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Review

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Indocyanine green and near-infrared fluorescence imaging in minimally invasive gastric cancer surgery: a narrative review

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Abstract

Background: The popularity of minimally invasive surgery for gastric cancer has been on the rise due to its advantages in faster recovery and improved outcomes. However, the lack of tactile sensation poses challenges for tumor identification and anatomical recognition. Indocyanine green (ICG) with near-infrared (NIR) fluorescence imaging has emerged as a potential solution to address these challenges. This review summarizes the current status, limitations, and future prospects of ICG and NIR fluorescence imaging in minimally invasive surgery for gastric cancer. Search strategy: This narrative review searched the PubMed database for relevant articles related to ICG and NIR fluorescence imaging in minimally invasive gastric cancer surgery, published through 2023. The search criteria comprised “indocyanine green”, “ICG”, “near-infrared fluorescence imaging”, “gastric cancer”, “gastrectomy”, and “minimally invasive surgery”. Findings: ICG with NIR fluorescence imaging offers three main applications in gastric cancer surgery. Firstly, it aids in real-time intraoperative tumor identification when injected locally around the tumor, surpassing traditional tattooing techniques. Secondly, ICG facilitates lymph node mapping, particularly in identifying sentinel lymph nodes, which could reduce unnecessary lymphadenectomy. Thirdly, ICG angiography enables the assessment of blood perfusion during reconstructive surgery, evaluating

anastomosis sites and potentially reducing anastomotic leakage risk. Conclusions: ICG and NIR fluorescence imaging have shown promising advancements in enhancing the precision and safety of minimally invasive gastric cancer surgery. However, standardized analysis methods and further prospective studies are needed to fully establish their clinical significance. Overall, ICG and NIR fluorescence imaging hold potential as valuable tools to improve patient outcomes in minimally invasive gastric cancer surgery.

Keywords: Indocyanine green, near-infrared fluorescence imaging, gastric cancer, gastrectomy, minimally invasive surgery

INTRODUCTION

In recent years, the popularity of minimally invasive surgery for gastric cancer has risen due to its faster recovery and improved patient outcomes. Types of minimally invasive surgery, including laparoscopic and robotic surgery, allow surgeons to have a wider and clearer field of view and to resect tumors more accurately, which potentially contributes to better long-term results in gastric cancer treatment[1]. However, minimally invasive surgery for gastric cancer also poses a few challenges, including the lack of tactile sensation necessary for the identification of tumors and anatomical structures[2]. Current intraoperative visualization methods, such as near-infrared (NIR) fluorescence imaging, are gaining interest as they strive to address these difficulties. Fluorescence imaging necessitates the use of a fluorescent dye to enhance specific tissues, along with a fluorescent camera system. The fluorescent dyes utilized can be categorized into specific binding dyes and non-specific binding dyes. As a non-specific dye, indocyanine green (ICG) is not selective for tissues, but it can fluorescently enhance tissues by perfusion into tissues or excretion from the liver and kidneys. This technique is widely used in clinical practice[3].

ICG emits strong fluorescent light, peaking at 830 nm when excited in the NIR range and allowing deep signal penetration and minimal tissue autofluorescence interference. Fluorescence can be detected during surgery using a specially developed device such as an NIR camera, which serves to supplement the senses of surgeons. An ICG solution contains trace amounts of iodine and is considered to be contraindicated in cases where allergy to iodine has been confirmed. However, in clinical practice, the occurrence of severe adverse reactions, notably anaphylactic reactions from ICG injection, is reported to be below 0.05%, demonstrating a high level of safety[4].

With regards to digestive surgery, ICG has become popular, especially for its use during esophageal and colorectal surgery. During operation, ICG aids in the evaluation of real-time blood perfusion before anastomosis to reduce the rate of anastomotic leakage[5-7]. For hepatobiliary surgery, it allows the visualization of hepatic segmental boundaries and biliary tree structures, enhancing the precision and ease of hepatectomy and cholecystectomy[8,9]. Additionally, ICG is currently utilized as an indicator for three different aspects of gastric cancer surgery: intraoperative tumor identification, lymph node mapping, and blood perfusion assessment during reconstruction. Despite its common use, there are no current reports comprehensively summarizing the role, the advantages, or the limitations of ICG in gastric cancer surgery. Here, the objective of this review is to provide a comprehensive overview of the present state of ICG and NIR fluorescence imaging in minimally invasive gastric cancer surgery and to discuss its clinical significance.

SEARCH STRATEGY

This study is a narrative review. We conducted a search using the electronic database PubMed to retrieve relevant articles published until 2023 on this topic. The search criteria comprised “indocyanine green”,

"ICG", "near-infrared fluorescence imaging", "gastric cancer", "gastrectomy", and "minimally invasive surgery". Articles were collected in full text and selected and reviewed for alignment with these essential topics.

INTRAOPERATIVE TUMOR IDENTIFICATION

As recommended by Japanese guidelines, proximal resection margins should be at least 2 cm and 3-5 cm for early and advanced gastric cancer, respectively[10]. However, appropriate margins are difficult to determine due to the absence of tactile feedback during laparoscopic or robotic gastrectomy. Thus, a variety of methods have been devised for locating the tumor during operation[11]. Recent studies have demonstrated that ICG is an effective method for intraoperative tumor identification[11-20]. When ICG is injected locally around the tumor, a portion of it binds to albumin in the tissue, allowing intraoperative NIR imaging to identify the tumor in real time.

ICG tattooing

The first method utilized for localization in gastrointestinal surgery was tattooing with dye prior to the surgery through an endoscope, which continues to be a common technique. In Japan, endoscopic tattooing with India ink is still the most common procedure. However, marking with India ink does not allow for an easy adjustment of the amount of ink needed to be visible on the surface of the serosa. As a result, unexpected blotting and spreading may occur. Because ICG is permeable to tissues, it is possible to inject smaller volumes of ICG, avoiding the problem that India ink has of not being able to control the amount. In contrast to India ink, ICG is both a visible and fluorescent dye. According to previous reports, ICG can be observed under an NIR camera within 1-3 days after injection[12]. Furthermore, ICG does not appear to darken the color of that region or interfere with macroscopic observation.

Several studies have used endoscopic ICG tattooing, together with an NIR fluorescence imaging system, to detect gastric cancer[13-17,21-23]. Table 1 summarizes these results. Submucosal injection into four quadrants near the tumor one to three days before surgery has been the most commonly adopted method[13-15,17]. The dose of ICG injection was usually 0.5 mL per puncture site at a concentration of 0.05 mg/kg. Tanaka *et al.* reported that 0.1 mL ICG per puncture site at a concentration of 1.0 mg/mL also produced satisfactory results[16]. The median proximal ICG diffusion distance in these studies was about 20-25 mm, which was adequate for obtaining sufficient resection margins. Cho *et al.* reported that three patients, among a total of 503 early gastric cancer patients, had a positive margin at resection. However, the leading cause of these three positive margin cases was the underestimation of tumor sizes by the endoscopist before surgery, not the ICG tattooing itself[17].

