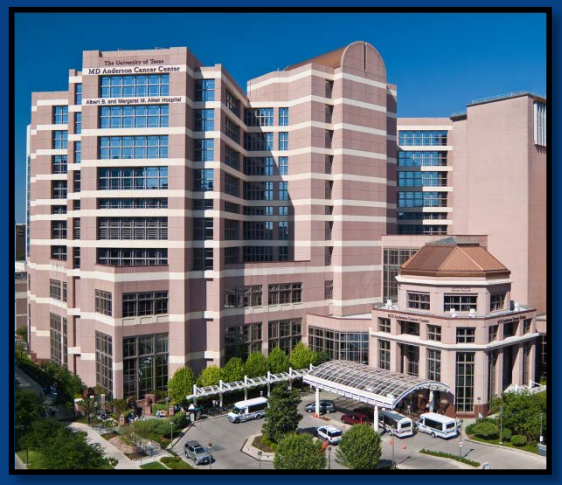

Intraoperative Use of Indocyanine Green for Lymphatic Mapping in Cervical and Uterine Cancers

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Overview

- Issue with current codes
- Indocyanine Green (ICG) imaging agent
- Lymphatic mapping
- FILM Trial results

Issue with Current Codes

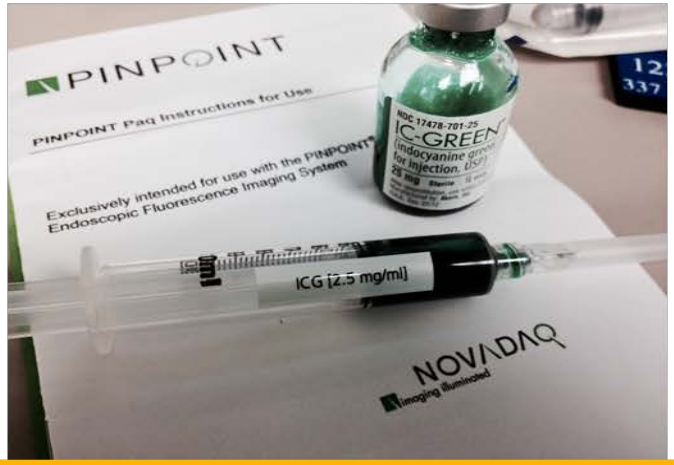
Existing codes below fail to capture the intraoperative use of ICG during lymphatic mapping

- **07JN8ZZ** Inspection of Lymphatic, Via Natural or Artificial Opening Endoscopic
- **4A1685Z** Monitoring of Lymphatic Flow, Via Natural or Artificial Opening Endoscopic

New codes will help coding professionals capture the use of ICG during this procedure and help providers further evaluate its associated patient outcomes

Intraoperative Use of the PINPOINT Imaging System and ICG Imaging Agent

PINPOINT is currently indicated for use to provide real time endoscopic visible and near-infrared fluorescence imaging



FDA approval expected before the end of this year for cervical and uterine lymphatic mapping

Increased Intraoperative Precision

Current FDA indications for ICG: **intravenous** injection to determine cardiac output, to evaluate perfusion of solid organs, and to perform ophthalmic angiography

FDA submission: on-label use of **interstitial** injection of ICG *combined with near infrared imaging* for the identification of lymph nodes during lymphatic mapping in cervical and uterine cancers

Gynecological Cancers

- Uterine Cancer
  - Most prevalent gynecologic cancer
  - 61,380 estimated new cases in 2017[1]
  - Mortality rates rising an average 1.4% annually[1]

- Cervical Cancer
  - Affects fewer women
  - 12,820 estimated new cases last year[1]

1. Surveillance, Epidemiology, and End Results (SEER) Program Cancer Stat Facts: Uterine Cancer. National Cancer Institute. Bethesda, MD. Available from: http://seer.cancer.gov/statfacts/html/corp.html. Accessed on August 17, 2018.

