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Vascular Virtual Endoluminal Visualization of Invasive Colorectal Cancer on MDCT Colonography

OBJECTIVE. The purpose of this study was to assess the utility of vascular views for visualization of invasive colorectal cancers on contrast-enhanced MDCT colonography.

CONCLUSION. By means of Hounsfield-transparency settings, we obtained virtual endoluminal images that show vascular structures and delineate invasive cancers of the colorectal wall, and we call these images "vascular views." Using this technique for contrast-enhanced MDCT colonography, we found that the increase in flow and pooling of blood related to angiogenesis of cancerous lesions is easy to identify and that this finding is useful in the detection of invasive colorectal cancers.

CT colonography, a technique for visualizing colorectal lesions using 3D volumetric data generated by helical CT, has developed rapidly over the past several years [1, 2]. This method has been reported to be useful for improving the diagnosis of colonic polyps and is now being considered for colorectal cancer screening in the United States [3, 4]. This potential has been markedly enhanced by the advent of MDCT, which allows acquisition of entire images of the colorectum during a single breath-hold [5]. A major merit of MDCT is its high acquisition speed that can be used to cover large volumes with thin collimation, resulting in good spatial resolution and reduction of the partial volume effect artifact [6]. The thinness of the reconstructed axial CT slices has allowed an increase in the image quality of CT colonography to depict colonic tumors more accurately. Furthermore, in contrast-enhanced studies with MDCT, the ability to scan through the entire abdomen in 20 sec or less means that data for the whole colon can be acquired within the time generally regarded as the arterial-dominant phase.

Detection of lesions on CT depends on lesion size, slice thickness, and contrast differentiation [7]. By means of Hounsfield-transparency settings, we obtained virtual endoluminal images that show vascular structures and delineate invasive cancers of the colorectal wall, called "vascular views," on contrast-enhanced MDCT colonography. Using this technique, we found that the increase in flow and pooling of blood related to angiogenesis of cancerous lesions is easy to identify and that this is useful in the detection of invasive colorectal cancers.

The purpose of this study was to assess the utility of vascular views for the visualization of invasive colorectal cancers on contrast-enhanced MDCT colonography.

Materials and Methods

From January to March 2002, 28 consecutive patients presenting with 30 invasive colorectal carcinomas underwent contrast-enhanced MDCT examinations at our hospital for preoperative staging. The series included 15 men and 13 women, ranging in age from 37 to 77 years (median, 60 years). Of these patients, 22 (78.6%) underwent MDCT after preoperative colonoscopic examinations with standard bowel preparation of up to 3 L of a polyethylene glycol–electrolyte solution, and the remaining six patients (21.4%) with advanced colorectal carcinomas underwent MDCT without preparation. Patients with rectal cancers underwent MDCT in the prone position, whereas a supine position was used for those with colon cancers. Before treatment, patients re-

Received October 22, 2003; accepted after revision August 10, 2004.

Supported in part by grants for Scientific Research Expenses for Health and Welfare Programs and the Foundation for the Promotion of Cancer Research and by the third-term Comprehensive 10-Year Strategy for Cancer Control from the Ministry of Health, Labor and Welfare.

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AJR 2005;184:1194–1198

0361–803X/05/1844–1194

ceived muscular injection of anticholinergic drugs, and room-air insufflation via the anus was performed just before each scan.

Pathologic diagnosis with endoscopic biopsy or surgically resected specimens was confirmed in each case. All colonic tumors had been initially diagnosed at colonoscopy, and the presence and site of the lesion were known at the time of the CT examination.

CT colonography was performed on an MDCT scanner (Aquilion, Toshiba Medical Systems). The scans were obtained through the abdomen and pelvis with the following parameters: 120 kV, 250–350 mA with automatic exposure control [8], 4 rows × 2-mm collimation, and helical pitch of 5 (pitch factor, 1.25). All patients received an IV bolus injection of 150 mL

Fig. 1.—Colonoscopic view and surface and vascular virtual endoluminal images for representative case of advanced colorectal cancer in 60-year-old woman.
A, Colonoscopic view shows advanced cancer in sigmoid colon.
B, Surface virtual endoluminal image shows lesion.
C, Vascular virtual endoluminal image clearly shows blood pooling of tumor and vessels (*arrow*) in colorectal wall.

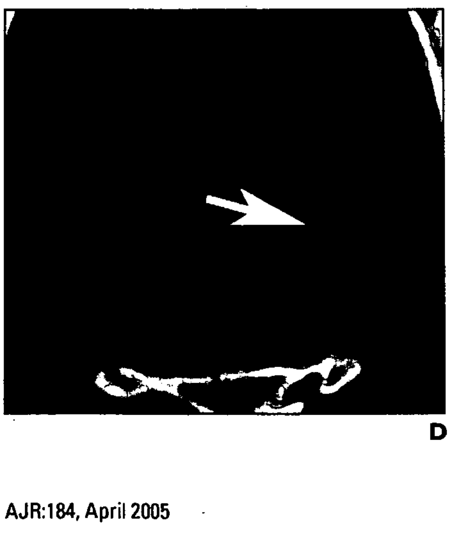


Fig. 2.—64-year-old man with colorectal cancer who underwent MDCT after colonoscopy.
A, Colonoscopic view shows small sessile lesion with central depression in lower rectum.
B, Surface virtual endoluminal image clearly shows lesion, although it is less than 2 cm in diameter.
C, Vascular virtual endoluminal image dramatically shows blood pooling of lesion in colorectal wall.
D, Axial MDCT image also shows lesion (*arrow*) as polypoid mass in insufflated rectum.

of iohexol 350 (Omnipaque, Daiichi Pharmaceutical) with a power injector at a rate of 3 mL/sec through a 20-gauge plastic IV catheter placed in an antecubital vein, and the whole abdomen was scanned 50 sec after this introduction of contrast material during the arterial phase. All images were reconstructed at a thickness of 1 mm, and the slices were transferred to an image workstation (M900/Pegasus, AMIN) for generation of 3D images of each patient.

We used virtual endoluminal images obtained with Hounsfield-transparency settings in MDCT colonography to show a surface or vascular view of the colorectal wall on a videotape monitor (Figs. 1–5). Hounsfield-transparency settings are based on Hounsfield units, which are the CT attenuation values. First, we adjusted the CT monitor's transparency and opacity setting to a value of 1 to display only the contour of the lumen and the mucosa. Next, we adjusted the transparency and opacity setting to a value of 2 to display only the arterial-dominant blood with contrast medium. Third, we adjusted the spatial parameters to display only to a depth of 3 mm surrounding the lumen and the mucosa, which corresponds to the thickness of the intestinal wall. Fourth, we overlaid the data displayed in steps one through three to produce a surface and vascular view of the colorectal wall, and then we reduced the surface opacity to produce an unobstructed vascular view.

The workstation was also equipped with navigation software for virtual colonoscopy, and the two types of virtual endoluminal images were displayed on the monitor. Two radiologists retrospectively evaluated primary lesions using the virtual endoluminal images with or without the Hounsfield-transparency settings—first, with a conventional surface view and then with a vascular view. Consensus interpretations were rated against all clinical information, including the results of colonoscopy; pathologic findings from biopsy and surgically removed specimens served as the gold standard.

