

# Assessment of the Completeness of Lymph Node Dissection Using Indocyanine Green in Laparoscopic and Robotic Gastrectomy for Gastric Cancer – A Review

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## ABSTRACT

More recently, few scientists have attempted to figure out how to improve the careful recognizable proof of the lymphatic waste courses and lymph node stations during radical gastrectomy in this way beginning another examination outskirts in this field called “navigation surgery”. Among the distinctive detailed arrangements, the presentation of the indocyanine green has drawn consideration for its attributes, a fluorescence colour that can be identified in the near-infrared spectral band. A fluorescence imaging innovation has been coordinated with frameworks of lymph node dissection in laparoscopic and robotic gastrectomy surgery for gastric cancer. Current confirmations uncover that ongoing vessel navigation by using indocyanine green fluorescence during laparoscopic gastrectomy was demonstrated doable with negligible complications. Its utilization may empower the presentation of fruitful robotic or laparoscopic pylorus-preserving gastrectomy with a decrease in unintended intraoperative wounds, for example, second rate polar dead tissue of the spleen during laparoscopic gastrectomy. The clinical ramifications of utilization of indocyanine green in laparoscopic and robotic gastrectomy for gastric cancer was, in any event, for surgeons with a significant level of involvement with laparoscopic D2 dissection, the near-infrared imaging framework can fill in as a complimentary apparatus to affirm total lymphatic node dissection in patients with atypical life structures. With some restrictions the incorporated innovation of indocyanine green fluorescence with near-infrared imaging systems was practical and a promising strategy for lymphatic mapping in laparoscopic and robotic gastrectomy for gastric cancer.

## Keywords:

indocyanine green; gastric cancer; laparoscopic gastrectomy; near-infrared image; robotic gastrectomy.

## Background

Gastric disease stays a test for oncology area being the fifth most as often as possible analyzed malignancy (10,33,701 new cases in 2018) and the third driving reason for malignancy passing (7,82,685 passings) of all malignancies overall [1]. Its frequency shifts generally among worldwide areas, with the most noteworthy occurrence in East Asia, Eastern Europe, and parts of Latin America. In Western nations, the rate of gastric malignant growth is on the ascent; around 25,000 new cases are analyzed every year in the US [2].

Precise clinical organizing of gastric malignancy is of vital significance to choose the best treatment. Various demonstrative modalities are utilized to accomplish precise preoperative clinical organizing. Data for T and N arranging can be acquired utilizing endoscopic ultrasound without or with fine-needle goal biopsy. N and M stages are assessed by processed tomography of the chest, midriff and pelvis. In suitable cases, extra tests and systems, for example, a positron discharge tomography scan and symptomatic laparoscopy might be sought after to get progressively exact M staging data. The National Comprehensive Cancer Network (NCCN) accord rules give further proposals and clarifications of assessment and workup, just as treatment for gastric cancer [3]. Gastric cancer will in general present at later stages since its side effects are vague [4].

Surgery is the main healing alternative for subjects with gastric adenocarcinoma. Excise of the tumor is generally joined by lymphadenectomy and the careful methodology relies upon the area and phase of the tumor and the experience and choice of the surgeon. Beginning stage tumors that have an exceptionally okay of lymph node metastasis are regularly treatable by endoscopic resection [5]. Lymph node dissection for cutting edge cases; The degree of lymphadenectomy for gastric cancer depends for the most part in front of an audience, however the perfect degree for cutting edge cases stays questionable. Kitano et al detailed the first laparoscopic gastrectomy for early gastric cancer in 1994, the procedure has become an elective choice for treating gastric cancer [6].

The utilization of robotic technology for gastric adenocarcinoma was first portrayed in 2003 [7,8] and the primary use in the US was accounted for in 2007 [9]. Many experienced laparoscopic surgeons have embraced robotic assisted surgery for treating gastric cancer since robotic gastrectomy has been seen as a safe and reasonable option in contrast to regular laparoscopic gastrectomy [10,11].

