Image guided surgery: probes, sentinel node and anastomosis

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Disclosures

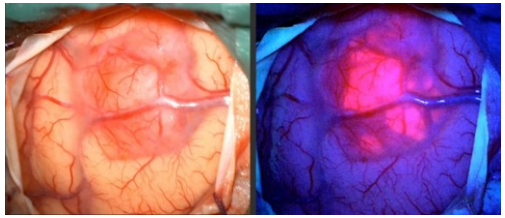
- Board member Surgical Science


CAUTION LANE CLOSED!
CONGESTION AHEAD ESTIMATED 15 MINUTE DELAY
60
SLOW

Probes used in fluorescence-guided surgery (FGS)

FDA-approved probes (2022)

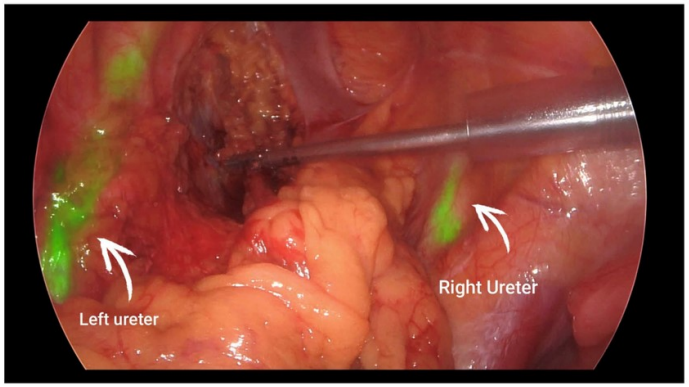
- Indocyanine green (ICG)
- Methylene blue
- 5-aminolevulinic acid (5-ALA)
- 5-ALA hexyl ester
- fluorescein sodium

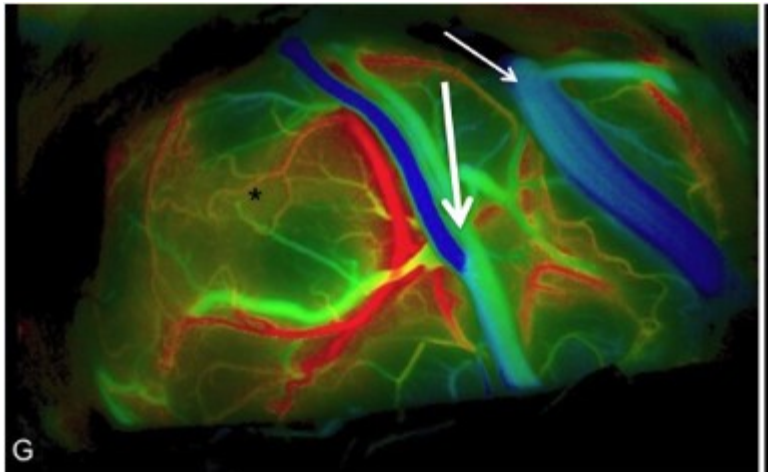


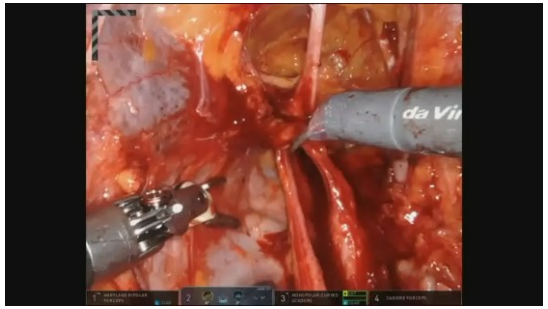
Neurosurgery

Indocyanine green (ICG)

- Water soluble, easy to handle
- Absorbs near-infrared (NIR) light at 800nm
- Emits fluorescence at 830nm
- Fluorescent pictures used as overlays may be captured using dedicated cameras
- Multiple applications in various medical fields
- In gynecologic oncology: sentinel nodes, compartment-based surgery, anastomosis perfusion assessment



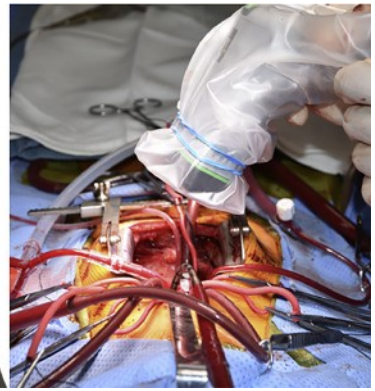




NIR detectors

Laparoscopy

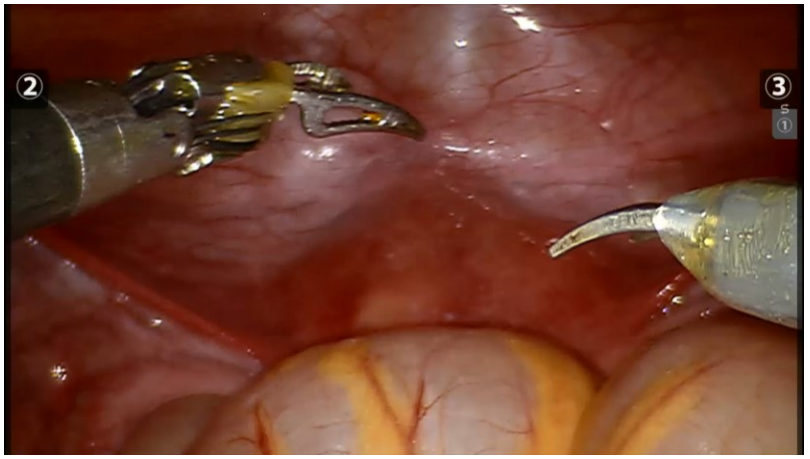
Robotics



Open

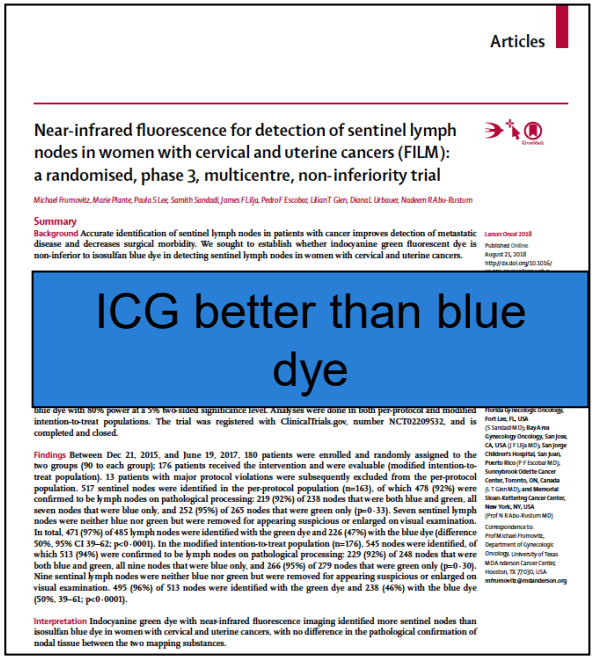
Sentinel lymph node detection in GYN oncology

- Cervical injection of ICG - superior to fundal
- Superficial injection adequate
- 2-4 injections
- Various amounts in different studies



	FIRES	SHREC
n injections	2	4*
Volume	2 ml	1 ml*
Amount ICG	1 mg	2,5 mg*
Mapping	52%	94%

SLN in endometrial cancer – landmark studies



Articles

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

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

Summary

Background Accurate identification of sentinel lymph nodes in patients with cancer improves detection of metastatic disease and decreases surgical morbidity. We sought to establish whether indocyanine green fluorescent dye is non-inferior to isosulfan blue dye in detecting sentinel lymph nodes in women with cervical and uterine cancers.