Although ICG tattooing has become common, there still remain some challenges. For example, it requires special equipment and is more expensive than India ink. Also, ICG readily diffuses into the lymphatic vessels surrounding the gastric tissue, meaning that if the time following injection exceeds three days, it will not be possible to localize the tumor accurately. Nonetheless, the results presented here indicate that ICG tattooing is a safe and feasible method of determining tumor location and surgical margin.

Endoscopic clip equipped with ICG

In open abdominal surgery, the placement of metallic clips, which can be verified by direct touch, is a beneficial technique for preoperative marking of tumors. However, in minimally invasive surgery, the clips are not visible from the surface of the gastrointestinal tract and are not tactile, making it challenging to pinpoint the precise location of the tumor.

Table 1. Summary of endoscopic ICG tattooing studies of gastric cancer

	Tumor stage (early/ advanced)	Tumor location	Injection time	Injection site	Injection depth	ICG manufacturer	ICG Conc. (mg/mL)	ICG amount (mL)	ICG-related complication	Positive resection margin	Near-infrared system
Ono *et al.* (2018)[13]	8/4	2 (L), 10 (M), 2 (U)	Three days before surgery	Four sites [proximal(2), distal(2)]: 0.5 mm away from tumor edge	Submucosal	Dai-Ichi Sankyo Pharm, Tokyo, Japan	0.05	0.5	N/A	0	PDE system (Hamamatsu Photonics, Japan), NIR camera system (Shinko Optical, Japan)
Ushimaru *et al.* (2019)[14]	55/29	32 (L), 52 (M)	One day before surgery	Four sites [proximal(1), distal(1), and bilateral(2)]: just at the tumor edge	Submucosal	Dai-Ichi Sankyo Pharm, Tokyo, Japan	0.05	0.5	0	0	IMAGE1 SPIES™ System (KARL STORZ, Germany)
Omori *et al.* (2022)[15]	65/42	107 (U)	One day before surgery	Four sites [proximal(1), distal(1), and bilateral(2)]: just at the tumor edge	Submucosal	Dai-Ichi Sankyo Pharm, Tokyo, Japan	0.05	0.5	0	0	IMAGE1 SPIES™ System (KARL STORZ, Germany)
Tanaka *et al.* (2020)[16]	29/0	5 (U), 24 (M)	One-three days before surgery	One site (proximal) or two sites [proximal(1) and distal(1)]: 1 cm away from tumor edge	Submucosal	Dai-Ichi Sankyo Pharm, Tokyo, Japan	1.0	0.1	0	0	KARL STORZ, Germany
Cho *et al.* (2022)[17]	456/47	263 (L), 15 (M), 86 (U)	One day before surgery	Four quadrants around the tumor	Submucosal	Dongindang Pharm, Siheung-si, Korea	0.625	0.6	0	3	da Vinci Si/Xi Surgical System® (Intuitive Surgical, USA), PINPOINT® Fluorescence Imaging System (Novadaq, Canada)
Chen *et al.* (2022)[21]	8/10	13 (L), 3 (M), 2 (U)	One day before surgery	Four sites	Submucosal	N/A	1.25	0.5	0	0	N/A
Yoon *et al.* (2022)[22]	21/2	11 (L), 12 (M)	One day before surgery	Four sites [proximal(1), distal(1), and bilateral(2)]: within 1 cm from the borders of tumors	Submucosal	Dongindang Pharm, Siheung-si, Korea	0.5	0.1	0	0	N/A
Nakanishi *et al.* (2022)[23]	6/0	6 (M)	One to three days before surgery	One site	Submucosal	Dai-Ichi Sankyo Pharm, Tokyo, Japan	1.0	0.1	0	0	da Vinci Xi Surgical System® (Intuitive Surgical, USA), Firefly® (Intuitive Surgical, USA)

Conc.: Concentration; ICG: indocyanine green; L: lower third; M: middle third; N/A: not available; NIR: near-infrared; U: upper third.

Recently, Narihiro *et al.* created an innovative endoscopic clip integrated with resin-conjugated ICG (ZEOCLIP FS; Zeon Medical Co., Ltd., Tokyo, Japan)[18,24]. The fluorescent resin is introduced at the ends of the fastening claws of the standard clip and sinks into the mucosa by holding the clip on the mucosal surface. In a study with eight cases of gastrointestinal cancer, the ICG fluorescent signal was detected in six patients (three gastric and three rectal)[19]. In another study of 37 cancer patients (23 colonic and 14 gastric), 33 of them (89.1%) had clear fluorescent clip marking at first glance during operation, and

fluorescence was visualized in another three patients (8.1%) after surgical dissection[20]. Therefore, this kind of clip can achieve a high rate of identification.

Fluorescent clips prevent spillage and local spread of dyes within the gastrointestinal tract, which can interfere with the accurate localization of the lesion. As should be noted, NIR fluorescence penetrates the tissues at a distance of approximately 5 to 10 mm. When the stomach wall is thicker than 10 mm, image visualization via NIR fluorescence is difficult. Additionally, fluorescence visibility depends on the angle between the stomach wall and the fluorescence laparoscope. To improve fluorescence visibility, it is important to observe at an angle that is as close to a right angle as possible and to stretch the stomach wall so that it becomes thinner.

LYMPH NODE MAPPING

The lymph node metastasis status plays a crucial role as a prognostic factor, significantly impacting the treatment decision for gastric cancer. The Japanese Gastric Cancer Guideline recommends different lymph node dissection strategies based on the stage of the disease. Generally, it is recommended that D1 or D1+ lymphadenectomy be used for early gastric cancer and D2 lymphadenectomy be used for advanced gastric cancer[25]. When ICG is injected locally, part of it enters into the small lymphatic vessels. As lymph flows slowly and the existence of lymph nodes, ICG can remain in the lymphatic system for long periods, allowing it to be used for lymph node mapping.

Sentinel lymph node mapping

A fact that cannot be ignored is that despite D1 or D1+ lymphadenectomy being performed in patients with early gastric cancer, postoperative pathology revealed that only about 10% of patients had positive lymph nodes[25]. In other words, most early gastric cancer patients are unnecessary for lymph node dissection. Sentinel lymph node (SLN) biopsy is an excellent way to avoid unnecessary lymphadenectomy and is now accepted as a standard method for breast cancer and melanoma[26,27]. Since 2000, many studies have been undertaken to investigate the potential of SLN biopsy in the management of gastric cancer. However, whether SLN biopsy is clinically applicable in gastric cancer is still yet to be determined due to significant heterogeneity among studies[28-30].

