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# The Use of Indocyanine Green in Colorectal Surgery

*Sinziana Ionescu*

## Abstract

This chapter looks at the use of indocyanine green (ICG) in colorectal surgery, by exploring at first the definition of vital dyes generally used in the surgical field, afterward the benefits of fluorescence-guided surgery, and furthermore, it enumerates several uses of ICG in the broad surgical field. The identification of tumor nodules in the peritoneum can help with proper cancer staging, and the same advantage is brought by the accurate detection of the sentinel lymph node, which concerns the use of ICG specifically in colorectal surgery, and this can be summed up through the following assets brought by the technique: (a) intraoperative fluorescence angiography as an adjuvant in the process of anastomosis, (b) fluorescence-guided detection of lymph node metastases in colorectal cancer and the sentinel lymph node technique, which was proved better than formal methods in some studies, (c) the positive fluorescence of a liver nodule as small as “only” 200 tumor cells, (d) the help in diagnosing a fistula, (e) the possibility to be used for tumor tattooing also, and (f) the help in maintaining a clean surgical field and preventing wound infection in abdominoperineal resection.

**Keywords:** colorectal, fluorescence, ICG, ICG-NIR, colorectal surgery, intraoperative staining

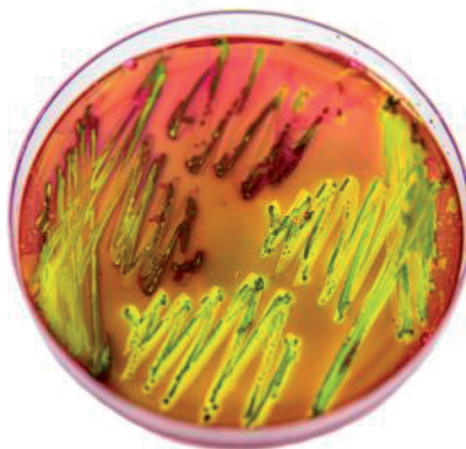
## 1. Introduction

As the general surgical techniques have polished with more and more precise gestures, which in time lead to the appearance and development of even robotic surgery, the same phenomenon happened when it comes to adjuvant methods to better identify, visualize, and resect a specific structure/tissue during the intervention. Fluorescence can bring important assets when it comes to seeing better—the vessels, the lymph nodes, and the tumor itself. Some organs, such as the case of the ureter, are also much better underlined with the technique of NIR-ICG (near-infrared light and indocyanine green [ICG]), and therefore, the risk of producing a lesion secondary to incomplete visualization is smaller. This chapter closely looks at the literature on the theme of ICG in colorectal surgery, offering also a general frame made out of significant research, mainly systematic reviews and randomized controlled trials about the use of ICG in visceral surgery.

## 2. Types of dyes used in surgery

### 2.1 Classical dyes

According to the definition given by the Merriam-Webster dictionary, a dye or a stain is able to penetrate living cells or tissues without inducing immediate obvious degenerative changes and thus, it is also called a vital stain. Supravital staining implies the removal of living cells from an organism, whereas intravital staining involves injecting (or otherwise administering) the dye into the organism. The term “vital stain” is sometimes used to refer to an intravital stain, and in some other situations, it is interchangeable with a supravital stain, the main idea being that the cell being looked at is still alive. In a more strict way of speaking, the term “vital staining” has a meaning which is opposite to “supravital staining.” If living cells take up the stain during supravital staining, living cells exclude the dye during “vital staining”; for example, they color negatively and only dead cells color positively, and hence, viability can be measured by counting in percentage the amount of total cells that stain negatively. Because the nature of the dye defines if the staining is either supravital or intravital, a mix of supravital and vital dyes can be employed to better categorize cells into various groups (e.g., viable, dead, dying) (**Figures 1 and 2**).



**Figure 1.**  
*Metallic green sheen characteristic colonies of Escherichia coli on eosin methylene blue agar (EMB) in close-up.*



**Figure 2.**  
*A vial of methylene blue.*

Tissue staining, also known as chromoscopy, can be used as an adjuvant technique in gastrointestinal endoscopy to help with the recognition of subtle lesions, such as is the case with polyps or, more so, allows to directly target biopsies, which may happen in the case of Barrett's esophagus, in order to increase the precision of the diagnosis. Four endoscopic staining techniques have been described—vital staining (the use of an agent that is absorbed by the intestinal epithelium), contrast staining (the use of a substance to accentuate the aspect of the surface), reactive staining (the use of an agent that can fire chemical reactions), and tattooing (a technique using agents such as India ink to underline a special lesion on the mucosa).

Tissue stains used in gastrointestinal surgery, as mentioned by Fennerty [1], can be classified as follows:

a. tattooing agents

1. India ink is used for permanent marking of the mucosal site for relocalization at the time of surgery or endoscopy, also used in the esophagus, stomach, and colon, which is safe without side effects.
2. Indocyanine green is a shorter-duration tattooing agent with more information offered in the following section.

b. absorptive stains

1. Lugol's iodine (stains normal glycogen containing squamous mucosa of the esophagus, allowing recognition of abnormal squamous epithelium—dysplasia—or metaplastic epithelium—Barrett's esophagus),
2. methylene blue and toluidine blue (stains the absorptive epithelium small bowel and colon), allowing the identification of metaplastic epithelium in the esophagus (Barrett's esophagus) and stomach (gastric intestinal metaplasia), can also find a negative stain in gastric metaplasia at the level of the duodenal bulb.

c. contrast stains

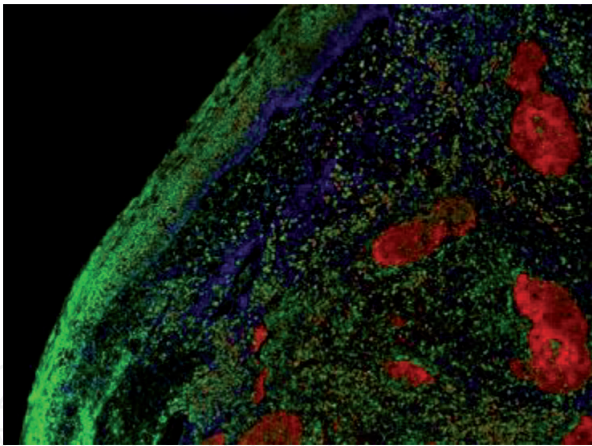
1. indigo carmine and cresyl violet (accentuates mucosal topography, allowing recognition of abnormal small bowel sprue and colonic mucosa inflammatory bowel disease, polyps).

d. reactive stains

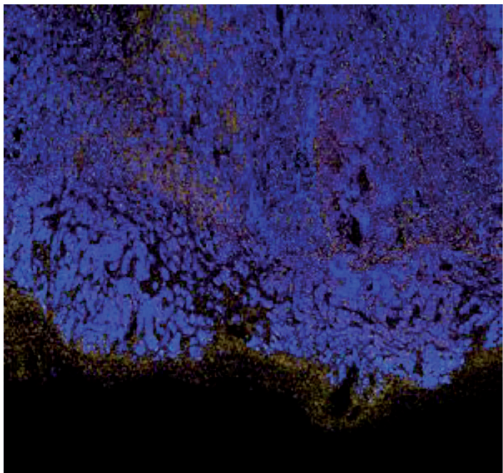
1. Congo red (identifies acid-secreting portions of the stomach postoperatively and documents achlorhydria) and
2. phenol red (identifies alkaline areas of the stomach).

