Estimating the Depth of Myometrial Involvement by Endometrial Carcinoma: Efficacy of Transvaginal Sonography vs MR Imaging

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OBJECTIVE. In this study we compare transvaginal sonography with MR imaging for use in detecting the depth of myometrial involvement by endometrial carcinoma.

SUBJECTS AND METHODS. Forty-two consecutive patients with stage I endometrial carcinoma had transvaginal sonography and MR imaging at 0.5 T. All the patients had a hysterectomy within 1–10 days after the imaging studies. The results of histologic examination of the surgical specimen were considered the gold standard of the study. We compared transvaginal sonography and MR imaging for use in assessing myometrial invasion by endometrial carcinoma by means of the staging classification of the International Federation of Gynecology and Obstetrics: stage Ia (tumor limited to endometrium), stage Ib (invasion of less than half the myometrium), stage Ic (invasion of more than half the myometrium). The overdiagnoses and the underdiagnoses for both techniques were calculated. We also evaluated the sensitivity and specificity of the two techniques for assessing the presence of myometrial invasion (stage Ib + stage Ic) and the presence of deep myometrial invasion (stage Ic). The diagnostic indexes evaluated and the differences between them were analyzed by using McNemar's test and 95% confidence intervals. The staging diagnoses based on MR imaging and sonographic findings were compared with staging diagnoses based on histologic examination, and a score was assigned to each diagnosis: these scores were then evaluated with Wilcoxon's signed rank test for paired data.

RESULTS. Histologic examination showed that six of the 42 patients had tumor confined to the endometrium (stage Ia), 14 had involvement of the inner half of the myometrium (stage Ib), and 22 had involvement of the outer half of the myometrium (stage Ic). The staging was concordant between the two imaging techniques in 32 cases (concordance, 76%). Among the 10 discordant cases, diagnosis was correct in six cases for MR and four cases for sonography. Overall staging based on sonography was correct with respect to histologic staging in 29 cases (69%; 95% confidence interval, 52–81%). Five tumors (12%) were underdiagnosed and eight (19%) were overdiagnosed. Staging based on MR findings was correct with respect to histologic staging in 31 cases (74%; 95% confidence interval, 58–85%). Five tumors (12%) were underdiagnosed, and six (14%) were overdiagnosed.

CONCLUSION. In our experience, there is no difference in the staging diagnoses of transvaginal sonography and MR imaging. Also, concordance with histologic staging diagnoses and sensitivity and specificity indexes did not show statistical differences between the two techniques, although these last results have to be considered with caution because of the low power of the statistical tests.

Endometrial carcinoma is the most common malignant neoplasm of the female genital tract [1, 2]. The prognosis and treatment of the disease are based mainly on three factors: histologic grading of the neoplasm, the extent of myometrial invasion, and the presence of nodal metastasis [1, 2].

The depth of myometrial involvement is one of the most important aspects, because the prevalence of pelvic and lumboaortic nodal metastases is directly related to this parameter [1, 2]. The revised staging classification of the International Federation of Gynecology and Obstetrics (FIGO) for endometrial carcinoma considers three degrees of myometrial invasion: stage Ia, no invasion; stage Ib, endometrial carcinoma involving the inner half of the myometrium; and stage Ic,

carcinoma reaching the outer half of the myometrium. If the myometrium is not invaded, nodal metastases are present in about 3% of patients. If the invasion is deep (stage Ic), nodal metastases are present in about 40% of cases [2, 3].

Previous authors [4–8] described the use of transvaginal high-frequency probes for sonographic evaluation of gynecologic neoplasms. The reported concordance with histologic examination of transvaginal sonography for determining the depth of myometrial involvement by endometrial carcinoma is 80–84% [6, 9].

MR imaging is a reliable technique in local staging of endometrial carcinoma. The reported MR concordance with histologic examination in distinguishing superficial from deep myometrial invasion is about 78–82% [3, 10–12].

