



EUROPROBE

Double Detection of Sentinel Lymph Nodes
by Gamma and Fluorescence

Corporate Profile

- EuroMedical Instruments has been a **major player in the field of intraoperative detection** for almost 20 years.
- **As the global distributor of the Europrobe system** for surgeons and doctors, we have been forerunners in the detection of sentinel lymph nodes.
- Since 2014, we offer a unique system that allows **bimodal gamma and fluorescence detection**.



Sentinel Lymph Node (SLN) Detection

- In terms of SLN detection the Gold Standard is the **dual detection** with gamma (Technetium ^{99m}Tc) detection combined to a colorimetric detection, with methylene blue.
- The radiolabelled colloids allow preoperative mapping and intraoperative SLN detection thanks to a **portable gamma probe**.
- Preoperative administration of the **blue dye** provides the surgeon with an additional visual identification of the SLN.



Drawbacks with the Blue Dye

- A blue lymphatic vessel deeply located will be **difficult to find**, and its removal may be difficult.
- Methylene blue causes a significant level of **anaphylactic shocks**, making its usage somewhat tricky.
- It **stains** the injection site for months.
- SLN's do **not always absorb** dye, for example in the neck.
- The detection rate of **false negatives** in patients with melanoma is high: **9% - 21%**.



Fluorescence Detection

- To circumvent usage of methylene blue a new colorimetric method is emerging: **Fluorescence-based** detection.
- The injection of indocyanine green (ICG), shortly before the operation is **simple and its diffusion is fast**.
- The occurrence of **side effects**, such as anaphylactic shocks, with ICG is **significantly lower** than with the blue dye, and estimated to be less than 1 in 10,000.
- However, the visualization of fluorescence required the use of a camera and therefore the introduction into the operating field of additional **bulky and expensive equipment**.



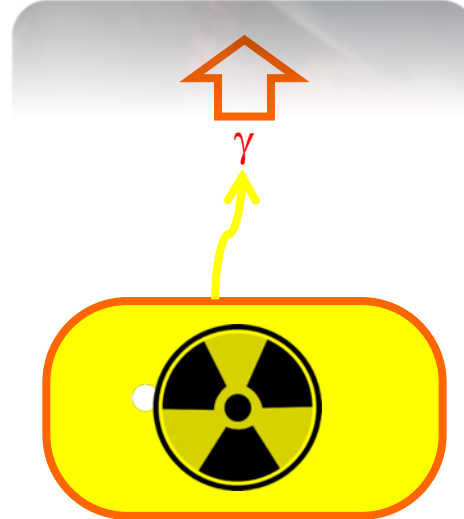
IndoCyanine Green

- Indocyanine green is a dye widely **used in medical diagnostics**. ICG absorbs mainly between 600 nm and 900 nm and emits fluorescence between 750 nm and 950 nm.
- Side-effects such as anaphylactic shock, hypotension, tachycardia are rare, and **rate of severe side-effects is <0.05%**.
- It is a **non radioactive** molecule.
- The product may directly be injected by the surgeon, and SNL detection becomes **no longer reliant on nuclear medicine**.

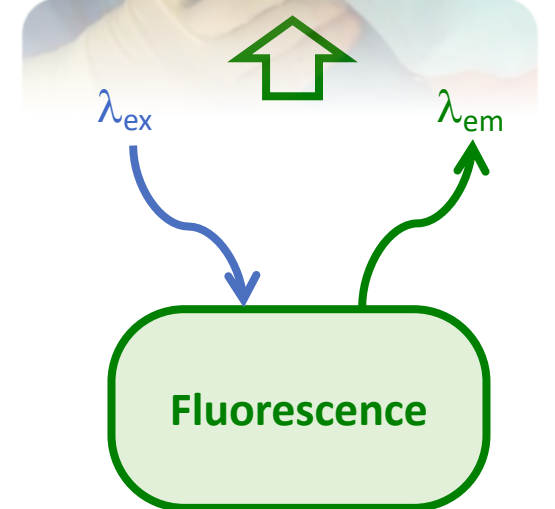


Detection Methods

Up until now, different tracers required different methods of detection and distinct separate devices.



