

Accuracy of magnetic resonance imaging for the evaluation of myometrial invasion in endometrial carcinoma

Takashi Fujimoto ¹⁾, Mitsuharu Tamagawa ²⁾, Miho Kimura ¹⁾, Ryoichi Tanaka ¹⁾, Kota Umemura¹⁾, Eiki Ito ¹⁾, Takahiro Suzuki ¹⁾, Masato Hareyama ²⁾, Tsuyoshi Saito ¹⁾

¹⁾ Department of Obstetrics and Gynecology,

²⁾ Department of Radiology,

Sapporo Medical University School of Medicine, S-1, W-16, Chuo-ku, Sapporo 060-8543, Japan

ABSTRACT

Endometrial carcinoma is the most common gynecologic malignancy and accounts for 6% of all cancers in women. In patients with endometrial cancer, preoperative knowledge of myometrial tumor extension has important prognostic and therapeutic implications. The aim of this retrospective study is to assess whether magnetic resonance (MR) imaging is useful to assess the depth of myometrial invasion by endometrial carcinoma. Sixty patients between 2003 and 2005 were included in the study. All patients were proven histopathologically endometrial carcinoma and underwent preoperative MR imaging and all data was compared in all cases. The histological results showed no myometrial invasion in 8 cases, myometrial invasion of less than 50% in 35 cases, and myometrial invasion of more than 50% in 17 cases. In the cases of no myometrial

invasion, MR T2 weighted imaging had a sensitivity of 87.5%, a specificity of 86.5%, a positive predictive Value (PPV) of 50.0% and a negative predictive value (NPV) of 97.8%. In the cases of myometrial invasion of less than 50%, MR T2 weighted imaging had a sensitivity of 82.9%, a specificity of 72.0%, PPV of 80.6% and NPV of 75.0%. By contrast, in the cases of myometrial invasion of more than 50%, the sensitivity, specificity, PPV and NPV of MR T2 weighted imaging were 58.8%, 100%, 100% and 86.0% respectively. Errors in MR findings when determining myometrial tumor spread were more frequently underestimations rather than overestimations.

Our results indicate that MR imaging is useful for the preoperative assessment of the depth of myometrial invasion in patients with endometrial carcinoma.

Key words : Endometrial carcinoma, MRI, Myometrial invasion

CORRESPONDENCE TO : Takashi Fujimoto,
Department of Obstetrics and Gynecology,
Sapporo Medical University School of Medicine
South 1, West 17, Chuo-ku
Sapporo 060-8556, Japan
E-mail : aae77220@pop21.odn.ne.jp
TEL : 011-611-2111(ext. 3368, 3373)

INTRODUCTION

Endometrial carcinoma is the most common gynecologic malignancy and accounts for 6% of all cancers in women. Most cases are first seen in the early stage, because of symptomatic abnormal bleeding¹⁾. Prognosis may be affected by several factors, including histological type, tumor grade and depth of myometrial invasion²⁾. The histological type and tumor grade may be determined at the time of diagnostic endometrial curettage, whereas myometrial invasion can be evaluated definitively only on surgical extirpation of the uterus. However, preoperative knowledge of the depth of myometrial invasion could play a great importance in the treatment plan. This retrospective study was designed to determine the sensitivity, specificity, PPV and NPV of MR imaging in assessing myometrial invasion in patients with endometrial cancer.

MATERIAL and METHODS

Patients

Sixty patients from January 2003 to December 2005 with clinical stage I endometrial carcinoma were considered for inclusion in this retrospective study. All patients were referred for preoperative diagnostic endometrial curettage and MR imaging. Following these preoperative examination, hysterectomy was performed.

Staging of endometrial carcinoma was assessed surgically according to the International Federation of Gynecology and Obstetrics (FIGO) staging system (Table 1)³⁾. The patients were

33–85 years of age (mean, 60.2 years). Nine patients were pre- or perimenopausal, and fifty-one were postmenopausal. Fifty-seven had endometrioid adenocarcinoma, and three had clear cell adenocarcinoma.