Results

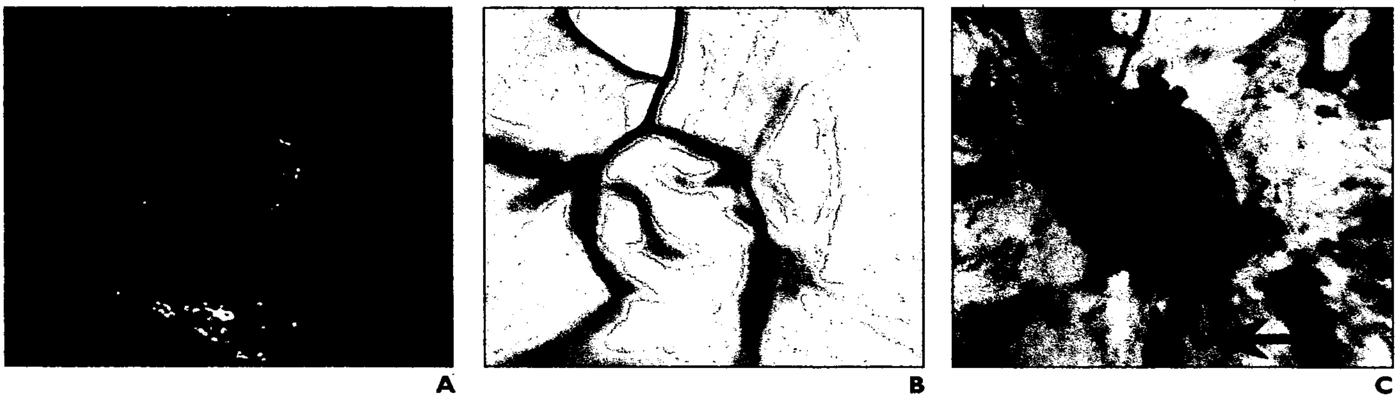
In the 28 patients, a total of 30 invasive carcinomas were confirmed by the preoperative colonoscopic examinations. Of the 30 lesions, 18 were in the rectum, five in the sigmoid colon, four in the transverse colon, and three in the ascending colon. The number of lesions over 2 cm in diameter was 21 (70.0%). Of the total, 19 (63.3%) were well differentiated and 11 (36.7%) were moderately differentiated on histologic diagnosis.

Lesions showing invasion limited to the submucosal layer were defined as early invasive colorectal cancer, whereas invasion farther than the submucosal layer was characterized as advanced colorectal cancer. Among the 30 lesions, 23 (76.7%) were advanced colorectal cancer lesions and seven (23.3%) were early invasive colorectal cancer lesions. Invasive lesions larger than 2 cm are generally of more advanced stage, but four (44.4%) of nine small lesions, 2 cm or smaller, were found to be advanced colorectal cancer.

Of the 30 confirmed cancerous lesions, 22 were revealed on conventional surface virtual endoluminal images, whereas 28 could be identified with vascular views (Table 1). The respective figures for lesions 2 cm or smaller were 44.4% (4/9) and 77.8% (7/9). Of lesions larger than 2 cm, three (14.3%) of 21 were missed on surface virtual endoluminal images,

TABLE 1 Detection of Colorectal Lesions Using Conventional Surface Versus Vascular Views for Virtual Endoluminal Imaging with Lesions Categorized by Size

Size of Lesion	No. (%) of Lesions Detected on Virtual Endoluminal Images	
	Conventional Surface View	Vascular View
≤2 cm	4/9 (44.4)	7/9 (77.8)
>2 cm	18/21 (85.7)	21/21 (100)
Total	22/30 (73.3)	28/30 (93.3)



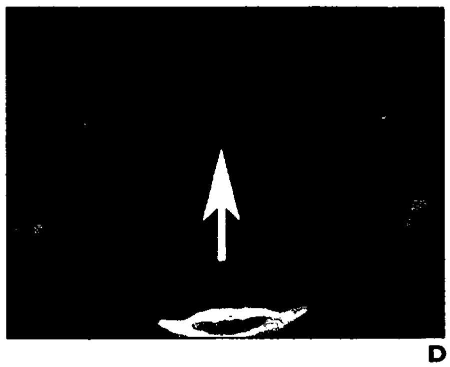


Fig. 3.—50-year-old man with colorectal cancer who underwent MDCT after colonoscopy.
A, Colonoscopic view shows irregularly shaped sessile lesion with central ulceration in lower rectum.
B, Surface virtual endoluminal image shows polypoid lesion.
C, Vascular virtual endoluminal image clearly depicts blood pooling and small vessels (*arrows*) in colorectal wall.
D, Axial MDCT image shows lesion (*arrow*) as enhanced mass in wall.

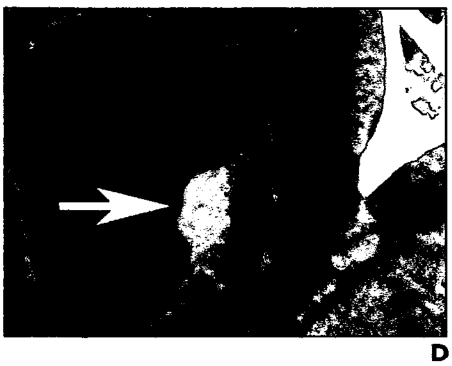


Fig. 4.—59-year-old man with colorectal cancer who underwent MDCT without preparation.
A, Colonoscopic view shows nodular protrusion in lower rectum.
B, It is hard to recognize lesion in residual stool (*arrows*) on surface virtual endoluminal image.
C, Vascular virtual endoluminal image successfully shows lesion as mass having blood pooling in colorectal wall.
D, Axial MDCT image shows lesion (*arrow*) as enhanced mass in colorectal wall.

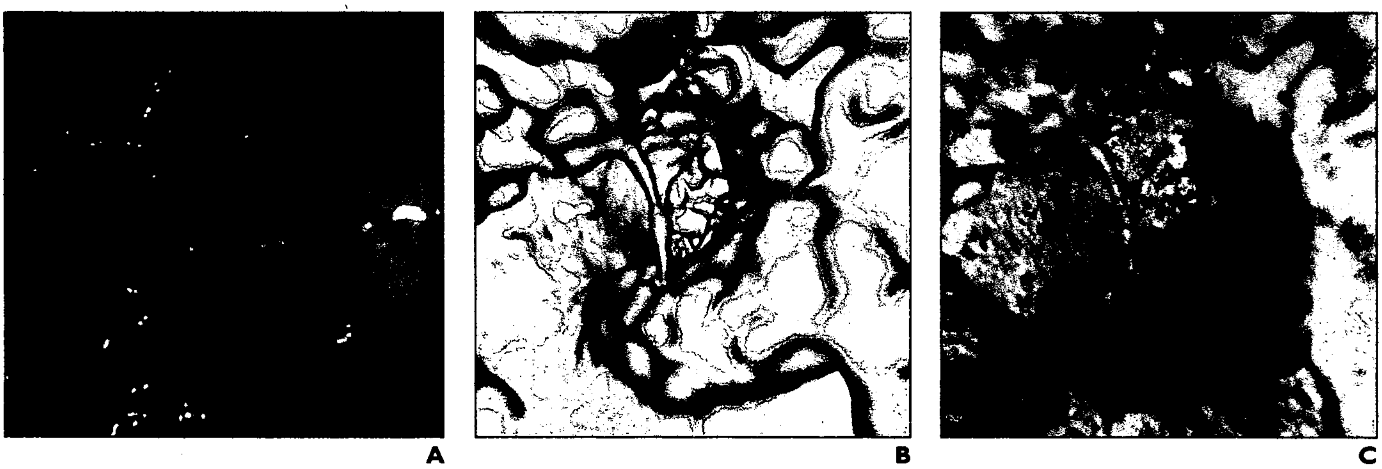


Fig. 5.—63-year-old man with colorectal cancer who underwent MDCT without preparation.
A, Colonoscopic view shows large mass with central ulceration in upper rectum.
B, Because of stool material, lesion cannot be identified on surface virtual endoluminal image.
C, Vascular virtual endoluminal image dramatically distinguishes lesion from stool.
D, Axial MDCT image shows lesion (*arrow*) as irregular thickening of rectal wall.

TABLE 2 Detection of Colorectal Lesions Using Conventional Surface Versus Vascular Views for Virtual Endoluminal Imaging with Lesions Categorized by Severity of Invasion

Severity of Colorectal Cancer	No. (%) of Lesions Detected on Virtual Endoluminal Images	
	Conventional Surface View	Vascular View
Early invasive		
With preparation	3/7 (42.9)	5/7 (71.4)
Advanced		
With preparation	17/17 (100)	17/17 (100)
Without preparation	2/3 (33.3)	6/6 (100)
Total	22/30 (73.3)	28/30 (93.3)

but all could be visualized on the vascular views. Invasive lesions larger than 2 cm are generally considered to have high potential for malignancy. However, even with the small lesions (≤ 2 cm), almost half were advanced colorectal cancers, so the use of the vascular approach allowed identification of most lesions that should be treated as a high priority (Table 1).

Of the 30 lesions, three of the seven early invasive colorectal cancer lesions were revealed on conventional surface virtual endoluminal images, whereas five of seven could be identified with vascular imaging. All 17 advanced colorectal cancer lesions in cases with preparation could be recognized on the surface and vascular virtual endoluminal images. This finding is especially noteworthy because among six advanced colorectal cancer lesions in patients without preparation, four (66.7%) were missed with the conventional surface approach, but all could be visualized on the vascular virtual endoluminal images (Table 2).

