Endorectal Ultrasonography for the Assessment of Wall Invasion and Lymph Node Metastasis in Rectal Cancer

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Endorectal ultrasonography (ERUS) with a flexible-type radial scanner (Aloka Co. Ltd., Tokyo, Japan; 7.5 MHz) was applied to 120 patients with rectal cancer for the assessment of wall invasion and pararectal lymph node metastasis. Normal rectal wall was described as a five- or seven-layer structure excluding the lowest part within 3 cm from the anal verge. Loss of normal layers basically indicated the existence of cancer invasion. According to UICC classification, we divided the depth of wall invasion into four ultrasonographic levels (uT1–uT4), and results were correlated with histopathologic findings. Overall accuracy of the assessment was 92.0 percent (103/112). Overestimation occurred in 5 of 60 cases with T3 cancer (8.3 percent), and underestimation occurred in 1 of 19 cases with T2 cancer (5.3 percent) and 3 of 60 cases with T3 cancer (5 percent). Inflammatory cell infiltration was found around the cancer in a considerable number of cases. However, the assessment of wall invasion was hardly affected in our hands. Because the muscularis propria of the rectal wall was often recognized as a three-layer structure, uT2 cancer was subdivided into three subgroups of uPM1, uPM2, and uPM3. The assessment of invasion of sublayers in muscularis propria was possible in 14 of 19 cases (73.7 percent), and correct assessment was achieved in 57 percent of the cases. The ultrasonographic demonstration of pararectal lymph nodes was studied on 98 patients. No swollen lymph nodes were detected ultrasonographically in 35 of 98 cases (35.7 percent), but cancer metastasis was found histopathologically in 5 of these 35 cases (14.3 percent). The metastasis was observed more frequently in lymph nodes with a diameter of more than 5 mm (53.8 percent) and in those with a well-defined boundary and with an uneven and markedly hypoechoic pattern (72.3 percent). Although unable to detect minimal cancer foci, ERUS was considered a very useful tool for the assessment of the depth of cancer invasion in the rectal wall and pararectal lymph node metastasis. [Key words: Endorectal ultrasonography; ERUS; Rectal cancer; Depth of wall invasion; Pararectal lymph node metastasis]

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The preoperative assessment of the depth of cancer invasion in the rectal wall and regional lymph node metastasis is very important to determine the surgical policy for rectal cancer. However, a fully reliable procedure has not been developed. With computed tomography, it is still hard to delineate clearly the layer structure of the rectal wall and to detect precisely the regional metastatic lymph nodes.[1-4]

Recently, endorectal ultrasonography (ERUS) has been introduced as a useful procedure for such assessment in rectal cancer. The preliminary study reveals that ERUS is able to describe the normal rectal wall as a five- or seven-layer structure. It will surely contribute to more accurate assessment of wall invasion by rectal cancer,[5-7] but over- or underestimation of cancer invasion has frequently been reported. It is just the same with the assessment of lymph node metastasis.[8] Accordingly, we carried out an extensive study on the assessment of wall invasion and lymph node metastasis in rectal cancer and evaluated the usefulness of ERUS for these purposes.

PATIENTS AND METHODS

From April 1986 to December 1989, ERUS was applied to 120 patients with rectal cancer preoperatively. In eight patients, the procedure could not be adequately practiced because of nearly complete obstruction of the rectal lumen or high location of the tumor. Fourteen patients with early-stage cancer who received local excision or polypectomy were excluded from the study on pararectal lymph node metastasis.

The ERUS apparatus was composed of a radial scanner, an imaging unit SSD-520, and an ultrasound probe ASU-59 (Aloka Co. Ltd., Tokyo, Ja-

pan). The endorectal probe conducted 360° scans transversely in reference to the longitudinal axis of the rectum. The transducer emitting a 7.5-MHz beam was attached on the end of a flexible rod measuring 65 cm in length and 10.4 mm in diameter.

The rectum was evacuated with a glycerin enema prior to the examination. Patients were placed in the lithotomy position on a consulting bed for urologic use. The rectum was first filled with 150 to 200 ml of water slowly injected through small holes attached near the end of the probe. The ultrasonogram was obtained by a transducer in the probe that was covered with a disposable latex sheath filled with water. To determine the depth of cancer invasion and lymph node metastasis accurately, several levels of the tumor-bearing rectum were scanned by carefully moving the probe up and down.

