

I See Green: Intra-operative use of Indocyanine Green and Near Infrared Spectroscopy in Head and Neck Surgery

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Disclosures

No financial disclosures or conflicts of interest

Nonfinancial: The presenter has no relevant nonfinancial relationship to disclose

I mention brand name devices as illustrative points only

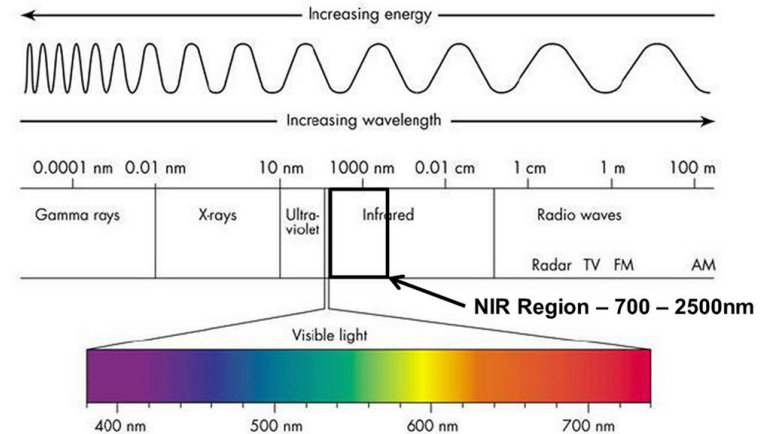
Overview

- Review Near Infrared Technology
- Review applications of near infrared fluorescence imaging in head and neck oncologic surgery
 - Sentinel Lymph Node Biopsy
 - Parathyroid Preservation
 - Tumor delineation
 - Nerve Identification
- Review application of near infrared spectroscopy and fluorescence imaging in head and neck reconstruction
- Conclusions



Overview of near infrared

- 740-1400 nm wavelengths excite organic chemical bonds
- **Near-Infrared Spectroscopy (NIRS):** Exposing a sample to NIR light and measuring how much light is absorbed or reflected by different molecular bonds, providing a unique fingerprint for the substance
- **Near-Infrared Fluorescence (NIRF) Imaging:** Utilizes a fluorescent dye, which is excited by NIR light and emits longer-wavelength infrared light which can be detected with specialized cameras
- **Near-Infrared Autofluorescence (NIRAF):** tissue has inherent fluorescence which can be measured by a sensor



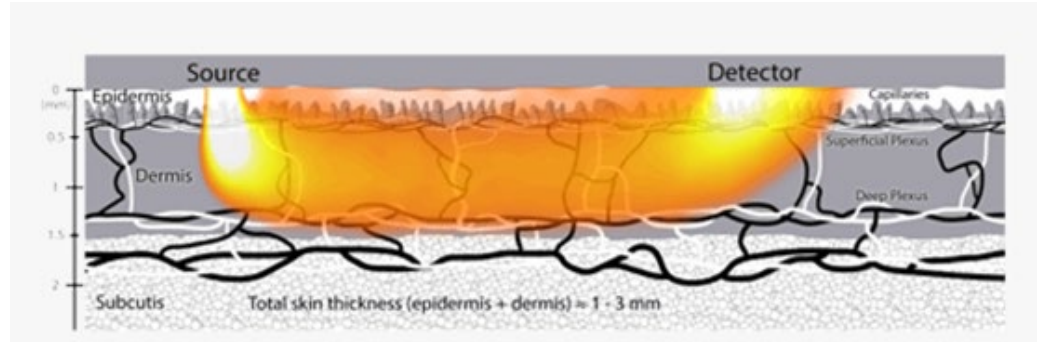
How it works

Near Infrared Spectroscopy NIRS

Example Vioptix

Near infrared light excited chromophores specifically oxygenated and deoxygenated hemoglobin which absorb and reflect different wavelengths. A sensor captures these different signals and a ratio of the signals determines the tissue oxygen saturation or StO₂.

