ICG Fluorescence Imaging in Colorectal Surgery: A Snapshot from the ICRAL Study Group

Gian Luca Baiocchi (✉ gianluca.baiocchi@unibs.it)
University of Brescia

Research Article

Keywords: colon cancer, rectal cancer, laparoscopy, fluorescence guided surgery, ICG

DOI: https://doi.org/10.21203/rs.3.rs-124542/v1

License: ☺️ This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

Background

Fluorescence-guided visualization represents a recently proposed technology in colorectal surgery. Possible uses include perfusion evaluation, lymph node navigation and search for hepatic metastases and peritoneal spread. Despite the absence of high-level evidence, this technique gained considerable popularity among colorectal surgeons, due to its significant reliability, easy and safe use and the relatively low cost. However, the actual use of this technique in daily clinical practice has not been reported to date.

Methods

The survey was conducted on April 2020 among 44 centres dealing with colorectal diseases, participating to the Italian ColoRectal Anastomotic Leakage (iCral) study group. Surgeons were about equally divided on the basis of a geographical criterion from multiple Italian regions, with a large proportion of public (89.1%) and non-academic (75.7%) centres. They were invited answering to an online survey in order to make a snapshot of their current behaviours regarding the use of fluorescence-guided visualization in colorectal surgery. Questions about technological availability, indications and techniques, personal approach and feeling were collected in a 23-item questionnaire.

Results

Questionnaire replies were received from 37 institutions, and partially answered by 8 of them, who don't have the fluorescence technology (21.6%). Out of the remaining 29 centres (78.4%), fluorescence is utilized in all laparoscopic colorectal resections by 72.4% of surgeons and only in selected cases in the remaining 27.6%, while 62.1% of respondents don't use fluorescence in open surgery (unless the perfusion is macroscopically doubtful with the naked eye for 41.4% of them). The survey also suggests that there is no agreement on dilution, dosing and timing, as many different practices are adopted, based on personal belief. Only about half of surgeons reported reduced leak rate with fluorescence perfusion assessment, but 65.5% of them strongly believe that this technique will become a minimum requirement in colorectal surgery in the future.

Conclusion

The survey confirms that fluorescence is becoming a widely used technique in colorectal surgery. However, both the indications and methods still vary considerably; furthermore, the surgeons’ perception of results is still not enough to consider this technology essential. This survey emphasizes the need for further research to reach recommendations based on solid scientific evidences.

Background
Indocyanine green (ICG), approved for clinical use by the Food and Drug Administration (FDA) since 1959, is the most commonly used fluorescent probe. It is a low-cost molecule, easy to use, widely available and with negligible toxicity (1). ICG binds primarily to serum albumin and other serum globulins such as alpha1-lipoprotein, and then it circulates behaving like a macromolecule (2). In recent years, ICG fluorescence-guided visualization has gained a predominant role in visceral surgery. With particular reference to colorectal surgery, the main use of this technology is a real time intraoperative angiography that allows to assess the perfusion of the anastomotic stumps before and after anastomosis (3). Another possible use is the search for superficial liver metastases (4) and small peritoneal metastases after intravenous injection performed in different times before surgery (5); finally, intra-tumour injection of ICG allows to visualize the tumour itself and the draining regional lymph nodes (6). The wide availability of this technology (now present in nearly all new laparoscopic systems), its ease of use, the low cost of the molecule and the excellent visual yield, have meant that this technology spread rapidly, while no robust scientific evidence is provided from randomized controlled clinical trials.

The Italian ColoRectal Anastomotic Leakage (iCral) Study Group collects Italian surgeons particularly interested and experienced in colorectal surgery (7–9), working in 44 centres from nearly all Italian regions. It represents, therefore, an ideal background for a survey aimed to show a snapshot of the current diffusion of this technology in Italy.

The aim of this study is to obtain a picture of how and to what extent ICG fluorescence-guided visualization is used in colorectal surgery, to understand if the indications and the methods of use are sufficiently consistent and uniform to make prospective clinical studies unnecessary or outdated by daily clinical practice. The secondary aims are to analyse the technology availability, to detect organizational problems and highlight unsolved problems, to collect colorectal surgeon's opinion about the actual usefulness and the future developments of this technology.

