review

QUANTITATIVE METHODS FOR THE USE OF ICG IN COLORECTAL SURGERY- an updated literature review

Sinziana Ionescu [1,*];

[1]Ist Clinic of General Surgery and Surgical Oncology, Bucharest Oncology Institute, 022328 Bucharest, Romania and "Carol Davila" University of Medicine and Pharmacy, 050474 Bucharest, Romania; sinzianaionescu30@gmail.com (S.I.);

* Correspondence: sinzianaionescu30@gmail.com (S.I.);

Abstract: This review looks at the use of indocyanine green (ICG) in colorectal surgery, from a quantitative point of view. The main benefits of the ICG technique in colorectal surgery, can be summarized as follows: a)in the realization of the intraoperative fluorescence angiography as adjuvant in the process of anastomosis, b)in the fluorescence guided detection of lymph node metastases in colorectal cancer and, also, the sentinel lymph node technique, which was proven better than formal methods in some studies, c) marking with positive fluorescence a liver nodule as small as "just" 200 tumor cells, d) offering assistance in the diagnosis of a fistula, e)in the possibility to be used for tumour tattooing also, f)providing help in maintaining a clean surgical field and preventing wound infection in abdominoperineal resection. Apart from the qualitative intraoperative use of ICG, the method can be employed in association with quantitative methods, such as: maximum intensity, relative maximum intensity and various parameters of the inflow (time-to-peak, slope, and t1/2max) , this latter cathegory being more significantly associated with anastomotic leakage.

Keywords: colorectal 1; fluorescence 2; ICG 3; ICG-NIR 4; colorectal surgery 5; intraoperative staining 6; q-ICG 7;

1. Introduction

As general surgical techniques have become more refined with increasingly precise movements, eventually leading to the emergence and development of robotic surgery, the same phenomenon has occurred with adjunctive methods to better identify, visualize, and resect a specific structure/tissue during the intervention. With the aid of fluorescence, the vessels, lymph nodes, and tumor itself can all be seen more clearly. The NIR-ICG (near infrared light and indocyanine green) technique significantly improves the visibility of certain organs, such as the ureter; consequently, the risk of creating a lesion due to inadequate visibility is diminished. The quantitative parameters discussed in the current medical literature used for the quantitative use of ICG were separated into four categories: time to fluorescence, contrast-to-background ratio, pixel intensity, and numeric classification score. This review examines extensively different studies on the use of ICG in colorectal surgery and provides a general framework based on substantial research.

2. Materials and Methods

Envisaging the goal of performing an updated literature review on the theme of quantitative ICG use in colorectal surgery, the following searches were conducted: 1)a search for relevant terms on www.pubmed.gov which only resulted in a few answers to the quest; 2) the terms "ICG quantitative colorectal surgery" were searched for on www.sciencedirect.com, with 399 results; 3) the terms indocyanine green AND colorectal AND surgery AND quantitative"were looked on www.oxfordjournals.com and 4) the terms "indocyanine AND green aND colorectal AND surgery AND quantitative" were looked upon on www.scopus.com, from 2022-2018, in English and this last search returned 397 results. All the above mentioned returned results were summarized into principal matters according to the subject treated, and the main ideas and concepts are presented in the next session.

3. Results

Optical imaging currently refers to a variety of noninvasive techniques for monitoring specific physiologic, pathologic, and molecular processes, as well as the behavior of specific cell populations, as presented by Ottobrini [1] and Pirovano[2]. These techniques rely on the detection of photons in the visible range, up to the near-infrared (400-1700 nm), emitted by fluorescent and bio/chemo-luminescent molecules.

As described by Morales-Conde [3]in the 2022 guidelines on the use of fluorescence dyes in general surgery, with visibility in near-infrared light, Indocyanine Green is a fluorescent substance. It is helpful at: 1.the identification of anatomical structures (biliary tract, ureters, parathyroid, thoracic duct), 2. appreciating the tissue blood supply(anastomosis in colorectal, esophageal, gastric, bariatric surgery, in plastic surgery procedures , liver resection, in strangulated hernias and in intestinal ischemia), as it can be noticed in figures 1.a and 1.b.), and 3.can help with minute tumor identification (liver, pancreas, stomach, breast, colon, rectum, esophagus and skin cancer).

The evidence found so far is very encouraging; however, standardization of its use and randomized studies with a larger number of patients are necessary to reach definitive conclusions regarding its use in general surgery.

In an Informed opinion given by Ghuman[4] on the use of fluorescence in colorectal surgery, it is mentioned that this technology's versatility improves on numerous aspects of colorectal procedures. Historically, white light was the only modality for the visualization of tissue perfusion, tumor implants, and important, relevant structures, such as the ureters and lymph nodes. The near-infrared spectrum's ability to penetrate biological tissues enables the injection of fluorophores to identify these structures. The two most commonly used fluorophores (intravenously) are methylene blue and indocyanine green. In addition, novel tumor marker-specific fluorophores are being researched for cancer detection.

Thammineedi [5]calls fluorescence guided cancer surgery (FGS) a new paradigm and focuses research on its use in the context of abdominal-thoracic malignancies. Martinez Lopez [6]underlines that new FGS applications are being created to aid in the detection of peritoneal metastases and in the proper evaluation of tumor resection margins, as demonstrated in figures 2.a-g.

Heeman [7]discusses the importance of a uniform fluorescence imaging protocol and data collection in clinical trials.

Lutken[8] looked at the new technique of quantitative indocyanine green angiography (Q-ICG) that provides surgeons with an objective evaluation of tissue perfusion.

By means of a systematic review, he sought to determine the optimal Q-ICG methodology. A total of 1216 studies were evaluated, and 13 were ultimately included. Maximum intensity and relative maximum intensity were unable to identify patients with anastomotic leakage, according to the studies. In contrast, the parameters of the inflow (time-to-peak, slope, and t1/2max) were significantly associated with anastomotic leakage. Only two studies performed intraoperative Q-ICG, while the rest used video recordings to perform Q-ICG retrospectively. The designs, Q-ICG parameters, and patient populations of the studies varied. No randomized studies were identified, and the overall level of evidence was rated as low to moderate. While the results are diverse, they all appear to point in the same direction. Fluorescence intensity parameters are unstable and do not accurately represent clinical endpoints. In contrast, inflow parameters are robust in a clinical setting and more accurately reflect clinical endpoints. From this previous research in 2020, the research field of quantitative ICG evolved exponentially.

A research by Noltes [9]aims to develop a reproducible and generalizable Workflow model of ICG-angiography incorporating Standardization and Quantification (WISQ) that can be applied uniformly within the surgical innovation domain regardless of the user. WISQ must be prospectively validated in larger series before it can support clinical decision-making to predict and prevent postoperative organ function impairment in a large and diverse surgical population.

A systematic review by Slooter [10]sought to identify all methods for quantifying intraoperative fluorescence angiography (FA) of the gastrointestinal anastomosis and to identify potential thresholds for predicting patient outcomes, such as anastomotic leakage and necrosis. The quantitative parameters were separated into four categories: time to fluorescence (twenty studies), contrast-to-background ratio (three studies), pixel intensity (two studies), and numeric classification score (2). The first category was divided into: manually measured time (7 studies) and software-generated fluorescence–time curves (13). To predict patient outcomes, cutoff values were derived for manually assessed time (speed in gastric conduit wall) and derivatives of the fluorescence–time curves (Fmax, T1/2, TR, and slope). Conclusion: Time to fluorescence appears to be the most promising metric for quantifying FA. Future research could concentrate on fluorescence–time curves, as numerous parameters can be derived and fluorescence intensity persistence can be avoided. To enable future data comparison, however, consensus on study design, calibration of fluorescence imaging systems, and software validation is required. A study by Ahn[11] concluded that, since quantitative parameters of ICG angiography are affected by a variety of conditions, a standardized protocol is necessary. Fluorescence images can be optimized through the application of ICG-specific modes at a fixed distance of 4-5 cm.