## 2.2 Fluorescent dyes

According to the definition offered by [www.britannica.com](http://www.britannica.com), fluorescence is the emission of electromagnetic radiation, usually visible light, caused by the excitation of atoms in a material, which then reemit almost immediately (within about 10 s). The initial excitation is frequently determined by the absorption of energy from



**Figure 3.**  
*High-resolution fluorescent microscope image of clusters of tumor cells in red surrounded by normal cells and normal skin in green. Photo source: [www.shutterstock.com](http://www.shutterstock.com).*



**Figure 4.**  
*Research sample slide of tumor tissue where cells have been stained for different proteins using a fluorescently tagged antibody. Presented as false-color image on white background.*

incident radiation of particles, as is the case with X-rays or electrons (**Figure 3**). Due to the fact that reemission happens so quickly, the fluorescence stops when the exciting source is removed, unlike the phenomenon of phosphorescence (**Figure 4**), which later persists as an afterglow.

### 3. The use of ICG in surgery

#### 3.1 General aspects

Fluorescence imaging techniques have become increasingly common in recent years. ICG-based fluorescence, in particular, is now widely used in a variety of diagnostic and treatment procedures, according to the research made by Nowaka and co [2]. ICG is currently the most commonly used fluorescent agent due to its gradual degradation and the rarity of the severe adverse effects described. ICG is a water-soluble, amphiphilic tricyanocyanine probe with a molecular weight of 776 Da, relatively nontoxic, unstable compound, a dye in clinic use bound by albumin in the intravascular space until rapid clearance by the liver. Severe allergic reactions associated with the use of ICG are very rare (1:10,000) with an incidence of 0.05% and mostly occur in patients allergic to iodine. It has various applications in different



fields, such as cardiology, ophthalmology, and neurosurgery, but its fluorescent properties have only recently been applied to the intraoperative estimation of tissue blood supply. Apart from ICG, other substances can act as fluorophores (fluorescent chemical compounds that are able to reemit light upon light excitation), such as methylene blue, five-aminolevulinic acid, fluorescein sodium.

What is fluorescence-guided surgery (FSG)? FSG is employed because white visible light makes various tissues appear either identical or highly similar, and proper tumor identification can be difficult, according to [www.isfgs.org](http://www.isfgs.org) [3]. Moreover, the surgeon just sees the tissues from the superficial layers under natural light. Nonetheless, structures that were previously invisible can be seen now and recognized by using ICG in a different light length. By combining visual abilities with special dyes, it is now possible to avoid such organs or structures during the surgical process in order to avoid harming them. Other benefits of the FSG include the ability to minimize operative time and the need for second-look procedures by facilitating the rapid detection of structures and lesions while avoiding excessive harm.

### **3.2 The use of ICG in general surgery interventions, outside the colorectal area**

ICG has found application in several fields of general surgery, especially colorectal surgery (seen in the next section of the present article), esophageal surgery, and emergency evaluation of intestinal perfusion in cases of mesenteric ischemia, kidney transplantation, hepatobiliary, and endocrine surgery.

#### *3.2.1 ICG in peritoneal carcinomatosis*

ICG can improve the harvesting of tumors during surgery and can properly adjust both the indications, as the extent of the intervention. In a systematic review performed in 2020 by Baiocchi [4], which took into account 192 screened papers with six series meeting the eligibility criteria, there were analyzed in total 353 peritoneal nodules, the neoplasms in question being—colorectal, hepatocellular, ovarian, endometrial. The above-mentioned study had as a purpose to look at the available clinical data regarding the value of ICG fluorescence imaging for intraoperative detection of peritoneal carcinomatosis during open surgery and the main aspects studied settled to the conclusion that sensitivity varied from 72.4 to 100%, while the specificity ranged from 54.2 to 100%.

#### *3.2.2 ICG in liver surgery*

The ICG fluorescence method is being used more and more in liver surgery due to the fact that it permits the real-time display of the segmental anatomy of the organ, depending on the tumor's characteristics, and, more so, it is possible to perform direct or indirect identification of hepatic lesions and metastases. Additionally, ICG imaging allows more sensitive detection of tumor foci and, therefore, also a higher R0 resection rate. However, in a systematic review of the literature on the application of ICG imaging in open and laparoscopic liver surgery performed by Sucher et al. [5], the conclusion was drawn toward the aspect that the application resulted mainly useful for superficial lesions, as the depth of penetration of NIR is only 8–10 mm. In liver resections, post-hepatectomy liver failure (PHLF) can occur although an adequate liver volume is kept in place. Diverse dynamic functional tests, such as the indocyanine green test (ICG), could only appreciate globally the liver function, with no definition toward the functional ability of the hepatic remnant. Magnetic resonance imaging (MRI) with liver-specific

contrast agents makes the evaluation of both liver function and volume possible. A preoperative combination between dynamic quantitative tests, such as ICG, with MRI or HBS (hepato-bilio-scintigraphy), should provide a more complete functional evaluation. One should opt for various functional tests to predict PHLF that should be selected according to patient's characteristics, disease, and center experience, as shown by Tomassini and the team [6].

### *3.2.3 ICG-NIR to assess skin flap perfusion*

The incidence of skin flap necrosis after mastectomies can reach 11–24%. Laser-assisted ICG angiography appears as a promising technique to assess skin flap perfusion. In a systematic review performed by Driessen et al. [7], it was found that all studies looking at the current ICG methodology and ability to predict outcome showed a substantial decrease in skin necrosis when the ICG was used.

### *3.2.4 ICG-NIR to assess peritoneal endometriosis*

Endometriosis is a very commonly encountered disease that is found in up to 10% of the female population. The use of (ICG) has been advocated for the proper location of endometriotic lesions intraoperatively. NIR-ICG is useful in appreciating the blood supply of bowel anastomoses after segmental resection, according to a systematic review done by Ianieri et al. [8] that looked at 53 studies.

### *3.2.5 ICG to identify the ureter*

Iatrogenic ureteral injury in abdominal surgery is rare at the moment, although it can still result in significant morbidity and mortality. Inspection and palpation are two traditional methods of measuring iatrogenic ureteral damage, which can be difficult during laparoscopic procedures. The use of NIRF imaging to aid in better visualization of the ureters is currently being investigated. The report's goal performed by Slooter et al. [9] was to picture the currently available and experimental dyes in ureter visualization and to further evaluate their feasibility of using them and, more so, to look at their effectiveness.