The surgical specimens were sliced 3 to 5 mm thick following fixation in formalin, and the histopathologic depth of cancer invasion was correlated with the depth assessed by ERUS. The degree of inflammatory cell infiltration seen around the cancer was classified into three categories, i.e., markedly infiltrative, moderately infiltrative, and minimally infiltrative. The largest cross-section of lymph nodes was used for histopathologic study, and the findings were also correlated with ultrasonographic images.

Statistical significance was assayed by using the chi-squared test, and a P value below 0.01 was considered significant.

RESULTS

Ultrasonogram in the Normal Rectal Wall

Generally, the normal rectal wall was described as a five-layer structure by ERUS excluding the lowest part within 3 cm from the anal verge. In some cases, however, the wall was described as a seven-layer structure, in which the fourth layer of muscularis propria was further divided into three layers by an intramuscular hyperechoic band.

Ultrasonographic Assessment of Cancer Invasion in the Rectal Wall

Rectal cancer was usually demonstrated as a hypoechoic lesion, but the echogenicity was stronger than the normal layer of muscularis propria. De-

struction or disappearance of the normally existing layer was one of the most reliable findings which indicated the depth of cancer invasion. However, normal hyperechoic layers of the rectal wall disappeared in some cases because of inflammatory cell infiltration around the cancer. Although the area of inflammatory cell infiltration often presented with an appearance simulating the cancer, we could distinguish the former from the latter in nearly all the cases by perceiving small differences in echogenicity. The cancer echo was always stronger than the echoes of normal muscularis propria and the area of inflammatory cell infiltration.

Accuracy of Assessment of Wall Invasion by ERUS

According to UICC classification, we divided the grade of wall invasion by rectal cancer determined with ERUS into four categories, i.e., uT1, uT2, uT3, and uT4 (T1, T2, T3, and T4, when determined histopathologically).[9] The uT1 cancer indicated the lesion with invasion confined to the mucosa or submucosa, and uT2 cancer was the lesion with invasion to the muscularis propria. The uT3 cancer was the lesion penetrating the rectal wall and infiltrating the perirectal fat tissues (Fig. 1), and uT4 cancer was the lesion infiltrating further into the neighboring organ (Fig. 2).

The predicting value of positive rate in the assessment of wall invasion was 96.2 percent in uT1, 85.7 percent in uT2, 100 percent in uT3, and 61.5 percent in uT4 cancer. The assessment was correct in 103 of 112 cases, the overall accuracy being 92.0 percent. Overestimation occurred in 5 of 60 cases with T3 cancer (8.3 percent), and underestimation occurred in 1 of 19 cases with T2 cancer (5.3 percent) and 3 of 60 cases with T3 cancer (5 percent) (Table 1).

