

## Case Report

# A Case of Rectal Cancer with Vaginal Invasion Using Indocyanine Green to Determine the Extent of Resection

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### Abstract

Here we report a case of locally advanced rectal cancer with vaginal invasion, which was successfully resected via laparoscopic surgery using intraoperative indocyanine green (ICG) navigation to determine the vaginal cut line. Based on preoperative examinations, an 81-year-old female was diagnosed with locally advanced rectal cancer with vaginal invasion. After preoperative chemoradiotherapy, the lesion was judged to be resectable. During surgery, the gynecologist transvaginally injected ICG into the vaginal submucosa to determine the caudal margin of the vaginal invasion, and laparoscopically dissected under the near-infrared image of the stained area. Pathological analysis of the resection specimen revealed negative resection margins. One year after surgery, there has been no recurrence.

### Keywords

colorectal cancer, ICG, vaginal invasion

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## Introduction

In cases of advanced rectal cancer, laparoscopic surgery is reportedly less invasive during the perioperative period compared to open surgery[1]. Additionally, laparoscopic surgery is non-inferior to open surgery in terms of short-term and long-term outcomes in cases of rectal cancer, when T4 cases are excluded[2].

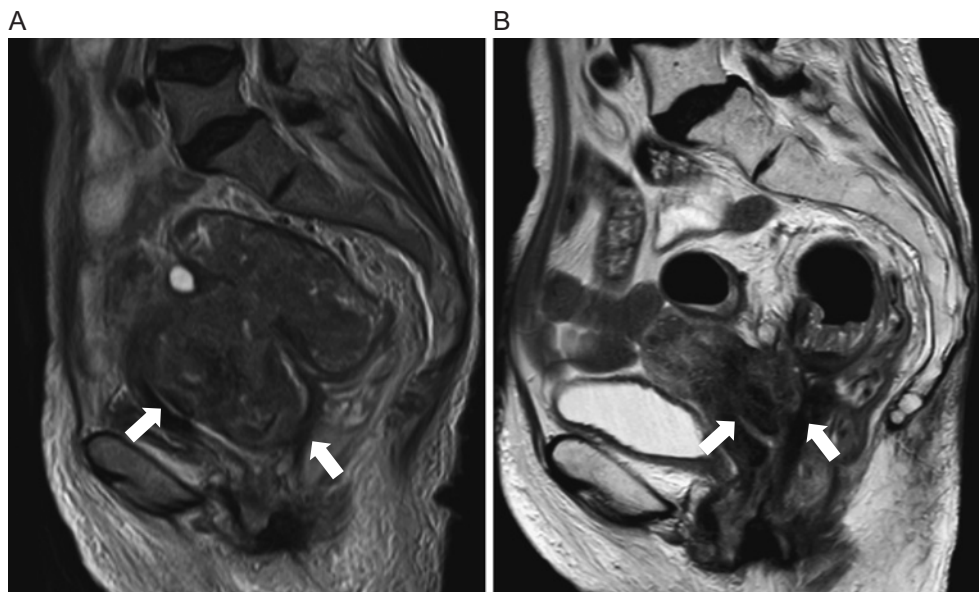
In about 15% of cases, rectal cancer invades adjacent organs[3], and surgical treatment with concomitant resection of the invaded organ is recommended[4]. Although palpation is useful and definitive for determining the degree and area of invasion of other organs, fine palpation is specific to conventional open laparotomy.

Here we report a case of rectal cancer with vaginal invasion, in which we used indocyanine green (ICG) to ascertain

margins during a complicated resection. While performing laparoscopic surgery without intraperitoneal palpation, we locally injected ICG into the prearranged margin of the vagina, and used near-infrared imaging to confidently determine the cut end line. Local injection of ICG was performed under the part of the clinical trials. The study protocol of this study was consistent with the principles of the Declaration of Helsinki and was approved by the Ethics Committees of Osaka University Hospital (No. 16379-3). All methods were performed in accordance with the relevant guidelines and regulations.

## Case Report

An 81-year-old female had previously visited another hospital with bilateral lower leg edema and frequent urination



**Figure 1.** A, Magnetic resonance imaging (T2 emphasis, sagittal section) before chemotherapy, white arrows indicate massive tumoral invasion to the vagina. B, MRI (T2 emphasis, sagittal section) after chemoradiotherapy. The tumor has been reduced in size but invasion remains (white arrows).

for several months. She had a history of polyarteritis nodosa and deep vein thrombosis. Computed tomography (CT) and magnetic resonance imaging (MRI) (Figure 1A) scans revealed a mass extending from the rectum to the uterus and vagina. Colonoscopy revealed a type 2 tumor at the middle rectum, and biopsy analysis indicated an adenocarcinoma. KRAS was wild-type, however, we were unable to analyze for genetic mutations other than KRAS. The tumor was also observed transvaginally. Immunohistochemical staining of a transvaginal biopsy specimen revealed that this tumor was an adenocarcinoma of rectal origin (CDX2<sup>+</sup>, CK7<sup>-</sup>, CK20<sup>+</sup>, PAX8<sup>-</sup>, ER<sup>-</sup>, and PgR<sup>-</sup>). The patient was referred to our hospital with a diagnosis of rectal cancer with vaginal invasion.