In 2004, a multicenter clinical trial (JCOG0302) was carried out by the Japan Clinical Oncology Group to assess the feasibility and accuracy of diagnosing T1 gastric cancer using SLN biopsy. In this study, ICG was injected into the subserosa intraoperatively as a visible dye, and SLN biopsy was performed using a conventional pick-up method. Nevertheless, this trial was halted because of a high rate of false negatives[31]. Several factors contributed to this outcome, including a short learning period for SLN identification and only one frozen section being analyzed. The concept of sentinel basin nodes (SBNs) was proposed by Miwa *et al.*, in which SLN basins were found to contain actual metastatic nodes even in patients with false-negative SLN biopsy results[32]. Since then, numerous studies have demonstrated that SBN biopsy is more accurate at detecting SLN metastasis than pick-up SLN biopsy[33-35]. In 2013, another multicenter clinical trial conducted by the Japan Society for Sentinel Node Navigation Surgery demonstrated that SBN dissection was deemed appropriate without jeopardizing the potential cure for cT1N0 gastric cancer in patients with no prior treatment history[36]. In this study, the lymph node mapping procedure utilized the dual tracer method, combining technetium 99m-labeled tin colloid and 1% isosulfan blue dye. However, blue dye degrades rapidly, and radioactive colloid results in a shine-through effect during the detection of hot nodes using a γ probe. These drawbacks restrict their effectiveness for laparoscopic SLN biopsy. In a meta-analysis of 10 studies with 643 patients utilizing ICG and NIR fluorescence imaging for SLN identification, it was found that the pooled identification rate, sensitivity, and specificity were 99%, 87%, and 100%,

respectively[37]. Although the included studies primarily focused on the pick-up method, they support the increasing recognition of the value of ICG and NIR fluorescence imaging in SLN identification.

In 2013, In South Korea, a significant and prospective phase III trial (SENORITA TRIAL) was initiated to conduct a comparative study between laparoscopic sentinel node navigation surgery (LSNNS) and standard laparoscopic gastrectomy combined with lymph node dissection for early gastric cancer[38]. In this study, if all the retrieved SBNs showed no signs of tumor presence, stomach-preserving primary tumor resection rather than standard gastrectomy was then carried out. The final result showed that both groups were comparable in surgical outcomes, including postoperative complications, three-year overall survival, and three-year disease-specific survival rates. However, LSNNS had better long-term quality of life (QOL) and nutrition than conventional laparoscopic gastrectomy with lymph node dissection[39,40]. In this trial, the dual-tracer method (ICG and radiolabeled human serum albumin) was applied for SLN mapping. In a recent survey conducted by the International Society for Fluorescence Guided Surgery, some consensus was reached regarding fluorescence imaging and ICG during gastric cancer surgery[41]. According to the consensus, fluorescence imaging with ICG was an acceptable single-agent method for detecting SLN, and the SBN biopsy method was preferred. However, SLB dissection is restricted to T1 gastric cancer and tumors measuring ≤ 4 cm in diameter. Technically, ICG should be injected into four quadrants near the tumor, administered on the same day as surgery, injected endoscopically into the submucosa at a total volume of 1 to 5 mL of 5 mg/mL concentration, and repeated if SLN imaging remains insufficient. In all, these data show that SBN can be beneficial in the treatment of early gastric cancer. Yet, more research is necessary to determine ICG-specific applications in SBN and to compare ICG with other dyes.

ICG-guided lymph node harvesting

The existing Union for International Cancer Control (UICC) classification suggests a requirement of at least 16 lymph nodes or more for precise pathological staging in gastric cancer[42]. However, Miftode *et al.* conducted a study that indicated the lack of justification for a minimum threshold of 16 examined lymph nodes[43].

They emphasized the importance of performing accurate lymphadenectomy and thoroughly examining the surgical specimen. Macalindong *et al.* examined the number of lymph nodes harvested (1-30, 31-45, > 45) in relation to five-year disease-free survival and overall survival[44]. They observed that a higher number of harvested lymph nodes correlated with improved survival in gastric cancer patients at intermediate stages.

In a randomized trial (FUGES-012), Chen *et al.* demonstrated that ICG increases the number of lymph nodes (mean 50.5 *vs.* 42.0, $P < 0.001$) harvested by surgeons and reduces the rate of lymph node noncompliance in patients undergoing D2 lymphadenectomy for gastric cancer[45]. Several authors have reported similar findings[46-48]. Park *et al.* studied infrapyloric lymph node dissection with and without ICG in laparoscopic distal gastrectomy. They found that although there was no significant difference in the number of lymph nodes dissected between the two groups, the use of ICG significantly shortened the operative time and decreased bleeding during dissection[49]. In a robotic gastrectomy study, fluorescent lymphography using ICG and NIR imaging produced similar results, with more lymph nodes retrieved and a reduction in the rate of lymph node noncompliance[50]. Fujimoto *et al.* reported a prospective non-randomized cohort study on the quality of lymph node dissection in robot-assisted distal gastrectomy (RDG) with ICG tracer guidance using the da Vinci surgical system with Firefly system (Intuitive Surgical, Sunnyvale, CA, USA)[51]. They concluded that the use of the Firefly system led to an increase in the number of retrieved lymph nodes and a decrease in lymph node noncompliance rate, thereby improving the quality of lymph node dissection. Similarly, Zhang *et al.* conducted a systematic review and meta-analysis,

confirming the safety and efficacy of ICG and NIR fluorescence imaging-guided lymph node dissection in robot-assisted gastrectomy for gastric cancer[52]. Regarding the prognostic impact of combined ICG fluorescence, Park *et al.* reported the results of a retrospective analysis of 5,678 gastric cancer patients[53]. They have found that ICG fluorescence-guided lymphadenectomy has provided better survival outcomes, especially in stage III patients, due to more accurate staging with stage migration, extensive lymph node excision, the larger number of lymph nodes harvested, and more sensitive detection of metastatic lymph nodes. Thus, while many favorable reports can be found for ICG-guided lymph node harvesting in the surgical treatment of gastric cancer, there are also several reports that are skeptical as to its clinical significance. Recently, Sposito *et al.* reported the results of a phase 2 trial (Greeneye) focusing on the clinical benefits of ICG-guided D2 lymphadenectomy in distal gastrectomy. The authors conclude that the true benefit of ICG-guided lymphadenectomy is limited in the presence of adequate D2 lymph node dissection, making it difficult to justify the widespread use of this technique[54]. Moreover, Lan *et al.* observed no significant difference in the number of harvested lymph nodes between patients who underwent robotic gastrectomy with or without the application of NIR/ICG technology[55]. While the number of lymph nodes harvested is an important aspect in harvesting lymph nodes, it is also necessary to examine the rate of identification of metastatic lymph nodes. The FUGES-012 trial results indicated that there was no substantial difference in the number of metastatic lymph nodes between the two groups, as the ICG group exhibited similar numbers to the non-ICG group at each station. Furthermore, the diagnostic sensitivity and specificity for the fluorescence and metastatic lymph nodes of the ICG group were reported as 56.3 and 46.1, respectively. ICG fluorescence suffers from a limitation in accurately differentiating metastatic lymph nodes, which may result in the inadvertent removal of a significant number of normal lymph nodes during surgery.