Several software options for quantifying fluorescence have emerged, but they have not been compared previously. The comparison of the outcomes of quantitative ICG-FI analysis of relative perfusion in an experimental setting using two distinct software-based quantification algorithms was the objective of a study (FLER and Q-ICG) by Gosvig[12].When perfusion was either extremely high or extremely low, the quantitative fluorescence analysis of the two software packages differed considerably. The clinical significance of these variations is unclear.

Gorspas [13]emphasizes the fact that FGS offers high sensitivity, contrast, and specificity without exposing the patient to radiation. It can also identify the borders and reflect the position of superficial lesions during a surgical procedure, providing the technical means for early detection and precise resection of small lesions. It is anticipated that the validation of FGS technology's performance through both imaging equipment development and standardization and clinical trials will reduce iatrogenic trauma and improve postoperative survival rates and quality of life.

3.1. Rectocolonic perfusion

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In a study by Gomez-Rosado [14]that had as a purpose to quantify fluorescence angiography with indocyanine green (ICG) in colorectal cancer anastomosis, an identification was made of the influential factors in its temporary intensity and pattern. The research also did an evaluation of the ability to predict the AL(anastomotic leak) , and establishing the cut-off levels for high- or low-risk groups. To stratify risk of AL, quantitative analysis of ICG fluorescence during colorectal surgery is safe and feasible.The intensity of fluorescence at the point of section is affected by hypertension and the anastomosis site (the nearest to rectum, the most intensity detected). When fluorescence intensities at the point of section are less than 169 U or slopes are less than 14.4 U/s, a change of division site should be considered to prevent AL due to vascular causes.

Another research, conducted by Mo Son[15], aimed at quantitatively evaluating colon perfusion patterns using indocyanine green (ICG) angiography in order to identify the most accurate predictor of anastomotic complications following laparoscopic colorectal surgery.The use of laparoscopic fluorescence imaging on colorectal cancer patients. ICG (0.25 mg/kg) was injected slowly into peripheral blood vessels, and the fluorescence intensity of colonic flow was measured sequentially using a video analysis and modeling tool to generate perfusion graphs. On the basis of their fluorescence slope, T1/2MAX and time ratio (TR = T1/2MAX/TMAX), colon perfusion patterns were classified as fast, moderate, or slow. Analyses of clinical and quantitative perfusion variables were performed to identify predictors of anastomotic complications. The conclusion was that quantitative analysis of ICG perfusion patterns using T1/2MAX and TR can be used to identify segments with inadequate perfusion, thereby reducing anastomotic complications during laparoscopic colorectal surgery.

Nerup [16]conducted a study in which the aim was an investigation of whether ICG-FA and q-ICG could improve blood supply evaluation by surgeons of different training levels. In a porcine model, thirteen small bowel segments with varying degrees of devascularization and two healthy sham segments were constructed. Blinded to the degree of devascularization, the study recruited students, residents, and surgeons to perform perfusion assessments of the segments in white light (WL), with ICG-FA, and after q-ICG. The conclusion was that Q-ICG seems to guide surgeons, regardless of experience level, to safely perform resection in healthy tissue, compared with standard WL.

The conclusion of a research presented by Tang[17] was that ICG can effectively reduce the incidence of AL, without prolonging the operative time or increasing postoperative complications in colorectal surgery, an idea also presented by Vargas[18] . A meta-analysis by Trastulli [19]found that ICG-FA used in colorectal surgery lead to a significant reduction in anastomotic leakage and in the need for surgical reintervention for anastomotic leak, especially in patients with low or ultra-low rectal resections. Similarly, sigmoid and rectal resections can have an improved AL(lower rates of fistullae) secondarily to ICG-NIFA technology, as presented by Neddermeyer[20].

Low anastomoses and preoperative radiotherapy are crucial risk factors for leakage.

Numerous surgeons frequently perform an unnecessary protective ileostomy, which raises costs and necessitates a second operation for recanalization. A study by Brescia [21] aimed to evaluate the role of indocyanine green in assessing bowel perfusion, even in the presence of a low anastomosis on radiotherapy-treated tissue.

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Even in the highest-risk cases, indocyanine green appears to be safe and effective for assessing the perfusion of colorectal anastomoses, potentially reducing the rate of ileostomy.

The primary limitation is the absence of a universally replicable standard evaluation.

The conclusion of a research by Meijer [22]was that the difficulty in interpreting uncorrected fluorescence signals is demonstrated by the fact that similar intraoperative fluorescence results may lead to different surgical treatment strategies. In the near future, surgeons may benefit from the quantification and standardization of NIR fluorescence perfusion imaging in real time.

A study by Cheon Kim[23]underlined that quantitative analysis of indocyanine green fluorescent imaging may help prevent anastomotic complications during robot-assisted sphincter-saving operations, and may be of particular value in patients with a short descending mesocolon and high-class ASA. A study by Ishii [24] found that ICG fluorescence angiography has the potential to reduce the rate of AL in patients undergoing laparoscopic rectal cancer surgery.

Higashijima [25] evaluated 79 patients who underwent laparoscopic colorectal resection for colon cancer using a double-stapling technique were evaluated retrospectively. By measuring indocyanine green fluorescence time, blood flow in oral stumps was assessed (FT). The authors analyzed correlations between FT and AL risk factors and performed a comprehensive investigation of AL cases. The conclusions drawn were towards the idea that :patients with delayed FT (.60 seconds or 50-60 seconds with _3 risk factors) may require revision of the anastomosis (stoma diversification or additional resection) to prevent AL. Aiba[26] looks at the assessment of blood supply where there isn't a clear demarcation line and conducts a study where the clinical effect of the time to arterial perfusion (TAP) on anastomotic leakage (AL) was assessed, particularly in patients without ICG demarcation. The methods employed were: Using ICG-A, the TAP in 110 patients undergoing colorectal surgery was evaluated. The transection line had to be altered for ICG demarcation, and the TAP was measured at the new stump. According to the arterial route, the patients were divided into marginal flow (MF) and direct flow (DF) groups. The third quartile or slower TAP within each group was defined as delayed TAP. The conclusions were that, in patients without ICG demarcation, delayed TAP may be useful for predicting high-risk AL patients in the MF group; however, a diverting stoma or strict observation may be a reasonable response.

To prevent AL, numerous solutions, including ICG angiography and transanal drainage tubes (TDT), have been proposed. Although it was recently recognized that microbiota play a role in the pathogenesis of AL, primarily based on the results of animal models, it is still unknown whether this mechanism can occur in humans, and a research by Kawada [27] analyzed this aspect. The need for a proximal shift of the transection site due to insufficient intestinal perfusion was significantly associated with high fecal volume, which may reflect the correlation between intestinal perfusion and postoperative diarrhea. In addition, the intensity of ICG fluorescence at the site of transection was significantly correlated with fecal volume as measured by TDT.

Grafitsch [28] decided to look into the aspects of visible light spectroscopy(VLS) to evaluate serosal oxygen saturation patterns during colorectal resections. Regarding the

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materials and procedures employed, those involved: the use of VLS on the colonic serosa, the bowel perfusion of patients undergoing left-sided colorectal resections was evaluated at various timepoints during surgery.