Gamma signal detection

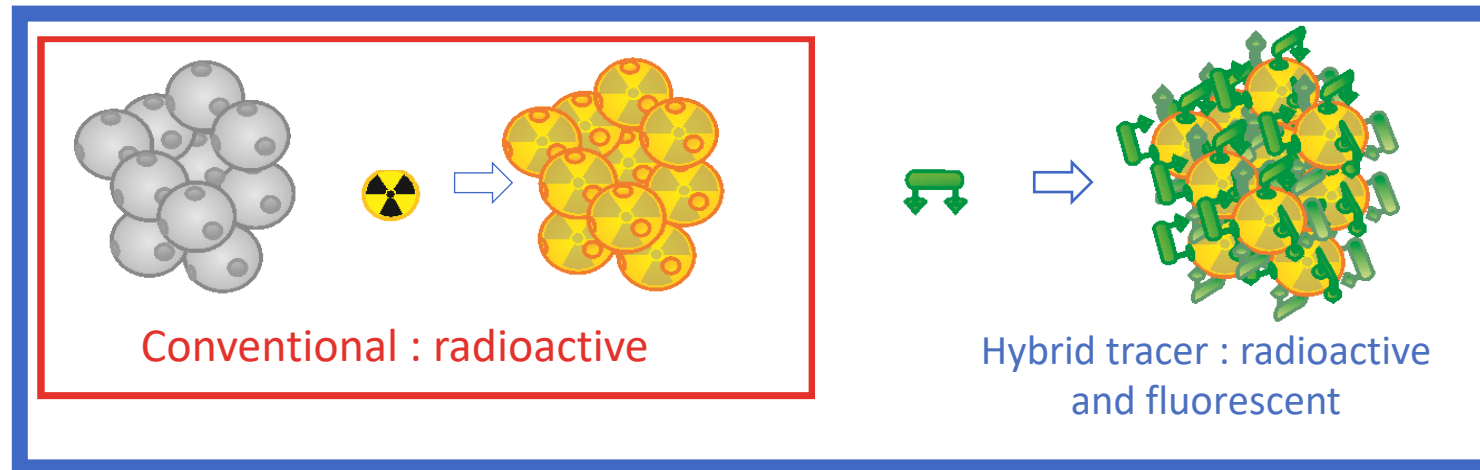


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- 1) Excitation wavelength
- 2) Collection of the emission signal

ICG as a Hybrid or Stand-Alone Tracer

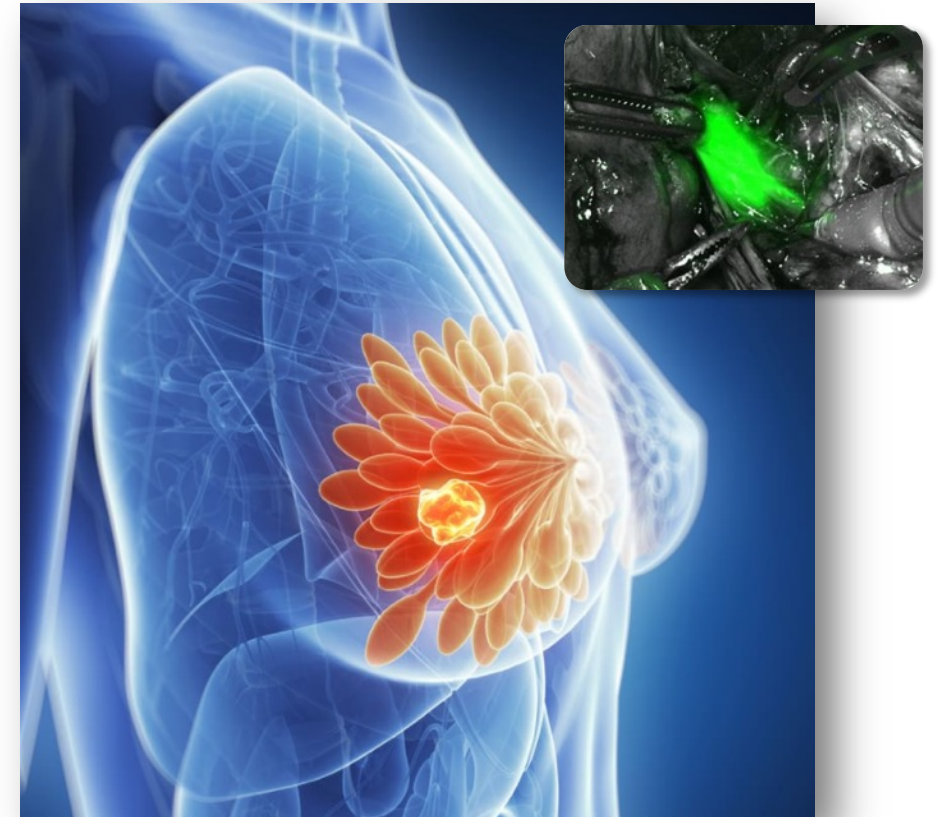
- ICG can be combined with the radioisotope for a simultaneous injection to the patient.



- The two tracers, ICG and the radioisotope, may also be administered separately.