Discussion

Amin et al. [9] first described the merits of dynamic contrast-enhanced CT study with the air-insufflation technique for the detection of colorectal cancers. Subsequently, the same group reported the value of contrast-enhanced CT colonography for the improvement of colorectal polyp detection [10]. With contrast-enhanced CT studies, the advent of MDCT allows acquisition of images of the entire abdomen during a single breath-hold, which is regarded as the arterial-dominant phase. The resulting thinner-collimated transverse images with blood flow information provide better-quality MDCT colonographic data than conventional CT, and these data should further increase the ability to detect not only colonic polyps but also invasive lesions more accurately. In addition, we can manipulate the 3D volumetric data on an image workstation with navigation software for virtual endoscopy or with various display modes including Hounsfield-transparency settings, such as the vascular views, to show information about the blood flow within and around the colorectal wall.

With conventional surface virtual endoluminal images of CT colonography, a surface is just that—a surface. However, as shown in this study, pooling of blood related to angiogenesis of invasive cancers and small vessels of the colorectal wall can be more clearly visualized with vascular views of within the colorectal wall. With the introduction of 16-MDCT scanners, the image quality of virtual endoluminal images is expected to improve even further; therefore, vascular views are going to be more and more in demand not only by radiologists and gastroenterologists, but also by patients who, we believe, will be happy that vascular views require no preparatory fasting, because vascular views are not confused by the absence or presence of stool.

Vascular views also have a great potential for using blood flow information to detect small invasive cancers with computer-aided diagnosis, which is expected to improve radiologists' and gastroenterologists' diagnostic performance enormously [11, 12]. We therefore believe that a focus on the blood supply with the vascular views should be used in conjunction with conventional surface virtual endoluminal images whenever diagnostic or screening contrast-enhanced MDCT is performed until safer contrast media are developed.

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Diseases of the Colon & Rectum

Denervation of the Neorectum as a Potential Cause of Defecatory Disorder Following Low Anterior Resection for Rectal Cancer

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PURPOSE: The aim of this study was to determine whether denervation of the sigmoid colon during low anterior resection contributes to the postoperative motility characteristics of the neorectum and to the defecatory function of patients. METHODS: Sixty-seven patients who underwent either low or ultralow anterior resection for rectal cancer were evaluated. In accordance with the length of denervated neorectum, each patient was assigned to either the short-denervation or long-denervation group, determined by whether the inferior mesenteric artery was divided. Colonic propagated contraction was then measured by means of intraluminal pressure monitoring. Transit time was calculated with orally administered radiopaque markers. RESULTS: Propagated contraction down to the neorectum was significantly less common in the long-denervation group (14/36) than in the short group (12/15, $P < 0.05$), whereas spastic minor contraction at the neorectum was significantly more common in the long-denervation group (21/36) than the in short group (3/15, $P < 0.05$). Colonic transit time below the sigmoid colon was significantly longer in long group (6.4 hours) than in the short group (3.4 hours, $P < 0.01$). Although motility disorder of the neorectum was correlated with clinical defecatory malfunctions, including multiple evacuations, urgency, and soiling, no significant correlation was noted between the length of the denervated neorectum and the defecatory disorders. CONCLUSIONS: Motility of the neorectum following low anterior resection appears degraded by intraoperative maneuvers that cause denervation of the remnant sigmoid colon. Motility disorder of the neorectum, but not the length of the denervated neorectum causing the disorder, correlates well with several defecatory malfunctions. This finding suggests that postoperative defecatory disorder as a result of low anterior resection is caused by many factors in addition to denervation of the neorectum. [Key words: Rectal cancer; Low anterior resection; Defecatory function; Neorectum; Denervation; Motility disorder]

During standard low anterior resection (LAR) for rectal cancer, most of the rectum and some distal part of the sigmoid colon are removed along with accompanying vessels and nerve supplies during lymph node dissection. Because the healthy rectum and sigmoid colon are double innervated with ascending fibers from the pelvic plexus and descending fibers that run along the internal mesenteric artery (IMA),[1] the surgery-related maneuvers result in a denervated colonic segment of a length that varies from case to case (Fig. 1).

When the IMA is transected at its origin during removal of the specimen, most of the remaining sigmoid colon and the descending colon become a denervated colonic segment when the ascending fibers from the pelvic plexus and the descending fibers around the IMA are transected. In some cases, the

Supported in part by a grant-in-aid for Scientific Research from the Japanese Ministry of Education (#115591376) and a grant-in-aid from the Japanese Ministry of Health, Labor, and Welfare (#14-13).

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Dis Colon Rectum 2005; 48: 210–217
DOI: 10.1007/s10350-004-0814-6

Published online: 7 February 2005

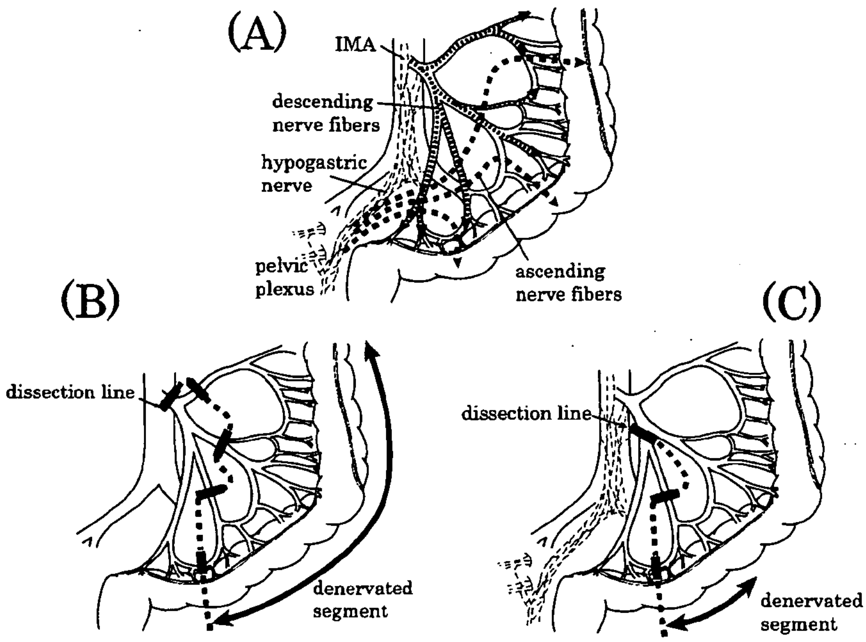

Figure 1. A. Innervation of healthy rectum and sigmoid colon. Both are double innervated with both ascending nerve fibers from the pelvic plexus and descending nerve fibers which run along the internal mesenteric artery (IMA). B. Long denervation of the neorectum when the IMA is transacted at its origin during removal of the specimen. C. Short denervation of the neorectum when the IMA and some sigmoid colon arteries are preserved together with the descending nerve fibers.

denervated colonic segment may be short if the IMA and some sigmoid colon arteries have been preserved along with the descending nerve fibers. However, the ascending nerve fibers originating from the pelvic plexus are always compromised (Figs. 1B, 1C). In most cases, the neorectum is reconstructed with the denervated sigmoid colon segment, thus the functionality of the neorectum may contribute to the patient's defecatory status following LAR for rectal cancer.

In the present study, we evaluated the correlation between motility characteristics and the length of the denervated neorectum to determine whether functional disorders of the neorectum contribute to postoperative defecatory status. Possible surgical maneuvers for LAR that preserve postoperative defecatory function are also discussed.

PATIENTS AND METHODS

Patients

Sixty-seven patients (35 men and 32 women; age range, 40–81 years; median age, 63 years) who underwent either LAR (n = 45) or ultralow anterior resection (n = 22) for middle or lower rectal cancer were enrolled in the present study. Informed consent was obtained from all patients. A colonic J-pouch of 6 to 7 cm in size was constructed with a side-to-side colocolic anastomosis by use of a linear stapler in 11 patients; 4 of these patients underwent pouch-anal anastomosis *via* the transanal handsewn method and the remaining 7 patients underwent a mechanical anastomosis with a circular stapler. A side-to-end anastomosis with a short stump was performed with a stapler in 18 cases and a straight end-to-end anastomosis by means of the double-stapling technique was performed in 38 cases. In this series, 11 patients received preoperative radiation therapy. The interval between initial surgery and postoperative physiologic study was one year in 31 cases (46 percent), two years in 10 cases (15 percent), and more than three years in 26 cases (39 percent) (Table 1).