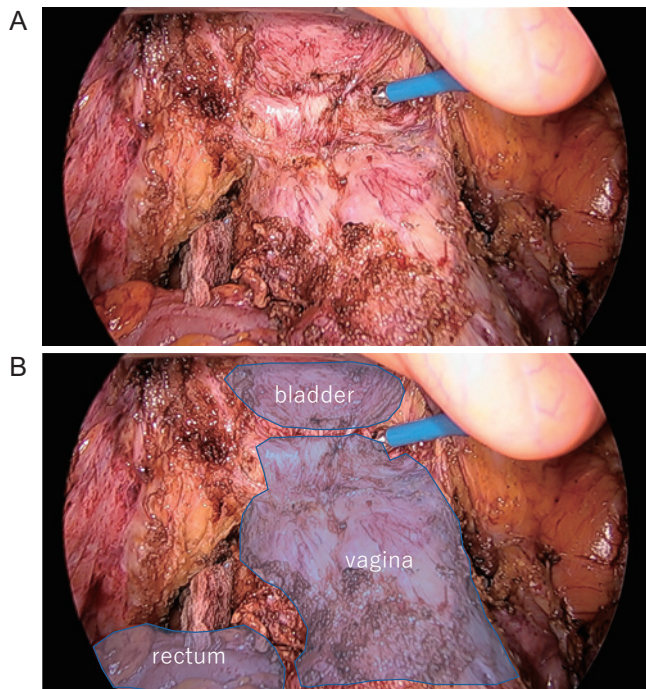
Close examination revealed no lymph node metastasis or distant metastasis, and the patient was diagnosed with rectal cancer cT4b (uterine and vaginal) N0M0 cStage IIc (Japanese classification, 9<sup>th</sup> edition). To maximize resectability, we decided to perform preoperative chemoradiotherapy (CRT) with six courses of TS-1 plus cetuximab plus radiation therapy (45 Gy/25 Fr). After CRT, the tumor remained but was diminished in size, and thus the therapeutic effect was deemed a partial response (PR) (Figure 1B). No distant metastatic lesions were found, the lesion was judged to be resectable, and surgical treatment was planned.

We performed laparoscopic low anterior rectal resection (D3 dissection); combined uterine, vaginal, and bilateral adnexal resection; and transverse colostomy. Lateral lymph node dissection was not performed, because the primary lesion was confined to the middle rectum. The surgery was performed in a standard multiport fashion[5]. Starting from

a medial-to-lateral approach, the inferior mesenteric artery and vein were divided, and Japanese D3 dissection was performed. During pelvic manipulation, direct invasion of the tumor into the vagina was confirmed, and thus we dissected the space between the vagina and the cystic bladder.

The vaginal invasion of the tumor was also transvaginally confirmed. The vaginal submucosa was circumferentially dissected and tightly sutured at 2 cm from the tumor on the distal side (Figure 2). Then, the gynecologist (E. K.) thoroughly washed the area with saline, and locally injected ICG (1.25 mg/0.5 ml, Diaginogreen<sup>®</sup>, Daiichisankyo, Tokyo, Japan) at the prearranged cut line. We shifted to laparoscopic manipulation, and the vagina was dissected at the distal side from the point of rectal cancer invasion, under near-infrared fluorescence image guidance (Figure 3). Upon completion of vaginal dissection, we performed low anterior resection of the rectum in the standard fashion, and extracted the specimen. Anastomosis was performed using a double-stapling technique, a drain was placed on the posterior surface of the anastomosis, and the wound was closed. Finally, we created a diverting transverse colostomy. The patient exhibited a generally good postoperative course.

Postoperative pathology revealed adenocarcinoma, tub1> tub2, ypT4b (uterus, vagina), ypN0, INFb, Ly0, V0, PN0, pPM0, pDM0, pRM0, M0 ypStage IIc, and the treatment effect was Grade 1b. Notably, the cut end line of the vagina provided sufficient distance from the site of cancer invasion (Figure 4). After one year of careful screening, no obvious recurrence has been observed.

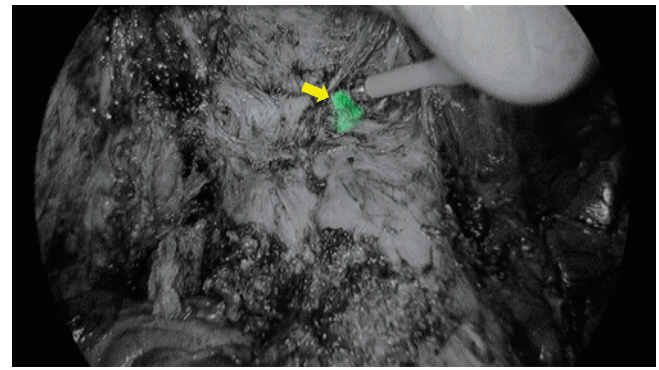


**Figure 2.** A, Intraoperative pelvic field of view. The fibers have been stripped between the vagina and bladder. B, Illustration of the same field.