Consequently, extensive studies with substantial sample sizes are required to evaluate whether the excessive harvesting of lymph nodes contributes to the long-term prognosis of patients. Additionally, skip metastasis occurs in up to 11% of lymph node metastases in patients with gastric cancer exhibiting a dominant lesion on the lesser curvature, particularly in the lower part of the gastric body or the entire circumference of the stomach[56]. Addressing these distinct lymph node metastases of gastric cancer through the utilization of ICG and NIR fluorescence imaging represents a crucial concern for the future.

The optimal approach for ICG injection is yet to be determined. According to Tajima *et al.*, submucosal injection of ICG before surgery exhibited higher accuracy in detecting SLNs compared to the intraoperative subserosal injection of ICG[57]. Nevertheless, several retrospective studies endorse the utilization of submucosal injections of ICG one day prior to the surgical procedure for fluorescence-guided lymphadenectomy[46]. Chen *et al.* carried out a prospective randomized clinical trial (FUGES-019) aiming to compare the effectiveness of ICG injection using the preoperative submucosal and intraoperative subserosal approaches for lymph node tracing during laparoscopic gastrectomy. The result showed no difference in terms of the ability to use ICG submucosally or subserosally[58].

Neoadjuvant chemotherapy is frequently used in the treatment of advanced gastric cancer. Chemotherapy-induced profibrotic reactions and cytotoxicity often complicate lymph node dissection[59]. It is doubted that ICG is able to reach the fibrotic lymph nodes, leading to lymph node omission. Therefore, ICG-guided lymph node harvesting may not be ideal for such patients. Despite this, Huang *et al.* recently studied the impact of ICG on lymph node harvesting during laparoscopic D2 radical gastrectomy after adjuvant chemotherapy. They found that for patients with no remission, ICG administration during laparoscopic radical gastrectomy can enhance the lymph node harvest count, decrease the rate of lymph node noncompliance, and reduce intraoperative bleeding. For patients with remission, the number of lymph nodes harvested and the rate of lymph node noncompliance in the ICG group were comparable to those in

the non-ICG group[60]. Puccetti *et al.* reported, based on the results of a retrospective study of laparoscopic total gastrectomy with D2 lymphadenectomy, that while ICG-guided lymphadenectomy increased the extent of lymph node detection, some factors such as preoperative chemotherapy and positive lymph node metastasis rates possibly limit the technical efficacy of ICG[61]. An international multicenter prospective study, including both surgery as first treatment and surgery after neoadjuvant treatment, is currently underway to examine the clinical role of NIR/ICG technology for advanced gastric cancer surgery[62].

BLOOD PERFUSION ASSESSMENT DURING RECONSTRUCTIVE SURGERY

Anastomotic leakage, which correlates closely with anastomosis blood perfusion, is one of the most severe complications in gastrointestinal surgery. Traditional blood perfusion evaluation methods are mainly based on peristalsis, color, artery pulsation, or end bleeding. These methods rely primarily on the experience of surgeons and can be inaccurate. When ICG is injected intravenously, it binds rapidly to plasma lipoproteins, enabling the visualization of vessels that contain ICG (angiography). In recent years, ICG angiography with NIR fluorescence imaging, which allows real-time and visual assessment of organ blood perfusion, has been used in digestive surgery, particularly esophagectomy and colectomy. There are several reviews of these topics[6,7,63,64], with some demonstrating that ICG fluorescence angiography helped reduce anastomotic leakage[65-67].

It is still under debate as to how to define anastomosis blood perfusion by ICG, and no standardized analysis method has been established. Sherwinter *et al.* proposed a scoring system comprising a fluorescence score ranging from 1 to 5 (1 indicated no uptake, 5 indicated maximum uptakes, and the scoring was based on a subjective assessment) to evaluate mucosal perfusion of the colon, rectum, and the anastomotic staple line. In this study, a total of twenty patients underwent technically successful ICG angiograms, four of whom had abnormal angiograms. In two of these cases, protective loop ileostomies were performed, and there was no evidence of anastomotic leakage. The two other patients with diverting loop ileostomies were found on CT scans to have peri-anastomotic collections consistent with anastomotic leaks. Based on their findings, the authors concluded that transanal ICG angiography was viable and enabled imaging of mucosal and anastomotic blood flow[68]. Huh *et al.* used the same scoring system and a laparoscopic system with a NIR function to assess the anastomotic perfusion in 30 ICG-guided gastrectomies (distal gastrectomy with B-I or B-II, total gastrectomy with Roux-en-Y, and pylorus-preserving gastrectomy). Seven patients (23.3%) had abnormal ICG visualization. However, no modifications were recommended to the surgical plan, and anastomotic leakage occurred in one patient with high clinical and fluorescence scores. The authors concluded that when the fluorescence assessment showed sufficient perfusion, the anastomosis was considered to have a healthy blood supply. However, careful monitoring of the anastomotic site is warranted to detect any focal changes. On the contrary, in cases where the fluorescence assessment indicated inadequate perfusion, the clinician could not definitively determine that all anastomoses are unhealthy. Alternatively, closely monitoring the anastomotic site and implementing additional precautionary measures were deemed necessary[69].

In other studies, blood perfusion was assessed according to the perfusion time point[70]. Noma *et al.* used ICG angiography to evaluate gastric conduit blood perfusion prior to esophagogastric anastomosis. Every effort was made to complete the anastomosis within 30 seconds of the line. The result showed that the incidence of anastomotic leakage in the ICG group was significantly lower compared to the non-ICG group[70]. Similar results were obtained in a study by Luo *et al.* in which a 60-second line was selected as a point of differentiation between zones with good and poor perfusion. They used this 60-second rule for McKeown minimally invasive esophagectomy with cervical anastomosis for esophageal cancer. Anastomotic leakage was significantly lower in the ICG group than in the non-ICG group (1.2% *vs.*

10.4%)[71]. Kumagai *et al.* proposed a 90-second rule that all anastomoses should be constructed within 90 seconds (ideally within 60 seconds) after the first fluorescent enhancement is observed at the root of the right gastroepiploic artery. The incidence of anastomotic leakage was 1.4% (1/70) when the anastomosis was carried out in the region where ICG perfusion was identified using fluorescence angiography within 90 seconds[72]. It should be noted that the reconstructed techniques and time calculation methods in these studies were not all the same, so it is difficult to determine which time point was more accurate.