The aim of our study was to compare transvaginal sonography and MR imaging in the preoperative assessment of myometrial infiltration by the tumor in proved cases of endometrial carcinoma.

Subjects and Methods

Fifty-one consecutive patients with histologically proved endometrial carcinoma were considered for inclusion in this prospective study. Nine patients in whom pathologic examination of the surgical specimen showed the presence of advanced disease were excluded. The remaining 42 women (33–72 years old; mean, 61.8 years) were included in the study. Thirty-one (74%) were postmenopausal; 11 (26%) were premenopausal.

Diagnosis was based on the results of pathologic examination of specimens obtained during dilatation and curettage. All 42 patients had both transvaginal sonography and MR imaging in order to assess the depth of myometrial involvement of tumor. The studies were performed 1–10 days before surgery. Radical hysterectomy was performed in each case.

Sonograms were obtained using 5-MHz phased-array sector and convex endovaginal transducers and commercially available units (RT 3000 GE Medical Systems, Milwaukee, WI, and SAL 100/SAL 250 Toshiba Medical System, Tokyo). Each patient had a cleansing enema and then was examined supine when her bladder was empty. A physician expert in transvaginal scanning who did not

know the MR results performed sonography. The longitudinal, transverse, and anteroposterior diameters of the uterus were imaged. As described by Fleischer et al. [13], the presence and continuity of the hypoechoic halo that surrounds the outer layer of the endometrium was assessed and classified as intact (Fig. 1), partially disrupted (Fig. 2A), or totally disrupted (Fig. 3A). The extent of myometrial involvement was estimated by measuring the distance from the central lumen of the uterus to the distal junction between tumor and normal myometrium. All the sonograms were prospectively evaluated, and the data obtained were classified according to FIGO criteria as stage Ia (tumor limited to endometrium), stage Ib (invasion of less than half the myometrium), or stage Ic (invasion of more than half the myometrium).

MR was performed on a 0.5-T unit (MRT 50A, Toshiba Medical Systems, Tokyo, Japan). T2-weighted spin-echo images (1500–2000/40–90 [TR/TE], 256 × 192 matrix, two excitations, and 35-cm field of view) were acquired. The uterus was examined in both sagittal and axial planes. Contiguous slices 5.0 or 7.5 mm thick were imaged. Two experts on pelvic disease who did not know the sonographic findings prospectively evaluated the MR images in conference. They examined the signal intensity of the endometrium and the continuity of the hypointense band (junctional zone) that lines the endometrium–myometrium interface [3] (Figs. 2 and 3). If the junctional zone was partially or totally disrupted, the thickness of myometrial invasion was measured, and the tumor was classified according to FIGO criteria. When the junctional zone was poorly delineated, the myometrial invasion was judged on the basis of the minimal thickness of residual myometrium. The two observers reached a consensus in each case.

After hysterectomy, the pathologist examined radial thin sections of the uterus from the endometrial cavity to the serosal surface of the myometrium. Myometrial tumor spread was evaluated histologically and graded as absent (tumor limited to the endometrium), superficial (invasion of less than half the myometrium), or deep (invasion of more than half the myometrium). The pathologist had no knowledge of the sonographic or MR findings. The results of histologic examination of the surgical specimens were considered the gold standard for the study.

The concordance of staging of myometrial invasion based on transvaginal sonographic and MR imaging findings with histologic staging was calculated by dividing the total number of correct estimations obtained with each technique by the total number of cases.
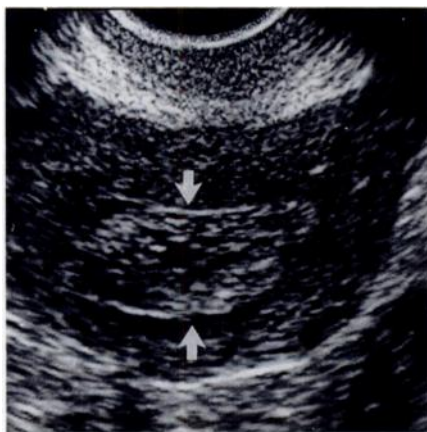

A

B

Fig. 1.— Axial transvaginal sonogram of a patient with endometrial carcinoma shows an uninterrupted hypoechoic halo (arrows). Tumor was correctly classified as stage Ia.

