2,550 primary colorectal carcinoma patients were treated at our institution. Patient information and follow-up data were prospectively collected and added to the department database. Of those patients, the present study selected 541 (21.2%) cases of UICC stage I colorectal carcinoma undergoing curative resection combined with surgical lymph node clearance, in order to review the time and form of recurrence, the changes in CEA levels at recurrence, and the rate of re-resectability. For analysis, the 541 cases of UICC stage I colorectal carcinoma were divided into two groups: 313 patients with stage Ia colorectal carcinoma (pT1N0M0) and 228 patients with stage Ib colorectal carcinoma (pT2N0M0).

In terms of the follow-up of a patient with stage I colorectal carcinoma, we routinely conducted a periodic check-up every six months until two years after the operation, and subsequently once per year from the 3rd to 5th postoperative year. Clinical examination, abdominal ultrasound, and CEA measurement were performed at each visit, and chest X-ray was performed once per year. CEA was defined as positive when the level was increased above the cut-off value. Colonoscopy or barium enema was conducted once within one year of the first surgery, and was repeated at intervals of one to two years depending on the findings of the prior examination. When a patient complained of a symptom that suggested recurrence or had an increased level of CEA without symptoms, we employed other types of examinations in addition to the periodic check-up.

The clinicopathologic parameters were compared using Student's t test and the Fisher's exact test as appropriate. Cancer-specific survival curves and disease-free survival curves were estimated using the Kaplan-Meier technique and were compared by means of the log-rank test. For cancer-specific survival, only cancer-related deaths were considered; data on the patients who died from other causes or who were still alive at the end of the study were censored. A P value of less than 0.05 was considered significant.

TABLE 1. Patient's Characteristics

		UICC stage Ia patients	UICC stage Ib patients	P value
Number of patients		313	228	
Sex ratio (Male:Female)		201:112	129:99	0.0750
Age (yr; mean and range)		60.7 (33-88)	62.0 (23-91)	0.1641
Location	Cecum	16	14	0.0003*
	Ascending colon	23	15	
	Transverse colon	18	7	
	Descending colon	7	5	
	Sigmoid colon	122	53	
	Upper rectum	28	23	
	Middle rectum	34	31	
	Lower rectum	65	80	
Operative procedures	Partial resection	45	4	
	Ileocecal resection	11	4	
	Right hemicolectomy	15	25	
	Transverse colectomy	3	5	
	Descending colectomy	7	2	
	Left hemicolectomy	0	4	
	Sigmoid colectomy	105	49	
	Anterior resection	91	93	
	Abdominoperineal resection	14	35	
	Abdominosacral resection with coloanal anastomosis	4	2	
	Transsacral partial resection	17	0	
	Hartmann's operation	1	4	
	Total pelvic exenteration	0	1	
Follow-up time (mo; range and median)		3-189 (80)	1-201 (85)	
Recurrence	Positive	9	12	0.1793
	Negative	304	216	
Sites of First Tumor Recurrence	Liver	7	5	
	Lung	1	6	
	Local			
	Pelvis	1	2	
	Anastomosis	1	1	
	Para-aortic lymph node	0	1	
Oncologic outcome	5-Year disease-free survival (%)	96.9	94.9	0.1575
	5-Year cancer-specific survival (%)	99.3	97.6	0.0354

*colon and upper/middle rectum *vs.* lower rectum.

RESULTS

The patient demographics are summarized in **Table 1**. Compared with the UICC stage Ia group, the UICC stage Ib group included significantly more patients with lower rectal carcinoma (p=0.0003). Recurrence occurred in 9 of 313 (2.9%) UICC stage Ia group, and in 12 of 216 (5.6%) UICC stage Ib group. However, the difference between the two groups was not significant (p=0.1793). Disease-free survival rates at 5 years were 96.9% for the UICC stage Ia group and 94.9% for the UICC stage Ib group **(Figure 1a)**, with no significant difference between the two groups (p=0.1575). Cancer-specific survival rates at 5 years were 99.3% for the UICC stage Ia group and 97.6% for the UICC stage Ib group **(Figure 1b)**; there was a significant difference between the two groups (p=0.0354).

The performance rate of curative-intent salvage surgery for recurrent lesions in these recurrent carcinoma patients was 61.9% (13/21) **(Table 2)**. Recurrence was found at a median time of 19 months (range 6-66) after primary carcinoma resection. Only one patient with pelvic and hepatic recurrence was found after five-year routine follow-up.

Since the proportion of lower rectal carcinoma patients was significantly elevated in the UICC stage Ib group, we divided the sites of carcinoma into the lower rectum and other parts to evaluate recurrence rates and prognoses **(Table 3)**. Recurrences occurred in 10 of 145 (6.9%) patients with lower rectal carcinoma, and in 11 of 396 (2.8%) patients with colon or upper/middle rectal carcinoma. Between these two groups, the difference in the recurrence rate was significant (p=0.0415). Disease-free survival rates at 5

years in patients with lower rectal carcinoma were 92.6%, and 97.3% in patients with colon or upper/middle rectal carcinoma **(Figure 2a)**, with the difference between the two groups significant ($p=0.0304$). However, the cancer-specific survival rates at 5 years were not significantly different between the groups ($P=0.2402$) **(Figure 2b)**.

Among the 21 recurrent cases, 13 (61.9%) individuals were CEA positive at the time of recurrence **(Table 4)**. With regard to the recurrent site and CEA positive rate, patients with hepatic recurrence showed a significantly higher rate of CEA positivity, compared with the patients with recurrence at other sites ($p=0.0272$). Between the patients who were CEA positive and those who were CEA negative at the time of recurrence, no significant difference in the prognosis after the detection of recurrence was found **(Figure 3a)**, in addition to in the prognosis after the first surgery **(Figure 3b)**.

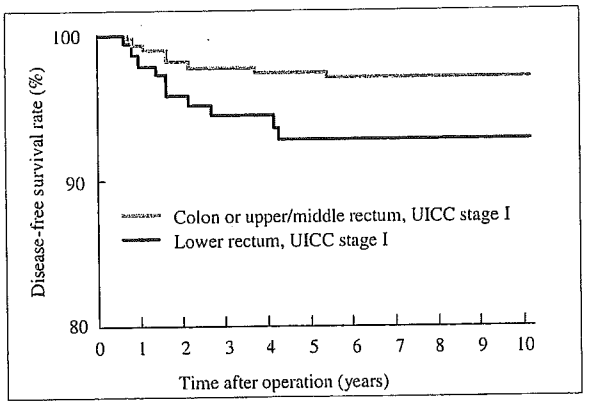

FIGURE 2a Cumulative disease-free survival curves for patients with lower rectal carcinoma and colon or upper/middle rectal carcinoma. The difference between the two groups was significant ($p=0.0304$).

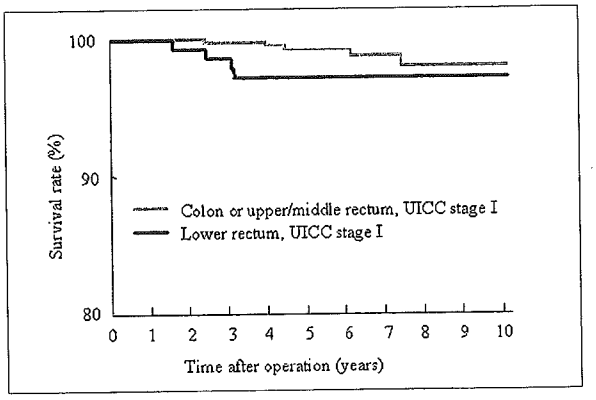

FIGURE 2b Cancer-specific survival curves for patients with lower rectal carcinoma and colon or upper/middle rectal carcinoma. The difference between the two groups was not significant ($p=0.2402$).

FIGURE 1a Cumulative disease-free survival curves for UICC stage Ia group and UICC stage Ib group. The difference between the two groups was not significant ($p=0.1575$).

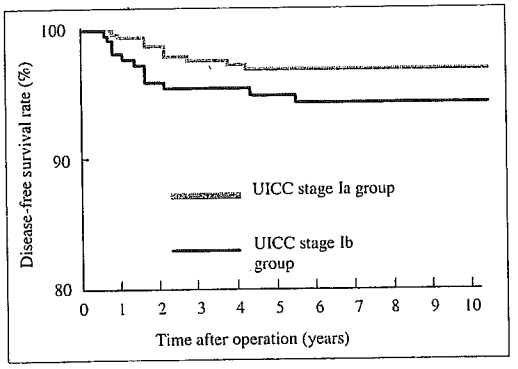

FIGURE 1b Cancer-specific survival curves for UICC stage Ia group and UICC stage Ib group. The difference between the two groups was significant ($p=0.0354$).

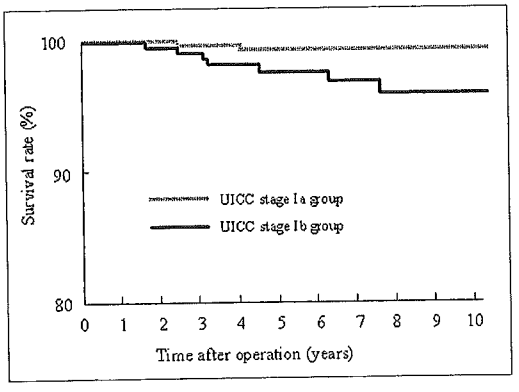

TABLE 2 Treatment of Recurrent Cancers

Treatment	No. of patients
Resection	
APR+radiation	3 (2*)
TPE+combined resection of sacrum	1 (1)
hepatic resection	9 (7*)
lung resection	5 (5)
Systemic chemotherapy	2
Hepatic artery infusion	2
Pelvic radiotherapy	1

( ), number of patients having curative-intent salvage surgery. *two patients underwent curative-intent salvage surgery for pelvic and hepatic recurrences.

DISCUSSION

For surveillance after curative surgery for colorectal carcinoma, a cost-effective method of follow-up should be established for consideration of the risk for recurrence. The probable subjects that the numbers of times and follow-up examinations can be reduced are UICC stage I patients. In the present study, we carried out follow-up examinations of a large number of UICC stage I patients over a long period at a single institution, and analyzed the data to clarify an appropriate method of surveillance. The present findings demonstrated that compared with the UICC stage Ia group, the UICC stage Ib group had a significantly lower rate of 5-year cancer-specific survival. In addition, lower rectal carcinoma involved a significantly higher incidence of recurrence. A recent study by Wichmann *et al.* (19) reported that between UICC stages Ia and Ib, there was an approximately 10% difference in the 5-year survival rate, although the difference did not achieve significance due to the small number of study patients. In the present study, however, the number of UICC stage I patients who were investigated was

much larger compared with the numbers reported in former studies, suggesting that the present study findings may help establish a method of follow-up for UICC stage I patients in the future.