The primary outcome measure was the serosal oxygen saturation (StO2) at the anastomosis at various timepoints during surgery. The conclusion was that: during colorectal resections, the researchers observed an increase in colonic StO2 during surgery. The absence of an association between the onset of AL and a decrease in StO2 demonstrates the multifactorial nature of AL development. Seeliger [29] aimed to quantify potential differences in mucosal and serosal perfusion levels in an ischemic colon segment. Mucosal ischemic zones were larger than serosal ischemic zones. These findings suggest that an evaluation of bowel perfusion from the serosal side alone may underestimate the severity of ischemia. Additional research is necessary to determine the optimal resection margin and anastomotic site.

High ligation (HL) and low ligation (LL) of the inferior mesenteric artery (IMA) continue to be debated in the field of rectal cancer surgery in terms of perfusion and anastomosis leakage. Han [30] made a study on this aspect by using ICG. Randomization was used to assign patients with rectosigmoid or rectal cancer to the high or LL group.

Before and after IMA ligation, ICG was injected, and ROI values were measured using an image analysis program (HSL video).F max did not differ significantly between the two groups, but T max was significantly greater and Slope max was significantly lower in the HL group compared to the LL group. Significant associations were found between anastomosis leakage and neoadjuvant chemoradiation and F max. T max increased and slope max decreased significantly in the HL group following IMA ligation.

Nonetheless, the intensity of perfusion (F max) was not affected by the degree of IMA ligation. Munechika[31] presented a study in which he demonstrated the safety and feasibility of high ligation of the IMA for descending colon cancer without sacrificing additional distal colon using fluorescence evaluation of blood flow in the remnant colon.

AL is arguably the most challenging complication of anterior resection (AR). Before implementing the double-stapling technique anastomosis, ICG was injected intravenously and blood flow on the rectal stump was evaluated laparoscopically.

Iwamoto[32] conducted a quantitative analysis of the association between various parameters and AL. The results showed that T0, the time between when the ICG was injected intravenously and when the ICG disappeared from the injection route, was significantly longer in the AL group than in the non-AL group (P =.03). No other significant differences existed between the AL and non-AL groups. T0 was longer in patients with AL compared to those without the disease. If prolonged T0 can be identified intraoperatively, only appropriate patients will be able to receive DS.

In Japan, lower rectal cancer with lateral lymph node metastasis is regarded as a local disease, and lateral lymph node dissection is recommended (LLND). Nevertheless, laparoscopic procedures are relatively challenging. To preserve the autonomic nerve and ureter, the hypogastric fascia and ureter must be dissected from the vesical-hypogastric fascia. In addition, lymph node dissection close to the internal iliac artery is difficult because the internal iliac artery branches in numerous patterns.

Using a near-infrared ray fluorescent ureteral catheter (NIRFUC) and indocyanine green, Ryu [33] and Gila-Bohorquez [34]investigated the utility of fluorescence ureter and vessel navigation (ICG). The conclusions of the study was that fluorescence navigation of vessels and the ureter is feasible in laparoscopic LLND and may increase patient safety. Figures 3.a and 3.b depict the use of fluorescent ureteral intraoperative devices for improved identification of the anatomic structures and enhanced and more secure dissection.

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In patients with locally advanced rectal cancer, a research by Kim[35] used fluorescence to evaluate the learning process for performing robotic total mesorectal excision with lateral pelvic node dissection.

Subjective visual assessment (SVA) of color, pulsations, and bleeding from cut edges during colon pull-up surgery for corrosive oesophageal strictures is unreliable for predicting conduit perfusion.

The conclusion of a research by Kumar [36] was that ICG-FI can enhance the subjective visual assessment of conduit perfusion by detecting subtle hypoperfusion defects.

The goal of a study by Spagnolo [37] was to examine the current understanding of the function of fluorescence imaging for intraoperative intestinal assessment in gynecological surgery. All articles describing the application of indocyanine green (ICG) to bowel evaluations in gynecology or endometriosis surgery were evaluated. The results were that ICG is an effective tool for assessing bowel vascularization, thereby potentially preventing anastomotic leakage and recto-vaginal fistula, and is thus useful for endometriosis surgery and bowel assessment in gynecological oncology procedures, a finding also described by Ianieri[38].

Real-time characterization of the hypovascular pattern of endometriotic nodules has been correlated with larger nodule size and lower microvessel density, thereby assisting surgeons in selecting the optimal transecting line and technique.

ICG angiography permits a laparoscopic and intrarectal assessment of the bowel, which can serve as a double check of bowel perfusion and enable the evaluation of mucosa vascularization.

ICG fluorescence can direct intraoperative decision-making following intestinal anastomosis, discoid resection (also shown by Raimondo[39]), and rectal shaving, thereby preventing anastomotic leakage and postoperative recto-vaginal fistula in low anterior resections.

3.2. To improve detection of cancer tissue and target treatment

Endoscopic imaging is the primary technique for detecting gastrointestinal diseases that are detrimental to human health, and several enhancements and additional methods are further presented by Li[40].

White light endoscopy (WLE) was the first method used for endoscopic examination and remains the first step in the clinical examination of gastrointestinal diseases. Due to its poor correlation with histopathological diagnosis, it is unable to accurately diagnose gastrointestinal disorders. In recent years, numerous innovative endoscopic techniques have been developed to enhance the detection accuracy of endoscopy. Using biocompatible dye agents, chromoendoscopy (CE) increases the contrast between normal and diseased tissues. Narrow band imaging (NBI) can enhance the contrast between capillaries and submucosal vessels by modifying the light source acting on the tissue through the use of special filters to visualize the vascular structure. Flexible spectral imaging color enhancement (FICE) technique uses reflectance spectrum estimation to obtain individual spectral images and three selected spectral images to reconstruct an enhanced image of the mucosal surface. Utilizing the different reflective properties of normal and diseased tissues, the i-Scan technology obtains images and enhances image contrast through post-processing algorithms.

In a subset of patients with colorectal peritoneal metastases, complete cytoreduction has been the most important prognostic factor influencing long-term outcomes.

Imaging with indocyanine green fluorescence appears useful for detecting small subclinical peritoneal implants in these patients.

Nonetheless, quantitative fluorescence analysis has not yet been standardized. A study by Gonzales-Abos [41] had as a purpose to determine the sensitivity and specificity of quantitative indocyanine green fluorescence in the detection of peritoneal metastases

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of non-mucinous colorectal origin. Indocyanine green was administered intravenously 12 hours prior to surgery. Cytoreduction was accomplished by identifying nodules under white light and then indocyanine green. Finally, fluorescence ex vivo was evaluated. In total, 52 nodules were resected, with histopathological analysis diagnosing 37 (71,1 percent) as malignant. Five (13.5%) were undetectable under white light and could only be identified through fluorescence. Under white light, a total of 15 noncancerous nodules were detected, 8 of which were negative for fluorescence (53.3%). Fluorescence greater than 181 units may be the threshold for malignancy, with a sensitivity and specificity of 89.0 and 85.0 percent, respectively, while uptake less than 100 units appears to correlate with a benign pathology. Quantitative indocyanine green appears useful for assessing colorectal peritoneal metastases that are not mucinous. Fluorescence uptake above 181 units appears to correlate with malignancy, while uptake below 100 units appears to correlate with a benign pathology. Similar results were found also by Moran [42]. Lieto[43] finds that the diagnostic performance of ICG-FI was significantly superior to both preoperative ($p = 0.027$) and intraoperative ($p = 0.042$) conventional procedures, suggesting that intraoperative ICG-FI may improve outcomes for patients undergoing CS for PC from CRC.