Fig. 2.— Tumor in a patient with histologically proved endometrial carcinoma that was correctly classified as stage Ib on basis of both sonographic and MR findings.
A, Axial transvaginal sonogram shows tumor invading myometrium (arrows).
B, Axial T2-weighted (2000/90) MR image shows interruption (arrowheads) of hypointense junctional zone.
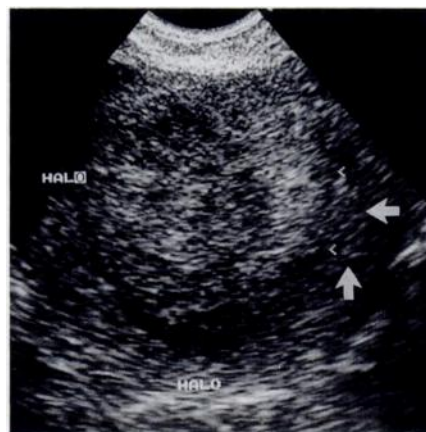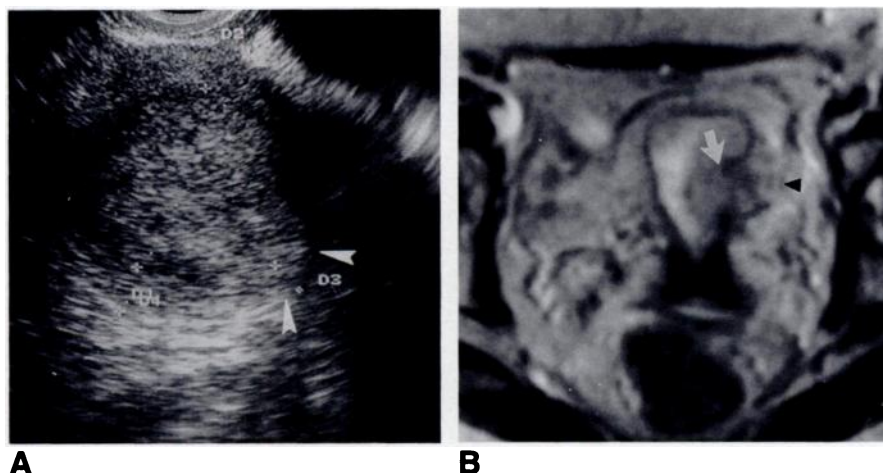
Fig. 3.— Tumor in a patient with histologically proved endometrial carcinoma that was correctly classified as stage Ic on basis of both sonographic and MR findings.

A, Oblique transvaginal sonogram shows tumor invading outer half of myometrium (*arrowheads*).

B, Axial T2-weighted (2000/90) MR image shows that junctional line is interrupted (*arrow*) and that tumor reaches serosal surface of myometrium (*arrowhead*).

The overdiagnoses and underdiagnoses with both techniques were calculated.

We also evaluated the sensitivity and specificity of the two techniques for assessing the presence of myometrial invasion (stage Ib + stage Ic) vs the absence of myometrial invasion (stage Ia) and the presence of deep myometrial invasion (stage Ic) vs superficial or no invasion (stage Ia + stage Ib). Ninety-five percent confidence intervals of these accuracy indexes and of overall concordance of the two techniques with histologic examination were calculated. Ninety-five percent confidence intervals of the differences between the diagnostic indexes evaluated were calculated also [14].