**Methods**

A 23-item questionnaire was sent to the referring surgeons of all the 44 centres participating to the iCral study group. The study protocol was performed in accordance with the relevant guidelines. The Institutional Review Board of the University of Brescia, Department of Clinical and Experimental Sciences, approved the study protocol. A waiver on written informed consent was granted by the ethics committee of University of Brescia.

The questionnaire was structured in 4 sections: 1) Hospital trait, size, mission; surgical unit, operating rooms and Intensive Care Unit (ICU) hallmark. 2) Effective availability of technology necessary for fluorescence visualization in the operating room: brand, number of laparoscopic columns, sharing with other specialties, the possibility of performing multiple operations at the same time and multiple operations on the same day; 3) Indications for use: in all interventions/in selected cases, in open/laparoscopy, only for the evaluation of perfusion/other uses; 4) technical aspects: dilution, dosage,
timing; 5) personal opinion of the surgeon about the usefulness and future developments. Forty-eight hours were granted for filling the questionnaire.

The datasets used and analysed during the current study is available from the corresponding author on request.

**Results**

Questionnaire replies were received from 37 institutions (response rate 84.1%). Table 1 reports the participating features. Surgeons were about equally divided on the basis of a geographical criterion, with a large proportion of public (89.1%), non-academic (75.7%) centres. More than 50 cases/year were declared by 89.2% centres (70.3% declared more than 80 cases/year). Only 21.6% of centres have no availability for fluorescence technology, therefore the analysis was conducted on the remain 78.4% of centres (10.8% of them had the technology available only on trial). Table 2 describes the availability and technical characteristics of the utilized tools. More than half of respondents have the technology always available, including contemporary or same-day surgery (62.1% of centres), and have ICG vials in the OR (96.5%). Seven centres have more than one laparoscopic system which is able to visualize fluorescence. Table 3 provides data on indications for fluorescence utilization. Only 27.6% of surgeons said that the use of fluorescence is limited to selected cases, while the remaining use the fluorescence check of perfusion in all interventions. However, this is limited to laparoscopic approach: only 37.9% of surgeons provide fluorescence also in open interventions (usually by laparoscopic instruments). The few surgeons suggesting a selective utilization of fluorescence usually program the utilization before starting the intervention, in high-risk patients (37.5%) and/or in high-risk cases (43.7%); only 18.7% of them pick up the instruments during the intervention, in case of doubtful perfusion. About half of the survey participants use fluorescence only for perfusion evaluation, while 35.5% also mark the site of the neoplasm, and 16.1% would like to identify potentially affected lymph nodes. Nobody uses fluorescence to search for small peritoneal carcinosis that cannot be seen with the naked eye. The majority (78.6%) of those who use fluorescence also for purposes other than perfusion evaluation do not believe that it limits the quality of perfusion evaluation.
Table 1
Thirty-seven institutions answered the survey