A study by Lwin [44] describes molecular biomarkers associated with fluorescence in pre-clinical and clinical evaluation. For the illumination of target lesions, an impressive number of fluorescently labeled antibodies, peptides, particles, and other molecules related to cancer hallmarks have been developed, as shown by Mieog[45] , Privitera[46], Nagaya[47] and Tipirneni[48] . Zhang [49]researches on the theme of the recent progress of activable molecular probes, with applications from fluorescence guided surgery to endoscopy and tissue biopsy.

Despite the fact that only a few of these imaging agents have advanced beyond early-phase clinical trials, new methods are being implemented to bring them to the clinic.

For this translational process to be successful, target selection, imaging agents and their associated detection systems, and clinical implementation must work in perfect unison to enable real-time intraoperative visualization that is beneficial to patients.

The metal-organic framework-mediated chemo-photothermal therapy guided by photoacoustic imaging (PAI) is an accurate and effective method for tumor inhibition, which can synergistically achieve immunogenic cell death and result in an increasing infiltration of immune cells into the tumor microenvironment, thereby enhancing the sensitivity for immune checkpoint blockade (aPD-L1) therapy.

This type of therapy can not only reduce the systemic toxicity caused by conventional treatments, but it can also address the issue of immune checkpoint blockade's poor efficacy in colorectal cancer (CRC). As described by Liu[50], metal-organic structure oxaliplatin (OXA) and indocyanine green (ICG) were loaded into hyaluronic acid (HA)-modified MIL-100 (Fe) nanoparticles in order to obtain multifunctional nanoparticles (OIMH NPs). The OIMH NPs exhibited sensitive photoacoustic imaging (PAI) for imaging-guided therapy and exhibited a favorable synergistic effect when chemotherapy was combined with photothermal therapy (PTT) to eradicate tumor cells. Immunogenic cell death (ICD) and T-cell activation induced by chemo-photothermal therapy may sensitize to immune checkpoint blockade (aPD-L1) response, thereby inducing systemic antitumor immunity. The combination of chemotherapy, PTT, and aPD-L1 was finally responsible for the observed inhibition of tumor growth.

3.3. For Lymph node mapping and lymph node metastasis

In numerous types of cancer, indocyanine green has been widely utilized as a safe and straightforward technique for mapping sentinel lymph nodes.

In spite of this, the use of Indocyanine green has not been fully implemented due to the heterogeneous findings of published studies. Consequently, the purpose of a meta-analysis by Villegas-Tovar [51] was to evaluate the overall performance of Indocyanine green for sentinel lymph node mapping and node metastasis in colorectal cancer patients undergoing surgery. Unrestricted by time constraints, a comprehensive systematic search was conducted to identify relevant studies in English and Spanish.

A hierarchical summary receiver operating characteristic curve (HSROCs) was constructed for the meta-analysis, and random effects models were used to synthesize quantitative data. Specificity, sensitivity, positive likelihood ratio, and negative likelihood ratio were derived from the respective HSROC. The conclusion indicated that, indocyanine green for the detection of sentinel lymph node mapping is more accurate when applied laparoscopically, and to colon cancer.However, its overall performance for lymph node metastasis detection is poor.

A study by Li[52] describes a method for fluorescently staining excised lymph nodes using paired-agent molecular imaging principles, which involve co-administration of a molecular-targeted imaging agent and a suitable control (untargeted) agent, with the signal from the control agent accounting for any nonspecific retention of the targeted agent.

Dual-needle continuous infusion of either an antibody-based imaging agent pair (epidermal growth factor receptor (EGFR) targeted agent: IRDye-800CW labeled Cetuximab; control agent: IRDye-700DX-IgG) or an Affibody-based imaging agent pair (EGFR targeted Affibody® agent: ABY-029; control agent IRDYN-700DX carboxylate) .The results indicated the possibility of achieving >99% sensitivity and >95% specificity for the detection of a single micrometastasis (0.2 mm in diameter) in a whole lymph node within 22 minutes of tissue processing.

The detection capabilities offer significant enhancements over existing intraoperative lymph node biopsy techniques (e.g., frozen pathology has a micrometastasis sensitivity of 20%).

3.4. In inflammatory bowel disease (IBD)

After a restorative proctocolectomy and ileal J-pouch, an anastomotic leak (AL) increases morbidity and the risk of pouch failure. Consequently, a perfusion assessment is essential during J-pouch formation. Although indocyanine green near-infrared fluorescence (ICG-NIRF) has demonstrated the potential to reduce ALs, its applicability in a restorative proctocolectomy is still uncertain.

The objective of a study by Eder [53]was to develop a standardized method for investigating ICG-NIRF and ALs in pouch surgery. The methods used were the following: patients undergoing a restorative proctocolectomy with an ileal J-pouch for ulcerative colitis at an IBD-referral center were enrolled in a prospective study with the primary outcome being an AL within 30 days postoperatively. Standardized perfusion visualization with ICG-NIRF was performed intraoperatively and videotaped at three time points for postoperative analysis. The correlation between quantitative clinical and technical variables (secondary outcome) and the primary outcome was determined by descriptive analysis and logistic regression. The definition and classification of AL of the J-pouch have been modified. A pouchoscopy was routinely performed postoperatively to screen for AL. In 25 patients, neither intraoperative ICG-NIRF-visualization, nor its postoperative visual analysis indicated an AL. In all cases of ALs, the anastomotic site appeared completely fluorescent with a strong fluorescence signal (category 2). (4 of 25). The anastomotic site remained unchanged. ICG-NIRF visualization was standard and reproducible. The data obtained in the study indicated that the visual interpretation of ICG-NIRF alone may not detect pouch ALs in all cases; in the future, quantitative and objective methods of interpretation may be required.

A conclusion from a research by Spinelli [54] was that FA may aid in reducing perfusion-related anastomotic leaks during IPAA surgery and that a prospective randomized study is required.

3.5. Studies that intent quantification of perfusion through the association of fluorescence and other methods

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Traditional methods for determining colonic perfusion rely on the surgeon's visual examination of tissue. Fluorescence angiography provides qualitative information, but there is still disagreement regarding how to interpret the observed signal. It is unknown whether fluorescence correlates with physiological tissue properties, such as oxygen saturation. A study by Soares [55] sought to establish a correlation between fluorescence intensity and colonic tissue oxygen saturation. The arrival time of indocyanine green in tissues is presented as a potential quantification index for tissue oxigenation by Egi [56], who measured the tissue oxygen saturation (StO2) in the intestinal tract using near-infrared spectroscopy, because it is able to measure the oxygen concentration precisely and displays objective data immediately.

In this study, we hypothesize that the time required for ICG to reach the anastomotic site after intravenous injection is an effective parameter for quantifying ICG fluorescence angiography when compared to the data of StO2 in the gastrointestinal tract.

Acute mesenteric ischemia is a challenging condition that is frequently caused by intestinal vessel occlusion.In therapeutic algorithms, revascularization of the occluded vessel and surgical removal of necrotic intestine are included. Necrotic intestine can be difficult to identify visually in different clinical settings.

In a research by Mehdorn [57], it was found that, for objective intraoperative evaluation of intestinal perfusion, tools such as hyperspectral imaging (HSI) and indocyanine green fluorescence angiography (ICGFA) may be useful.

