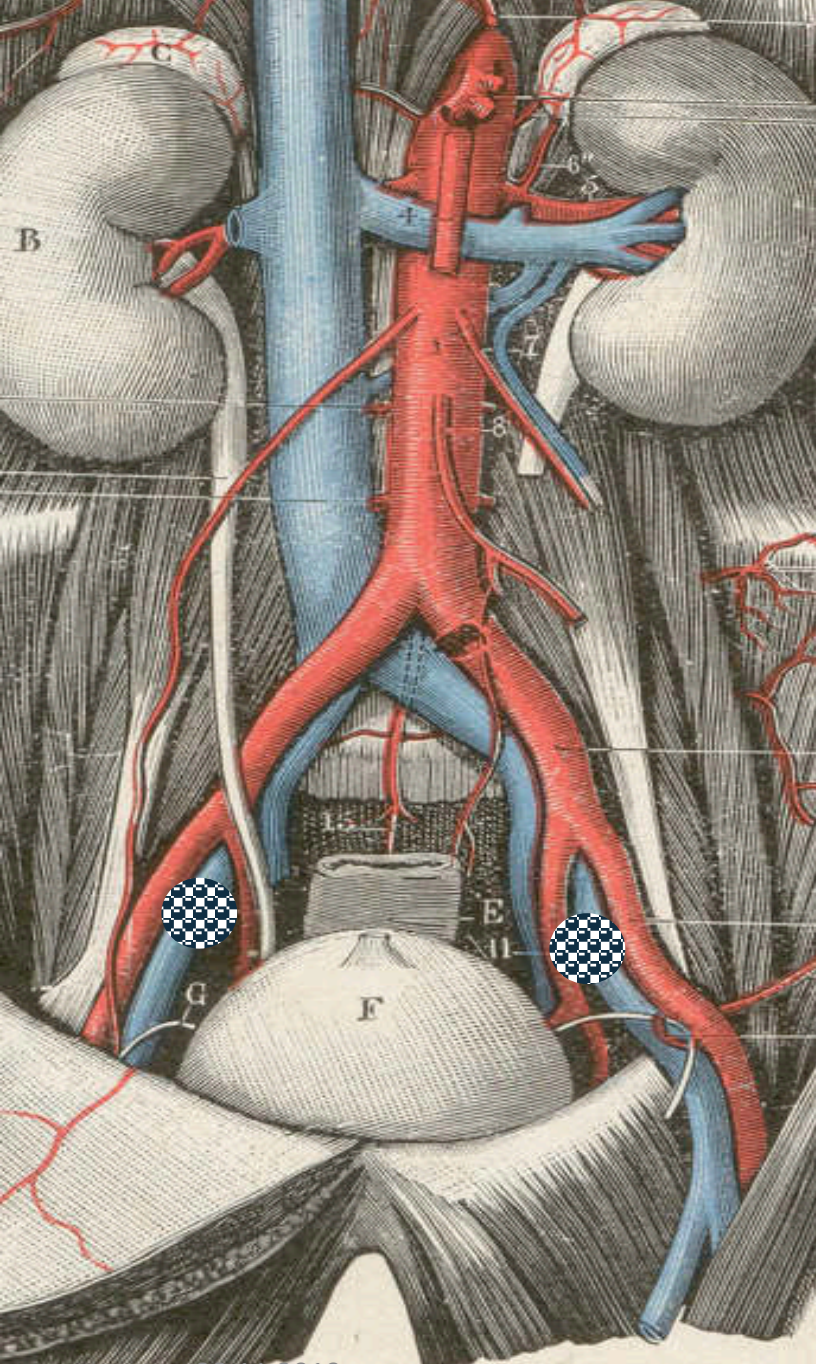
Michael Frumovitz, Marie Plante, Paula S Lee, Samith Sandadi, James F Lilja, Pedro F Escobar, Lilian T Gien, Diana L Urbauer, Nadeem R Abu-Rustum

