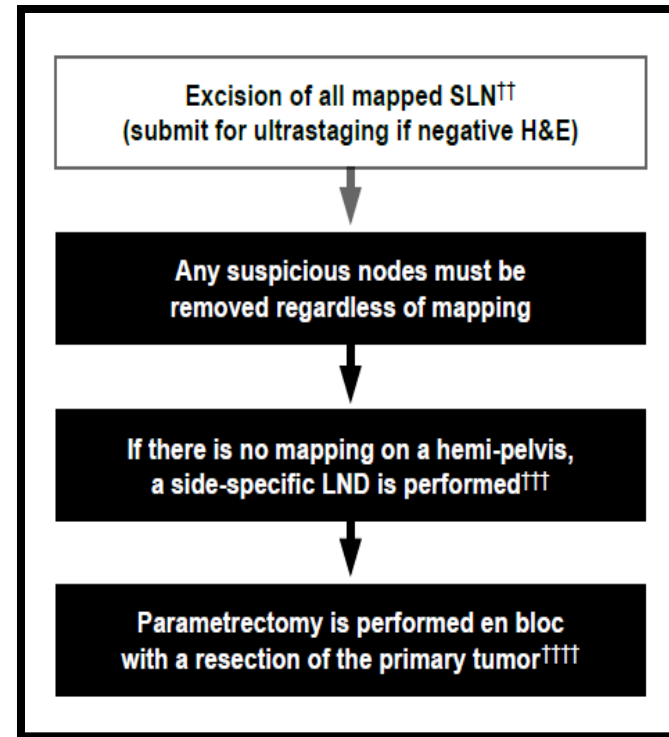
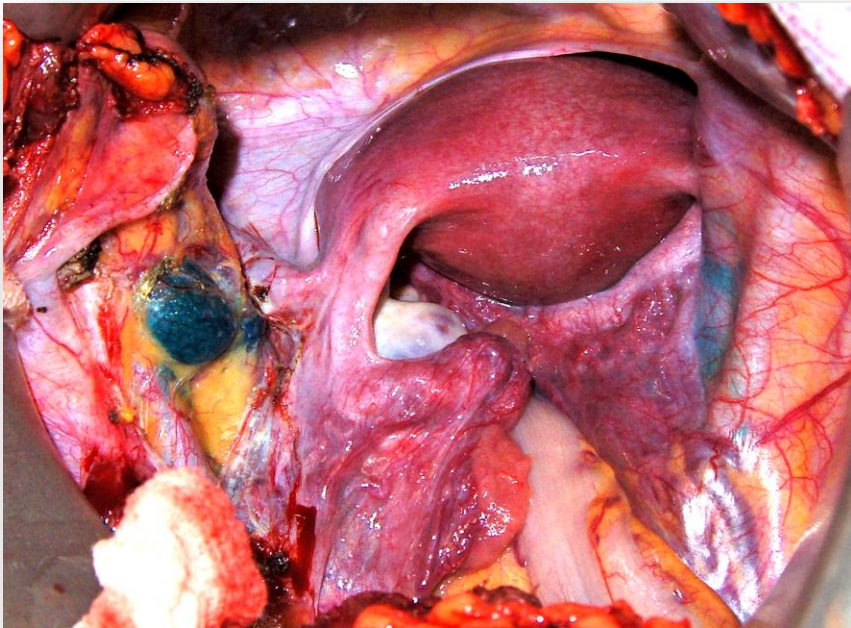


SLN Mapping in Cervical Cancer

Nadeem R. Abu-Rustum, M.D.



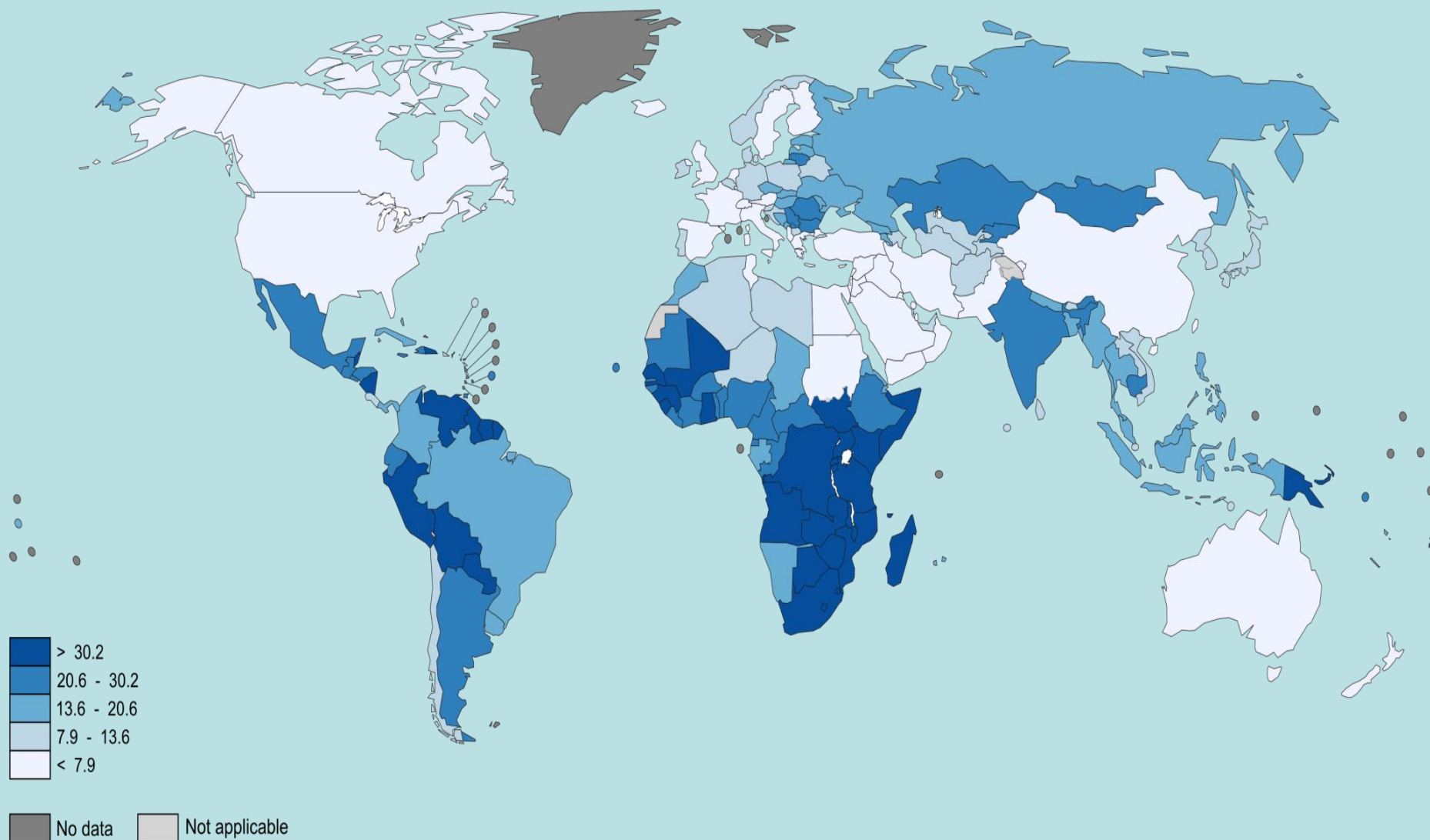
Memorial Sloan Kettering Cancer Center
New York, USA

Conflict of Interest Disclosure

Nadeem R. Abu-Rustum, M.D.

I have no financial relationships with a commercial entity producing health-care related products and/or services.

Incidence of cervix cancer



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data source: GLOBOCAN 2012
Map production: IARC
World Health Organization



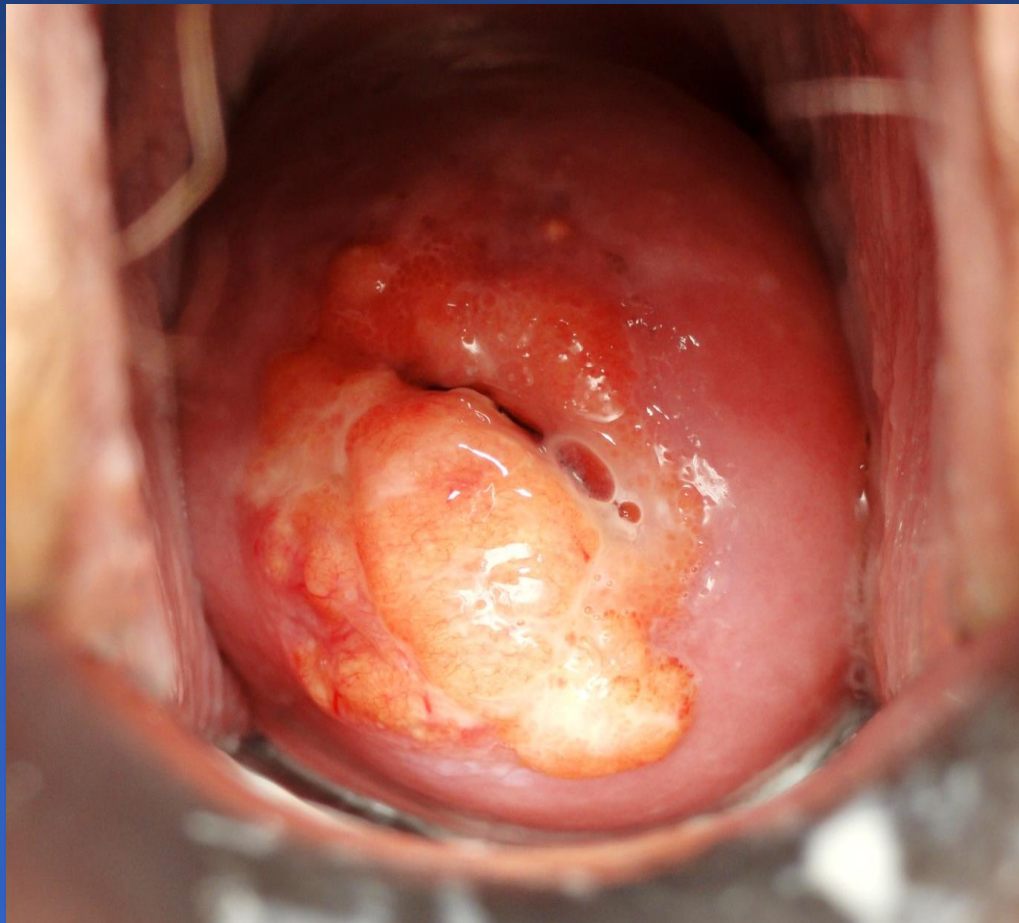
© WHO 2015. All rights reserved

Surgical Questions in Stage I Cervical Cancer 2018

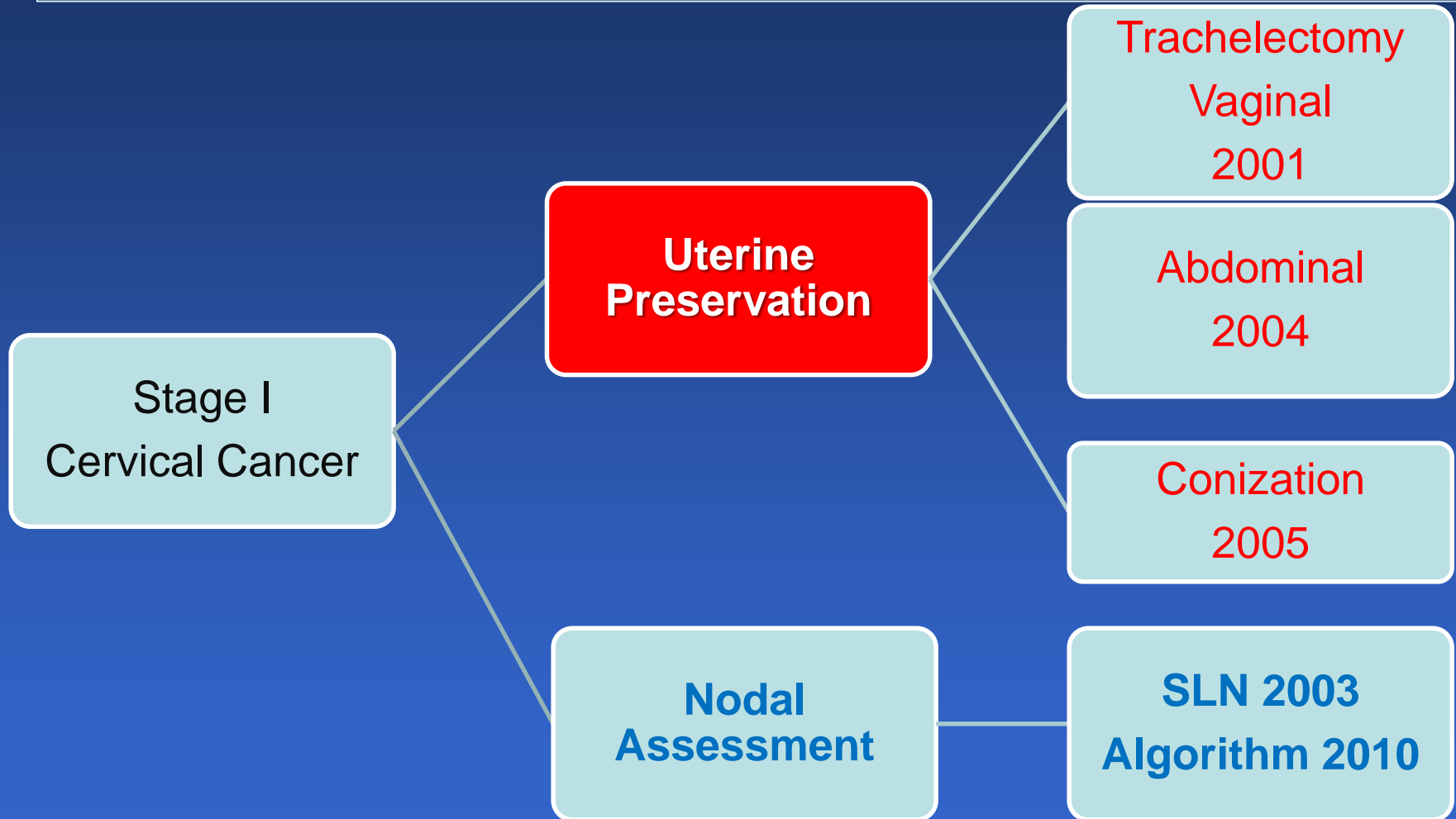
1. Decrease or tailored radicality of resections
2. Sentinel lymph node (SLN) mapping
3. Improving QOL:
 - Nerve Sparing Radical Hysterectomy
 - Minimally Invasive Surgery vs. Open Radical Surgery

Surgery Generally for Stage I Cervical Cancer

FIGO stage IB1 (2-3cm adenoca)



Changes in Surgical Approach Stage I 2001-2018



2013 NCCN Guidelines



National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 2.2013 Cervical Cancer

CLINICAL STAGE

PRIMARY TREATMENT (FERTILITY SPARING)^c

Stage IA1
(no lymphovascular
space invasion
[LVSI])



Cone biopsy with negative margins
(preferably a non-fragmented specimen with 3-mm negative margins)
(If positive margins, repeat cone biopsy or perform trachelectomy)



[See Surveillance \(CERV-10\)](#)

Stage IA1
(with LVSI)
and
Stage IA2



Cone biopsy with negative margins
(preferably a non-fragmented specimen with 3-mm negative margins)
+ pelvic lymph node dissection
or
Radical trachelectomy + pelvic lymph node dissection
(± para-aortic lymph node sampling [category 2B])



[See Surveillance \(CERV-10\)](#)

Stage IB1^d



Radical trachelectomy
+ pelvic lymph node dissection
± para-aortic lymph node sampling



[See Surveillance \(CERV-10\)](#)

^cNo data support a fertility-sparing approach in small cell neuroendocrine tumors or minimal deviation adenocarcinoma (also known as adenoma malignum). Total hysterectomy after completion of childbearing is at the patient's and surgeon's discretion, but is strongly advised in women with continued abnormal pap smears or chronic persistent HPV infection.

