

# The use of near-infrared angiography in evaluating bowel anastomosis during a gynecologic oncology surgery

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## ABSTRACT

Reducing anastomotic leak rates after bowel resection is a priority among patients undergoing gynecologic oncology surgery. While near-infrared (NIR) angiography has been investigated in the colorectal literature, more recent work has demonstrated promising results when used in gynecologic cancer surgery. It has been repeatedly shown to be a safe intervention that can offer real time assessment of bowel perfusion, offering the surgeon the opportunity to act on the results in the hopes of decreasing the risk of complications.

## 1. Background

Surgical resection has been repeatedly shown to play an integral role in the treatment of advanced gynecologic malignancy. The success of surgical resection in the treatment of advanced uterine or ovarian malignancy has been demonstrated to depend on maximizing the amount of tumor resected with the best survival outcomes being linked to achieving no gross residual (Bristow et al., 2023; Rajkumar et al., 2019). In order to achieve such goals, some form of bowel resection is frequently required. In addition, we often find ourselves performing bowel resections in the setting of bowel obstruction as well as other disease- or treatment- related complications. Given the integral role that bowel resections have on patients in an already fragile state, it is of the utmost importance that we work to minimize their potential for complications. Among these detrimental complications are anastomotic leaks. Rates in the gynecologic literature vary, ranging up to 7 % in patients undergoing debulking surgery for ovarian cancer (Grimm et al., 2017). The mortality rate associated with an anastomotic leak ranges from 3 % up to 21 %, most often secondary to sepsis (Blumetti et al., 2014). In addition anastomotic leaks are associated with increased hospital cost, length of hospital stay, readmission, reoperations, and a longer time to start of adjuvant chemotherapy (Grimm et al., 2017). Given these detrimental impacts, identifying possible interventions to help intra or *peri*-operatively diminish the risk of an anastomotic leak have undergone investigation.

Among these is the use of near-infrared (NIR) angiography in

evaluating bowel anastomosis during a gynecologic oncology surgery. Poor oxygenation due to diminished blood supply is believed to play a role in the risk of an anastomotic leak (Kingham and Pachter, 2009; Vignali et al., 2000). The use of NIR offers the surgeon a method by which to assess anastomotic perfusion intraoperatively. This provides an opportunity to act on abnormal findings intraoperatively, such as the implementation of a diverting ileostomy or revision of anastomosis in the case of abnormal perfusion findings.

## 2. Technology

Indocyanine green (ICG) has been used in medicine since the late 50 s for a multitude of procedures from measuring cardiac output to studying the anatomy of the retinal vessels. ICG absorbs light in the NIR spectrum between 790 and 805 nm and re-emits electromagnetic energy at 835 nm, which can be visualized by its fluorescence in the vasculature using NIR irradiation (Alander et al., 2012). Its half-life in humans is 3–5 min, and the rate of allergic reaction is approximately 1 in 333,000 (Keller et al., 2017; Yamaguchi et al., 2021).

An endoscopic fluorescence imaging system is then used to visualize ICG perfusion. The system provides high-definition white-light and NIR-light rapid image sequencing, creating a superimposition of NIR-on-white-light views using false-green signal coloring to allow an enhanced intraoperative assessment of perfusion. ICG perfusion with NIR assessment is an available option whether an open or minimally invasive surgical technique (Keller et al., 2017; Boni et al., 2016). This review

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will focus on the use of ICG with NIR angiography for low anterior resections, however this technique has additionally been demonstrated in other bowel surgeries such as small bowel anastomosis, sleeve gastrectomy and esophagectomy (Aleassa and El-Hayek, 2020).

### 3. Technique

This intervention is used to assess perfusion of colonic tissue at two critical steps: the first is to assess the proximal and distal stumps after transection, and the second is for low anterior resections, after completion of the anastomosis to assess the integrity of the mucosal aspect via proctoscopy. Both the NIR angiographic examination of the bowel serosa in the first step, and NIR endoscopic examination of the anastomosed bowel mucosa in the second step promote a comprehensive evaluation of bowel perfusion. This two-step technique was used in the retrospective study by Moukarzel et al. (2020).