MR imaging

All patients were imaged with a 1.5-T system (Signa; GE Medical Systems, WI) and phased array coil was used as a body. T1-weighted spin-echo images with a repetition time of 400–600 msec and an echo time of 8 msec (400–600/8) were obtained in the axial plane. T2-weighted fast spin-echo images (4,000–5,000/100) were obtained in the axial and sagittal planes. Imaging parameters were two signals acquired with a 384 x 256 matrix, of 6.0-mm section thickness, 1.5–2.5 mm intersection gap, and a 22–24 cm field of view (the smallest field of view possible; it was dependent on patient size). MR images were interpreted retrospectively by a single experienced radiologist who was blinded to the pathologic results. Images were analyzed for the signal intensity of the tumor relative to that of the myometrium, the status of the junctional zone (JZ), the presence of leiomyoma and adenomyosis. Myometrial invasion of endometrial carcinoma was staged with MR imaging according to established criteria (Table 2)⁴⁾.

Pathological review

Two experienced pathologist, who were blinded to the clinical information and the MR

Table 1 FIGO staging system for endometrial carcinoma

stage	Characteristics
stage I	The tumor is confined to the uterine fundus
I A	The tumor is limited to the endometrium
I B	The tumor invades less than one-half of the myometrial thickness
I C	The tumor invades more than one-half of the myometrial thickness
stage II	The tumor extends to the cervix
II A	Cervical extension is limited to the endocervical glands
II B	Tumor invades the cervical stroma
stage III	There is regional tumor spread
stage IV	There is bulky pelvic disease or distant spread

Table 2 MRI staging criteria

stage	findings
IA	Intact JZ, normal MT
IB	Interrupted JZ, invasion \leq 50% of MT
IC	Interrupted JZ, invasion $>$ 50% of MT

JZ:junctional zone, MT:myometrial thickness

findings, reviewed the 60 cases. They estimated microscopically the depth of myometrial invasion, histological type, grading, the presence of leiomyoma and adenomyosis. Furthermore, the pattern of myometrial invasion was distinguished between solid pattern and diffuse pattern, as described previously⁵⁾.

Statistical analysis

Sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each of the three myometrial invasion groups.

RESULTS

Comparison of the MR and pathologic findings of depth of myometrial invasion in our series of sixty patients with clinical stage I endometrial carcinoma is presented in Table 3. Pathological findings revealed the cancer to have intramucosal localization in 8 cases, myometrial invasion of less than 50% in 35 cases and invasion of more than 50% in 17 cases. By MR findings, intramucosal tumor was diagnosed in 14 cases, myometrial invasion of less than 50% in 36 cases and myometrial invasion of more than 50% in 10 cases. The MR diagnoses concurred with the pathological results in 46/60

Table 3 Comparison of MR imaging and Pathological staging in depth of myometrial invasion

MR stage	Pathological Stage		
	IA	IB	IC
IA (n=14)	7	6	1
IB (n=36)	1	29	6
IC (n=10)	0	0	10

of the cases (76.7%).

Statistical indexes of the accuracy of MR imaging are shown in Table 4. The sensitivity and specificity of MR and the positive and negative predictive values for no myometrial invasion were 87.5%, 86.5%, 50.0% and 97.8% respectively. The sensitivity and specificity of MR and the positive and negative predictive values for myometrial invasion of less than 50% were 82.9%, 72.0%, 80.6% and 75.0% respectively. The sensitivity and specificity of MR and the positive and negative predictive values for myometrial invasion of more than 50% were 58.8%, 100%, 100% and 86.0% respectively.

Mismatch cases between MR imaging and pathological staging are shown in Table 5. 13 cases were underestimated by MR imaging (Table 5-A). In six of the cases of myometrial invasion of less than 50%, the MR result showing no myometrial invasion was proven to be wrong by pathological examination of the specimens. Among these 6 cases, 4 showed only slight invasion and in the other two multiple intramural leiomyomas were present in the uterine horn.