^dFertility-sparing surgery for stage IB1 has been most validated for tumors ≤2 cm.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

2014 NCCN Guidelines



National
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NCCN Guidelines Version 1.2014 Cervical Cancer

CLINICAL STAGE	PRIMARY TREATMENT (FERTILITY SPARING) ^d	
Stage IA1 (no lymphovascular space invasion [LVSI])	Cone biopsy ^e with negative margins (preferably a non-fragmented specimen with 3-mm negative margins) (If positive margins, repeat cone biopsy or perform trachelectomy)	See Surveillance (CERV-10)
Stage IA1 (with LVSI) and Stage IA2	Cone biopsy ^e with negative margins (preferably a non-fragmented specimen with 3-mm negative margins- if positive margins, repeat cone biopsy or perform trachelectomy) + pelvic lymph node dissection ± para-aortic lymph node sampling (category 2B) (Consider sentinel lymph node mapping [category 2B]) ^f Radical trachelectomy + pelvic lymph node dissection^f (± para-aortic lymph node sampling [category 2B]) (Consider sentinel lymph node mapping [category 2B]) ^f	See Surveillance (CERV-10)
Stage IB1 ^c	Radical trachelectomy + pelvic lymph node dissection ^f ± para-aortic lymph node sampling (Consider sentinel lymph node mapping [category 2B]) ^{f,9}	See Surveillance (CERV-10)

^cFertility-sparing surgery for stage IB1 has been most validated for tumors ≤2 cm. Small cell neuroendocrine histology and adenoma malignum are not considered suitable tumors for this procedure.

^dNo data support a fertility-sparing approach in small cell neuroendocrine tumors or minimal deviation adenocarcinoma (also known as adenoma malignum). Total hysterectomy after completion of childbearing is at the patient's and surgeon's discretion, but is strongly advised in women with continued abnormal pap smears or chronic persistent HPV infection.

^eCold knife conization (CKC) is the preferred method of diagnostic excision, but LEEP is acceptable, provided adequate margins and proper orientation are obtained.

^f[See Principles of Evaluation and Surgical Staging \(CERV-A\).](#)

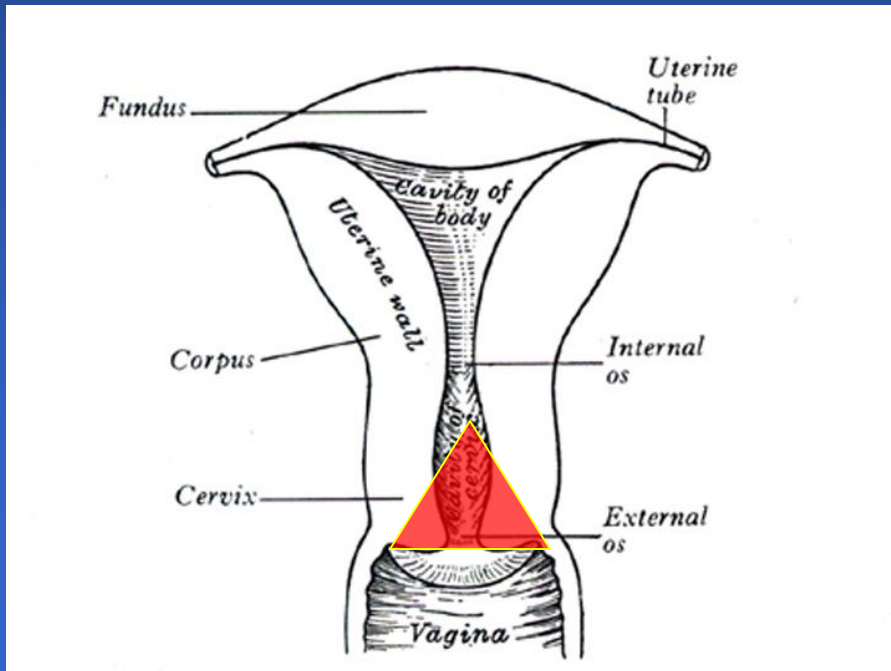
⁹For SLN mapping (category 2B), the best detection rates and mapping results are in tumors <2 cm.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Stage IA1 No Lymphovascular Invasion (LVI)

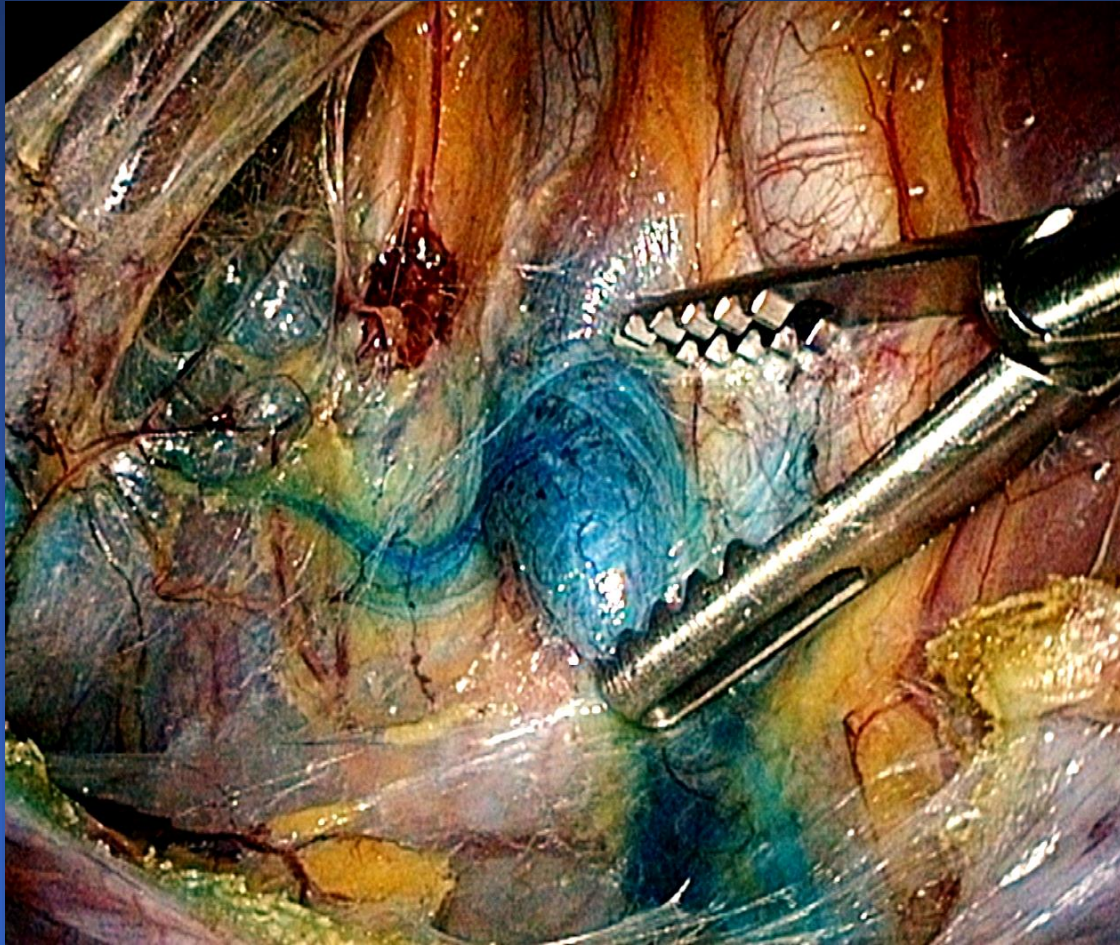
- Can be treated with Cone
- Review Pathology



Stage IA1 with LVI

SLN Mapping & Conization

SLN mapping is Category 2A recommendation



“Less is more....”

2011: 1st SENTICOL Study Cervical SLN Algorithm were Published

- No false-negative results were observed when SLN were identified bilaterally.
- When the SLN algorithm was applied, all patients with lymph node metastasis were detected.

•Lecuru F, et al. JCO 2011.
•Diaz JP, et al. (MSKCC) Gynecol Oncol 2011.
•Cormier B. et al. (MSKCC) Gynecol Oncol 2011.

SENTICOL Study

- 139 patients
- Intraoperative radioisotope-blue dye mapping detected at least one SLN in 98%, 23 of whom had true-positive results and two who had false-negative results, yielding 92.0% sensitivity and 98.2% NPV.
- No false-negative results were observed in the 104 patients (76.5%) in whom SLN were identified bilaterally.
- SLN biopsy was fully reliable only when SLNs were detected bilaterally.

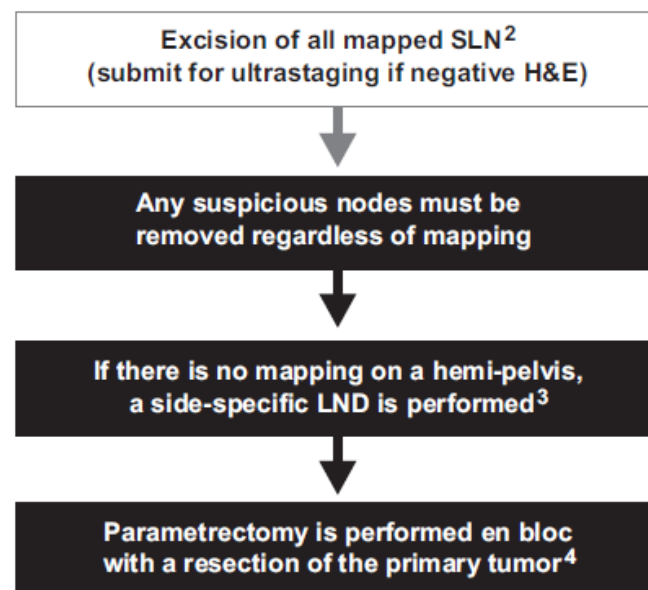
MSKCC SLN Algorithm

- 122 patients were included. Median SLN count was 3 and median total LN count was 20.
- At least one SLN was identified in 93%
- Optimal (bilateral) mapping was achieved in 75% of cases.
- SLN correctly diagnosed 21 of 25 patients with nodal spread.
- When the algorithm was applied, all patients with LN metastasis were detected
- With optimal mapping, bilateral pelvic LND could have been avoided in 75% of cases.

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 Cancer¹



H&E: Hematoxylin and eosin staining
LND: Lymphadenectomy
SLN: Sentinel lymph node

¹Reproduced with permission from Comier B, Diaz JP, Shih K, et al. Establishing a sentinel lymph node mapping algorithm for the treatment of early cervical cancer. Gynecol Oncol. 2011 Aug;122:275-280.

²Intracervical injection with dye, 99m technetium, or both.

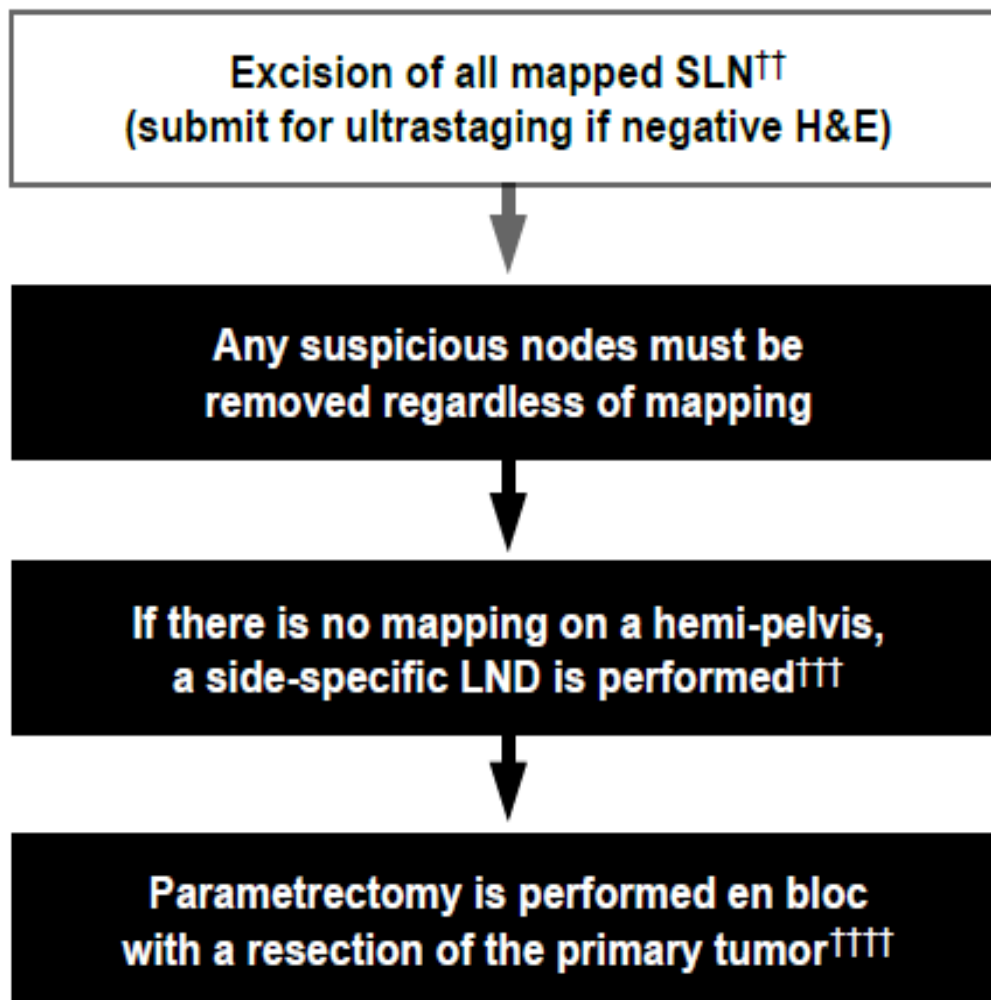
³Including interiliac/subaortic nodes.