In most carcinomas other than colorectal carcinoma, when recurrence is discovered after resection of the primary lesion, they are treated as a systemic disease and salvage surgery is infrequently indicated for the recurrent lesion. However, in colorectal carcinoma, resection of the recurrent lesion may improve patient prognosis. In this respect, research is required to determine whether intensive follow-up for detecting recurrence earlier and initiating the treatment of it will lead to improvement in prognosis for colorectal carcinoma patients. In earlier studies, the numbers of examinations and times of the check-up conducted were different (1-13). As a matter of course, it should be recognized that with advances in technologies, the precisions diagnostic examinations are being enhanced, and new effective methods of examination are being developed. Moreover, the treatment regimens have been changing rapidly; in recent years the indications for aggressive surgical resection for recurrent lesions have been expanded, and new chemotherapies that are useful for improving patient prognosis have been identified (20-23). For the reasons mentioned above, a study that retrospectively confirms the usefulness of follow-up will not able to avoid a bias caused by the times when the study was performed.

TABLE 3 Site of the Primary Tumor and Recurrence

	Colon and upper/ middle rectum	Lower rectum	*P* value
Number of patients	396	145	
Recurrence			
Positive	11	10	0.0415
Negative	385	135	
Oncologic outcome			
5-Year disease-free survival (%)	97.3	92.6	0.0304
5-Year cancer-specific survival (%)	99.1	97.1	0.2402

TABLE 4 Recurrent Disease and Results of Tumor Marker Monitoring at the Time of Recurrence

Tumor marker monitoring	Elevation	No elevation	*P* value
Number of patients	13	8	
Sites of recurrence			
Liver	11	1	0.0272
Lung	2	5	
Local (Pelvis and anastomosis)	3	2	
Para-aortic lymph node	1	0	
Interval to recurrence (mo; range and median)	6-66 (19)	9-32 (18)	0.3348
Oncologic outcome 5-Year survival following first recurrence (%)	52.7	87.5	0.2734
5-Year survival after primary surgery (%)	61.5	87.5	0.3558

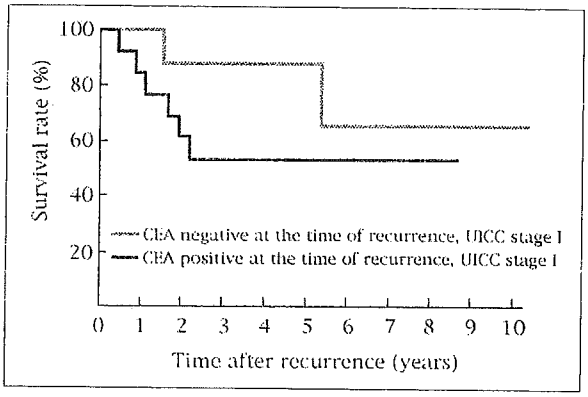

FIGURE 3a Cancer-specific survival curves after the detection of recurrence for patients who were CEA positive and CEA negative at the time of recurrence. The difference between the two groups was not significant ($p=0.2734$).

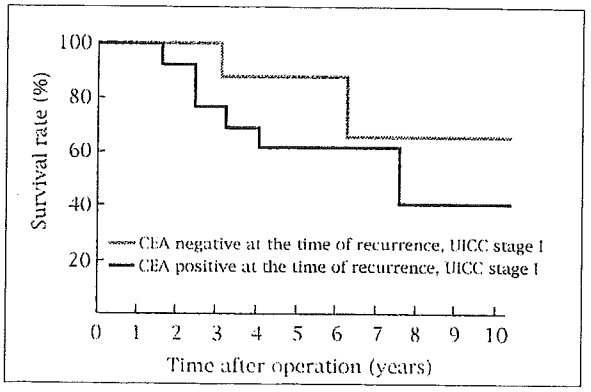

FIGURE 3b Cancer-specific survival curves after the first surgery for patients who were CEA positive and CEA negative at the time of recurrence. The difference between the two groups was not significant ($p=0.3558$).

With regard to the value of CEA in the postoperative surveillance, some benefits have been reported from the viewpoint of earlier detection of recurrence and cost-effectiveness in detecting potentially curable recurrent disease (24-26). However, no conclusion has been reached whether the earlier detection of recurrence using CEA may influence the prognosis. In the present study, 62% (13/21) of patients with recurrence showed an increased CEA level at the time of recurrence. In these patients, the follow-up that used CEA alone might have enabled the confirmation of recurrence if diagnostic imaging was performed at the point when an increased level of CEA was recorded. However, the question here is about those cases in which recurrence was confirmed first by diagnostic imaging without showing an increased level of CEA. Of these patients, 75% (6/8) remain disease-free to date, and there is a possibility that with the follow-up using CEA alone, asymptomatic recurrences without CEA elevation may not be detected. However, these 6 patients comprised only 1.1% (6/541) of all study patients, and it may therefore be inefficient to conduct the usual postoperative surveillance while burdening the remaining 99% patients with huge costs and effort. In all UICC stage I carcinoma patients, there was a low recurrence rate of 3.9% (21/541), and in addition,

because two-thirds of recurrences could be identified using CEA, the CEA test alone may be adequate at each visit, at least for UICC stage I patients.

Another problem in the CEA examination is that encountering a patient who shows false-positivity is inevitable. Moertel *et al.* (27) reported that when the preoperative CEA level was 5ng/mL or higher, false-positivity may appear approximately in 30% of such cases. If a UICC stage I patient shows an increased CEA level during the follow-up that uses CEA alone, it may be necessary to perform examinations for other carcinoma occurrences in addition to the metastasis and recurrence of the primary colorectal carcinoma.

A noteworthy aspect of the present study was that the patients with lower rectal carcinoma showed a significantly higher incidence of recurrence. Wichmann *et al.* (19) also reported that although there was no significant difference across UICC stage I patients, rectal carcinoma involved a higher rate of recurrence, with particularly more local recurrence, compared with colon carcinoma. The CEA positive rate in patients with local recurrence of rectal carcinoma was not as high as that in patients with hepatic metastasis (2,27,28). Hence, especially in conducting follow-up examinations of patients with lower rectal carcinoma, special attention should be paid to local recurrence, and when any symptom such as pain, hemorrhage, or change in bowel habit appears, necessary examinations should be performed early.

In the present study, the UICC stage Ia group included a significantly smaller number of patients with lower rectal carcinoma. This may be because some patients who had pT1 carcinoma at the lower rectum were followed up after undergoing trans-anal resection alone. The treatment of T1 and T2 carcinoma of the lower rectum is controversial, and several studies have suggested satisfactory tumor control after local excision for lower rectal T1 and T2 carcinoma (29,30). However, recent studies suggested that local excision of T1 and T2 rectal carcinoma is followed by a much higher recurrence rate than previously reported (31,32). In our institution, a radical surgery of low anterior resection or abdominoperineal resection is often indicated for T2 lesions and most T1 lesions with adverse risk factors, especially poorly differentiated carcinoma, lymphovascular invasions, incomplete excision, or massive invasion of carcinoma to the submucosal layer. Although most patients with T1 and T2 carcinoma lesions in the lower rectum in whom local recurrence develops after local excision can be salvaged by radical resection, the long-term outcome remains unknown (33).

In the field of the postoperative follow-up examination, the value of colonoscopy has been discussed. Periodic colonoscopy may be useful for detecting anastomotic and locoregional recurrences after colorectal carcinoma operation in addition to finding metachronous colorectal carcinoma (34,35). However, in UICC stage I patients, the anastomotic and locoregional recurrences have involved a very low proportion of 1% to 3%, according to previous and the present study (19). Particularly in patients with colonic carcinoma, there have been no anastomotic or locoregional recurrences observed at our institution. Performing colonoscopy is not warranted for the purpose of detecting anastomotic and locoregional recurrences in UICC stage I patients.

In conclusion, for UICC stage I patients, the incidence of recurrence was lower, and it is therefore possible to reduce the times and screening examinations for the postoperative surveillance. Regarding screening examinations, the CEA measurement every six months until two years after the operation, and subsequently once per year until the 5th postoperative year appears to be sufficient. Nevertheless, for patients with UICC stage Ib disease and those with lower rectal carcinoma, oncologists need to pay special attention because the rates of recurrence are significantly higher.

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Original Report

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Thin-Section MRI with a Phased-Array Coil for Preoperative Evaluation of Pelvic Anatomy and Tumor Extent in Patients with Rectal Cancer

OBJECTIVE. The aim of our study was to assess the accuracy of thin-section MRI performed with a phased-array coil as a technique for the preoperative evaluation of pelvic anatomy and tumor extent in patients with rectal cancer.

CONCLUSION. Thin-section MRI with a phased-array coil is accurate and reliable for preoperative evaluation of pelvic anatomy and depth of transmural tumor invasion. Thus, it may be helpful in the selection of the appropriate treatment for patients with rectal cancer.

The principal problems associated with rectal cancer treatment are tumor recurrence and impairment of anorectal and genitourinary functions after surgery. For a patient with rectal cancer to achieve a better prognosis and quality of life, the extent of surgery should accurately reflect the disease status. The internal and external anal sphincters, which are essential for anorectal function, are adjacent to the rectum. The pelvic autonomic nervous system—consisting of the hypogastric plexus, hypogastric nerves, and pelvic plexuses—is essential for genitourinary functions and is adjacent to the mesorectal fascia surrounding the mesorectum [1]. The mesorectum is defined as the lymphovascular, fatty, and neural tissue that is circumferentially adherent to the rectum [2]. Therefore, excessive resection easily leads to unnecessary damage of anorectal and genitourinary functions, whereas insufficient resection inevitably leads to tumor recurrence. Indeed, reported incidences of permanent stoma, erectile dysfunction, urinary dysfunction, and local recurrence generally are 34% [3], 45% [4], 58% [5], and 22–27% [6, 7], respectively. However, the incidences of these outcomes in a series of patients who received ideal treatment from experts were reported to be only 6% [8], 13% [9], 5% [9], and 5–7% [9, 10], respectively.

Treatment options should be selected according to the extent of the tumor. In general, T1 tumors invading the superficial submucosa can be effectively treated by local excision, which is minimally invasive and promises excellent maintenance of anorectal and genitourinary functions [11]. T1 tumors invading the deep submucosa, T2 tumors invading the muscularis propria, or T3 tumors invading the perirectal fat slightly but remaining within the mesorectal fascia can be treated by mesorectal excision, which maintains good genitourinary functions and fair anorectal function if the anal sphincter can be preserved [8–11]. Patients with T3 tumors invading the mesorectal fascia or T4 tumors invading the neighboring organs require more radical surgery, and preservation of genitourinary functions is more difficult.