Lancet Oncol 2018

Published Online August 21, 2018

ICG better than blue dye

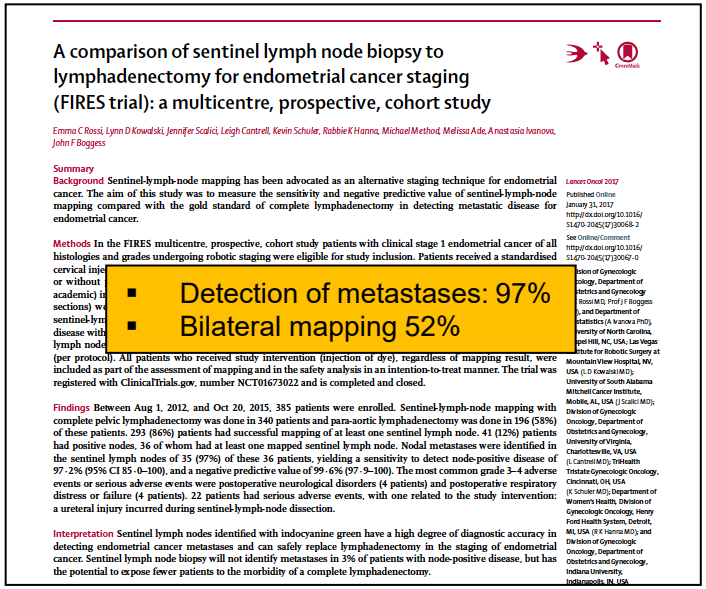
blue dye with 80% power at a 5% two-sided significance level. Analyses were done in both per-protocol and modified intention-to-treat populations. The trial was registered with ClinicalTrials.gov, number NCT02209532, and is completed and closed.

Findings Between Dec 21, 2015, and June 19, 2017, 180 patients were enrolled and randomly assigned to the two groups (90 to each group); 176 patients received the intervention and were evaluable (modified intention-to-treat population). 13 patients with major protocol violations were subsequently excluded from the per-protocol population. 517 sentinel nodes were identified in the per-protocol population (n=163), of which 478 (92%) were confirmed to be lymph nodes on pathological processing: 219 (92%) of 238 nodes that were both blue and green, all seven nodes that were blue only, and 252 (95%) of 265 nodes that were green only (p<0·33). Seven sentinel lymph nodes were neither blue nor green but were removed for appearing suspicious or enlarged on visual examination. In total, 471 (97%) of 485 lymph nodes were identified with the green dye and 226 (47%) with the blue dye (difference 50%, 95% CI 39–62; p<0·0001). In the modified intention-to-treat population (n=176), 545 nodes were identified, of which 513 (94%) were confirmed to be lymph nodes on pathological processing: 229 (92%) of 248 nodes that were both blue and green, all nine nodes that were blue only, and 266 (95%) of 279 nodes that were green only (p=0·30). Nine sentinel lymph nodes were neither blue nor green but were removed for appearing suspicious or enlarged on visual examination. 495 (96%) of 513 nodes were identified with the green dye and 238 (46%) with the blue dye (50%, 39–61; p<0·0001).

Interpretation Indocyanine green dye with near-infrared fluorescence imaging identified more sentinel nodes than isosulfan blue dye in women with cervical and uterine cancers, with no difference in the pathological confirmation of nodal tissue between the two mapping substances.

Florida Gynecologic Oncology, Fort Lee, FL, USA (S Sandadi MD); Bay Area Gynecology Oncology, San Jose, CA, USA (J F Lilja MD); San Juego Children's Hospital, San Juan, Puerto Rico (P F Escobar MD); Sunnybrook Odette Cancer Center, Toronto, ON, Canada (L T Gien MD); and Memorial Sloan-Kettering Cancer Center, New York, NY, USA (Prof N R Abu-Rustum MD)

Correspondence to: Prof Michael Frumovitz, Department of Gynecologic Oncology, University of Texas MDA nderson Cancer Center, Houston, TX 77030, USA mfrumovitz@mdanderson.org



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

Summary

Background Sentinel-lymph-node mapping has been advocated as an alternative staging technique for endometrial cancer. The aim of this study was to measure the sensitivity and negative predictive value of sentinel-lymph-node mapping compared with the gold standard of complete lymphadenectomy in detecting metastatic disease for endometrial cancer.

Lancet Oncol 2017

Published Online January 31, 2017

- Detection of metastases: 97%
- Bilateral mapping 52%

(per protocol). All patients who received study intervention (injection of dye), regardless of mapping result, were included as part of the assessment of mapping and in the safety analysis in an intention-to-treat manner. The trial was registered with ClinicalTrials.gov, number NCT01673022 and is completed and closed.

Findings Between Aug 1, 2012, and Oct 20, 2015, 385 patients were enrolled. Sentinel-lymph-node mapping with complete pelvic lymphadenectomy was done in 340 patients and para-aortic lymphadenectomy was done in 196 (58%) of these patients. 293 (86%) patients had successful mapping of at least one sentinel lymph node. 41 (12%) patients had positive nodes, 36 of whom had at least one mapped sentinel lymph node. Nodal metastases were identified in the sentinel lymph nodes of 35 (97%) of these 36 patients, yielding a sensitivity to detect node-positive disease of 97·2% (95% CI 85·0–100), and a negative predictive value of 99·6% (97·9–100). The most common grade 3–4 adverse events or serious adverse events were postoperative neurological disorders (4 patients) and postoperative respiratory distress or failure (4 patients). 22 patients had serious adverse events, with one related to the study intervention: a ureteral injury incurred during sentinel-lymph-node dissection.

