Role of Indocyanine Green Fluorescence in Enhancing Surgical Margin

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ABSTRACT

Improvements in preoperative imaging and intraoperative navigation, identifying malignant and normal tissues during surgery particularly during minimally invasive surgery—remains challenging. Indocyanine green fluorescence imaging has become a novel intraoperative imaging modality that enables real-time, high-resolution imaging of anatomical structures, tissue perfusion, and tumor margins, thus improving surgical accuracy and safety. ICG is a water-soluble, sterile tricarbocyanine dye that fluoresces in the near-infrared range with peak emission at around 835 nm after excitation between 750 and 810 nm. With rapid binding to plasma proteins upon intravenous injection, tissue penetration of approximately 5–10 mm and low background interference are achieved. First approved in the U.S. by the FDA in 1959 for cardiac output and assessment of liver function, ICG has now become a general-purpose intraoperative imaging adjunct to various surgical specialties. ICG-assisted liver surgery also enables precise identification of hepatocellular carcinoma and metastatic lesions, demystifying resection margins and unveiling occult tumors not identified by traditional imaging. In thoracic surgery, ICG makes intersegmental plane delineation precise during lung segmentectomy and thereby improves parenchymal preservation and oncological precision. The application of ICG also comes to neurosurgery, where the "Second Window ICG (SWIG)" method provides delayed tumor-targeted uptake such that near-infrared visualization of gliomas and meningiomas is possible.

Keywords: Indocyanine green fluorescence, colorectal, gastric cancer surgery, cholecystectomy, Hepatobiliary surgery, pulmonary surgery, neurosurgery, neurosurgery, prostatectomy, lymphadenectomy

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INTRODUCTION

Surgical resection is still an integral component of treatment in solid malignancies with the extent of tumor excision namely the attainment of negative margins at surgery being an important determinant of long-term oncological success incomplete margin clearance raises the threat of local recurrence affects survival and commonly requires adjuvant treatments that can burden patients with further physiological psychological and economic loads despite the progression of preoperative imaging and intraoperative navigation precise discrimination between neoplastic and normal tissues intraoperatively particularly under minimally invasive techniques continues to be an important challenge indocyanine green ICG fluorescence imaging has been gaining momentum in recent years as a potential additional tool to traditional surgical methods providing real-time high-resolution anatomical structure visualization tissue perfusion and tumor margins is a sterile water-soluble Tri carbocyanine dye cleared by the united states food and drug administration FDA in 1959 binds quickly to plasma proteins after intravenous administration and fluoresces at the near-infrared wavelengths peak emission at 835 nm upon irradiation at wavelengths of 750810 nm [1] this provides deep tissue penetration of about 510 mm with little interference from ambient light or endogenous autofluorescence which allows for a range of surgical uses initially formulated for cardiac output determination and liver function testing ICG has been adapted to many intraoperative uses during hepatobiliary surgery icg fluorescence cholangiography has become more and more widespread in laparoscopic cholecystectomy and hepatectomy allowing for definitive visualization of the biliary tree and minimizing bile duct injury one of the most dangerous complications of gallbladder surgery[2][3].