| Survey answers                                      | Num | %   |
|-----------------------------------------------------|-----|-----|
| **Type of hospital**                                |     |     |
| Public, academic                                    | 9   | 24.3|
| Public, non-academic                                | 24  | 64.8|
| Private                                             | 4   | 10.9|
| **Region**                                          |     |     |
| Northern Italy                                      | 21  | 56.7|
| South-Central Italy                                 | 16  | 43.2|
| **Total beds number**                               |     |     |
| < 201                                               | 2   | 5.4 |
| 201–500                                             | 18  | 48.6|
| 501–1000                                            | 11  | 29.7|
| > 1000                                              | 6   | 16.3|
| **OR number/week**                                  |     |     |
| < 3                                                 | 4   | 10.8|
| 4–5                                                 | 7   | 18.9|
| 6–10                                                | 18  | 48.6|
| > 11                                                | 8   | 21.6|
| **Colorectal cancer case/year**                     |     |     |
| < 50                                                | 4   | 10.8|
| 50–80                                               | 7   | 18.9|
| > 80                                                | 26  | 70.3|
| **Technology for fluorescence available in 2019**   |     |     |
| No                                                  | 8   | 21.6|
| Yes, on trial                                       | 4   | 10.8|
| Yes                                                 | 25  | 67.6|
| Table 2 | Availability of fluorescence technology in 29 colorectal surgical units |
|----------------|-----------------------------|
| **Fluorescence system (7 centres have more than 1 system)**<sup>1</sup> | **Num** | **%** |
| Karl Storz | 13 | 44.8 |
| Stryker | 5 | 17.2 |
| Surgical Intuitive/Firefly | 8 | 27.6 |
| Olympus | 9 | 31.0 |
| Novadaq | 3 | 10.3 |
| **Fluorescence systems number in the multidisciplinary ORs** | | |
| 1 | 9 | 31.0 |
| 2 | 16 | 55.2 |
| >2 | 4 | 13.8 |
| **Fluorescence systems always available for the general surgery OR** | **Yes** | 17 | 58.6 |
| **No** | 12 | 41.4 |
| **Fluorescence system available for more than 1 simultaneous colorectal interventions** | **Yes** | 18 | 62.1 |
| **No** | 11 | 37.9 |
| **Is ICG (Verdy, 25 mg) always available in OR?** | **Yes** | 28 | 96.5 |
| **No** | 1 | 3.5 |

<sup>1</sup> More than one answer accepted
| Clinical indications for fluorescence perfusion assessment | Num | % |
|---------------------------------------------------------|-----|---|
| What colorectal operation is scheduled with fluorescence technology? | All colorectal resections | 14 | 48.3 |
| | All colorectal resections, if available | 7 | 24.1 |
| | In selected cases | 8 | 27.6 |
| Selected cases in which fluorescence perfusion is utilized\(^1\) | High risk patient | 6 | 75.0 |
| | High risk intervention (rectum/transverse) | 7 | 87.5 |
| | Intraoperative doubtful perfusion | 3 | 37.5 |
| Does the surgical approach matter? Fluorescence is utilized | Both in open and laparoscopy | 11 | 37.9 |
| | Only in laparoscopy | 6 | 20.7 |
| | In laparoscopy and in open doubtful cases | 12 | 41.4 |
| Fluorescence perfusion assessment is most important in\(^2\) | Rectal resection | 8 | 27.6 |
| | Transverse colon and left flexure resection | 11 | 37.9 |
| | Extended right or left hemicolecotomy | 10 | 34.5 |
| Other uses of fluorescence in colorectal resections\(^3\) | Yes, nodal navigation | 5 | 17.2 |
| | Yes, peritoneal carcinomatosis assessment | 0 | 0 |
| | Yes, tumour tattooing | 11 | 37.9 |
| | No | 15 | 51.7 |
| In case of tumour marking by ICG, is perfusion assessment impaired? | Yes | 3 | 21.4 |
| | No | 11 | 78.6 |

\(^1\) Answers were provided only by 8 surgeons answering “In selected cases” to the previous question. More than one answer was accepted
\(^2\) Only one answer was accepted
\(^3\) More than one answer was accepted
From a technical point of view (Table 4), there is no agreement on how to use fluorescence for perfusion evaluation. The dilution varies from 0.25 mg/ml to 2.5 mg/ml (51.8% use the lower dilution), the dosage is independent of weight for 79.3% of surgeons, but it varies from 5 mg (most used dosage, 39.1% of surgeons) to 25 mg. The remaining 20.7% of respondents decide for the weight-based dosing: the majority of those use 0.2–0.3 mg/kg. Finally, even on the timing of the injection (1, 2 or 3 injections, before or after the anastomosis, laparoscopically or endoscopically) there is no a clear preference.
Table 4  
Technical features of perfusion assessment by fluorescence