The results of transvaginal sonography and MR imaging were compared by using McNemar's test [15] with a two-by-two table in which the staging diagnoses with each technique were classified as correct or incorrect (underdiagnosis or overdiagnosis) in comparison with histologic staging diagnoses. The power of this McNemar's test was calculated also [16]. Moreover, the staging diagnoses based on MR and sonographic findings were compared with histologic staging diagnoses, and a score was assigned to each diagnosis, representing the distance from the histologic diagnosis: when the diagnosis was correct, the score was zero; when the histologic stage differed from the stage obtained with one imaging technique by one degree (e.g., stage Ia instead of stage Ib), the score was 1; when the histologic stage differed from the stage obtained with one imaging technique by two degrees, the score was 2. When the error was an overstage error, a plus sign (+) was added; when it was an understage error, a minus sign (−) was added.

The differences between the absolute values of these scores were then assessed with a single tail Wilcoxon's signed rank test for paired data [14].

Results

Histologic examination showed that six of the 42 patients had tumor confined to the endometrium (FIGO stage Ia), 14 had involvement of the inner half of the myometrium (stage Ib), and 22 had involvement of the outer half of the myometrium (stage Ic) (Table 1). All the sonographic examinations were adequate. Endometrial carcinoma appeared coarsely hyperechoic in most patients.

Although the quality of seven MR examinations was suboptimal because of motion artifacts, all 42 examinations were included in the study. On T2-weighted MR images, the junctional zone was poorly delineated in 17 cases (40%). The signal intensity of the tumor was always higher than that of normal myometrium.

The results of staging based on sonographic and MR findings are reported in Table 1.

Overall, staging based on sonography was correct in 29 cases (concordance with histologic staging, 69%; 95% confidence interval, 52–81%). Five tumors (12%) were underdiagnosed and eight (19%) were overdiagnosed. Staging based on MR findings was correct in 31 cases (concordance with histology, 74%; 95% confidence interval, 58–85%). Five tumors (12%) were underdiagnosed, and six (14%) were overdiagnosed.

The difference between concordance with histologic staging of the two techniques was 5% (95% confidence interval, −10–20%). The number of cases that were understaged or overstaged is reported in Table 2. Of the 20 patients with stage Ia or Ib disease (i.e., those in the study who could possi-

TABLE 1: Depth of Myometrial Invasion in Stage I Endometrial Carcinoma: Comparison of Transvaginal Sonography, MR Imaging, and Histologic Findings

Histologic Examination (%)	Transvaginal Sonography			MR Imaging		
	Ia	Ib	Ic	Ia	Ib	Ic
Ia						
6 (14)	**3**	1	2	**4**	1	1
Ib						
14 (33)	2	**7**	5	3	**7**	4
Ic						
22 (52)	1	2	**19**	1	1	**20**

Note.—Ia, no tumor invasion of myometrium; Ib, invasion to the inner half of the myometrium; Ic, invasion to the outer half of the myometrium. Boldface numbers indicate correct diagnoses.

TABLE 2: Cases of Endometrial Carcinoma Incorrectly Staged on the Basis of Sonographic and MR Imaging Findings

Examination	Underdiagnoses		Overdiagnoses	
	Stage Ib (%)	Stage Ic (%)	Stage Ia (%)	Stage Ib (%)
Sonography	2 (14)	3 (14)	3 (50)	5 (36)
MR imaging	3 (21)	2 (9)	2 (33)	4 (29)

Note.—Ia, no tumor invasion of myometrium; Ib, invasion to the inner half of the myometrium; Ic, invasion to the outer half of the myometrium.
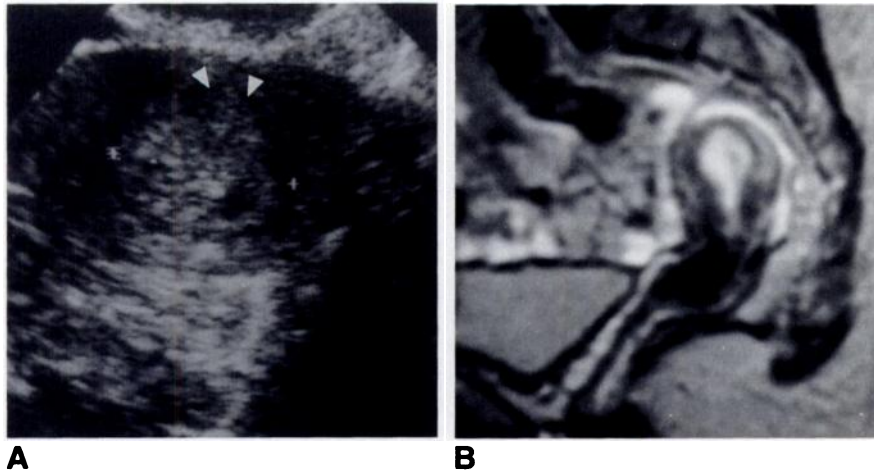
A   B