### *3.2.6 ICG to identify a bleeding site in the GI area*

Several studies, among which the one performed by Copaescu [10], aimed to look at the reliability of a novel fluorescence-guided laparoscopic technique to correctly find the site of unknown gastrointestinal bleeding, with the help of the vascular washout properties of indocyanine green (ICG). The bleeding site was correctly identified and the patient benefited from a minimally invasive technique, and it was, therefore, possible to avoid an open surgical exploration.

### *3.2.7 ICG in sentinel lymph node in different neoplasms*

This represents another important topic in different surgical fields, for instance, urology, gynecology, and general surgery.

#### *3.2.7.1 Breast cancer*

In the early stage of breast cancer, ICG-fluorescence-based sentinel lymph node (SLN) detection is being considered. A systematic review looking at 2301 patients from 19 studies found that ICG-fluorescence could complement the radioisotope

method or provide an alternative. Another study regarding the ICG lymph node technique in breast cancer was a literature review presented by Benson [11] in which a significantly better sentinel node detection rate was found with ICG than with the standard radioisotope method (**Figure 5**).

### 3.2.7.2 Cervical cancer

Techniques that combine the ability to identify technetium-99 and a blue dye have been widely used for sentinel lymph node biopsy (SLNB), but there has recently been a surge of interest in the use of fluorescent staining, such as indocyanine green (ICG), to improve the rate of SLN detection. Even though recent guidelines recommend sentinel lymph node biopsy in addition to PLND, SLN biopsy alone is not yet the gold standard because there is insufficient prospective evidence, especially in terms of long-term oncological protection. The prospective randomized clinical trial SENTICOL III will answer to these signaled issues, as a study by Balaya et al. [12] mentions. In addition to the facts mentioned above, the prospectively randomized FILM trial evaluated ICG to be superior in lymph node detection compared to isosulfan blue dye in patients with stage I endometrial or cervical cancer, an evaluation performed by Frumovitz and team [13]. Meanwhile, the study's conclusions created a context for the FDA's approval of ICG for lymph node mapping. NCCN guidelines mention sentinel lymph node mapping by ICG in cervical cancer patients, according to Koh et al. [14].

## 3.3 The use of ICG in colorectal surgery

### 3.3.1 Intraoperative fluorescence angiography in colorectal surgery used for the evaluation of the anastomosis

Anastomotic leakage remains among the most feared and challenging complications after colorectal resection. The etiology of leaks includes patient factors, technical factors, and anastomotic perfusion. The known etiology of leaks includes the following: different patient factors, technical factors, and anastomotic blood supply. An intact anastomotic irrigation pattern is particularly vital in the process of anastomotic healing. The air leak testing and intraoperative colonoscopy are



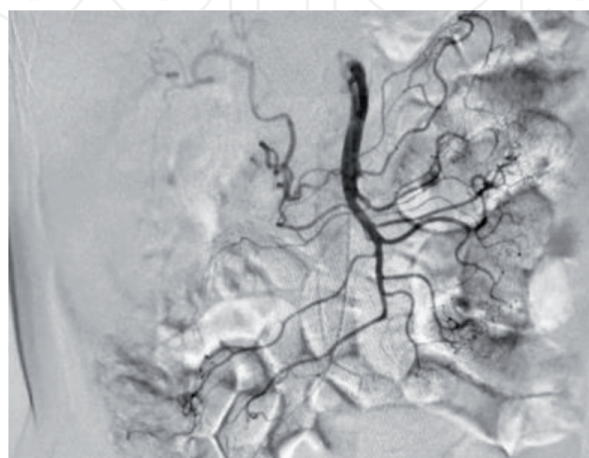
**Figure 5.**  
*The surgeon uses a portable fluorescence imaging device during breast removal. Photo source: [www.shutterstock.com](http://www.shutterstock.com).*



methods that can be done to establish the anastomotic integrity intraoperatively. Among the major causes of anastomotic leakage is impaired vascularization and a minimal deficit in blood supply, both aspects being difficult to detect under white light. Fluorescence angiography with indocyanine green (ICG-FA) is employed in colorectal surgery in order to evaluate the blood supply in the area of an anastomosis. Studies with ICG-FA in open and laparoscopic interventions indicated a lower rate of anastomotic leakage; for example, the PILLAR II study reported a leakage rate of 1.4%. There were researches in this field, such as is the case of Carus and Pick [15] that reported impressive results in clinical outcome and patient prognosis. Likewise, the use of ICG-FA in the group of patients studied potentially led to a reduction of the leakage rate by 48%. Another systematic review from Blanco-Colino and Espin-Basany [16] looks at 1302 patients from five nonrandomized studies in which fluorescence imaging significantly decreased the anastomotic leak in cases operated on for colorectal cancer. Lower leak rates were found in rectal cancer surgery, as well (ICG 1.1% vs. non-ICG 6.1%;  $p = 0.02$ ) (**Figure 6**).

### 3.3.2 Fluorescence-guided detection of lymph node metastases in colorectal cancer and the sentinel lymph node technique

Indocyanine green fluorescence imaging can also be used as a potential tool for enhancing the accuracy of the staging of patients with primary colorectal cancer through the detection of sentinel lymph nodes. The search in electronic databases was performed and eligible data were taken from 248 patients in a review published by Emile et al. [17], which looked at the overall sensitivity and specificity of (ICG) (NIR) fluorescence in sentinel lymph node detection in colorectal cancer. The median values for the sensitivity, specificity, and accuracy rates were 73.7, 100, and 75.7, respectively. Other several studies, even though none was a prospective one, considered the ICG method feasible in colorectal cancer and also for lower rectal tumors, especially in order to detect the lymphatic drainage across the lateral lymph nodes, as studied by the teams of Nagata et al. [18], Kawahara et al. [19], Cahill et al. [20], and Liberale et al. [21]. Another method used in correctly and precisely identifying the lymph node involvement is one-step nucleic acid (OSNA), as it can offer a quick method of characterization of the lymph nodes. On the other hand, near-infrared (NIR) laparoscopy, together with indocyanine green (ICG), can identify relevant nodal tissue *in situ* during surgery. The association between the OSNA, laparoscopy, and NIR-ICG was studied in an RCT by Yeung et al. [22],



**Figure 6.**

*X-ray angiography of the inferior mesenteric artery (IMA) with contrast media. Its supplies arterial blood to organs of hindgut-distal 1/3 of the transverse, splenic flexure, descending colon, sigmoid, rectum.*

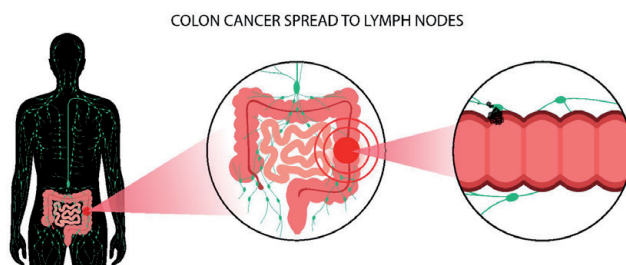
a research during which ICG was administered around the tumor, while endoscopy was conducted at a moment previous to the operation. NIR-identified fluorescent lymph nodes were first labeled and then sent for whole-node OSNA review. Both traditional histology and OSNA were used to examine and analyze “fresh” lymph nodes dissected from the typical resection specimen. Furthermore, the fluorescent lymph node status was compared to that of non-ICG nodes in order to determine their predictive value. OSNA is concordant with normal histology, but only a minority of nodes detectable by complete pathological examination was identified for OSNA on fresh dissection, according to the study’s findings. To provide an intraoperative evaluation of nodal tissue in patients with colorectal cancer, OSNA can be performed at the same time as NIR and ICG lymphatic mapping. Patients with colorectal cancer can benefit from this treatment.