|                            | Num | %     |
|-----------------------------|-----|-------|
| **Dilution**                |     |       |
| 0.25 mg/ml                  | 4   | 13.8  |
| 0.5 mg/ml                   | 5   | 17.2  |
| 1 mg/ml                     | 5   | 17.2  |
| 2.5 mg/ml                   | 15  | 51.8  |
| **ICG dosing**              |     |       |
| Standard                    | 23  | 79.3  |
| Depending on patient weight | 6   | 20.7  |
| **Standard ICG dosage**     |     |       |
| 5 mg                        | 9   | 39.2  |
| 10 mg                       | 5   | 21.7  |
| 15 mg                       | 3   | 13.1  |
| 20 mg                       | 1   | 4.3   |
| 25 mg                       | 5   | 21.7  |
| **ICG dosage depending on patient weight** |     |       |
| 0.1 mg/kg                   | 1   | 16.7  |
| 0.2–0.3 mg/kg               | 4   | 66.6  |
| >0.3 mg/kg                  | 1   | 16.7  |
| **Timing of injection in ileo-colic and colo-colic anastomosis** |     |       |
| Before proximal and distal colonic section (1 injection) | 14 | 48.3  |
| Before proximal and distal colonic section/after anastomosis (2 injections) | 13 | 44.8  |
| After anastomosis (1 injection) | 2 | 6.9   |
| **Timing of injection in colorectal anastomosis** |     |       |
| Before proximal colonic section (1 injection) | 8  | 27.6  |
| Before proximal colonic section/before anastomosis (2 injections) | 13 | 44.9  |
| Before proximal colonic section/after anastomosis by endoscopy (2 injections) | 3  | 10.3  |
| Before proximal colonic section/before anastomosis/after anastomosis by endoscopy (3 injections) | 5  | 17.2  |

Participating surgeons were also asked for their opinion on the effectiveness of this method (Table 5). Only 41.4% and 55.2% stated that visceral perfusion assessment reduced the leak rate (statistically and based on personal non-statistical assessment, respectively). However, 65.5% of them believe that in the
future this method will become mandatory, especially in the face of medico-legal considerations. Finally, there is no agreement on which type of intervention benefits most from it (Table 3).

Table 5
General opinion on fluorescence value in colorectal surgery

| Did in your experience perfusion assessment by fluorescence reduced anastomotic leak rate by statistical analysis? | Num | %  |
|-----------------------------------------------------------------------------------------------------------------|-----|----|
| Yes                                                                                                              | 12  | 41.4|
| No                                                                  | 17  | 58.6|

| Did in your experience perfusion assessment by fluorescence reduced anastomotic leak rate by personal feeling?     | Num | %  |
|-----------------------------------------------------------------------------------------------------------------|-----|----|
| Yes                                                                                                              | 16  | 55.2|
| No                                                                  | 13  | 44.8|

| Do you believe perfusion assessment by fluorescence will become a minimum requirement in colorectal surgery?        | Num | %  |
|-----------------------------------------------------------------------------------------------------------------|-----|----|
| Yes                                                                                                              | 19  | 65.5|
| No                                                                  | 10  | 34.5|

Discussion

Fluorescence-guided surgery allows real time intraoperative enhanced visualization of anatomical structures and/or vascular perfusion (3–6). In this technique, the operative field is exposed to near-infrared light, while the target is injected by Indocyanine Green, the most commonly used fluorescent dye. Fluorescence can be visualized both directly on the operative field, in open surgical procedures, both on the screen, in minimally invasive procedures. Due to the low cost and large availability, in the last few years fluorescence-guided surgery has become widespread in many surgical specialties (10, 11). In colorectal procedures, one of the most feared complications are anastomotic leaks, which incidence is accepted at a 5–7% rate, even in high volume centres (12); about half of anastomotic leaks are believed to be related to an insufficient vascular supply, not detected with the naked eye while performing anastomosis. The bowel perfusion can be evaluated intraoperatively by ICG intravenous injection and fluorescence detection. This ICG-based angiography might provide the optimal resection site on both anastomotic sides (changes in the transection line are reported in 5–15% of cases (13)), and represents a promising technique for reducing leak rate. Some phase II trials confirmed the feasibility, low cost and high success rate of this procedure (14–17), reporting a leakage rate (< 3%) lower than expected on the basis of historical series, with particular reference to rectal anastomosis. Some randomized prospective controlled trials are going to be published (18), and some other efforts are finalized to a better understanding of dynamic information of perfusion (19).