In another six cases MR revealed myometrial invasion of less than 50%, however pathological examination of these surgical specimens disclosed invasion of more than 50%. The following factors made the evaluation difficult. In two cases, the junctional zone was absent. In two other cases, multiple intramural leiomyomas were present. Two had adenomyosis. One had myometrial invasion of only slightly more than 50%. In 4 cases, the form of invasive carcinoma was particularly diffuse. When carcinoma is spread diffusely, assessment of myometrial invasion by MR imaging may be difficult. In one

Table 4 Statistical indexes of the accuracy of MR imaging

stage	Sensitivity	Specificity	PPV	NPV
I A	87.5	86.5	50.0	97.8
I B	82.9	72.0	80.6	75.0
I C	58.8	100	100	86.0

PPV:Positive Predictive Value, NPV:Negative Predictive Value

All Values are percentages

Table 5–A Mismatch cases between MR imaging and pathological staging

Underestimated cases of MR imaging

Patient	MR staging	Pathological staging	JZ	absence	Leiomyoma	Adenomyosis	Histroygy	Grade	Invasion form
1	I A	I B	No	No	No	No	Endomet	G2	Solid
2	I A	I B	No	No	No	Yes	Endomet	G1	Solid
3	I A	I B	No	No	No	No	Endomet	G1	Solid
4	I A	I B	No	No	No	No	Endomet	G1	Solid
5	I A	I B	No	Yes	No	No	Endomet	G1	Solid
6	I A	I B	Yes	Yes	No	No	Endomet	G1	Solid
7	I A	I C	No	Yes	No	No	Endomet	G1	Diffuse
8	I B	I C	Yes	No	No	No	Endomet	G2	Diffuse
9	I B	I C	No	Yes	No	No	Endomet	G2	Diffuse
10	I B	I C	Yes	No	Yes	Yes	Endomet	G2	Diffuse
11	I B	I C	No	Yes	No	No	Endomet	G1	Diffuse
12	I B	I C	No	No	Yes	Yes	Endomet	G2	Solid
13	I B	I C	No	No	No	No	Endomet	G2	Solid

JZ : junctional zone, Endomet : Endometrioid adenocarcinoma

Table 5–B Mismatch cases between MR imaging and pathological staging

Overestimated cases of MR imaging

Patient	MR staging	Pathological staging	JZ	absence	Leiomyoma	Adenomyosis	Histroygy	Grade	Invasion form
1	I B	I A	Yes	Yes	Yes	No	Endomet	G1	Solid

JZ : junctional zone, Endomet : Endometrioid adenocarcinoma

case, no myometrial invasion was seen on MR imaging, but invasion of more than 50% was pathologically confirmed in the surgical specimen. This case was a diffusely spread form and had multiple intramural leiomyomas.

One case was overestimated by MR imaging (Table 5–B). This case had intramural leiomyoma and junctional zone absence.

DISCUSSION

Prognosis of endometrial carcinoma may be affected by several factors, including histological type, tumor grade and depth of myometrial invasion²⁾. Though the histological type and tumor grade may be determined at the time of diagnostic endometrial curettage, myometrial invasion can be evaluated definitively only on surgical extirpation of the uterus. Thus, preoperative knowledge of the depth of myometrial invasion could be of great importance in the treatment plan. In the present study, we evaluated

the efficiency of MR imaging for the preoperative diagnosis of myometrial invasion. In previous studies, the accuracy of MR imaging for the evaluation of myometrial invasion in endometrial carcinoma varied between 58% and 89%^{6–13)}. In present study, we used T2-weighted images to estimate the depth of myometrial invasion. Our results are similar to those of previous studies^{6–13)}.