	Blue	Green	<i>p</i>
>1 SLN	75 %	95 %	<0.001
Bilateral SLNs	31 %	84 %	<0.001

Funding Novadaq

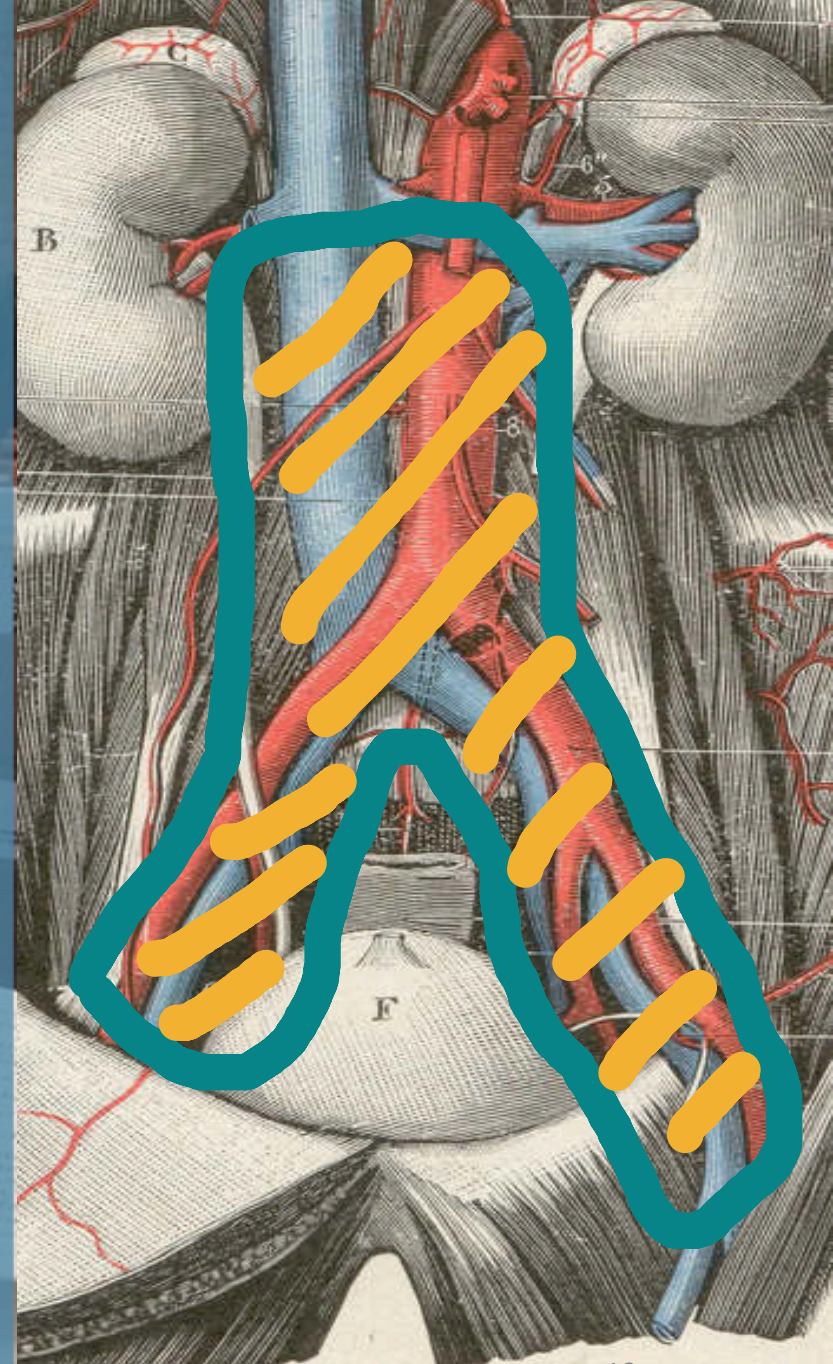
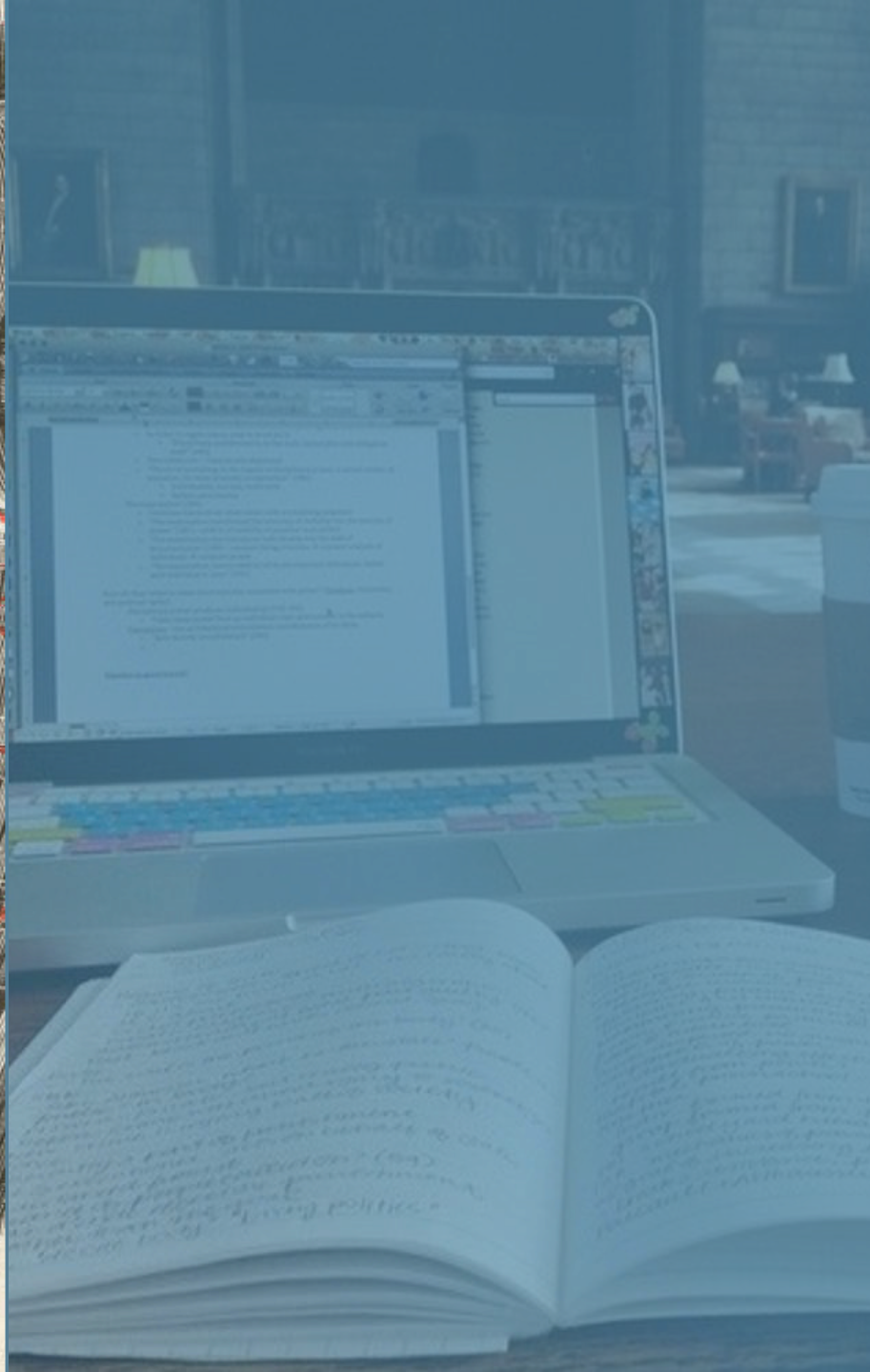
The Most Important Concern





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HISTOIRE NATURELLE (6^e Éd.)



19

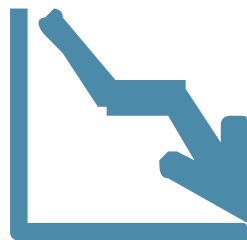
HISTOIRE NATURELLE (6^e Éd.)

False Positive SLN

10%



Poster 202
N=202 women with EC
Harold JA et al.



Click on image to zoom

#

36 cases
SLN detection: 91.6%
Bilateral detection: 55.5%

Prospective assessment of lymphatic dissemination in endometrial cancer: A paradigm shift in surgical staging

Andrea Mariani, Sean C. Dowdy, William A. Cliby, Bobbie S. Gostout, Monica B. Jones, Timothy O. Wilson, and Karl C. Podratz*

Division of Gynecologic Surgery, Mayo Clinic, Rochester, Minnesota, USA



2267/8 %

n=281 with 'risky' EEC

Isolated Paraaortic Metastasis

Kumar, 2013	Hirateke, 1997	Matsumoto, 2002
Dogan, 2012	22/851 3 %	Fotopoulou, 2010
	Turan, 2011	

Endometrioid		Non-endometrioid	
MI > 50 %		MI<50%	MI>50%
G 2	4/32 12.5%	1/26 4%	0/14
G 3	3/11 27%		