Interpretation Sentinel lymph nodes identified with indocyanine green have a high degree of diagnostic accuracy in detecting endometrial cancer metastases and can safely replace lymphadenectomy in the staging of endometrial cancer. Sentinel lymph node biopsy will not identify metastases in 3% of patients with node-positive disease, but has the potential to expose fewer patients to the morbidity of a complete lymphadenectomy.

http://dx.doi.org/10.1016/S1470-2045(17)30068-2

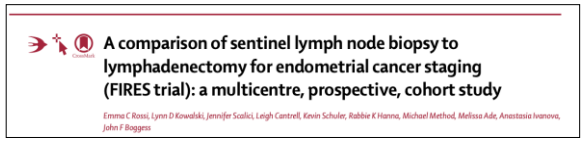
See Online/Comment http://dx.doi.org/10.1016/S1470-2045(17)30067-0

...ology, Department of ...stetrics and Gynecology ...Rossi MD, Prof J F Boggess ..., and Department of ...statistics (A Ivanova PhD), ...versity of North Carolina, ...pel Hill, NC, USA; Las Vegas ...ttute for Robotic Surgery at Mountain View Hospital, NV, USA (L D Kowalski MD); University of South Alabama Mitchell Cancer Institute, Mobile, AL, USA (J Scalici MD); Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Virginia, Charlottesville, VA, USA (L Cantrell MD); TriHealth Tristate Gynecologic Oncology, Cincinnati, OH, USA (K Schuler MD); Department of Women's Health, Division of Gynecologic Oncology, Henry Ford Health System, Detroit, MI, USA (R K Hanna MD); and Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Indiana University, Indianapolis, IN, USA

FILM: Frumowitz et al 2018 Lancet Oncol

FIRES: Rossi et al 2017 Lancet Oncol

Endometrial cancer: SLN algorithms may replace LND



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

European Journal of Cancer 116 (2019) 77–85

Available online at www.sciencedirect.com

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journal homepage: www.ejcancer.com

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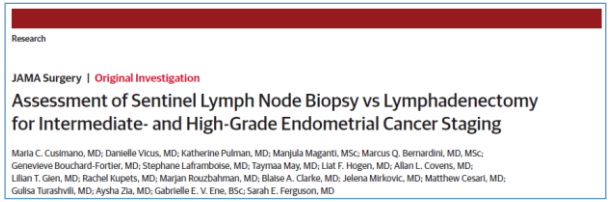
Original Research

Pelvic Sentinel lymph node detection in High-Risk Endometrial Cancer (SHREC-trial)—the final step towards a paradigm shift in surgical staging

Jan Persson [a,b,*], Sahar Salehi [c], Michele Bollino [a,b], Celine Lönnerfors [a,b], Henrik Falconer [c], Barbara Geppert [a,b]



Research

JAMA Surgery | Original Investigation

Assessment of Sentinel Lymph Node Biopsy vs Lymphadenectomy for Intermediate- and High-Grade Endometrial Cancer Staging

Maria C. Cusimano, MD; Danielle Vicus, MD; Katherine Pulman, MD; Manjula Maganti, MSc; Marcus Q. Bernardini, MD, MSc; Genevieve Bouchard-Fortier, MD; Stephane Laframboise, MD; Taymaa May, MD; Liat F. Hogen, MD; Allan L. Covens, MD; Lilian T. Glen, MD; Rachel Kupets, MD; Marjan Rouzbahman, MD; Blaise A. Clarke, MD; Jelena Mirkovic, MD; Matthew Cesari, MD; Gulisa Turashvili, MD; Aysha Zia, MD; Gabrielle E. V. Ene, BSc; Sarah E. Ferguson, MD

- Reinjection
- Surgical experience

	FIRES	SHREC	SENTOR
n cases	340	257	156
Bilat mapping	54%	94%	78%
n LN+	36	54	26
Sensitivity	97%	100%	96%
NPV	99%	100%	99%

Adhering to the SLN algorithm

- Surgical proficiency crucial
- Reinjection in case of failed mapping
- Pay attention to atypical SLN positions
- LPP probably not important
- Recognising and removing macro metastases critical
- Ultrastaging

Defining the learning curve for successful staging with sentinel lymph node biopsy for endometrial cancer among surgeons at an academic institution

PDF

Katherine Tucker[1], Stuart-Allison Staley[1], Paola A Gehrig[1], John T Soper[1], John F Boggess[1], Anastasia Ivanova[2] and Emma Rossi[1]

Author affiliations

Abstract

Background Sentinel lymph node (SLN) biopsy is increasingly used in endometrial cancer staging; however, success of the technique is variable, and the learning curve needs to be better understood. Success is defined as identification of a SLN specimen containing nodal tissue in bilateral hemi-pelvises.

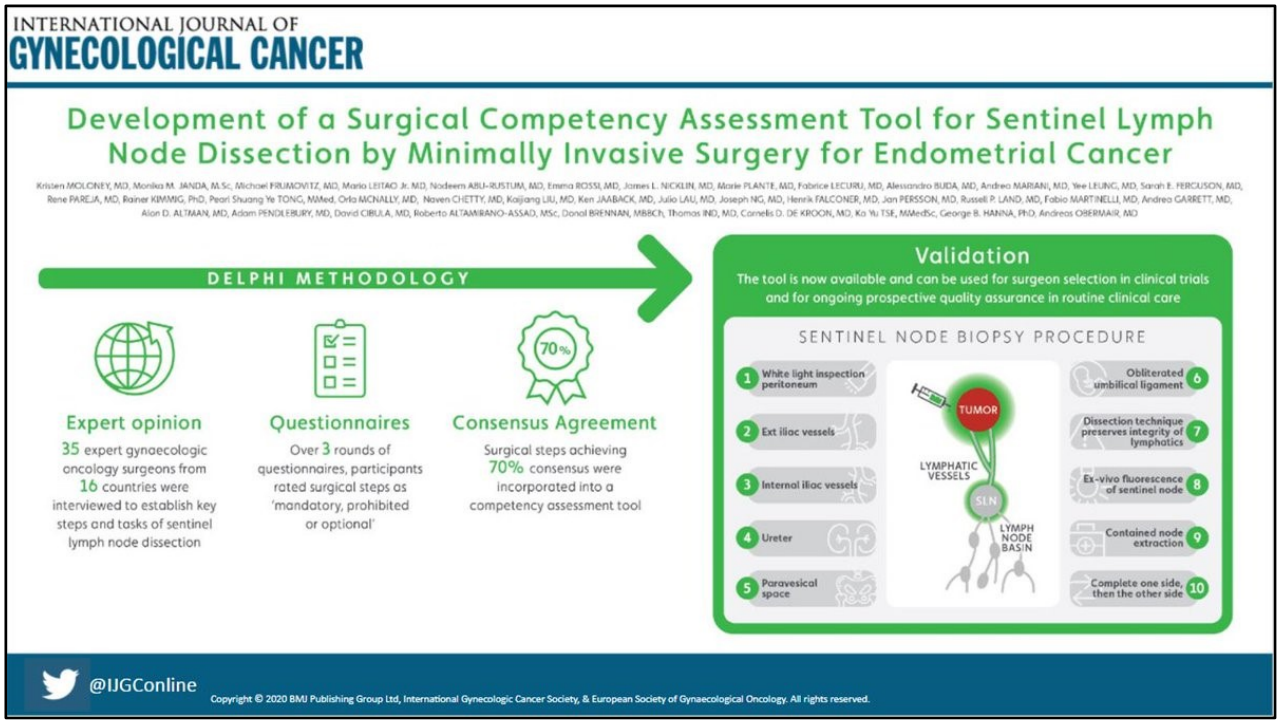
Objective To assess the learning curve of surgeons at an academic institution in performing successful SLN mapping and biopsy during robotic staging for endometrial cancer.