NIR is able to penetrate ~1 cm of soft tissue



How it works

Near Infrared Fluorescence NIRF

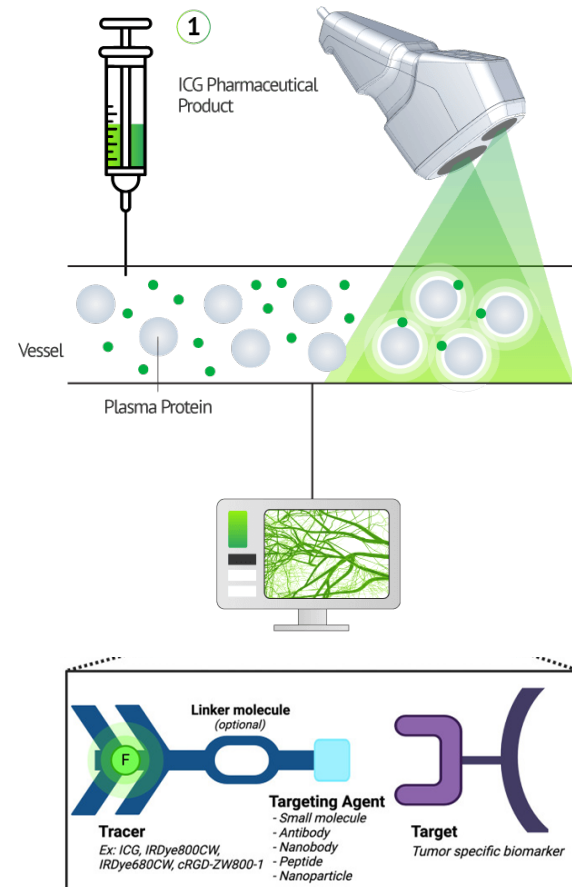
Fluorescent dyes eg Indocyanine Green (ICG)

Different dyes will have proprietary properties making them best suited for their target application. Often a fluorophore bound to a targeting agent

ICG is a water soluble dye that binds with albumin in the bloodstream and is **metabolized in the liver with half-life of ~3-4 minutes**. When excited with NIR light it emits infrared light that can be detected.

FDA approved ICG detection systems include:

Stryker SPY Elite, SurgVision Explorer Air, Hamamatsu PDE-Neo, Firefly Imaging System, Quest Spectrum, Stryker PinPoint, and VisionSense Iridium

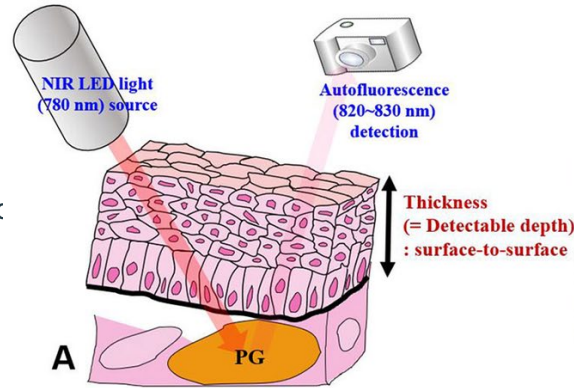


How it works cont

Near Infrared Autofluorescence

Examples PTeye™ and Fluobeam LX

NIR light is directed at tissue and causes the tissue to autofluoresce. Tissues have unique properties which allow them to be distinguished from surrounding tissues.