The main goal of this paper is to describe protocols for handling ICG fluorescence imaging in colorectal interventions within Italian Departments of General Surgery participating to the iCRAL group. Fluorescence-guided surgery has forcefully entered daily clinical practice, without being supported by high-level scientific evidence that certifies its usefulness (20). One of the reasons why there is a lack of high-quality studies in this field is the absence of agreement on usage protocols, which make it
impossible to compare multicentric series. Before proposing prospective studies based on rigid use of protocols, it is necessary to know current daily practice.

The present questionnaire reliably represents a cross-section snapshot of Italian centres performing colorectal surgery. The composition of the iCRAL Group reflects the national public/private hospitals and the academic/non-academic hospital relationship. Most of the involved surgeons work in medium to large hospitals (only 2 surgeons work in hospitals with less than 200 beds, only 6 in hospitals with more than 1000 beds). Participating should be considered colorectal medium-high volume centres, with scientific and cultural interest on the subject (7–9). Participation in the iCral study group requires that from 2017 onwards all cases are included in a web-based prospective database, so the few questions in this survey that require a numerical analysis are immediately available and reliable.

The first consideration that emerges from the questionnaires analysis is that fluorescence technology is now extremely widespread: with reference to the year 2019, only 21.6% of surgeons declared that they did not have the technology for fluorescence-guided surgery. Where available, in 69% of cases there are more than one laparoscopic system, in 58.6% of cases at least one column is always available, and in 62.1% of cases multiple operations are possible at the same time. On the other hand, there is no uniqueness on the system brand; apart from a slight prevalence of Karl Storz, Stryker/Novadaq, Surgical Intuitive and Olympus are equally distributed. We can therefore report a satisfactory diffusion of fluorescence technology, which makes it even more important to clarify the indications and techniques of use.

As for the indications, 72.3% of surgeons use fluorescence by default in all laparoscopic interventions, while only 37.9% use it by default also in open procedures. Instead, 27.6% of surgeons consider fluorescence only in selected cases, but there is no agreement on which ones they are (high-risk patients, high-risk interventions, intraoperative doubt). Few surgeons also take into account features different from than perfusion evaluation, such as lymph node navigation (16.1%) and tumour labelling (35.5%). Basically, the most widespread practice involves the use of fluorescence for the anastomotic perfusion evaluation in all laparoscopic colorectal surgery.

However, there is no agreement on the ideal timing for the perfusion assessment: in ileocolic anastomosis, about half of surgeons proceed with a single injection before the anastomosis, and half proceed with two injections, before and after the anastomosis (48.3% and 44.8%, respectively). In colorectal anastomosis, the majority of surgeons (44.9%) perform the injection before the proximal colon section and before the anastomosis, while 27.6% perform it only before the proximal colon section, 10.3% perform 2 injections, of which one endoscopically after the anastomosis, and 17.2% perform 3 injections. Further discrepancies are also found in dilution and dosages, as reported in Table 4. It is evident that the discrepancy between these techniques limits the possibility of comparing the results between the different centres.

A final interesting note relates to the perception of Italian surgeons of the efficacy of fluorescence in preventing anastomotic leaks: surprisingly, only 65.5% believe that this method should be implemented to the point of becoming a minimum essential requirement in colorectal surgery. However, this is
understandable if we consider the subjective perception and statistical evidence relating to the reduction of anastomotic leaks: as many as 44.8% and 58.6% of the interviewed surgeons declared that they did not detect a reduction in leaks, from a subjective impression and from a statistical perspective, respectively.

In conclusion, the assessment of visceral perfusion by means of fluorescence after intravenous injection of ICG represents an extremely widespread intraoperative technique, yet applied with a considerable variability of protocols that prevents a correct multicentric data collection aimed at statistical demonstration of its usefulness. Multilateral scientific action is required, coordinated and supported by the scientific societies of the surgical area, to harmonise the application techniques.