Paraaortic SLN mapping

Cervical injection + *Fundal injection*



0 - 2,8 %

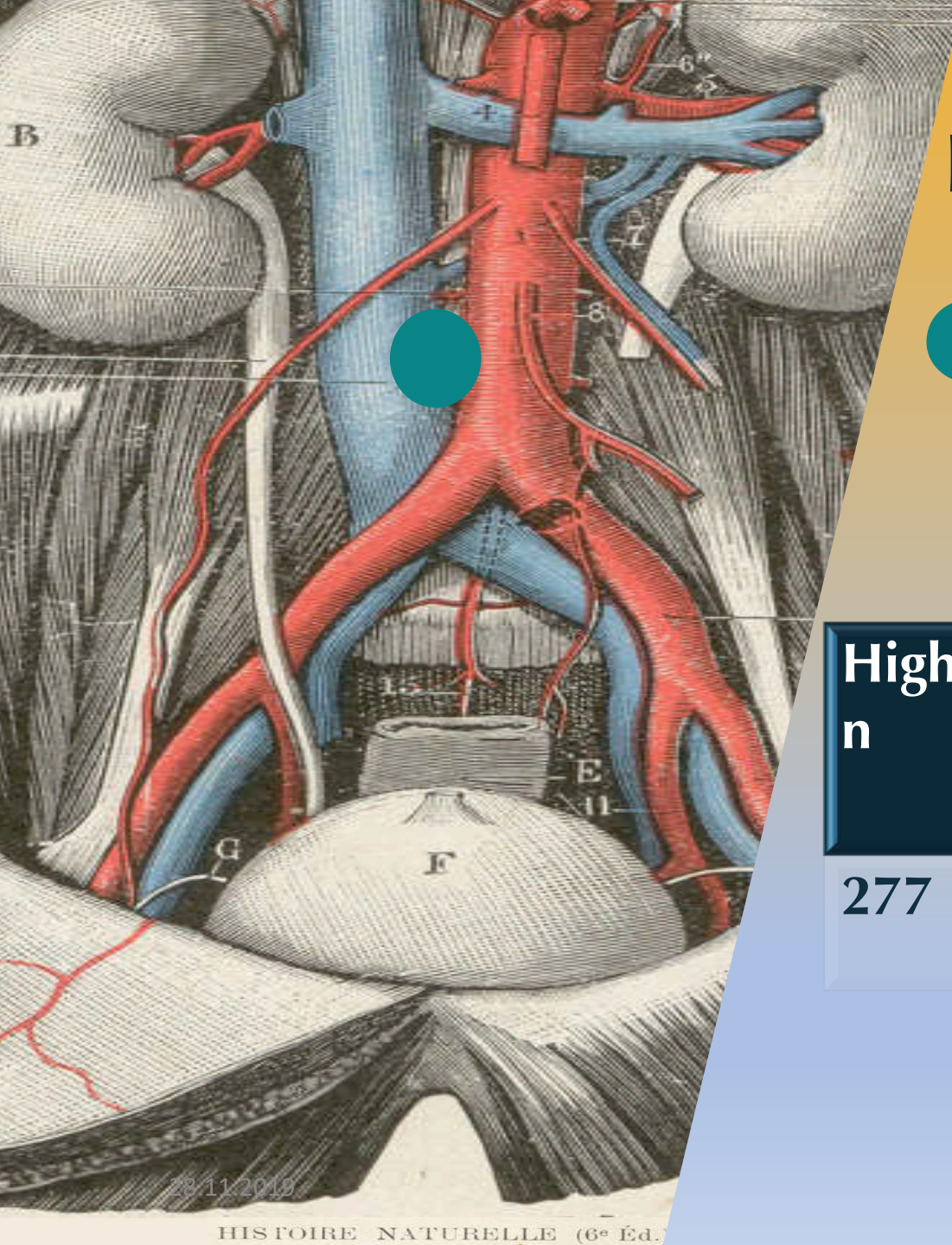
55 %

0,9 %

Holloway et al. Gynecol Oncol 2016
Rossi EC et al. FIRES trial. Lancet Oncol 2017
Soliman et al. Gynecol Oncol 2017

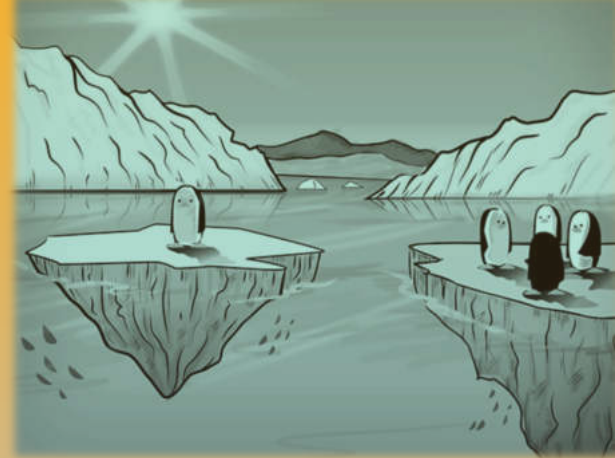
Togami et al. IJGO 2018

Personal experience²⁴



Is it really isolated ?

? *What if ultrastaging would be performed*



**High grade,
n**

277

**Non-
endometrioid,
n**

169

**Positive
node**

27 %

**Isolated PA
positive
node**

0

Holloway et al. Gynecol Oncol 2016
Rossi EC et al. FIRES trial. Lancet Oncol 2017
Soliman et al. Gynecol Oncol 2017
Baiocchi et al. Ann Surg Oncol 2017