Study showed that ICG cholangiography delineated biliary anatomy by means of direct biliary injection in 100 of patients and intravenous administration in 83.3 of patients thus improving surgical safety and accuracy[2]. In colorectal surgery incorporation of ICG imaging has been demonstrated to be of considerable value in evaluating bowel perfusion especially during the formation of anastomosis impaired perfusion at the anastomotic region is a principal cause of postoperative anastomotic leakagea condition whose occurrence has been reported in 1 to 20 of cases with additional morbidity mortality and hospital costs[1][4]. By providing for real-time imaging of blood flow ICG helps surgeons choose well-perfused segments of bowel for resection and anastomosis faber et al also suggested quantification protocols for standardizing interpretation since conventional dependence on subjective fluorescence measurement has been demonstrated to provide poor interobserver correlation[4]. The advantages of ICG fluorescence go beyond the evaluation of perfusion in oncologic surgery particularly in gastrointestinal thoracic and genitourinary oncologic procedures ICG has shown value in intraoperative lymphatic mapping and tumor identification for instance during a randomized controlled trial of 266 patients with gastric cancer who underwent laparoscopic gastrectomy icg-directed lymph node dissection yielded significantly more resected nodes mean 505 vs 420 p 0001 and reduced lymph node noncompliance rates but no increased complication rates these data highlight ICG capacity to optimize surgical completeness without compromising safety in addition in reconstructive surgery of the upper urinary tract demonstrated that intraureteral ICG injection permitted accurate identification of strictures and ureteral margins with reduced intraoperative identification time and hospital stay in neurosurgery of high-complexity cases presented the second window ICG swig technique which allows for tumor-specific uptake of ICG in high-grade gliomas and meningiomas and aids in their resection with improved tumor-margin visualization in thoracic surgery ICG fluorescence has been incorporated into robot-assisted minimally invasive esophagectomy ramie to assess gastric conduit perfusion and inform optimal site selection for anastomosis reported that ICG changed the surgical strategy in 14 of patients and identified a relationship between delayed fluorescence and increased risk of anastomotic leakage the same techniques have been used in ventral hernia repair and breast reconstruction to determine flap viability and prevent ischemic complications these applications indicate a convergence toward augmented reality surgery in which real-time functional visualization is incorporated in the operative field the success of ICG-guided fluorescence imaging depends on various factors correct dosing timing of injection compatibility of imaging equipment and surgeon skill in interpreting fluorescence signals ICG is most commonly administered at doses between 01 and 05 mg/kg with visualization within minutes of injection because of its rapid plasma clearance and hepatic excretion even with demonstrated efficacy limitations exist fluorescence signal intensity is modulated by technical parameters like camera position distance ambient illumination and thickness of tissue additionally standardization between surgical specialties is not present this review discusses the bidirectional role of ICG fluorescence in optimizing surgical margins in various procedures based on the recent data and developing clinical uses[5][6][7].

1. COLORECTAL: Indocyanine Green (ICG) fluorescence imaging is increasingly being utilized in colorectal cancer surgeries. It boosts visibility during operations, refines surgical margins, and minimizes the risk of anastomotic leaks (AL). When ICG is exposed to near-infrared (NIR) light, it latches onto plasma proteins and begins to fluoresce. This allows for an immediate assessment of tumor size and blood flow in the tissues.In a study conducted by Nagata and colleagues, ICG fluorescence successfully pinpointed the tumor in every patient (n=24), even in cases where India ink fell short in 10 instances. It proved to be both safe and reliable. Anastomotic leaks continue to be the most severe complication following colorectal surgery, primarily because of insufficient perfusion. Fluorescence imaging provides objective measurement of bowel viability.[8][10] A Delphi survey of 35 international experts validated a strong consensus on the utility of ICG in assessing anastomotic perfusion and the risk of leakage. Furthermore, quantified fluorescence intensity curves in studies determined three different patterns of bowel perfusion, providing a more objective methodology than subjective surgeon analysis, which revealed only moderate concordance. ICG fluorescence is non-toxic with no known adverse effects and enables intraoperative fine-tuning according to the findings of perfusion. The ideal dose is 5–10 mg injected 30–60 seconds before imaging. Its use is applicable in both open and minimally invasive procedures, utilizing dedicated laparoscopic imaging equipment[9].

2. GASTRIC CANCER SURGERY: This is a new surgical navigation method to increase the accuracy of excision of stomach cancer due to ICG fluorescence imaging. It gives better lymphatic mapping and lymph node dissection, thus giving definite surgical margins [11]. Better Lymph Node Dissection: In a randomized trial for laparoscopic radical gastrectomy, the mean number of lymph nodes that were retrieved in the ICG-treated group was 50.5 versus only 42.0 in the non-ICG group, thus increased lymphadenectomy. Identification of Missed Malignant Lymph Nodes: The procedure has a higher significance when it comes to identifying sentinel lymph nodes (SLNs) outside the typical surgical field of intervention. One pilot study showed that ICG picked up malignant SLNs in cases who would otherwise have been missed, thus directly influencing the completeness of the resection[12]. Technical Feasibility: The development of technology has introduced ways of performing ICG-guided surgery into the mainstream. The newer equipment allows the procedure to be done under normal room illumination, giving a cheap, easy tool for lymphatic mapping for procedures like laparoscopic gastrectomy without increasing surgical complications[11][13].