Received February 8, 2004; accepted after revision June 2, 2004.

Supported in part by a Grant-in-Aid for Clinical Research for Evidence-Based Medicine and a Grant-in-Aid for Cancer Research from the Ministry of Health, Labor, and Welfare and a grant from the Foundation for Promotion of Cancer Research in Japan.

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AJR 2005;184:531–538

0361–803X/05/1842–531

Randomized controlled studies have shown that adjuvant preoperative radiation therapy is effective for reducing local recurrence and prolonging survival in patients with rectal cancers, especially those with T3 tumors or node-positive cancer [6, 7]. Thus preoperative radiation therapy is becoming standard treatment for advanced rectal cancer. However, surgery alone can achieve local control in almost all T1 or T2 tumors and in many cases in T3 tumors as well. In addition, radiation therapy is complicated by toxicity [12], so the adjuvant therapy adopted also should reflect the accurate disease status.

The extent of tumor spread is generally evaluated using digital examination, endorectal sonography, CT, and MRI. The accuracy rates of endorectal sonography in the evaluation of the depth of transmural tumor invasion have been reported to be 82–88% [13, 14], and the technique has been described as superior to others for preoperative staging [15–17]. However, endorectal sonography is not applicable for stenosing tumors; further improvements are necessary for optimum tailoring of treatment for the individual patient.

Recent advances in medical imaging have shown that thin-section MRI performed with a phased-array coil is accurate and useful for preoperative evaluation of the extent of rectal cancer [18, 19]. Thus, we used a new phased-array coil that originally was developed to permit the early diagnosis of pancreatic cancer. Our previous study [unpublished] showed that this coil is superior to the conventional body coil, as indicated by the signal intensity distributions. The purpose of this study was to evaluate accuracy of thin-section MRI performed with this coil for the preoperative evaluation of pelvic anatomy and tumor extent in patients with rectal cancer.

TABLE 1 TNM Classification of Transmural Tumor Invasion Depth

T Stage	Definition
Tis	Carcinoma in situ
T1	Tumor invading submucosa
T2	Tumor invading muscularis propria
T3	Tumor invading through muscularis propria into subserosa or into nonperitonealized pericolic or perirectal tissues
T4	Tumor directly invading other organs or structures and/or perforating visceral peritoneum

TABLE 2 Criteria for MRI Staging of Rectal Cancer

T Stage	MRI Criteria
T1	Tumor signal intensity confined to submucosal layer—signal intensity low compared with high signal intensity of the adjacent submucosa
T2	Tumor signal intensity extends into muscle layer, with loss of interface between submucosa and circular muscle layer
T3	Tumor signal intensity extends through muscle layer into perirectal fat, with obliteration of interface between muscle and perirectal fat
T4	Tumor signal intensity extends into adjacent structure or viscus

Subjects and Methods

Between June 2001 and April 2002, 34 consecutive patients with primary rectal cancer proven by biopsy were examined with thin-section MRI using a phased-array coil for the preoperative evaluation of tumor extent. The patients were 25 men and nine women with a median age of 57 years (age range, 34–82 years). Of the 34 tumors in the patients, two were in the upper rectum, or 10–15 cm from the anal verge; seven were in the middle rectum, or 5–10 cm from the anal verge; and 25 were in the lower rectum, or less than 5 cm from the anal verge. None of the patients received preoperative radiation therapy. Informed consent was obtained from all patients.

MRI was performed preoperatively and interpreted by one gastrointestinal radiologist and one colorectal surgeon who were blinded to the findings of the digital rectal examination, endorectal sonography, and CT. The resected specimens were histopathologically examined by pathologists who were blinded to the findings of the preoperative evaluation of tumor extent. The depth of transmural tumor invasion was assessed according to the TNM classifications [20] (Table 1) for both MRI and histopathologic examinations, and results were compared prospectively.

MRI Methods

The patients received a 150-mL glycerin enema before examination and were placed in a supine, head-first position. No air insufflation was used, but an intramuscular antispasmodic was administered. We used a 1.5-T whole-body system (VISART/EX Scanner, Toshiba Medical Systems) and placed a wraparound quadrature phased-array coil (Pancreatic QD paired array coil, Toshiba Medical Systems) at the patient's pelvis. Initially, sagittal T2-weighted fast spin-echo images (TR/TE, 4,000/120; echo-train length, 23; slice thickness, 6 mm; gap, 1.2 mm; signal averages; 4; matrix, 166 × 256; field of view, 15 × 15 cm) of the pelvis were obtained. These images were used to plan T2-weighted thin-section axial imaging. Axial T2-weighted thin-section fast spin-echo images (9,500/120; echo-train length, 23; slice thickness, 3 mm; gap, 0 mm; signal averages; 4; matrix, 166 × 256; field of view, 15 × 15 cm) of the pelvis were then obtained.

MR Image Interpretation

One experienced gastrointestinal radiologist and one experienced colorectal surgeon who had no knowledge of the clinical and histopathologic data interpreted each MR image in consensus on the workstation monitor. Distance was measured with electronic calipers. The reviewers assessed the visualization of the rectal mucosa, submucosa, muscularis propria (inner circular and outer longitudinal muscle layers), and mesorectal fascia; depth of the transmural invasion by the tumor; mesorectal involvement by the tumor; visualization of the branches of the named arteries such as the superior rectal and the internal iliac arteries; visualization of the mesorectal and extramesorectal lymph nodes; numbers of detected lymph nodes; and smallest short-axis diameters of the lymph nodes.

The depth of transmural invasion by each tumor was categorized according to the TNM classification [20] (Table 1) and was assessed according to the reported criteria [18] (Table 2). In accordance with the findings of Brown et al. [18], we did not regard the presence of spiculation within the fat alone as sufficient evidence of extramural invasion. Small interruptions of the outer contours of the muscle coat were also not regarded as sufficient for diagnosis of a T3 lesion. To further evaluate agreement in the assessment of invasion depth, reviewers performed second interpretations after an interval of at least 4 months.

Histopathologic Study

All patients underwent radical surgery. The median interval between MRI and surgery was 22 days (range, 1–55 days). Procedures performed were mesorectal excision [8–10] in 30 patients (low anterior resection in 24 and abdominoperineal resection in six), pelvic exenteration in three, and pelvic exenteration with partial sacrectomy in one. Immediately after surgery, resected specimens were opened on the side opposite the tumor and fixed in 10% formalin. After fixation, we obtained serial slices through the whole tumor in Tis–T2 cases or through more than two sections of the deepest part of the tumor in T3 or T4 cases. The slices were embedded in paraffin, sectioned, and examined histologically after H and E staining. The depth of

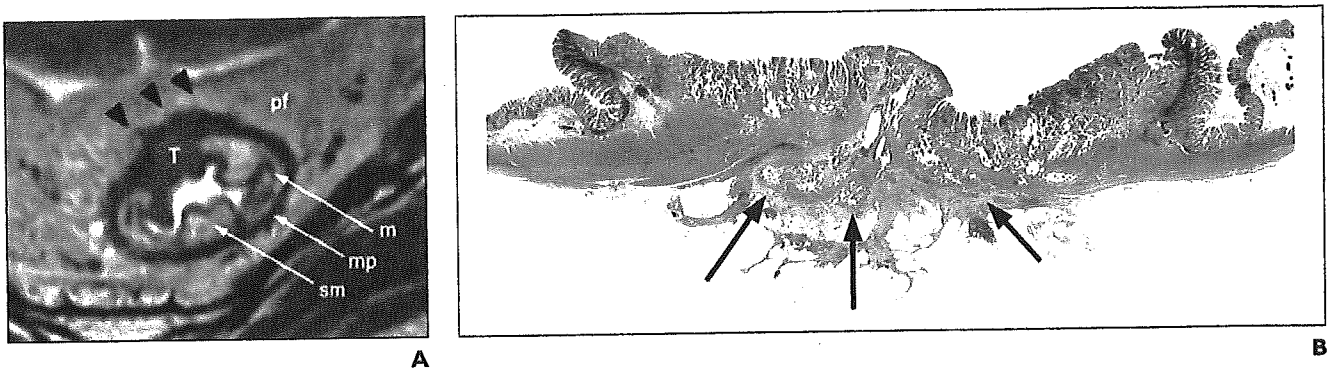


Fig. 1.—64-year-old woman with pT3 rectal carcinoma.
A, Unenhanced T2-weighted fast spin-echo image shows rectal mucosa (m) as low-intensity, submucosa (sm) as high-intensity, muscularis propria (mp) as low-intensity, and perirectal fat (pf) as high-intensity layers. Signal intensity of tumor (T) is higher than that of proper muscle layer but lower than that of submucosa. Tumor is seen invading through muscularis propria (*arrowheads*).
B, Photograph of histologic specimen reveals tumor invading through muscularis propria (stage pT3) (*arrows*).

transmural tumor invasion was classified according to the TNM classification (Table 1) [20].

Identification of the Pelvic Plexuses

Postoperative MR images were compared with ones obtained preoperatively in two patients so that the exact locations of the pelvic plexuses—which are essential for genitourinary function—could be identified. During surgery, metal hemostatic clips had been applied to the cut ends of the middle rectal arteries and veins on the inner surfaces of the pelvic plexuses. These clips facilitated identification of the pelvic plexuses on postoperative MR images.

Statistical Methods

The agreement regarding MRI-determined and histologically determined tumor stage was assessed with the weighted kappa statistic, as was the agreement between the first and second interpretations.

