

# The Use of Preoperative Endoscopic Tattooing in Laparoscopic Colorectal Cancer Surgery for Endoscopically Advanced Tumors: A Prospective Comparative Clinical Study

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## Abstract

**Background:** Endoscopic India ink marking techniques are often used for the intraoperative location of colonic polyps and early stage neoplasms. The aim of this study was to compare how effective this technique is compared with conventional localization methods, as well as its influence on the results of colorectal laparoscopy (LSCRC) for endoscopically advanced tumors.

**Methods:** From January 2003 to January 2005, 47 patients with colorectal carcinomas were included in the study. In one group, lesions were localized preoperatively by endoscopic India ink tattooing (n = 21; tattooed group, TG), while conventional methods were used in the others (n = 26; non-tattooed group, NTG). Patients' perioperative clinical and pathoanatomical data were prospectively collected.

**Results:** Both groups were comparable in age, sex distribution, American Society of Anesthesiologists (ASA) score, body mass index (BMI), technique performed, tumor size and proportion of patients who had previous abdominal surgery. Three patients presented ink spillage without clinical repercussions. Visualization of the correct resection site was higher in the TG (100% vs. 80.8%,  $P = 0.03$ ). Operative time ( $147.3 \pm 46.2$  vs.  $187.0 \pm 52.7$  minutes,  $P = 0.02$ ) and blood loss ( $99.3 \pm 82.8$  vs.  $163.6 \pm 96.6$  cc,  $P = 0.03$ ) were lower in the TG. There were no differences between groups regarding peristalsis, introduction of oral intake, hospital stay or intra- and postoperative complication rates. No differences were observed amongst pathoanatomical data studied.

**Conclusions:** Preoperative endoscopic tattooing is a safe and effective technique for intraoperative localization of advanced colorectal neoplasms, improving the operative results of LSCRC.

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In colorectal cancer surgery, exact lesion location is essential for oncologically correct surgery and adequate tumor and lymph node resection margins.<sup>1</sup> In laparoscopic surgery, the inability to touch makes it harder for surgeons to locate lesions during surgery, even advanced tumors. A secure and effective method is therefore essential for solving this problem.<sup>2</sup>

Effective preoperative colonoscopy depends on many factors, such as expertise of the endoscopist, intestine length, endoscope flexibility or bowel cleansing, and is considered an insufficient method for exact lesion localization.<sup>3</sup> Traditionally, barium enemas have also been used, although they are problematic for diagnosing small or flat tumors, and patients have to endure a second colon preparation with lavage solution.<sup>4</sup>

Many papers have addressed the usefulness and safety of preoperative endoscopic tinting for localizing lesions during surgery. Used initially to mark polyps or early-stage tumors, more recent papers have proved it is useful in laparoscopic surgery on advanced neoplasms.<sup>5-7</sup> However, the value of endoscopic tattooing of advanced tumors compared with conventional methods has not been researched, nor has its possible influence on the perioperative results of colorectal laparoscopy (LSCRC). Therefore, the purpose of this paper is to research these two issues.

## PATIENTS AND METHODS

Patients included in the study had been endoscopically diagnosed as having advanced stage colorectal carcinoma (protuberant, ulcerated or diffusely infiltrating type tumors, appearing endoscopically more advanced than type 0 [superficial] lesions, as defined by the Japanese classification of colorectal carcinoma),<sup>8</sup> the location of which was susceptible to being mistaken during surgery. Rectal tumors located less than 12 cm from the anal verge ( $n = 20$ ), measured with a rigid rectoscope, as well as tumors adjacent to the ileocecal valve ( $n = 1$ ) were excluded from the study. Patients were also excluded in the following cases: when found to have tumors not susceptible for laparoscopic surgery due to perforation or obstruction ( $n = 1$ ); when tumor size was greater than 8 cm ( $n = 1$ ); and when tumors were preoperatively diagnosed to be infiltrating neighboring organs ( $n = 1$ ). Finally, patients were also excluded when there was an anesthetic contraindication for the pneumoperitoneum. From January 2003 to January 2005, 47 patients were eventually included in the study, out of the 71 with colorectal neoplasms initially assessed.

A single diagnostic endoscopy was performed on each patient by 1 of 4 gastroenterologists with 5+ years of specialist experience. Two of them performed preoperative marking and the other two conventional colonoscopies. Patients were distributed in order of admission by endoscopy unit administrative staff.