Evaluation of Defecatory Dysfunction

Within one month before or after each examination, patients were interviewed with a self-administered questionnaire about their recent defecatory status. The patients were then categorized into groups according to the degree of defecatory dysfunction. The questionnaire consisted of 20 questions about bowel movement frequency, degree of urgency, multiple evacuations, and fecal soiling. Patients were first divided into three groups as follows: "severe urgency," in which a patient always or often could not defer defecation for ten minutes; "mild urgency," in which a patient only sometimes experienced such urgency; and "no urgency," in which a patient was always able to defer defecation for ten minutes. Next patients were divided into two groups

Table 1.
Patient Background and Length of Denervated Neorectum

Factor	Length of Denervated Neorectum Short (n = 17)	Long (n = 50)	*P* Value[a]
Gender			<0.05
Male	6	33	
Female	11	17	
Period from operation			<0.01
1 year	15	16	
2 years	0	10	
>3 years	2	24	
Operation method			NS
Low anterior resection	9	36	
Ultralow anterior resection	8	14	
Reconstruction			NS
End-to-end	4	34	
Side-to-end	10	8	
J-pouch	3	8	
Preoperative radiation			NS
Yes	1	10	
No	16	40	

NS = not significant.
[a]Chi-squared test.

on the basis of evacuation frequency as follows: "multiple evacuations," in which a patient needed to use the toilet more than three times an hour for completion of evacuation, and "negative multiple evacuations," in which a patient was able to evacuate each time satisfactorily with one or two toilet visits. Fecal soiling was categorized on the basis of previously reported criteria, which take into account the degree and frequency of incontinence,[2] as follows: "soiling," in which a patient experienced fecal incontinence with liquid stool more than once a month, and "negative soiling," in which a patient rarely or never experienced incontinence. In addition, patients also categorized their own defecatory status as excellent, good, fair, poor, or totally unsatisfactory.

Monitoring of Contraction Waves

A 3-mm-wide pressure transducer that consisted of four sensors 20 cm apart was specially manufactured. At the time of postoperative follow-up colonoscopy performed on patients who underwent low or ultralow anterior resection, the tip of the catheter was introduced up to the cecum. Following completion of the routine examination, the position of the catheter was adjusted under x-ray so that the fourth sensor was located inside the neorectum, which was approximately 10 cm from the anal edge. In most cases, the first sensor was located at the transverse colon, the second around the descending colon close to the splenic flexure, and the third around the sigmoid colon–descending colon junction. The catheter was then connected to a pressure amplifier (Nihon Koden Inc., Tokyo, Japan) and contractions of the colon were recorded as variations in intraluminal pressure. Patients were then asked to lie quietly for 30 to 60 minutes to monitor colonic motility. Waves with high amplitude (≥20 mmHg) of more than ten seconds in duration were regarded as contraction waves. Contraction waves that originated at sensor 1 or 2 and propagated accordingly down to the neorectum (sensor 4) were called "propagated waves." When there was at least one propagated wave seen during the examination period, the patient was allocated to the positive propagated-wave group. The monitoring of contractions was successfully performed in 51 patients from whom consent was obtained.

Calculation of Transit Time

Colonic transit time was determined in 48 patients by means of Sitzmarks capsules (Konsyl Pharmaceuticals Inc., Fort Worth, TX), which consist of 20 radiopaque markers within a gelatin capsule. On three consecutive days, a Sitzmarks capsule was taken with water after dinner. On Day 4, two flat-plate abdominal x-rays were taken of the patient in the supine and upright positions. From one day before to the day of completion of the examination, patients were asked not to take laxatives or other medicines that might affect intestinal motility. Segmental colonic transit time was calculated with the computerized Sitzmarks Analysis Program (Kaigen Inc., Osaka, Japan), which is based on Arhan *et al.*'s theory.[3] In this theory, the number of markers that pass through one intestinal point exhibits a bell-shaped distribution curve. By measuring the total time for all radiopaque markers to pass each colonic segment, the mean passage time in the corresponding colonic segment was calculated. The transit times of the ascending colon, transverse colon, descending colon, and neosigmoid colon and neorectum were calculated.

Statistical Analysis

Continuous variables were analyzed with the Student's *t*-test. Categoric variables were analyzed with the chi-squared test. Ordered categories were ana-

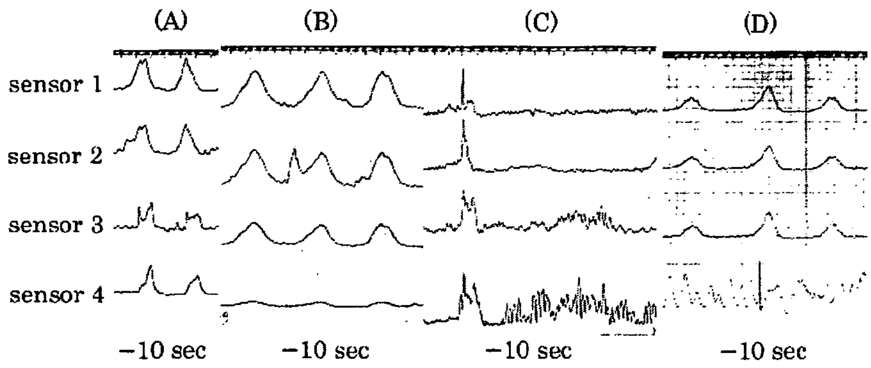

Figure 2. Pattern of contraction waves seen in patients who underwent low or ultralow anterior resection for rectal cancer. A. Typical propagated contraction waves down to the neorectum (sensor 4, n = 17). B. Vanished propagated waves at the neorectum (n = 9). C. Propagated waves followed by minor spastic waves (n = 9). D. Minor spastic waves without any propagated waves (n = 16).

lyzed with Wilcoxon's signed-rank test. All statistical calculations were performed by means of the SPSS® program (SPSS, Inc., Chicago, IL) under the direction of a statistician. A P value of <0.5 was considered to indicate statistical significance.

RESULTS

Length of Denervated Neorectum

Of the 67 patients, the IMA was divided at its origin in 35 patients with advanced-stage tumor and N2 (more than 3) lymph node metastases suspected either preoperatively or intraoperatively. In another 15 patients with N1 (1 to 3) lymph node metastases suggested, the IMA was preserved but the surrounding tissue was removed for lymph node dissection. In 50 patients, the descending nerve fibers that otherwise would have serviced the neorectum were compromised during lymph node dissection. Thus, the neorectums of these 50 patients were composed of long denervated segments of sigmoid colon (the long-denervation group; Fig. 1B). In contrast, in the remaining 17 patients without any lymph node metastases diagnosed preoperatively or intraoperatively, the superior rectal artery was divided at its origin, thereby preserving the descending nerve fibers that service the neorectum. The descending nerve fibers along with the IMA and several sigmoid colon arteries were preserved in these patients (the short-denervation group; Fig. 1C). Table 1 summarizes patients' characteristics based on the theoretical length of the denervated neorectum. Male patients who had received the operation more than three years ago tended to have a long denervated neorectum.

Pattern of Colonic Motility After Low Anterior Resection

Of the 67 patients, colonic motility was measured in 51 cases by a pressure transducer. Figure 2 summarizes the pattern of colonic contractions following LAR. In this examination, we focused on two major findings: existence of strong propagated contractions down to the neorectum (sensor 4), and existence of spastic minor waves in the neorectum (sensor 4; Fig. 2). Contraction waves were categorized and detected as follows: Type A, strong contraction waves that propagated down to the neorectum without any spastic waves, found in 17 patients; Type B, strong contractions that diminished at the neorectum and were not associated with spastic waves, found in 9 patients; Type C, strong contractions accompanied by spastic-waves at the neorectum, found in 9 patients; and Type D, spastic waves only irregularly seen at sensor 4 without any propagated waves, found in16 patients.

Segmental Colonic Transit Time and Colonic Motility

The mean segmental colonic transit time in relation to propagated contraction down to the neorectum is summarized in Table 2. The transit time at the neosigmoid colon or neorectum was longer (with marginal statistical significance) in patients who did not have propagated contraction waves down to the neorectum (Type B or Type D) than in patients who had propagated contractions (Type A or Type C). No other difference in transit time was observed at any other colonic segment among the various motility patterns; spastic waves did not correlate with segmental colonic transit time (data not shown).