Results

All patients tolerated the thin-section MRI examination well. The total scanning time was about 20 min. Although motion artifacts complicated findings in five patients (15%), the images were of sufficient quality to allow assessment. The histologic diagnoses were well-differentiated adenocarcinoma in 11 patients, moderately differentiated adenocarcinoma in 16, poorly differentiated

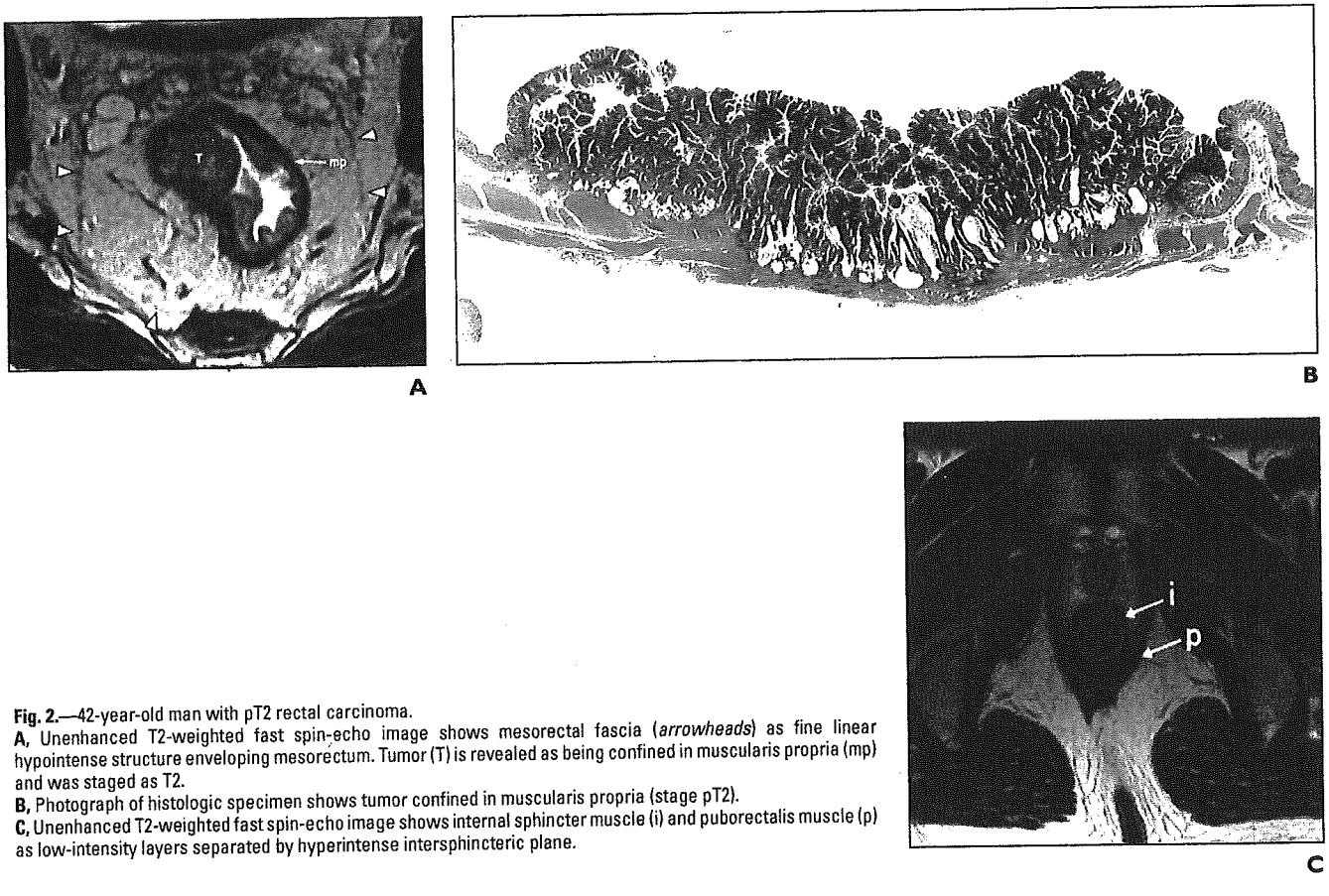


Fig. 2.—42-year-old man with pT2 rectal carcinoma.
A, Unenhanced T2-weighted fast spin-echo image shows mesorectal fascia (*arrowheads*) as fine linear hypointense structure enveloping mesorectum. Tumor (T) is revealed as being confined in muscularis propria (mp) and was staged as T2.
B, Photograph of histologic specimen shows tumor confined in muscularis propria (stage pT2).
C, Unenhanced T2-weighted fast spin-echo image shows internal sphincter muscle (i) and puborectalis muscle (p) as low-intensity layers separated by hyperintense intersphincteric plane.

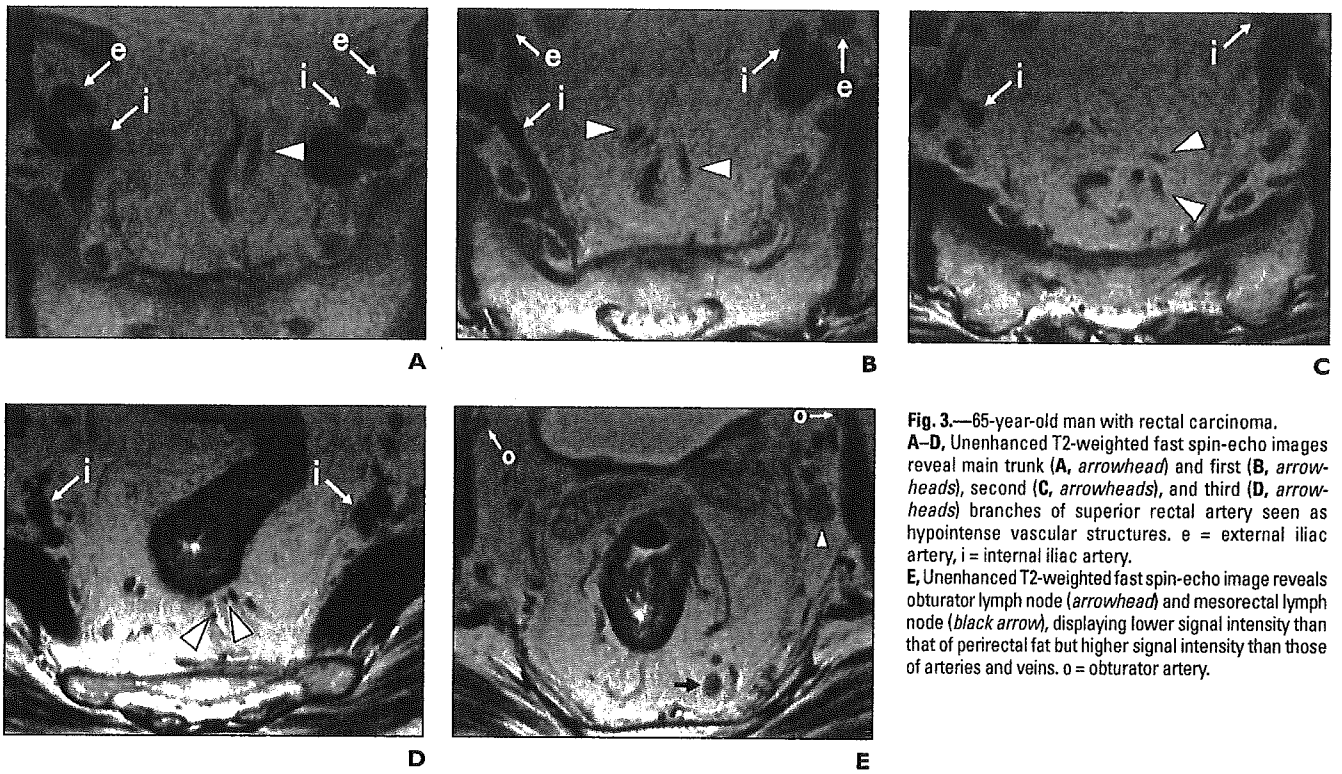


Fig. 3.—65-year-old man with rectal carcinoma.
A–D, Unenhanced T2-weighted fast spin-echo images reveal main trunk (**A,** *arrowhead*) and first (**B,** *arrowheads*), second (**C,** *arrowheads*), and third (**D,** *arrowheads*) branches of superior rectal artery seen as hypointense vascular structures. e = external iliac artery, i = internal iliac artery.
E, Unenhanced T2-weighted fast spin-echo image reveals obturator lymph node (*arrowhead*) and mesorectal lymph node (*black arrow*), displaying lower signal intensity than that of perirectal fat but higher signal intensity than those of arteries and veins. o = obturator artery.

adenocarcinoma in two, mucinous adenocarcinoma in four, and linitis plastica carcinoma in one. The histologic transmural invasion depths were pT1 in four patients, pT2 in nine, pT3 in 15, and pT4 in six. The mesorectal fascia was involved in eight patients. The median tumor diameter was 4.1 cm (range, 1.5–9.0 cm).

Visualization of the Pelvic Anatomy

In all patients, the rectal mucosa was visualized as a low-intensity layer; the submucosa, as a high-intensity layer; the muscularis propria, as a low-intensity layer; and the perirectal fat, as a high-intensity layer (Fig. 1). However, the inner circular muscle and outer longitudinal muscle layers could be distinguished only in three patients (9%). The mesorectal fascia was consistently depicted as a fine linear hypointense structure enveloping the mesorectum in all patients (Fig. 2A). In all patients, the internal and external sphincter muscles were shown as low-intensity layers separated by a hyperintense intersphincteric plane (Fig. 2C).

The first, second, third, and fourth branches of the superior rectal artery were seen as hypointense vascular structures in 34 (100%), 34 (100%), 31 (91%), and 11 patients (32%), respectively (Figs. 3A–3D). The bilateral obturator arteries branching from the internal iliac arteries were shown as hypointense vascular structures in all patients (Fig. 3E).

The lymph nodes were identified as having lower signal intensity than the perirectal fat but as having higher signal intensity than the arteries and veins (Fig. 3E). In patients with mucinous carcinoma, metastatic lymph nodes were shown as hyperintense nodules alone or as hyperintense nodules within hypointense nodules. The shapes of the lymph nodes were

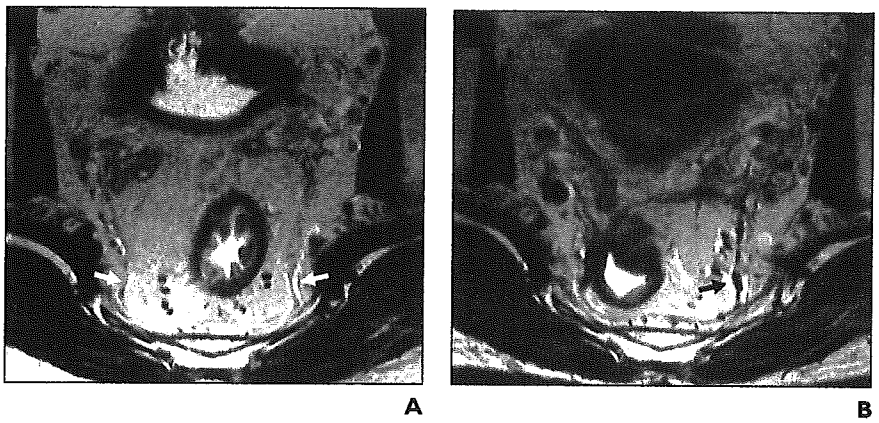


Fig. 4.—42-year-old man with rectal carcinoma.
A and **B,** Comparison of pre- and postoperative MR images show pelvic plexuses are located just outside mesorectal fascia. MR image obtained before surgery (**A**) shows pelvic plexuses (*white arrows*). Postoperative MR image (**B**) shows one of metal hemostatic clips that were applied to inner surfaces of pelvic plexuses during surgery to mark their exact locations (*black arrow*).

spherical or spheroidal, so that they could be distinguished easily from vascular structures. The mesorectal lymph nodes were apparent in all patients (Fig. 3E); the median number detected was five (range of nodes detected, 1–12). The median short-axis diameter of the smallest detected lymph nodes was 2.7 mm (range, 1.3–8.3 mm). The iliac or obturator lymph nodes were detected in only nine patients (33%) (Fig. 3E); the median number detected was 0 (range of nodes detected, 0–4). The median short-axis diameter of the smallest detected lymph nodes was 0 mm (range, 0–8.2 mm).