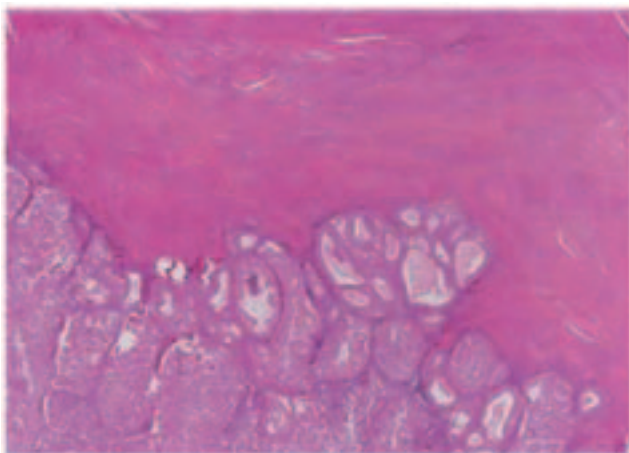
In each stage, statistical indexes of the accuracy of MR imaging show almost acceptable results. However, in the estimation for no myometrial invasion, the positive predictive value was low (50.0%). Accurate diagnosis for no myometrial invasion has become more important recently because the number of young endometrial carcinoma patients has been increasing. Since, standard therapies for endometrial carcinoma are hysterectomy, bilateral salpingo-oophorectomy or more pelvic lymphadenectomy, even if patients have a strong

desire to bear children, they cannot retain their fertility after surgery. However, in recent years, conservative progesterone treatment including high-dose medroxyprogesterone therapy for well-differentiated stage Ia adenocarcinoma was reported to be effective¹⁴⁻¹⁷. Conservative progesterone treatment is a safe and effective alternative for the patient, especially for those who wish to preserve their fertility of the 14 cases diagnosed as no myometrial invasion by MR imaging, seven cases were underestimated, six were myometrial invasion of less than 50%, and one was myometrial invasion of more than 50%. Improvement of stage Ia diagnostic rate is a problem which needs to be resolved.

As stated above, MR imaging is useful for the evaluation of myometrial invasion, however, it is not a completely satisfactory method. To clarify which factors cause the misdiagnosis of MR imaging, we analyzed the mismatch between MR imaging and pathological results (Table 5). The presence and depth of myometrial invasion can be assessed on T2 weighted images as an interruption of the junctional zone, which appears hypointense, compared with en-

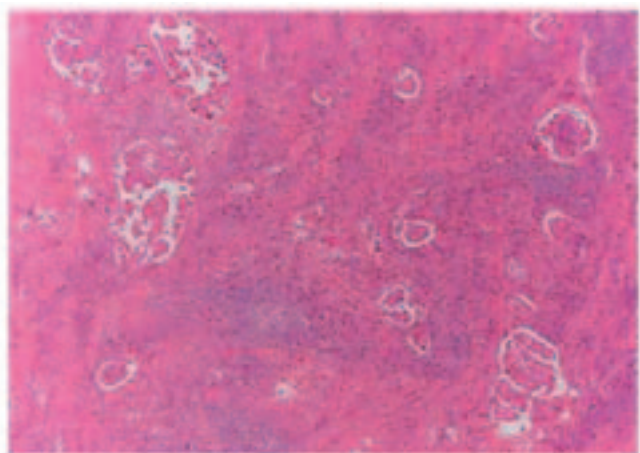
dometrial adenocarcinoma, which appears hyperintense. However, in postmenopausal women the junctional zone may not be easily visible and the myometrium may be thinned due to uterine atrophy, making the presence and depth of myometrial invasion more difficult to assess. In fact, in our mismatch cases, the junctional zone was not clearly visible in four (28.6%) of 14 patients. Meanwhile, uteruses with endometrial carcinoma complicating with leiomyoma or adenomyosis are occasionally deformed and estimation of the presence and depth of myometrial invasion seems to be more difficult. As shown in Fig. 1, we classified two patterns, solid and diffuse. The solid pattern shows a clear division between carcinoma tissue and normal myometrium. On the other hand, the diffuse pattern shows loose invasion, with no clear division between carcinoma tissue and normal myometrium. In our underestimated cases, a diffuse patterns of invasion was present in five (35.7%) of 14 patients. This is due to the fact that the border between tumor and normal myometrium is unclear in cases of diffuse pattern. Previous studies suggest that cases with diffuse pattern have a poorer prog-

Fig.1 The pattern of myometrial invasion



A) Solid pattern

Solid pattern shows surface growth with clear division between carcinoma tissue and normal myometrium.



B) Diffuse pattern

Diffuse pattern shows loose invasion with no clear division between carcinoma tissue and normal myometrium.

nosis than those with solid pattern⁵⁾ so careful detection of the diffuse pattern is important.