A study performed by Vuijk et al. [23] looking at the lymph node involvement in gastrointestinal tumors assessed the sentinel lymph node technique with Nanocoll, and ICG- and CEA-targeted fluorescent imaging, and settled to the following conclusions: sentinel lymph node interventions in gastric cancer resections using indocyanine green (ICG) linked to Nanocoll outperformed normal ICG, but could not offer details on possible lymph node metastasis. Besides that aspect, the carcinoembryonic antigen (CEA)-targeted fluorescent imaging technique by using SGM-101 was successful in both pancreatic and colorectal cancers. A large phase III multicenter trial with the corresponding results would be able to complete the missing data.

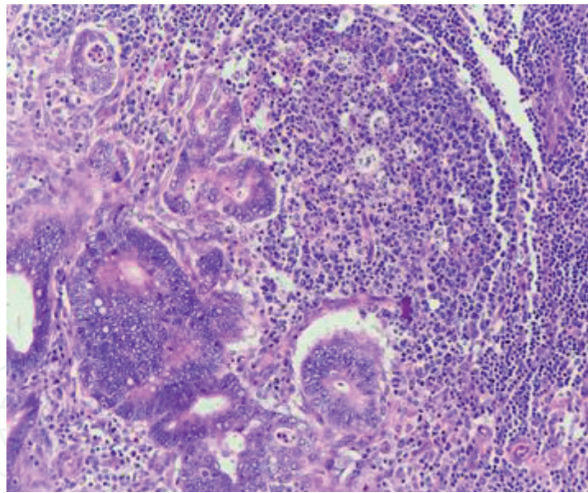
Simultaneously, in which concerns lymph node invasion, the concept of ultrastaging appeared recently in the specific literature. Furthermore, studies were compiled, such as the one by Hirche et al. [24], in which regards ultrastaging of colon cancer by sentinel node biopsy using fluorescence navigation with ICG. Overall, the ICG fluorescence technique found a mean of 1.7 sentinel lymph node (SLN) in 25 out of 26 patients (with a detection rate of 96%). Metastatic involvement of the SLN was detected in 9 out of 11 nodal positive patients by conventional histopathology. The sensitivity of the method was 82% in the case of colon carcinoma. The drawn conclusion of the abovementioned study was that the ICG fluorescence technique is a new but feasible method for SLNB of colon carcinoma and permits ultrastaging with improved accuracy, but with limited validity (so far) due to the small number of cases (**Figures 7 and 8**).

### 3.3.3 ICG in metastatic colorectal cancer

ICG is metabolized by the liver and accumulates in areas of slower bile metabolism, a situation that can be encountered in primary liver cancers and colorectal secondary determinations (metastases), as found by the teams of Peloso et al. [25] and van der Vorst [26]. A tumor cluster of cells as small as 200 tumor cells can be identified by ICG, allowing surgeons to find foci of a minimum of 1 mm,



**Figure 7.** Colorectal cancer concept. Development of cancer from the colon or rectum to the whole large intestine. Stages of spreading tumor to the lymph nodes and vector flat illustration of other internal organs.



**Figure 8.**

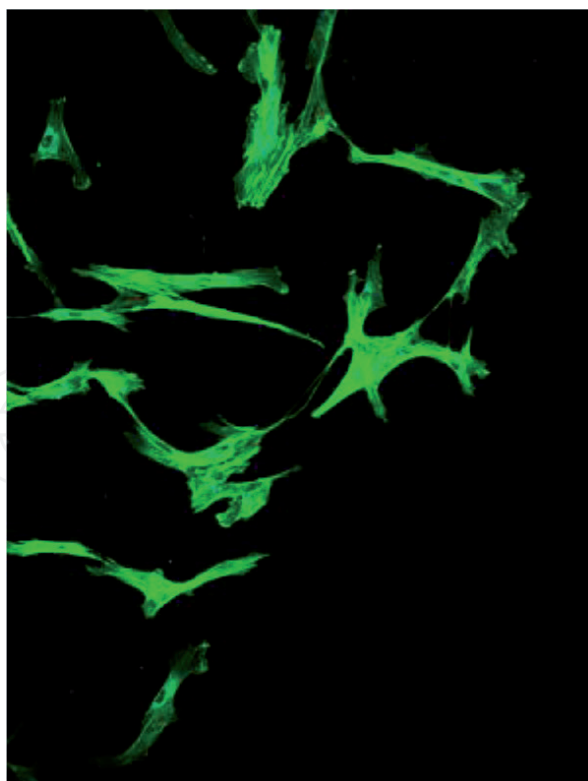
*Metastatic colon carcinoma, in lymph node. Tumor component is on the left and lymphoid component is on the right, magnification 200x.*

as it was shown by Ishizawa et al. [27]. The practical aspect of finding liver masses is that they have to be superficial, and the fluorescence methods can look at the maximum depth of infiltration of up to 10 mm. A combination of the application of intraoperative ultrasound and fluorescence techniques was shown to increase the identification rate of colorectal metastatic lesions, as it was researched by Kaibori et al. [28]. In patients suffering from liver fibrosis, nevertheless, areas that have a slow bile metabolism might give false-positive fluorescence. ICG fluorescence can be employed to qualitatively and quantitatively depict changes at a molecular and cellular level in the living organism, and to objectively display liver tumor information, to define hepatic tumor boundaries, and to detect residual tumors, achieving an intraoperative real time coloration and the successful navigation of the liver parenchyma in the targeted zone, as mentioned by Shizawa et al. [29]. A recent meta-analysis included studies on 587 patients showing that ICG fluorescence in the field of liver surgery does decrease operative time, blood loss, hospital stay, and postoperative complications if we are to mention a study done by Qi et al. [30]. As mentioned in subchapter 3.2.2 (ICG in liver surgery), the ICG fluorescence technique is for sure viewed as an intraoperative method that allows the detection of additional superficial hepatic metastases of colorectal cancer, a fact underlined by Liberale and team [31] in an article in which PubMed and Medline literature databases were searched for articles on the use of ICG in the setting of clinical studies on CRC (**Figures 9 and 10**).