Lymph node metastasis is one of the most significant prognostic factors in gastric cancer [12]. In early gastric cancer (T1), the recurrence of lymph node metastasis was 4.9% in cases with T1a lacerations and 21.4% in cases with T1b injuries [13]. For cutting edge gastric cancer, the recurrence of lymph node metastasis ought to be higher. As the longing increments for negligibly obtrusive gastrectomy in cutting edge gastric cancer, there is a developing interest for an intraoperative guide for lymphadenectomy for surgeons. Indocyanine green lymphatic mapping by sentinel node navigation surgery with infrared beam perception under laparoscopic view was accounted for to be a sufficient strategy for lymph

node dissection for gastric cancer [14-16].

Indocyanine green is a famous, clinically affirmed demonstrative reagent and unfavourably susceptible responses to ICG are less in comparison with blue dyes, for example, Lymphazurin (isosulfan blue) [17,18]. The dye guided strategy is sheltered, helpful and savvy, while lawful contemplations and radioactive substances' expenses limit the probe guided technique in all clinics [19,20]. A few advantages of the indocyanine green are: diminished harmfulness, nonappearance of radioactivity, minimal effort, safe organization that includes intravenous and endoscopic both through the submucosa or subserosa, binding of protein with no change in sub-atomic structures and cooperation of macrophages at the lymph node level. In spite of the fact that indocyanine green demonstrated fast and broad scattering with sufficient titration and measurement, near-infrared encouraged view can be sent to the working screen to permit the recognizable proof of anatomical structures just where the dye is available.

Presently, near-infrared fluorescence imaging innovation has been incorporated into laparoscopic frameworks by certain makers and a couple of specialists have endeavoured to apply this developing innovation to gastric surgery. In gastric cancer surgery, the identification of sentinel nodes through the laparoscopy utilizing indocyanine green fluorescence is previously revealed by Miyashiro et al [21]. Rino et al during esophagectomy utilized indocyanine green fluorescence imaging to envision the supply of blood course to the recreated stomach [22]. With this context, the present article reviews the practicality of near-infrared imaging with indocyanine green infusion in completeness of lymph node dissection in laparoscopic and robotic assisted gastrectomy for gastric cancer.

## Gastric cancer treatment

In laparoscopic SN biopsy, Indocyanine green is an appropriate tracer. Lately, indocyanine green fluorescence sentinel node mapping has been created [16,23,24]. Indocyanine green transmits maximum fluorescence at 840 nm wavelength when it ties to plasma proteins. Indocyanine green fluorescence imaging was resuscitated after the innovation of the camera framework known as the Photodynamic Eye. Kusano et al exhibited high compassion for this indocyanine green fluorescence sentinel node mapping in gastric cancer [16].

Complete dissection of the infra-pyloric zone is in fact provoking inferable from anatomical dissimilarities in the vasculature and conjoining of embryologic planes, while nodal metastasis to the privilege gastroepiploic vessels is visit in lower-and center third gastric cancer [25,26]. Pylorus-preserving gastrectomy has a higher probability of deserting delicate tissues after dissection than distal gastrectomy and expelling tissues from the little parts of the corridor and vein while saving them requires a more elevated level of careful expertise [27,28]. As of late, intraoperative vascular imaging with the indocyanine green fluorescence method has been acquainted with beaten this obstacle [29].

Gastric cancer surgery is developing from observationally based to ongoing explored activities alongside propels in

imaging gadgets. Presently, a robotic surgical platform is an agent get together for constant careful imaging through the TilePro™ (Intuitive Surgical Inc.) and Firefly™ innovations (Intuitive Surgical Inc.). TilePro™ is a sort of multi-input show mode that permits preoperative processed tomography pictures to be incorporated into the robotic surgical comfort, empowering surgeons to see both the registered tomography pictures and the careful view all the while during the activity. Kim et al revealed 12 instances of picture guided robotic gastric cancer surgery utilizing TilePro™ and 3D-reproduced vascular pictures [30]. Herrera-Almario et al reported that, Firefly™ was applied to the reaping of lymph nodes for lymphadectomy as an aide to the recognizable proof of important lymph node bowls continuously during robotic gastrectomy [31].