Comparisons of preoperative and postoperative MR images showed the pelvic plexuses to be located just outside the mesorectal fascia (Figs. 4A and 4B). However, even with metal hemostatic clips applied during surgery, the plexuses themselves could not be visualized on thin-section MRI.

Assessment of the Depth of Transmural Tumor Invasion

All rectal cancers were detected on thin-section MRI and, in most patients, showed higher signal intensity than the proper muscle layer but lower signal intensity than the submucosa (Fig. 1A). However, linitis plastica carcinoma showed signal intensity as low as that of the proper muscle layer, and mucinous carcinoma showed a signal intensity that was higher than that of the submucosa in parts of the mucous lakes.

At the first interpretation, MRI staging agreed with the histologic staging in 28 (82%) of 34 patients (weighted $\kappa = 0.82$; 95% confidence interval [CI], 0.69–0.95). Detailed results of the MRI staging are shown in Table 3. Sensitivity, specificity, overall accuracy rate, positive predictive value, and negative predictive value for detection of proper muscle invasion (T2) were 97% (29/30), 100% (4/4), 97% (33/34), 100% (29/29), and 80% (4/5), respectively (Fig. 2). Those values for detection of perirectal fat invasion (T3) were 95% (20/21), 77% (10/13), 88% (30/34), 87% (20/23), and 91% (10/11), respectively (Fig. 1). For detection of adjacent organ invasion (T4), the respective values were 100% (6/6), 96% (27/28), 97% (33/34), 86% (6/7), and 100% (27/27). The values for detection of the mesorectal fascia involvement were 100% (8/8), 100% (26/26), 100% (34/34), 100% (8/8), and 100% (26/26), respectively ($\kappa = 1.0$) (Fig. 5).

At the second interpretation, MRI staging agreed with the histologic staging in 29 (85%) of 34 patients (weighted $\kappa = 0.85$; 95% CI, 0.74–0.97). Sensitivity, specificity, overall accuracy rate, positive predictive value, and negative predictive value for detection of proper muscle invasion (T2), adjacent organ invasion (T4), and mesorectal fascia involvement were the same as those for the first interpretation. Those values for detection of perirectal fat invasion (T3) were 95% (20/21), 85% (11/13), 91% (31/34), 91% (20/22), and 92% (11/12), respectively. The agreement of the first and second interpretations on the depth of transmural invasion depth was good ($\kappa = 0.87$; 95% CI, 0.73–1.0).

Of the six cases in which staging errors were encountered at the first interpretation, four were overstaged, and two were understaged (Table 3). Histologic review of the specimens revealed that in three of the overstaged cases, the tumor invaded close to the deeper uninvolved layer and reactive changes were present in the connective tissue around the tumor, including inflammatory cell aggregation, desmoplastic change, and hypervascularity (Fig. 6). In addition, the deepest part of the tumor was not sectioned vertically on MRI but was sectioned obliquely, so that interpretation was difficult (Fig. 7). Histologic review of the two understaged cases revealed that they had only microscopic invasion beyond the estimated involved layers and that reactive changes of the connective tissue around the tumor were either only very slight or absent.

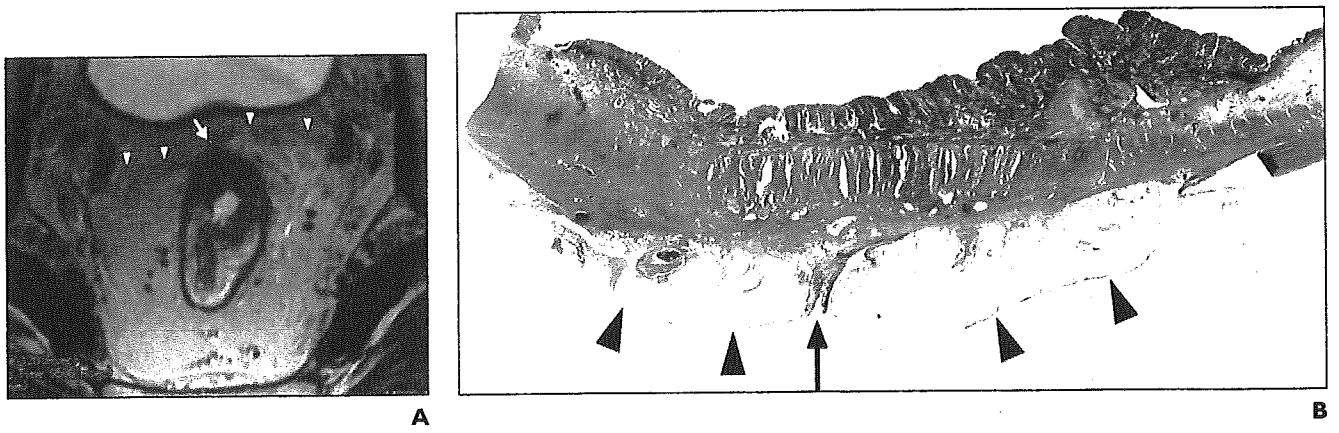
TABLE 3 **Depth of Transmural Tumor Invasion in Rectal Cancer: Comparison of MRI and Histopathologic Findings**

Histology		MRI			
pT	*n*	T1	T2	T3	T4
pT1	4	4			
pT2	9	1	5	3	
pT3	15		1	13	1
pT4	6				6

Note.—*n* = number of patients, T = MRI classification, pT = pathologic classification.

Discussion

As these results show, thin-section MRI performed with a quadrature phased-array coil has sufficient accuracy to depict fine details of the rectal wall (mucosa, submucosa, and muscularis propria), the anal sphincter, the mesorectum (perirectal fat; superior rectal artery and vein and their branches; lymph



A B

Fig. 5.—44-year-old man with pT3 rectal carcinoma involving mesorectal fascia.
A, Unenhanced T2-weighted fast spin-echo image shows tumor (*arrow*) involving mesorectal fascia (*arrowheads*).
B, Photograph of histologic specimen reveals tumor (*arrow*) involving mesorectal fascia (*arrowheads*).

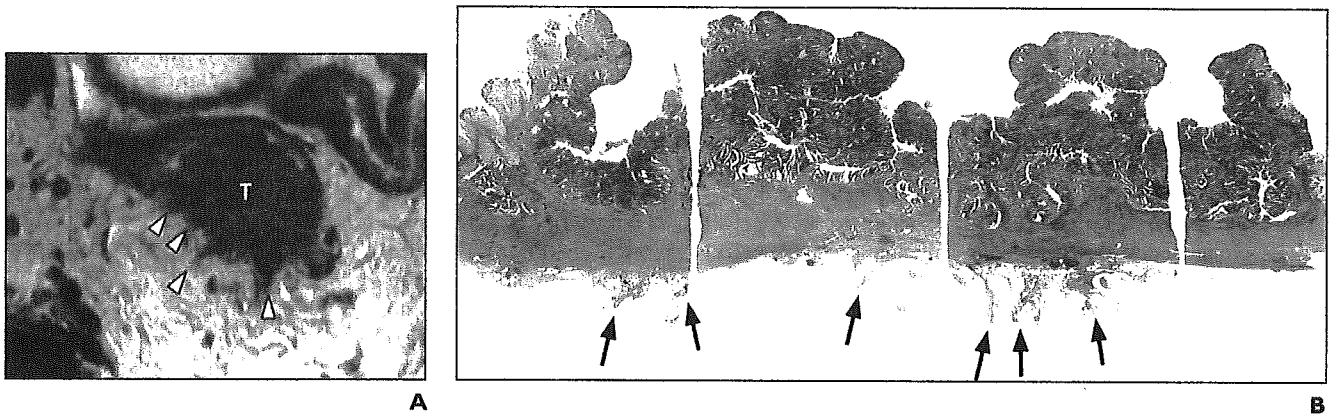


Fig. 6.—80-year-old man with pT2 rectal carcinoma.
A, Tumor (T) was overstaged as T3 because spiculation (*arrowheads*) was interpreted as cancer invasion on unenhanced T2-weighted fast spin-echo image.
B, Photograph of histologic specimen reveals tumor confined in muscularis propria (stage pT2). However, reactive changes in connective tissue around tumor, including desmoplastic change and hypervascularity (*arrows*), can affect MRI findings and mimic tumor invasion.

node; and mesorectal fascia), and the extramesorectal structures (internal iliac artery and vein and their branches; and lymph node) clearly in every patient. Fourth branches of the inferior mesenteric artery and lymph nodes measuring 2 mm could be visualized in most patients. In addition, although the pelvic plexuses per se could not be visualized on our thin-section MRI, we identified their exact locations just outside the mesorectal fascia via metal hemostatic clips placed on their inner surfaces during surgery and comparisons of preoperative and postoperative MR images.

Previous studies using similar instruments also provided precise images of the rectal and pelvic anatomy [18, 19]. Brown et al. [18] reported that their technique had an in-plane resolution of 0.6 × 0.6 mm and allowed differentiation of the inner circular and outer longitudinal muscle layers. We could distinguish the layers in only 9% of the patients, but such differentiation is not clinically important because treatment for the tumor invading the inner muscle is the same as that for the tumor invading the outer muscle.

All intraluminal cancers measuring more than 1.5 cm were detected. Most tumors showed a signal intensity that was higher than that of the proper muscle layer but lower than that of the submucosa, as has been reported previously [18, 19]. In addition, we found that linitis plastica carcinoma had a signal intensity that was as low as that of the proper muscle layer and that mucinous carcinoma had a signal intensity higher than that of the submucosa in parts of the mucous lakes. These findings are useful for predicting histologic diagnosis and may contribute to treatment selection because they are risk factors for a poor prognosis [21–23]. However, whether the histology of the tumor affects staging accuracy could not be determined because of the limited number of patients studied.