⁴Exceptions made for select cases (see [CERV-A 1 of 7](#)).

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

The key to a success
in cases of failed m



H&E: Hematoxylin and eosin
LND: Lymphadenectomy
SLN: Sentinel lymph node

[†]Reproduced with permission from
Gynecol Oncol. 2011;
^{††}Intracervical injection
^{†††}Including interiliac/s
^{††††}Exceptions made for

Note: All recommendations
Clinical Trials: NCCN

specific nodal dissection

of early cervical cancer.

[Continued](#)

CERV-B
4 OF 7

R. de Freitas & G. Baiocchi (Brazil)

ASO 2015

- 57 patients, and 19% LN metastases.
- SLN identified in 84%, bilateral in 58%.
- The false-negative rate was 4.2%.
- Patient specific analysis - Applying the NCCN Algorithm identified 100% of patients who had (+) LN.
- **CONCLUSIONS: Safe and accurate and increases detection of LN+**

G. Salvo & P. Ramirez (MDACC)

Gyn Onc 2017

- 188 patients, 35 (19%) LN metastases.
- SLN identified in 90%, bilateral in 62%.
- The false-negative rate was 3.6% (1 case).
 - Sensitivity of 96%, NPV of 99%.
- Applying the NCCN Algorithm identified 100% of patients who had (+) LN.
- **CONCLUSIONS:** We believe it is time to change the standard of care for women with early-stage cervical cancer to SLN biopsy only.



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.⁸⁻¹¹ This simple technique utilized 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.^{2,12}

Figure 1: Options of SLN Cervical Injection Sites[†]

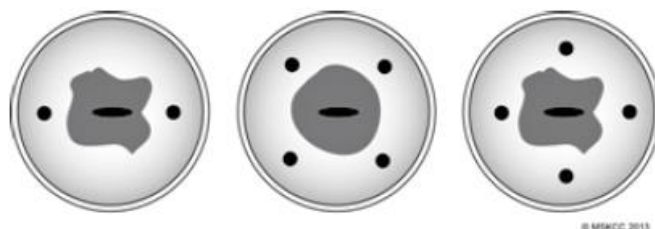
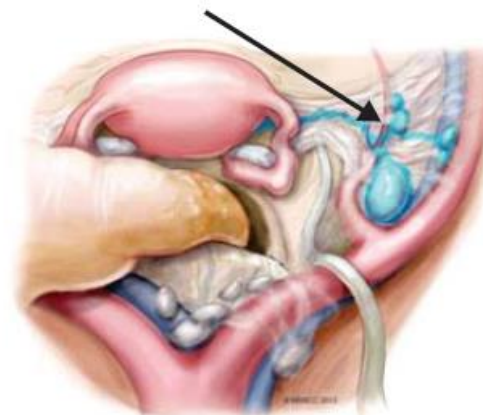


Figure 2: SLNs (blue, arrow) After Cervical Injection Are Commonly Located Medial to the External Iliac, Ventral to the Hypogastric, or in the Superior Part of the Obturator Space[†]



[†]Figures 1 and 2 are reproduced with permission from Memorial Sloan-Kettering Cancer Center. © 2013 Memorial Sloan-Kettering Cancer Center.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

2014 NCCN Principles of Surgical Staging

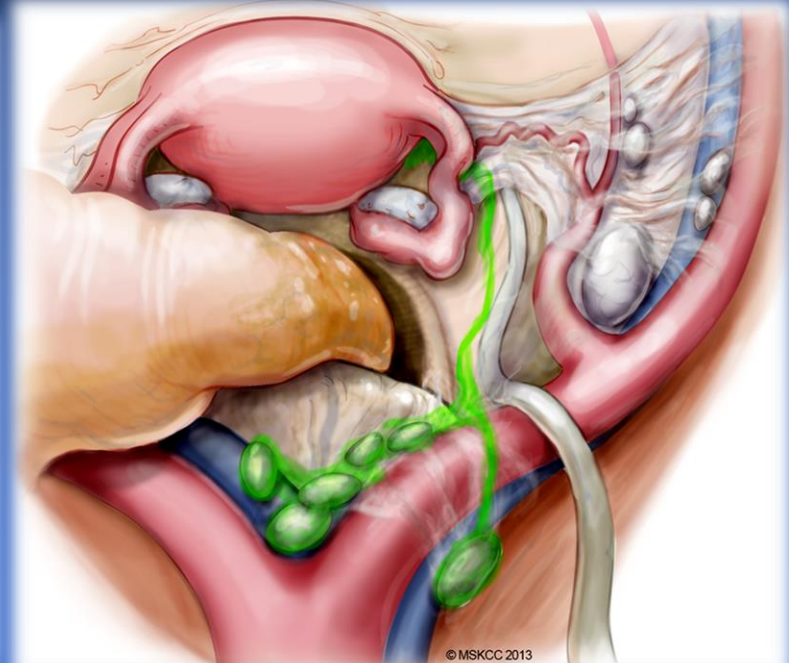
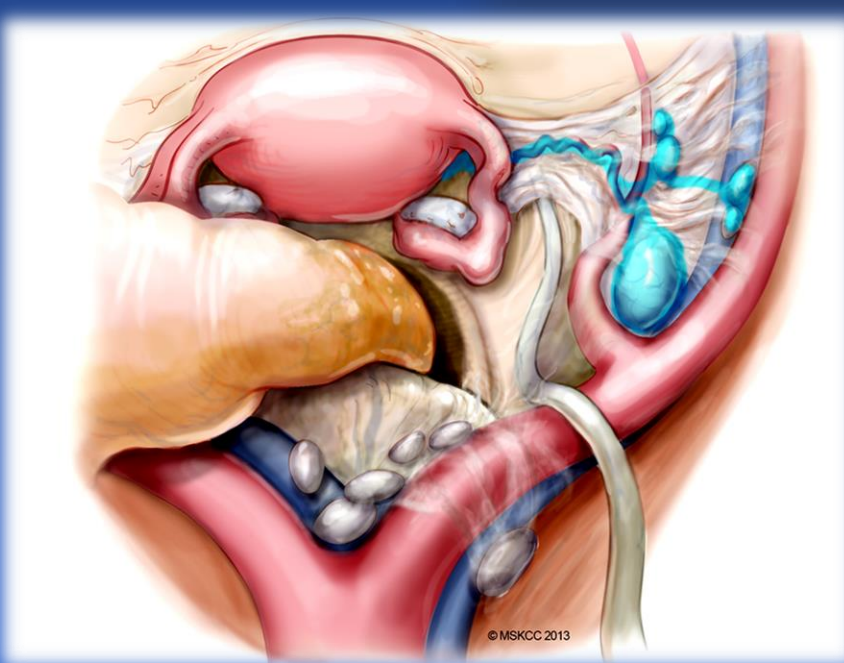
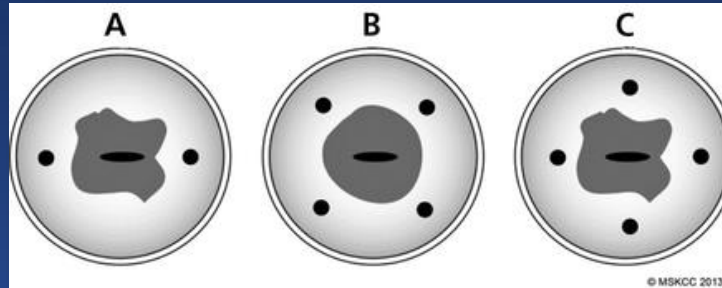
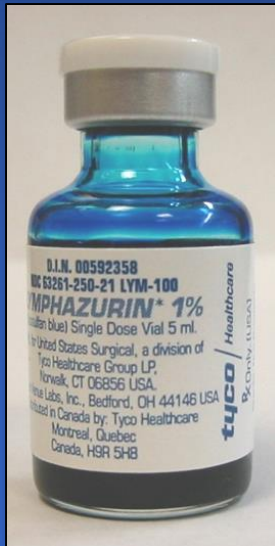
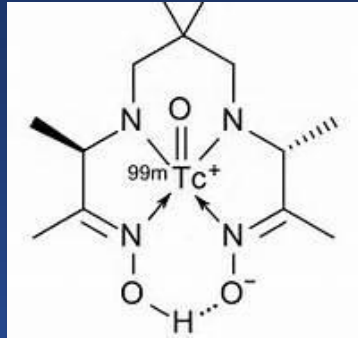