Table 2.
Mean Segmental Colonic Transit Time in Relation to Propagated Contraction Waves

	Mean Transit Time (hours)		
Colonic Segment	Positive Propagated Contractions (n = 14)	No Propagated Contractions (n = 18)	*P* Value[a]
Ascending colon	12.9 ± 9.6	13.1 ± 5.4	NS
Transverse colon	8.7 ± 4.2	8.6 ± 5.9	NS
Descending colon	4.3 ± 3.5	5.9 ± 4.6	NS
Sigmoid colon/neorectum	3.7 ± 2.1	6.5 ± 5.0	0.06
Total	29.7 ± 8.8	34.5 ± 10.8	NS

NS = not significant.
[a]Student's *t*-test.

Length of Denervated Neorectum and Colonic Motility

Monitoring of colonic contraction with a pressure transducer revealed that 12 of 15 patients (80 percent) who belonged to the short-denervation group had propagated contraction waves (Types A and C; Fig. 2), which was a significantly higher percentage than that seen in the long-denervation group (38.9 percent; $P < 0.01$; Table 3).

In contrast, 21 of 36 patients (58.3 percent) in the long-denervation group showed spastic waves at the neorectum (Types C and D; Fig. 2) irrespective of the existence of propagated contraction waves, which was a significantly higher percentage than that seen in the short-denervation group (20 percent; $P < 0.05$; Table 3).

The mean transit time in relation to length of the denervated neorectum is summarized in Table 4. The transit time at the neosigmoid colon or neorectum was greatly prolonged in patients with a long denervated neorectum. In contrast, the transit time at the transverse colon was only slightly prolonged in patients with a short denervated neorectum.

Motility of Neorectum and Defecatory Function

Table 5 summarizes the correlation between colonic contraction pattern and defecatory disorders. The loss of propagated contraction correlated well with urgency and slightly with multiple evacuations. There was no correlation seen between propagated contraction and soiling. By contrast, spastic minor contractions in the neorectum correlated significantly with several major defecatory disorders, specifically urgency, multiple evacuations, and major soiling ($P < 0.01$). The loss of propagation and occurrence of spastic minor contractions in the neorectum also correlated with patients' self-assessment of bowel function. The majority of patients who did not have a spastic neorectum (24/26) and most patients with propagated waves (23/26) replied that theirfunction was either satisfactory or fair.

Length of Denervated Neorectum and Defecatory Functions

Table 6 summarizes the correlation between length of the denervated neorectum and clinical defecatory disorders seen in patients. Patients with a long denervated neorectum tended to have multiple evacuations; however, the difference did not reach statistical significance.

DISCUSSION

Functional disorders in defecation following LAR for rectal cancer have often been discussed as postoperative sphincter malfunctions. Manometric studies have revealed that anal resting pressure and maximum squeeze pressure are both degraded following surgery,[4] with reduced anal sensation[5] or reduced physiologic rectoanal inhibitory reflex.[6] These sphincter malfunctions may be caused by direct injury during surgery[7] or be a result of denervation to the internal sphincter,[8] which is controlled by the hypogastric nerve.[9] In addition to postoperative malfunction of the sphincter, compliance of the neorectum constructed at the LAR is also reported to contribute to postoperative defecatory function,[10] although low compliance may recover with time, unlike damage to the anal sphincter.[11] Similarly, the volume[12] and diameter[13] of the neorectum have been reported to correlate with postoperative bowel functioning.

More recently, efforts have been made to evaluate

Table 3.
Length of Denervated Neorectum and Colonic Contraction Pattern

	Contraction Pattern of Neorectum			
	Pattern A	Pattern B	Pattern C	Pattern D
Long denervation (n = 36)	8	7	6	15
Short denervation (n = 15)	9	2	3	1

Table 4.
Mean Colonic Transit Time in Relation to Length of Denervated Neorectum

	Mean Transit Time (hours)		
Colonic Segment	Short-Denervation Group (n = 11)	Long-Denervation Group (n = 37)	*P* Value
Ascending colon	12.4 ± 6.7	13.4 ± 7.1	NS
Transverse colon	11.7 ± 5.3	8.6 ± 5.9	<0.05
Descending colon	4.9 ± 3.4	6.6 ± 5.3	NS
Sigmoid colon/ neorectum	3.4 ± 1.6	6.4 ± 5.4	<0.01
Total	30.1 ± 7.4	34.4 ± 11.1	NS

NS = not significant.

Table 5.
Colonic Contraction Pattern and Defecatory Disorders

	Propagated Contractions			Spastic Neorectum		
	Yes (n = 26)	No (n = 25)	*P* Value	Yes (n = 25)	No (n = 26)	*P* Value
1) Urgency			<0.01[a]			<0.01[a]
None	16	8		7	17	
Mild	9	12		12	9	
Severe	1	5		6	0	
2) Multiple evacuations			<0.05[b]			0.01[b]
Yes	8	16		17	7	
No	18	9		8	19	
3) Major soiling			NS[b]			<0.01[b]
More than sometimes	4	6		9	1	
Almost none	22	19		16	25	
4) Patients' self-assessment of defecation			<0.01[a]			<0.01[a]
Excellent	7	5		2	10	
Good	11	11		11	11	
Fair	5	2		4	3	
Poor	3	6		7	2	
Unsatisfied	0	1		1	0	

NS = not significant.
[a]Wilcoxon's signed-rank test.
[b]Chi-squared test.

the motility of the neorectum. Oya *et al.* reported that the time-activity curve of evacuation seen in cases of a neorectum closely correlated with postoperative bowel functions following anterior resection.[14] Seike *et al.* showed that patients who complain of evacuation difficulty postoperatively tend to have a high volume of left-sided colon gas, which suggests a motility disorder at the neosigmoid or neorectum.[15] In healthy individuals who have not undergone any surgery, rectal function has been reported to play a major role in fecal continence[16] and chronic constipation.[17]

In the present study, we evaluated the dynamic motility characteristics of the neorectum in conjunction with motility of the oral colonic segments to determine if collaborative movements of the postoperative residual colon correlate with evacuative malfunction following LAR. We found that the propagated contraction waves that originated from the up-

Table 6.
Length of Denervated Neorectum and Defecatory Disorders

	Length of Denervated Neorectum		
	Long (n = 50)	Short (n = 17)	*P* Value
1) Urgency			NS[a]
None	20	10	
Mild	21	7	
Severe	9	0	
2) Multiple evacuations			0.07[b]
Yes	27	5	
No	23	12	
3) Major soiling			NS[b]
More than sometimes	12	2	
Almost none	38	15	
4) Patients' self-assessment of defecation			NS[a]
Excellent	8	5	
Good	19	9	
Fair	11	2	
Poor	11	1	
Unsatisfied	1	0	

NS = not significant.
[a]Wilcoxon's signed-rank test.
[b]Chi-squared test.

per part of the colon disappeared at the neorectum in 25 of 51 patients (Fig. 1). The loss of propagation at the neosigmoid colon or neorectum seemingly correlated with the tardiness of transit in that part of the bowel. Clinically, most patients who showed a loss of propagating waves also experienced multiple evacuations and urgency, which suggests that their evacuation each time was incomplete because of a motility disorder of the neorectum. We would like to emphasize that the patients who showed loss of propagating waves predominantly had a long denervated neorectum, in which the IMA was either divided or its surrounding tissue was removed for lymph node dissection at the time of surgery (Table 3).

The other important finding regarding contraction pattern was the existence of spastic minor contractions at the neorectum. Although having a spastic neorectum did not correlate with segmental transit time, a spastic neorectum was very closely associated with clinical symptoms such as multiple evacuations, urgency, and major soiling. Importantly, spastic contraction was more commonly seen in patients with a long denervated neorectum (Table 3). This finding suggests that denervation of the neorectum during surgery may be a causative factor of the spastic neorectum and of the loss of contraction waves to the neorectum.