In our prospective study, we performed unenhanced thin-section MRI (slice thickness, 3 mm) on a 1.5-T scanner with a quadrature phased-array coil. The depth of transmural tumor invasion and mesorectal fascia involvement were predicted correctly in 82% and 100% of the patients, respectively. In their retrospective evaluation, Beets-Tan et al. [19] used contrast-enhanced thin-section MRI (slice thickness, 3 mm) on a 1.5-T scanner with a quadrature phased-array spine coil and

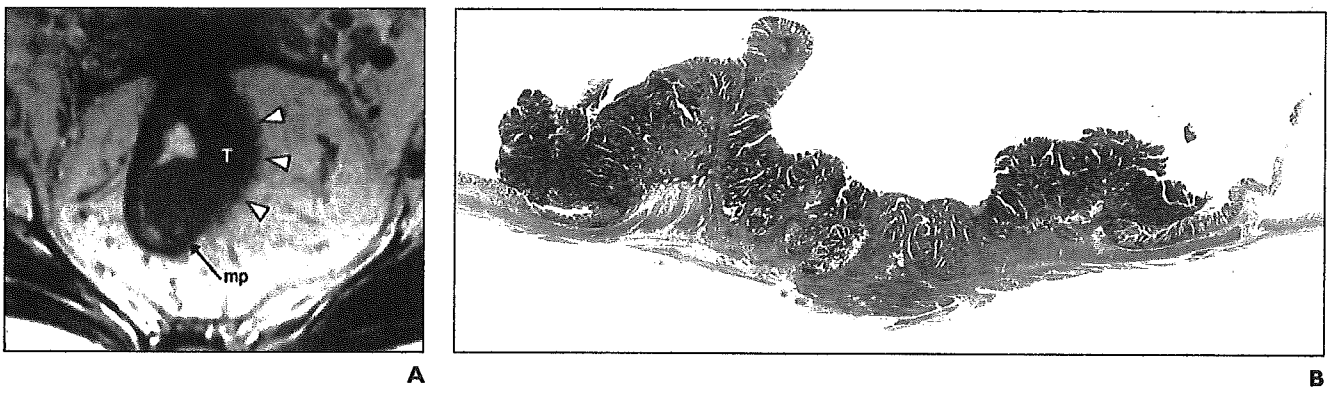


Fig. 7.—56-year-old woman with pT2 rectal carcinoma.
A, Tumor (T) was overstaged as T3 because site of deepest invasion (*arrowheads*) was sectioned obliquely on MRI and mimicked cancer invasion beyond muscularis propria (mp).
B, Photograph of histologic specimen reveals tumor confined in muscularis propria (stage pT2).

reported that the depth of transmural tumor invasion and mesorectal fascia involvement were predicted correctly in 83% and 100% of their patients, respectively. Brown et al. [18] used unenhanced thin-section MRI (slice thickness, 3 mm) on a 1.5-T scanner and a four-element flexible wraparound surface coil and conducted a retrospective study that found correct invasion depth assessment was attained in 100% of their cases. Thus, thin-section MRI performed on a 1.5-T scanner with a phased-array coil in general can be considered to provide moderate to good accuracy in the prediction of invasion depth and good accuracy in the prediction of mesorectal fascia involvement. These data are comparable to accuracy rates of 82–88% [13, 14] obtained with endorectal sonography for the prediction of invasion depth. However, endorectal sonography is not applicable for stenotic or obstructive tumors and cannot visualize the mesorectal fascia and obturator space because of the limitations of sonographic attenuation [14]. In addition, good-quality sonograms can be guaranteed only if the images are acquired by a skilled operator [14]. Therefore, thin-section MRI can be concluded to be clinically more useful than endorectal sonography.

As to reproducibility, we did not evaluate interobserver agreement, but concordance between the first and second interpretations was good for both invasion depth ($\kappa = 0.87$) and mesorectal fascia involvement ($\kappa = 1.0$). Brown et al. [18] evaluated only interobserver agreement and reported good agreement between experienced reviewers for invasion depth ($\kappa = 1.0$). Beets-Tan et al. [19] assessed both intraobserver and interobserver agreement. For assessment of invasion depth, intraobserver agreement was good ($\kappa = 0.8$) for a radiologist experienced in pelvic MRI but was only moderate ($\kappa = 0.49$) for an inexperienced radiologist; interobserver agreement was moderate ($\kappa = 0.53$). In contrast, intraobserver and interobserver agreements for the prediction of involvement of circumferential resection margin [24–26] (the same as mesorectal fascia involvement in patients who undergo mesorectal excision [8–10]) were good, because intraclass correlation coefficients for the experienced reviewer, inexperienced reviewer, and both reviewers were 0.99, 0.91, and 0.93, respectively. Therefore, examinations for invasion depth should be interpreted by a reviewer experienced in pelvic MRI; involvement of the circumferential resection margin or mesorectal fascia is more easily interpretable.

Thin-section MRI is sufficiently accurate and reliable to provide clinically useful information. Prediction of involvement of the mesorectal fascia, adjacent organs, or circumferential resection margin is especially important [24–26]. Involvement of these structures requires surgery more radical than mesorectal excision [8–10], preoperative adjuvant therapy, or both to reduce local recurrence and overall recurrence [27]. Prediction of an absence of such involvement allows performance of mesorectal excision alone [8–10], reducing the incidence and severity of anal and genitourinary dysfunctions [9] and preventing toxicity from unnecessary adjuvant radiation therapy [28, 29], chemotherapy, or both. Accurate prediction of invasion depth of T1 tumors ensures proper assignment of candidates for local excision to enhance patient survival and quality of life [11].

Although thin-section MRI is very accurate, it is not perfect. In our series, two thirds of staging errors in invasion depth resulted from overstaging and were most common with pT2 tumors, as has been reported for endorectal sonography [13, 14]. Reactive changes in the connective tissue around the tumor, including inflammatory cell aggregation, desmoplastic change, and hypervascularity, mimic tumor invasion on MR images. Such reactive changes have also been previously noted as a main cause of overstaging on sonography [14, 30] and MRI [18, 19]. Contrast enhancement may be helpful for differentiating these reactive changes from true tumor invasion. However, Beets-Tan et al. [19], who used gadolinium as a contrast medium, reported that MRI could not be used to distinguish reliably between fibrosis with and fibrosis without tumor cells. The best results were reported by Brown et al. [18], who could differentiate between desmoplastic spiculation and true invasion. Therefore, the best technique may be the one described in their report or may involve more precise image acquisition and administration of effective contrast material. In addition, the direction of MRI sectioning is important. Obliquely sectioned images make contours of tumors obscure and interpretation difficult, as seen in our study. This difficulty may be overcome by more precise image acquisition and 3D data accumulation.

One third of the staging errors in our study involved underestimation that was mostly attributable to microscopic invasion that is fundamentally undetectable on MRI or difficulties in attaining a complete examination with the 2D rather than 3D approach, so that we obtained not continuous images but rather interrupted images. To reduce overstaging and understaging, investigators need to address the possibility of using an image matrix smaller than 166 × 256, a slice width thinner than 3 mm, techniques for achieving a higher signal-to-noise ratio, 3D data accumulation, effective contrast material, and a shorter scanning time. MRI with an endorectal coil may have higher signal-to-noise ratio near the coil and produces better visualization of the rectal wall structure [31, 32]; however, its limited field of view makes assessment of the mesorectal fascia and surrounding structures difficult, and insertion of the coil is difficult in patients with annular stenotic lesions. Therefore, approaches using thin-section MRI with a phased-array coil still seem better.

Although our study concerned a relatively small number of patients, we conclude that thin-section MRI with a phased-array coil is accurate and reliable for the preoperative evaluation of the pelvic anatomy and the depth of transmural tumor invasion Thus, it may be helpful in the selection of the appropriate treatment for patients with rectal cancer. However, the accuracy of this technique is not perfect, so further investigation to improve accuracy is warranted. In addition, for validation, a multiinstitutional prospective study is necessary.

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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 breathhold [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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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

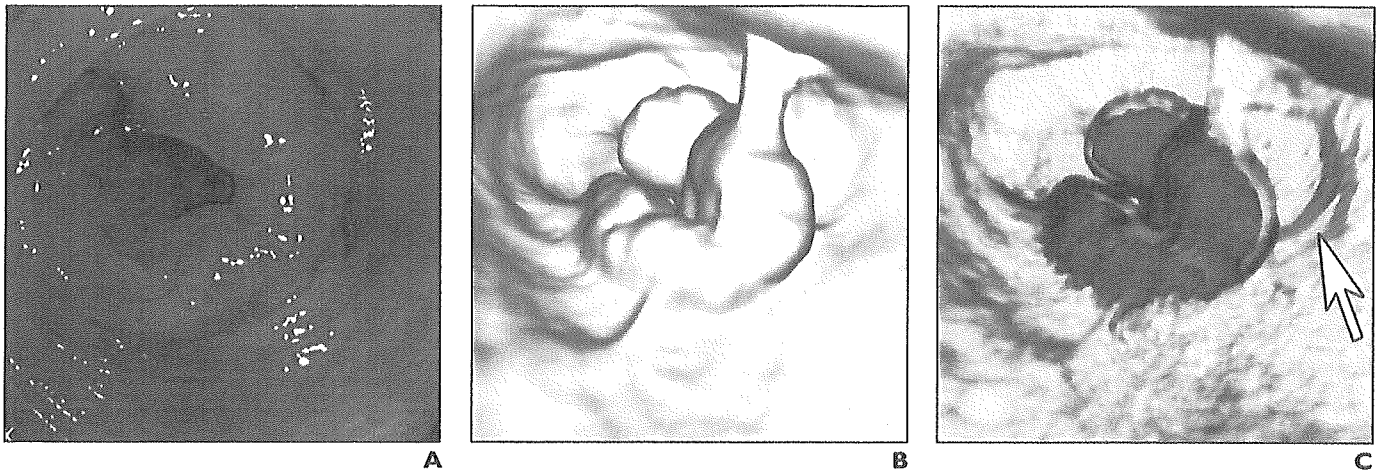

Fig. 1.—Colonoscopic view and surface and vascular virtual endoluminal images for representative case of advanced colorectal cancer in 60-year-old woman.
A, Colonoscopic view shows advanced cancer in sigmoid colon.
B, Surface virtual endoluminal image shows lesion.
C, Vascular virtual endoluminal image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

