

# INPLASY PROTOCOL

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**Conflicts of interest:**  
None declared.

## INTRODUCTION

**Review question / Objective:** We aimed to investigate whether ICG NIR fluorescence imaging is safe and effective in guiding lymph nodes (LNs) resection during robotic gastrectomy.

## Safety and Efficacy of Indocyanine Green Near-infrared Fluorescent Imaging-guided Lymph Nodes Dissection During robotic gastrectomy for Gastric Cancer: A Systematic Review and Meta Analysis

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**Review question / Objective:** We aimed to investigate whether ICG NIR fluorescence imaging is safe and effective in guiding lymph nodes (LNs) resection during robotic gastrectomy.

**Rationale:** The use of ICG in lymph node dissection for gastric cancer patients undergoing robotic gastrectomy is still in its infancy. According to our literature searches, the relevant articles are small samples, single-center studies. The purpose of our study was to evaluate the safety and efficacy of ICG NIR fluorescence imaging-guided lymph node dissection in robotic radical gastric cancer surgery by means of a meta-analysis. The primary outcome was the total number of LNs retrieved, and the secondary outcomes included operative time, intraoperative blood loss, and postoperative complications.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 November 2021 and was last updated on 15 August 2022 (registration number INPLASY2021110062).

**Rationale:** The use of ICG in lymph node dissection for gastric cancer patients undergoing robotic gastrectomy is still in its infancy. According to our literature searches, the relevant articles are small samples, single-center studies. The purpose of our study was to evaluate the

safety and efficacy of ICG NIR fluorescence imaging-guided lymph node dissection in robotic radical gastric cancer surgery by means of a meta-analysis. The primary outcome was the total number of LNs retrieved, and the secondary outcomes included operative time, intraoperative blood loss, and postoperative complications.

**Condition being studied:** Gastric cancer is the fourth-leading cause of cancer-related mortality globally and the fifth-most prevalent malignant tumor. Accurate staging of gastric cancer benefits from adequate lymph node dissection and new research has demonstrated that greater lymph node dissection is advantageous for accurate gastric cancer lymph node staging as well as improving patients' long-term prognosis. Compared with traditional laparoscopy, the da Vinci robot performs radical gastric cancer resection, which has a finer anatomy, easier vascular choroidization, and more thorough lymphatic dissection. However, because the stomach has complex anatomy and a rich blood vessel supply, how to carry out safe and adequate lymph node dissection is a difficult point and hot spot in the radical resection of gastric cancer in robots. Indocyanine green (ICG) is an FDA-approved dye for use in vivo that allows for precise assessment of blood and lymphatic vessels. Since longer near-infrared wavelengths are able to better penetrate lymph nodes within thick adipose tissue, it has been found that ICG under near-infrared imaging provides better lymph node development for lymphoid tissue under visible light than with the naked eye. ICG fluorescence imaging shows its superiority in a variety of tumor surgeries. During the lymphatic dissection process of robotic gastric surgery, fluorescence mode can be used to assist in finding the correct anatomical gap for lymph node dissection; When it is difficult to distinguish blood vessels from lymph nodes, use fluorescence mode for screening; After the sweep is complete, a fluorescence pattern can be used to check for missing lymph nodes. This results in a more thorough lymphatic dissection and a safer cleaning

process. However, the use of ICG in lymph node dissection for gastric cancer patients undergoing robotic gastrectomy is still in its infancy.

## METHODS

**Search strategy:** Through July 2022, all relevant studies from Embase, Web of Science, PubMed, and the Cochrane Library were systematically reviewed. The search strategy contained two core components, which were linked using the AND operator: 1) stomach neoplasms (e.g., neoplasm, stomach, stomach neoplasm, neoplasms, stomach, gastric neoplasms, gastric neoplasm, neoplasm, gastric, neoplasms, gastric, stomach cancers, cancer of stomach, gastric cancer, cancer, gastric, cancers, gastric, gastric cancers, stomach cancer, cancers, stomach, cancer, stomach, cancer of the stomach, gastric cancer, familial diffuse), 2) indocyanine green (e.g., green, indocyanine, wofaverdin, vofaverdin, ujoeveridin, vofaverdin, cardio-green, cardio green, cardiogreen). For each of the two core components, controlled vocabulary (i.e. Medical Subject Headings terms) and title/abstract were identified. The search was developed initially for PubMed and then adapted for each of the other three databases by mapping the search terms to additional controlled vocabulary and subject heading terminology.

**Participant or population:** Patients with gastric cancer who underwent robotic radical gastrectomy.

**Intervention:** Patients with indocyanine green tracer-guided lymphadenectomy.

**Comparator:** Patients without indocyanine green tracer-guided lymphadenectomy.

**Study designs to be included:** Either randomized controlled trials (RCTs), cohort studies, or comparative studies all will be included.

**Eligibility criteria:** The Cochrane Handbook was used to evaluate quality of randomized controlled studies (RCTs). If the study

scored 4 or more out of a maximum of 6 points, it is considered as a high quality research and will be included. For non-randomized controlled studies such as retrospective studies, the Newcastle-Ottawa scale was used to evaluate quality and Studies with scores  $\geq 7$  were deemed high in quality.

**Information sources:** All relevant medical studies from Embase, Web of Science, PubMed, and the Cochrane Library were systematically reviewed through July 2022.

**Main outcome(s):** The total number of harvested lymph nodes.

**Additional outcome(s):** The number of metastatic lymph node dissection; Operative time; Intraoperative blood loss; Postoperative complications; Postoperative hospital stay.

**Quality assessment / Risk of bias analysis:** The Cochrane Collaboration Risk of Bias Tool and Newcastle Ottawa Scale (NOS) were used to assess the quality of included RCT studies and observational studies, respectively. Pooled analyses were conducted using random and fixed effect models with the Mantel-Haenszel method when appropriate. Statistical heterogeneity was investigated using the Cochran's Q test ( $P < 0.10$ ) and the I<sup>2</sup> statistic ( $> 50\%$ ). Sensitivity analysis was conducted based on the low risk of bias. Subgroup analyses were conducted based on surgical approach, study design and countries. Potential publication bias was assessed by visually inspecting the funnel plots in Review Manager. Publication bias in this meta-analysis was assessed using a funnel plot based on primary outcomes.

**Strategy of data synthesis:** The odds ratio (OR) and mean difference (MD) with their 95% confidence interval (CI) were used to evaluate dichotomous and continuous variables, respectively. For studies that only reported median and range, data were converted into mean and standard deviation (SD) following the method reported by Wan et al. [28]. Heterogeneity among studies was assessed by  $\chi^2$  and I<sup>2</sup>

statistics. I<sup>2</sup>  $> 50\%$  indicates significant heterogeneity. For this, a random-effects model was used; otherwise, a fixed-effects model was performed. For the assessment of publication bias, a funnel plot was conducted. A p value  $< 0.05$  was considered significant. All of the statistical analyses were performed by Review Manager Software, version 5.3 (Cochrane, London, UK).

**Subgroup analysis:** Subgroup analyses were conducted based on surgical approach, study design and countries.

**Sensitivity analysis:** Sensitivity analysis was performed by removing one study at a time and repeating the meta-analysis to assess whether at least one study significantly affected the pooled estimates.

**Language:** English.

**Country(ies) involved:** China.

**Keywords:** Indocyanine green; Robotic gastrectomy; Lymph node; Gastric cancer; Meta-analysis

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