The incidences of inflammatory cell infiltration according to the histopathologic depth of cancer invasion are shown in Figure 3. Overestimation of the depth of cancer invasion with ERUS occurred in 1 of 19 cases of T2 cancer associated with a moderate degree of inflammatory cell infiltration (5.3 percent) and 3 of 60 cases of T3 cancer with a moderate degree of inflammatory cell infiltration (5 percent). Underestimation also occurred only occasionally irrespective of the degree of inflammatory cell infiltration.
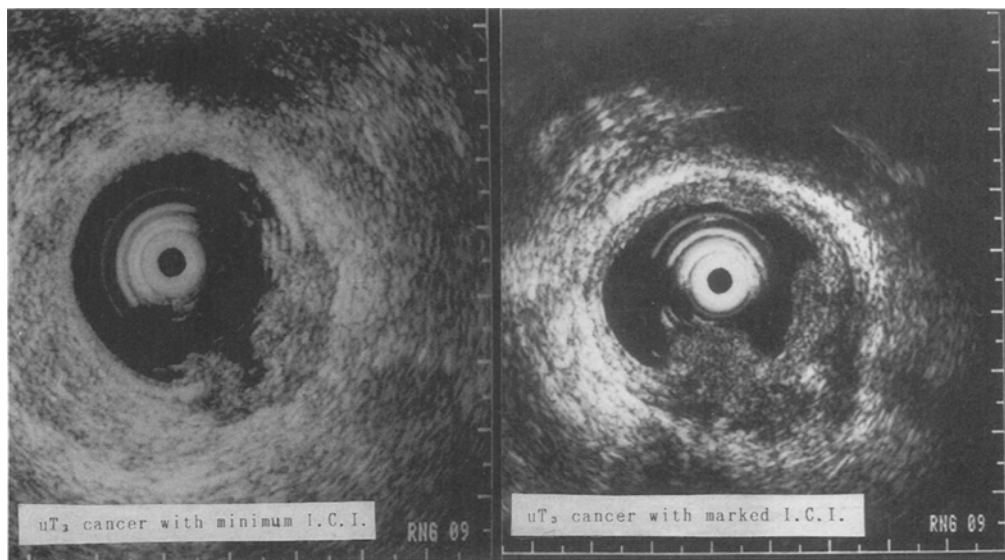
Figure 1. Ultrasonograms showing uT3 cancer. Left. The layer of muscularis propria is invaded by the tumor completely, and the outermost hyperechoic band disappears in the central area of the tumor. Right. The tumor is surrounded by hypoechoic bands produced by inflammatory cell infiltration (I.C.I.), so that the outermost band disappears even in the peripheral area of the tumor, where cancer invasion does not exist.
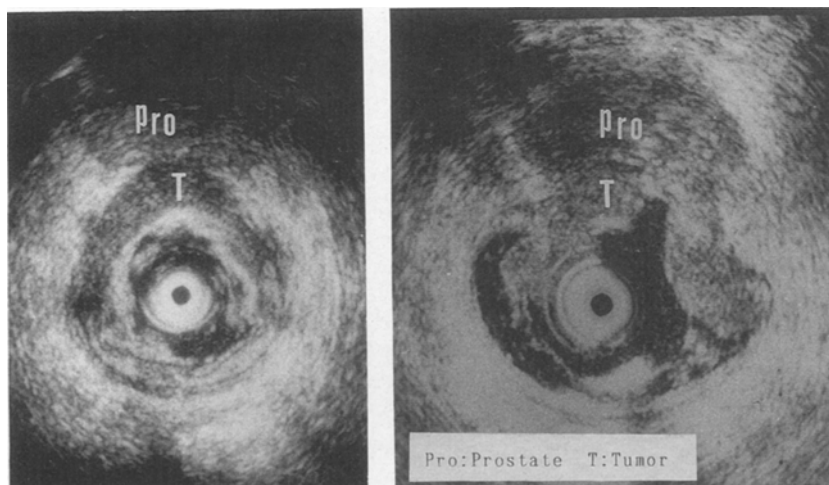
Figure 2. Ultrasonograms showing uT4 cancer. In both cancers, the hyperechoic band between the tumor and prostate disappears, so that it is impossible to distinguish the former from the latter because of their similar echogenicity. Histopathologically, the tumor of the right side invaded the prostate deeply, whereas the prostate was not involved by the tumor of the left side.
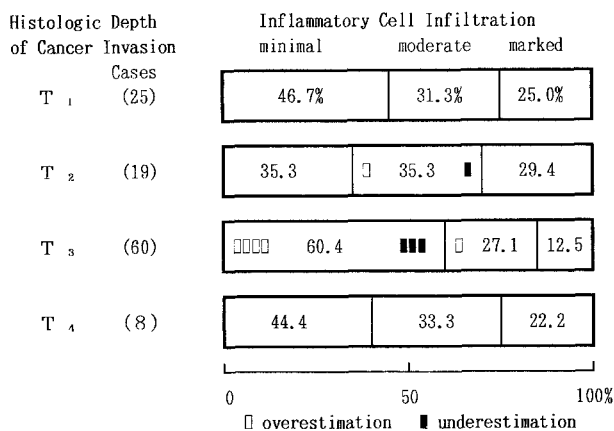
Assessment of Invasion in the Layer of Muscularis Propria by ERUS

Because the layer of muscularis propria in the rectal wall was described as a three-layer structure with ERUS, the depth of cancer invasion in this layer was also subdivided into three categories, *i.e.*, uPM1, uPM2, and uPM3 (PM1, PM2, and PM3, when determined histopathologically). The uPM1 cancer indicated that the lesion invaded the internal layer of muscularis propria only superficially,

and uPM3 cancer indicated that the lesion deeply invaded the outer layer of muscularis propria. The uPM2 cancer indicated the lesion with findings between uPM1 and uPM3 invasions. In 4 of 21 cases with invasion into the muscularis propria, reliable findings were not obtained, and these cases were excluded from the study. The ultrasonograms of two patients with uPM2 cancer are shown in Figures 4 and 5. The predictive value of positive rate in the assessment of invasion in the layer of muscularis propria was 66.7 percent in uPM1, 70