One group was marked with India ink proximally and distally to the tumor—the tattooed group (TG,  $n = 21$ ), while the other had a conventional colonoscopy without tattooing—the non-tattooed group (NTG,  $n = 26$ ). In all cases, patients in the NTG had a contrast enema and CT for tumor localization. All patients were duly informed of the study and gave written consent accepting the risks of lower digestive tract endoscopy. Patients also explicitly authorized any diagnostic and/or therapeutic maneuvers deemed necessary during the test.

In each case, patients' preoperative procedures routinely included: physical examination; analyses with liver function tests; chest X-rays and electrocardiograms; carcinoembryonic antigen and abdominal CT to assess liver involvement and, in the NTG, for tumor localization. All NTG patients had a contrast enema for primary tumor localization. TG patients only had a barium enema when suffering stenosing tumors for which colonoscopy was incomplete.

Data on demographic, clinical, and pathoanatomical variables of both groups were collected prospectively into a database. Variables on patients' characteristics included age, sex, American Society of Anesthesiologists (ASA) score, body mass index (BMI) and previous abdominal surgery records. Clinical variables covered operative data, tumor visualization (defined as tattoo identification or unequivocal indirect tumor signs in the colonic serosa, such as thickening and retraction of the colonic wall), operative time, blood loss and conversion rates, as well as data regarding return of peristalsis, reintroduction of oral intake, average hospital stay and perioperative transfusion. Data on perioperative morbidity were collected, as well as readmissions and reoperations. Pathoanatomical data such as specimen length, number of lymph nodes studied, and proximal and distal margins were analyzed.

Quantitative variable results are expressed as mean/standard deviation. Categorical variable results are expressed as percentages.

Quantitative variables between groups (TG/NTG) were compared using Student's *t*-test. Group comparisons (TG vs. NTG) were calculated using the Chi-squared or Fisher's exact test. Statistical analyses were performed using the SPSS 11.0.1 statistical software package.

## Tattooing Techniques

Preoperative tattooing was performed as described by Fu *et al.*<sup>9</sup> In brief, 3 ml of normal saline were injected into the submucosal layer with a 23G 4-mm needle (NM-200U-0423; Olympus, Japan), in order to create a bleb (see Fig. 1). The syringe was then replaced by another containing sterilized 90% India ink and 0.2–0.5 ml were injected. Finally, the ink was pushed into the preformed bleb by further injecting 2 ml of saline.

Tattooing was performed at each of two points approximately 2 cm away from both the anal and oral edge of the lesion. Stenosing cancers were marked only on the anal side (see Fig. 2).

## Surgical Technique

All patients were prepared with a lavage solution the day prior to surgery and received antibiotic prophylaxis during anesthetic induction. All surgical procedures were performed under general anesthesia. Specimens were extracted for extracorporeal resection in every case. While left-side colectomies had intracorporeal anastomoses, for right-sided colectomies they were extracorporeal. In all procedures, a gastrointestinal anastomosis vascular stapler load was used to perform intracorporeal hemostasis of the main vessel. Perioperative care was identical in both groups.

## RESULTS

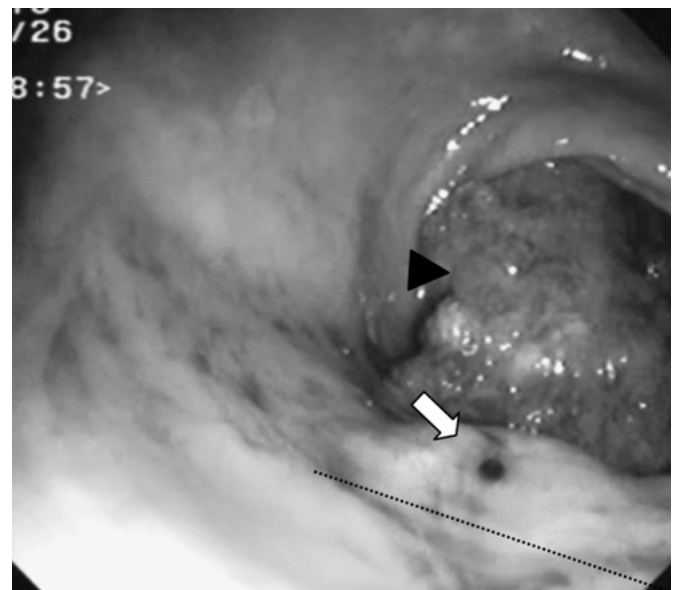
Ultimately, 47 of the 71 patients initially assessed were included in the prospective comparative study. Both groups were comparable regarding demographic characteristics, age, sex, ASA score, BMI, TNM (tumor, node, metastases) staging, as well as technique performed, tumor size, and proportion of patients with previous abdominal surgery (Table 1).