Sentinel Lymph Node Biopsy

Standard practice for SLNB

Lymphoscintigraphy with a radiolabeled isotope

Traditionally, studies demonstrate increase SLN identification when blue dye is combined with radioisotope (Peek)

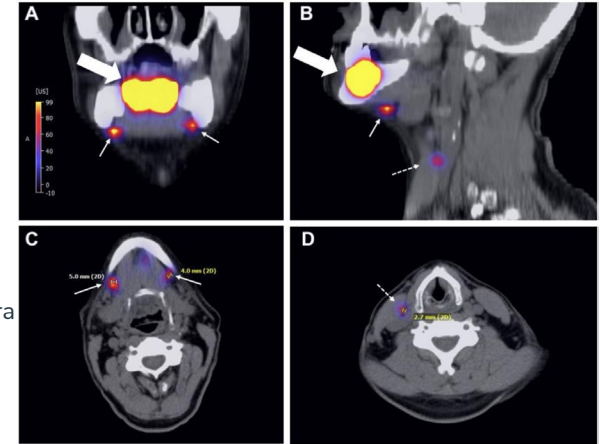
Blue dye carries risk of tattooing and anaphylaxis (0.06%)

Visualization of SLN is superior with ICG compared to blue dye (Marion)

Breast SLNB have demonstrated similar outcomes when comparing ICG with radiolabeled isotopes. (Samora)

Targeted dyes may have a role in identifying occult nodal metastatic disease

- Targeted fluorophores such as panitumumab IRDye800 have been studied in small trials for the identification of SLNs and for predicting occult metastatic disease. Dye has been injected peritumoral and intravenously with high sensitivity and specificity for occult metastasis.



How I Do It

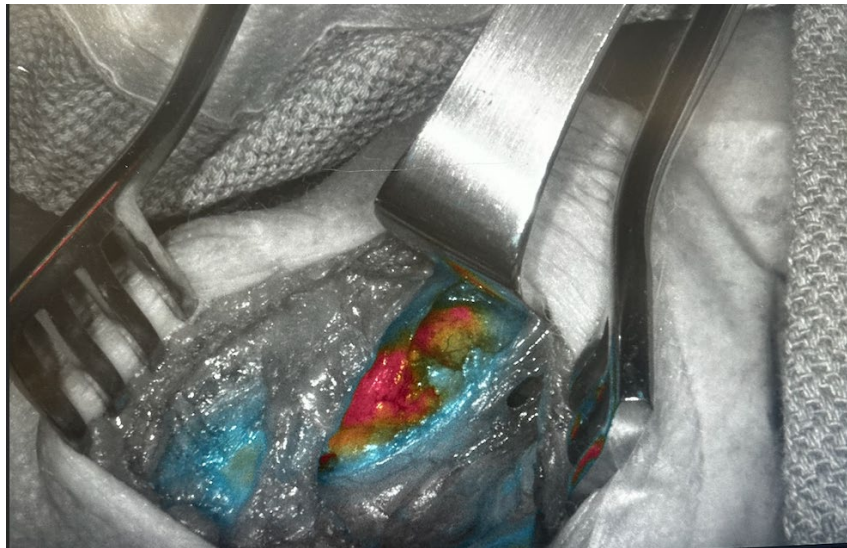
Immediately after intubation ICG 2.5mg/mL 0.4 cc (0.1 cc aliquots) injected into 4 quadrants around the tumor at the site of lymphoseek injections

Resection of the primary performed in standard fashion.

- Less tissue staining compared to blue dye.

NIR Device used in conjunction with gamma probe for SLN identification.

- Particularly useful for floor of mouth primaries where shine through from the primary can impact gamma probe utility.
- I have not found lymphatic mapping in real time to be helpful
- Given tissue penetration limitations I would not perform this without radioisotope especially for cutaneous

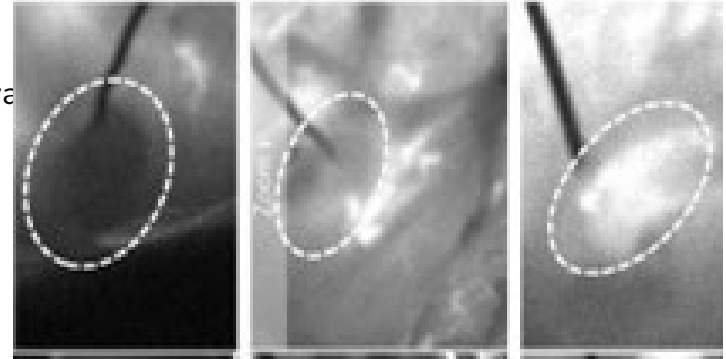


Parathyroid Preservation

- Hypoparathyroidism is a common complication after total thyroidectomy
- Two principle problems devascularization and inadvertent removal