Methods After institutional review board approval, patients who underwent staging with robotic SLN mapping using indocyanine green at a single academic program between July 2012 and December 2017 were identified. Demographic, pathologic, and surgical data were retrospectively collected from the medical records. Descriptive and comparative statistics were performed. Surgeon rates of successful bilateral SLN mapping and removal of lymphoid-containing SLN specimens were compared. A logistic model was used to analyze the probability of successful SLN mapping and removal of lymph node-containing tissue with increasing number of procedures performed.

Results Three hundred and seventeen patients met the eligibility criteria. Most had early-stage, low-grade endometrial cancer. A total of 194 (61%) patients had successful bilateral mapping. Among seven surgeons, a plateau in rates of successful bilateral mapping was achieved after 40 cases. No linear correlation was seen between the number of surgeries performed and the rate of removal of lymph node-containing tissue among surgeons. Each additional 10 procedures performed was associated with a 5% and an 11% increase in the odds of successful SLN mapping and removal of lymph node-containing tissue, respectively.

Discussion The successful removal of lymph node-containing specimens appears to be a surgeon-specific phenomenon. The plateau of the learning curve for successful bilateral mapping seems to be reached at around 40 cases. These first 40 cases offer a time for auditing of individual rates of SLN mapping and removal to identify surgeons who may benefit from procedure-specific remediation.

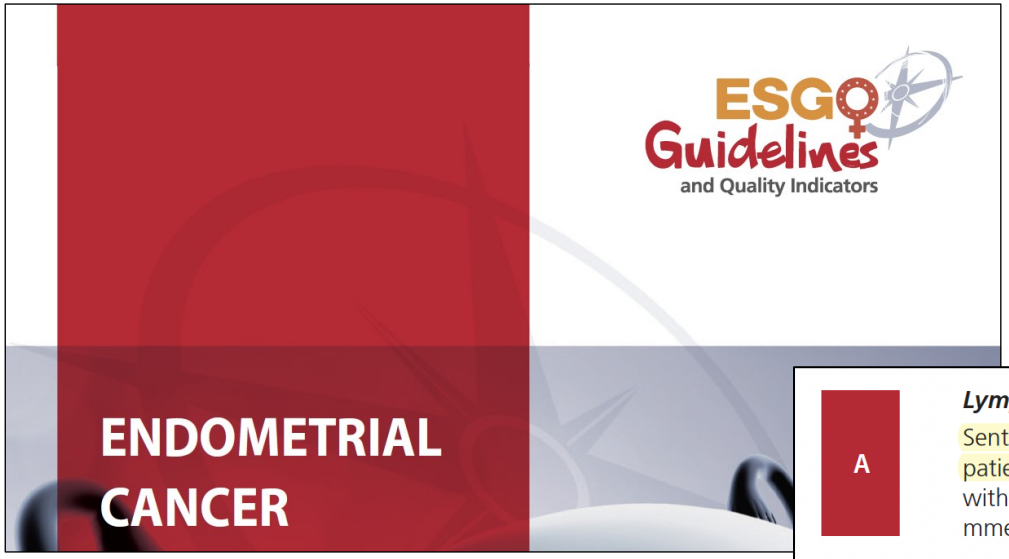
Competency assessment tools

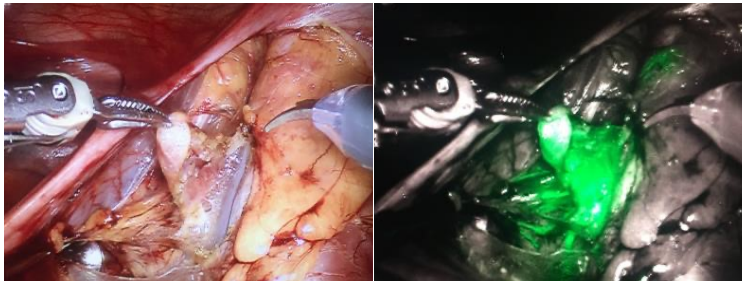


Moloney et al al IJGC 2021

- Developed through Deplhi methodology: 35 experts from 16 countries
- Consensus agreement identified 21 mandatory and 3 prohibited steps to complete SLN
- May be used for surgeon selection in clinical trials and routine clinical care

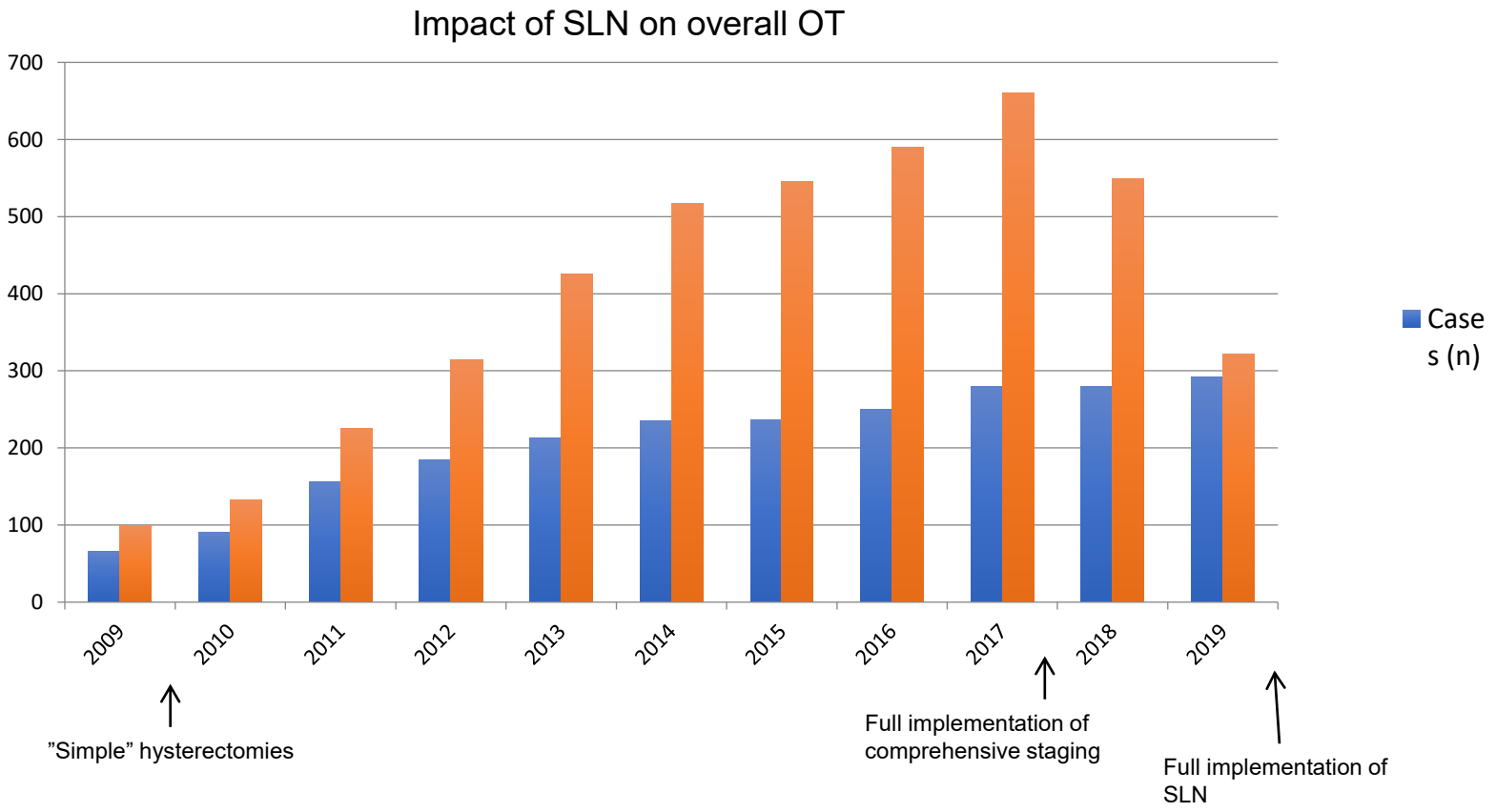
ESGO guidelines SLN in endometrial cancer