Image Guided Surgery



1981 FDA



1891
Not FDA

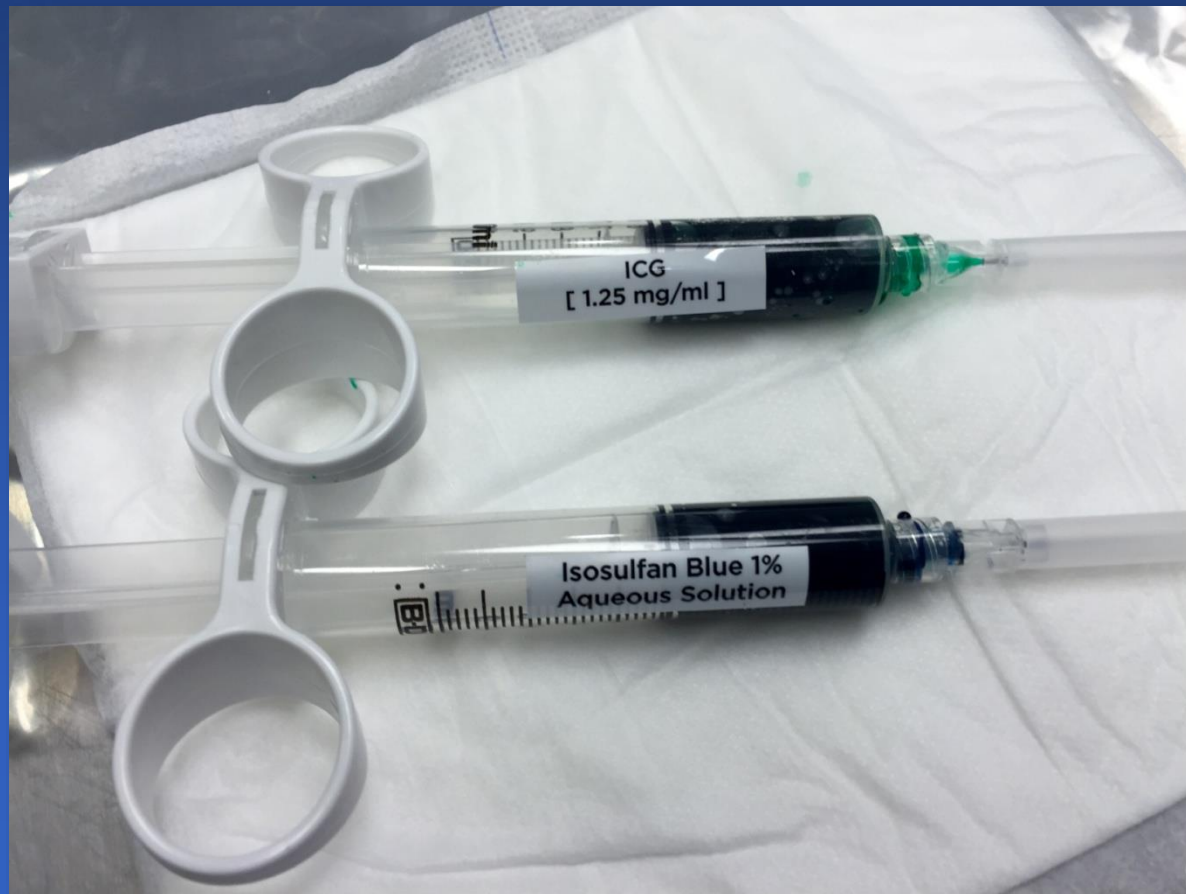


1959 FDA
for liver & cardiac

Colored Dye: Simple Setup

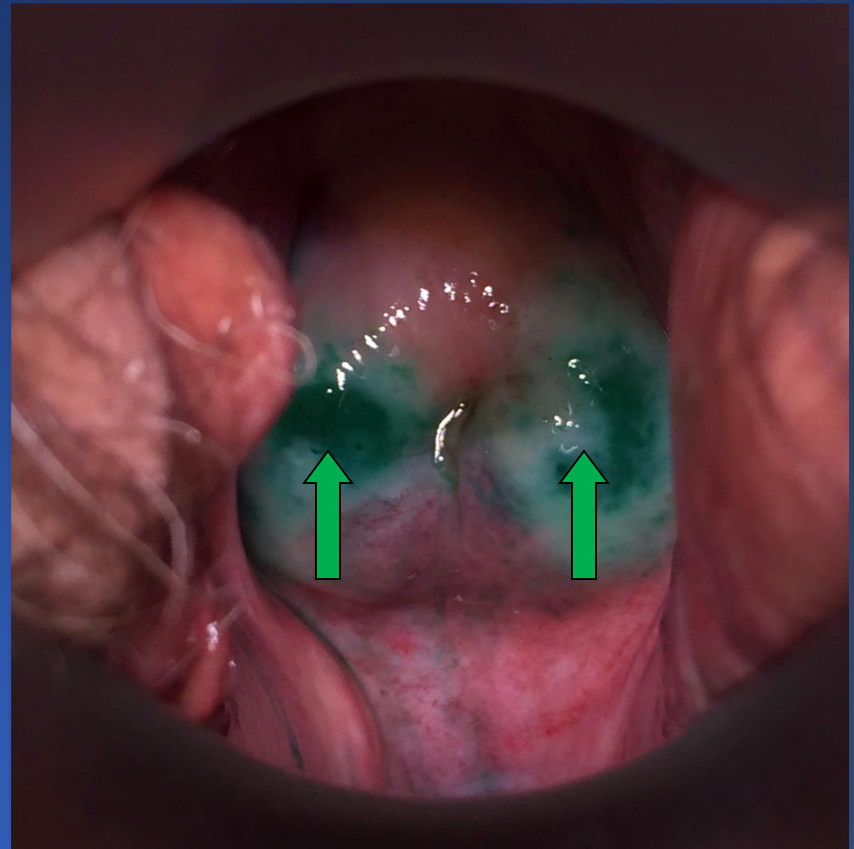
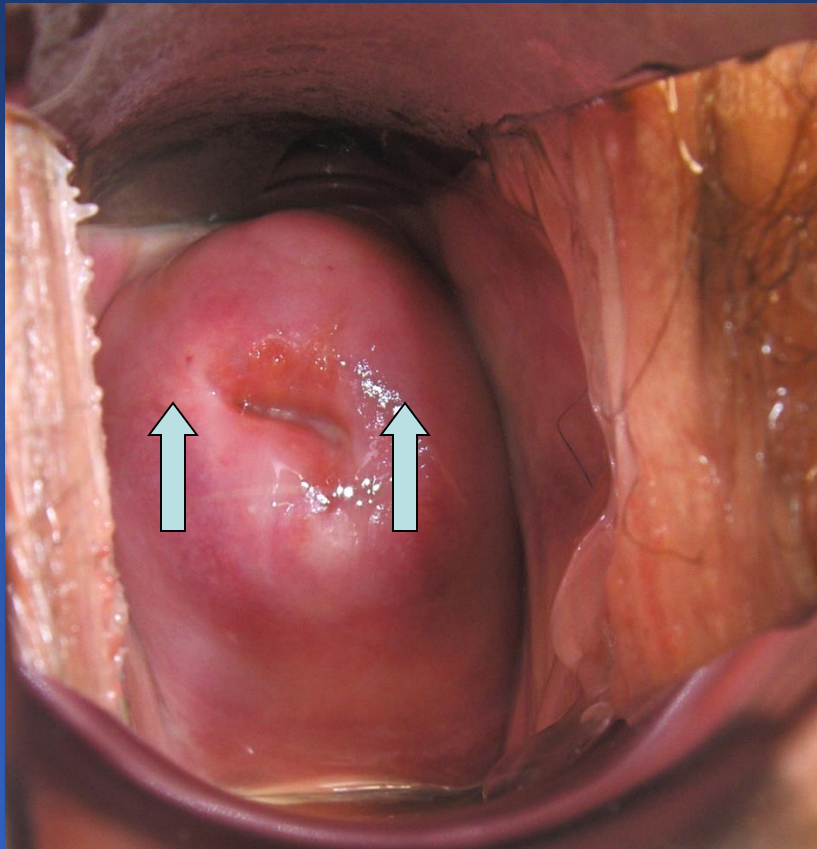


ICG is FDA approved for IV administration
ICG Interstitial injection for lymphatic
mapping is off-label

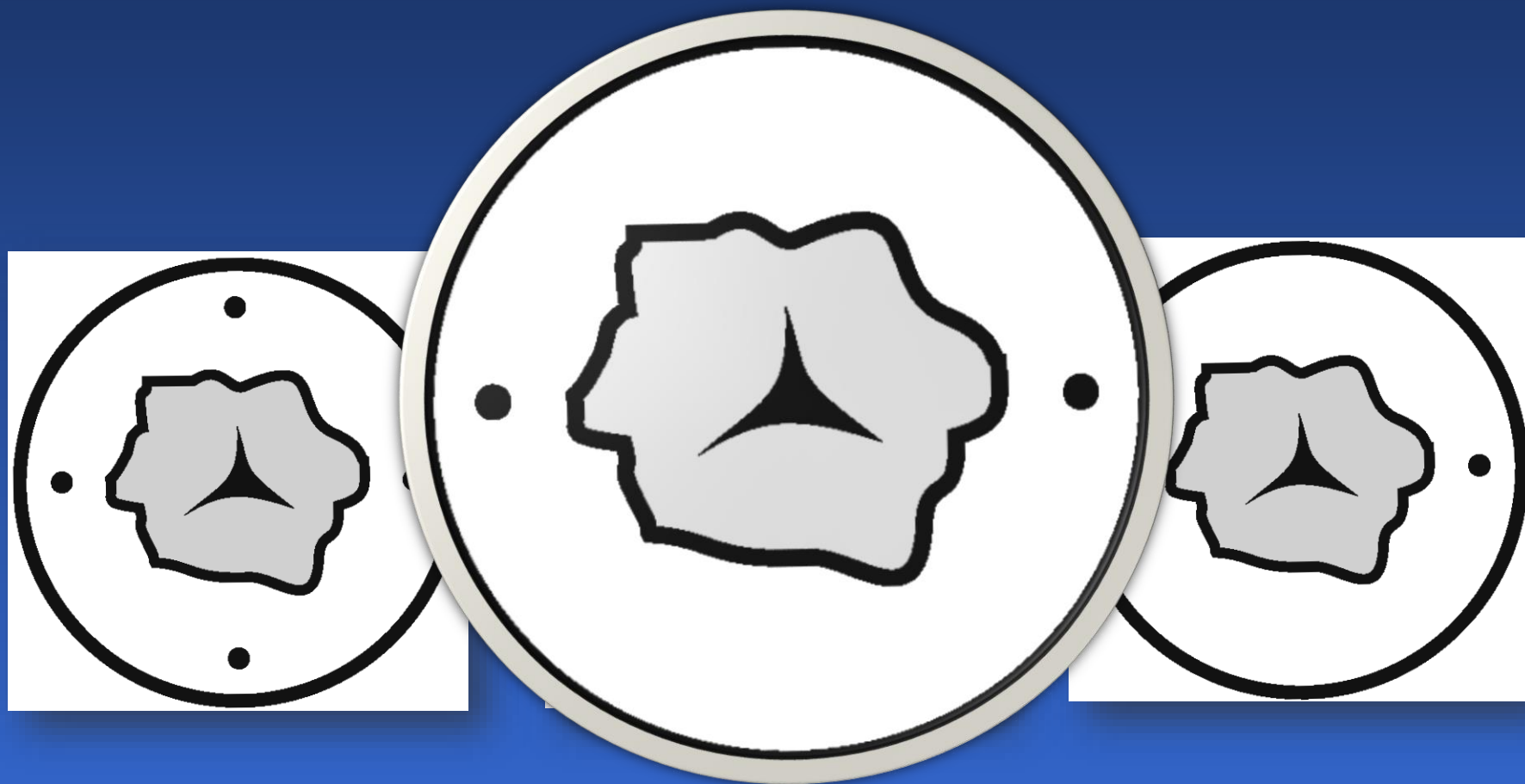




Use 22G Spinal Needle
3 & 9 O'clock total 4 cc
1cc superficial & 1cc deep on each side