2012

28.11.2019

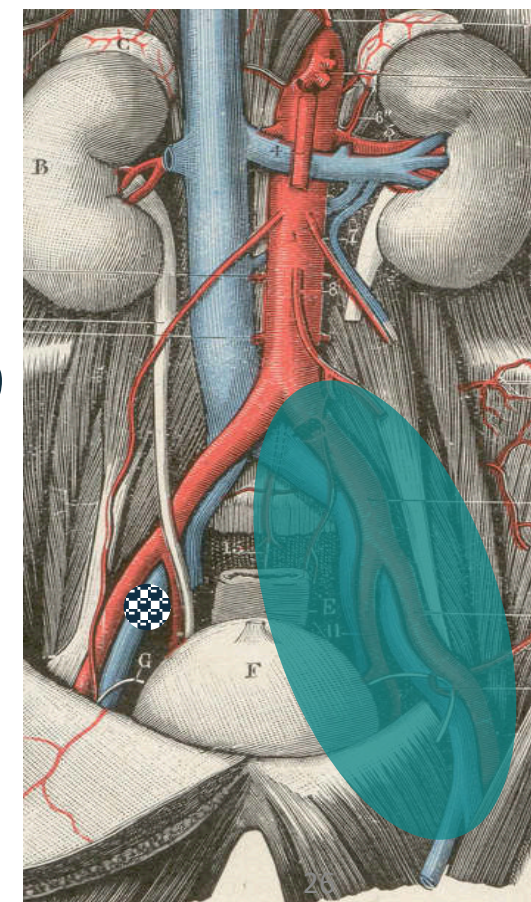


SLN Algorithm

Including high risk cases



- Sensitivity **98%**
- False negative %**1.9**



Barlin et al. Gynecol Oncol 2012



MIS in EC

2008

2009

2010

**Operative
time,
minutes**

Operative time, minutes

**Median
nodal count**

Median nodal count

**Detection of
stage III**

Detection of stage III

Validation Studies of the MSKCC Algorithm

Vidal F et al. IJGC 2013

Sadeghi R. Gynecol Oncol 2014

Eitan R et al. EJSO 2015

Eriksson AG et al. Gynecol Oncol 2016

Hagen B et al. Gynecol Oncol 2016

Tschernichovsky R et al. AJCO 2016

Ducie J et al. Gynecol Oncol 2017

Rossi E et al. Lancet Oncol 2017

Geppert B et al. Gynecol Oncol 2017

Holloway R et al. Gynecol Oncol 2017

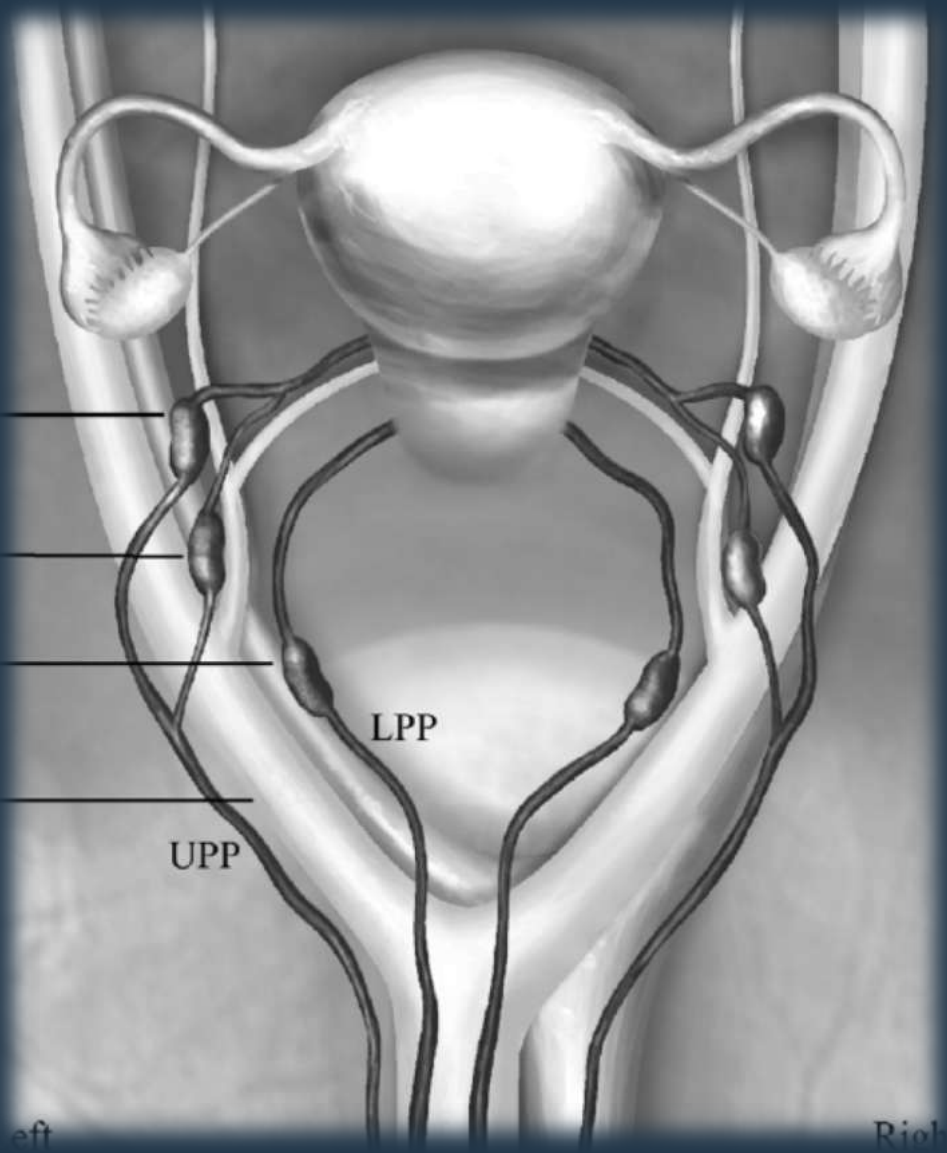
How J et al. Gynecol Oncol 2017

Liu C et al. Gynecol Oncol 2017

Soliman P et al. Gynecol Oncol 2017

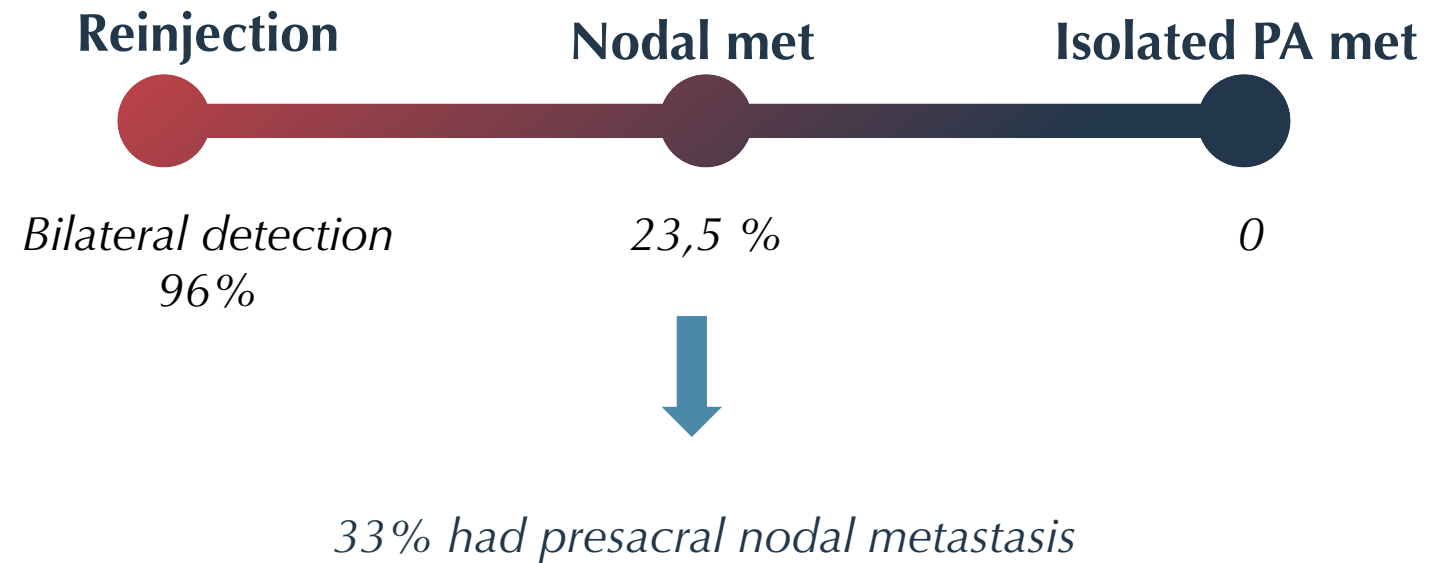
Buda A et al. Gynecol Oncol 2018

Papadia A et al. J Cancer Res Clin Oncol 2018



Anatomically Based Algorithm

High risk cases
n= 102



ORIGINAL ARTICLE – GYNECOLOGIC ONCOLOGY

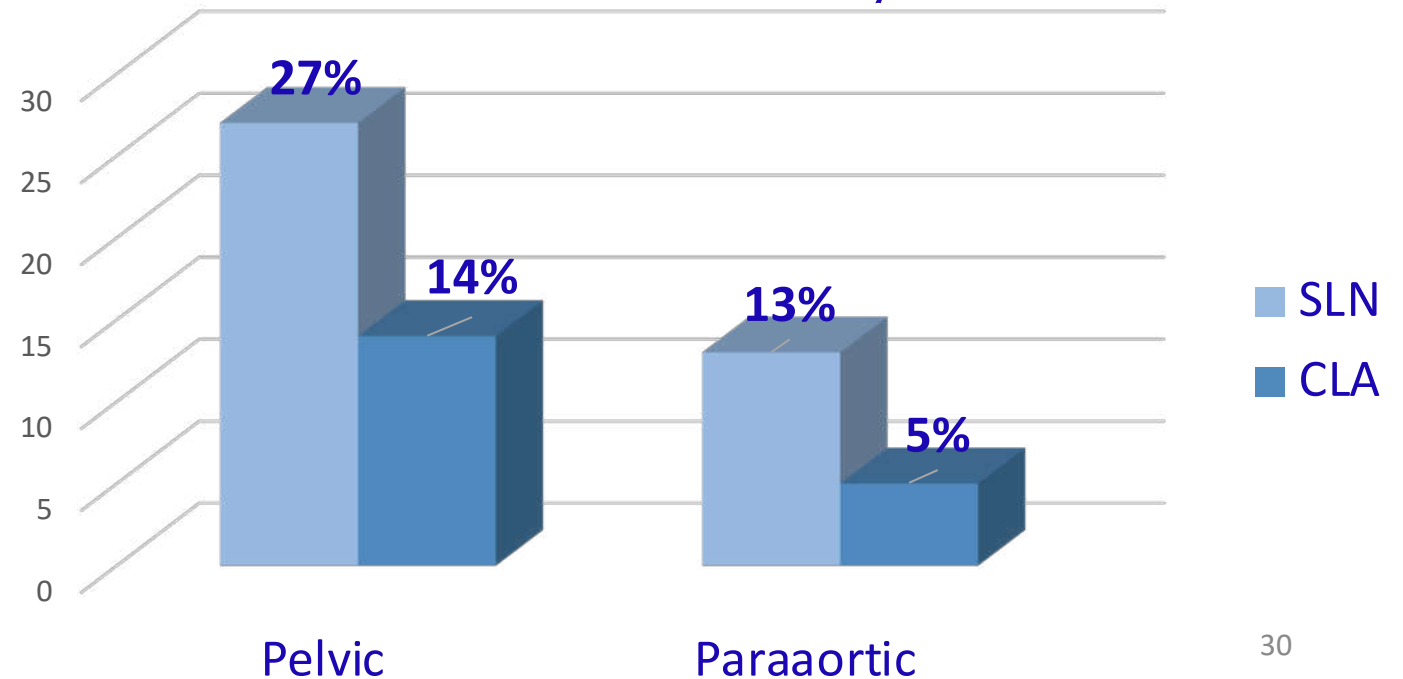
The Impact of Sentinel Node-Mapping in Staging High-Risk Endometrial Cancer

Glauco Baiocchi, MD, PhD¹ , Henrique Mantoan, MD¹, Lillian Yuri Kumagai, MD¹, Bruna Tirapelli Gonçalves, RN, MSc¹, Levon Badiglian-Filho, MD, PhD¹, Ademir Narciso de Oliveira Menezes, MD¹, Carlos Chaves Faloppa, MD¹, Louise De Brot, MD, PhD², and Alexandre Andre Balieiro Anastacio da Costa, MD, PhD³

- LVSI
- MI>50%
- Serous, clear cell, cs