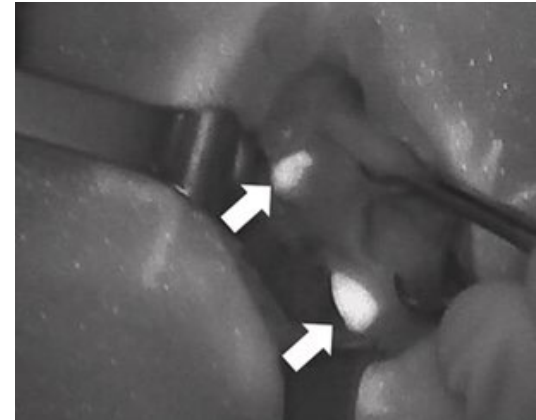
ICG/NIRF

- May be useful in determining perfusion of parathyroid glands
- Not well studied whether intra-operative implementation affects outcomes



NIRAF

- When irradiated with light at a wavelength of 785 nm, PGs can emit fluorescence that is 2–11 times stronger than the fluorescence of the thyroid gland with parathyroid identification >95%
- Imaging-based systems and a probe-based systems
- Multi-institutional trial (Benmiloud):
 - parathyroid autotransplantation (3.3% vs. 13.3%),
 - inadvertent removal (2.5% vs. 11.7%)
 - transient hypocalcemia (9.1% vs. 21.7%)
 - *no difference in permanent hypocalcemia
 - Added 8 minutes on average



Tumor Delineation

Positive tumor margins occurs in ~13% of oral cavity cancers (Orosco, 2018)

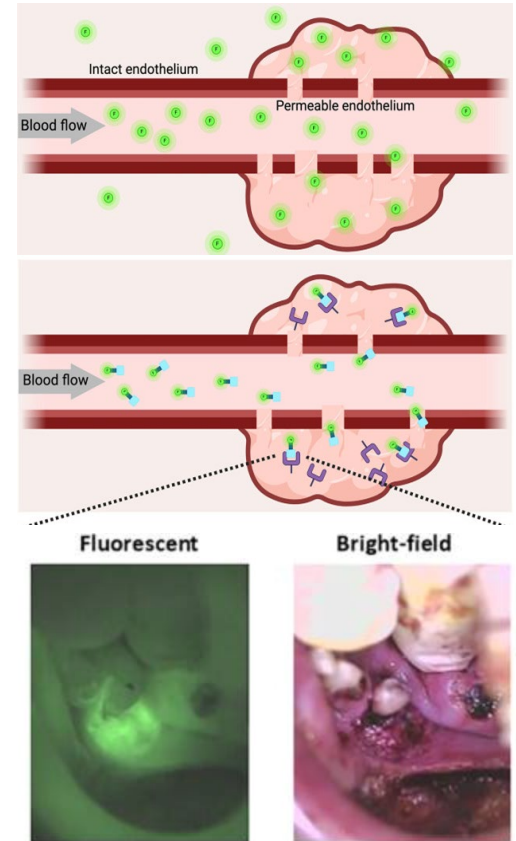
NIRF

IV dye is administered 1-5 days ahead of surgery. At the time of surgery in vivo (tumor and tumor bed) and ex vivo (back table) analysis have been studied .

ICG (nonspecific) and targeted fluorophores (EGFR, 5-ALA, pH sensitive agents and c-MET) are being studied.

Overall this is a promising field of research with ongoing multi-institutional trials which hope to address the significant heterogeneity and small study size of prior studies.

Limitations of this technology include costs associated with equipment requirements, background noise from OR lighting, tumor heterogeneity and limited depth of penetration of NIR light.