3. CHOLECYSTECTOMY: Laparoscopic cholecystectomy (LC) is the standard treatment for gallbladder disorders, though it carries a 0.2–1.5% risk of bile duct injury, most often due to misinterpretation of anatomy. To minimize this, indocyanine green (ICG) near-infrared fluorescence cholangiography has been introduced, allowing real-time mapping of biliary structures. After intravenous administration, ICG is excreted in bile, highlighting the cystic and common bile ducts. A typical dose of 2.5 mg given 30–60 minutes before surgery provides good visualization (~83%), while direct intrabiliary injection through gallbladder puncture, PTGBD, or ENBD yields nearly complete delineation of ducts. Clinical studies show that ICG fluorescence enhances biliary identification, lowers the risk of ductal injuries, and avoids the disadvantages of conventional X-ray cholangiography. The method is safe, practical, cost-effective, and particularly valuable in technically challenging procedures. Limitations include weaker imaging in obese patients and acute inflammation, along with the absence of standardized dosing protocols[14].

4. HEPATOBILIARY SURGERY: Hepatobiliary surgery is technically demanding due to the complexity of liver and biliary anatomy, making accurate visualization essential for safe and effective outcomes. The use of indocyanine green (ICG) fluorescence imaging has emerged as a major advancement, offering surgeons real-time guidance, enhanced safety, and improved oncological precision. During liver resections, ICG assists in detecting hepatocellular carcinoma and metastatic lesions, particularly those located deep within the parenchyma or in posterior segments where conventional laparoscopic views are limited. It enables clearer definition of tumor boundaries, facilitates accurate parenchymal transection, and can reveal occult or extrahepatic metastases not identified on preoperative imaging, thereby improving staging and completeness of resection[3][15]. In biliary procedures, ICG fluorescence cholangiography provides a radiation-free method of visualizing the biliary tree, including the cystic duct and common bile duct, reducing the risk of bile duct injury during complex cholecystectomies and aiding resections around the hepatic hilum. Direct instillation into the gallbladder has been shown to yield sharper delineation of biliary anatomy compared with systemic administration. From an oncological perspective, ICG can outline microscopic tumor spread, peribiliary infiltration, and small nodules invisible to standard imaging, helping ensure margin adequacy.[16] The disappearance of fluorescence following resection also serves as an intraoperative marker of oncological clearance. Limitations of this approach include shallow tissue penetration and interference from background fluorescence in the liver. The best dose and timing of administration are still under evaluation, though injection several hours prior to surgery remains common practice. Future developments such as integration with advanced imaging systems and artificial intelligence are expected to broaden its application and standardize its use[17].

5. HERNIA: ICG fluorescence imaging is getting more attention these days for real-time surgery visuals, especially in tricky areas like hernia repairs. It’s been around for liver and gut surgeries, but now people are seeing how it helps with hernias too. Two recent studies show how this works for both inguinal and ventral types. For laparoscopic inguinal repairs, stuff like bleeding or tearing the hernia sac stays a big worry, especially when dealing with complex cases or repeat surgeries where scar tissue messes 17 patients getting TEP repair using ICG They diluted the dye, injected it, and then used special cameras to light up blood vessels around the groin area. Basically, it helps spot the spermatic cord vessels, epigastric ones, and that tricky corona mortis spot. This lets surgeons map out hernia sac edges better, cut down dissection time, and keep blood loss crazy low, like 5 ml on average. Surgery took about 42 minutes; nobody had sac ruptures, and follow-ups showed no seromas or comebacks. Turns out fluorescence imaging cuts down on complications during surgery. Also speeds up dissection time while keeping blood flow normal in key areas Ventral hernias are another story, especially when you’re doing redo surgeries or separating muscle layers. The real headache there is finding those nerve and blood vessel bundles hidden under scar tissue or old mesh. ICG angiography is used here too. They found that shooting dye and then using infrared cams gives a live view of blood flow patterns. Helps avoid slicing through important vessels mid-surgery. Plus, it acts like a teaching tool for newer surgeons, showing them exactly where everything is. Timing matters, though. The best images pop up in the first minute after the dye goes in, before it washes out. Studies suggest ICG’s got real value for different hernia types. For groin hernias, it stops bleeding, makes sac removal cleaner, and protects delicate structures. In belly wall cases it maps out hidden vessels, cutting accidental injuries. The tech even helps train surgeons while making tough surgeries faster and safer. ICG looks promising for hernia fixes. By lighting up what’s what during surgery, it makes things more precise, cuts problems down, and could become standard care for complex cases. Especially redos But we’ll need more proof before everyone jumps on board[7][18].