The long denervated neorectum, which is the result of dissection of the IMA or its surrounding tissue, may cause motility disorders in the neorectum constructed during LAR for rectal cancer. No significant correlation was noted between the length of the neorectum and the manifestation of defecatory disorders, which suggests that many other factors also contribute to postoperative defecatory function. Denervation to the neorectum may be one factor that indirectly relates to and exerts influence on postoperative function. Therefore, IMA and the surrounding nerve fibers should be preserved whenever feasible. Further study is warranted to elucidate the influence of IMA dissection on functional outcome for defecation. In addition, a time-course study is needed to investigate whether these motility disorders will recover with time, given that patients' clinical symptoms sometimes gradually improve.

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特集　最新　直腸癌手術

新しい肛門温存術
—Total Intersphincteric Resection—

白水和雄*　緒方　裕**　荒木靖三**

はじめに

肛門にきわめて近い下部直腸癌や肛門管癌に対する手術法は，腹会陰式直腸切断術が一般的であるが，最近，このような癌に対しても，肛門管へメスを入れて内外の肛門括約筋間を剝離しながら内肛門括約筋（内括約筋）を切除するintersphincteric resection（以下，ISR）が試みられている[1)~6)]。この術式は従来の経肛門吻合術（CAA；coloanal anastomosis）[7)8)]と異なり歯状線を含めて肛門管を全摘する新しい術式であるために，その手術方法には，これまでどんな成書にも記載されていない特殊な技術やコツが要求される。本書では，肛門管癌に対して内括約筋を全切除するtotal intersphincteric resectionについて実際の手術の写真を紹介し，手術方法について解説する。

I. 手術術式

直腸の剝離は前後壁，側壁とも通常の低位前方切除術と同じであるので，簡単に述べる。

1. 直腸後壁の剝離

直腸後壁は仙骨前面の静脈叢を損傷しないように注意深く行う。仙骨前面の静脈叢が薄い膜1枚で覆われていれば，正しい剝離層である。Waldeyer筋膜を穿破して肛門挙筋を十分に露出する。

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2. 直腸前壁，側壁の剝離

Total intersphincteric resectionを施行するには，直腸前壁の剝離が重要である。まず腹膜翻転部を切開し，Denonvilliers筋膜を直腸壁につけて剝離する。男性では精嚢・前立腺，女性では腟後壁を露出する。直腸前壁の無理な剝離は止血に難渋し，出血量を増加させることになるので細心の注意を要する。ついで，精嚢・腟後壁の剝離層を直腸の両側に延長し，直腸側壁にある膀胱直腸間隙を鋏で押し広げながら開窓する。この時点で，直腸は側方靱帯で固定された状態となり，この靱帯を切離すると，挙筋前腔が開大し肛門挙筋が十分に露出され，前壁の剝離がさらに可能となる。注意深く行えば男性でも女性でも歯状線近傍まで前壁の剝離が可能である。

3. 肛門管の剝離

この手術における独特の剝離法である。肛門挙筋を十分に露出したのち，6時方向に注目する。この方向が肛門管への入り口の突破口である。図1に示すように，6時方向の尾骨直腸靱帯を肛門挙筋から切離し，この切離部を腸ベラ（鉤）で腹側に圧排すると，肛門管の後壁が露出される。ついで図2に示すように，肛門管の後壁から側壁にかけて，肛門挙筋と直腸縦走筋の間をツッペルや電気メスを使用しながら，注意深く肛門側に向かって剝離する。この操作はきわめてむずかしく，肛門管癌の場合には剝離層が内側に入り過ぎると，外科的剝離面に癌が遺残する。下部直腸癌のように遠位側断端の距

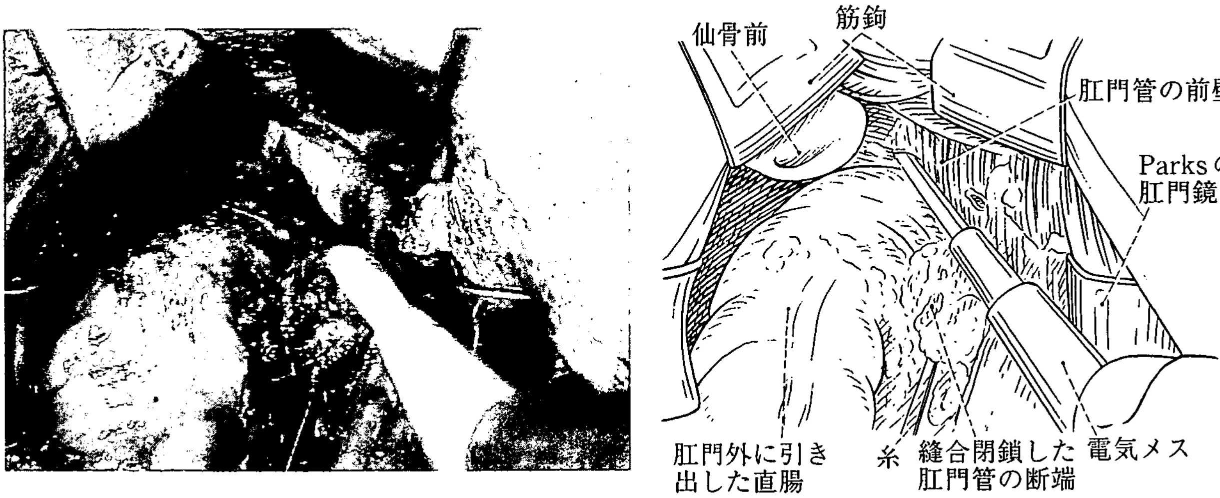

図 7　肛門管前壁の剝離
腹会陰式直腸切断術の要領で肛門管の前壁を剝離する。

図 8　J 型結腸囊（-またはストレート型結腸）・肛門吻合
6，12 時方向で肛門皮膚粘膜，皮下外肛門括約筋，結腸全層の順で 4-0 バイクリル糸をかけ，折り返し結腸粘膜と肛門皮膚粘膜のマットレス縫合を行う。3，9 時方向も同様に行い，4 点縫合を施行する。

直腸引き出し法”と名づけたが[5)]，この手術を容易ならしめる重要で簡単な操作である。肛門管が 4/5 周性に切除されているため直腸を十分に肛門外に引き出すことが可能で，また直腸前壁が blind にならず容易に観察できる。ついで図 7 に示すように，腹会陰式直腸切断術の要領で肛門管の前壁を剝離する。男性では前立腺後壁を，女性では膣後壁を切離すると直腸を完全に摘出できる。前立腺や膣後壁の剝離の際に出血をみることがあるが，視野が十分なため容易に止血可能である。

5．経肛門的結腸肛門吻合

J 型結腸囊肛門吻合あるいは，結腸肛門端々吻合（ストレート）を施行する。結腸を肛門側に引き出し，図 8 に示すように，まず 6 時，12 時方向で肛門皮膚粘膜，皮下外肛門括約筋，結腸全層の順で 4-0 バイクリル糸をかけ，折り返し結腸粘膜と肛門皮膚粘膜のマットレス縫合を行う。3，9 時方向も同様に行い，4 点縫合を施行する。ついで，4 点縫合部の両隣を縫合する。そのつど結紮しておくとあとの操作が容易である。糸は切らずに支持糸とする。12 針縫合が終了したのち，支持糸を牽引し肛門全体を眺めながら，間隙のある不十分な箇所を追加縫合する。図 9 に示すように，合計で 16～20 針程度縫合し吻合が完了する。20 針以上縫合すると肛門狭窄の原因となるので注意を要する。

II．内括約筋切除症例

術前の注腸造影は，図 10 a に示すように下部直腸肛門管癌（Rb-P）を示す。切除標本では図 10 b に示すように，腫瘍は 2 型を呈し，

腫瘍下縁は歯状線から1cmの距離に存在する。歯状線は全周性に切除され，肛門側断端の距離は十分に確保されている。病理所見は，図10cに示すように腫瘍は深達度mpの癌で，歯状線を含めて内括約筋切除が完璧に施行されており，外科的剥離面に問題はない。

おわりに

内括約筋合併切除による結腸肛門吻合術は新しい肛門温存術式である。従来の経肛門的直腸切除・吻合術（経肛門吻合術）が歯状線を温存し，あるいは歯状線の直上で内肛門括約筋を部分切除する術式であるのに対し，この術式は歯状線を含めて内括約筋を全摘するものである。従来の経肛門吻合術に比べ，より低位の下部直腸癌や肛門管癌に本術式が適応可能である。第1のポイントは，腹腔内から肛門管への突破口である尾骨直腸靱帯を切離する。第2のポイン