## Discussion

Randomized control trials in patients with rectal cancer (excluding T4 cases) show that laparoscopic surgery and open surgery have similar rates of local recurrence, disease-free survival, and overall survival[2]. Adjacent organ invasion occurs in about 15% of rectal cancer cases[3]. When rectal cancer with organ invasion is judged to be resectable, surgical treatment with combined resection is recommended[4]. Palpation is useful for determining the extent of resection of invaded organs, but is limited to open surgery. Our present case involved vaginally invasive rectal cancer in an elderly patient, and thus we sought a way to avoid laparotomy and maintain the minimally invasive nature of laparoscopy.

Other preoperative marking techniques, including colorectal tattooing with the India ink method and the clipping method, have been widely used to address this issue in laparoscopic colorectal surgery. However, the India ink method has the disadvantage that the ink diffuses to the surrounding area. Additionally, the clipping method can be difficult to identify under laparoscopy, and the clip often migrates or dislodges within a short period of time[6]. Another marking method might be sticking a needle to the Vagina to determine the planned resection line. However, it is presumed that it is extremely difficult to puncture the tissue perpendicularly with the needle because of the limited space in the lumen of a hollow organ.



**Figure 3.** Images of the abdominal cavity after injection of indocyanine green (ICG) into the vaginal mucosa. Resection of the vaginal area was performed caudal to the ICG-stained area (yellow arrow).

In the present case, we were able to laparoscopically determine the extent of resection through local injection of ICG at the presumed resection margin of vaginal invasion. The ICG fluorescence method has been increasingly clinically applied in recent years due to the widespread use of near-infrared observation equipment. Common uses include the identification of sentinel lymph nodes, evaluation of aneurysms, identification of gallbladder ducts and hepatocellular carcinoma, and evaluation of blood flow in the intestinal tract[7]. Within the field of colorectal cancer, ICG fluorescence is clinically applied for the evaluation of blood flow and lymphatic flow in the anastomotic intestine[8].

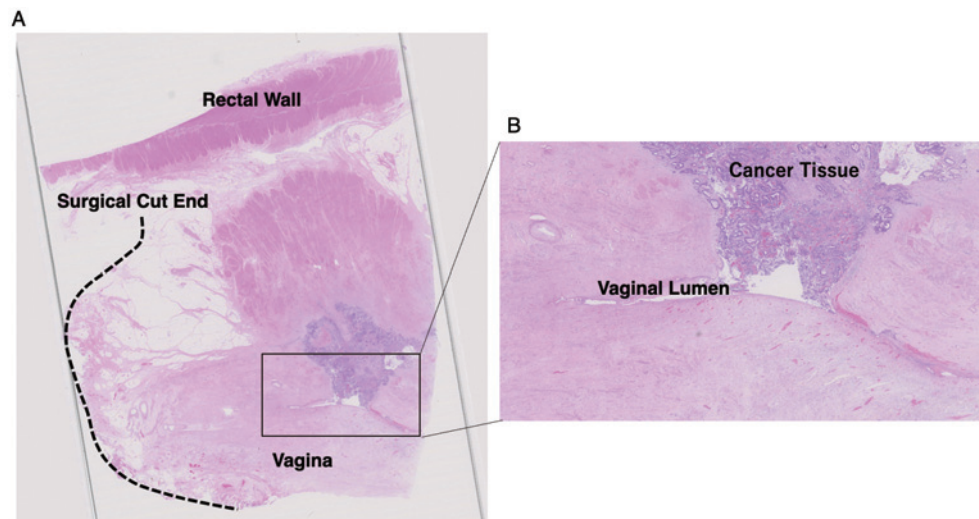
We describe the successful use of local ICG injection to determine the distal margin of the vagina, which was a merged resection organ. The vagina was previously palpated to determine the extent of the resection; however, the additional use of ICG injection enabled us to perform a complicated resection while maintaining a good field of view and fine manipulation of the laparoscope. Prior reports describe the securing of surgical margins by ICG accumulation at the primary tumor in liver tumors and lymphatic teratomas[9,10]. However, we found no prior report of the use of ICG to determine the resection margins for cancer invading other organs, as in our present method. This case supports that the combined use of ICG and laparoscopy is a useful option for rectal cancer with invasion of other organs, and to facilitate the performance of optimal resection.

### Conflicts of Interest

There are no conflicts of interest.

### Author Contributions

Hidekazu Takahashi wrote the manuscript with support from Yuki Sekido, Eiji Kobayashi, Tsuyoshi Hata, Atsushi Hamabe, Takayuki Ogino, Norikatsu Miyoshi, Mamoru Uemura, Hirofumi Yamamoto, Yuichiro Doki, Hidetoshi



**Figure 4.** Resection pathological specimen, showing that rectal cancer tissue has invaded the vaginal lumen. A,  $\times 4$  image. B,  $\times 400$  image.

Eguchi. All authors discussed the results and commented on the manuscript.

Approval by Institutional Review Board (IRB)

All procedures used in this research were approved by the Ethical Committee of Osaka University Hospital.

Informed Consent

The patient gave written informed consent for the publication of this case report and any accompanying images.

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