Contrast enema located 24 (92.3%) tumors in the NTG. CT located 17 tumors (80.9%) in the TG and 22 (84.6%) in the NTG.

In 18 TG patients India ink marking was correct and was limited to the colonic wall. Two patients had ink spillage into the peritoneum and one into the retroperitoneum, although this did not prevent correct tumor localization (see Fig. 3). Tumors were visualized successfully and precisely in all TG cases and oncologic tumor resections were correct. In the NTG, only 21 tumors were visualized (100% vs. 80.8%,  $P = 0.3$ ), while 5 mobilizations were performed without intraoperative



**Figure 1.** Submucosal bleb with a 23 G 4-mm needle (India ink) indicated with an *arrow*.



**Figure 2.** Stenosing cancer marked (India ink) only on the anal side with four-quadrant technique (*arrows* indicate one quadrant marked). *Black arrowhead* shows the stenosing tumor.

tumor visualization. Of these, 2 resulted in incorrect resections: 1 unnecessary resection of a healthy segment of the colon and another with inadequate resection margins.

As for perioperative variables, operating time ( $147.4 \pm 46.2$  vs.  $187.0 \pm 52.7$  minutes,  $P = 0.02$ ) and operating blood loss were lower in the TG ( $99.3 \pm 82.8$  vs.  $163.6 \pm 96.6$  cc,  $P = 0.03$ ). There were no differences

**Table 1.**  
Patient characteristics

	Tattooed group (n = 21)	Non-tattooed group (n = 26)	Difference ( <i>P</i> value)
Age (years)	65.1 ± 6.8	68.5 ± 12.9	ns
Sex (female/male)	8/11	12/14	ns
ASA score	2.3 ± 0.6	2.1 ± 0.9	ns
BMI (kg/m <sup>2</sup> )	26.7 ± 3.6	26.1 ± 3.6	ns
TNM staging			
I	4	4	ns
II	10	12	ns
III	6	7	ns
IV	1	3	ns
Surgical technique			
Sigmoidectomy	6 (28.5)	11 (42.3)	ns
Right colectomy	6 (28.5)	5 (19.2)	ns
Left colectomy	5 (23.8)	4 (15.4)	ns
HAR	4 (19.0)	6 (23.1)	ns
Size (cm)	3.5 ± 1.4	4.2 ± 1.3	ns
Previous abdominal surgery, n (%)	7 (33.3)	5 (19.2)	ns

ASA: American Society of Anesthesiologists; BMI: body mass index; TNM: tumor, node, metastases; HAR: high anterior resection.

between the groups with regard to return of peristalsis, reintroduction of oral intake, intra- and postoperative morbidity or hospital stay, or readmission and reoperation rates (Table 2).

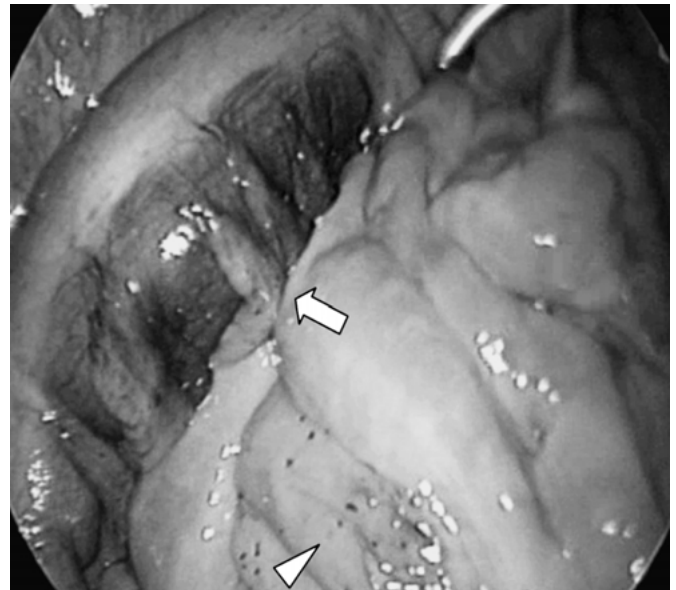
There were no differences in the variables studied in histological specimen examinations (resection length, proximal and distal margins and number of lymph nodes harvested, Table 3).