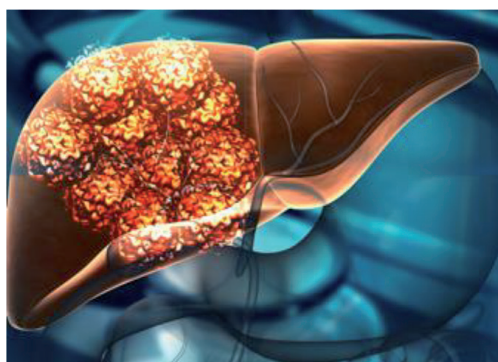
#### *3.3.4 Evidence of ICG usefulness in robotically assisted colorectal surgery*

As previously shown in the previous subsections of the chapter, ICG fluorescence imaging is increasingly being used, tested, and documented in different areas of abdominal surgery. The constant improvement in the method and in the technological possibilities enables easy use and facilitates operative decision-making, also in robotically assisted colorectal surgery, as it is communicated in a study published by Vilz et al. [32]. Additional information offered there was that the first individual studies underlined an important reduction in the incidence of anastomotic leakage after colorectal anastomosis through the use of ICG fluorescence angiography (FA, 9.1% vs. 16.3%;  $p = 0.04$ ). First feasibility research studies also emphasized lymph node detection or navigation, as well as the possibility to visualize the ureter (**Figure 11**).





**Figure 9.**  
*Immunofluorescence of multiple human tumor metastatic cells growing in tissue culture for research purposes.*



**Figure 10.**  
*Human liver cancer cell growth. 3D illustration.*

### *3.3.5 Evidence of ICG usefulness in laparoscopic colorectal resection*

In regard to tumor localization, ICG-coated endoscopic clips can bring a promising new technique, as seen in a study by Lee et al. [33]. The precise localization of a tumor before surgery is vital, more so in the early stages of cancer, and the amplitude of the surgical intervention must be established. The accurate localization of a colorectal lesion ensures proper margins for resection and prevents surgical removal of healthy segments of the colon; furthermore, it can reduce the duration of surgery and prevent unnecessary colon traction and tumor handling, which could result in dissemination of tumor cells. The method abovementioned involves placing endoscopic clips coated or mounted with near-infrared fluorescent material, such as ICG, at the lesion site and determining the location of the tumor by consequently detecting the fluorescent signal through the intestinal wall (through the use of a near-infrared laparoscope).





**Figure 11.**  
*Robotic surgery in the operation room.*

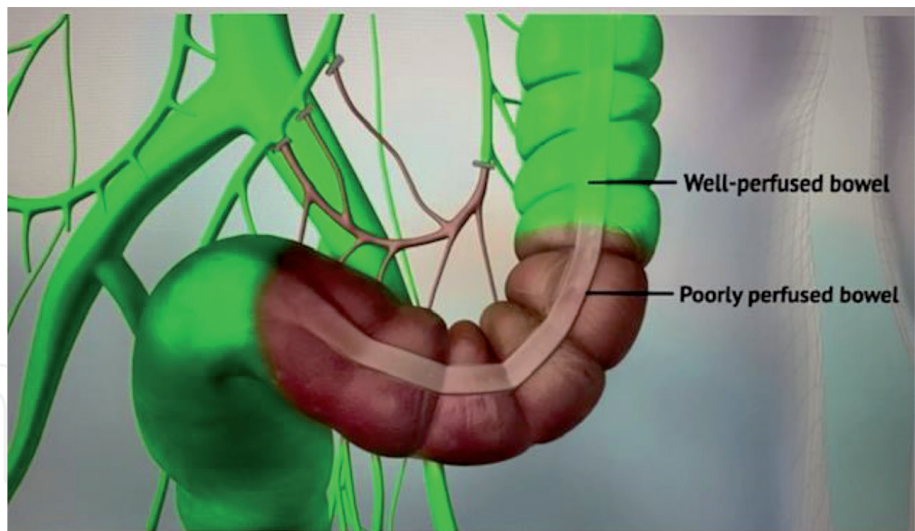
In a research by de Nardi and team [34], a randomized trial was formulated, involving 252 cases in which laparoscopic left-sided colon and rectal resection were performed. The algorithm randomized 1:1 to intraoperative ICG or to subjective visual evaluation of the bowel blood supply without ICG. The main results were the following: ICG angiography documented insufficient blood supply of the colic stump, which implied extended bowel resection in 13 cases (11%). In the control group, 11 patients (9%) had a fistula; meanwhile, in the study group, six patients (5%) developed one anastomotic leak ( $p = n.s.$ ).

Based on the general elements reviewed, it was summed up that intraoperative ICG fluorescence angiography can efficiently find correctly the vasculature of the colic stump and anastomosis in situations when colorectal resection is performed.

Despite the fact that this method guided proximal bowel resection in 13 instances, the ICG arm did not find a statistically meaningful decrease in anastomotic bowel leak rate. Transanal ICG angiography has been shown to be both feasible and effective in imaging the mucosal and anastomotic blood supply in research conducted by Sherwinter [35]. Future research in a larger community of patients is needed to fully understand the technique's potential to detect flaws in tissue perfusion that could lead to an anastomotic breakdown. Twenty patients with benign and malignant lesions underwent low anterior resection for the analysis. Indocyanine green (ICG) was injected through a peripheral iv catheter after the anastomosis was completed. Transanally, an endoscopic near-infrared imaging device (NIR) was used to test the blood supply at the level of the colon mucosa, the rectum, and the anastomotic staple axis (**Figure 12**).

### *3.3.6 ICG monitoring for perineal wound contamination in abdominoperineal resection*

The incidence of the incisional surgical site infections in colorectal surgery was reported between 5 and 26%. Surgical site infections (SSI) in an abdominoperineal resection (APR) appear more than in other types of interventions in the case of patients with colorectal cancer. Toshiyuki et al. [36] found that perineal wounds are the most vulnerable sites, and they may be triggered by stool contamination. Indocyanine green (ICG) fluorescence testing was employed as a marker of perineal wound contamination. The study had as a method to inject indocyanine green into the rectum transanally before the operation, and fluorescence images were obtained



**Figure 12.**  
*Schematics of fluorescence angiography in the colorectal area.*

during the operation in patients who underwent APR. The findings, though sparse, are promising: one subject had an SSI after having no clear gross contamination, and a trace of ICG fluorescence was found in the perianal skin.

The other two cases were free of SSI, and skin treatment was carried out thoroughly before ICG contamination was removed in those cases.

Even after the normal antiseptic skin preparation, a trace of stool contamination can remain in the perineal skin area, according to the study's findings.

Furthermore, careful skin preparation is needed and it is compulsory if we are to minimize stool contamination in APR subjects (**Figure 13**).