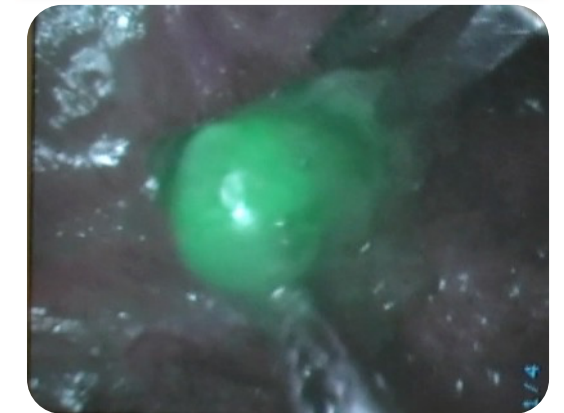
Bi-Modal Detection

- A complete **modular system** combining:
 - Gamma detection
 - Fluorescence dye detection
- The Opto-Nuclear Probe is **the first modality** tailored for the detection of **hybrid tracers**.
- Fluorescence tracing works in **ambient light**.
- The Opto-Nuclear Probe is the only device in the world that allows to detect SNL via fluorescence **without the need for cumbersome imaging systems**.



Clinically Established

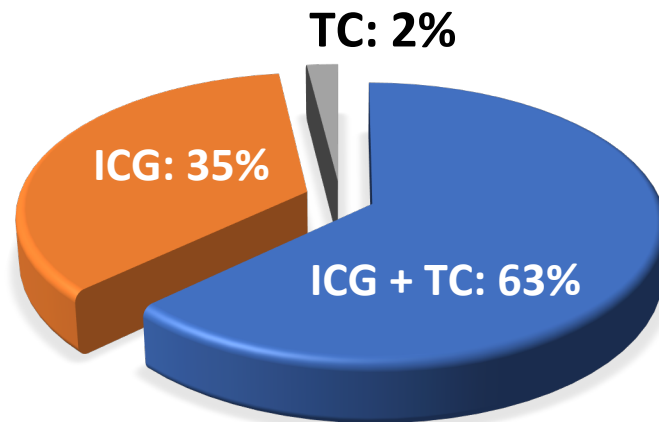
- ICG – 99mTc-nanocolloid enables both preoperative SLN mapping and intraoperative SLN identification in patients with melanoma.¹
- Optical identification of the SLNs through the fluorescent signature of the hybrid tracer is superior compared with SLN identification with blue dye.¹
- ICG - 99mTc-NanoColloid improve the SLN detection accuracy up to 98%.²
- Fluorescence imaging enabled intraoperative identification of the SLNs in the areas where acoustic gamma tracing is inefficient.²
- In the other areas fluorescence helped identify the exact location of the SLNs with a higher precision.²
- Higher rate of SLN identification: 99,8 %.³
- A sharp decrease of the rate of False Negatives³:
 - 2,8 % for bi-modal detection
 - 10 % for radioisotope only
 - 6,7 % for ICG Only



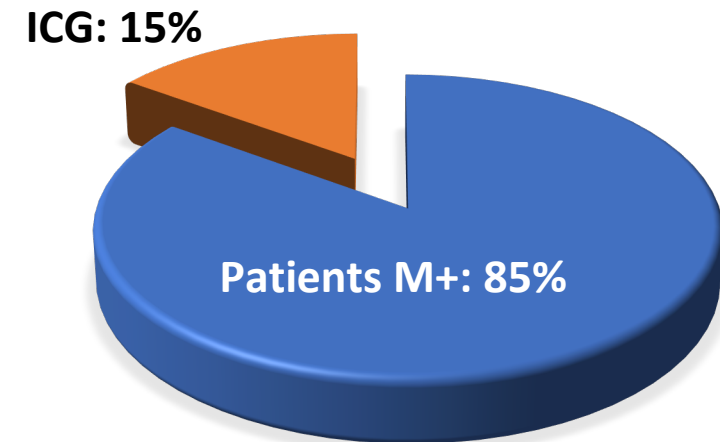
Paris Breast RV 2018 - Comparative Study ICG vs Gamma Detection of SLN

- 63% of SLN detected by both modalities
- 35% detection by ICG only
- **For Metastatic patients, 15% of M+ SLN detected by ICG only**

SLN Analysis



Metastatic Patients



123 patient study in Charleroi Hospital (Belgium) and San Carlo Hospital (Milano), by Dr. Luciano Mazzeo Cicchetti.

ICG

- Injection in the Operating Room 15mn before intervention
- Injection by a nurse
- Direct access to the OR
- In combination with gamma detection, NO RISK of adverse effect.