- Endometrioid grade 3

SLN+CLA
(n=75)
VS
CLA only
(n=161)

Nodal Positivity





Survival

28.11.2019

European Journal of Surgical Oncology 44 (2018) 1562–1567

Contents lists available at ScienceDirect

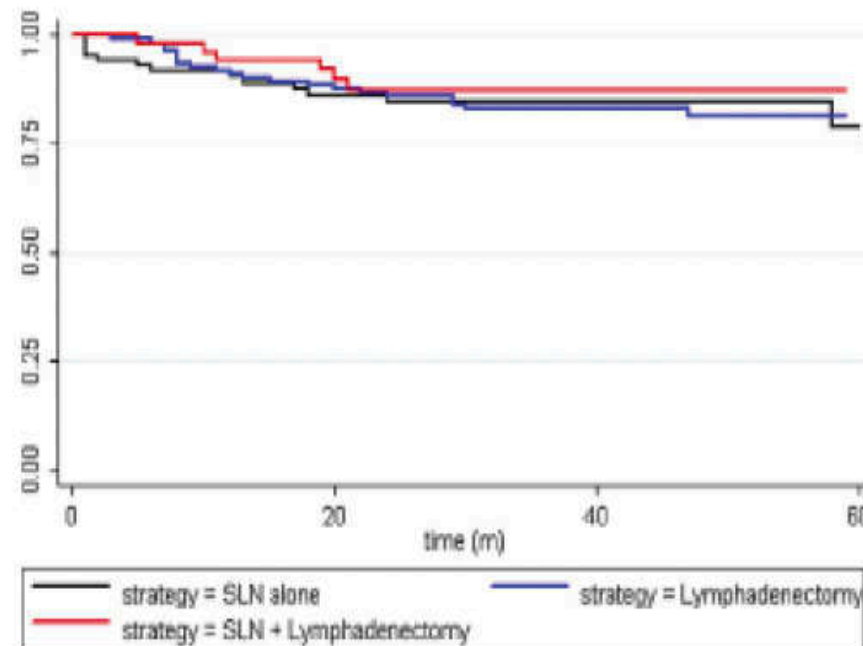
European Journal of Surgical Oncology

journal homepage: www.ejso.com

The impact of the type of nodal assessment on prognosis in patients with high-intermediate and high-risk ESMO/ESGO/ESTRO group endometrial cancer. A multicenter Italian study

Alessandro Buda ^{a,*}, Stefano Restaino ^b, Giampaolo Di Martino ^a, Elena De Ponti ^c, Giorgia Monterossi ^d, Giorgia Dinoi ^d, Sonia Magni ^a, Lorena Quagliozzi ^d, Federica Dell'Orto ^a, Francesca Ciccarone ^d, Maria Lamanna ^a, Giovanni Scambia ^d, Fabio Landoni ^a, Francesco Fanfani ^e

Check for updates



n= 200
3-year DFS: 84 %

Similar



**Complete LND
(Mayo)
VS
SLND
(MSKCC)**

Intermediate risk (Any grade, MI $\geq$ 50 %)

	Mayo	MSKCC	P
N	107	82	
Nodal (+), %	28	29	0,21
PA nodal (+), %	20,8	10,7	0,23

High risk (Serous or clear cell)

	Mayo	MSKCC	P
N	103	120	
Nodal (+), %	19,4	21,7	0.68
PA nodal (+), %	15,9	17,9	0.76

SLN in Deeply Invasive EEC



2004

2008

2013

Mayo- LND n= 94

MSKCC- SLN Algorithm n= 82



33 %

(+) Pelvic Node

14%

3.7 %

(+) PA Node

15 %

75 %

3-year PFS

81 %

92 %

3-year OS

83 %

Retrospective series – High-risk cases

	No.	High-risk	Tracer	False neg.	Sensitivity
Naoura, 2015	34	ESMO	Blue+Tc99	20%	-
Ehrisman, 2016	36	G3, or type 2	Blue ICG	7.7%	92.3%
Touhami, 2017	128	G3, or type 2	Any	5%	95%
Papadia, 2018	42	G3, or type 2	ICG	10%	90%