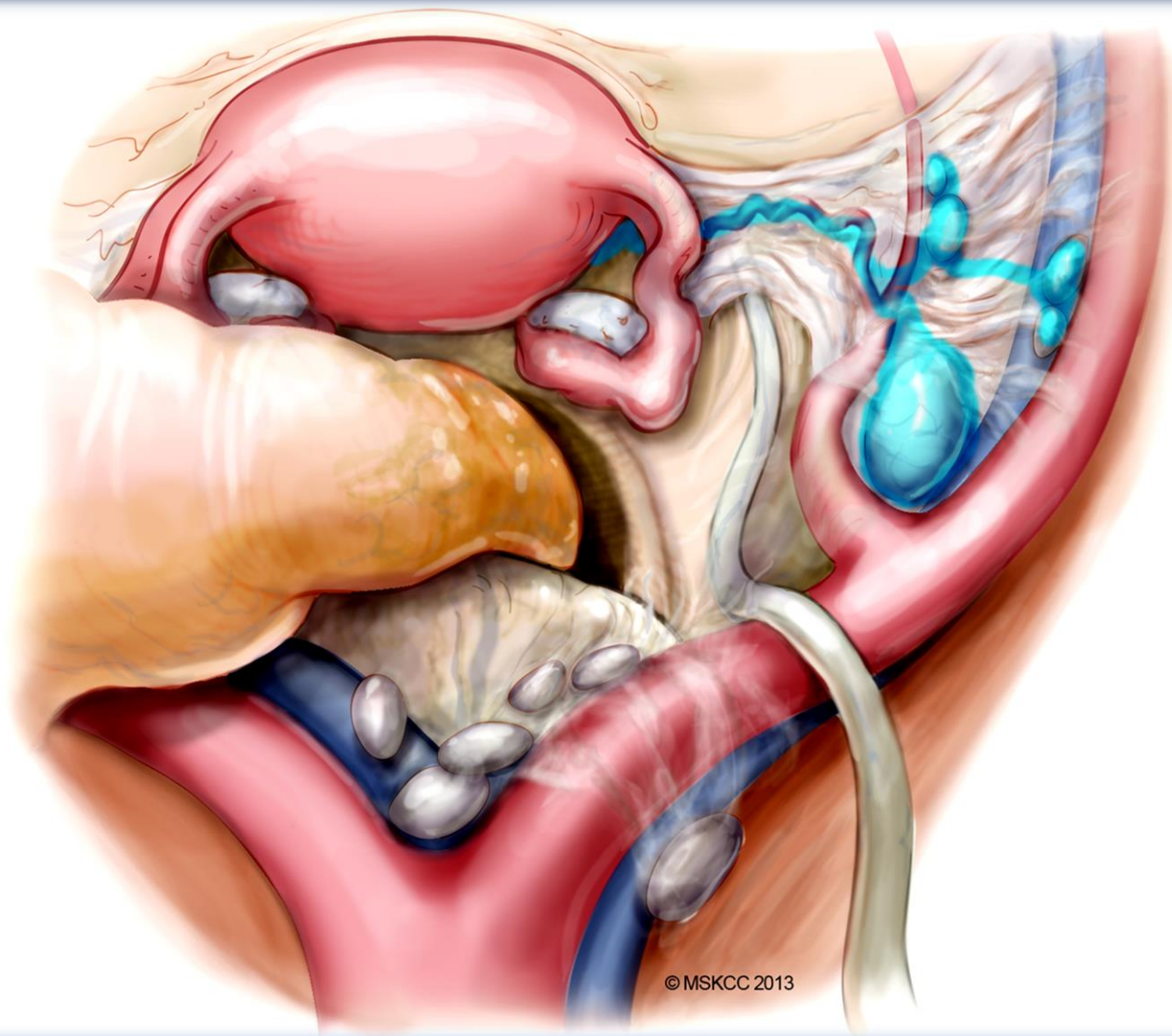


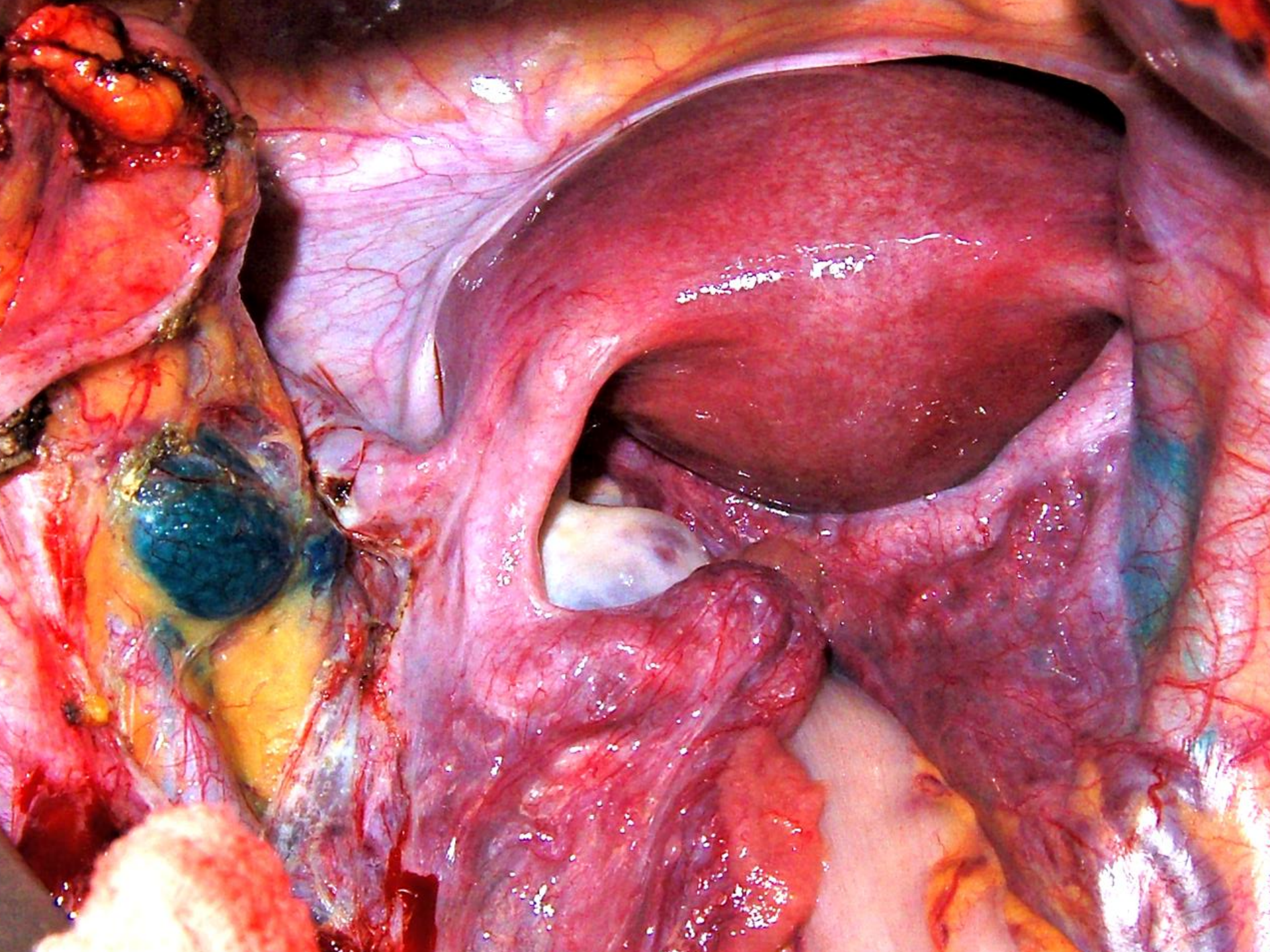
Cervical Injection Sites

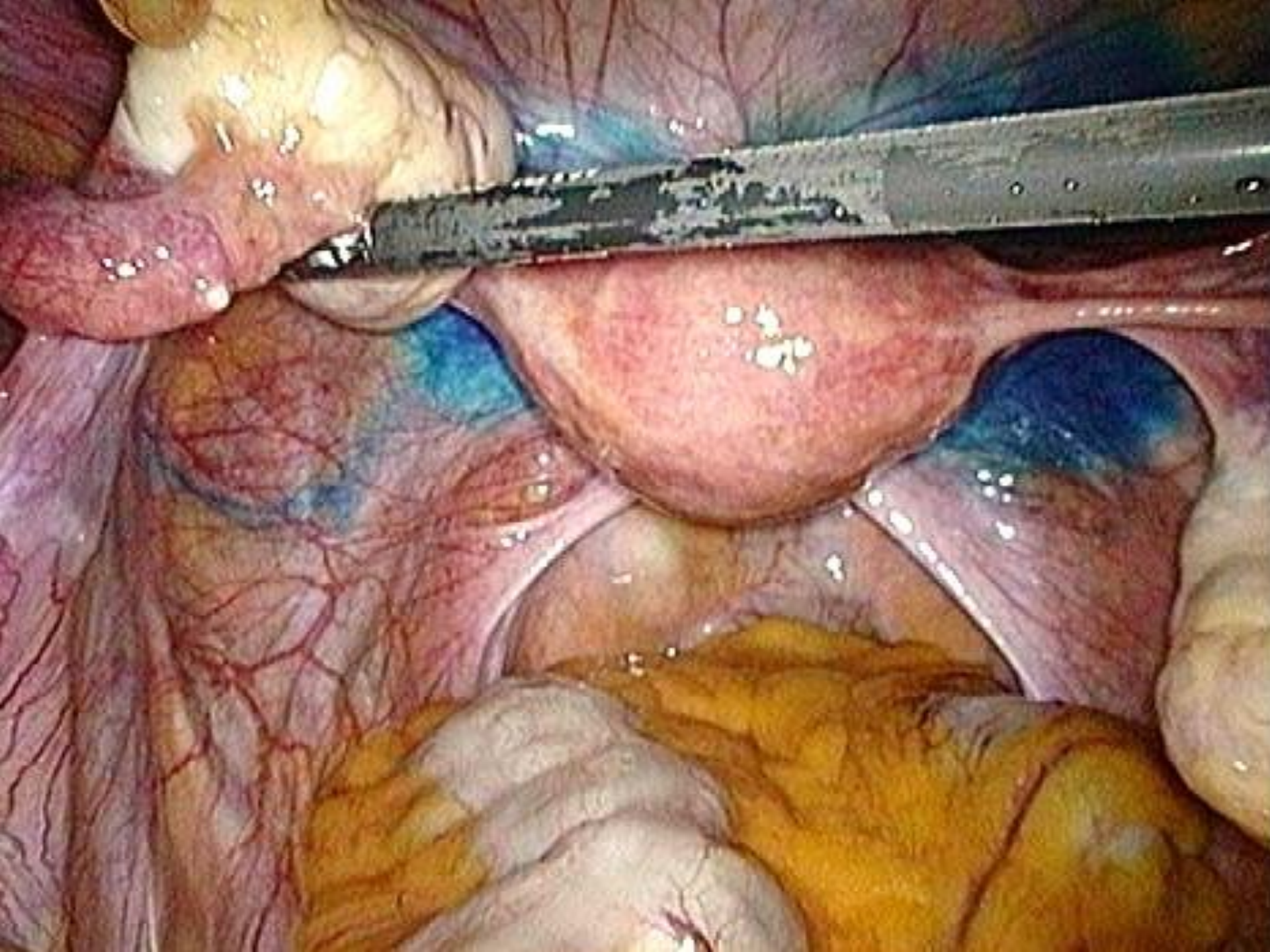


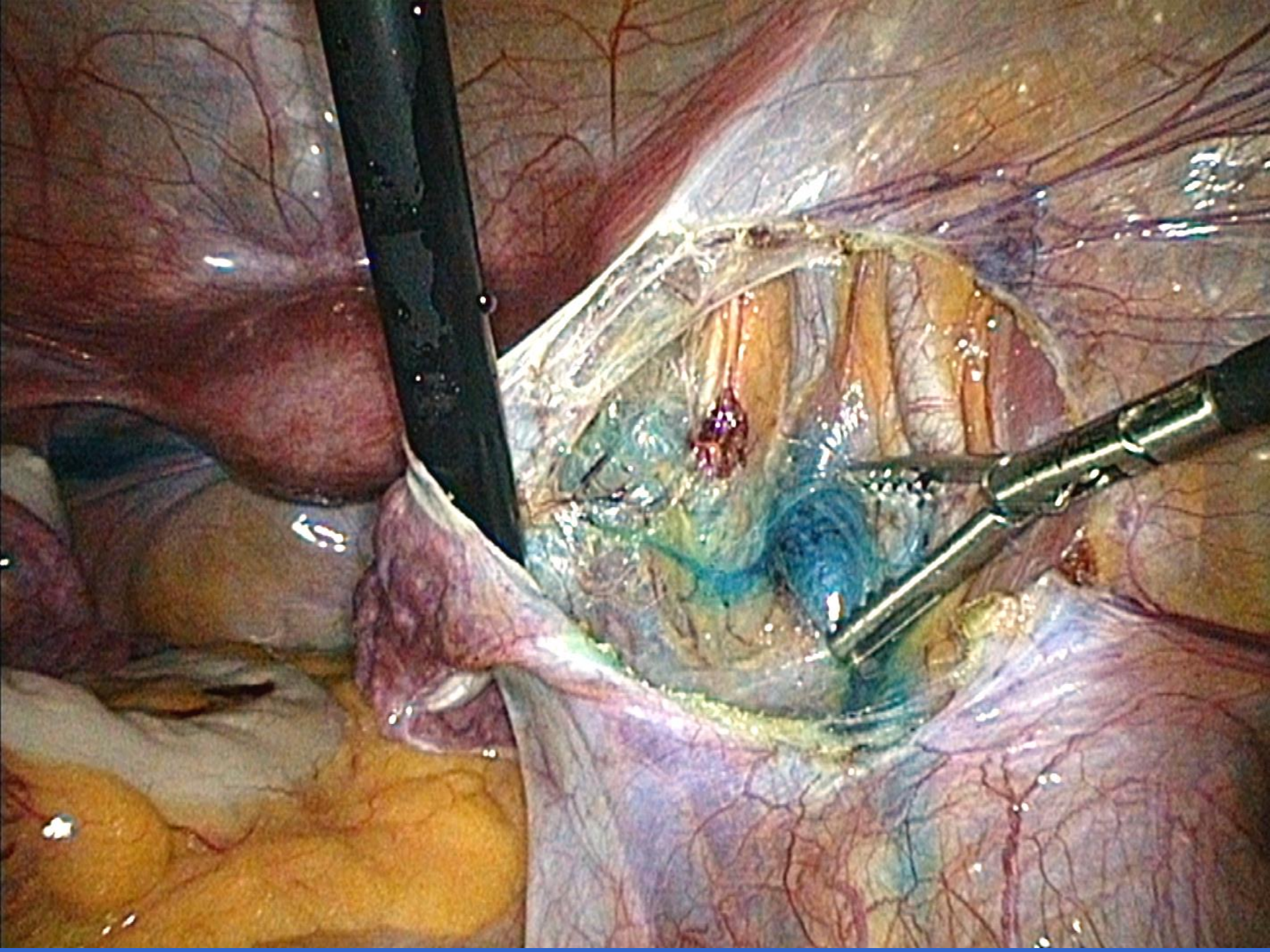
Abu-Rustum NR, Rob L.
Atlas of Procedures in Gynecologic Oncology
3rd Edition 2013

Most Common Drainage

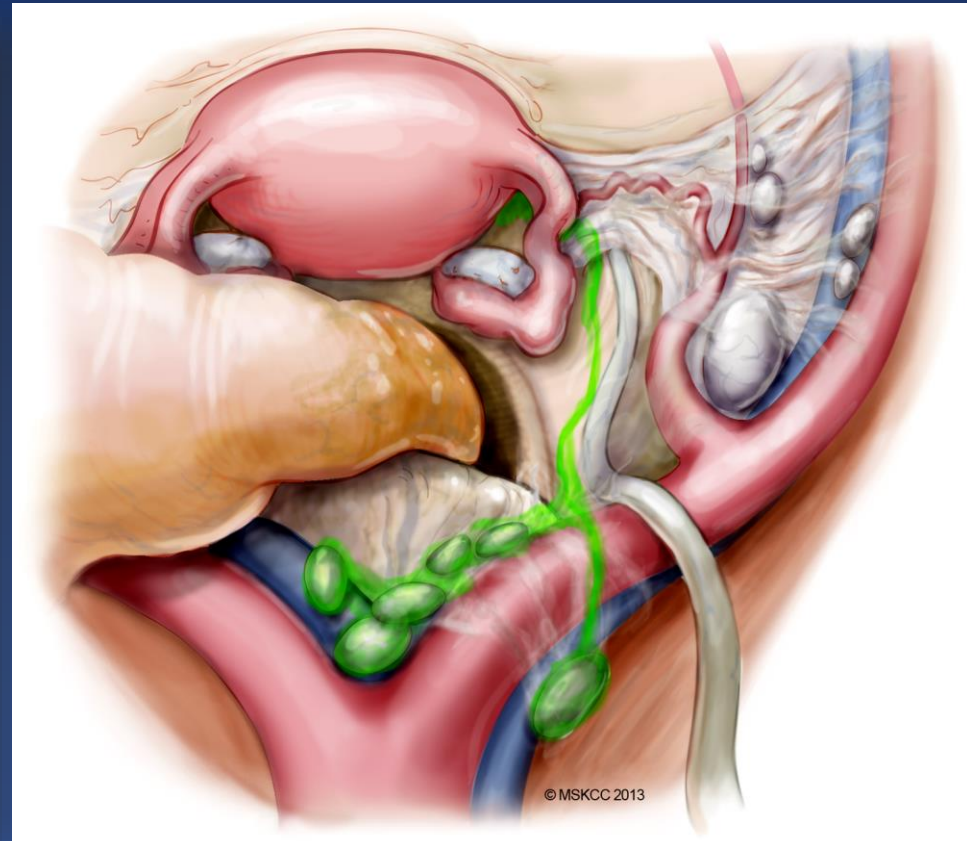
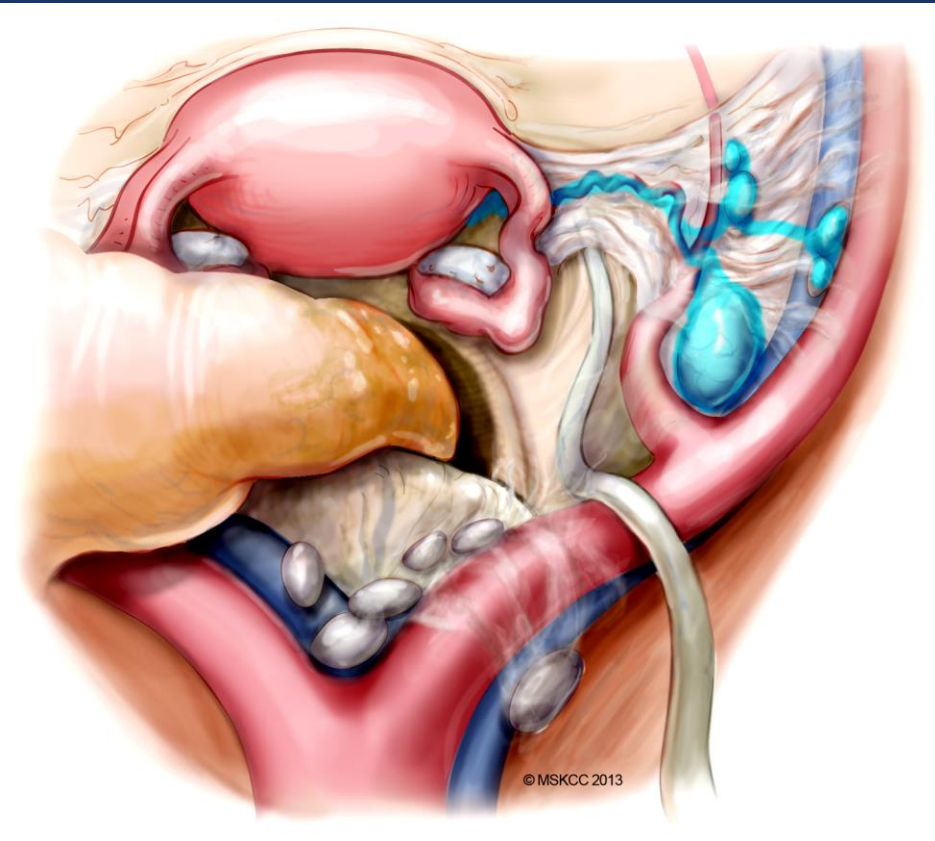