Mori *et al.* retrospectively evaluated ICG fluorescence of anastomosis on 100 laparoscopic gastrectomies, including distal gastrectomy, proximal gastrectomy, and total gastrectomy. The reconstruction method included B-I, B-II, and Roux-en-Y. The authors injected 0.5 mg/kg of ICG solution after the anastomosis was completed[73].

ICG fluorescence image patterns were categorized into homogeneous, heterogeneous, and faint groups, determined by the fluorescence intensity observed on the proximal and distal sides of the anastomosis at 60 seconds. The ratios of anastomotic leak in the homogeneous, heterogeneous, and faint groups were 1.6% (1/61), 2.7% (1/37), and 100% (2/2), respectively. Additionally, the authors reported a risk of anastomotic leakage in situations where there was a considerable time gap between the staining of the oral and anal sides of an organ utilized in anastomosis with ICG. Hayakawa *et al.* assessed blood perfusion on the lesser-curvature side of the duodenum following a B-I anastomosis with delta anastomosis[74]. This study observed that the duodenal wall on the lesser curvature side was the final area to be stained with ICG at the anastomotic site, suggesting that this region was particularly susceptible to altered blood flow. Consequently, this susceptibility led to complications related to the anastomotic site in patients who underwent RDG following delta-shaped anastomosis. It stated that time to fluorescence showed the most favorable potential as a category for quantifying fluorescence angiography[74].

Compared to esophagus and colorectal surgery, there are fewer gastric surgery studies that have adopted ICG to assess blood perfusion for reconstruction[75]. This may be due to the fact that the stomach has a rich network of vessels in its submucosa, and the rate of anastomotic leakage is much lower than that of esophagectomy or colorectal resection. In addition, the assessment method of ICG in blood perfusion is not standardized at the moment. In our department, we routinely use ICG for blood flow assessment during an esophagectomy. In some gastrectomy cases involving a high risk of anastomotic leakage, such as higher esophagojejunostomy, ICG angiography is also performed [Figure 1]. Considering the disastrous consequences of anastomotic leak after gastric surgery, it is still worth exploring the use of ICG fluorescence for assessing anastomotic blood supply in the future.

ONGOING TRIALS AND PERSPECTIVE

Ongoing clinical trials include those for advanced and remnant gastric cancer, as well as clinical trials comparing lymph node dissection by ICG infusion method and site. The POLA trial (NCT05720598) is investigating the safety and feasibility of ICG-guided SLN detection in patients with advanced gastric cancer undergoing multimodal therapy[76]. In addition, the NCT05687617 trial is a multicenter prospective study in Canada that utilizes ICG fluorescence for the retrieval of peritoneal dissemination in diagnostic laparoscopy. The iGreenGO (indocyanine Green Gastric Observation) study (NCT04943484) investigates the rate of change in surgical techniques in ICG tracer-guided lymph node dissection for remnant gastric cancer if the NIR/ICG technique is activated during surgery after macroscopic D2 lymph node dissection[62]. The NCT04219332 trial is investigating the impact of ICG injection sites in laparoscopic gastrectomy on lymph node retrieval by comparing submucosal or subserosal injection sites in laparoscopic gastrectomy. The NCT05229874 trial is a study of the efficacy and safety of carbon nanoparticle suspension

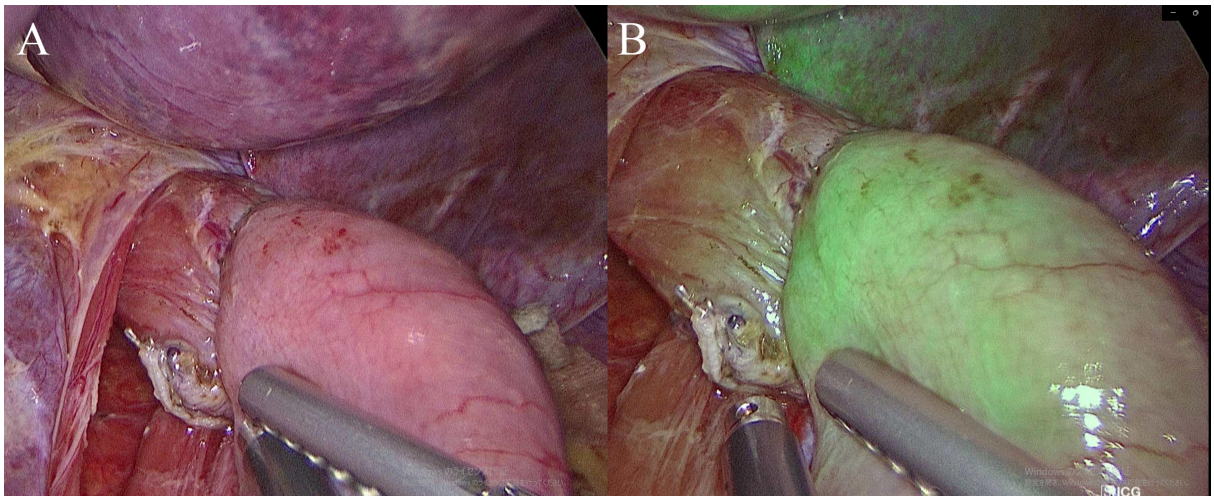

Figure 1. (A) Spectrum of images in the usual form of esophagojejunostomy anastomosis; (B) Esophagojejunostomy seen with indocyanine green (ICG) image-guided fluorescence.

injection during robot-assisted gastrectomy compared to ICG tracer-guided lymph node dissection with the number of dissected lymph nodes as the main outcome. These multifaceted trials are expected to contribute to further evidence-based development of ICG-related surgical treatment for gastric cancer in the near future.

CONCLUSION

Current research shows that NIR fluorescence imaging using ICG is a safe and promising technology in minimally invasive gastric cancer. Intraoperative visualization of tumors is possible using ICG administered in a small amount under the mucosa. ICG-equipped endoscopic clips prevent spillage and local dye spread, allowing more accurate lesion localization. The lymphatic node is visualized efficiently using ICG without contaminating the operating field. ICG can identify SLNs for early gastric cancer and greatly facilitate lymph node dissection for advanced gastric cancer. Perfusion patterns after ICG angiography can help assess the blood supply of anastomotic areas and predict leakage. Despite the numerous benefits, this method has yet to be established as a golden standard. Therefore, further research should be conducted to provide the additional evidence that is needed to confirm its clinical efficacy.