6. PULMONARY SURGERY: Lung segmentectomy is getting more popular these days, especially with all these small nodules; they’re finding early cancers too, plus metastatic stuff, you know. The big issue is always figuring out where exactly to cut between segments; you have to balance tumor margins against saving healthy lung. Old-school methods like inflation-deflation lines don’t cut it sometimes, especially with emphysema patients whose lungs don’t expand right, which messes up visibility. Turns out ICG fluorescence works better here. They tie off the target artery pump in the dye, and bam, non-target areas light up bright green while the target stays dark, giving surgeons clear edges[19]. The dye lit up fast, like 20 seconds after injection, and stuck around nearly three minutes, long enough to mark everything. No bad reactions either from the ICG, which matters. Then there’s this Russian group that did 86 cases. Same deal, over 95% success rate. Even COPD patients showed decent borders, though the glow didn’t last as long. They found upping the ICG dose helped when things got tricky visibility-wise. So now ICG is basically standard in VATS and robotic surgeries and lets them chop exactly what needs chopping without taking extra lung. Pretty much textbook precision stuff these days[20].

7. NEUROSURGERY: Attainment of clear surgical margins is probably the most significant objective in cancer surgery. In brain tumors and other complex lesions, it is even more difficult because the tumor-non tumor interface is not always discernible to the naked eye. Incomplete removal is a cause of recurrence, and overly aggressive surgery can compromise critical structures. This is where the new imaging modality such as fluorescence guidance has revolutionized surgical practice. Indocyanine Green (ICG) is not a novel agent. It has been used for decades in the application of angiography to image vasculature. What distinguishes it for surgical margin signification is its near-infrared (NIR) fluorescence function (excitation at ~805 nm, emission at ~835 nm). Unlike visible light fluorophores such as 5-aminolevulinic acid (5-ALA) or fluorescein, NIR light penetrates deeper into tissue and produces less background interference from normal brain autofluorescence. This allows surgeons to see beneath the surface and identify tumor tissue that lies behind normal structures. Historically, ICG was administered as a rapid bolus during angiography. When administered in the form of a larger dose (approximately 5 mg/kg) 16–30 hours before operation, ICG does something else. ICG leaks and becomes sequestered in tumor tissue through the EPR effect due to the tumor's abnormal, leaky vasculature. This creates a "second window" when tumors emit bright light under NIR cameras during operation, allowing surgeons to visualize residual tumor at margins. SWIG examinations in meningiomas, metastases, pituitary tumors, and gliomas demonstrate that the technique significantly increases the detection of tumor tissue. For high-grade gliomas, SWIG identified areas of tumor with a 98% sensitivity, and few tumors were left undetected.