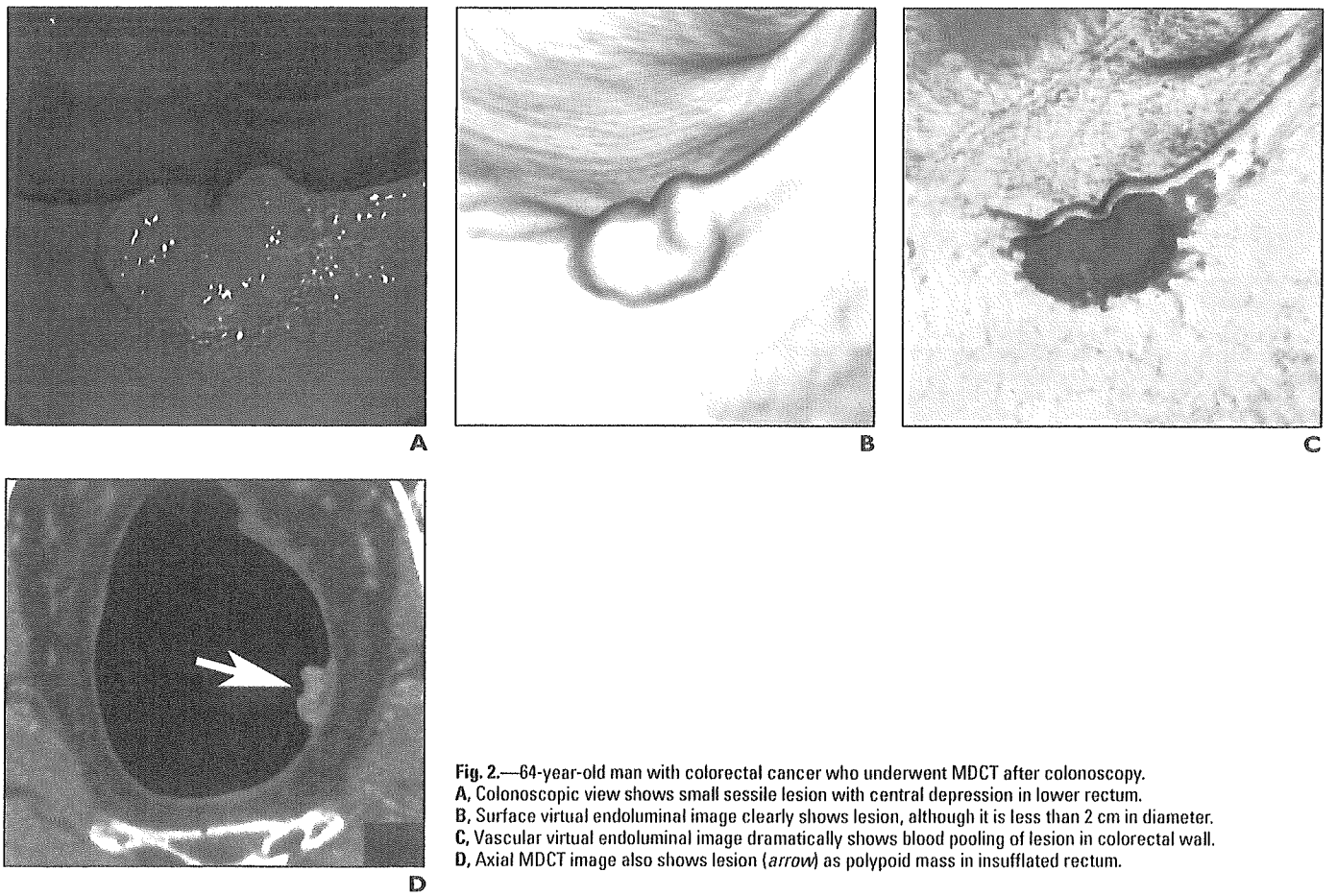

Fig. 2.—64-year-old man with colorectal cancer who underwent MDCT after colonoscopy.
A, Colonoscopic view shows small sessile lesion with central depression in lower rectum.
B, Surface virtual endoluminal image clearly shows lesion, although it is less than 2 cm in diameter.
C, Vascular virtual endoluminal 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)

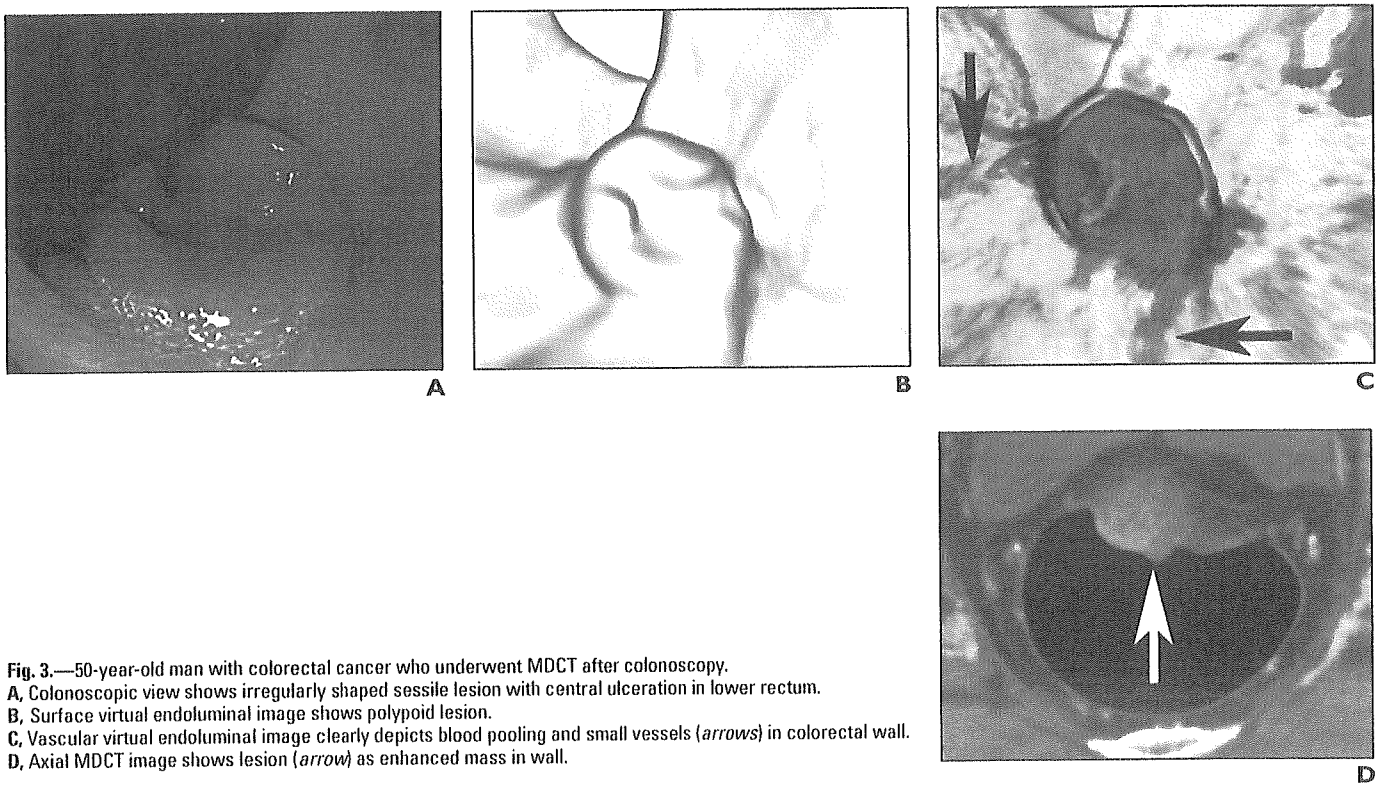

Fig. 3.—50-year-old man with colorectal cancer who underwent MDCT after colonoscopy.
A, Colonoscopic view shows irregularly shaped sessile lesion with central ulceration in lower rectum.
B, Surface virtual endoluminal image shows polypoid lesion.
C, Vascular virtual endoluminal image clearly depicts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

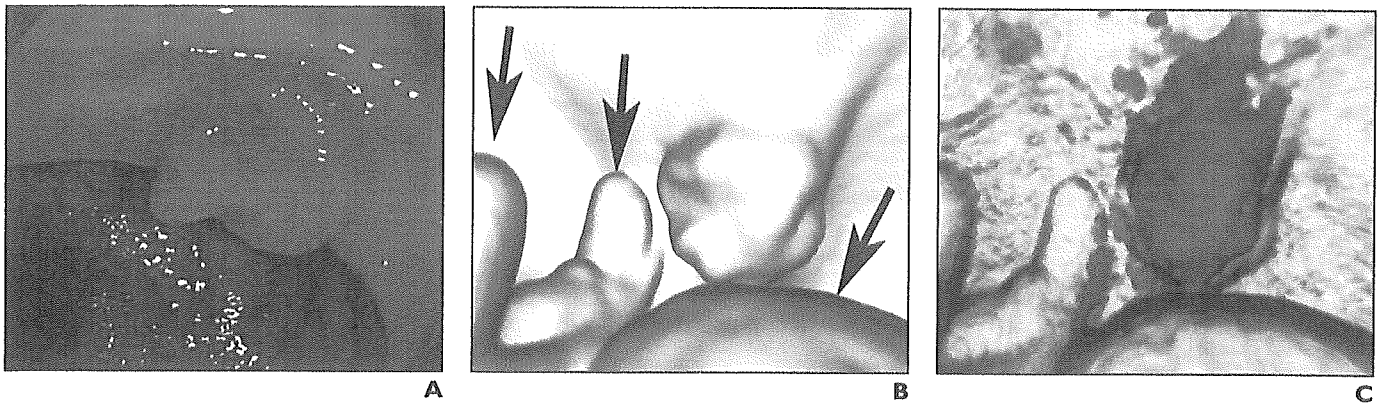

Fig. 4.—59-year-old man with colorectal cancer who underwent MDCT without preparation.
A, Colonoscopic view shows nodular protrusion in lower rectum.
B, It is hard to recognize lesion in residual stool (*arrows*) on surface virtual endoluminal image.
C, Vascular virtual endoluminal image successfully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