## DISCUSSION

Advanced colonic neoplasms can sometimes be difficult to localize during laparoscopic surgery, especially in areas close to the splenic and hepatic flexures or in the sigmoid colon, especially when tumors do not surpass the serosa or when there are visceral or wall adhesions as a result of previous laparotomies. This difficulty for localization requires lengthy mobilization of the colon, which can increase operative time unnecessarily.<sup>9</sup>

In a survey carried out on members of the American Society of Colon and Rectal Surgeons, 6.5% of those questioned said they had experienced some cases of erroneous resection of healthy colon segments.<sup>10</sup>

Laparoscopic approaches to colorectal cancer are nonetheless increasingly common in the clinical practice of surgical departments, due to research evidence demonstrating results comparable to those of conventional surgery in terms of survival and recurrence.<sup>11,12</sup> However, the intraoperative localization of lesions is a problem yet to be solved.



**Figure 3.** Laparoscopic visualization of advanced-stage colonic tumor (arrow). Arrowhead shows ink spillage in the peritoneum.

In view of the shortcomings of conventional diagnostic colonoscopy, many methods have been used for the preoperative localization of lesions. Traditionally, barium enemas were used, but, although they are a good method for exophytic and stenosing lesions, they are less effective for the localization of early or flat tumors.<sup>13</sup> Additionally the correlation between radiological imaging and intraoperative findings is not always easily established, especially in the transverse and sigmoid colon.<sup>4</sup> Other

**Table 2.**  
Perioperative clinical results

	Tattooed group (n = 21)	Non-tattooed group (n = 26)	Difference ( <i>P</i> value)
Operative time (minutes)	147.4 ± 46.2	187 ± 52.7	0.02
Blood loss (cc)	99.3 ± 8.8	163.6 ± 96.6	0.03
Transfusion (%)	2 (9.6)	1 (3.8)	ns
IO complications (%)	1 (4.8)	3 (11.5)	ns
Rectal perforation	1 (4.8)	0 (0.0)	
Stapling problems	0 (0.0)	1 (3.8)	
Tumors not located <sup>a</sup>	0 (0.0)	1 (3.8)	
Inadequate margin <sup>a</sup>	0 (0.0)	1 (3.8)	ns
Conversion	1 (4.8)	1 (3.8)	
Peristalsis (hours)	33.9 ± 14.8	33.0 ± 17.1	ns
Oral intake (hours)	43.8 ± 21.2	52.2 ± 22.5	ns
P.O. complications <sup>b</sup> (%)	5 (23.8)	6 (23.1)	ns
Wound infection	2 (9.6)	2 (7.6)	
CVA	1 (4.8)	1 (3.8)	
IAM	0 (0.0)	1 (3.8)	
Evisceration	0 (0.0)	1 (3.8)	
Anastomoses leakage	1 (4.8)	0 (0.0)	
Others	1 (4.8)	2 (7.6)	
Hospital stay (days)	5.8 ± 2.1	5.9 ± 2.7	ns
Mortality (%)	0 (0.0)	1 (3.8)	ns
Readmission (%)	1 (4.8)	0 (0.0)	ns
Reoperation (%)	1 (4.8)	1 (3.8)	ns

IO: intraoperative; PO: perioperative; CVA: cerebrovascular accident; IAM: acute myocardial infection.

<sup>a</sup>Complications related to non-visualized tumors.

<sup>b</sup>Proportion of patients with complications.