DECLARATIONS

Authors' contributions

Designed the review, collected and analyzed the data, drafted the article: Yamauchi S, Wu Z
Revised all manuscripts as a native English language proofreader: Fedor C
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REFERENCES

1. Kim HH, Han SU, Kim MC, et al. Effect of laparoscopic distal gastrectomy vs open distal gastrectomy on long-term survival among patients with stage I gastric cancer: the KLASS-01 randomized clinical trial. *JAMA Oncol* 2019;5:506-13. DOI PubMed PMC
2. Hamed OH, Gusani NJ, Kimchi ET, Kavic SM. Minimally invasive surgery in gastrointestinal cancer: benefits, challenges, and solutions for underutilization. *JSLS* 2014;18:e2014.00134. DOI PubMed PMC
3. Alander JT, Kaartinen I, Laakso A, et al. A review of indocyanine green fluorescent imaging in surgery. *Int J Biomed Imaging* 2012;2012:940585. DOI PubMed PMC
4. Paumgartner G. The handling of indocyanine green by the liver. *Schweiz Med Wochenschr* 1975;105:1-30. PubMed
5. Kitagawa H, Yokota K, Marui A, Namikawa T, Kobayashi M, Hanazaki K. Near-infrared fluorescence imaging with indocyanine green to assess the blood supply of the reconstructed gastric conduit to reduce anastomotic leakage after esophagectomy: a literature review. *Surg Today* 2023;53:399-408. DOI PubMed
6. Quan YH, Han KN, Kim HK. Fluorescence Image-Based Evaluation of Gastric Tube Perfusion during Esophagogastrostomy. *Korean J Thorac Cardiovasc Surg* 2020;53:178-83. DOI PubMed PMC
7. Iwamoto M, Ueda K, Kawamura J. A narrative review of the usefulness of indocyanine green fluorescence angiography for perfusion assessment in colorectal surgery. *Cancers* 2022;14:5623. DOI PubMed PMC
8. Majlesara A, Golriz M, Hafezi M, et al. Indocyanine green fluorescence imaging in hepatobiliary surgery. *Photodiagnosis Photodyn Ther* 2017;17:208-15. DOI
9. Serban D, Badiu DC, Davitoiu D, et al. Systematic review of the role of indocyanine green near-infrared fluorescence in safe laparoscopic cholecystectomy (review). *Exp Ther Med* 2022;23:187. DOI PubMed PMC
10. Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2021 (6th edition). *Gastric Cancer* 2023;26:1-25. DOI PubMed PMC
11. Jeong SH, Seo KW, Min JS. Intraoperative tumor localization of early gastric cancers. *J Gastric Cancer* 2021;21:4-15. DOI PubMed PMC
12. Barberio M, Pizzicannella M, Laracca GG, et al. Endoscopic preoperative tattooing and marking in the gastrointestinal tract: a systematic review of alternative methods. *J Laparoendosc Adv Surg Tech A* 2020;30:953-61. DOI PubMed
13. Ono H, Kusano M, Nihei M, et al. [Effectiveness of indocyanine green fluorescence in endoscopic marking in gastric cancer surgery:a feasibility study for replacing India ink]. *Nihon Shokakibyo Gakkai Zasshi* 2018;115:385-93. DOI PubMed
14. Ushimaru Y, Omori T, Fujiwara Y, et al. The feasibility and safety of preoperative fluorescence marking with indocyanine green (ICG) in laparoscopic gastrectomy for gastric cancer. *J Gastrointest Surg* 2019;23:468-76. DOI PubMed
15. Omori T, Hara H, Shinno N, et al. Safety and efficacy of preoperative indocyanine green fluorescence marking in laparoscopic gastrectomy for proximal gastric and esophagogastric junction adenocarcinoma (ICG MAP study). *Langenbecks Arch Surg* 2022;407:3387-96. DOI PubMed
16. Tanaka C, Kanda M, Funasaka K, et al. Detection of indocyanine green fluorescence to determine tumor location during laparoscopic gastrectomy for gastric cancer: results of a prospective study. *Asian J Endosc Surg* 2020;13:160-7. DOI PubMed
17. Cho M, Kim KY, Park SH, Kim YM, Kim HI, Hyung WJ. Securing resection margin using indocyanine green diffusion range on gastric wall during NIR fluorescence-guided surgery in early gastric cancer patients. *Cancers* 2022;14:5223. DOI PubMed PMC
18. Narihiro S, Yoshida M, Ohdaira H, et al. Near-infrared fluorescent clip guided gastrectomy: report of 2 cases (Case reports). *Ann Med Surg* 2020;55:49-52. DOI PubMed PMC
19. Namikawa T, Iwabu J, Hashiba M, et al. Novel endoscopic marking clip equipped with resin-conjugated fluorescent indocyanine green during laparoscopic surgery for gastrointestinal cancer. *Langenbecks Arch Surg* 2020;405:503-8. DOI PubMed
20. Ryu S, Okamoto A, Nakashima K, et al. Usefulness of preoperative endoscopic fluorescent clip marking in laparoscopic gastrointestinal surgery. *Anticancer Res* 2020;40:6517-23. DOI PubMed
21. Chen X, Zhang Z, Zhang F, et al. Analysis of safety and efficacy of laparoscopic radical gastrectomy combined with or without indocyanine green tracer fluorescence technique in treatment of gastric cancer: a retrospective cohort study. *J Gastrointest Oncol*