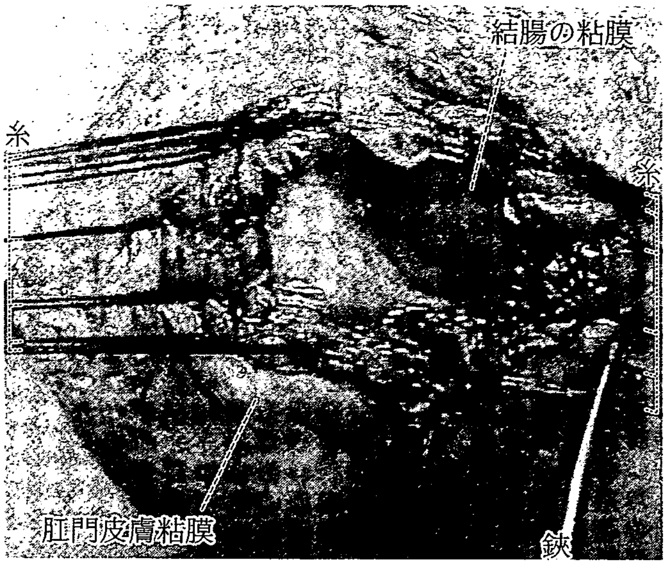

図9　吻合完了
16～20針程度縫合し吻合が完了する。

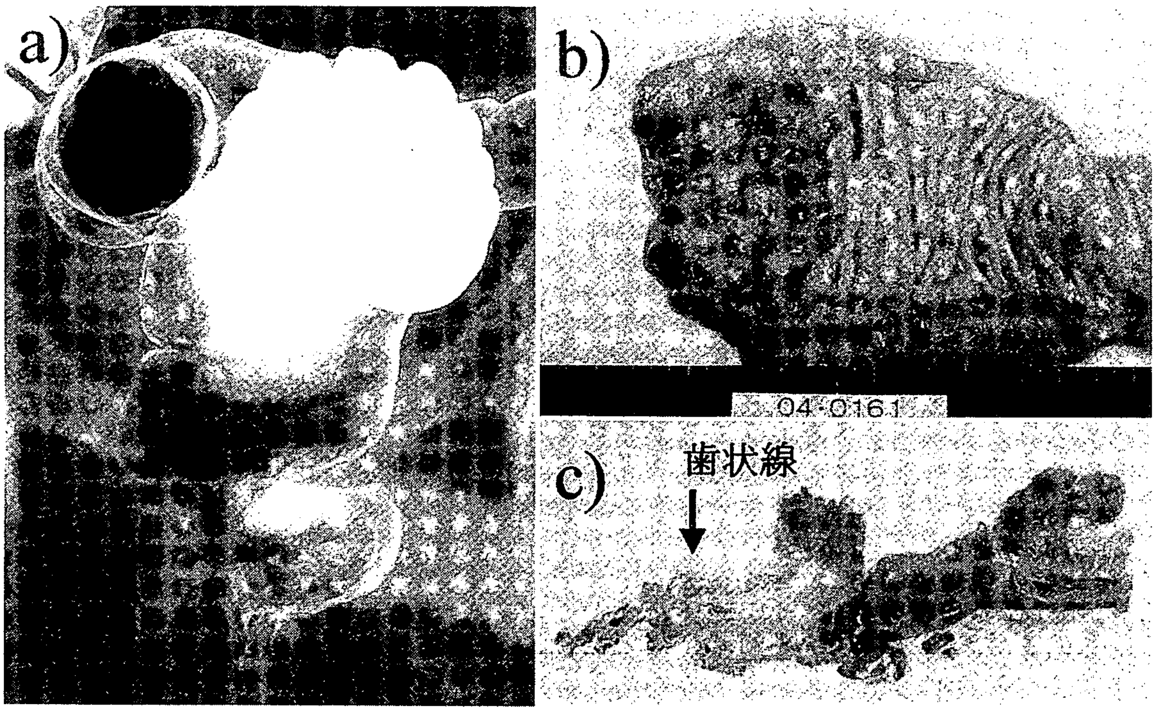

図10　内括約筋切除症例
a）注腸造影で下部直腸癌（Rb-P）を示す。　b）切除標本を示す。
c）病理所見で腫瘍は内括約筋に止まる深達度mpの癌である。歯状線を含めて内括約筋が完璧に切除され，外科的剥離面に問題はない。

トは，経肛門的操作において前壁以外の括約筋間溝を4/5周性に切開する。第3のポイントは，肛門管切離断端を埋没縫合したのち，Parksの肛門鏡を仙骨前に挿入しなおす。第4のポイントは，肛門外に直腸を引き出すことである。

また，本術式の適応は厳密に決定されなければならない。癌の浸潤が筋層を越えて外括約筋に及ぶ場合には，本術式では癌遺残の危険性が残るため適応外であり，外括約筋を含めた内外括約筋切除術が施行されなければならない[9]。癌の浸潤が筋層を超えないSM癌やMP癌に対しては，腫瘍学的にみても十分な根治性が得られると考えられ[10]，本術式のよい適応と思われる。

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Feasibility of autonomic nerve-preserving surgery for advanced rectal cancer based on analysis of micrometastases

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Background: Autonomic nerve preservation has been advocated as a means of preserving urinary and sexual function after surgery for rectal cancer, but may compromise tumour clearance. The aim of this study was to determine the incidence of micrometastasis in the connective tissues surrounding the pelvic plexus.

Methods: The study included 20 consecutive patients who underwent rectal surgery with bilateral lymph node dissection for advanced cancer. A total of 78 connective tissues medial and lateral to the pelvic plexus and 387 lymph nodes were sampled during surgery. All connective tissue samples and 260 lymph nodes were examined for micrometastases by reverse transcriptase–polymerase chain reaction (RT–PCR) after operation. All patients were followed prospectively for a median of 36·0 months.

Results: Of 245 histologically negative lymph nodes, 38 (15·5 per cent) were shown by RT–PCR to harbour micrometastases. However, micrometastases to tissues surrounding the pelvic plexus were detected in only two (3 per cent) of 78 tissues, that is in two of 20 patients. Clinical follow-up showed that the two patients had a poor prognosis owing to distant metastases.

Conclusion: Autonomic nerve-preserving surgery may be feasible for advanced rectal cancer, but study of more patients positive for micrometastases is required.

Paper accepted 20 June 2005
Published online 26 September 2005 in Wiley InterScience (www.bjs.co.uk). **DOI:** 10.1002/bjs.5141

Introduction

The complex flow patterns of lymphatic fluid around the rectum were investigated in 1951 by Sauer and Bacon[1]. They regarded the lateral ligament as the tissue in which the inflow of lymphatic fluid from the rectum first occurs *en route* to the internal iliac artery. However, the high incidence of urinary and sexual dysfunction after rectal cancer surgery gradually led surgeons to realize that the lateral ligament plays an important role in postoperative urinary and sexual function[2]. The pelvic autonomic nerve system is comprised of the superior hypogastric plexus, hypogastric nerves, pelvic plexus (inferior hypogastric plexus) and pelvic splanchnic nerves[3]. The lateral ligament of the rectum consists of a neurovascular bundle derived from the combined redistributing sympathetic and parasympathetic nerves of the system, and dissection injury to these nerves may cause problems.

Inclusion of total mesorectal excision (TME) in rectal cancer surgery can improve the rate of cure[4]. Dissection of the rectum at the layer of TME allows preservation of the pelvic autonomic nerves, reducing postoperative urinary and sexual morbidity[5–7]. Extensive pelvic lymphadenectomy involving resection of both pelvic autonomic nerves and lateral lymph nodes was employed in Japan from the 1970s to the early 1980s with the aim of reducing local recurrence of rectal cancer[8]. However, postoperative urinary and sexual dysfunction invariably ensued, leading to marked reduction in quality of life. More recently, efforts have been made to preserve urinary and sexual function and to achieve local control of cancer, by a combination of autonomic nerve-preserving surgery and lateral lymph node dissection[9–12].

Recent pathological studies have warned against autonomic nerve preservation because histologically proven cancer foci might exist in the autonomic nerves and surrounding connective tissues, and lead to local recurrence[13,14]. To aim of the present study was to examine the incidence of micrometastases in the region of the pelvic plexus by reverse transcriptase–polymerase chain reaction (RT–PCR) analysis, which is more sensitive than conventional histological diagnosis[15,16].