**Table 3.**  
Histological examination of patients

	Tattooed group (n = 21)	Non-tattooed group (n = 26)	Difference ( <i>P</i> value)
Specimen length (cm)	21.3 ± 7.9	19.3 ± 5.2	ns
Number of lymph nodes	8.0 ± 7.7	6.9 ± 4.3	ns
Distal margin (cm)	4.4 ± 2.3	4.6 ± 1.8	ns
Proximal margin (cm)	10.7 ± 8.0	9.2 ± 4.2	ns

methods of facilitating intraoperative detection, such as magnetic marking clips, ultrasonography or endoscopy, are too sophisticated and require learning the technique or they hamper laparoscopic handling due to insufflation.<sup>14–17</sup>

India ink marking during diagnostic endoscopy seems to be the simplest, safest and most effective method. Although there are various tinting methods, two-step ink injection, which includes injecting saline previously in order to form a submucosal bleb, is better than other techniques of tumor visualization and also creates fewer ink spillage problems.<sup>17</sup> In our research, we did not observe pericolonic inflammation in the two cases in which ink spilled into the peritoneum. Scattered ink stains were found, but they did not hinder resection in any way. In the case of spilling into the retroperitoneum, a larger pres-

ence of ink was noted. Cases in which the technique described was used are scarce and we believe acquired experience will reduce the number further still. Additionally, we find India ink markings easier to visualize than the sterile carbon compounds used by other authors.<sup>6</sup> The overall procedure is extended by not more than 5 minutes when performed by an experienced endoscopist.

In previous studies the use of preoperative tattooing in the localization of colorectal lesions, using both conventional and laparoscopic approaches, is reported to have been effective in over 90% of cases.<sup>7,9,17</sup> Contrary to our study, these papers did not gather information regarding size or stage of the tumors operated on; nor did they study the influence of marking on patients' perioperative clinical variables. In all TG cases, including the three subclinical cases of ink spillage, marked areas were

successfully visualized, allowing for correct resection without having to worry about visualizing or palpating the tumor. In 5 NTG cases, however, tumors were not visualized, despite carcinomas being at an advanced stage: 2 tumors were close to the hepatic flexure; a further 2 in the sigmoid and transverse colon respectively; and 1 was an upper-third rectal tumor. In these cases the segment thought to be affected was mobilized. In the transverse tumor case—a T3 stage tumor measuring 4 cm in its largest diameter, visualized by contrast enema and CT—an erroneous extracorporeal colectomy of a healthy segment was performed. This was due to a thickened and fibrotic epiploon caused by previous peritonitis that had involved the colonic wall, which hindered manual palpation of the tumor. Conversion of the procedure to a standard laparotomy was required in order to perform resection correctly. Non-visualization in the rectal tumor case (size 2 cm, stage T2, not visualized by enema or CT), led to rectal resection too close to the tumor. Therefore, a more distal laparoscopic resection was performed to achieve a distal margin greater than 2 cm. In our experience, a high percentage of endoscopically advanced neoplasms (19.2%) are not identified during the laparoscopic approach and this can lead to resection errors, especially in left-sided procedures, where distal colon resection is performed intracorporeally. The specimen is then extracted and the procedure is finished extracorporeally.

Previous marking of lesions led to an important reduction in operative time and blood loss. We believe that increased blood loss in the NTG is related to longer and more laborious surgery. This is due to the dissection and mobilization maneuvers required when attempting to identify unmarked tumors that are difficult to locate owing to size, location or presence of adhesions. Nonetheless, the increase did not correlate with a larger number of patients requiring transfusion. Furthermore, we believe that marking leads to more correct surgery, since it avoids tumor handling as well as unnecessary colon traction and desquamation of tumor cells, which can be caused by palpating when attempting to locate non-visualized tumors.

Although endoscopic tumor tattooing served as a guide for resection margins, we did not encounter differences in histological examination between the two groups.

Our study does have its weaknesses. One the one hand, the reduced number of patients does not allow valid conclusions to be drawn regarding some of the variables we believe may benefit from the routine lesion tattooing, such as conversion and intraoperative com-

plication rates. On the other hand, the fact that colonoscopic diagnoses were carried out by different specialists could introduce a certain degree of bias dependent on the endoscopist performing the test, although we feel that the non-selective assignment of patients on behalf of personnel from outside the investigation team dampens this effect. Moreover, we feel our results are validated by the equal distribution between groups of the variables that might have influenced perioperative results (Table 1).

Although it has been proved to be a useful technique, at present preoperative tattooing is not frequent in clinical practice, as can be seen in results reported by the COLOR Study Group, where less than 5% of lesions had been tattooed.<sup>18</sup>

To conclude, our study suggests that endoscopic India ink tattooing is a safe and effective technique for the intraoperative localization of advanced colorectal neoplasms. It reduces mobilization of the colon when tumors have not been successfully visualized and improves the surgical results of LSCRC. We therefore believe that endoscopic India ink tattooing should be considered a useful alternative when using this surgical approach.

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