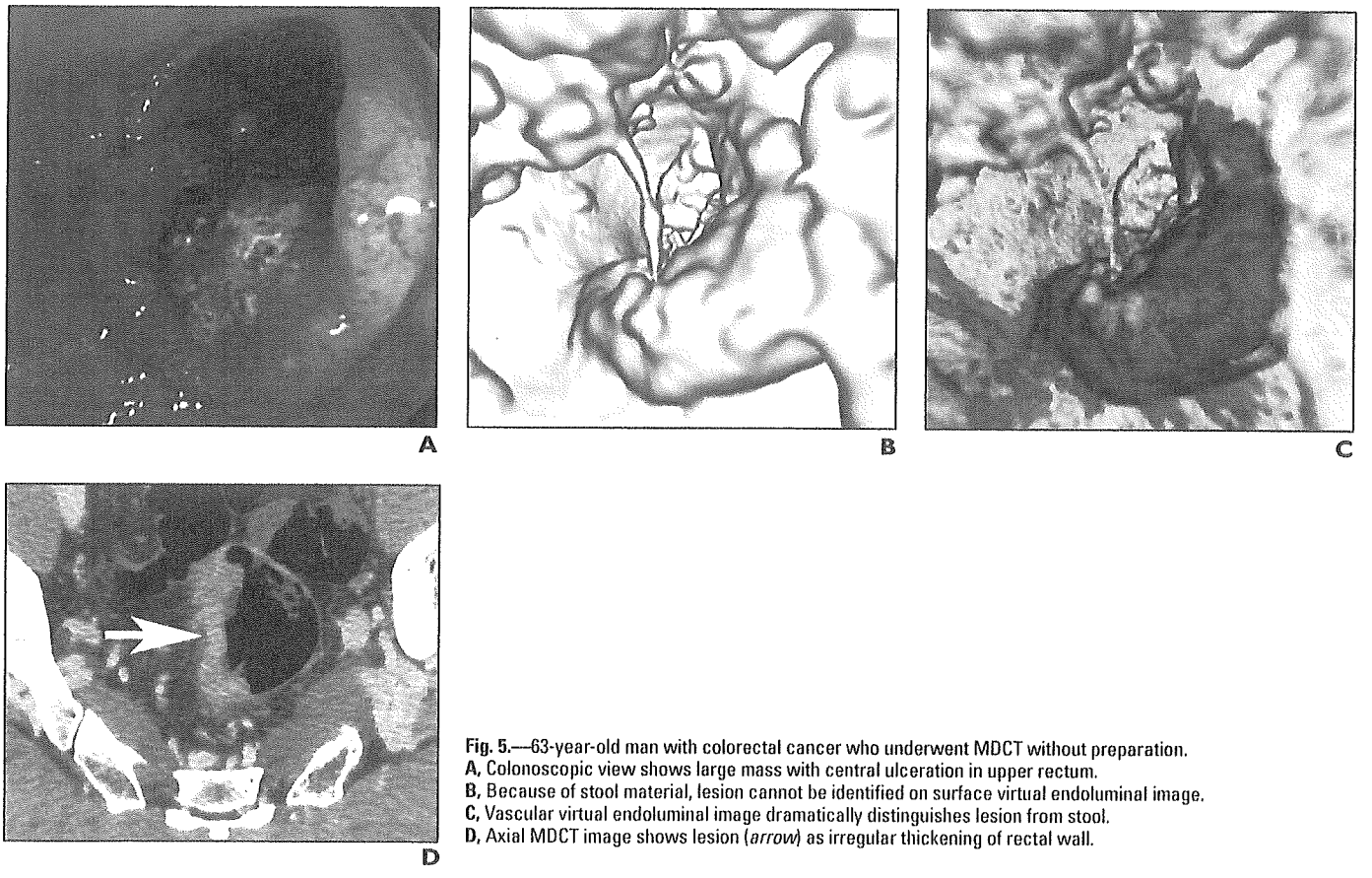

Fig. 5.—63-year-old man with colorectal cancer who underwent MDCT without preparation.
A, Colonoscopic view shows large mass with central ulceration in upper rectum.
B, Because of stool material, lesion cannot be identified on surface virtual endoluminal image.
C, Vascular virtual endoluminal image dramatically 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

CD10 Expression in Colorectal Carcinoma Correlates With Liver Metastasis

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PURPOSE: If it were possible to identify the features of primary colorectal carcinoma that were associated with liver metastasis, these features could be used as predictors of liver metastasis. METHODS: From January 1995 to December 1997, 648 consecutive cases of colorectal carcinoma were recorded at the Department of Surgery, National Cancer Center Hospital, Tokyo, Japan. We evaluated clinicopathologic and immunohistochemical factors (age, gender, tumor location, gross type, size, histologic type, dedifferentiation of invasive front, depth of invasion, lymphatic invasion, venous invasion, lymph-node metastasis, and expression of CD10, MUC2, and human gastric mucin) in 505 of these patients who had undergone resection of T2/T3/T4 colorectal carcinomas to clarify the correlation between these factors and liver metastasis. RESULTS: Liver metastases, including unresectable, were detected in 122 patients (24 percent), all of whom had been followed for at least five years. Univariate analysis revealed that liver metastasis was significantly associated with tumor size, histologic type, dedifferentiation of invasive front, depth of invasion, lymphatic invasion, venous invasion, lymph-node metastasis, and CD10 expression. Multivariate analysis revealed that invasion deeper than the subserosa, venous invasion, lymph-node metastasis, and CD10 expression were significantly associated with liver metastases. CONCLUSIONS: CD10 expression in colorectal carcinoma is a good predictor of liver metastasis. [Key words: Colorectal carcinoma; Liver metastasis; Predictive factor; CD10 expression; Immunohistochemistry]

The prognosis of patients with colorectal cancer is influenced not only by surgery for primary tumors but also by treatment of liver metastases, because 20 to 23 percent of patients with colorectal cancer exhibit liver metastases simultaneously or metachronously.[1,2] The treatment strategy for liver metastases from colorectal carcinoma is still controversial. In the case of surgically resectable tumors, hepatic resection is generally recommended.[1–4] The outcome of hepatic resection for colorectal metastases has improved because of recent advances in hepatic surgery and diagnostic technology. Five-year survival rates after curative resection of hepatic metastases are reported to be 27 to 48 percent.[1–9]

Risk factors for liver metastasis include serosal invasion, venous invasion, and lymph node metastasis.[10–17] A high incidence of liver metastasis in venous-invasion-positive cases has been reported previously,[10,11] and the presence of venous invasion is one of the most important risk factors for various distant metastases in colorectal carcinoma.[12] The presence of extracolonic lymph node metastasis has

Supported in part by a Grant-in-Aid for Cancer Research from the Ministry of Health, Labor and Welfare, Japan.

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Dis Colon Rectum 2005; 48: 1883–1889
DOI: 10.1007/s10350-005-0141-6

Published online: 2 September 2005

been reported to be associated with liver metastasis in patients with colorectal cancer.[13]

Expression of such phenotypic markers as CD10, MUC2, and human gastric mucin (HGM) was recently reported to be correlated with the histologic features and biologic behavior of colorectal carcinomas.[18–22] CD10 glycoprotein is a 100-kD cell metalloendopeptidase that inactivates a variety of biologically active peptides. It was initially identified as the common acute lymphoblastic leukemia antigen (CALLA).[23] Subsequent studies, however, have shown that it also is strongly expressed on the brush borders of small intestinal epithelial cells (absorptive cells) and the germinal centers of lymphoid follicles and microvilli of the kidney.[24–26] MUC2 glycoprotein, also known as "intestinal-mucin-related protein antigen," is an intestinal apomucin and is expressed in the supranuclear areas of goblet cells.[27–29] 45M1 recognizes the mucin epitope located in the peptide core of HGM, and the antibody is known to react with surface foveolar cells in the stomach.[30] Hanski *et al.*[20] reported that the *MUC2* gene is strongly suppressed in liver and lymph node metastases of colorectal carcinomas. Yao *et al.*[19] suggested that patients with colorectal adenocarcinoma with CD10 expression are at increased risk of liver metastasis. However, their study included only patients with resected liver metastases and did not include those with liver metastases that were unresectable because of peritoneal dissemination, paraaortic lymph-node metastasis, and distant metastasis. In addition, their study lacked multivariate-type analysis, therefore, their results were not reliable enough to conclude that expression of MUC2 or CD10 was a good predictor of liver metastasis in patients with colorectal carcinoma.

This study was designed to clarify the correlation between phenotypic markers, such as CD10, MUC2, and HGM, and liver metastasis from colorectal carcinoma by using a larger series of consecutive patients with colorectal carcinoma at a single institution.

METHODS

From January 1995 to December 1997, a total of 648 consecutive cases of colorectal carcinoma were recorded at the Department of Surgery, National Cancer Center Hospital, Tokyo, Japan. These patients underwent surgery without previous radiotherapy or chemotherapy, with the exception of 11 patients who did not undergo resection of the primary lesion (2 who received probe laparotomies, 7 stomas, and 2 bypasses). Therefore, the clinical records and histologic specimens of 637 patients were available for review. From among these, we excluded 49 patients with intramucosal carcinoma, 80 with submucosal invasive carcinoma, and 3 whose paraffin-embedded blocks were missing.

Our study population consisted of 505 patients (306 males; age range, 21–93 (mean, 61) years) with resected T2/T3/T4 colorectal carcinomas, according to the TNM classification.[31] The clinicopathologic and immunohistochemical examinations were performed by four observers (YF, YN, SS, and TS) without previous knowledge of the patients' clinical information. The results were compared, and any discrepancies were resolved by consensus at a meeting after further histopathologic review.

The resected tissue specimens were subjected to conventional processing. Histologic sections were cut from samples containing the deepest site of cancer invasion, and then stained with hematoxylin and eosin. Tumor location (colon or rectum), gross type (polypoid or ulcerative), and tumor size were evaluated on the resected specimens. Microscopic factors included histologic type, dedifferentiation of invasive front, depth of invasion, lymphatic invasion, venous invasion, and lymph node metastasis. Histologic type was defined by the histologic features constituting >50 percent of the tumor area (Fig. 1). We defined the "dedifferentiation" unit as a single cancer cell or a solitary trabecular form at the invasive front. The tumor was designated as positive for dedifferentiation when, in the section containing the deepest site of cancer invasion, >10 percent of the area of the invasive front consisted of dedifferentiation units (Fig. 2).

Representative tissue sections, each containing the deepest site of cancer invasion, were subjected to immunohistochemical staining using the avidin-biotin-peroxidase complex (ABC) method.[32] These sections were autoclaved for 10 minutes with heat-induced epitope retrieval in 10 mmol/L citrate buffer, pH 6.0, before reaction with the primary antibodies (except in the case of antibody against gastric mucin). The mouse monoclonal antibodies 56C6 (Novocastra, Newcastle, United Kingdom; diluted 1:200), Ccp58 (Novocastra; diluted 1:200), and 45M1 (Novocastra; diluted 1:100) were used to detect CD10 glycoprotein, MUC2 glycoprotein, and HGM expression, respectively. Sections containing small intestinal brush borders, intestinal goblet cells, and gastric foveolar cells were used as positive controls for 56C6, Ccp58, and