Table 1.
Results of Assessment of Rectal Wall Invasion

(UICC) Histologic Depth of Invasion	Ultrasonic Diagnosis				
	uT1	uT2	uT3	uT4	Total
T1: Confined to submucosa	25				25
T2: Confined to muscularis propria	1	18			19
T3: Beyond muscularis propria		3	52	5	60
T4: Extension to adjacent organ				8	8
Total	26	21	52	13	112
Predicting value of positive rate (%)	96.2	85.7	100	61.5	92.0

Histologic Depth of Cancer Invasion	Cases	Inflammatory Cell Infiltration minimal moderate marked
T₁	(25)	46.7% 31.3% 25.0%
T₂	(19)	35.3 ☐ 35.3 ∎ 29.4
T₃	(60)	☐☐☐☐ 60.4 ∎∎∎ ☐ 27.1 12.5
T₄	(8)	44.4 33.3 22.2

0   50   100%
☐ overestimation ∎ underestimation

Figure 3. Incidences and degrees of inflammatory cell infiltration (ICI) in relation to histopathologic depth of cancer invasion. Overestimation of wall invasion occurs in one case of T2 cancer with moderate ICI, four cases of T3 cancer with minimal ICI, and one case of T3 cancer with moderate ICI. Underestimation occurs in one case of T2 cancer with moderate ICI and three cases of T3 cancer with moderate ICI.

percent in uPM2, and 25 percent in uPM3 cancer (Table 2).

Ultrasonographic Assessment of Pararectal Lymph Node Metastasis

The ultrasonographic demonstration of pararectal lymph nodes was studied on 98 patients. No swollen lymph nodes were detected in 35 of them. However, lymph node metastasis was found histopathologically in 5 of these 35 patients (14.3 percent). Lymph nodes detected were measured on the ultrasonogram and divided into three groups according to the diameters of ≤4 mm, 5 to 9 mm,

and ≥10 mm. The incidence of lymph node metastasis was 18.2 percent in the small-sized group, 45.7 percent in the middle-sized group, and 70.6 percent in the large-sized group. The incidence of metastasis in lymph nodes with a diameter of more than 5 mm was significantly higher than in those ultrasonographically negative or with a diameter of less than 4 mm ($P < 0.01$) (Table 3).

Accuracy of Assessment of Lymph Node Metastasis by ERUS

Ninety-six lymph nodes with a diameter of more than 5 mm detected by ERUS were divided into two types (A and B) according to their ultrasonographic features. Type A lymph nodes exhibited an ill-defined boundary and an even and hyperechoic intranodal pattern, whereas Type B lymph nodes showed a well-defined boundary and an uneven and markedly hyperechoic intranodal pattern (Fig. 6). The incidence of metastasis was 72.3 percent in Type B lymph nodes and was significantly higher than 18.4 percent in Type A lymph nodes ($P < 0.01$) (Table 4).

DISCUSSION

An increasing interest has recently been shown in ERUS for the assessment of cancer invasion through the rectal wall or staging of rectal cancer. The findings are particularly useful for surgical options available for the conservative management of the disease. Saitoh et al.[6] first demonstrated that the normal rectal wall could be described as a five- or seven-layer structure with a 7.5-MHz radial scanner. Yamashita et al.[7] divided the depth of cancer invasion in the rectal wall into four levels and obtained an accuracy of 77.9 percent in the assessment of wall invasion. It should be noted, however, that the depth of invasion was overestimated in as many as 21 of 122 cases (17.2 percent).