### **Successful lymphatic node dissections using ICG**

Kim et al revealed the completeness of lymphatic node dissection of the infra-pyloric area at the time of laparoscopic pylorus-preserving gastrectomy (LPPG) in addition to that during laparoscopic distal gastrectomy (LDG). Kim et al highlights their knowledge and important factors with which success of lymph node dissection using near-infrared imaging with indocyanine green in laparoscopic gastrectomy for gastric cancer can be achieved; conveyance of the tracer was an important aspect for effective lymphatic mapping. The concentration and dosage of infusion are related with timing and dispersion level. Right concentration and dose ought to be adjusted by the structure and reason for the examination. The indocyanine green concentration was embraced at the most reduced point of confinement of preclinical investigation i.e. 0.05 mg/mL to get an ideal result from 4 to 6 numerous injections along the area of the stomach. Secondly, the submucosal injection aptitude is significant. Profound injection leads to intravascular injection, which brings about complete fogginess of adjoining organs. In instances of extraluminal spillage, even limited quantities can taint the activity field. In the meantime, when indocyanine green was injected uniquely inside the surface of the mucosa, a slack time in the perfusion of indocyanine green into the laminal progression of the lymphatic framework was recorded, making it hard to decide if the strategy was effective [32].

In a pilot study reported by Kim M et al with the goal to govern the assistant role of indocyanine green fluorescence in gastric surgery to reduce the time of operation and loss of blood, chiefly for unpractised surgeons in laparoscopy-assisted pylorus-preserving gastrectomy or for beginners who are untried in laparoscopic infrapyloric dissection. The foundation of the investigation planned to utilize indocyanine green fluorescence system. In the present examination, it had the option to effortlessly recognize the nearness or nonattendance of an adornment splenic artery by applying indocyanine green fluorescence and the ligation level of the left gastroepiploic vessels had the option to be resolved with the end goal that no splenic dead tissue happened. Besides, it was discovered that the procedural occasions, which also includes the interim and blood vessel stage times, contrasted by the

area of the vessel. The interim and arterial phase times were shorter essentially for the gastroepiploic vessels at left side in comparison with the gastroepiploic vessels at right side [33].

### **Role of indocyanine green in completion of surgeries**

With indocyanine green - upgraded fluorescence until the finish of the activity, surgeons ready to carry out a somewhat agreeable & safe surgery attributable to a virtual lymphangiogram, which enabled the surgeons to separate the lymphatic structures from other anatomical structures & maintain a strategic distance from damage of the new vascular life structures. The extra visual data gave a more significant level of affirmation for the operative personnel to maintain a strategic distance from potential damage and draining during the execution of D2 dissection, which could be useful in any event, for exceptionally experienced gastric surgeons. This near-infrared technical procedure can furnish direction in the lymphatic tissues' dissection with safe visual affirmation and can enhance intraoperative basic leadership at the time of complex lymphatic dissections [32].

The benefits of indocyanine green fluorescence imaging are lower recurrence of unfavourably susceptible responses than that with blue dye, capacity to distinguish bright nodes under fat tissue, clear representation, simple location of splendid nodes and lymphatic channels, greater affectability to identify minute convergences of indocyanine green and signal strength [16,23,24]. Signal strength is the most momentous benefits of indocyanine green fluorescence SN mapping over dye or blend mapping [24].

Kinami et al. cautiously studied indocyanine green fluorescence SN mapping for gastric cancer. It was concluded by authors that for early gastric cancer the indocyanine green fluorescence sentinel node biopsy is practicable in open and laparoscopic surgery both, and the optimal tracer setting to use with the PDE is an endoscopic submucosal injection of 0.5 mL of 50 µg/mL indocyanine green at 4 points surrounding the tumor on the day before surgery [34].