A	***Lymph node staging*** Sentinel lymph node biopsy can be considered for staging purposes in patients with low-risk/intermediate-risk disease. It can be omitted in cases without myometrial invasion. Systematic lymphadenectomy is not recommended in this group.
B	Surgical lymph node staging should be performed in patients with high–intermediate-risk/high-risk disease. Sentinel lymph node biopsy is an acceptable alternative to systematic lymphadenectomy for lymph node staging in stage I/II.

GYN robotic service Karolinska



Do patterns of SLN differ between endometrial and cervical cancer?

Contents lists available at ScienceDirect

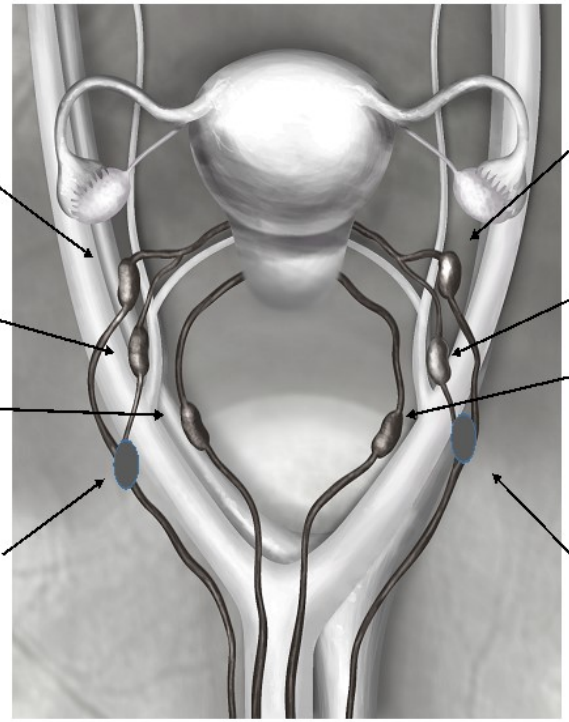
Gynecologic Oncology

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

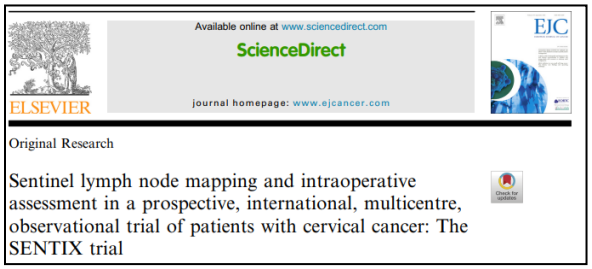
Similar distribution of pelvic sentinel lymph nodes and nodal metastases in cervical and endometrial cancer. A prospective study based on lymphatic anatomy

Oscar Lührs [a,c], Michele Bollino [b,c], Linnea Ekdahl [c], Céline Lönnerfors [c], Barbara Geppert [c], Jan Persson [c,*]

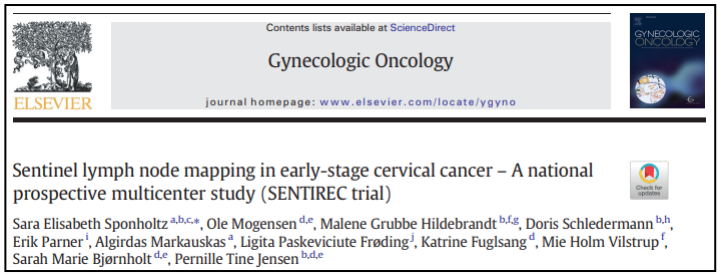
Positions of SLN in cervical cancer following cervical injection of ICG



SLN in cervical cancer: mapping and accuracy



SENTIX: Cibula 2020



SENTIREC: Sponholtz 2021

- Prospective observational multicenter (47 sites)
- SLN only for CC 1A-IB2
- 395 patients
- Bilateral mapping 91% (all tracers)
- Frozen section: 46% sensitivity N1

- Prospective observational multicenter (3 sites)
- CC >20mm: SLN + full LND
- 245 patients
- Bilateral mapping 82% (ICG only)
- Sensitivity 96.3 % (NPV 98.7%
- PET-CT: 14% sensitivity N1