In conclusion, the accuracy obtained in this study was similar to previous studies. MR imaging is an adequate method for estimation of the depth of myometrial invasion in endometrial carcinoma. However, in case with a junctional zone absence, an intramural leiomyoma and diffuse form of invasion more care should be taken when estimating the depth of myometrial invasion.

REFERENCES

1. Shepherd JH: Revised FIGO staging for gynecological cancer. *Br J Obstet Gynaecol* 1989; 96: 889-892.
2. Boronow RC, Morrow CP, Creasman WT, Disaia PJ, Silverberg SG, Miller A, Blessing JA. Surgical staging in endometrial cancer: clinical-pathologic findings of a prospective study. *Obstet Gynecol* 1984; 63:825-832.
3. Creasman WT. New gynecologic cancer staging. *Obstet Gynecol* 1990; 75:287-288.
4. Seki H, Kimura M, Sakai K. Myometrial invasion of endometrial carcinoma: assessment with dynamic MR and contrast-enhanced T1-weighted images. *Clin Radiol* 1997; 52: 18-23.
5. Sagae S, Saito T, Sato M, Ikeda T, Kimura S, Mori M, Sato N, Kudo R. The reproducibility of a binary tumor grading system for uterine endometrial endometrioid carcinoma, compared with FIGO system and nuclear grading. *Oncology* 2004; 67: 344-50.
6. Yamashita Y, Harada M, Sawada T, Takahashi M, Kohiji M, Okamura H. Normal uterus and FIGO stage I endometrial carcinoma dynamic gadolinium-enhanced MR imaging. *Radiology* 1993; 186: 495-501.
7. Hricak H, Stern JL, Fisher MR, Shapeero LG, Winkler ML, Lacey CG. Endometrial carcinoma staging by MR imaging. *Radiology* 1987; 162: 297-305.
8. Sinori S, Toccagni G, Garancini P. Myometrial invasion by endometrial carcinoma: assessment by MR imaging. *AJR Am J Roentgenol* 1992; 158: 565-569.
9. Ito K, Matsumoto T, Nakada T, Nakanishi T, Fujita N, Yamashita H. Assessing myometrial invasion by endometrial carcinoma with dynamic MRI. *J Comput Assist Tomogr* 1994; 18(1): 77-86.
10. Taieb S, Ceugnart L, Leblanc E. MR imaging of endometrial carcinoma: role and limits. *Bull Cancer* 2002; 89: 963-968.
11. Takahashi S, Murakami T, Nerumi Y. Pre-operative staging of endometrial carcinoma: diagnostic effect of T2w fast spin echo MRI. *Radiology* 1998; 206: 539-547.
12. Joja I, Asakawa T, Shiraiwa M. Endometrial carcinoma: multisection dynamic MRI using a three-dimensional FLASH technique during breath holding. *Radiat Med* 1999; 17: 211-218.
13. Sinori S, Colombo G, Villa G. Myometrial invasion by endometrial carcinoma: assessment with plain and gadolinium-enhanced MR imaging. *Radiology* 185: 207-212.
14. Niwa K, Tagami K, Lian Z, Onogi K, Mori H, Tamaya T. Outcome of fertility-preserving treatment in young women with endometrial carcinomas. *BJOG* 2005; 112: 317-320.
15. Benshushan A. Endometrial adenocarcinoma in young patients: evaluation and fertility-preserving treatment. *Eur J Obstet Gynecol Reprod Biol* 2004; 117: 132-137.
16. Ramirez PT, Frumovitz M, Bodurka DC, Sun CC, Levenback C. Hormonal therapy for the management of grade 1 endometrial adenocarcinoma: a literature review. *Gynecol Oncol* 2004; 95: 133-138.
17. Sardi J, Anchezar Henry JP, Panices G, Gomez Rueda N, Vighi S. Primary hormonal treatment for early endometrial carcinoma. *Eur J Gynaecol Oncol* 1998; 19: 565-568.

(Accepted for publication, Dec. 27, 2006)