Declarations

Ethics approval and consent to participate

The Institutional Review Board of the University of Brescia, Department of Clinical and Experimental Sciences, approved the study protocol. A waiver on written informed consent was granted by the ethics committee of University of Brescia.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and / or analyzed during the current study available from the corresponding author on reasonable request

Competing interests

No

Funding

Not applicable

Authors' contributions
This survey was organized within the ICRAL (Italian ColoRectal Anastomotic Leakage) collaborative group. Baiocchi GL and Catarci M conceived the idea. Baiocchi GL and Guercioni G wrote the questionnaire. All the following Authors equally contributed to the paper by answering the questionnaire, and all the following Authors read and approved the final version of the manuscript:

The ICRAL collaborative group

Gian Luca Baiocchi¹, Gianluca Guercioni², Nereo Vettoretto³, Stefano Scabini⁴, Paolo Millo⁵, Andrea Muratore⁶, Marco Clementi⁷, Giuseppe Sica⁸, Paolo Delrio⁹, Graziano Longo¹⁰, Gabriele Anania¹¹, Vittoria Barbieri¹², Pietro Amodio¹³, Carlo Di Marco¹⁴, Gianandrea Baldazzi¹⁵, Gianluca Garulli¹⁶, Alberto Patriti¹⁷, Felice Pirozzi¹⁸, Raffaele De Luca¹⁹, Stefano Mancini²⁰, Corrado Pedrazzani²¹, Matteo Scaramuzzi²², Marco Scatizzi²³, Lucio Taglietti²⁴, Michele Motter²⁵, Graziano Ceccarelli²⁶, Mauro Totis²⁷, Andrea Gennai²⁸, Diletta Frazzini²⁹, Gianluca Di Mauro³⁰, Gabriella Teresa Capolupo³¹, Francesco Crafa³², Pierluigi Marini³³, Giacomo Ruffo³⁴, Roberto Persiani³⁵, Felice Borghi³⁶, Nicolò de Manzini³⁷, Marco Catarci*².

¹Department of Clinical and Experimental Sciences, University of Brescia, Italy;
²General Surgery Unit, CG Mazzoni Hospital, Ascoli Piceno
³General Surgery Unit, ASST Spedali Civili, Montichiari (BS), Italy
⁴General & Oncologic Surgery Unit, National Cancer Center “San Martino”, Genova
⁵General Surgery Unit, Aosta Regional Hospital
⁶General Surgery Unit, Agnelli Hospital, Pinerolo (TO)
⁷General Surgery Unit, University Hospital, L’Aquila
⁸General Surgery Unit, Policlinico Tor Vergata University Hospital, Roma
⁹Colorectal Surgical Oncology Unit, IRCCS G. Pascale Foundation, Napoli
¹⁰General Surgery Unit, Policlinico Casilino, Roma
¹¹General Surgery Unit, University Hospital, Ferrara;
¹²General Surgery Unit, Cardinale G.Panico Hospital, Tricase (LE)
¹³General Surgery Unit, Belcolle Hospital, Viterbo
14 General Surgery Unit, Conegliano Hospital (TV) ULSS2 Marca Trevigiana
15 General Surgery Unit, ASST Nord Hospital, Sesto San Giovanni (MI)
16 General Surgery Unit, Infermi Hospital, Rimini
17 General Surgery Unit, Marche Nord Hospital, Pesaro e Fano (PU)
18 General Surgery Unit, ASL Napoli2 Hospital, Pozzuoli (NA)
19 General Surgery Unit, IRCCS Istituto Giovanni Paolo II, Bari
20 General & Oncologic Surgery Unit, San Filippo Neri Hospital, Roma
21 General Surgery Unit, University Hospital, Verona
22 General Surgery Unit, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG)
23 General Surgery Unit, Santa Maria Annunziata Hospital, Firenze
24 General Surgery Unit, ASST Valle Camonica, Esine, Italy
25 General Surgery Unit 1, Santa Chiara Hospital, Trento
33 General Surgery Unit, San Giovanni Battista Hospital - Foligno PG
27 General Surgery Unit, San Gerardo Hospital, Monza
28 General Surgery Unit, Sant’Andrea Hospital, La Spezia
29 General Surgery Unit, Ospedale Civile di Pescara
30 General Surgery Unit, Ospedale di Ragusa
31 Colorectal Surgery Unit, Policlinico Universitario Campus Bio Medico, Roma
32 General & Oncologic Surgery Unit, San Giuseppe Moscati Hospital, Avellino
33 General Surgery Unit, San Camillo Hospital, Roma
34 General Surgery Unit, IRCCS Sacro Cuore Don Calabria Hospital, Negrar di Valpolicella (VR)
35 Minimally Invasive Oncologic Surgery Unit, IRCCS Policlinico Gemelli Foundation, Roma
36 General Surgery Unit, Santa Croce e Carle Hospital, Cuneo
Acknowledgements