2022;13:1616-25. DOI PubMed PMC
22. Yoon BW, Lee WY. The oncologic safety and accuracy of indocyanine green fluorescent dye marking in securing the proximal resection margin during totally laparoscopic distal gastrectomy for gastric cancer: a retrospective comparative study. *World J Surg Oncol* 2022;20:26. DOI PubMed PMC
23. Nakanishi K, Tanaka C, Kanda M, et al. Preoperative indocyanine green fluorescence injection to accurately determine a proximal margin during robotic distal gastrectomy. *Asian J Endosc Surg* 2023;16:152-6. DOI PubMed
24. Narihiro S, Yoshida M, Ohdaira H, et al. Effectiveness and safety of tumor site marking with near-infrared fluorescent clips in colorectal laparoscopic surgery: a case series study. *Int J Surg* 2020;80:74-8. DOI PubMed
25. Kinami S, Nakamura N, Tomita Y, et al. Precision surgical approach with lymph-node dissection in early gastric cancer. *World J Gastroenterol* 2019;25:1640-52. DOI PubMed PMC
26. Jatoi I, Kunkler IH. Omission of sentinel node biopsy for breast cancer: historical context and future perspectives on a modern controversy. *Cancer* 2021;127:4376-83. DOI PubMed
27. Wong SL, Faries MB, Kennedy EB. Sentinel lymph node biopsy and management of regional lymph nodes in melanoma: American society of clinical oncology and society of surgical oncology clinical practice guideline update summary. *J Oncol Pract* 2018;14:242-5. DOI PubMed
28. Lirosi MC, Biondi A, Ricci R. Surgical anatomy of gastric lymphatic drainage. *Transl Gastroenterol Hepatol* 2017;2:14. DOI PubMed PMC
29. Ichikura T, Morita D, Uchida T, et al. Sentinel node concept in gastric carcinoma. *World J Surg* 2002;26:318-22. DOI PubMed
30. Ryu KW, Eom BW, Nam BH, et al. Is the sentinel node biopsy clinically applicable for limited lymphadenectomy and modified gastric resection in gastric cancer? A meta-analysis of feasibility studies. *J Surg Oncol* 2011;104:578-84. DOI
31. Miyashiro I, Hiratsuka M, Sasako M, et al. High false-negative proportion of intraoperative histological examination as a serious problem for clinical application of sentinel node biopsy for early gastric cancer: final results of the Japan Clinical Oncology Group multicenter trial JCOG0302. *Gastric Cancer* 2014;17:316-23. DOI PubMed
32. Miwa K, Kinami S, Taniguchi K, Fushida S, Fujimura T, Nonomura A. Mapping sentinel nodes in patients with early-stage gastric carcinoma. *Br J Surg* 2003;90:178-82. DOI PubMed
33. Kelder W, Nimura H, Takahashi N, Mitsumori N, van Dam GM, Yanaga K. Sentinel node mapping with indocyanine green (ICG) and infrared ray detection in early gastric cancer: an accurate method that enables a limited lymphadenectomy. *Eur J Surg Oncol* 2010;36:552-8. DOI PubMed
34. Lee YJ, Ha WS, Park ST, Choi SK, Hong SC, Park JW. Which biopsy method is more suitable between a basin dissection and pick-up biopsy for sentinel nodes in laparoscopic sentinel-node navigation surgery (LSNNS) for gastric cancer? *J Laparoendosc Adv Surg Tech A* 2008;18:357-63. DOI PubMed
35. Niihara M, Takeuchi H, Nakahara T, et al. Sentinel lymph node mapping for 385 gastric cancer patients. *J Surg Res* 2016;200:73-81. DOI PubMed
36. Kitagawa Y, Takeuchi H, Takagi Y, et al. Sentinel node mapping for gastric cancer: a prospective multicenter trial in Japan. *J Clin Oncol* 2013;31:3704-10. DOI PubMed
37. Skubleny D, Dang JT, Skulsky S, et al. Diagnostic evaluation of sentinel lymph node biopsy using indocyanine green and infrared or fluorescent imaging in gastric cancer: a systematic review and meta-analysis. *Surg Endosc* 2018;32:2620-31. DOI PubMed
38. Park JY, Kim YW, Ryu KW, et al. Assessment of laparoscopic stomach preserving surgery with sentinel basin dissection versus standard gastrectomy with lymphadenectomy in early gastric cancer-a multicenter randomized phase III clinical trial (SENORITA trial) protocol. *BMC Cancer* 2016;16:340. DOI PubMed PMC
39. An JY, Min JS, Hur H, et al. Laparoscopic sentinel node navigation surgery versus laparoscopic gastrectomy with lymph node dissection for early gastric cancer: short-term outcomes of a multicentre randomized controlled trial (SENORITA). *Br J Surg* 2020;107:1429-39. DOI PubMed
40. Kim YW, Min JS, Yoon HM, et al. Laparoscopic sentinel node navigation surgery for stomach preservation in patients with early gastric cancer: a randomized clinical trial. *J Clin Oncol* 2022;40:2342-51. DOI PubMed PMC
41. Sherwinter DA, Boni L, Bouvet M, et al. Use of fluorescence imaging and indocyanine green for sentinel node mapping during gastric cancer surgery: results of an intercontinental Delphi survey. *Surgery* 2022;172:S29-37. DOI PubMed PMC
42. Amin MB, Greene FL, Edge SB, et al. The eighth edition AJCC cancer staging manual: continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. *CA Cancer J Clin* 2017;67:93-9. DOI PubMed
43. Miftode S, Bruns H. Misclassification of nodal stage in gastric cancer: 16 lymph nodes is not enough. *Surg Exp Pathol* 2022;5:7. DOI
44. Macalindong SS, Kim KH, Nam BH, et al. Effect of total number of harvested lymph nodes on survival outcomes after curative resection for gastric adenocarcinoma: findings from an eastern high-volume gastric cancer center. *BMC Cancer* 2018;18:73. DOI PubMed PMC
45. Chen QY, Xie JW, Zhong Q, et al. Safety and efficacy of indocyanine green tracer-guided lymph node dissection during laparoscopic radical gastrectomy in patients with gastric cancer: a randomized clinical trial. *JAMA Surg* 2020;155:300-11. DOI PubMed
46. Jung MK, Cho M, Roh CK, et al. Assessment of diagnostic value of fluorescent lymphography-guided lymphadenectomy for gastric cancer. *Gastric Cancer* 2021;24:515-25. DOI PubMed
47. Maruri I, Pardellas MH, Cano-Valderrama O, et al. Retrospective cohort study of laparoscopic ICG-Guided Lymphadenectomy in gastric cancer from a Western country center. *Surg Endosc* 2022;36:8164-9. DOI PubMed