The above mentioned idea was studied comparatively by Barberio [58] , between quantitative fluorescence angiography and hyperspectral imaging in the assessment of bowel ischemia. Using hyperspectral imaging and fluorescence-based augmented reality, a segment of ischemic bowel created by dividing the arcade branches was imaged. Using a hyperspectral imaging system, tissue oxygenation values were obtained.Subsequently, fluorescence angiography was performed using a near-infrared laparoscopic camera and indocyanine green injected intravenously at a dose of 0.2 mg/kg. Using proprietary software, the time-to-peak fluorescence signal was analyzed to generate a perfusion map.This was superimposed on real-time images to create enhanced reality based on fluorescence. Simultaneously, nine adjacent regions of interest were chosen and superimposed onto the real-time video, resulting in hyperspectral-based augmented reality. The superimposition of fluorescence-based enhanced reality and hyperspectral-based enhanced reality allowed for a comparison of the two imaging modalities. Local lactate levels in capillaries were measured in regions of interest.

On the basis of both imaging systems, two prediction models utilizing the local capillary lactate levels were extrapolated. The study concluded that hyperspectral imaging and fluorescence angiography were used to quantify bowel perfusion. Fluorescence angiography produced less accurate results than hyperspectral imaging.Enhanced reality based on hyperspectral imaging may prove to be a valuable, contrast-free intraoperative tool for quantifying bowel ischemia.

As inadequate arterial blood supply and venous congestion both contribute to anastomotic complications, the objective of a study by Quero[59] was to evaluate a software-based analysis of the fluorescence signal to identify bowel ischemia patterns. Conclusions: The computer-assisted dynamic analysis of the fluorescence signal permits differentiation between various models of bowel ischemia.

Pfahl [60] studied hyperspectral and ICG quantitatively in order to make a more precise evaluation of tissue perfusion. Two data processing pipelines capable of reconstructing an ICG-FA correlating signal from hyperspectral data have been developed for the first time. Results were evaluated on a technical level and compared to data obtained during

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colorectal resections. In 87 percent of 46 data sets, the reconstructed images were similar to the original data. The combined application of ICG-FA and HSI within a single imaging system could provide supportive and complementary information regarding tissue vascularization, reduce perioperative mortality, and shorten surgical procedures.

Jansen-Winkeln [61] found that , in 115 patients undergoing colorectal resections, intraoperative HIS(hyperspectral imaging) is safe, reproducible, and does not interfere with the surgical workflow. In addition, it measures bowel surface perfusion. HSI could become an intraoperative guidance instrument, thereby preventing potential postoperative complications.

During colorectal surgery, the main limitation of perfusion assessment with indocyanine green fluorescence angiography is that the surgeon subjectively evaluates the quality of perfusion. The optimal intestinal viability test must be objective, minimally invasive, and reproducible. Kojima[62] assessed the quantitativity and reproducibility of laser speckle contrast imaging for perfusion evaluation during colorectal surgery. The conclusion of the research was that laser speckle contrast imaging is feasible for real-time, quantitative, and highly reproducible assessment of bowel perfusion during colorectal surgery without the use of contrast agents. On the contrary, Jonas Hedelund Ronn[63] finds that Q-ICG and LSCI (laser spectrum contrast imaging) are not interchangeable, but they can complement one another. Angle and distance have a significant influence on LSCI. q-ICG, on the other hand, is minimally affected by varying experimental conditions and is more readily applicable in minimally invasive procedures.

Joosten [64]looks at the use of ICG in acute setting and finds that intraoperative use of FA influences surgical decisions regarding bowel resection for intestinal ischaemia, potentially allowing bowel preservation in one-quarter of patients.

To optimize the best use of this technology for this indication and to establish standards for the interpretation of FA images and the potential need for second-look surgeries, prospective studies are required.

Vaassen [65] showed that, based on an intensity over time signal, quantitative FA appears to be a promising and objective method. Nonetheless, there is no agreement on the acquisition and interpretation of quantified FA parameters at this time. The author developed algorithms for the automatic extraction of inflow-based parameters, including the time to reach 50 percent of maximal intensity (T (1/2)) and the maximal normalized slope (slp n). These parameters provide a more accurate representation of clinical endpoints than direct intensity measurements. A changepoint detection algorithm was created to extract the beginning and endpoints of an intensity increase, enabling the calculation of T (1/2). In order to account for signal noise, the slope of the signal was estimated using least squares. FA was carried out on the small intestines of 38 individuals with normal intestinal perfusion. Comparison was made between the performance of the changepoint detection algorithm and manual extraction. The proposed method of using quantified FA to assess intestinal perfusion perioperatively is objective, practical, and appears extremely promising. The generation of immersive cartograms and direct access to objective information regarding bowel viability after vascular reconstruction are made possible by an automated method.

Various parameter-based perfusion analyses for quantitative evaluation have been studied in recent years, but the analysis results vary depending on the quantitative parameters used due to differences in vascular anatomical structure. Therefore, real-time microperfusion analysis based on artificial intelligence (AI) can help improve precision and consistency (AIRAM). The aim of a research by Park[66] was to evaluate the viability of AIRAM to predict anastomotic complication risk in patients undergoing laparoscopic colorectal cancer surgery.The results of the study showed that: AI-based risk and

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conventional quantitative parameters such as T1/2max, time ratio (TR), and rising slope (RS) were consistent when colonic perfusion was favorable and ICG curve pattern was steeply increasing. When the ICG graph pattern exhibited a stepped rise, the accuracy of conventional quantitative parameters declined, whereas the AI-based classification consistently maintained its accuracy. For predicting anastomotic complication risks, the receiver operating characteristic curves for conventional parameters and AI-based classification were comparable. The AI-based analysis improved the statistical performance verifications. AI analysis was determined to be the most accurate predictor of anastomotic complication risk. The F1 score of the AI-based algorithm improved by 31% for T1/2max, 8% for TR, and 8% for RS. AIRAM's processing time was measured to be 48.03 seconds, making it suitable for real-time processing. The conclusion of the research : AI-based real-time microcirculation analysis can be performed with greater precision and consistency than the conventional parameter-based method.

D'Urso[67] studied fluorescence-based enhanced reality (FLER) is a computer-based quantification method for evaluating bowel perfusion using fluorescence angiographies. During colorectal resections, the purpose of this prospective study was to assess the clinical feasibility and correlate FLER with metabolic perfusion markers. FLER enables the visualization of the quantified fluorescence signal in augmented reality and offers a reproducible estimation of bowel perfusion.

The purpose of a study by Tokunaga [68]was to demonstrate that measuring intestinal temperature via thermography is useful for assessing blood perfusion. Additionally, the authors investigated the relationship between intestinal temperature and ICG fluorescence time (FT). Using thermographic images, the temperature boundary could be easily identified. The residual intestinal tract temperature was significantly higher than that of the resected intestinal tract at the planned separation line (29.9 versus 27.3°C). In addition, there was an inverse relationship between the ICG FT and the residual intestine temperature. The conclusion was that bowel temperature measurement by thermography is a useful new method for assessing intestinal blood perfusion.

3.6. To estimate optimal resection in relation to liver function for colorectal metastases

In visceral surgery, it is primarily used to assess the perfusion of gastrointestinal anastomoses and to support lymph node dissection; however, preliminary studies suggest that it could also be used to detect liver metastases during staging laparoscopies or cytoreductive surgery, as shown by Knospe [69].