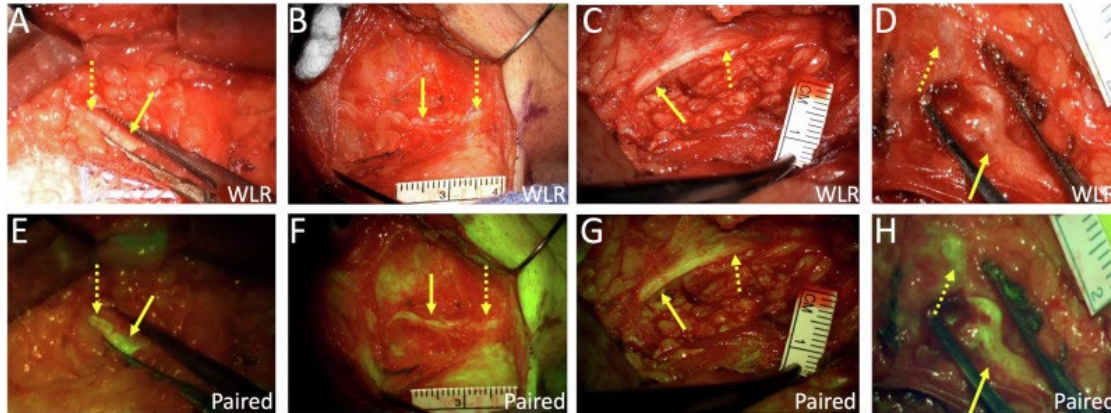
Intraoperative Nerve Identification

NIRF

Bevonescein is a protein bound fluorophore that specifically binds to the ECM of nerve cells independent of the myelin sheath.

Phase I trial of bevonescein completed

Currently enrolling patients in phase III trial to determine efficacy



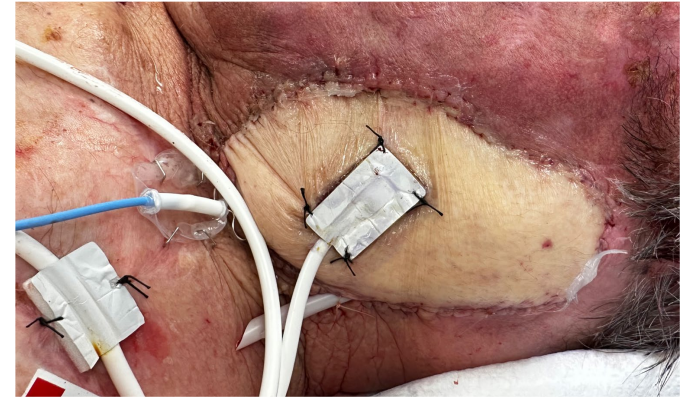
NIRF in Reconstructive Surgery

- Can help with qualitative assessment of flap perfusion and intraoperative use is associated with less severe flap necrosis
- Can be repeated several times due to short half-life of ICG
- Proprietary quantitative measures fluorescence can be made however there are not well established cutoff values.



NIRS in Reconstructive Surgery

- Continuous or intermittent monitoring post-operatively of flaps with skin paddles
- Good flap contact is paramount for reliable signal quality
- Keller et al. established criteria of a drop in 20% per hour sustained for 30 minutes as evidence of vascular compromise.
- StO₂ <60% predictive of skin necrosis, <40% predictive of flap failure
- Systematic review (mostly breast reconstruction)
 - Flap salvage rates 87.2% vs. 50.0%
 - Overall flap survival rates 98.1% vs. 96.3%
 - Earlier detection by NIRS to be 0.5–2.3 h before that of CM



Conclusion/?'s

Near infrared technology is in use in your ORs so try it out and see if it makes life easier.

I use it for:

SLNB

Flap debulking and local flaps

Parathyroid identification in advanced thyroid cancer (bilateral central neck dissection)

Monitoring pigmented skin paddles



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