Needless to say, it is of crucial importance to take a fine ultrasonogram and scrutinize it carefully for the accurate assessment of the depth of cancer invasion. For this purpose, we introduced a water-filled method, which made it possible to describe the rectal wall as a five- or seven-layer structure more clearly.[10] The method was especially useful for the visualization of a small and early-stage cancer or a pedunculated tumor. Although slightly complicated compared with the balloon method,
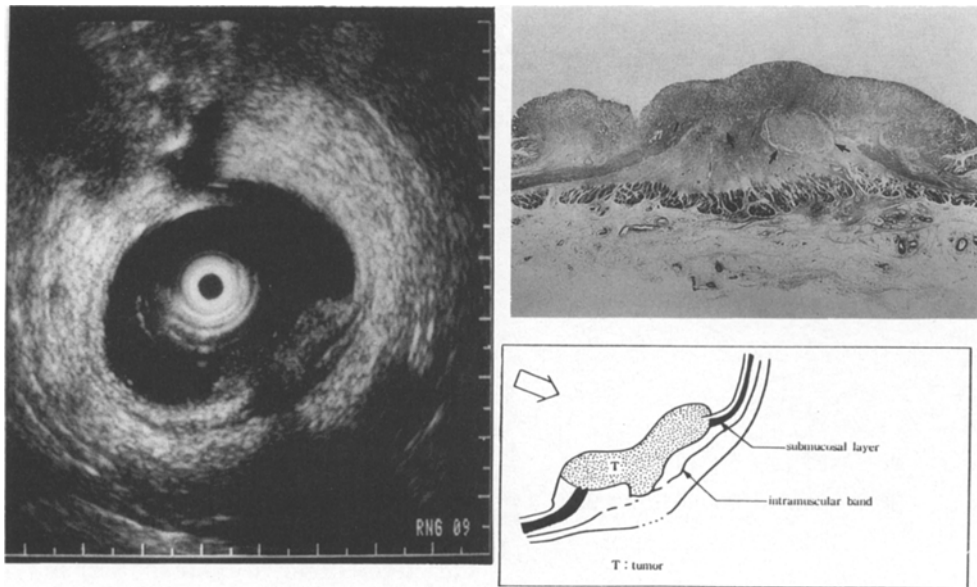
Figure 4. Ultrasonogram showing uPM2 cancer. The fourth hypoechoic layer (muscularis propria) is thickened markedly, and the intramuscular hyperechoic band is clearly seen on the right side of the tumor. However, this hyperechoic band disappears on the left side without tumor invasion. Histopathologically, marked inflammatory cell infiltration is observed in the intramuscular area, and cancer invasion is superficially seen in the outer muscle layer (PM2).
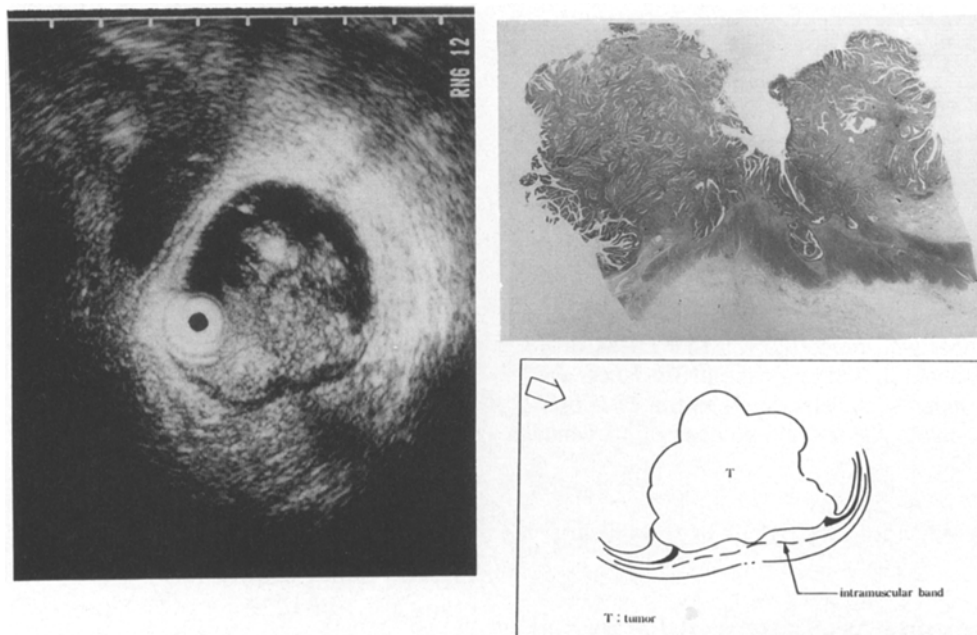
Figure 5. Ultrasonogram showing pedunculated uPM2 cancer. The fourth hypoechoic layer is thickened, and the intramuscular hyperechoic band is noted by careful observation. The outer muscle layer is assessed to be involved only slightly. However, deep invasion into the outer muscle layer is observed histopathologically (PM3).

it could be applied more easily and safely by using a consulting bed for urologic use.