*3.3.7 Surgical usefulness of ICG as an alternative to India ink for endoscopic marking*

India ink has been largely used for preoperative colonic tattooing, but different complications have been reported. A study performed by Miyoshi et al. [37] looked at the surgical usefulness of ICG as an alternative to India ink for endoscopic marking and evaluated 40 patients between the time of ICG marking and the intervention, the median time period was 4 days (range, 1–73 days).



**Figure 13.**  
*A perineal wound with infection and inflammation after colorectal surgery.*

At the time of surgery, all 29 patients who were operated on within 8 days of tattooing stained positive in green with ICG dye.

Positive staining was clearly obviated in just two of the remaining 10 cases after 9 days or more.

The staining faded over time and finally vanished.

There was no mention of the dye's perioperative side effects.

The authors concluded that this study supports the use of ICG as a safe approach that may be consistently detected within 8 days of endoscopic injection (**Figure 14**).

### 3.3.8 Preoperative detection of occult enterovesical fistulas in patients with Crohn's disease

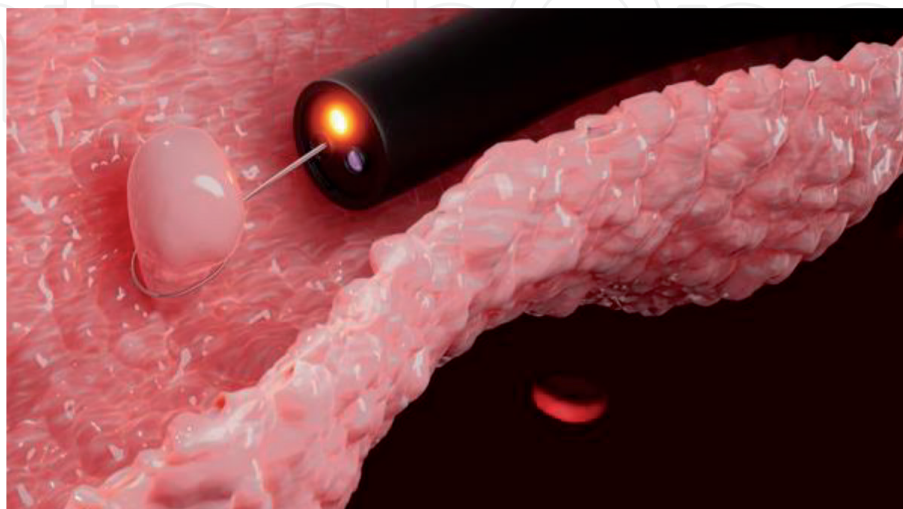
Efficacy of oral or rectal administration of indocyanine green solution. In a study realized by Sou et al. [38] whose objectives were to detect enterovesical occult microfistulas in patients with Crohn's disease before the fistulas had become readily apparent, nonhazardous enteral administration of indocyanine green solution was performed. The methods that were used collected a total of 12 patients with Crohn's disease who were suspected from their clinical manifestations of having enterovesical fistulas. Urine was collected and tested for contamination with indocyanine green by using a colorimeter to detect fistulas following oral or rectal administration of the indocyanine green solution. In addition, the efficacy of the indocyanine green test was compared to that of the "classical" X-ray sample.

The ICG test was positive in 11 of the 12 cases after either oral or rectal administration, resulting in a 92% correct diagnosis rate (11/12 patients).

The percentage of right diagnoses using an X-ray analysis, on the other hand, was just 17% (2/12 patients).

Furthermore, none of the eight patients with secret fistulas could be accurately diagnosed using an X-ray analysis, but all showed promising results when the indocyanine green approach was used.

The researchers concluded that the indocyanine green test had a 92% accuracy rate in diagnosing obscure fistulas and was highly diagnostic, while traditional examinations are often complicated and inaccurate (**Figure 15**).

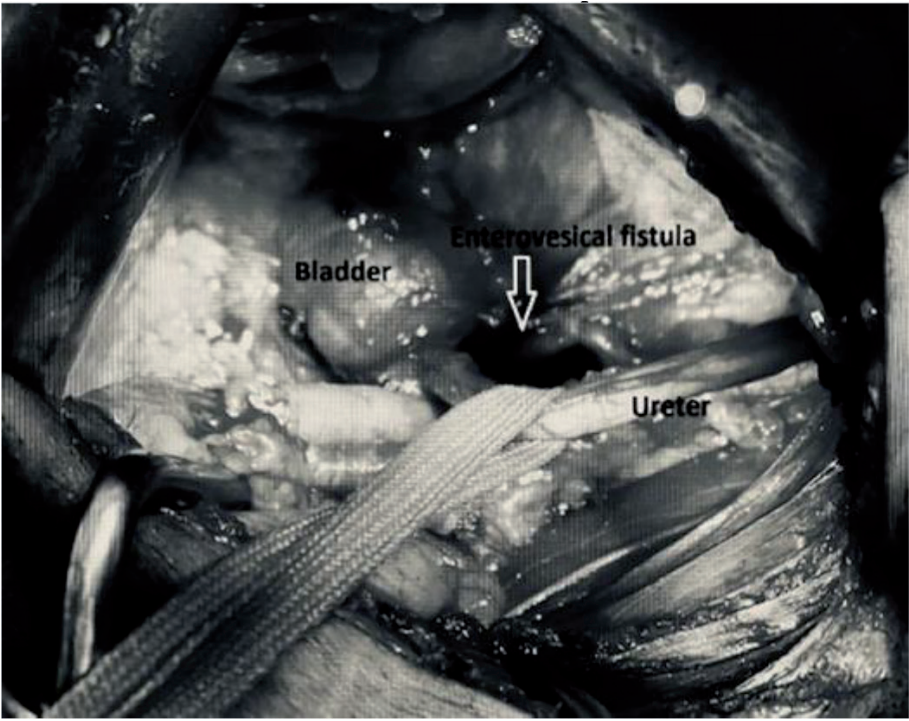


**Figure 14.**  
*Colon polyp removal. Endoscope inside colonoscopy for colon polyps.*

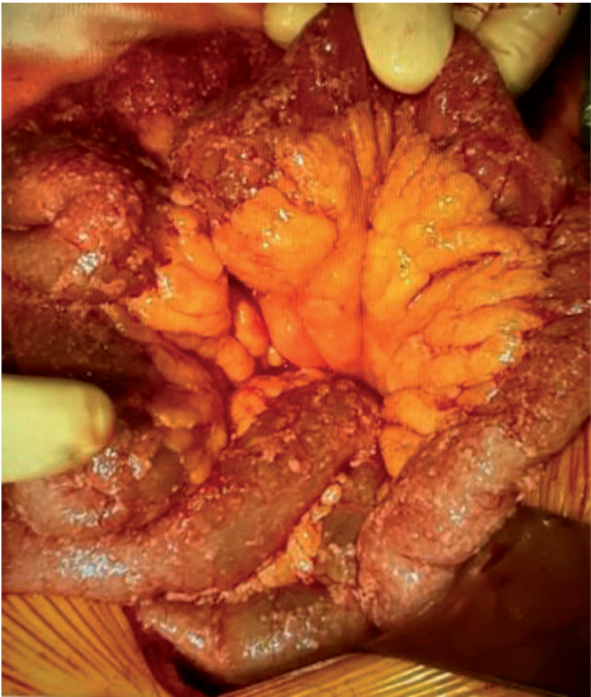


*3.3.9 The affinity of ICG in the detection of colorectal peritoneal carcinomatosis*

Peritoneal metastases can appear in 30–40% of patients with colorectal cancer and in a quarter of the patients might be the cause of death. ICG-guided surgery was able to detect additional lesions, and some studies reported up to 21.4% with a direct impact on modifying the surgical resection technique (**Figure 16**).