Tc99

- Injection day before intervention
- Injection by a nuclear doctor
- Compulsory stop at the scintigraphy room
- Complementary Blue Dye de, causes tattoo marks & Anaphylactic shock risks

- > **High Patient Comfort**
- > **Ease of Use**
- > **Much Safer Procedure**

Add-on cost of the DUAL Fluorescent Module:

- Module + probes (short + laparoscopic) : 25.000 € - 40.000 €
- Injection cost of ICG tracer : between 15 - 30 €
- Injection cost ^{99m}Tc : 200 € - 375 €

**-> Pay-back of Fluorescent module (vs Gamma) in 70 – 235 procedures
=> Cost Saving of 170 € to 360 € per procedure !**

- 1. Multimodal Surgical Guidance during Sentinel Node Biopsy for Melanoma: Combined Gamma Tracing and Fluorescence Imaging of the Sentinel Node through Use of the Hybrid Tracer Indocyanine Green–99mTc-Nanocolloid**
Nynke S. van den Berg et al, Radiology 2014
- 2. Intraoperative Laparoscopic Fluorescence Guidance to the Sentinel Lymph Node in Prostate Cancer Patients: Clinical Proof of Concept of an Integrated Functional Imaging Approach Using a Multimodal Tracer**
Vav der Poel et al, Europ Urol 2011
- 3. Détection du ganglion sentinelle dans le cancer du sein par sonde opto-nucléaire après injection de vert indocyanine et de technétium 99 m**
E. Barranger, M.-A.Poumellec et al., Gynecologie Obstétrique & Fertilité (2016)
- 4. First-in-human evaluation of a hybrid modality that allows combined radio-and (near infrared) fluorescence tracing during surgery**
VAN DEN BERG NS, et al, EUR.J Nucl Med Mol Imaging 2015
- 5. Accuracy and prognostic value of sentinel lymph node biopsy in head and neck melanomas**
R. Patuzzo et el, JSR 2014
- 6. Sentinel Lymph Node Biopsy in Vulvar Cancer Using Combined Radioactive and Fluorescence Guidance**
F. VERBEEK et al, International Journal of Gynecological Cancer / SLN Biopsy in Vulvar Cancer (2015)
- 7. The indocyanine green method is equivalent to the 99mTC-labeled radiotracer method for identifying the sentinel node in breast cancer : a concordance and validation study**
B.Ballardini et al. / EJSO 39 (2013) 1332-1336
- 8. Evaluation of sentinel node biopsy by combined fluorescent and dye method ans lymph flow for breast cancer**
T.Hojo et al. / The Breast (2010)
- 9. Impact of indocyanine green for sentinel lymph node mapping in early stage endometrial and cervical cancer : comparison with conventional radiotracer (99m)Tc and/or bue dye**
A.Buda et al. - Annals of surgical oncology- December 2015
- 10. Fluorescence imaging after indocyanine green injection for detection of peritoneal metastases in patients undergoing cytoreductive surgery for peritoneal carcinomatosis from colorectal cancer**
P.BOURGEOIS et al, Annals of surgery – January 2016



Specifications

Main Features:

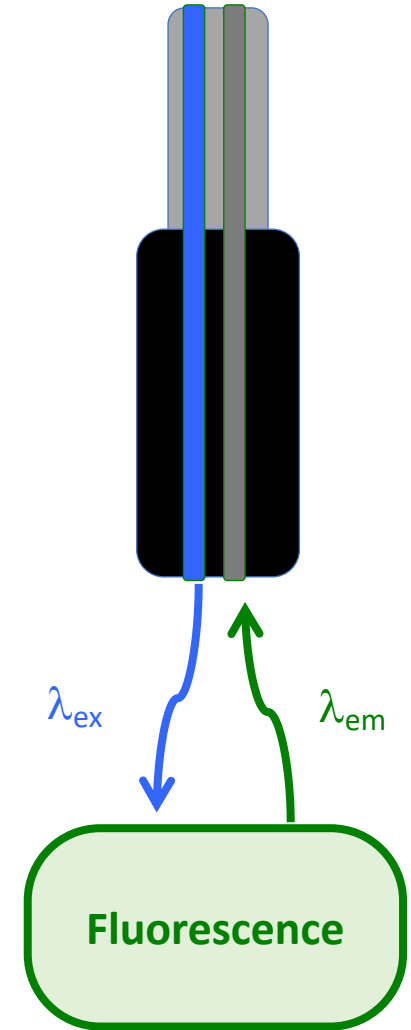
- Optional module placed underneath the Europrobe.
- Allows dual Gamma and Fluorescence detection.
- Selection of detection modality via a footswitch.
- Simple and identical use to Gamma gesture.
- Usable in ambient lighting conditions.
- Requires no specific set-up.
- Improved discrimination and sensitivity.

Technical specifications:

- Module height: 55mm.
- Weight: 1 Kg.
- Width / Depth: 233 mm / 270 mm.
- Suitable for of Indocyanine Green (ICG) detection.



Europrobe 3.2



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Europrobe 3.2

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