In the first step, following the transection and immediately prior to planning anastomoses, the surgeon performs the NIR angiography and assesses both the proximal and distal stumps for perfusion. This intervention can be used to assess perfusion of any segment of bowel prior to anastomosis. To assess the perfusion, a bolus of 3–7 ml at a concentration of 2.5 mg/ml of ICG followed by a 10 ml normal saline flush is administered intravenously by the anesthesiologist; recommended maximum dosing is <2 mg/kg (FDA, 2020). Using the endoscopic fluorescence imaging system, the time to ICG visualization should be noted with a goal of less than 60 s to complete perfusion. If perfusion is deemed satisfactory, then surgeon proceeds to perform the anastomoses in accordance with the surgeon's usual techniques (Fig. 1). If perfusion is deemed unsatisfactory, then the surgeon may decide to trim the distal portion of the stump (Fig. 2).

After completion of the anastomosis, anastomotic assessment is conducted in accordance with the surgeon's preference. For rectosigmoid resections the standard assessment includes visual inspection of tension at the anastomosis, an air bubble test, and, in some cases, visual assessment with rigid proctoscopy. After all anastomoses and standard assessment is complete, then the surgeon can choose to perform an additional assessment using NIR angiography, in step two.

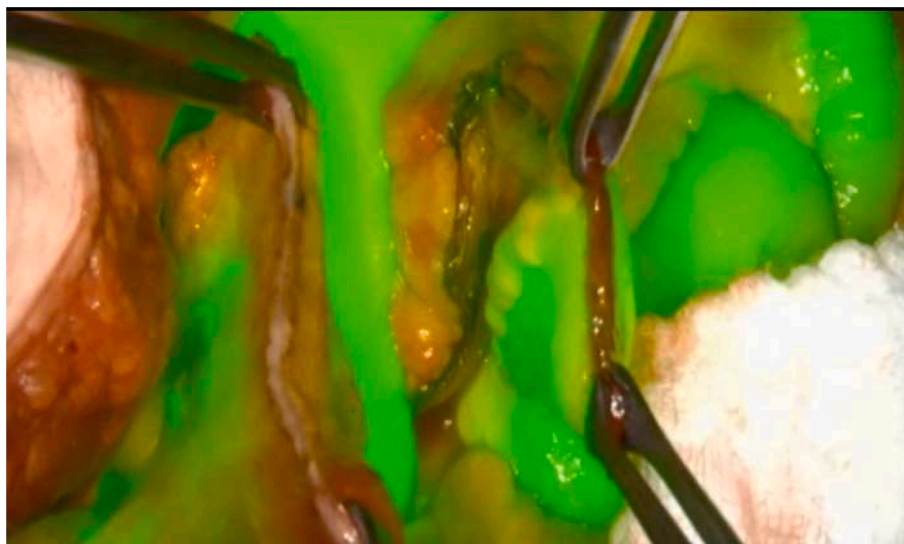
For a rectosigmoid resection, this subsequent assessment is performed via proctoscopy. The endoscopic fluorescence imaging system is inserted into the anus using a disposable endoscope and advanced to the staple line of the anastomosis. The surgeon obtains visualization of the proximal and distal ends of the rectosigmoid anastomosis with

visualization of the entire anastomosis. A second bolus of ICG is then re-administered intravenously by the anesthesiologist. The surgeon then assesses in real time the perfusion of the anastomosis. (Video 1,2). The surgeon would then decide on the surgical plan, such as to perform a revision of the anastomosis or perform a diverting ostomy.

### 4. Review of the literature & discussion

The use of this technique was originally developed in the colorectal literature where it was demonstrated to be safe with promising results in identifying anastomoses at risk, decreasing leak rates, and improving outcomes (Ris et al., 2018; Jafari et al., 2013; Jafari et al., 2015; Kudsuz et al., 2010). Recent studies have described a significant decrease in leak rates with the use of ICG imaging to assess anastomotic perfusion in rectal cancer surgery. The FLAG trial, a randomized control trial (RCT) in Russia investigating the use of NIR angiography for sigmoid or rectal neoplasms, found a decrease in AL rate from 16.3 % to 9.1 % in patients undergoing LAR (Alekseev et al., 2020). A meta-analysis reported a significant decrease in leak rates from 6.1 % to 1.1 % when ICG was used to evaluate anastomotic perfusion (Blanco-Colino and Espin-Basany, 2018). Results from the European IntAct RCT investigating the use of NIR angiography in laparoscopic colorectal cancer surgery are pending (Armstrong et al., 2018). While PILLAR III, a U.S. multicenter trial investigating the use of NIR angiography in LAR for colorectal malignancies, closed early due to slow accrual, the ICG-COLORAL study investigating the use of NIR angiography in benign and malignant colorectal surgery, is ongoing in Finland (Jafari et al., 2021; Kossi, 2018).