Using this method, we obtained an overall accuracy of 92.0 percent in the assessment of depth of cancer invasion in the rectal wall. When the accuracy of assessment was compared among four groups with different depths of cancer invasion (uT1–uT4), the result was most unfavorable in uT4 cancer. Since adjacent organs such as the prostate, seminal vesicles, and vagina exhibit hypoecho-

Table 2.
Results of Assessment of Wall Invasion in uT2 Cancer

Histologic Depth of Invasion	Ultrasonic Diagnosis			
	uPM1	uPM2	uPM3	Total
A part of internal muscle layer (PM1)	2	1		3
A part of outer muscle layer (PM2)	1	7	1	9
Deep outer muscle layer (PM3)		1	1	2
Beyond muscularis propria		1	2	3
Total	3	10	4	17
Predicting value of positive rate (%)	66.7	70.0	25.0	58.8

Table 3.
Relationship Between the Largest Diameter Detected by ERUS and Metastasis in Lymph Nodes

Size Measured by ERUS	Cases	Histologic Metastasis (%)		
		(−)	(+)	
Not detected	35	30	5	14.3
≤4 mm	11	9	2	18.2
				15.2 (7/46)
5–9 mm	35	19	16	45.7
≥10 mm	17	5	12	70.6
				53.8 (28/52)
Total	98	63	35	35.7

$P \leq 0.01$

Table 4.
Incidences of Metastasis in Type A and Type B Lymph Nodes

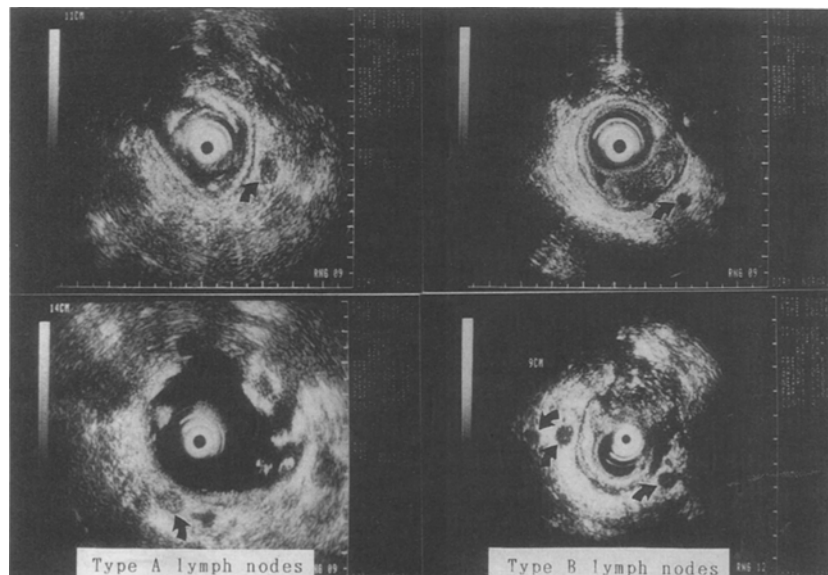| Lymph Node Size Measured by ERUS	Type A	Type B
5–9 mm	19.6% (9/46)	69.4% (25/36)
≥10 mm	0% (0/3)	81.8% (9/11)
Total	18.4% (9/49)	72.3% (34/47)

$P \leq 0.01$

genicity like the cancer, the assessment is very difficult in the tumor infiltrating deeply beyond the rectal wall.

Yamashita et al.[7] investigated the possible reason for overestimation in the assessment of the depth of cancer invasion in the rectal wall and found that the incidence increased in proportion to the degree of inflammatory cell infiltration around the cancer. We also paid special attention to this problem and observed that the existence of marked inflammatory cell infiltration around the cancer made hyperechoic layers in the normal rectal wall hypoechoic and indistinguishable. The hyperechoic layers disappeared completely without cancer invasion in some cases. However, the cancer echo was usually stronger than the echo of the normal layer of muscularis propria or inflammatory cell infiltration. It was thus possible to distinguish the cancer echo from two others with careful ob-

Figure 6. Ultrasonograms showing pararectal lymph nodes. Left. Type A lymph nodes. Right. Type B lymph nodes.

servation. Actually, the assessment of the depth of cancer invasion was hardly affected by the existence and degree of inflammatory cell infiltration in our series.