Fig. 4.— Tumor in a patient with histologically proved endometrial carcinoma that was incorrectly classified as stage Ib on basis of sonographic findings and correctly assessed as stage Ia on basis of MR findings.

A, Axial transvaginal sonogram shows apparent invasion of myometrium anteriorly (arrowheads).

B, Sagittal T2-weighted (2000/90) MR image shows intact hypointense junctional line is not interrupted.

bly have been overdiagnosed), staging based on sonographic findings was correct in only 10 (50%), and staging based on MR findings was correct in 11 (55%). Furthermore, staging based on sonographic findings gave eight (40%) overdiagnoses of these 20 patients, whereas staging based on MR findings gave overdiagnoses for six (30%) of 20 patients.

On the basis of sonographic findings, three tumors that histologic examination showed were infiltrating were considered noninfiltrating (false-negatives). In one case, endometrial carcinoma had infiltrated the myometrium for 18 mm over a total myometrial thickness of 25 mm (myometrial invasion, 72%). In the other two cases, myometrial infiltration was 2 over 20 mm (10%) and 1 over 10 mm (10%).

On the basis of MR findings, four tumors that histologic examination showed were infiltrating were considered noninfiltrating. Invasion of the myometrium was 2 over 17 mm of myometrial thickness (12%), 3 over 12 mm (25%), 2 over 15 mm (13%), and 12 over 19 mm (63%).

Three tumors classified as stage Ia on the basis of histologic findings were incorrectly classified as stage Ib or Ic (false-positives) on the basis of sonographic findings (Fig. 4). Two of these three cases were classified incorrectly (false-positives) on the basis of MR findings also.

The indexes of the accuracy of transvaginal sonography and MR imaging for the assessment of the presence of myo-metrial invasion (stage Ib + stage Ic vs stage Ia) or the presence of deep myometrial invasion (stage Ic vs stage Ia + Ib) are presented in Table 3. The 95% confidence intervals for the differences between the various diagnostic indexes evaluated are also presented in Table 3.

The sensitivity and specificity of staging based on MR imaging findings are in general slightly higher than the sensitivity and specificity of staging based on sonographic findings, but these differences are not significant. Table 4 shows the direct comparison in a three-by-three table format of the cases of endometrial carcinoma correctly or incorrectly staged with transvaginal sonograms and MR images. McNemar's test was calculated by considering together the over- and understaging errors. The test revealed that the overall staging capabilities of transvaginal sonography and MR imaging were not significantly different. This McNemar's test could detect a difference of more than 20%, with a 5% α error, a power of 90%, and a sample size of 42 pairs [16].

If we consider only the cases in which the two techniques were in agreement (30 patients), the concordance with histology is 83% (95% confidence interval, 64–94%), with five overdiagnoses and no underdiagnoses. The staging with the two techniques was the same in 32 (76%) of 42 cases (in 25 cases staging was equally correct; in seven cases staging based on both techniques was incorrect). Among the 10 dis-

TABLE 3: Indexes of the Accuracy of Transvaginal Sonography and MR Imaging for Correct Determination of Myometrial Invasion in Stage I Endometrial Carcinoma

	Myometrial Invasion			Deep Myometrial Invasion		
	Sonography	MR Imaging	Difference	Sonography	MR Imaging	Difference
Sensitivity	33/36	32/36	1/36	19/22	20/22	1/22
%	92	89	3	86	91	5
	(76; 97)	(73; 96)	(−20; 10)	(64; 96)	(69; 98)	(−20; 30)
Specificity	3/6	4/6	1/6	13/20	15/20	2/20
%	50	67	17	65	75	10
	(13; 86)	(24; 94)	(−30; 60)	(41; 84)	(50; 90)	(−10; 30)

Note.—Number in parentheses are 95% confidence intervals.