*Add-on completion
lymphadenectomy*

SGO Consensus 2017

*SLN algorithm
for high-grade*

*Completion of
paraaortic dissection*

*ICG is
preferable*

Detection rate and diagnostic accuracy of sentinel-node biopsy in early stage endometrial cancer: a prospective multicentre study (SENTI-ENDO)

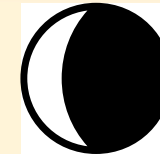
Lancet Oncol 2011; 12: 469-76

Marcos Ballester, Gil Dubernard, Fabrice Lécuru, Denis Heitz, Patrice Mathevet, Henri Marret, Denis Querleu, François Golfier, Eric Leblanc, Roman Rouzier, Emile Daraï

30%
High risk

All FN cases were in the high risk group

97% sensitivity 99.6% NPV



30%
G3 or type 2

A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES trial): a multicentre, prospective, cohort study

Emma C Rossi, Lynn D Kowalski, Jennifer Scalici, Leigh Cantrell, Kevin Schuler, Rabbie K Hanna, Michael Method, Melissa Ade, Anastasia Ivanova, John F Boggess

Lancet Oncol 2017; 18: 384-92



ELSEVIER

Contents lists available at ScienceDirect

Gynecologic Oncology

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

CrossMark

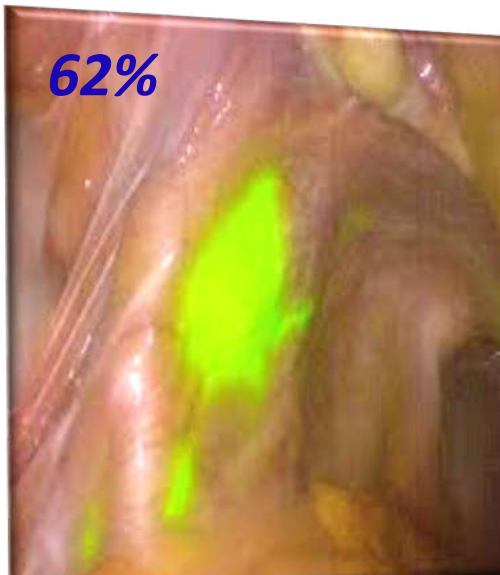
A prospective validation study of sentinel lymph node mapping for high-risk endometrial cancer☆

Pamela T. Soliman ^{a,*}, Shannon N. Westin ^a, Shayan Dioun ^a, Charlotte C. Sun ^a, Elizabeth Euscher ^b, Mark F. Munsell ^c, Nicole D. Fleming ^a, Charles Levenback ^a, Michael Frumovitz ^a, Pedro T. Ramirez ^a, Karen H. Lu ^a

- MI>50%
- Serous, clear cell, cs
- Endometrioid grade 3
- Cervical involvement

N=100

62%

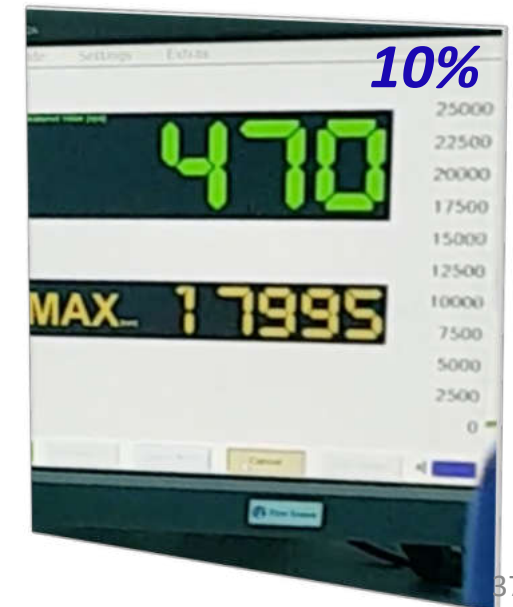


28.11.2019

28%



10%



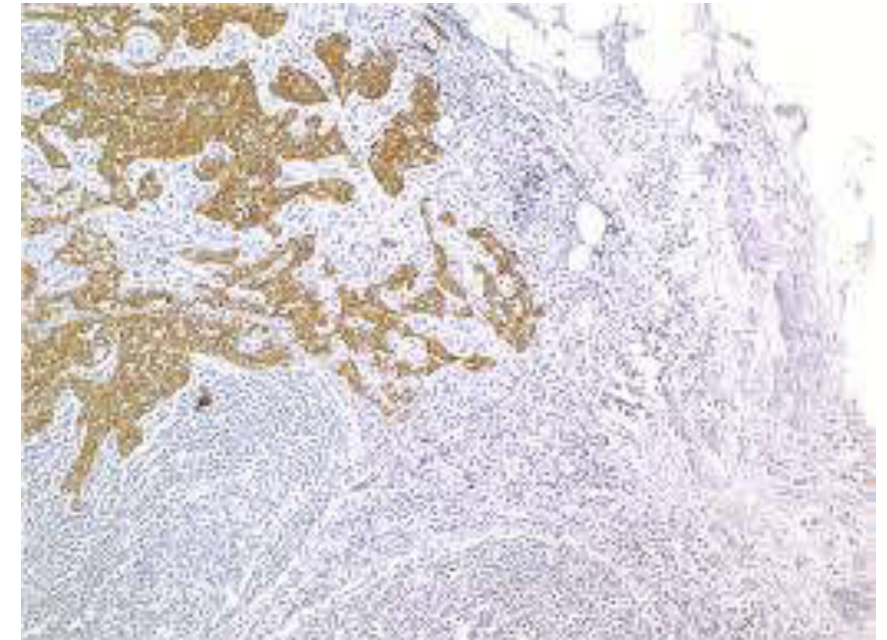
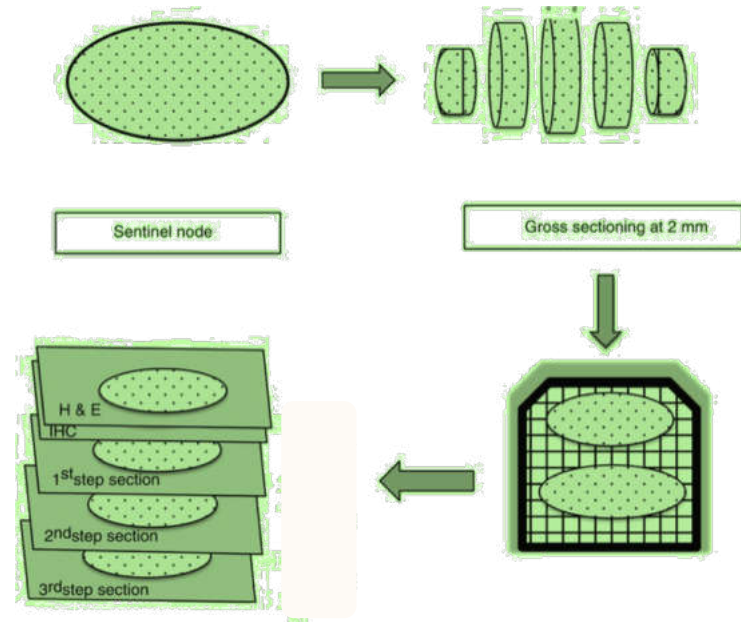
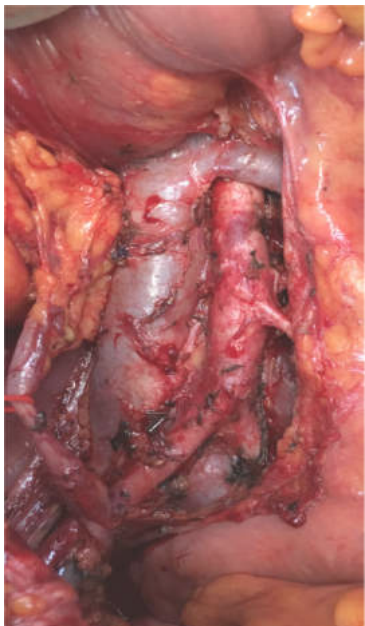
37