**Figure 15.**  
*Intraoperative macroscopic enterovesical fistula.*



**Figure 16.**  
*Extensive lesions of peritoneal carcinomatosis.*



## 4. Conclusions

Fluorescence-assisted surgery using near-infrared (NIR) light is a relatively new technique.

To improve the visible spectrum, this technique uses a combination of dyes and NIR imaging equipment.

As a result, it may provide more detailed anatomic and functional details, allowing for a more complete resection of a neoplasm or the protection of essential normal structures. Indocyanine green fluorescence technique is a surgical tool with increasing perioperative and intraoperative applications in colorectal surgical interventions. In colorectal surgery, in particular, several studies have shown that intraoperative fluorescence imaging is a safe and feasible method to evaluate anastomotic perfusion, and its use might positively affect the patient's clinical outcome by decreasing the incidence of anastomotic leaks. The number of virtual uses for indocyanine green is enhancing and developing, including new ways to detect and control colorectal metastases to the liver. All these advances expanded by the further evolution in time with more prospective trials could offer great information and value for both surgeons and patients, by improving the accuracy and outcomes of general surgery and surgical oncology.

## Conflict of interest

The author declares no conflict of interest.

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## References

- [1] Fennerty MB. Tissue staining (chromoscopy) of the gastrointestinal tract. *Canadian Journal of Gastroenterology*. 1999;**13**(5):423-429
- [2] Nowak K, Karampinis I, Gerken ALH. Application of fluorescent dyes in visceral surgery: State of the art and future perspectives. *Visceral Medicine*. 2020;**36**:80-87
- [3] [www.ifsg.org](http://www.ifsg.org)
- [4] Baiocchi GL, Gheza F, Molfino S, Arru L, Vaira M, Giacomuzzi S. Indocyanine green fluorescence-guided intraoperative detection of peritoneal carcinomatosis: Systematic review. *BMC Surgery*. 2020;**20**(1):158. DOI: 10.1186/s12893-020-00821-9
- [5] Sucher R, Brunotte M, Seehofer D. Indocyanine green fluorescence staining in liver surgery. *Chirurg*. 2020;**91**(6):466-473. DOI: 10.1007/s00104-020-01203-w
- [6] Tomassini F, Giglio MC, De Simone G, Montalti R, Troisi RI. Hepatic function assessment to predict post-hepatectomy liver failure: What can we trust? A systematic review. *Updates in Surgery*. 2020;**72**(4):925-938. DOI: 10.1007/s13304-020-00859-7. Epub 2020 Aug 4
- [7] Driessen C, Arnardottir TH, Lorenzo AR, Mani MR. How should indocyanine green dye angiography be assessed to best predict mastectomy skin flap necrosis? A systematic review. *Journal of Plastic, Reconstructive & Aesthetic Surgery*. 2020;**73**(6):1031-1042. DOI: 10.1016/j.bjps.2020.02.025. Epub 2020 Feb 18
- [8] Ianieri MM, Corte LD, Campolo F, Cosentino F, Catena U, Bifulco G, et al. Indocyanine green in the surgical management of endometriosis: A systematic review. *Acta Obstetrica et Gynecologica Scandinavica*. 2021;**100**(2):189-199. DOI: 10.1111/aogs.13971. Epub 2020 Sep 7
- [9] Slooter MD, Janssen A, Bemelman WA, Tanis PJ, Hompes R. Currently available and experimental dyes for intraoperative near-infrared fluorescence imaging of the ureters: A systematic review. *Techniques in Coloproctology*. 2019;**23**(4):305-313. DOI: 10.1007/s10151-019-01973-4. Epub 2019 Apr 27
- [10] Copăescu C, Bîrlog C, Turcu F, Săftoiu A. A novel indocyanine green fluorescence-guided laparoscopic technique to map the site of obscure. *Chirurgia (Bucur)*. 2021;**116**(1):89-101. DOI: 10.21614/chirurgia.116.1.89
- [11] Benson J. Indocyanine green fluorescence for sentinel lymph node detection in early breast cancer. *Annals of Surgical Oncology*. 2016;**23**(1):6-8
- [12] Balaya V, Guani B, Bonsang-Kitzis H, Deloménie M, Ngô C, Macias RM, et al. Sentinel lymph node biopsy in early-stage cervical cancer: Current state of art. *Bulletin du Cancer*. 2020;**107**(6):696-706. DOI: 10.1016/j.bulcan.2019.06.011. Epub 2019 Oct 15
- [13] Frumovitz M, Plante M, Lee PS, Sandadi S, Lilja JF, Escobar PF, et al. Near-infrared fluorescence for detection of sentinel lymph nodes in women with cervical and uterine cancers (FILM): A randomised, phase 3, multicentre, non-inferiority trial. *The Lancet Oncology*. 2018;**19**(10):1394-1403
- [14] Koh WJ, Abu-Rustum NR, Bean S, Bradley K, Campos SM, Cho KR, et al. Cervical Cancer, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network*. 2019;**17**(1):64-84