TABLE 4: Cases of Endometrial Carcinoma Correctly or Incorrectly Staged on the Basis of Transvaginal Sonography and MR Imaging in 42 Patients

MR Imaging	Transvaginal Sonography			
	Correct Staging	Understaging	Overstaging	Total
Correct staging	**25**	4	2	31
Understaging	4	**0**	1	5
Overstaging	0	1	**5**	6
Total	29	5	8	42

Note.—Boldface numbers indicate diagnostic agreement between the two techniques.

cordant cases, diagnosis was correct in six and four cases for MR and sonography, respectively (Table 4).

Regarding the seven cases in which staging was incorrect with both techniques, the staging error was the same in five cases (overstaging). In the last two cases, histologic examination showed a stage Ib tumor, whereas staging based on MR findings was Ia in one case and Ic in the other case; in these cases, staging based on sonographic findings was Ic and Ia, respectively.

Considering the score we assigned to each diagnosis, Wilcoxon's signed rank test for paired data resulted in a non-significant difference ($p = .34$). The sum of the scores obtained with staging based on sonographic findings was four; the sum of the scores obtained with staging based on MR imaging findings was one. These results reveal a slight tendency toward overstaging for sonography.

Discussion

Preoperative assessment of myometrial invasion by endometrial carcinoma is important because the prognosis and the surgical treatment (hysterectomy or hysterectomy plus lymphadenectomy) are based on the depth of infiltration [1]. Both sonography and CT have been used for local staging of endometrial carcinoma. The reported concordance with histologic examination is about 70% for transabdominal sonography [9, 13] and 7–76% for CT [17, 18]. Few studies [17, 18] have been published on the use of CT in evaluating the depth of myometrial infiltration. This might suggest wide interobserver variability for CT data.

Lewit et al. [7] and Higgins et al. [19] described the use of transvaginal sonography with high-frequency probes in the evaluation of gynecologic neoplasms. Visualization of pelvic structures was better than with the transabdominal examination, particularly for the evaluation of pregnancy and for early detection of ovarian carcinoma [19]. Tessler et al. [20] stated that endovaginal examination can effectively replace transabdominal examination as the initial approach for routine pelvic sonography. Transvaginal sonography has a number of potential advantages, including increased resolution, especially in obese women and in women with uterine retroversion [21]. Depiction of the endometrium is significantly better than with the transabdominal approach. In a study by Gordon et al. [6], 25 patients with endometrial carcinoma

had transvaginal sonography 1 week before hysterectomy. In 21 cases (84%), the depth of invasion of the myometrium was predicted correctly on the basis of the sonographic findings. Using the same technique, Cacciatore et al. [9] correctly detected myometrial invasion in 80% of cases. Fleischer et al. [13] reported a concordance with histologic examination of 80%. These studies did not compare the concordance of MR imaging with histologic examination against that of transvaginal sonography in the same patients. In the present study, the efficacy of transvaginal sonography and MR imaging in assessing myometrial invasion by tumor was evaluated in the same patients. In the study by Fleischer et al., however, the high rate of concordance of transvaginal sonography with histologic examination was probably due to the use of a measurement value of ±15% of the depth of the myometrial infiltration. In our study, the absolute value of invasion was calculated. Cacciatore et al. [9] also considered 15 cases that histologic examinations showed were stage II or higher, and they did not give separate data for patients with no invasion (Ia). This could have influenced the statististical values and makes their study not completely comparable with ours.