Even operating neurosurgeons could visualize fluorescence prior to opening the dura, which was not possible with earlier agents like 5-ALA. Maybe the most thrilling part of ICG is its application in margin evaluation. Once the surgeon believes that the tumor has been completely resected, the NIR system can image the surgical bed. If there is no fluorescence, the surgeon can be more certain that a GTR has been attained. This real-time feedback is beneficial because conventional methods such as neuronavigation can be misled by brain shifts during surgery. Increased penetration: NIR light penetrates tissue to 1 cm depth, so subcortical tumors become visible without further incisions. Real-time imaging: In contrast to MRI or frozen sections, it is real-time and does not disrupt the workflow. Widespread applicability: ICG binds a wide variety of tumors without requiring tumor-specific receptors. As good as it is, ICG has its limitations. Its biggest limitation is specificity. The dye will bind wherever there is breakdown of the blood-brain barrier, so it will light up tumor but also inflammation or necrosis. False positives may also be observed on the skin or dura. Also, the equipment involved a NIR imaging system is over $100,000 and proper training should be done to avoid errors such as incorrect gain settings or misreading of the signal. The Future Researchers are now creating tumor-specific NIR dyes that bind to cancer cell receptors specifically. Coupling the depth of NIR imaging with tumor specificity has the potential to revolutionize margin assessment. By contrast, SWIG with ICG is among the most convenient, easily available fluorescence-guided surgery systems[5].

8. UROLOGY: Clear margins are paramount in urologic oncology and reconstructive surgery, both oncologically and functionally postoperatively. Both—total eradication of malignant tissue with minimal sacrifice of healthy parenchyma—continue to be technical hurdles. Indocyanine Green (ICG) fluorescence imaging is a increasingly useful tool that provides real-time visualization of tissue, vascularity, and margin, allowing surgeons to attain accuracy in complex procedures[21]. ICG is an intravenous water-soluble contrast, which binds immediately with plasma proteins. It fluoresces on irradiation using near-infrared (NIR) light at around 807 nm to 820 nm with tissue penetration of 10 mm. It is useful for surgeons to visualize perfusion and tissue planes intraoperatively without the use of radiation or complicated setup[22].

9. PROSTATECTOMY AND LYMPHADENECTOMY: ICG also increases accuracy in prostate cancer surgery, when both lymph node dissection and prostate margin are equally important. Sentinel lymph node mapping with transrectal ICG injection offers real-time visualization of lymphatic drainage. The technique can identify risk nodes that would otherwise be missed during the process of routine dissection. For the operating surgeon, such high sensitivity ensures that important nodes are not left behind and may eliminate the necessity for aggressive dissections. Clinically, ICG fluorescence augments preoperative imaging and pathology and gives the surgeon assurance that margins are safe without causing morbidity[23].

DISCUSSION

ICG fluorescence imaging is totally shaking up how surgeons tackle tricky surgeries. Its main perk is super straightforward but effective: it provides live updates on blood flow, tissue condition, and tumor edges during surgery. turns out to be a handy tool for all sorts of fields In colorectal and esophageal surgery, for example, ICG helps surgeons assess blood supply at anastomosis sites more reliably than the traditional “eyeball test,” reducing the risk of leaks. In gastric and liver surgery, it's like a better map for lymph nodes and bile ducts, which makes the surgery safer and more complete. Neurosurgeons are now using this "second-window" ICG stuff to spot brain tumors better and see their edges more clearly, but occasionally it can still pick up on inflamed tissue and mess up the signals. Thoracic and urologic procedures have the same good stuff going for them in lung surgeries; ICG is great at marking the right spots, and for kidney and prostate stuff, it helps cut out the bad parts without taking out too much good tissue. In reconstructive surgery, where keeping blood flowing is super important, ICG lets docs check if the tissue's alive on the fly, which helps avoid nasty stuff like blockages or the surgery part not holding up.

CONCLUSION

ICG fluorescence is a trusty buddy for surgeons in the OR, giving them a superpower vision beyond what we can see with our own eyes. Making the margins, blood flow, and delicate parts easier to see while you're doing the surgery helps cut down on problems and boosts the odds of getting the whole tumor out without any issues. Its safety, easypeasy-ness, and super handiness in lots of different surgeries—like cancer removal or fixing up after surgery—prove it's a real go-to tool. Next step: we have to make sure we're using it all the time, like it's second nature, following the standard dosing and timing rules, plus making more hospitals able to use the imaging tech will spread the good stuff to more folks. With growing evidence of its impact on safety and precision, ICG fluorescence is well on its way to becoming a standard part of modern surgery—helping surgeons operate more confidently and patients recover more securely.

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