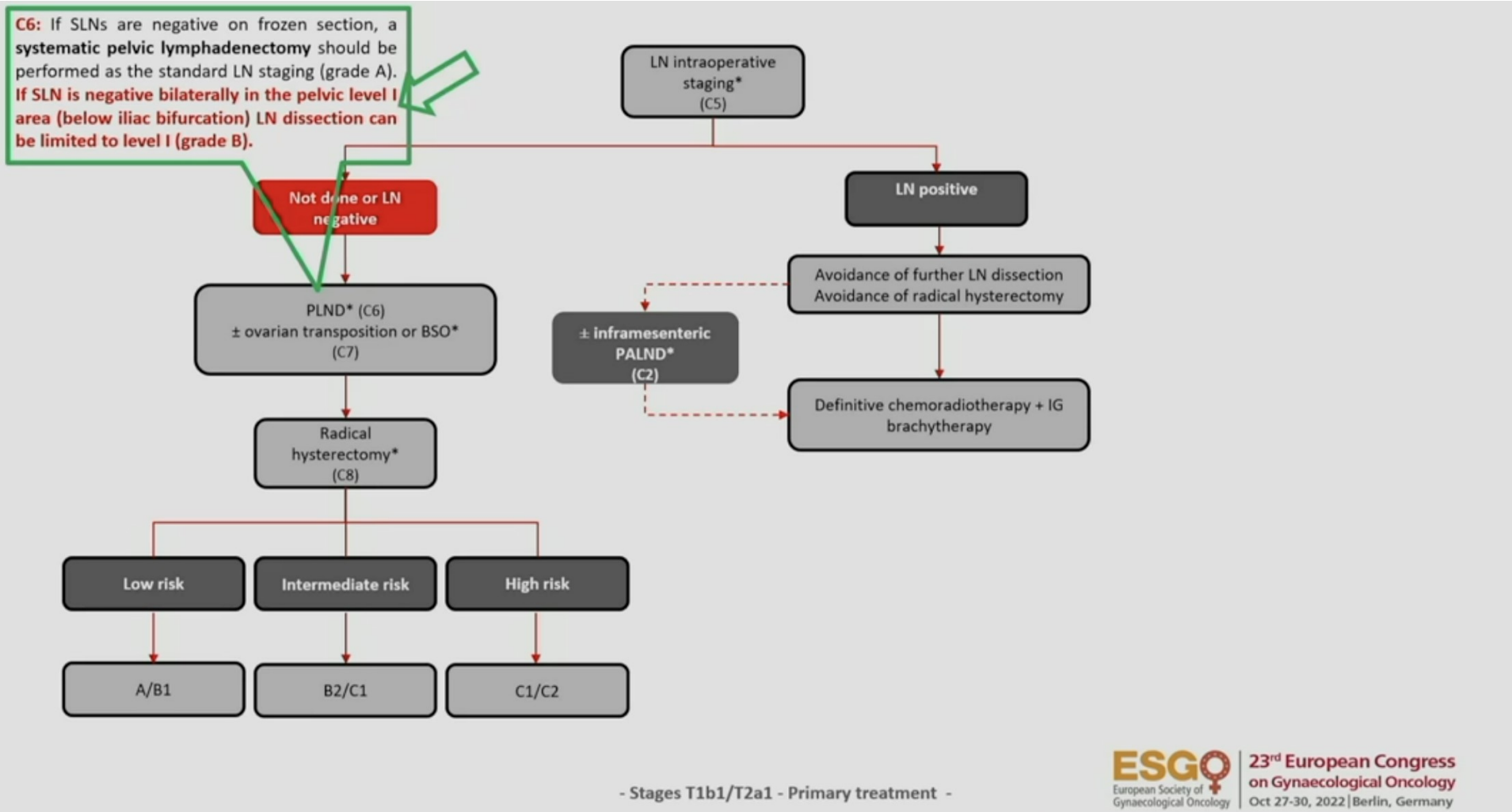
$$\mathrm{NPV} = \frac{\mathrm{specificity} \times (1 - \mathrm{prevalence})}{\mathrm{specificity} \times (1 - \mathrm{prevalence}) + (1 - \mathrm{sensitivity}) \times \mathrm{prevalence}}$$

SLN in cervical cancer: survival

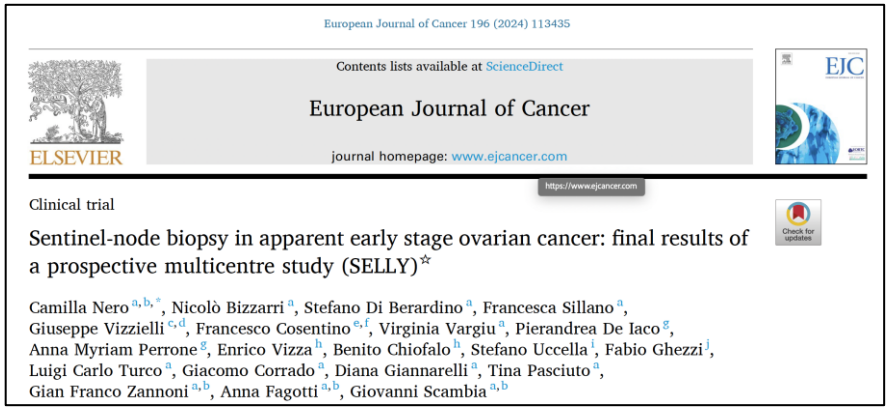
- Data expected from SENTIX (observational)
- Data expected from SENTICOL-3 (RCT)
- Data expected from PHENIX (RCT)

- SENTIX abstract ESGO: 2-year DFS 93.3%, OS 97.9%
- Data from SENTICOL-2: OS SLN 95% vs SLN+LND 96%
- Pooled data from senticol-1 and 2: DFS SLN 85% vs LND 80% (Balaya 2022)

SLN only in cervical cancer – limited to IA disease?



ICG and SLN in ovarian cancer



European Journal of Cancer 196 (2024) 113435

Contents lists available at ScienceDirect

European Journal of Cancer

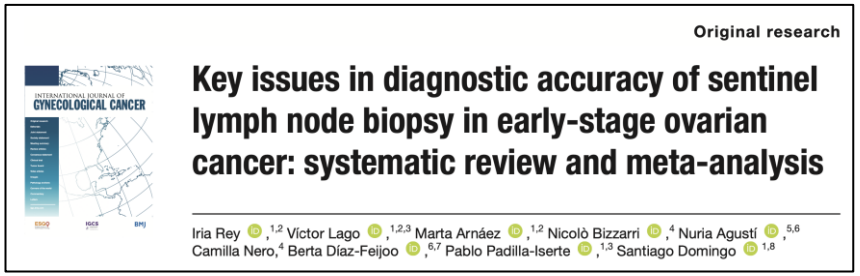
journal homepage: www.ejcancer.com

Clinical trial

Sentinel-node biopsy in apparent early stage ovarian cancer: final results of a prospective multicentre study (SELLY)☆

Camilla Nero [a,b,*], Nicolò Bizzarri [a], Stefano Di Berardino [a], Francesca Sillano [a], Giuseppe Vizzielli [c,d], Francesco Cosentino [e,f], Virginia Vargiu [a], Pierandrea De Iaco [g], Anna Myriam Perrone [g], Enrico Vizza [h], Benito Chiofalo [h], Stefano Uccella [i], Fabio Ghezzi [j], Luigi Carlo Turco [a], Giacomo Corrado [a], Diana Giannarelli [a], Tina Pasciuto [a], Gian Franco Zannoni [a,b], Anna Fagotti [a,b], Giovanni Scambia [a,b]

Conclusions: In a multicenter setting, identifying sentinel-lymph nodes in apparent early stage epithelial ovarian cancer did not reach the expected sensitivity: 1 of 4 patients might have metastatic lymphatic disease unrecognized by sentinel-lymph-node biopsy. Nevertheless, 35.0 % of node positive patients was identified only thanks to ultra-staging protocol on sentinel-lymph-nodes.