Traditionally, patients undergoing hepatic surgery have been evaluated using radiological and quantitative measures of liver function.As more complex and extensive surgery is now being performed, frequently in the presence of cirrhosis/fibrosis or after the administration of chemotherapy, it is questioned whether additional evaluations may be necessary prior to undertaking such procedures.

The purpose of a review by Morris-Stiff [70]was to determine the current state of knowledge regarding the pre- and post-operative quantitative assessment of hepatic function in patients undergoing hepatic resection and liver transplantation. The review has identified a number of different methods for dynamically assessing hepatic function, with indocyanine green clearance being the most common.

It is difficult to perform major hepatectomy on patients with marginal hepatic function. In certain instances, the procedure is contraindicated due to the possibility of postoperative liver failure. In a case report by Kato [71], the first patient is presented with marginal liver function (indocyanine green clearance retention rate at 15 minutes [ICGR15]: 28%), who was successfully treated with a right hepatectomy, resulting in the

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preservation of the entire caudate lobe. After chemotherapy, all metastatic lesions shrunk, but his ICGR15 and indocyanine green clearance rate (ICGK) were 21% and 0.12%, respectively. In addition, the residual liver volume was only 39 percent. Therefore, a right portal vein embolism (PVE) was suggested. Portography revealed the significant preservation of the right caudate lobe branch (PV1R) from the right portal vein's origin. After 18 days, the liver function was re-evaluated. During this period, the ICGR15 (21–28 percent) and ICGK rate (0.12–0.10 percent) declined. Significant enlargement of the right caudate lobe necessitated a total caudate lobe-preserving hepatectomy (TCPRx). TCPRx-eligible patients had (1) hepatocellular carcinoma or metastatic liver cancer, (2) no tumor in the caudate lobe, (3) marginal liver function (ICG Krem greater than 0.05 if TCPRx was adapted; otherwise, less than 0.05) and Child–Pugh classification category A, and (4) preserved PV1R and right caudate bile duct branch.The procedure consisted in: (A) precise estimation of the remnant liver volume preoperatively, (B) repeated intraoperative cholangiography to confirm the conservation of the biliary branch of the right caudate lobe (B1R), and (C) stapler division of posterior and anterior Glisson's pedicles laterally to avoid injury to the PV1R and B1R. Conclusions : For patients with marginal liver function, right hepatectomy with total caudate lobe preservation following PVE was a safe and viable surgical procedure.

A study by Li [72] aimed at evaluating the correlation between the intensity of indocyanine green (ICG) fluorescence in near-infrared fluorescence-guided surgery (NIRFGS) and preoperative liver function indicators. The absolute fluorescence intensity of mice in the model of liver injury was greater than that of mice in the control group. The clearance rate of ICG from the tumor in the liver injury model group was identical to the clearance rate in normal mice. However, the background clearance rate was slower than that of normal mice, extending the optimal time for the tumor-to-background ratio (TBR). In addition, correlation analysis was employed to determine which preoperative liver function parameters were most strongly correlated with hepatic ICG clearance. Conclusions: a liver injury does not have a significant effect on the maximum TBR, but it does extend the optimal TBR time, creating a wider and more stable surgical window. According to preoperative liver function testing using NIR fluorescence imaging technology, this study revealed that a delayed surgical start time is feasible.

3.7. To assess a flap

Gracilis muscle interposition (GMI) is a well-established option for the treatment and reconstruction of complex perineal fistulas. Complications such as necrosis, impaired wound healing, and fistula persistence or recurrence limit the outcome. There are no intraoperative quantitative methods for evaluating muscle flap perfusion. A study by Lobbes [73] evaluates a novel and objective software-based assessment of ICG-NIRF in GMI. The methods used: five patients with inflammatory bowel disease (IBD) undergoing GMI for perineal fistula and reconstruction had intraoperative ICG-NIRF visualization data analyzed retrospectively. By displaying the fluorescence intensity over time, new software was utilized to generate perfusion curves for the specific regions of interest (ROIs) of each GMI. In addition, pixel-to-pixel analysis and perfusion zone analysis were conducted. Clinical outcome was correlated with the findings. Four patients underwent GMI surgery without complications within three months. These novel perfusion indicators (curve shape, maximum slope value, distribution, and range) indicated adequate perfusion. In one patient, GMI was unsuccessful. Indicators of perfusion in this instance indicated impaired perfusion. The authors concluded that they present a novel, software-based method for assessing ICG-NIRF perfusion, identifying objective indicators of muscle flap perfusion that were previously unknown. This method is ready for intraoperative real-time use and has the potential to optimize GMI surgery in the future.

3.8. Experimental research and results hinting at future clinical achievements

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It is believed that decreased intestinal perfusion contributes to the pathogenesis of necrotizing enterocolitis (NEC). A research by Knudsen [74] aimed to evaluate intestinal perfusion assessment in NEC-lesions . Quantitative fluorescence angiography with indocyanine green (q-ICG) was used during laparoscopy and open surgery. To induce NEC, 34 preterm piglets were delivered by cesarean section and fed parenteral nutrition and increasing volumes of infant formula. Macroscopic NEC-lesions were evaluated during surgery using a validated macroscopic scoring system (1–6 for increasing NEC severity). The intestinal perfusion was evaluated using q-ICG and quantified using a validated computer algorithm for pixel intensity. The conclusion was that q-ICG appears to be a practical and useful method for assessing the perfusion of tissue with NEC-lesions. The authors discovered a dividing line between intestines with NEC scores of 1-3 and those with NEC scores of 3–6 in the colon and 3–4 in the small intestine.

Recently, it was discovered that nerves emit near-ultraviolet (NUV) light fluorescence. The objectives of a study by Dip [75]were to determine the degree to which nerves fluoresce brighter than background and vascular structures in NUV light and to determine the intensity of NUV light at which nerves are most distinguishable from other tissues. A fluorescence score of 200 is 100 percent accurate at distinguishing nerves from other anatomical structures in vivo at all NUV intensities 35%. In experimental settings on animal models, nerves were studied by determination of nerve signal- to- background ratios, as reported by Barth[76].

Wang [77] shows how a novel cyclic TMTP1 homodimer TMTP1-PEG4 ICG was successfully constructed and synthesized and exhibited more senzitive tumor detection than its monomer, it could also vizualize lymph node metastases from normal lymph node and proved to be an attractive photothermal agent to significantly inhibit tumor growth under NIR laser irradiation. Moreover, highly porous and injectable hydrogels derived from cartilage acellularized matrix exhibit reduction and NIR light dual resposive drug release in antitumor therapy, as demonstrated by Gulfam[78].

Current studies look into the multispectrum analysis of dyes for better accuracy of the results. For instance, Polom [79], by using one camera system for two distinct near-infrared wavelengths, employed two fluorophores — indocyanine green (ICG) and methylene blue (MB) — during different stages of colorectal surgery as described in our report. The study revealed a significant opportunity for the use of two distinct fluorophores in colorectal surgery, where the visualization of one does not affect the quantification analysis of the other.Utilizing two distinct dyes during a single procedure may aid in optimizing the fluorescent properties of both dyes when used for distinct applications. Visualization of different structures by different fluorophores appears to be the future of image-guided surgery and demonstrates progress in image-guided surgery's optical technologies. Van Beurden[80] discusses the combination of complementary fluorescent readouts during the same surgical procedure, also known as multi-wavelength fluorescence guidance, will present future challenges.