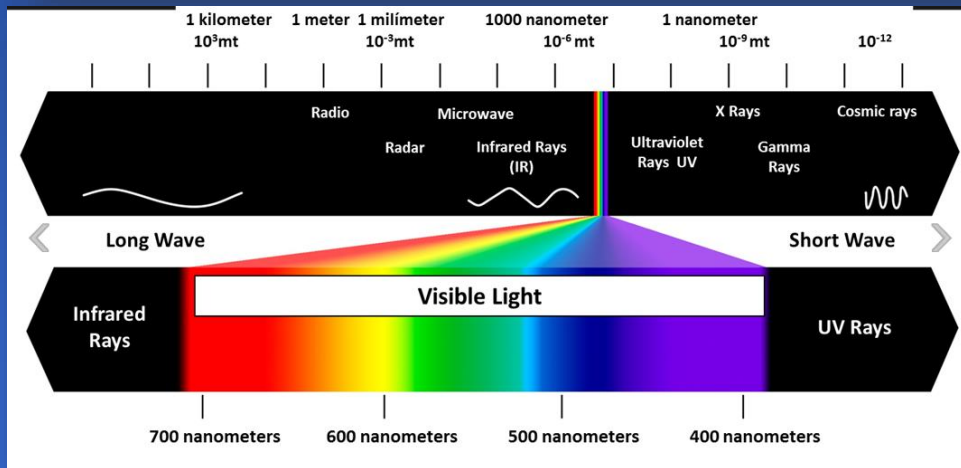


Lymphatic Drainage - Cervical Injection



Fluorescence Imaging Systems

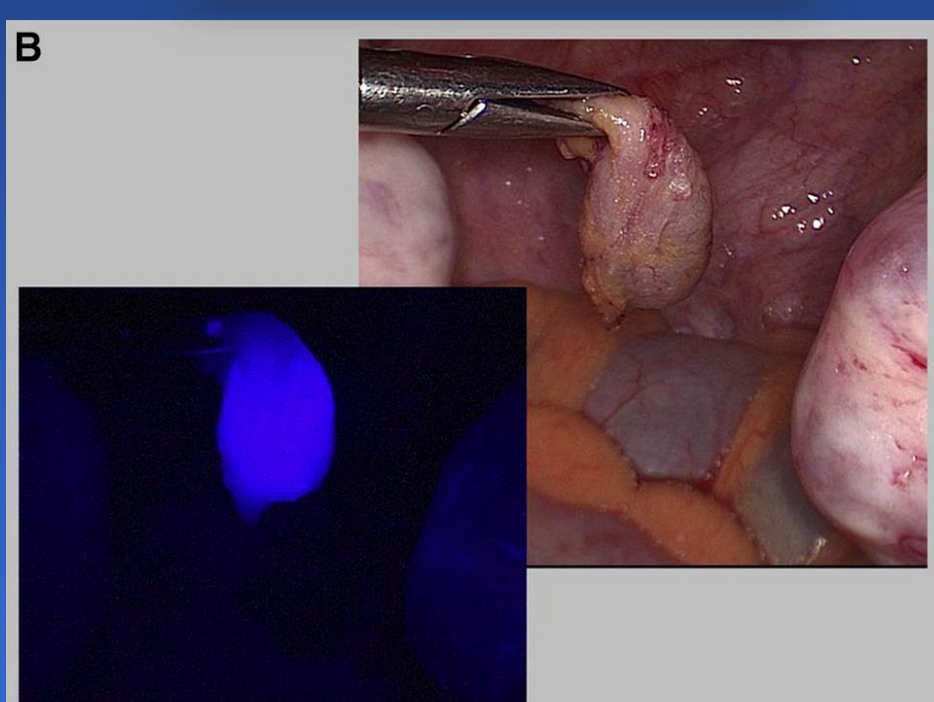
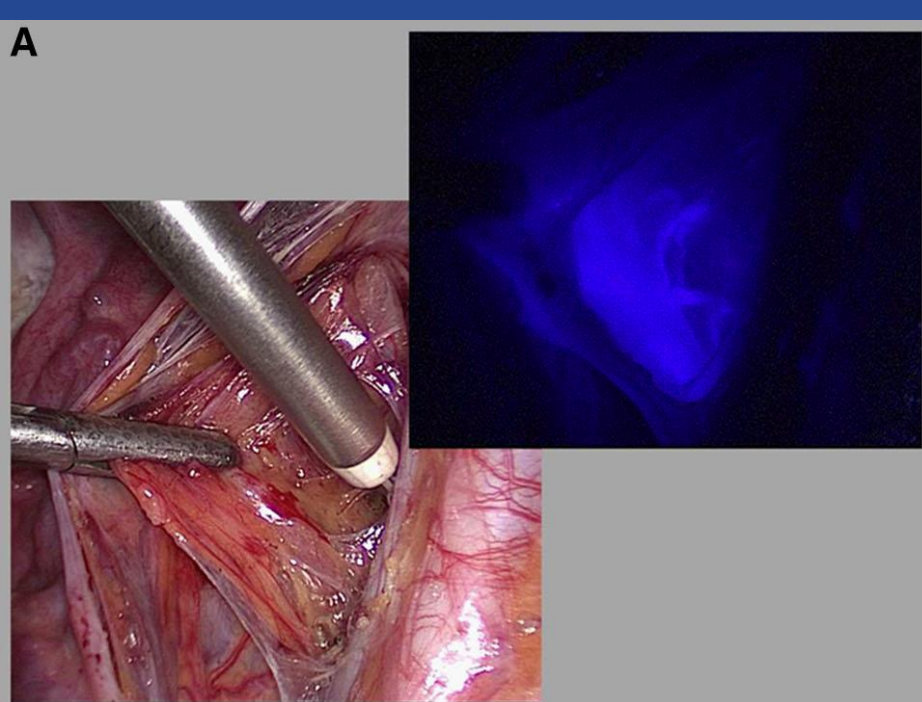
Indocyanine Green



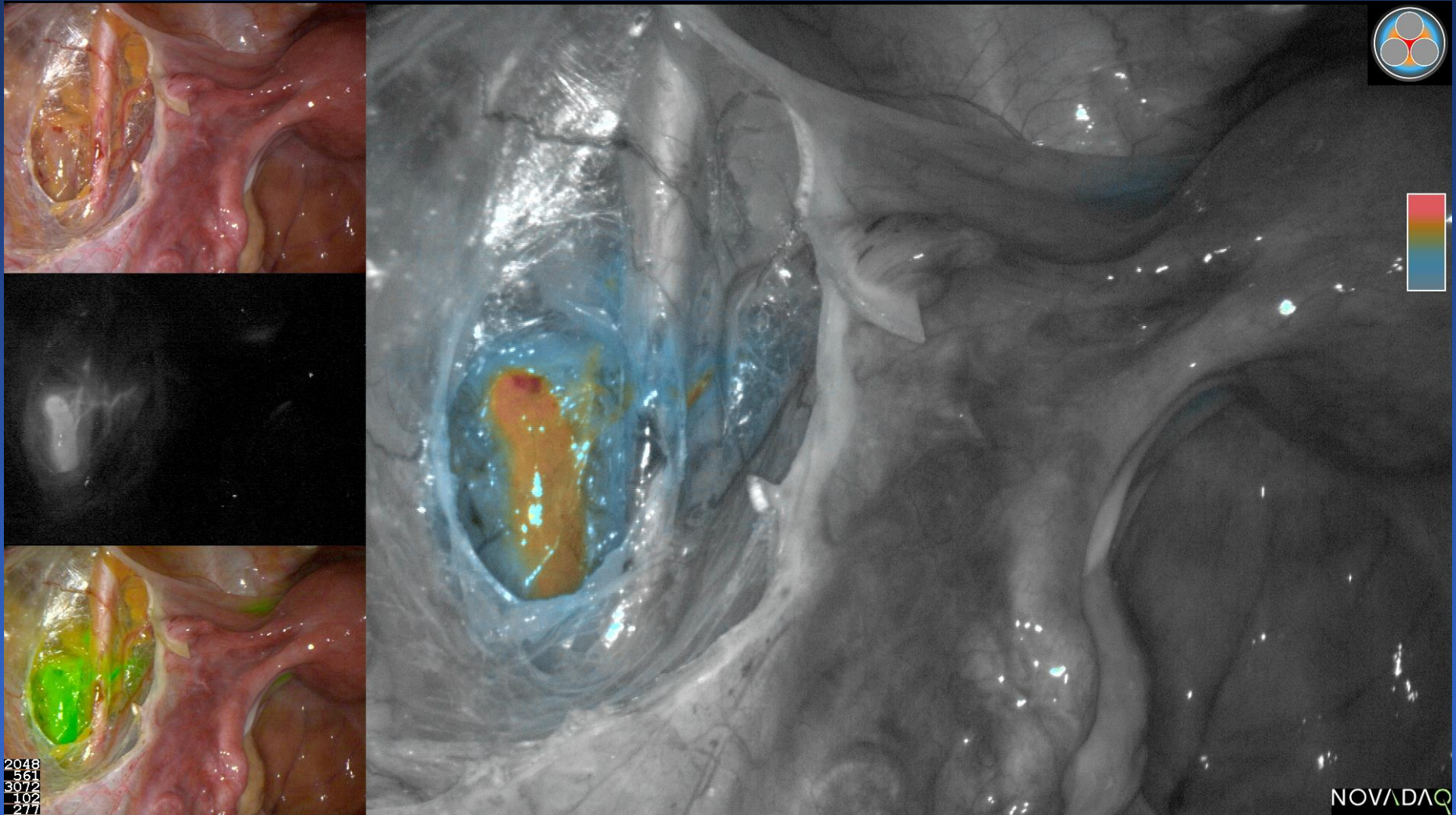
Near Infrared (NIR)



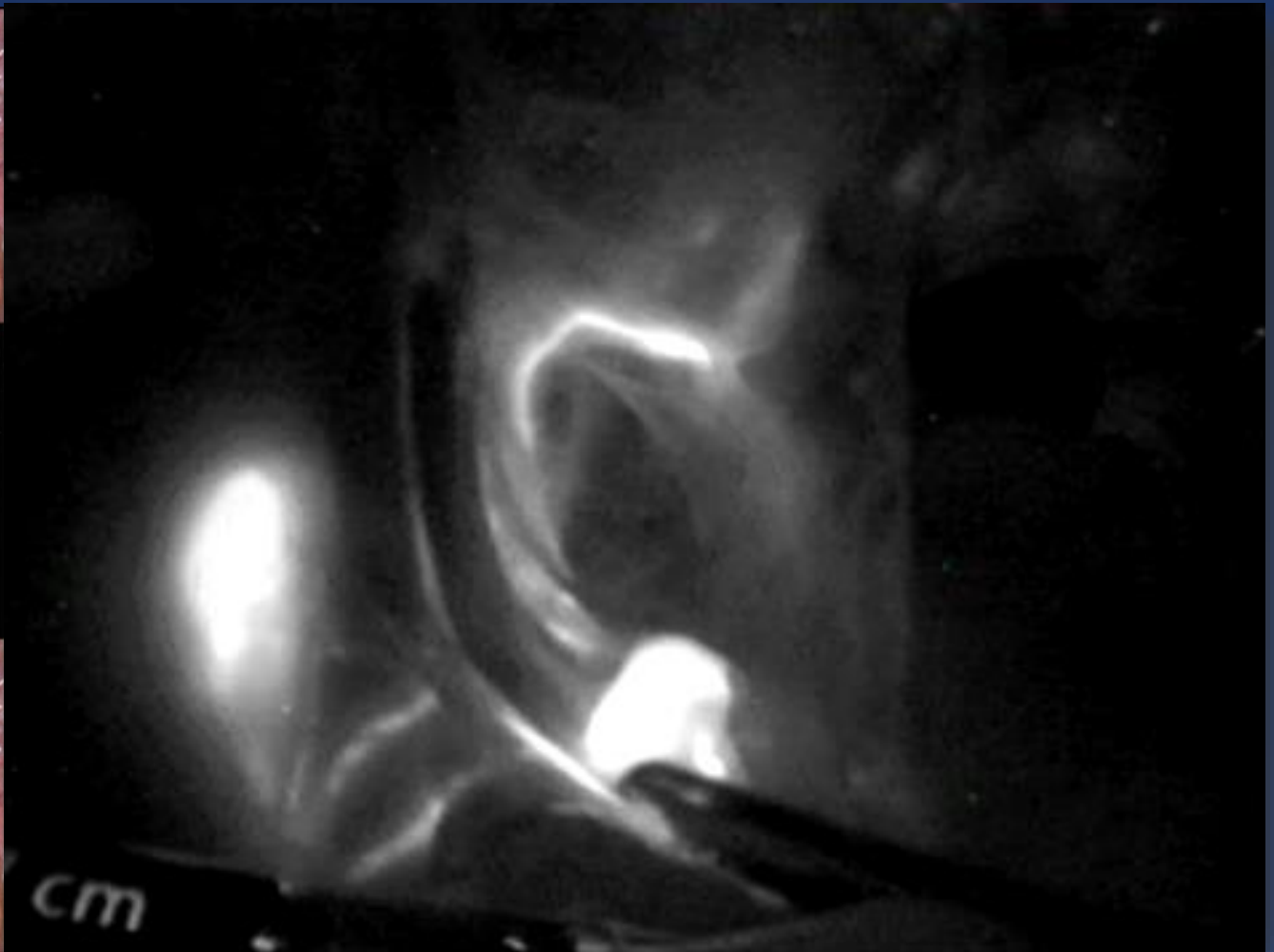
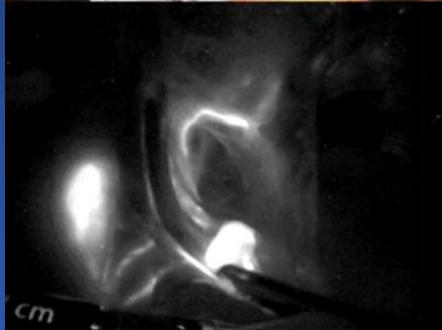
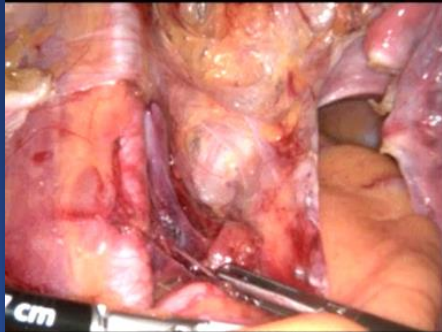
STORZ NIR - ICG



Indocyanine Green & NIR Mapping



SLN and Secondary Nodes



Sentinel Lymph Nodes

Nadeem Abu-Rustum (co-PI): MSKCC

Marie Plante: CHU de Quebec

Paula Lee: Duke Cancer Center

Samith Sandabi: Lee Memorial

James Lilja: O'Connor Hospital

Pedro Escobar: HIMA San Pablo

Lilian Gien: Sunnybrook HSC

The FILM Trial: A Phase III Multicenter Study Assessing Near Infrared Fluorescence in the Identification of Sentinel Lymph Nodes

- ICG is superior to blue dye in identifying SLNs
- ICG + blue dye is not better than ICG alone
- ICG identifies all metastatic nodes
- Interstitial injection of ICG is safe