Not applicable

References

1. Landsman ML, Kwant G, Mook GA, Zijlstra WG. Light-absorbing properties, stability, and spectral stabilization of indocyanine green. J Appl Physiol. 1976;40:575–583

2. Muckle TJ. Plasma proteins binding of indocyanine green. Biochem Med. 1976;15:17-21

3. Arezzo A, Bonino MA, Ris F, Boni L, Cassinotti E, Foo DCC, Shum NF, Brolese A, Ciarleglio F, Keller DS, Rosati R, De Nardi P, Elmore U, Fumagalli Romario U, Jafari MD, Pigazzi A, Rybakov E, Alekseev M, Watanabe J, Vettoretto N, Cirocchi R, Passera R, Forcignanò E, Morino M. Intraoperative use of fluorescence with indocyanine green reduces anastomotic leak rates in rectal cancer surgery: an individual participant data analysis. Surg Endosc. 2020 Jun 18. doi: 10.1007/s00464-020-07735-w. Online ahead of print.

4. Alfano MS, Molino S, Benedicenti S, Molteni B, Porsio P, Arici E, Gheza F, Botticini M, Portolani N, Baiocchi GL. Intraoperative ICG-based imaging of liver neoplasms: a simple yet powerful tool. Preliminary results. Surg Endosc. 2019 Jan;33(1):126-134. doi: 10.1007/s00464-018-6282-1. Epub 2018 Jun 22.

5. Baiocchi GL, Diana M, Boni L. Indocyanine green-based fluorescence imaging in visceral and hepatobiliary and pancreatic surgery: State of the art and future directions. World J Gastroenterol. 2018 Jul 21;24(27):2921-2930. doi: 10.3748/wjg.v24.i27.2921.

6. Baiocchi GL, Gheza F, Molfino S, Arru L, Vaira M, Giacopuzzi S. Indocyanine green fluorescence-guided intraoperative detection of peritoneal carcinomatosis: systematic review. BMC Surg. 2020 Jul 17;20(1):158. doi: 10.1186/s12893-020-00821-9.

7. The Italian ColoRectal Anastomotic Leakage (iCral) Study group. Anastomotic leakage after elective colorectal surgery: a prospective multicentre observational study on use of the Dutch leakage score, serum procalcitonin and serum C-reactive protein for diagnosis. BJS Open. 2020 Mar 5. doi:10.1002/bjs5.50269. [Epub ahead of print]

8. Caricato M, Baiocchi GL, Crafa F, Scabini S, Brisinda G, Clementi M, Sica G, Delrio P, Longo G, Anania G, de Manzini N, Amodio P, Lucchi A, Baldazzi G, Garulli G, Patriti A, Pirozzi F, Pavanello M, Carrara A, Campagnacci R, Liverani A, Muratore A, Siquini W, De Luca R, Mancini S, Borghi F, Di Cosmo M, Persiani R, Pedrazzani C, Scaramuzza M, Scatizzi M, Vettoretto N, Totis M, Gennai A, Marini P, Basti M, Viola M, Ruffo G, Catarci M; Italian ColoRectal Anastomotic Leakage (iCral) Study Group. Colorectal
9. The Italian ColoRectal Anastomotic Leakage (iCral) Study Group. Risk factors for adverse events after elective colorectal surgery: beware of blood transfusions. Updates Surg. 2020; in press.