Original research

Key issues in diagnostic accuracy of sentinel lymph node biopsy in early-stage ovarian cancer: systematic review and meta-analysis

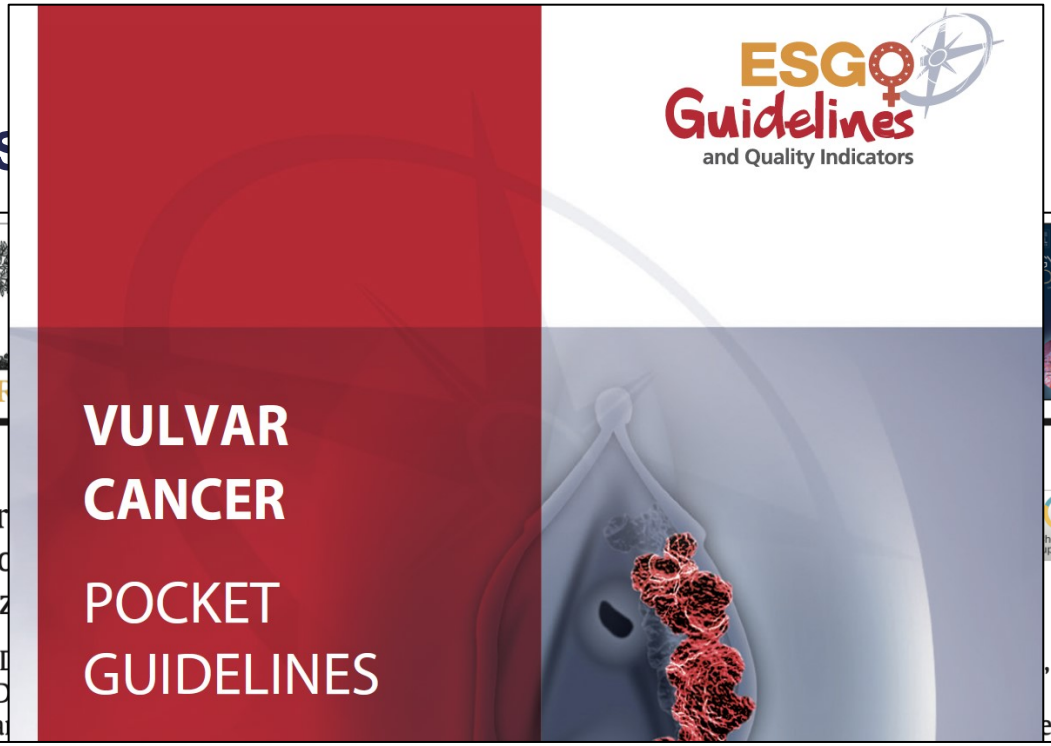
Iria Rey [1,2], Víctor Lago [1,2,3], Marta Arnáez [1,2], Nicolò Bizzarri [4], Nuria Agustí [5,6], Camilla Nero,[4] Berta Díaz-Feijoo [6,7], Pablo Padilla-Iserte [1,3], Santiago Domingo [1,8]

Results 239 patients from four studies were included. The SLN detection rate was 59.5% (95% CI 50.2 to 68.1%) and 64.4% (95% CI 58.2 to 70.2%) for the pelvic and para-aortic fields, respectively. The use of technetium-99

Conclusion The use of ^{99m}Tc in combination with a low volume injection (0.2–0.5 mL) of indocyanine green increased SLN detection rates. In apparent early stage epithelial ovarian cancer, SLN is a feasible technique with a high diagnostic accuracy.

- Multiple patterns of nodal dissemination
- Stage I disease rare
- Heterogenous situations (prior oophorectomy vs intact ovaries)
- Not part of most guidelines
- Minimally invasive surgery?

ICG and S



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SLN procedure

B	The SLN procedure is recommended in patients with unifocal cancers of <4 cm, >T1a, without suspicious inguinofemoral nodes.
C	There are insufficient data to confirm the efficacy and safety of the SLN procedure in the case of recurrent disease.
A	Use of radioactive tracer (Tc99/nanocolloid) is mandatory.
B	Combination detection techniques with isotope and either blue dye or indocyanine green (ICG) are recommended.

DOI: 10.1111/codi.16883

META-ANALYSIS

Indocyanine green fluorescence angiography could reduce the risk of anastomotic leakage in rectal cancer surgery: a systematic review and meta-analysis of randomized controlled trials

Alessio Lucarini[1,2] | Andrea Martina Guida[1,3] | Marion Orville[1] | Yves Panis[1]

Results: Four RCTs were included for analysis, with a total of 1510 patients (743 controls and 767 ICG patients). The rate of AL was 9% in the ICG group (69/767) and 13.9% (103/743) in the control group ($p = 0.003$, RR −0.5, 95% CI −0.827 to −0.172, heterogeneity test 0%, $p = 0.460$). The RD in terms of incidence of AL was significantly decreased by 4.51% ($p = 0.031$, 95% CI −0.086 to −0.004, heterogeneity test 28%, $p = 0.182$) when using ICG.

Conclusion: Our meta-analysis suggested that use of ICG during rectal cancer surgery could reduce the rate of AL.

Lancet 2024: Negative trial

ICG for bowel resections in GYN oncology

INTERNATIONAL JOURNAL OF
GYNECOLOGICAL CANCER

Assessment of Anastomotic Perfusion Using Indocyanine Green Fluorescence Angiography Following Bowel Resection for Gynecologic Malignancies: An Instructional Surgical Video

Elisabeth Spénard, Julie M.V. Nguyen, Taymaa May*

Objective:
Demonstrate a **step-by-step surgical approach** to the use of indocyanine green fluorescence angiography (ICG-FA)