In any event, for surgeons with a significant level of involvement with laparoscopic D2 dissections, the near infrared technique can fill in as a complimentary instrument to affirm complete dissection of lymph node in subjects with atypical life structures. In the meantime, for unpractised specialists, to carryout function-preserving surgeries, for example, LPPG, extra affirmation of complete dissection should profit the surgery to conquer the restriction of inadequate lymph node dissection [32].

### **Use of near-infrared imaging with fluorescent material**

IRobotic assisted techniques permit combination of practical imaging, for example, utilization of near-infrared imaging after indocyanine green infusion. Near-infrared imaging is utilized as a navigation tool for limitation of tumor and dissection of lymph node. Joined with the robotic visuals in negligibly obtrusive gastric cancer surgeries, it has altogether changed the comprehension of the example of lymphatic waste, just as expanding the quantity of collected lymph node. As legitimate lymphadenectomy is pivotal for a sufficient

oncological activity for gastric cancer, near- infrared imaging improvises representation of vascular life structures and lymph node distinguishing proof [31]. This innovation has been fused into different fortes also avoiding organ wounds, for example, to the ureter and biliary ducts [35]. In the colorectal surgery field, notwithstanding its utilization in essential surgery, near-infrared imaging has been utilized as a guide for resection of liver metastasis just as recognition of peritoneal carcinomatosis [36]. It additionally helps in distinguishing the lymphatic waste example of esophageal disease, which uncovered that most distal esophageal and esophagogastric intersection tumors channel into the left gastric lymph node, while other lymph node stations were less ordinarily included [37].

### **Image-guided surgery**

Acquired preoperatively or intraoperatively, registered tomography & MRI scans reconstructive pictures are utilized as a guide for essential dissection of tumor or lymph node by fusing them into the robotic system [38]. Image guided navigation serves to appropriately distinguish vasculature of stomach and take out the plausibility of vascular wounds [39,40]. These procedures are further developed in different fields, for example, neurosurgery & orthopaedic surgery. In gastric surgery, in any case, image-guided surgery still should be further investigated so as to measure the potential points of interest.

### **Limitations**

TMaximum error frequencies is one of the limitations of routine practice of indocyanine green as tracer in dissection of lymph node with near-infrared use in laparoscopic gastrectomy for gastric cancer. The high temperature of the energy device or forceful handling of the lymph nodes might have compromised the nodal structure, resulting in its deformity. Due to false positivity under this setting and because of dissection of unnecessary soft tissue in subjects with early gastric cancer that may result in additional injury. Application must thus be cautiously done to overcome such limitations [32].

Loss of perceivability in thick destiny and quick travel of the dye are different confinements related with dye guided surgeries. Hence, satisfactory preparing of the surgeons is required [41-43]. Plentiful experience is required to build up the specialized expertise and which is very important to make a high progress rate, implying that precision of the method relies upon the individual surgeon [44].

Contrasted with past modalities, the near-infrared camera can distinguish even a little part of indocyanine green from the field of activity, which may be befuddling in early use of this procedure. To beat this consequence, extra evaluation of indocyanine green sign could furnish corresponding data to recognize tissues with various degrees of fluorescence take-up. A measurement strategy can balance the false positive indocyanine green tissues and convey exact data about the focused tissues [32].

### **Conclusion**

In conclusion real-time vessel navigation utilizing

indocyanine green fluorescence while performing laparoscopic gastrectomy was proven practicable with negligible complications. Intraoperative vascular imaging with the help of indocyanine green fluorescence technique is of great use for the identification of shapes and origin of small vessels such as the IPA and an accessory splenic artery. Its' use may facilitate in performing robotic or laparoscopic pylorus-preserving gastrectomy successful with reduced accidental intraoperative injuries such as inferior polar infarction of the spleen at the time of laparoscopic gastrectomy. These discoveries energize researchers who are thinking about the utilization of indocyanine green fluorescence for lymph node dissection in robotic & laparoscopic gastrectomy for gastric cancer.

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DC, SL conceptualized and designed the study, acquired, and analyzed data, interpreted the study results, drafted and revised the manuscript.

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