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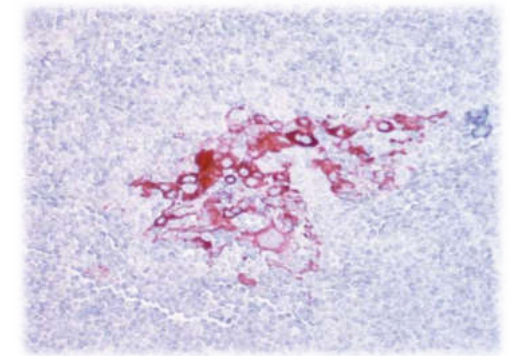
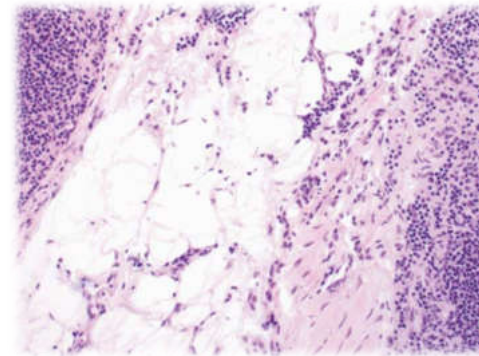
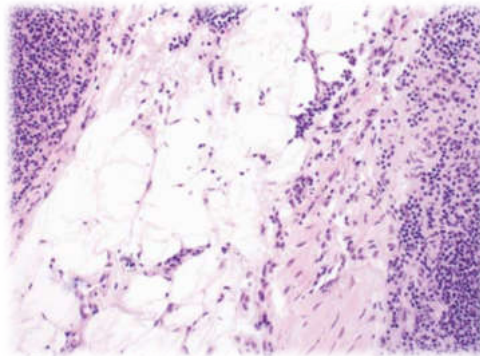
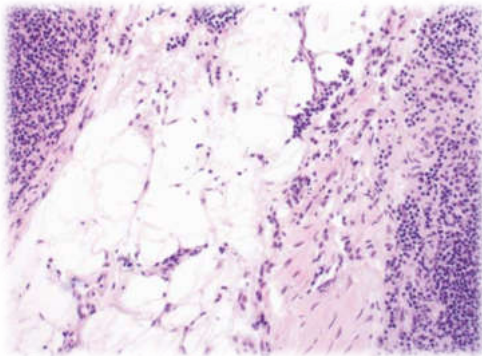
Gynecologic Oncology

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

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95% Sensitivity

98% NPV



- MI>50%
- Serous, clear cell, cs
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- Cervical involvement

5% FNR → *SLN ALONE*

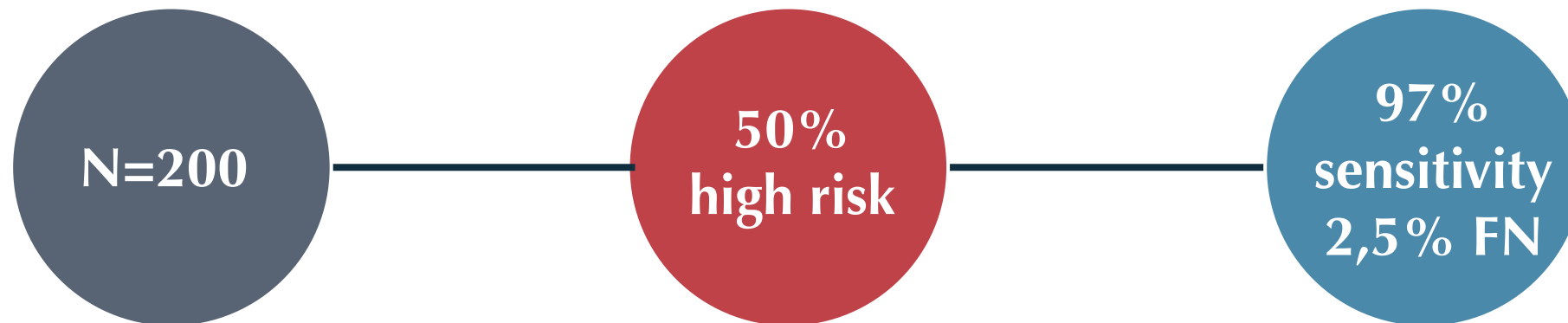
1.4% FNPV

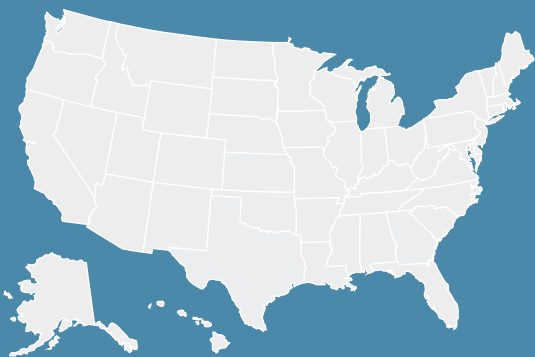


ORIGINAL ARTICLE – GYNECOLOGIC ONCOLOGY

A Prospective Cohort Study Comparing Colorimetric and Fluorescent Imaging for Sentinel Lymph Node Mapping in Endometrial Cancer

Robert W. Holloway, MD, Sarfraz Ahmad, PhD, James E. Kendrick, MD, Glenn E. Bigsby, DO, Lorna A. Brudie, DO, Giselle B. Ghurani, MD, Nicole M. Stavitzski, BS, Jasmine L. Gise, BS, Susan B. Ingersoll, PhD, and Julie W. Pepe, PhD





NCCN

*Algorithm
Maybe for high risk*

2018



ESGO

Experimental

2017



TRSGO

*By Experienced
Centers*

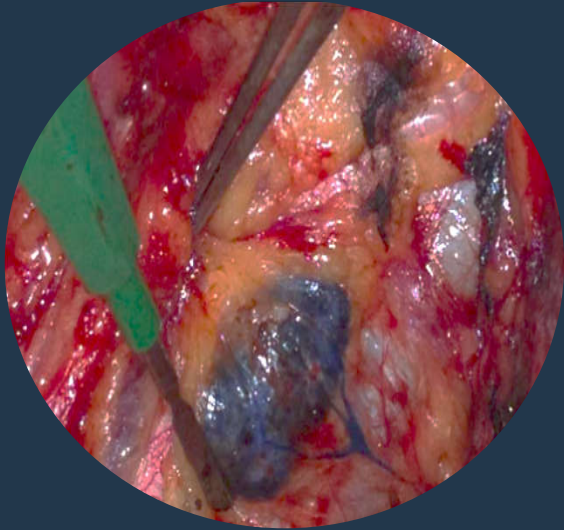
2018



Evidence



...