In uT2 (uPM) cancers, the accuracy of assessment of the depth of invasion was studied in three subgroups (uPM1, uPM2, and uPM3). The accuracy was exceedingly low (25 percent) in uPM3 cancer, compared with 66.7 percent in uPM1 cancer and 70 percent in uPM2 cancer. Because the number of cases studied was limited, the significance of results needs further investigation. Underestimation occurred in 5 of 17 cases (29.4 percent), but minimal invasion of cancer cells was the reason in three cases, and inflammatory cell infiltration was found only minimally in all cases.

The value of ultrasonographic assessment of pararectal lymph node metastasis seems superior to that of computed tomography, but only a few studies have been directed to this problem.[8, 10, 11] In the present study, we tried the ultrasonographic demonstration of pararectal lymph nodes in 98 patients with rectal cancer and obtained various useful information. No swollen lymph nodes were demonstrated ultrasonographically in 35 of 98 cases (35.7 percent), but cancer metastasis was found histopathologically in 5 of 35 cases (14.3 percent). The metastasis was observed more frequently in lymph nodes with a diameter of more than 5 mm (53.8 percent) than in those that were not demonstrated ultrasonographically or that were smaller in size with a diameter of less than 4 mm (15.2 percent). Furthermore, when lymph nodes were divided into Type A, with an ill-defined boundary and an even and hyperechoic intranodal pattern, and Type B, with a well-defined boundary and an uneven and markedly hypoechoic intranodal pattern, the incidence of cancer metastasis was significantly higher in Type B lymph nodes (18.4 percent *vs.* 72.3 percent).

In conclusion, although unable to detect minimal cancer foci, ERUS was considered a very useful tool for the assessment of the depth of cancer invasion in the rectal wall and pararectal lymph node metastasis.

REFERENCES

1. Clark J, Bankoff M, Carter B, Smith TJ. The use of computerized tomography scan in the staging and follow up study of carcinoma of the rectum. Surg Gynecol Obstet 1984;159:335–42.
2. Hori M, Watanabe S, Matsubara T, Ikeda T, Kajitani T. Staging of colorectal cancer with computed tomography. Stomach Intest 1984;19:1321–6.
3. Freency PC, Marks WM, Ryan JA. Colorectal carcinoma evaluation with CT. Radiology 1986;158: 347–53.
4. Hodgman CG, MacCarty RL, Wolff BG, *et al.* Preoperative staging of rectal carcinoma by computed tomography and 0.15T magnetic resonance imaging. Preliminary report. Dis Colon Rectum 1986;29: 446–50.
5. Hildebrant U, Feifel G. Preoperative staging of rectal cancer by intrarectal ultrasound. Dis Colon Rectum 1985;28:42–6.
6. Saitoh N, Okui K, Sarashina H, Suzuki M, Arai T, Nunomura M. Evaluation of echographic diagnosis of rectal cancer using intrarectal ultrasonic examination. Dis Colon Rectum 1986;29:234–42.
7. Yamashita Y, Machi J, Shirouzu K, Morotomi T, Isomoto H, Karegawa T. Evaluation of endorectal ultrasound for the assessment of wall invasion of rectal cancer: report of a case. Dis Colon Rectum 1988;31:617–23.
8. Ogiso M. A study of preoperative ultrasonographic evaluation of the depth of invasion and lymph node metastasis in rectal cancer. Tokyo Med Coll 1987; 45:191–203.
9. TNM Classification of Malignant Tumors. In: Hermanek P, Sobin LH, eds. International Union Against Cancer. Springer-Verlag, 1987.
10. Katsura Y, Ishizawa T, Yoshinaka H, Yamada K, Shimazu H. Diagnosis of mural invasion and lymph node metastasis of rectal cancer by endorectal ultrasonography. J Jpn Soc Colo-proctol 1990;43:388–95.
11. Hildebrandt U, Klein T, Feifel G, Schwarz H-P, Koch B, Schmitt RM. Endosonography of pararectal lymph nodes: *in vitro* and *in vivo* evaluation. Dis Colon Rectum 1990;33:863–8.