10. Nowak K, Karampinis I, Gerken ALH. Application of Fluorescent Dyes in Visceral Surgery: State of the Art and Future Perspectives. Visc Med. 2020 Apr;36(2):80-87. doi: 10.1159/000506910. Epub 2020 Mar 26.

11. Gossedge G, Vallance A, Jayne D. Diverse applications for near infra-red intraoperative imaging. Colorectal Dis. 2015 Oct;17 Suppl 3:7-11. doi: 10.1111/codi.13023. Review

12. Arezzo A, Migliore M, Chiaro P, Arolfo S, Filippini C, Di Cuonzo D, Cirocchi R, Morino M. The REAL (REctal Anastomotic Leak) score for prediction of anastomotic leak after rectal cancer surgery. Tech Coloproctol. 2019 Jul;23(7):649-663. doi: 10.1007/s10151-019-02028-4. Epub 2019 Jun 25.PMID: 31240416

13. Degett TH, Andersen HS, Gögenur I.. Indocyanine green fluorescence angiography for intraoperative assessment of gastrointestinal anastomotic perfusion: a systematic review of clinical trials. Langenbecks Arch Surg. 2016 Sep;401(6):767-75. doi: 10.1007/s00423-016-1400-9. Epub 2016 Mar 11.PMID: 26968863

14. Son GM, Kwon MS, Kim Y, Kim J, Kim SH, Lee JW . Quantitative analysis of colon perfusion pattern using indocyanine green (ICG) angiography in laparoscopic colorectal surgery. Surg Endosc. 2019 May;33(5):1640-1649. doi: 10.1007/s00464-018-6439-y. Epub 2018 Sep 10.PMID: 30203201

15. Hasegawa H, Tsukada Y, Wakabayashi M, Nomura S, Sasaki T, Nishizawa Y, Ikeda K, Akimoto T, Ito M. Impact of intraoperative indocyanine green fluorescence angiography on anastomotic leakage after laparoscopic sphincter-sparing surgery for malignant rectal tumors. Int J Colorectal Dis. 2020 Mar;35(3):471-480. doi: 10.1007/s00384-019-03490-0. Epub 2020 Jan 6.PMID: 31907595

16. Tsang YP, Leung LA, Lau CW, Tang CN.. Indocyanine green fluorescence angiography to evaluate anastomotic perfusion in colorectal surgery. Int J Colorectal Dis. 2020 Jun;35(6):1133-1139. doi: 10.1007/s00384-020-03592-0. Epub 2020 Apr 14.PMID: 32291508

17. Mangano A, Masrur MA, Bustos R, Chen LL, Fernandes E, Giulianotti PC. Near-Infrared Indocyanine Green-Enhanced Fluorescence and Minimally Invasive Colorectal Surgery: Review of the Literature. Surg Technol Int. 2018 Nov 11;33:77-83.PMID: 30029290

18. Alekseev M, Rybakov E, Shelygin Y, Chernyshov S, Zarodnyuk I. A study investigating the perfusion of colorectal anastomoses using fluorescence angiography: results of the FLAG randomized trial. Colorectal Dis. 2020 Mar 18. doi: 10.1111/codi.15037. Online ahead of print.

19. Lütken CD, Achiam MP, Svendsen MB, Boni L, Nerup N. Optimizing quantitative fluorescence angiography for visceral perfusion assessment. Surg Endosc. 2020 Jul 21. doi: 10.1007/s00464-020-07821-z. Online ahead of print.

20. Starker PM1,2, Chinn B3. Using outcomes data to justify instituting new technology: a single institution's experience. Surg Endosc. 2018 Mar;32(3):1586-1592. doi: 10.1007/s00464-017-6001-3.