- [15] Carus T, Pick P. Intraoperative fluorescence angiography in colorectal surgery. *Chirurg*. 2019;**90**(11):887-890. DOI: 10.1007/s00104-019-01042-4
- [16] Blanco-Colino R, Espin-Basany E. Intraoperative use of ICG fluorescence imaging to reduce the risk of anastomotic leakage in colorectal surgery: A systematic review and meta-analysis. *Techniques in Coloproctology*. 2018;**22**(1):15-23. DOI: 10.1007/s10151-017-1731-8. Epub 2017 Dec 11
- [17] Emile SH, Elfeki H, Shalaby M, Sakr A, Sileri P, Laurberg S, et al. Sensitivity and specificity of indocyanine green near-infrared fluorescence imaging in detection of metastatic lymph nodes in colorectal cancer: Systematic review and meta-analysis. *Journal of Surgical Oncology*. 2017;**116**(6):730-740. DOI: 10.1002/jso.24701. Epub 2017 Jun 1
- [18] Nagata K, Endo S, Hidaka E, Tanaka J, Kudo SE, Shiokawa A. Laparoscopic sentinel node mapping for colorectal cancer using infrared ray laparoscopy. *Anticancer Research*. 2006;**26**(3B):2307-11.55
- [19] Kawahara H, Nimura H, Watanabe K, Ko-bayashi T, Kashiwagi H, Yanaga K. Where does the first lateral pelvic lymph node receive drainage from? *Digestive Surgery*. 2007;**24**(6):413-7.56
- [20] Cahill RA, Anderson M, Wang LM, Lindsey I, Cunningham C, Mortensen NJ. Near-infra-red (NIR) laparoscopy for intraoperative lymphatic road-mapping and sentinel node identification during definitive surgical resection of early-stage colorectal neoplasia. *Surgical Endoscopy*. 2012;**26**(1):197-204
- [21] Liberale G, Galdon MG, Moreau M, Vankerckhove S, El Nakadi I, Larsimont D, et al. Ex vivo detection of tumoral lymph nodes of colorectal origin with fluorescence imaging after intraoperative intravenous injection of indocyanine green. *Journal of Surgical Oncology*. 2016;**114**(3):348-353
- [22] Yeung TM, Wang LM, Colling R, Kraus R, Cahill R, Hompes R, et al. Intraoperative identification and analysis of lymph nodes at laparoscopic colorectal cancer surgery using fluorescence imaging combined with rapid OSNA pathological assessment. *Surgical Endoscopy*. 2018;**32**(2):1073-1076. DOI: 10.1007/s00464-017-5644-4. Epub 2017 Jun 22
- [23] Vuijk FA, Hilling DE, Mieog JSD, Vahrmeijer AL. Fluorescent-guided surgery for sentinel lymph node detection in gastric cancer and carcinoembryonic antigen targeted fluorescent-guided surgery in colorectal and pancreatic cancer. *Journal of Surgical Oncology*. 2018;**118**(2):315-323. DOI: 10.1002/jso.25139. Epub 2018 Sep 14
- [24] Hirche C, Mohr Z, Kneif S, Doniga S, Murawa D, Strik M, et al. Ultrastaging of colon cancer by sentinel node biopsy using fluorescence navigation with indocyanine green. *International Journal of Colorectal Disease*. 2012;**27**(3):319-324. DOI: 10.1007/s00384-011-1306-5. Epub 2011 Sep 13
- [25] Peloso A, Franchi E, Canepa MC, Barbieri L, Briani L, Ferrario J, et al. Combined use of intraoperative ultrasound and indocyanine green fluorescence imaging to detect liver metastases from colorectal cancer. *HPB (Oxford)*. 2013;**15**(12):928-934
- [26] van der Vorst JR, Schaafsma BE, Hutteman M, Verbeek FP, Liefers GJ, Hartgrink HH, et al. Near-infrared fluorescence-guided resection of colorectal liver metastases. *Cancer*. 2013;**119**(18):3411-3418

- [27] Ishizawa T, Masuda K, Urano Y, Kawaguchi Y, Satou S, Kaneko J, et al. Mechanistic background and clinical applications of indocyanine green fluorescence imaging of hepatocellular carcinoma. *Annals of Surgical Oncology*. 2014;**21**(2):440-448
- [28] Kaibori M, Matsui K, Ishizaki M, Iida H, Oku-mura T, Sakaguchi T, et al. Intraoperative detection of superficial liver tumors by fluorescence imaging using indocyanine green and 5-aminolevulinic acid. *Anticancer Research*. 2016;**36**(4):1841-1849
- [29] Shizawa T, Fukushima N, Shibahara J, Ma-suda K, Tamura S, Aoki T, et al. Real-time identification of liver cancers by using indocyanine green fluorescent imaging. *Cancer*. 2009;**115**(11):2491-2504
- [30] Qi C, Zhang H, Chen Y, Su S, Wang X, Huang X, et al. Effectiveness and safety of indocyanine green fluorescence imaging-guided hepatectomy for liver tumors: A systematic review and first meta-analysis. *Photodiagnosis and Photodynamic Therapy*. 2019;**28**: 346-353
- [31] Liberale G, Bourgeois P, Larsimont D, Moreau M, Donckier V, Ishizawa T. Indocyanine green fluorescence-guided surgery after IV injection in metastatic colorectal cancer: A systematic review. *European Journal of Surgical Oncology*. 2017;**43**(9):1656-1667. DOI: 10.1016/j.ejso.2017.04.015. Epub 2017 May 8
- [32] Vilz TO, Kalff JC, Stoffels B. Evidence of indocyanine green fluorescence in robotically assisted colorectal surgery : What is the status? *Der Chirurg*. 2021;**92**(2):115-121. DOI: 10.1007/s00104-020-01340-2. Epub 2021 Jan 11
- [33] Lee DW, Sohn DK, Han KS, Hong CW, Park HC, Oh JH. Promising novel technique for tumor localization in laparoscopic colorectal surgery using indocyanine green-coated endoscopic clips. *Diseases of the Colon & Rectum*. 2021;**64**(1):e9-e13. DOI: 10.1097/DCR.0000000000001876
- [34] De Nardi P, Elmore U, Maggi G, Maggiore R, Boni L, Cassinotti E, et al. Intraoperative angiography with indocyanine green to assess anastomosis perfusion in patients undergoing laparoscopic colorectal resection: Results of a multicenter randomized controlled trial. *Surgical Endoscopy*. 2020;**34**(1):53-60. DOI: 10.1007/s00464-019-06730-0. Epub 2019 Mar 21
- [35] Sherwinter DA. Transanal near-infrared imaging of colorectal anastomotic perfusion. *Surgical Laparoscopy, Endoscopy & Percutaneous Techniques*. 2012;**22**(5):433-436. DOI: 10.1097/SLE.0b013e3182601eb8
- [36] Kitai T, Kawashima M, Fujii H, Mashima S, Shimahara Y. Indocyanine green fluorescence monitoring of perineal wound contamination in abdominoperineal resection: A preliminary report. *Surgery Today*. 2011;**41**(8):1037-1040. DOI: 10.1007/s00595-010-4417-7. Epub 2011 Jul 20
- [37] Miyoshi N, Ohue M, Noura S, Yano M, Sasaki Y, Kishi K, et al. Surgical usefulness of indocyanine green as an alternative to India ink for endoscopic marking. *Surgical Endoscopy*. 2009;**23**(2):347-351. DOI: 10.1007/s00464-008-9938-4. Epub 2008 Apr 29
- [38] Sou S, Yao T, Matsui T, Takemura S, Sakurai T, Takenaka K, et al. Preoperative detection of occult enterovesical fistulas in patients with Crohn's disease: Efficacy of oral or rectal administration of indocyanine green solution. *Diseases of the Colon & Rectum*. 1999;**42**(2):266-270. DOI: 10.1007/BF02237140