48. Liu M, Xing J, Xu K, et al. Application of near-infrared fluorescence imaging with indocyanine green in totally laparoscopic distal gastrectomy. *J Gastric Cancer* 2020;20:290-9. DOI PubMed PMC
49. Park SH, Berlth F, Choi JH, et al. Near-infrared fluorescence-guided surgery using indocyanine green facilitates secure infrapyloric lymph node dissection during laparoscopic distal gastrectomy. *Surg Today* 2020;50:1187-96. DOI PubMed
50. Kwon IG, Son T, Kim HI, Hyung WJ. Fluorescent lymphography-guided lymphadenectomy during robotic radical gastrectomy for gastric cancer. *JAMA Surg* 2019;154:150-8. DOI PubMed PMC
51. Fujimoto D, Taniguchi K, Takashima J, Kobayashi H. Indocyanine green tracer-guided radical robotic distal gastrectomy using the firefly™ system improves the quality of lymph node dissection in patients with gastric cancer. *J Gastrointest Surg* 2023; Online ahead of print. DOI PubMed
52. Zhang Z, Deng C, Guo Z, Liu Y, Qi H, Li X. Safety and efficacy of indocyanine green near-infrared fluorescent imaging-guided lymph node dissection during robotic gastrectomy for gastric cancer: a systematic review and meta-analysis. *Minim Invasive Ther Allied Technol* 2023:1-9. Online ahead of print. DOI PubMed
53. Park SH, Kim KY, Cho M, Kim YM, Kim HI, Hyung WJ. Prognostic impact of fluorescent lymphography on gastric cancer. *Int J Surg* 2023; Online ahead of print. DOI PubMed
54. Sposito C, Maspero M, Conalbi V, et al. Impact of indocyanine green fluorescence imaging on lymphadenectomy quality during laparoscopic distal gastrectomy for gastric cancer (greeneye): an adaptative, phase 2, clinical trial. *Ann Surg Oncol* 2023; Online ahead of print. DOI PubMed
55. Lan YT, Huang KH, Chen PH, et al. A pilot study of lymph node mapping with indocyanine green in robotic gastrectomy for gastric cancer. *SAGE Open Med* 2017;5:2050312117727444. DOI PubMed PMC
56. Lee SE, Lee JH, Ryu KW, et al. Sentinel node mapping and skip metastases in patients with early gastric cancer. *Ann Surg Oncol* 2009;16:603-8. DOI PubMed
57. Tajima Y, Yamazaki K, Masuda Y, et al. Sentinel node mapping guided by indocyanine green fluorescence imaging in gastric cancer. *Ann Surg* 2009;249:58-62. DOI PubMed
58. Chen QY, Zhong Q, Li P, et al. Comparison of submucosal and subserosal approaches toward optimized indocyanine green tracer-guided laparoscopic lymphadenectomy for patients with gastric cancer (FUGES-019): a randomized controlled trial. *BMC Med* 2021;19:276. DOI PubMed PMC
59. Li Z, Shan F, Ying X, et al. Assessment of laparoscopic distal gastrectomy after neoadjuvant chemotherapy for locally advanced gastric cancer: a randomized clinical trial. *JAMA Surg* 2019;154:1093-101. DOI PubMed PMC
60. Huang ZN, Su-Yan, Qiu WW, et al. Assessment of indocyanine green tracer-guided lymphadenectomy in laparoscopic gastrectomy after neoadjuvant chemotherapy for locally advanced gastric cancer: results from a multicenter analysis based on propensity matching. *Gastric Cancer* 2021;24:1355-64. DOI PubMed
61. Puccetti F, Cinelli L, Genova L, et al. Applicative limitations of indocyanine green fluorescence assistance to laparoscopic lymph node dissection in total gastrectomy for cancer. *Ann Surg Oncol* 2022;29:5875-82. DOI PubMed
62. Lombardi PM, Mazzola M, Nicastro V, et al. The iGreenGO study: the clinical role of indocyanine green imaging fluorescence in modifying the surgeon's conduct during the surgical treatment of advanced gastric cancer - study protocol for an international multicenter prospective study. *Front Oncol* 2022;12:854754. DOI PubMed PMC
63. Slooter MD, Eshuis WJ, Cuesta MA, Gisbertz SS, van Berge Henegouwen MI. Fluorescent imaging using indocyanine green during esophagectomy to prevent surgical morbidity: a systematic review and meta-analysis. *J Thorac Dis* 2019;11:S755-65. DOI PubMed PMC
64. Peltrini R, Podda M, Castiglioni S, et al. Intraoperative use of indocyanine green fluorescence imaging in rectal cancer surgery: the state of the art. *World J Gastroenterol* 2021;27:6374-86. DOI PubMed PMC
65. Ohi M, Toiyama Y, Mohri Y, et al. Prevalence of anastomotic leak and the impact of indocyanine green fluorescein imaging for evaluating blood flow in the gastric conduit following esophageal cancer surgery. *Esophagus* 2017;14:351-9. DOI PubMed PMC
66. Zehetner J, DeMeester SR, Alicuben ET, et al. Intraoperative assessment of perfusion of the gastric graft and correlation with anastomotic leaks after esophagectomy. *Ann Surg* 2015;262:74-8. DOI PubMed PMC
67. Kondo A, Kumamoto K, Asano E, Feng D, Kobara H, Okano K. Indocyanine green fluorescence imaging during laparoscopic rectal cancer surgery could reduce the incidence of anastomotic leakage: a single institutional retrospective cohort study. *World J Surg Oncol* 2022;20:397. DOI PubMed PMC
68. Sherwinter DA, Gallagher J, Donkar T. Intra-operative transanal near infrared imaging of colorectal anastomotic perfusion: a feasibility study. *Colorectal Dis* 2013;15:91-6. DOI PubMed
69. Huh YJ, Lee HJ, Kim TH, et al. Efficacy of assessing intraoperative bowel perfusion with near-infrared camera in laparoscopic gastric cancer surgery. *J Laparoendosc Adv Surg Tech A* 2019;29:476-83. DOI PubMed
70. Noma K, Shirakawa Y, Kanaya N, et al. Visualized evaluation of blood flow to the gastric conduit and complications in esophageal reconstruction. *J Am Coll Surg* 2018;226:241-51. DOI PubMed
71. Luo RJ, Zhu ZY, He ZF, Xu Y, Wang YZ, Chen P. Efficacy of indocyanine green fluorescence angiography in preventing anastomotic leakage after McKeown Minimally invasive esophagectomy. *Front Oncol* 2020;10:619822. DOI PubMed PMC
72. Kumagai Y, Hatano S, Sobajima J, et al. Indocyanine green fluorescence angiography of the reconstructed gastric tube during esophagectomy: efficacy of the 90-second rule. *Dis Esophagus* 2018;31:doy052. DOI PubMed
73. Mori M, Shuto K, Hirano A, et al. A novel parameter identified using indocyanine green fluorescence angiography may contribute to

predicting anastomotic leakage in gastric cancer surgery. *World J Surg* 2020;44:2699-708. DOI PubMed

74. Hayakawa S, Ogawa R, Ueno S, et al. Impact of the indocyanine green fluorescence method for anastomotic blood flow in robotic distal gastrectomy. *Surg Today* 2022;52:1405-13. DOI PubMed
75. Slooter MD, Mansvelders MSE, Bloemen PR, et al. Defining indocyanine green fluorescence to assess anastomotic perfusion during gastrointestinal surgery: systematic review. *BJS Open* 2021;5:zraa074. DOI PubMed PMC
76. Rawicz-Pruszyński K, Sędłak K, Pelc Z, et al. Staging laparoscopy to assess lymph node involvement in advanced gastric cancer (POLA) - study protocol for a single-arm prospective observational multicenter study. *PLoS One* 2023;18:e0285758. DOI PubMed PMC