Patients and methods

The study included 20 consecutive patients who underwent rectal cancer surgery with bilateral lymph node dissection at the Graduate School of Medicine, Osaka University between October 1999 and May 2001. Demographic data are shown in *Table 1*. Tumours were located 0–10 (median 6·5) cm above the anal verge and diagnosed before surgery as advanced cancer (T2,T3 and T4)[17]. The operative procedures are summarized in *Table 1*. Curative resection was performed in all patients. Tumour stages determined by postoperative histological examination are shown in *Table 1*[17]. Two patients with lateral node metastasis without distant organ metastasis were included in stage III (*Table 2*). Nine patients with stage III or IV tumours were treated with 5-fluorouracil-based chemotherapy but none had radiation therapy. The patients were reviewed at least every 3 months after operation with blood tests such as measurement of carcinoembryonic antigen (CEA), and underwent computed tomography (CT) or magnetic resonance imaging (MRI) every 6 months. The study protocol was approved by the Human Ethics Review Committee of Osaka University Graduate School of Medicine and a signed consent form for the study was obtained from each patient.

All patients underwent radical resection with autonomic nerve preservation and lymph node dissection[11]. The following is a brief description of the surgical procedures, with schematic presentation in *Fig. 1*, focusing on the collection of specimens. After isolating the sigmoid colon, the mesorectum was dissected from the parietal fascia of the sacrum at the layer of TME to preserve the hypogastric nerves, and the medial side of the pelvic plexus was exposed. At this stage, the connective tissues of the medial and lateral sides of the pelvic plexus were meticulously sampled taking care not to injure the plexus, with four specimens being obtained from each patient. However, if the tumour had macroscopically infiltrated the pelvic plexus, only tissue from the lateral side was collected because the infiltrated pelvic plexus was dissected *en bloc* with the tumour. The specimens were promptly frozen in liquid nitrogen and stored at −70°C pending RNA extraction. A total of 78 connective tissues were obtained from 20 patients (*Table 2*).

After removing the tumour and performing lateral node dissection, the lymph nodes were sampled from the mesorectum and the lateral area along the internal iliac artery and the obturator nerve outside the boundaries of TME (*Fig. 1*). In 12 patients, each of the 260 lymph

Table 1 Clinical characteristics of patients

Median (range) age (years)	63·5 (35–92)
Sex ratio (M : F)	15 : 5
Surgical procedure	
Low anterior resection	9
Abdominoperineal resection	7
Hartmann resection	3
Total pelvic exenteration	1
Autonomic nerve preservation	
Bilateral	18
Unilateral	2
TNM stage	
I	4
II	7
III	6
IV	3
Histological type	
Well differentiated	1
Moderately differentiated	16
Poorly differentiated	2
Mucinous	1
Tumour location (cm)*	
<6	9
≥6	11

*Distance from anal verge. TNM, tumour node metastasis.

Table 2 Metastasis to lymph nodes and tissues surrounding pelvic plexus

		Site of metastasis			Survival at 1 year	
TNM stage	No. of patients	Upper lymph nodes (HE)	Lateral lymph nodes (HE)	Tissues surrounding pelvic plexus (micrometastases)	Relapse free	Overall
I	4	0	0	0 (16)	4	4
II	7	0	0	0 (28)	6	7
III	6	6	2	0 (24)	5	6
IV	3	3	3	2 (10)	0	0

Values in parentheses are number of tissues; HE metastasis detected by histological examination with haematoxylin and eosin staining. TNM, tumour node metastasis.

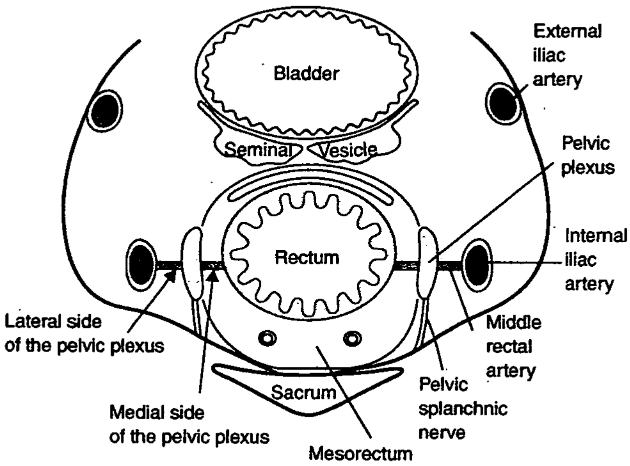

Fig. 1 Schematic presentation of the pelvic autonomic nerve system and connective tissues surrounding the pelvic plexus. The connective tissues comprise fat and lymphatic vessels including the middle rectal artery. The medial tissue is equivalent to the lateral ligament and the lateral tissue is located outside the boundaries of total mesorectal excision, between the plexus and internal iliac artery

node samples was halved, with one part being subjected to conventional histological diagnosis and the other being frozen in liquid nitrogen and stored at −70°C until extraction of RNA. In the other eight patients, 127 samples were collected and subjected to histological diagnosis only.

Total RNA was extracted by a single-step method as described previously[18]. Complementary DNA was generated with avian myeloblastosis virus RT using the procedure outlined by the supplier (Promega, Madison, Wisconsin, USA). *CEA* and *cytokeratin 20* (*CK-20*) transcripts were used as sensitive markers for micrometastases, and *phorphobilinogen deaminase* (*PBGD*) transcript was used to check for the presence of mRNA in samples[15]. PCR products were analysed by electrophoresis on 2 per cent agarose gels stained with ethidium bromide. The reproducibility of cDNA products was checked by repeated RT–PCR and gel electrophoresis. The sensitivity of PCR was determined by detecting *CEA* and *CK-20* transcripts in serial dilutions of a human colonic cancer cell line (HT29) mixed with human lymphocytes; the detection sensitivity was 100 HT29 cells among 10^6 lymphocytes.

Results

The presence of *PBGD* products was confirmed in all 78 connective tissue specimens and 260 lymph nodes examined for micrometastases by RT–PCR. The diagnosis was positive if bands specific for *CEA* or *CK-20* were present[15].

The 260 lymph nodes were collected from 12 patients (median 22 per patient). The appearance of both *CEA* and *CK-20* mRNAs was verified in all 15 histologically positive lymph nodes. Of the 245 histologically negative lymph nodes, 38 (15·5 per cent) harboured micrometastases (*Table 3*).

Metastases were identified histologically in the upper lymph nodes within the mesorectum in nine of 20 patients, and in the lateral lymph nodes along the internal iliac artery and the obturator nerve in five of 20, suggesting that many patients had very advanced cancer. Direct tumour invasion into the right or left pelvic plexus was observed macroscopically in two patients with stage IV disease. The pelvic plexus on the affected side was therefore resected *en bloc* with the tumour, whereas that on the other side was preserved.

Eighteen of 20 patients had neither *CEA* nor *CK20* mRNA in the four connective tissues surrounding the bilateral pelvic plexus. Two of three patients with stage IV disease were positive for both *CEA* and *CK20* mRNA in the lateral tissue from the resected pelvic plexus, but all other tissues surrounding the preserved pelvic plexus were negative. Micrometastases were identified in two (3 per cent) of 78 samples of connective tissue surrounding the pelvic plexus, that is in two of 20 patients (*Table 2*). All five patients with lateral node metastasis had metastasis to the upper lymph nodes, but only two had micrometastases to the connective tissues surrounding the pelvic plexus.

Median follow-up after surgery was 36·0 months. By 1 year after surgery, five of 20 patients had developed local recurrence or distant metastases, despite undergoing curative surgery and postoperative chemotherapy, and three had died from cancer (*Table 2*). Of three patients with pelvic recurrence, one patient showed relapse in the lateral area of the pelvis despite lateral node dissection, and two patients developed recurrent tumour in the rectum after a Hartmann's procedure. The autonomic

Table 3 Lymph node metastases detected by reverse transcriptase–polymerase chain reaction and histological examination with haematoxylin and eosin staining

	RT-PCR		
	Positive	Negative	Total
Haematoxylin and eosin			
Positive	15	0	15
Negative	38	207	245

RT–PCR, reverse transcriptase–polymerase chain reaction.