

Verdye™ (Indocyanine Green)

Use of ICG in Breast SLN Detection



Intraoperative identification of sentinel lymph nodes and visualisation of lymphatic pathways in breast cancer

The presence of lymphatic metastases is an important prognostic factor for the survival of breast cancer patients and their identification has a bearing on further treatment.¹ Sentinel lymph node biopsy (SLNB) remains a cornerstone in the management of early breast cancer and is the current standard of care for clinically and radiologically node-negative patients.² Importantly, compared with axillary lymph node dissection (ALND), SLNB enhances patient's quality of life without compromising diagnostic accuracy or prognostic information for node-negative patients.³

The gold standard for SLNB in patients with breast cancer is radio-guided surgery with radioisotope technetium-99m (Tc-99m) which has a reported sentinel lymph node (SLN) detection rate ranging from 85.0% to 100%.⁴ Some clinicians combine Tc-99m with blue dyes (usually methylene blue dye), increasing the detection rate to 96.0%-99.8%.^{4,5} However, the use of blue dyes might be associated with adverse effects,^{6,7} including skin necrosis, soft tissue necrosis, (permanent) skin tattooing at the injection site or systemic adverse effects making it infrequently utilised for routine surgical care.⁸ The use of Tc-99m places a considerable burden on both patients and hospitals, including challenges in sourcing due to lack of a nuclear medicine department, logistical difficulties related to pre-operative administration, occupational exposure risks to ionising radiation for healthcare professionals and stringent regulatory requirements for the handling and storage of radiopharmaceuticals.

In contrast, indocyanine green (ICG) fluorescence imaging has emerged as a safe and effective alternative for SLNB. Clinical studies have demonstrated that ICG provides SLN detection rates that are comparable to or even superior to those achieved with traditional radioisotope techniques.^{4,5,11,12,13} It also offers similar or improved accuracy in identifying pathological nodes, in both primary SLNB and in patients who have received neoadjuvant chemotherapy.^{4,12} Furthermore, ICG maintains its effectiveness in patients with a high body mass index (up to 40).^{4,12,14} In a recent meta-analysis involving 2168 patients undergoing ICG imaging procedures (5-10 mg per injection), the mean SLN detection rate was 97.4% and the mean number of sentinel lymph nodes detected per patient generally ranged between 2.0 and 3.0.¹⁴

ICG eliminates the need for radiation, significantly reduces logistical complexity, and avoids most of the adverse effects commonly associated with blue dyes. Its ability to provide real-time visualisation of lymphatic flow enhances surgical precision while improving patient experience. As such, ICG is increasingly being adopted as a preferred approach for sentinel lymph node mapping in early-stage breast cancer.^{11,12}

INDOCYANINE GREEN (ICG) APPROVED FOR BREAST SLN DETECTION

A recently approved method for detecting sentinel lymph nodes (SLNs) in breast cancer utilises ICG.¹⁴ In some European countries and UK only Diagnostic Green's Verdyne is now approved for intraoperative identification of sentinel lymph nodes ± visualisation of lymphatic pathways in breast cancer.



Preparation and administration of ICG for SLNB

Immediately prior to surgery, a 25 mg vial of ICG is prepared with 5mL of water for injections. Once the patient is anaesthetised, ICG (1-2 mL) is injected intradermally, subcutaneously, or peritumourally into a region upstream of the lymph nodes of interest which drain this area.

PROCEDURE

Holding the near infra-red (NIR) camera system above the injected tissue, lymphatic vessels containing ICG are visible transcutaneously (up to a depth of 1.0-1.5 cm¹⁵) and can be mapped to the axilla. By tracking the breast lymphatics it allows the user to visualise in real-time the flow of lymph through the vessels.

After the axilla is incised, the tissue is dissected until the axillary fascia is exposed. Using the NIR camera, the axilla is examined for tissue fluorescence (**Fig 1**) and the SLN can be identified (**Fig 2**).



Fig 1. Tissue dissection reveals fluorescent tissue

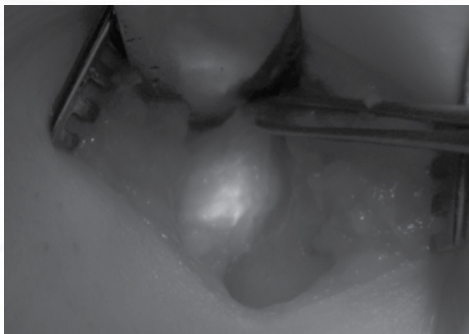


Fig 2. Fluorescent SLN identified

Figure 1 & 2 taken using the IC-Flow™ Imaging System. Courtesy of Mr. Chris Hoo, Consultant Plastic & Breast Surgeon, Belfast City Hospital.