To Decrease Lymphedema Avoid the Circumflex Iliac Nodes



Available online at www.sciencedirect.com



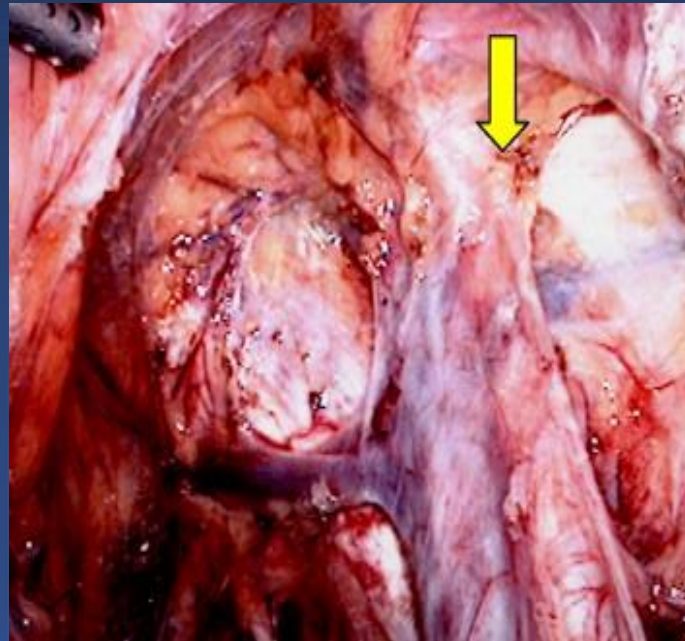
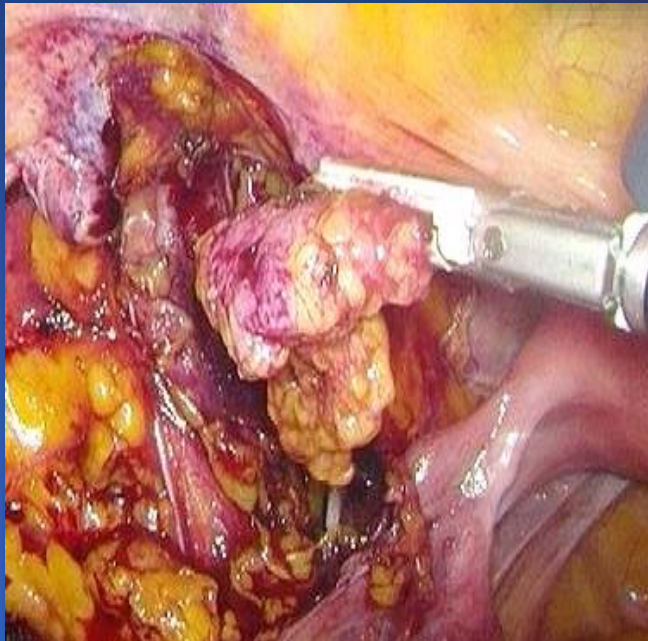
Gynecologic Oncology 106 (2007) 4–5

Gynecologic
Oncology

www.elsevier.com/locate/ygyno

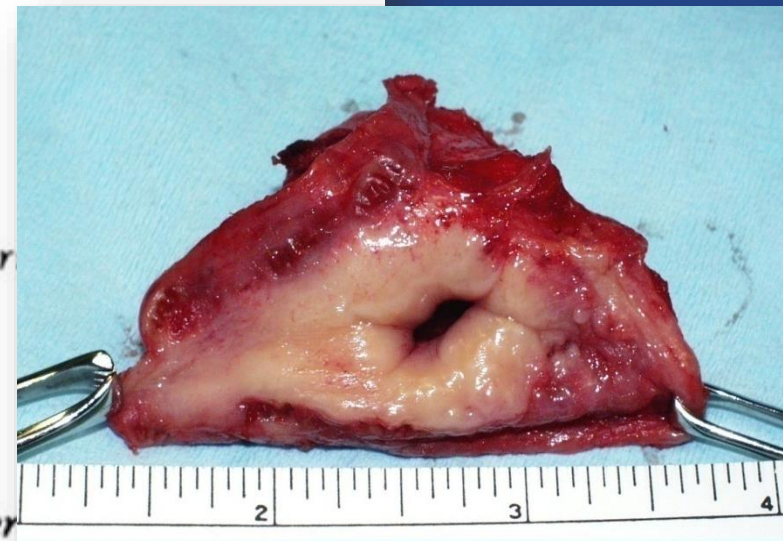
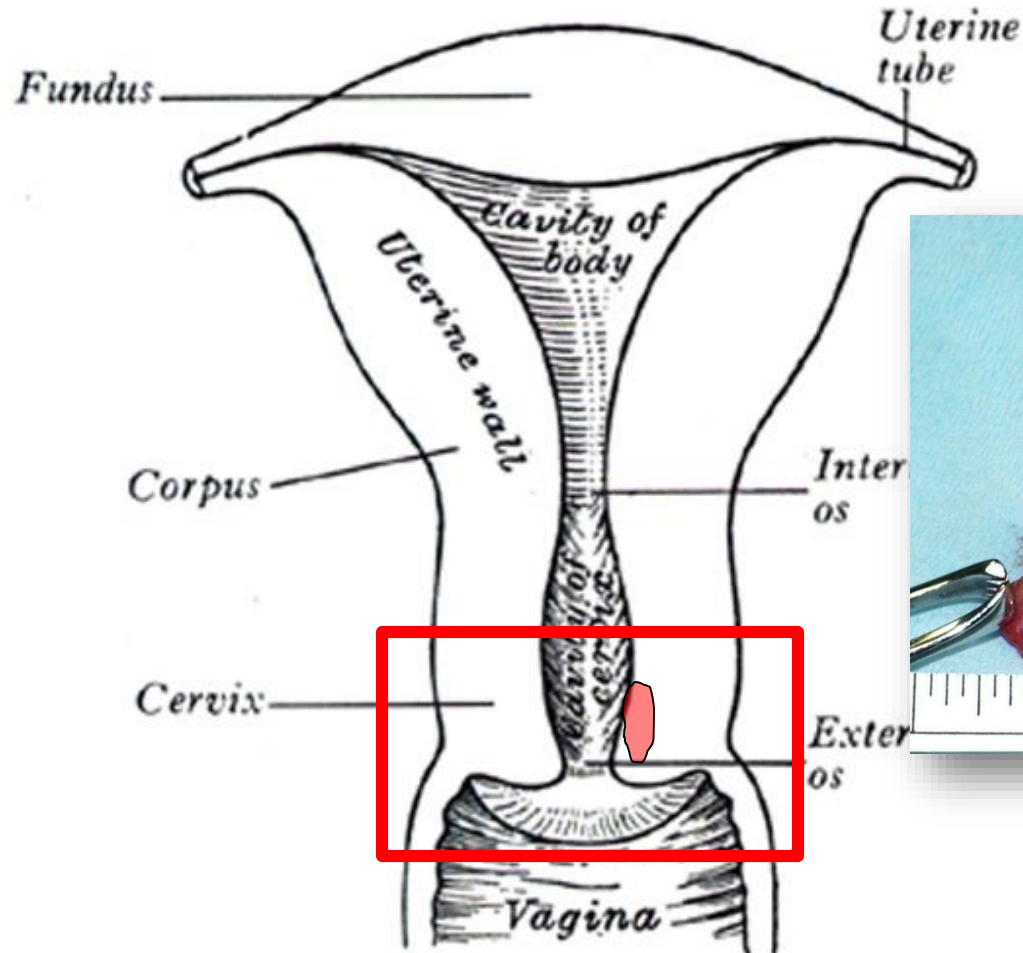
Editorial

Observations on the role of circumflex iliac node resection and the etiology of lower extremity lymphedema following pelvic lymphadenectomy for gynecologic malignancy

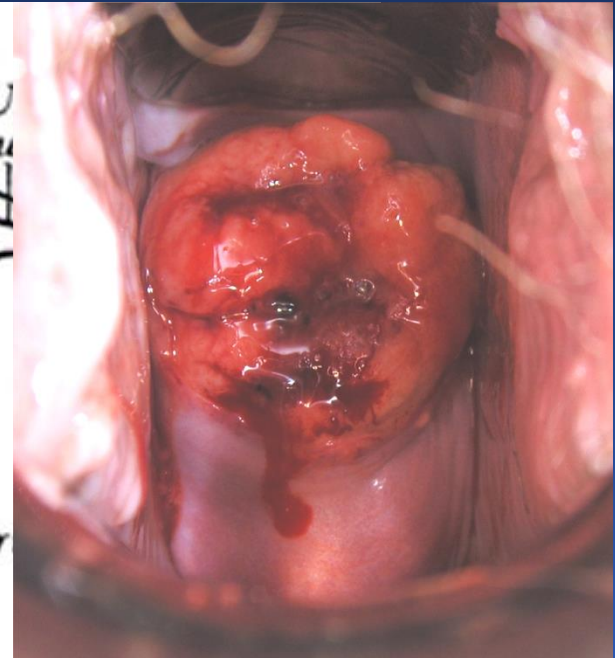
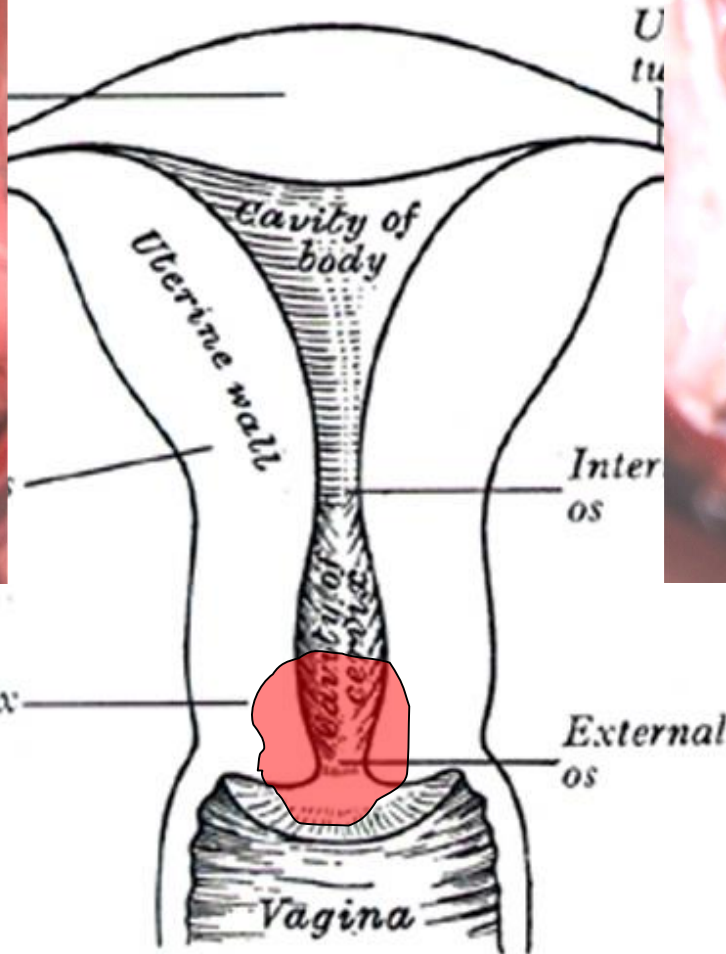
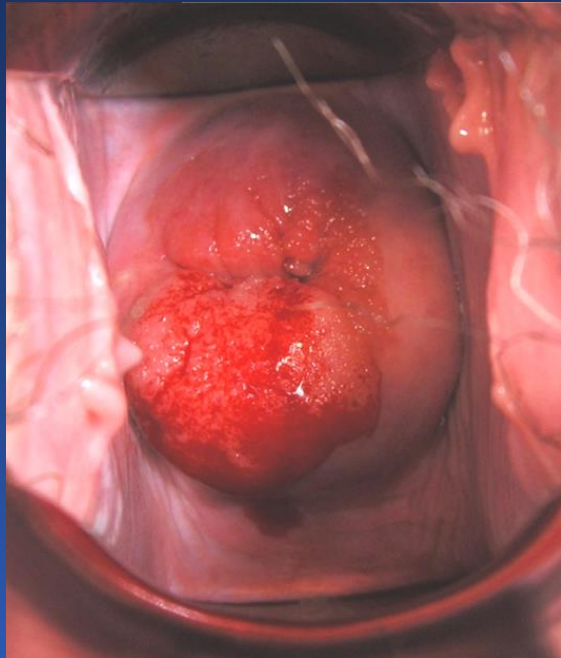


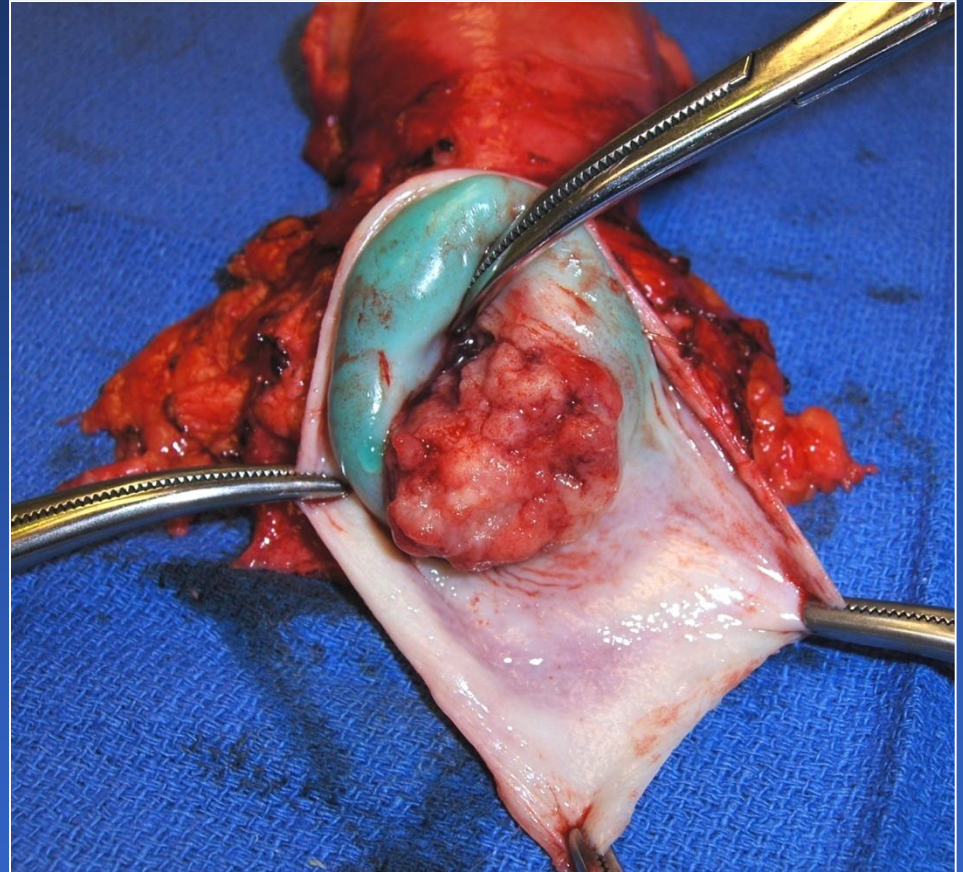
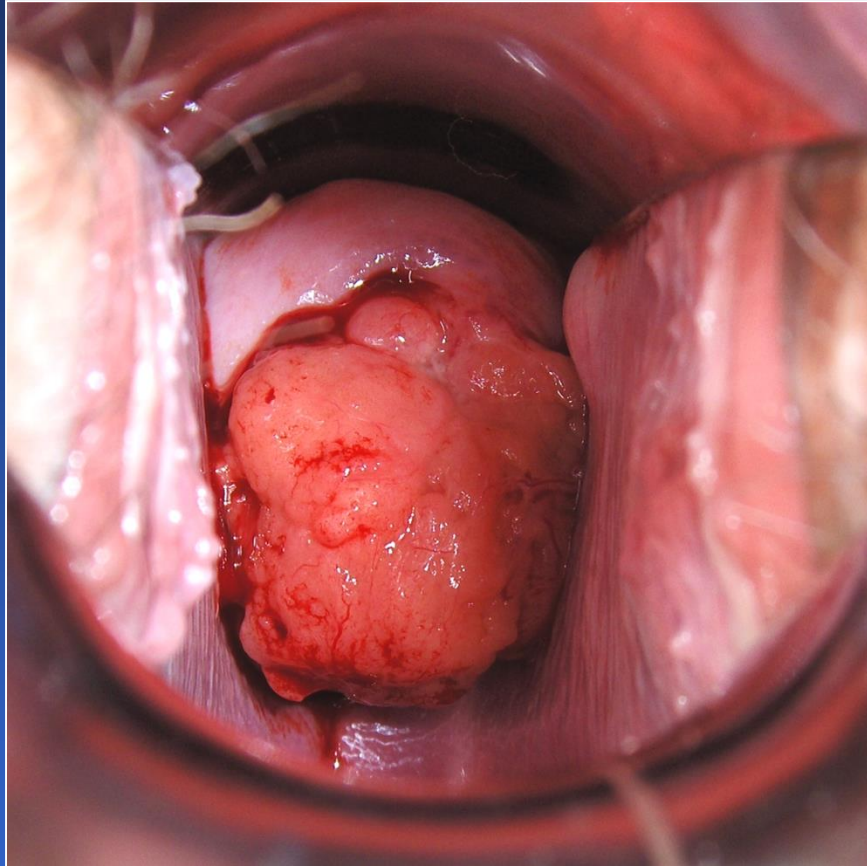
Stage IA2