Although laparoscopic resection is becoming more and more common for early gastric and colorectal cancers, it is difficult to detect tumors in the stomach and intestine due to the absence of tactile sensation. Lee[81] proposes the use of an indocyanine green (ICG)-loaded alginate hydrogel system as a fluorescence surgical marker for accurate laparoscopic procedures. Results: The optimal concentration of the ICG-HSA complex was determined to be 30 M, and the maximum fluorescence intensity of the complex was obtained with a mole ratio of 1:1 between HSA and ICG. Injecting ICG or ICG-HSA solution subcutaneously into mice caused the fluorescence signal to rapidly spread around the injection site within 3 hours, and 24 hours later, a weak fluorescence was detected at the injection site. In contrast, ICG-HSA-loaded alginate gel effectively prolonged the fluorescence detection time up to 96 hours post-injection, while preventing the diffusion of the injected ICG from the injection site.Even after three days, injection

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sites of the hydrogel in porcine stomach could be accurately detected in real time during laparoscopic surgery.Conclusions: This alginate hydrogel system has the potential to serve as an accurate and durable surgical marker for laparoscopic procedures.

The objective of a study by Marston[82] was to identify an optical imaging agent for the use of FGS technology on CRC. In which concerns the methods: the authors compared a panitumumab-IRDye800CW conjugate to an isotype control IgG-IRDye800CW conjugate.Mice were implanted with one of three CRC cell lines (LS174T, Colo205, and SW948), and open- and closed-filed fluorescence imaging systems were used to capture images.To quantify fluorescent contrast, the ratio between tumor and background fluorescence was calculated.The mice were sacrificed after 10 days, and their tumors were stained for microscopic imaging. Panitumumab-IRDye800CW produces significantly greater fluorescent contrast than IgG-IRDye800CW in a murine model of colorectal cancer and is an agent suitable for the application of FGS technology to CRC.

Optical imaging (OI) provides clinical imaging in real-time as well as simultaneous molecular, morphological, and functional data on disease processes.

Kan[83] presents a novel interventional OI technique that permits in vivo visualization of three distinct pathologic zones of ablated tumor periphery for immediate detection of residual tumors during radiofrequency ablation (RFA) treatment. Eight rabbits with orthotopic hepatic tumors were categorized into two groups: incomplete RFA and complete RFA. Interventional OI based on indocyanine green was used to distinguish between three pathological zones: ablated tumor, transition margin, and residual tumor or surrounding normal liver, with quantitative comparison of signal-to-background ratios between the three zones and between incompletely and completely ablated tumors.Ex vivo OI and correlation with pathology were performed to confirm the results of interventional OI. Interventional OI could differentiate partially or completely ablated tumor margins, allowing for the detection of residual tumor.This method may provide new opportunities for assessing tumor eradication during a single interventional ablation session.

Brain neuropeptides are secreted in a spatiotemporally coordinated manner during a stress response.For a precise understanding of peptide functions in a stress response, it is necessary to investigate their release, diffusion, and breakdown in the brain.

Indicators of genetically encoded fluorescent calcium have significantly advanced our understanding of the functions of specific neuronal activity in the regulation of behavioral changes and physiological responses during stress over the past two decades.In addition, numerous structural details regarding G-protein-coupled receptors (GPCRs) for neuropeptides have been uncovered.Utilizing conformational changes induced by ligand binding, fluorescent sensors with genetic encoding have been developed recently for the detection of neurotransmitters. For instance on the correlation between oxytocin(OT) and nerve development at the level of the bowel, OT is produced by enteric neurons, and both enteric neurons and enterocytes express developmentally regulated OT receptors (OTRs), as found by Welch [84] and Padurariu [85]. The findings suggest that OTR-mediated signaling is an important physiological regulator of enteric neuronal activity, mucosal homeostasis, intestinal permeability, and intestinal inflammation.

Bergenheim [86] and Raducanu[87], as part of the homeostatic process, intestinal stem cells located at the base of Lieberkühn crypts generate progeny that replace resident cells that are shed from the tip of villi.

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These stem cells can be propagated in vitro as organoids and orthotopic transplantation in murine models of mucosal injury revealed that intestinal organoids can spontaneously attach and integrate into the damaged epithelium, thereby accelerating the healing process and resulting in improved weight gain

This suggests that transplantation of intestinal stem cells may be applicable in humans to actively promote mucosal healing and could potentially be used to treat a wide range of gastrointestinal disorders, including inflammatory bowel disease, in which mucosal healing is a key treatment objective and the most important predictor of clinical remission

To assess engraftment efficiency and to monitor wound healing, it is essential to track transplanted cells in vivo, especially during the preclinical phase.

The feasibility of using a panel of fluorescent dyes and nanoparticles to label intestinal organoids for visualization with the clinically approved imaging modality, confocal laser endomicroscopy, was investigated (CLE).

Using CLE, the homogeneity, durability, cell viability, differentiation capacity, and efficiency of organoid formation were assessed, along with the visualization of labeled organoids in vitro and ex vivo.

It is highly feasible to use fluorescent dye-based labeling in conjunction with CLE to track intestinal organoids after transplantation in order to confirm implantation at the intestinal target site.

Any antibody or small molecule that targets cancer could theoretically be labeled with bioluminescent or fluorescent agents. Fluorescence imaging (FI) and bioluminescence imaging (BLI) have been used extensively in preclinical research for quantifying tumor bulk, evaluating the targeting of tumors by experimental agents, and differentiating between the primary and secondary effects of cancer treatments. Highly cancer-specific, fluorescent probes that can be imaged are being developed. This will enable the identification of tumors for staging, the monitoring of novel therapeutic agents, the facilitation of adequate surgical resection, and the performance of image-guided biopsies. According to a research by Woo[88] (1) a fluorescent protein that is biologically safe, stable, and clearly visible with a high target-to-background ratio, and (2) highly sensitive optical detectors are essential FI components.

Present research accomplishments have been reported by De Galitiis[89] in p53 gene mutations in colorectal cancer by means of FAMA=Fluorescence assisted mismatch analysis. In the author's personal opinion, an extensive study on p53 gene polimorphism in a defined population could be done using FAMA, by means of targetting a particular area(according to a geodemographic classification- for instance Romanian people and their genetic polimorphism, as described previously by Murarasu[90] [91]). An intervention as such could consistently help in cancer control in that area, because the identification of more prevalent mutations could imply earlier diagnosis and earlier treatment.

Also, another personal opinion is that q -ICG could very well be used in the diagnosis and treatment of a localized infection in the abdominal region, either with an intraperitoneal(Xie [92]) or retroperitoneal site(Marincas [93]).

4. Discussion

Near-infrared (NIR) light-assisted fluorescence surgery is a relatively new technique.