SIGNIFICANT BENEFITS OF USING ICG

- ⊙ **Real-time Imaging:** ICG provides real-time visualisation, allowing surgeons to precisely identify and remove SLNs during surgery.
- ⊙ **Accuracy:** Studies have shown that ICG is superior or at least non-inferior to all other options in identifying lymph nodes.^{4,5,11,12,13} Requires a small injection only, which can be administered whilst patient is anaesthetised, thus minimising patient discomfort.
- ⊙ **Excellent Safety Profile:** ICG has a more favourable safety profile compared with blue dyes.**
- ⊙ **Minimal Skin Staining:** Little or no tattooing with ICG, and when present it typically resolves within weeks. In contrast, blue dye tattooing can persist months to years,¹⁶ and Superparamagnetic Iron Oxide (SPIO) (e.g., Magtrace®) has reported up to 37.8% immediate and 9.4% long-term (36-month) skin staining after peritumoral injection in lumpectomy patients.¹⁷
- ⊙ **MRI-compatible Follow-up (vs SPIO):** ICG does not create MRI susceptibility artefacts, preserving image quality for postoperative/surveillance MRI. SPIO tracers can cause *persistent MRI artefacts* near injection or drainage sites that may render images nondiagnostic.¹⁸
- ⊙ **Streamlined Surgical Workflow (vs SPIO):** ICG can be administered intraoperatively with a short wait and typically no massage; SPIO labelling instructs ≥20 minutes wait plus 5 minutes of vigorous massage before SLN Biopsy, adding time and handling steps.¹⁸
- ⊙ **No Preoperative Procedure Required:** Using Tc-99m introduces logistical hurdles, regulatory requirements, and occupational radiation exposure risks for staff, ICG avoids these preoperative steps.

Summary of nine meta-analyses: 2016-2021*

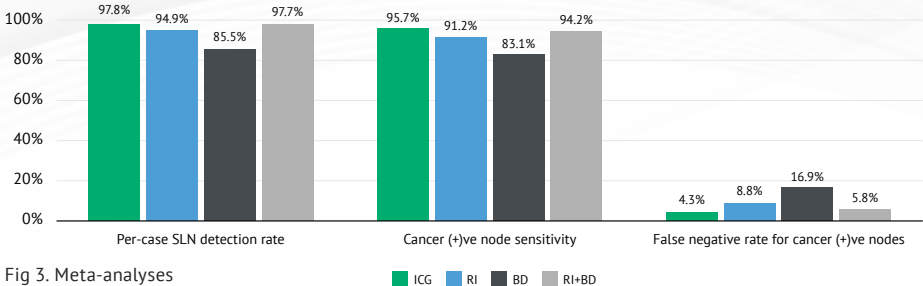


Fig 3. Meta-analyses

SUMMARY

In summary, ICG-based SLN detection offers several advantages to surgeons, including high accuracy (**Fig 3**), reduced invasiveness, enhanced patient comfort, reduced cost and safer alternatives to traditional radioactive tracers and blue dyes.¹³ These benefits contribute to better surgical outcomes and a higher quality of care for breast cancer patients. Studies have shown that ICG has high sensitivity in SLN detection, meaning it accurately identifies the SLN while reducing the chances of false-negative results. This reliability is crucial for making informed decisions about treatment and staging of breast cancer disease.

*Diagnostic Green. Data on File.

**Based on Diagnostic Green Pharmacovigilance data 25 Feb 2025, a single adverse reaction was identified in 12,500 patients.

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VERDYE ABBREVIATED PRESCRIBING INFORMATION

Verdye

5 mg/ml powder for solution for injection

Composition:

Active substance: Indocyanine green (ICG); vials containing 25 mg and 50 mg (to be reconstituted with 5 ml respectively 10 ml water for injections).

Indications:

Cardiac, circulatory and micro-circulatory diagnostic agent for measurement of cardiac output and stroke volume, circulating blood volumes and cerebral perfusion; liver function diagnostic agent for measurement of liver blood flow and excretory function of the liver; ophthalmic angiography diagnostic agent for measurement of perfusion of the choroid. Intraoperative identification of sentinel lymph nodes and visualization of lymphatic pathways in breast cancer (registered only in some European countries).

Posology:

Cardiac, circulatory, micro-circulatory and tissue perfusion diagnostics as well as cerebral blood flow (adults and children): 0.1-0.3 mg/kg body weight (BW) as single i.v. bolus per measurement; liver function diagnostics (adults and children): 0.25-0.5 mg/kg BW as single i.v. bolus per measurement; ophthalmic angiography (adults and children): 0.1-0.3 mg/kg BW as single i.v. bolus per measurement. Total daily dose: ≥ 12 yrs: < 5 mg/kg BW, 2-11 yrs: < 2.5 mg/kg BW, < 2 yrs: < 1.25 mg/kg BW. Identification of sentinel lymph nodes and visualization of lymphatic pathways regardless of BW (adults): 5-10 mg per single injection (intradermal, subcutaneous or peritumoral). Total daily dose: ≤ 10 mg.

Contraindications:

Hypersensitivity to ICG, sodium iodide or iodine, hyperthyroidism, autonomic thyroid adenomas, hyperbilirubinemia requiring exchange transfusion in premature infants or neonates, history of poor tolerance to Verdye.

Interactions:

Anticonvulsants, bisulphite compounds, haloperidol, heroin, pethidine, metamizole, methadone, morphine, nitrofurantoin, opium alkaloids, phenobarbital, phenylbutazone, cyclopropane, probenecid, rifamycin.

Undesirable effects:

Very rare (<1 in 10,000): nausea, urticaria, anaphylactic/anaphylactoid reaction, coronary arteriospasm. *Frequency not known:* injection site discoloration.

Prescription only.

This product information may differ in some countries. For detailed information see prescribing information by territory visit {website}.

Diagnostic Green Ltd.

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For full prescribing information go to www.diagnosticgreen.com

Diagnostic
Green

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