cancer invasion is 3-5 mm deep and < 7 mm wide

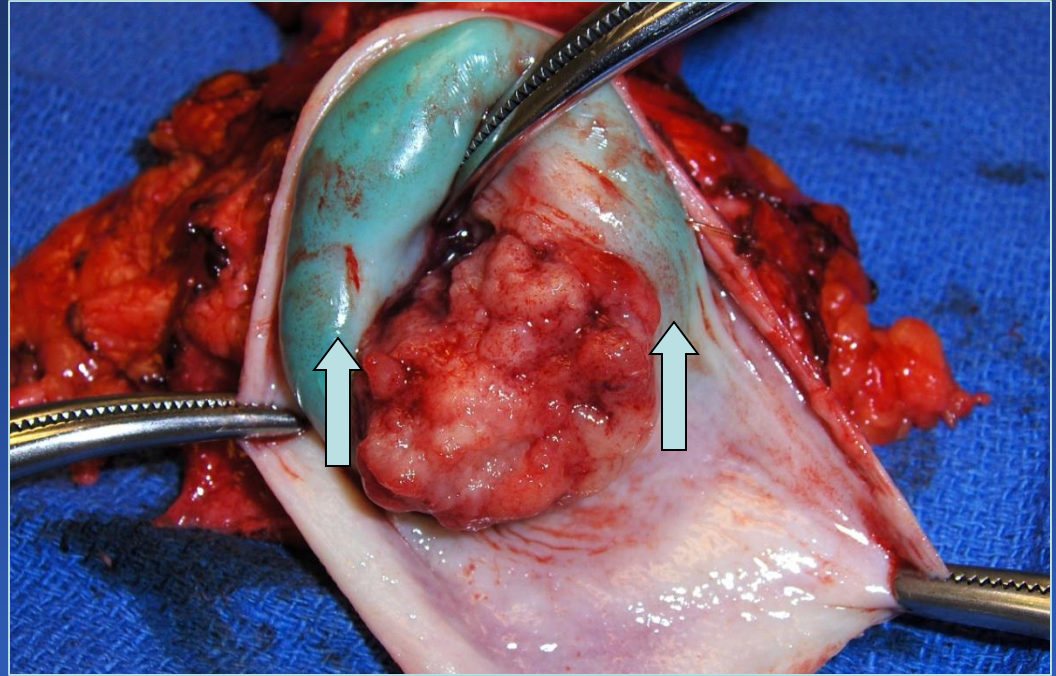
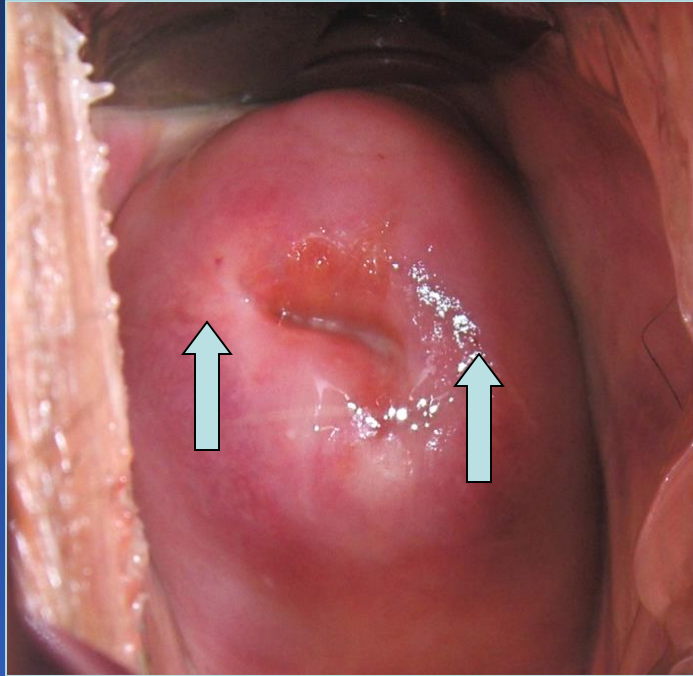


Stage IB1

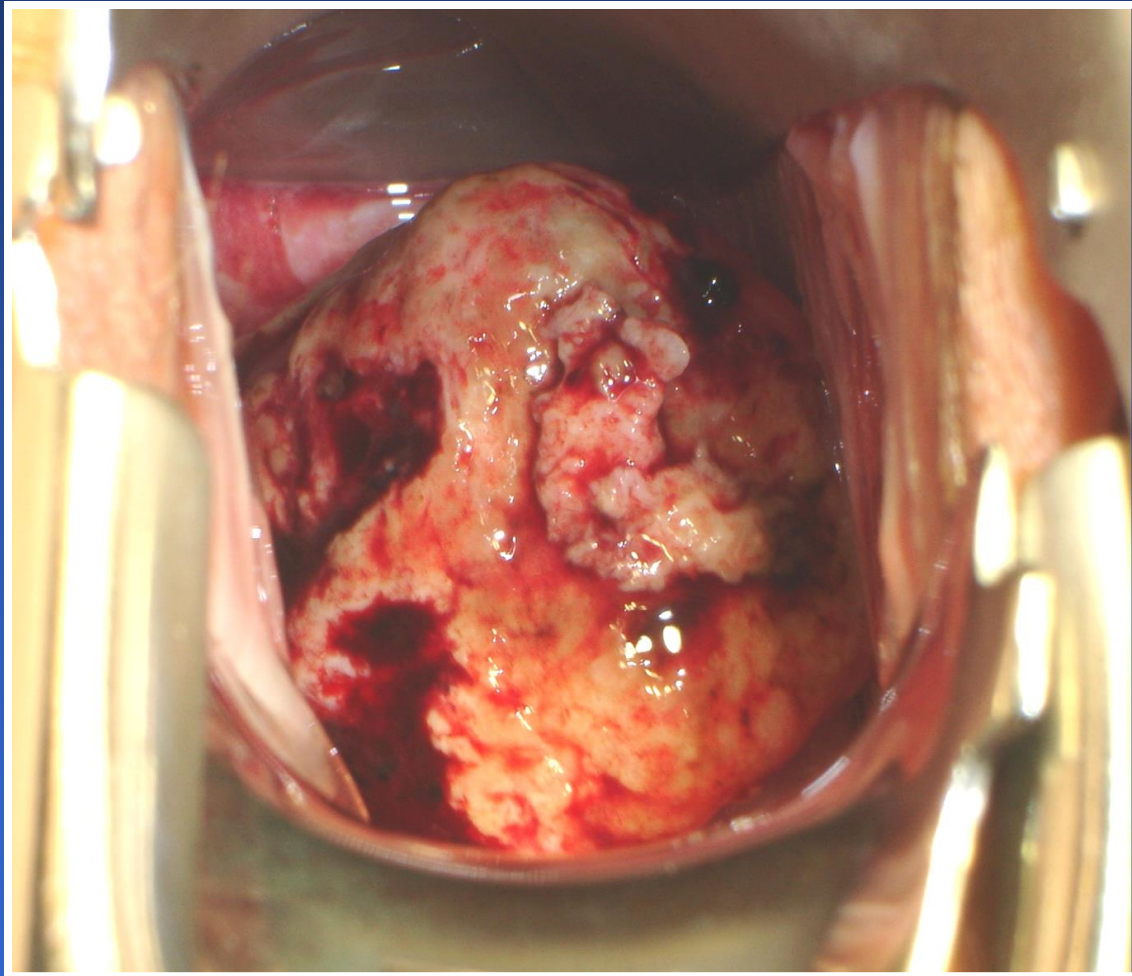




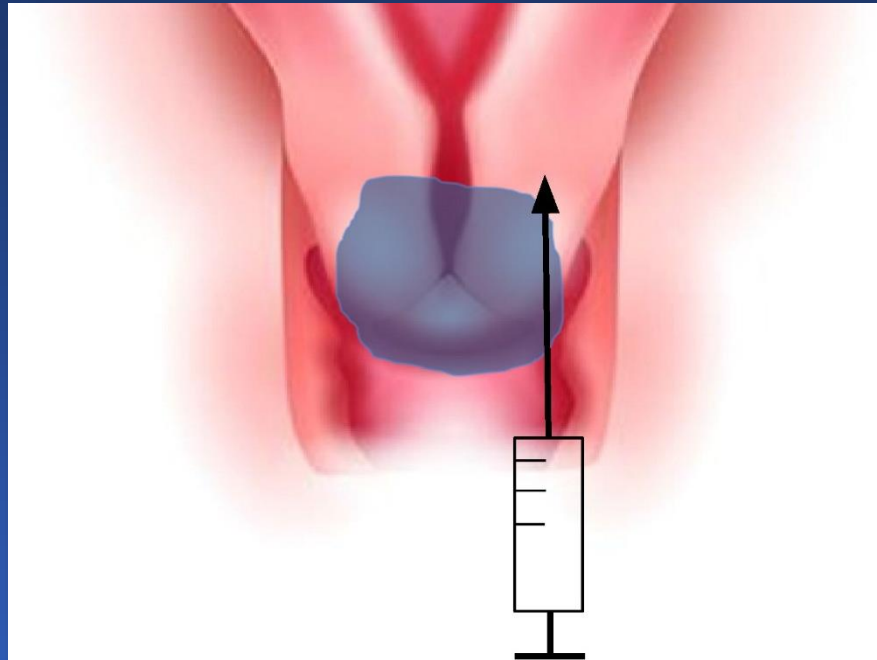
3 & 9 O'clock: 1cc superficial on each side



SLN for Large Lesions Stage IB2 Cervical Cancer



SLN biopsy in cervical cancer patients with tumors larger than 2cm and 4cm

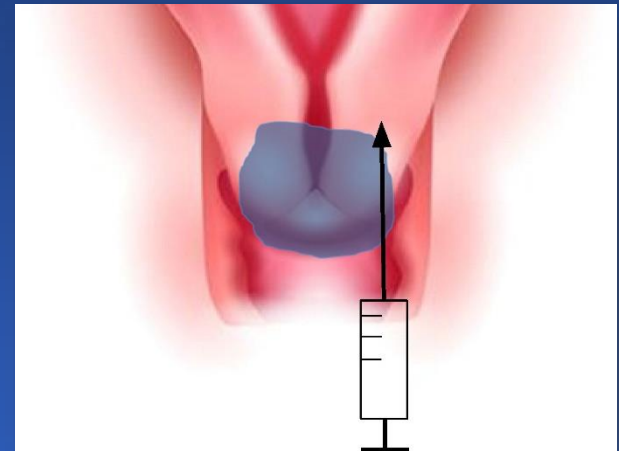


Diluted blue dye (2.5%, Guerbet, France) 5-10 mL using a (20 G) spinal needle.

The spinal needle lead through the tumor into the remaining cervical stroma according to sono topography.

SLN biopsy in cervical cancer patients with tumors larger than 2cm and 4cm

- 350 patients
- Macrometastases, micrometastases, ITC in 10%, 8%, and 4%.
- Bilateral SLN detection similar in tumors <2cm, 2-3.9cm, ≥ 4 cm (79%, 83%, 76%).
- FNR very low in all three subgroups (0.9%, 0.9%, and 0.0%).
- **CONCLUSIONS:** SLN biopsy can be equally reliable in pelvic LN staging in tumors smaller and larger than 2cm.



Ongoing Research: SENTICOL III

Accepted by the French National Cancer Institute (Fabrice Lécuru)

- A prospective multi-center international randomized study.
- Compare the outcome of patients with negative bilateral SLN (SLN Algorithm) vs. patients with negative SLN + Pelvic Lymph Node Dissection.

SENTIX Protocol

David Cibula

A prospective observational trial on sentinel lymph node biopsy in patients with early stage cervical cancer


- The null hypothesis is that the recurrence rate after SLN biopsy is non-inferior to the reference recurrence rate of 7 % (at the 24th month of follow-up) in patients after systematic pelvic lymphadenectomy, but that the less radical surgery is associated with significantly lower postoperative morbidity.


Summary: Cervical Cancer SLN

- SLN Algorithm is a standard of care in many practices.
- Its a reasonable strategy for Stage IA1 with LVI, IA2, and IB1 tumors.
- If you have not incorporated SLN mapping in your Gyn oncology practice, I encourage you to consider it.

SLN Future Directions

Fertility-Sparing Surgery in Stage I Cervical Ca

- For bigger lesions with no obvious metastasis by imaging:
 - SLN Algorithm
 - If (-)SLN  Neoadjuvant chemotherapy followed by radical trachelectomy or conization

- For smaller lesions:
 - SLN Algorithm
 - if (-) SLN  conization or simple trachelectomy

- For high-risk resected lesions:
 - Adjuvant chemotherapy, instead of radiation+chemo

Thank You



Memorial Sloan Kettering
Cancer Center™

MORE

SCIENCE.

LESS

FEAR.