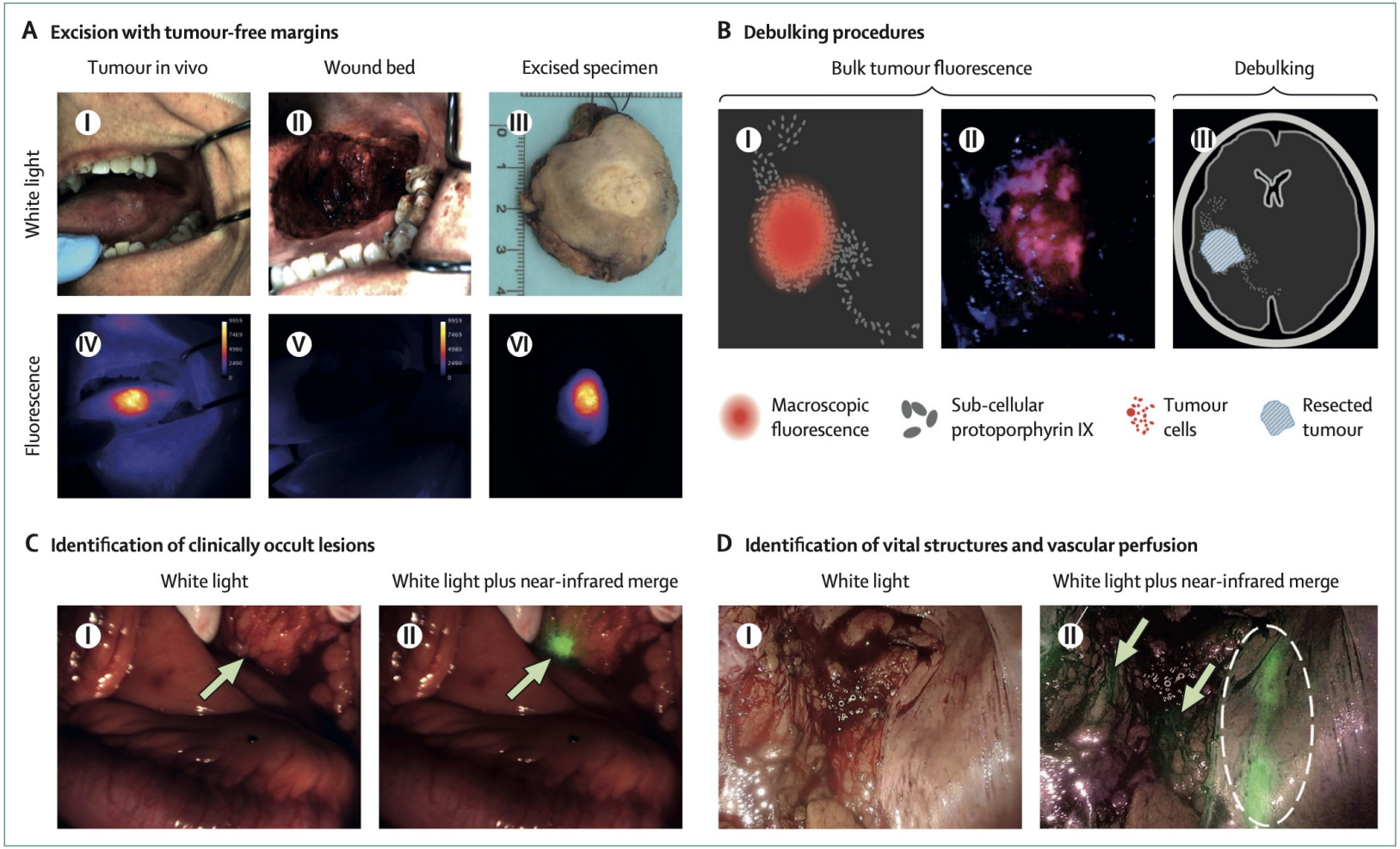
5-Step technique

1. Perform bowel anastomosis
2. Inspect and assess the anastomosis for mechanical integrity
3. Prepare near-infrared instruments and room setting
4. Administer 3 mL IV ICG (2.5mg/mL), followed by 10 mL NS
5. Observe and interpret anastomotic perfusion using near-infrared technology

For a **safe use** of ICG-FA:
- Dilute 25 mg ICG in 10 mL H20
- Maximum dose of ICG < 2mg/kg
- ICG is metabolised by the liver
- ICG contains sodium iodine

Conclusion:
- ICG-FA is **a safe technique** that can be used to aid intra-operative decision making in patients undergoing bowel resection
- ICG-FA is an important tool that **may decrease the risk of anastomotic leak** after bowel resection

Future perspectives: from diagnostic to therapeutic



original reports

A Phase III Study of Pafolacianine Injection (OTL38) for Intraoperative Imaging of Folate Receptor–Positive Ovarian Cancer (Study 006)

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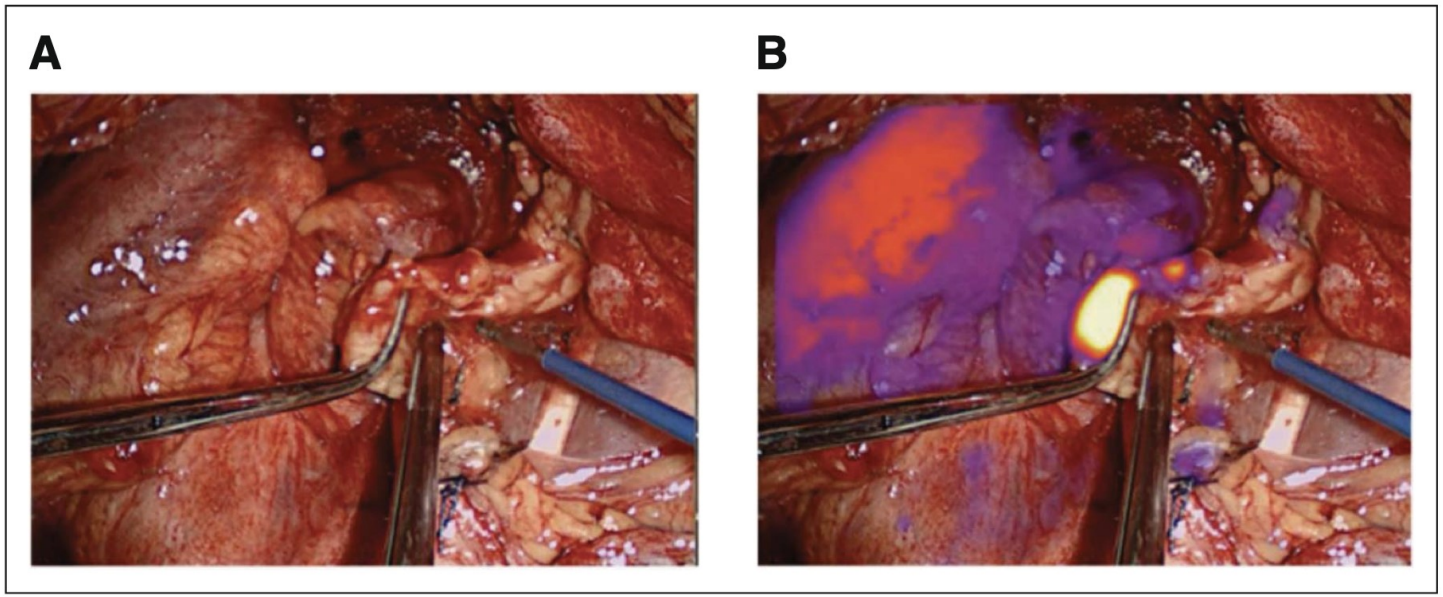

FIG 4. Visualization of ovarian cancer lesions in the right paracolic gutter using (A) normal white light compared with (B) NIR fluorescence imaging following pafolacianine injection. NIR, near-infrared imaging.

Thanks for the attention!

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