More recently the use of this technology has also been investigated during surgical debulking cases for ovarian and uterine carcinoma. In a retrospective review of 133 patients, Moukarzel et al., demonstrated the safety and feasibility of using NIR angiography as an adjunct to standard assessment of primary rectosigmoid anastomosis at the time of surgery for gynecologic malignancy (Moukarzel, 2020). In this study, NIR angiography use was associated with extremely low rates of anastomotic leak: 1.5 % in the NIR group and 4.7 % in the non-NIR cohort. This was accompanied by a lower total rate of intestinal diversion (6.8 % vs 19.9 %), fewer post-operative abscesses (6.0 % vs 15.9 %) and fewer post-operative interventional procedures (9.0 % vs 19.9 %) in the NIR group vs the non-NIR group. Additionally, there were no allergic reactions to ICG or intraoperative complications associated with the use of NIR angiography, further demonstrating the safety of NIR angiography.



**Fig. 1.** ICG should perfuse normal tissue within 60seconds of injection and should be cleared within 10 minutes. Image demonstrates circumferential perfusion throughout colonic stump.

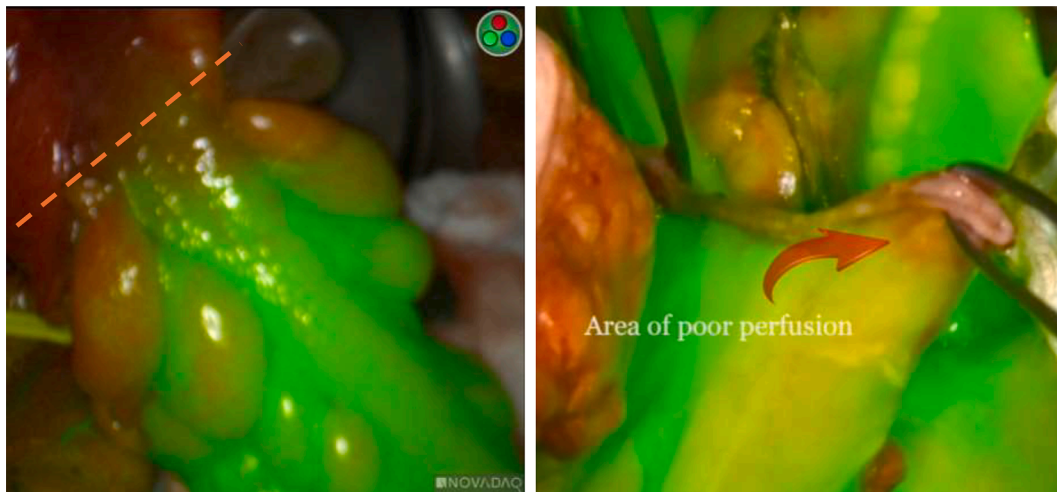


Fig. 2. Lack of satisfactory perfusion. A) Clear line of demarcation marked by dotted red line. B) Localized to corner of colonic stump.

These findings suggest that the use of NIR angiography reduces complications while resulting in fewer diverting ileostomies and the morbidity associated with them. Currently in the US, there is an ongoing multi-institutional randomized clinical trial investigating the use of this technology in gynecologic cancer surgery (NCT04878094) (Leitao et al., 2024).

## 5. Barriers to implementation

When considering barriers to implementation, the NIR angiography system and training to safely use this technology is critical. While start-up cost of the NIR angiography system is high, the cost of ICG per patient is minimal (Blanco-Colino and Espin-Basany, 2018). Additionally, the NIR angiography system is used in the gynecologic oncology field for sentinel lymph node mapping, and its use can be modified for the evaluation of bowel anastomosis. A recent cost analysis in colorectal surgery showed a per-case saving of \$192 with NIR angiography implementation (Liu et al., 2022). When the costs of NIR angiography are considered against the costs of anastomotic leak including prolonged antibiotic treatment and hospitalization, re-operation and other interventional procedures, NIR angiography implementation can result in significant benefit to the patient and healthcare system.

## CRedit authorship contribution statement

**Lea A. Moukarzel:** Writing – review & editing, Writing – original draft, Conceptualization. **Sarah Andres:** Writing – review & editing. **Oliver Zivanovic:** Validation, Supervision.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.gore.2024.101474>.

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