MR imaging seems to be a reliable method for the staging of uterine tumors [3, 10–12]. Its concordance with histologic examination is about 80% for staging endometrial carcinoma [3, 10, 11] and 82% for distinguishing superficial from deep myometrial invasion [3].

In a prospective study by Hricak et al. [3] in which myometrial invasion was evaluated by using MR imaging, concordance with histologic examination was 82%, superior to our 74%. Their study, however, considered all the stages of endometrial carcinoma. In a separate analysis of their 39 patients with stage I tumor, the concordance with histologic examination was 77%, similar to that reported in our study.

We previously [11] reported 86% concordance for MR imaging with histologic examination in assessing myometrial invasion; that study was retrospective, however, and a high-field-strength magnet (1.5 T) was used. On the other hand, in a recent prospective study [22], we obtained a staging sensitivity of 74% for MR imaging, equal to that reported by Hricak et al. [23] for a multicenter study.

For assessing the presence (stage Ib + Ic) vs the absence (stage Ia) of myometrial invasion, MR imaging had a sensitivity slightly superior to the sensitivity of transvaginal sonography (Table 3), but this difference is not statistically significant. The sensitivity and specificity of staging based on MR imaging in the detection of deep myometrial invasion (stage Ic vs stage Ia + Ib) are also slightly superior to those of staging based on sonographic findings, but again this difference is not significant.

In addition, the evaluation of the concordance with histologic examination between the two techniques did not show statistically significant differences (Table 4). All these results, however, are probably influenced by the relatively small number of patients in the study and by the proportion of patients in each group, especially the small number of patients with stage Ia endometrial carcinoma. The McNemar's test on the overall concordance with histologic examination had the power to detect a difference greater than

20%. This value is not precise, but the calculated number of patients required to detect a difference of at least 10% in a population of patients similar to the one of our study is about 200, and it is difficult to conduct such a large study.

An overall evaluation of the similarity in the performance of the two techniques was carried out by analyzing the concordance between the two techniques. The data revealed that in most cases (32 of 42) staging based on MR imaging findings was the same as staging based on sonographic findings (for 25 cases both were correct and for seven cases both were incorrect; Table 4). Only 10 cases had discordant diagnoses: of these, the number of cases in which MR imaging was correct (six) is similar to the number of cases in which sonography was correct (four), supporting the hypothesis that the two techniques are similar in staging endometrial carcinoma. In our experience, most errors with both techniques were overdiagnoses (Table 2).

False-positive diagnoses in detecting the presence of myometrial invasion result in more radical surgery, involving more risk for the patient who might not actually require lymphadenectomy. Three false-positive diagnoses were made on the basis of sonographic findings and two on the basis of MR findings. Two of the three tumors classified incorrectly on the basis of sonographic findings were misdiagnosed on the basis of MR findings also. These errors were probably due to the thinned myometrium in elderly patients.

False-negative diagnoses in detecting myometrial invasion can lead to conservative surgical treatment (transvaginal or transabdominal hysterectomy without lymphadenectomy) in patients who are actually at risk for lymph node metastases. We found that the false-negative diagnoses based on sonographic findings were different from those based on MR findings. In five of seven cases, the false-negative diagnoses involved lesions with myometrial invasion of 1–3 mm. These minimal amounts have little influence on the prognosis and prevalence of lymph node metastases. In the remaining two cases, however, the degree of myometrial invasion was relevant. This means that the staging errors may be due not only to insufficient spatial resolution of the techniques, but also to subjective interpretative mistakes.

If we consider only the 30 cases in which the two techniques were in agreement, the concordance with histology is higher than it is with either sonographic or MR imaging findings, suggesting a more accurate prediction of the histologic stage.

In conclusion, our study indicates that, as a whole, staging of myometrial tumor invasion based on transvaginal sonography is similar to that based on MR imaging. Further investigations with larger series of patients are needed in order to fully understand the respective roles of the two techniques in staging endometrial cancer.

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