Is it good enough ?

If SLN can replace...

All needed

Morbidity

Detection

Survival



30 Studies found for: sentinel lymph node | Endometrial Cancer

de, and ENDOMETRIAL CARCINOMA. [See Search Details](#)

5	☐	Recruiting	Sentinel Node Mapping in High Risk Endometrial Cancer	• Endometrial Cancer • Lymph Node Metastases	• Procedure: Sentinel Node Mapping • Procedure: Lymphadenectomy	• AC Camargo Cancer Center Sao Paulo, SP, Brazil
9	☐	Recruiting	Accuracy of Sentinel Lymph Node Biopsy in Nodal Staging of High Risk Endometrial Cancer	• Endometrial Cancer • Sentinel Lymph Node	• Biological: Indocyanine Green (ICG)	• Sunnybrook Health Sciences Center Toronto, Ontario, Canada • University Health Network - Princess Margaret Hospital Toronto, Ontario, Canada
11	☐	Recruiting	Evaluation of Sentinel Node Policy in Early Stage Endometrial Carcinomas at Intermediate and High Risk of Recurrence.	• Endometrial Carcinoma	• Drug: Pre-operative SN mapping with radionuclide • Drug: Intra-operative SN mapping with patent V blue dye • Drug: Intra-operative SN mapping with indocyanin green • (and 2 more...)	• Polyclinique Urbain V Avignon, France • Centre Hospitalier Régional Universitaire Besançon, France • Institut Bergonié Bordeaux, France • (and 16 more...)
21	☐	Not yet recruiting	Evaluation of the Efficacy for Sentinel Lymph Node Policy in High-risk Endometrial Carcinoma	• Endometrial Adenocarcinoma	• Procedure: SLN mapping	
24	☐	Active, not recruiting	PET/CT and Lymph Node Mapping in Finding Lymph Node Metastasis in Patients With High-Risk Endometrial Cancer	• Endometrial Clear Cell Adenocarcinoma • Endometrial Mixed Adenocarcinoma • Endometrial Serous Adenocarcinoma • (and 2 more...)	• Procedure: Computed Tomography • Drug: Indocyanine Green Solution • Other: Laboratory Biomarker Analysis • (and 3 more...)	• Lyndon Baines Johnson General Hospital Houston, Texas, United States • M D Anderson Cancer Center Houston, Texas, United States • The Woman's Hospital o Texas Houston, Texas, United States • (and 4 more...)



Clinicopathological features Age, stage, grade, LVSI	Mol Class 1 <i>POLE</i> mutant (i.e. <i>POLE</i> EDM)	Mol Class 2 MMRd (i.e. MSI)	Mol Class 3 NSMP (i.e. p53 wt)	Mol Class 4 p53 aberrant (i.e. p53 abn, p53-mutant)
Preoperative Low grade High grade	<u>Surgery</u>		Urgency and extent	
Stage I-II Low risk Intermediate risk High risk Stage III-IV	<u>Adjuvant treatment</u>		VBT/ EBT/ chemotherapy/ none	
	<u>Surveillance</u>		3 months/ 6 months/ annual/discharge	
Recurrent disease	<u>Targeted therapy</u>		Checkpoint inhibitors/ small molecules/ PARPi/ hormonal treatment/ mTOR inhibition	



Take Home Messages

1/

SLN mapping
ALGORITHM

2/

Isolated PA
metastasis

3/

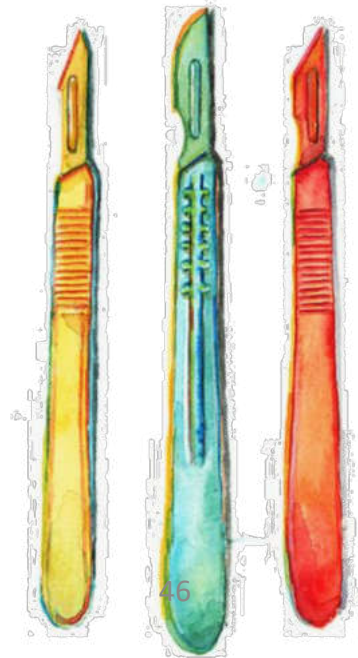
Cervical
injection

4/

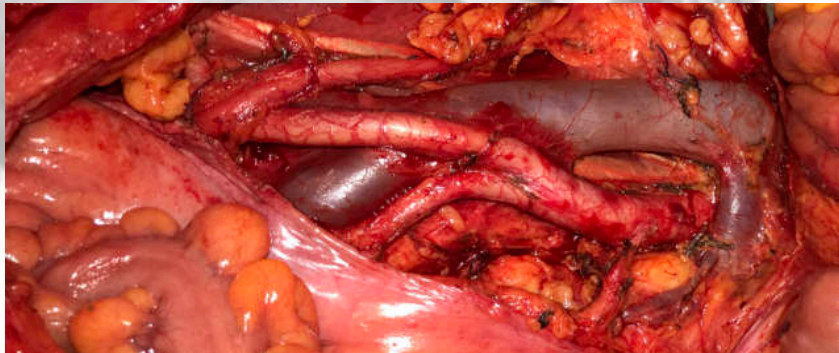
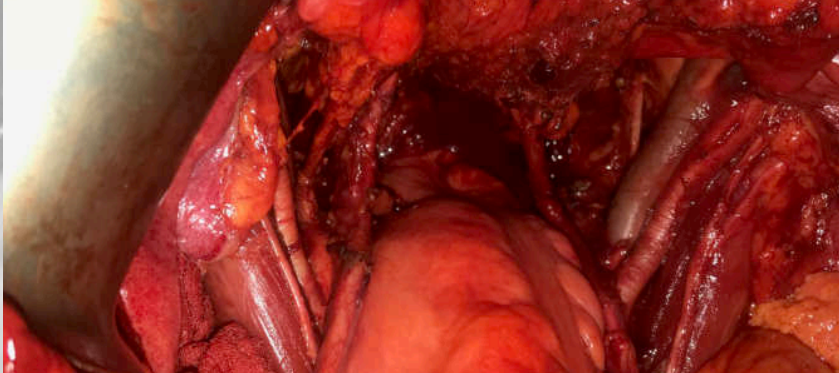
Adjuvant
treatment

5/

TRSGO



Adequacy of LA for Staging



40 negative nodes

QUALITY
~~QUANTITY~~

OR



a (+) node



1ST International
&
XVITH National Gynecologic
Oncology Congress

Thank you

Dr. İlker Kahramanoğlu
ilkerkahramanoglu@gmail.com
00905334746497