Historical Surgical Management: Lymphadenectomy

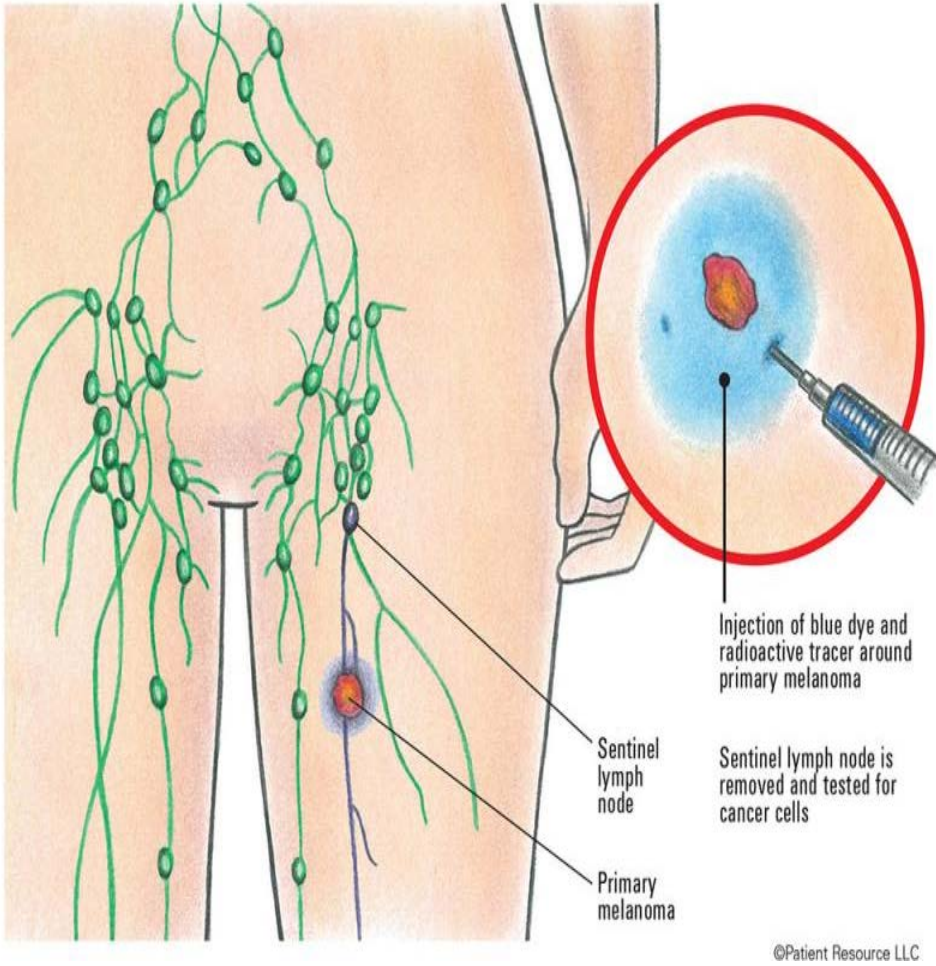
- **What is it?**
  - Removal of one or more groups of lymph nodes[2]

- Unwarranted excess costs due to comprehensive lymphadenectomy[2]
  - Prolonged operating room time
  - Prolonged anesthesia
  - Increased blood loss
  - Vascular and nerve damage
  - Increased conversion rate from laparoscopy to laparotomy to complete the operation successfully
  - Other serious adverse events
  - Increased risk of surgery-related morbidity or lymphedema or lymphocyst formation

2. Abu-Rustum NR. Sentinel Lymph Node Mapping for Endometrial Cancer: A Modern Approach to Surgical Staging. Journal of the National Comprehensive Cancer Network. 2014; 12(2):288-297.

Lymphatic Mapping: Compared to Complete Lymphadenectomy

- **What is lymphatic mapping?**
  - *Image-guided procedure* that uses dyes or tracers to optimize selective lymph node removal[3]
- **What is the concept behind it?**
  - The lymph drains in an orderly pattern *away from the tumor* through the lymphatic system to the first lymph node or lymph nodes (i.e., sentinel LNs or SLNs)[3]
- **How does it work?**
  - Inject a dye or tracer to identify lymph node normally very difficult to identify due to adipose tissue, inflammatory tissue, adhesions, etc.[3]
  - Observe the lymphatic flow through the channels as it incorporates into a lymph node[3]



3. National Cancer Institute. Sentinel Lymph Node Biopsy. https://www.cancer.gov/about-cancer/diagnosis-staging/staging/sentinel-node-biopsy-fact-sheet. Accessed August 17, 2018.

Why Lymphatic Mapping/SLN?

- Node status most important predictor of survival
  - Postoperative adjuvant therapy
- Most women with early gynecologic cancers are node negative
  - No need for lymphadenectomy
- Complete lymphadenectomy may not be best therapy for positive nodes
  - Therapeutic value of lymphadenectomy unknown

FILM Trial Overview

Fluorescence Imaging for Lymph Node Mapping

- Phase III **randomized**, international study
  - 8 sites in US, Canada, and Puerto Rico

- Compare detection of lymph nodes after interstitial ICG injection and interstitial isosulfan blue dye injection, the standard of care

- **Goal:** Demonstrate safety and clinical benefits of lymphatic mapping using ICG in cervical and uterine cancer surgery and to obtain FDA approval

ICG Identifies More SLNs than Blue Dye, and ICG+Blue Dye is not better than ICG Alone

	Blue Only	Green Only	Blue and Green	p-value
Number Nodes* (n=545)	9 (1.7%)	279 (51.2%)	248 (45.5%)	< 0.001
Pathologically Confirmed	100%	95.3%	92.3%	0.299

* 9 nodes neither blue nor green but suspicious by visualization and/or palpation

ICG Superior to Blue Dye in Identifying SLNs

ID of ≥ 1 SLN in Per Protocol Population (n=163)

ICG:	97.5%
Blue Dye:	76.1%

ID of ≥ 1 SLN in mITT Population (n=176)

ICG:	95.5%
Blue Dye:	74.4%

ICG Identifies ≥ 1 SLN and Bilateral SLNs More Often than Blue Dye

	Blue	Green	p-value
≥ 1 SLN	74.4%	95.5%	< 0.001
Bilateral SLNs	30.7%	78.4%	<0.001

Randomization Arm Did Not Affect Ability of Blue Dye or ICG to Detect Any or Bilateral SLNs

ICG Identifies All SLNs with Metastatic Disease

Sixteen patients (9%) had metastatic disease

– 21 total metastatic SLNs

Blue Only	Green Only	Blue and Green
0 (0%)	8 (38.1%)	13 (61.9%)

No Allergic Reactions or Adverse Events

FILM Study Conclusions

- ICG is superior to blue dye, the current standard of care, in identifying SLNs
  - $\geq$ 1 SLN and bilateral SLNs
- ICG + blue dye is not better than ICG alone
- ICG identifies all metastatic nodes
- Interstitial injection of ICG is safe