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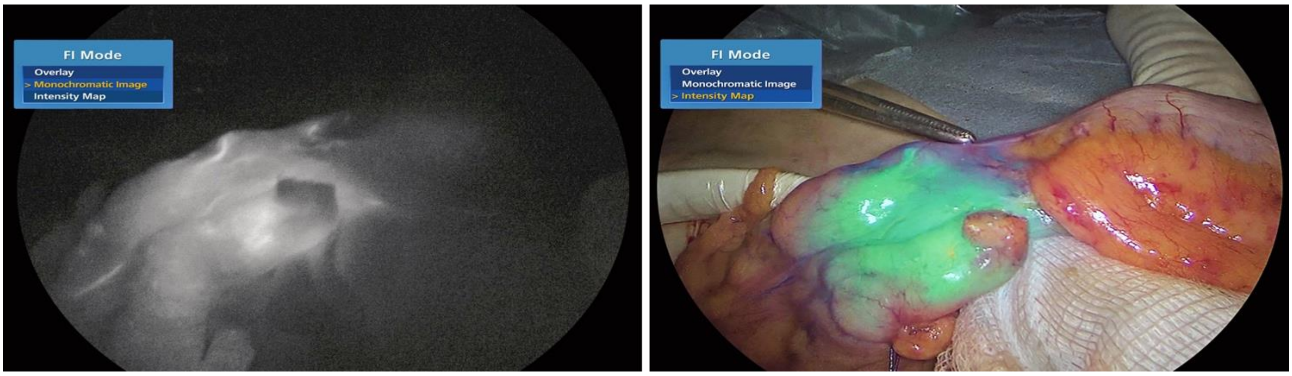
This technique combines dyes and NIR imaging equipment to improve the visible spectrum. Consequently, it may provide more precise anatomic and functional information, allowing for a more thorough resection of a tumor or the protection of vital normal structures.

The technique of indocyanine green fluorescence has increasing perioperative and intraoperative applications in colorectal surgical interventions, both from a qualitative as from a quantitative point of view.

Several studies have demonstrated that intraoperative fluorescence imaging is a safe and feasible method for evaluating anastomotic perfusion during colorectal surgery, and its use may improve the patient's clinical outcome by mainly reducing the incidence of anastomotic leaks.

The number of new indications for the use of indocyanine green continues to grow, including new options for detecting and guiding the management of colorectal liver metastases.

By enhancing the precision and efficacy of general surgery and surgical oncology, all of these developments could provide surgeons and patients with a wealth of information and benefit.



Figures 1.a and 1.b. ICG-enhanced fluorescence-guided evaluation of colonic perfusion following division of the mesentery during laparoscopic left colectomy. Images captured intraoperatively in Monochromatic NIR/ICG mode (a) and NIR/ICG Intensity Map mode (b). The tip of the forceps indicates the edge of the well-perfused region.

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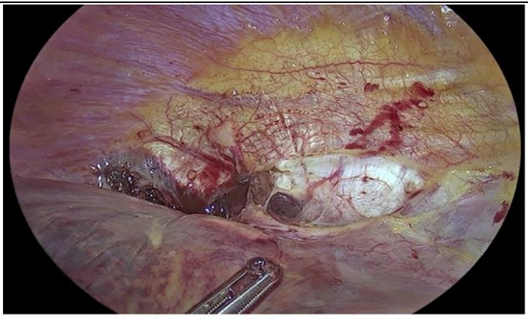
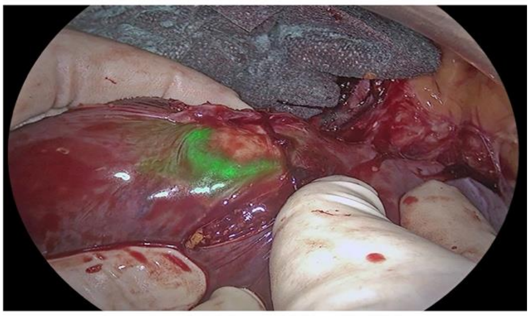
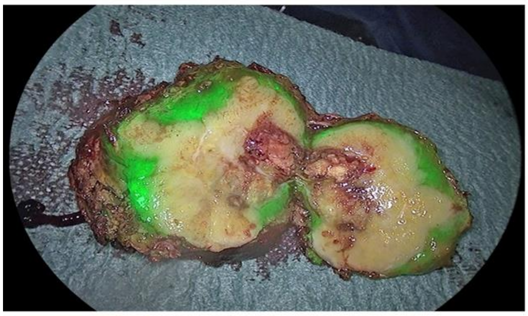
Figures 2.a and 2.b

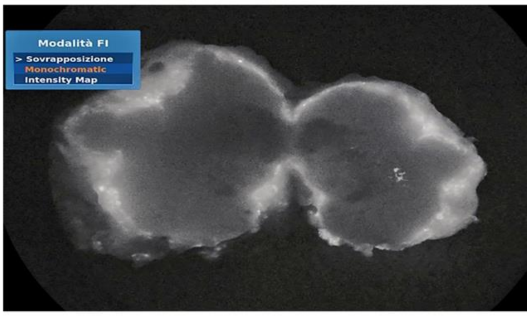


Figures 2.c and 2.d



Figures 2.e. and 2.f





Figures 2.g

(Fig. 2.a–g). In this case, ICG enhanced fluorescence imaging not only helps in localizing metastatic lesions, but also facilitates to determine the resection margins. Fig. 2. ICG-enhanced fluorescence-guided liver resection for metastatic hepatic lesions. The intraoperative images (a) to (g) were captured using the following visualization modes: a. White light mode. b. NIR/ICG Overlay mode. c. NIR/ICG Intensity Map mode. d. NIR/ICG Overlay mode (open surgery). e. NIR/ICG Overlay mode (macroscopic view of the surgical specimen after extraction). f. NIR/ICG Monochromatic mode showing the same specimen as in (e). g. NIR/ICG Intensity Map mode showing the same specimen as in (e).

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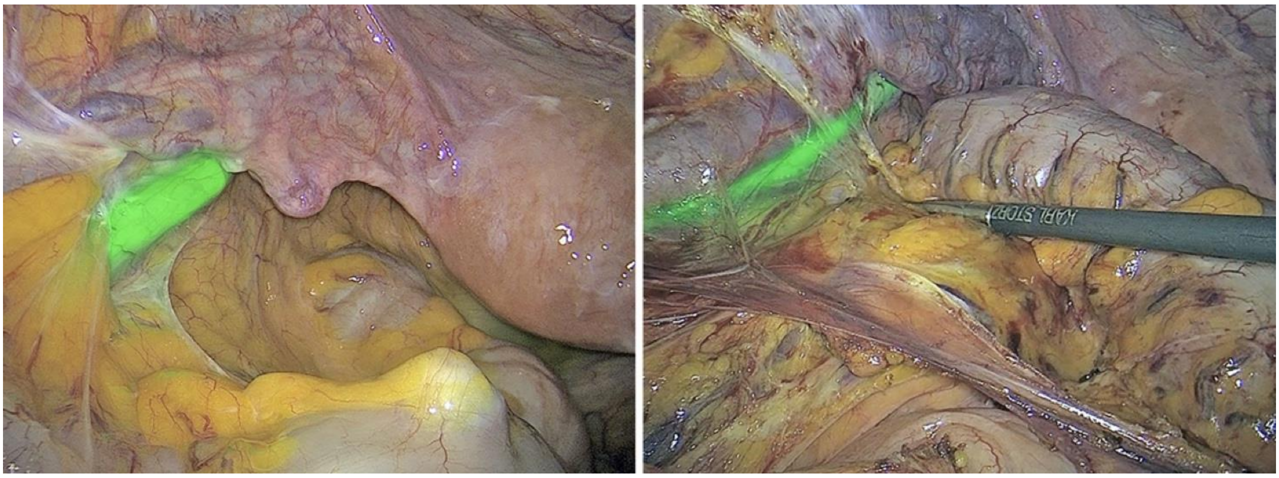

Figures 3.a and 3.b. ICG-enhanced fluorescence imaging for visualization of the left ureter during left colectomy. Intraoperative images (a, b) captured while using the green NIR/ICG Overlay mode

The images in figures 1,2, 3 and in their subsets are reproduced in this article courtesy of © KARL STORZ SE & Co. KG, Germany.

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