

# Stage IB1 cervical cancer patients with an MRI-measured tumor size $\leq 2$ cm might be candidates for less-radical surgery

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## Summary

**Objectives:** To examine the correlation between histopathology and magnetic resonance imaging (MRI) measured tumor size and define whether patients with Stage IB1 cervical cancer with an MRI-measured tumor size  $\leq 2$  cm can be candidates for less-radical surgery. **Materials and Methods:** The authors retrospectively reviewed 200 patients with Stage IB1 cervical cancer who underwent radical hysterectomy (class III) and pelvic lymphadenectomy. The largest diameter of the tumor was determined by MRI in 52 consecutive cases. **Results:** Regarding risk factors for parametrial involvement, only tumor size and age are known before definitive surgery without conization. Multivariate analysis of these risk factors revealed that both tumor size and old age were independently associated with parametrial involvement. Eighty-eight patients had a tumor size  $\leq 2$  cm and an age  $\leq 50$  years, two of which (2.3%) had parametrial involvement. In 52 consecutive patients, a significant correlation between histopathology- and MRI-measured tumor size was found ( $r = 0.787$ ). Twenty-three patients had an MRI-measured tumor size  $\leq 2$  cm, none of which had parametrial involvement. **Conclusions:** Patients with Stage IB1 cervical cancer lesions with a tumor size  $\leq 2$  cm measured by MRI and age  $\leq 50$  years can be treated with less-radical surgery.

**Key words:** Cervical cancer; Less-radical surgery; MRI.

## Introduction

Patients with Stage IB1 cervical cancer are commonly treated worldwide with radical hysterectomy and pelvic lymphadenectomy. The most frequent site of the local spread of cervical cancer is the parametrium; parametrial spread occurs via direct microscopic extension or lymphatic channels. Therefore, the removal of the parametrial tissue is considered to be of paramount importance in the treatment of cervical cancer. However, parametrectomy is the main cause of postoperative complications, including bladder dysfunction, sexual dissatisfaction, and anorectal mobility disorders, which are attributable to partial denervation of the autonomic nerve supply to the pelvic organs during parametrial resection [1, 2]. Recent studies question the efficacy and safety of radical hysterectomy due to the high rate of long-term postoperative complications [3, 4]. Although nerve-sparing surgery may minimize these complications, no prospective randomized controlled trial to evaluate this surgery has yet been conducted.

Stage IB1 cervical cancers are defined by a broad range of tumor characteristics such as tumor size, depth of invasion, lymph vascular space invasion (LVSI), lymph node metastasis, and parametrial invasion. Recently, the authors reported that patients with a tumor depth of invasion  $\leq 10$  mm (or tumor size  $\leq 2$  cm), no LVSI, and age  $\leq 50$  years could be considered for less-radical surgery, such as modified radical hysterectomy or simple hysterectomy with pelvic lymphadenectomy [5]. Although the depth of invasion and LVSI can be assessed by a pathological examination of the cone biopsy specimen,

tumor size may be determined by magnetic resonance imaging (MRI) before definitive surgery.

The objective of this study was to examine the correlation between tumor sizes measured by histopathology and MRI. In addition, the authors aimed to define whether patients with an MRI-measured tumor size  $\leq 2$  cm can be candidates for less-radical surgery.

## Materials and Methods

The study population consisted of 200 patients who presented with Stage IB1 cervical cancer according to the 1995 International Federation of Gynecology and Obstetrics (FIGO) staging system treated with radical hysterectomy (type III) and systematic pelvic lymphadenectomy at the Okayama University Hospital, Japan, between 1985 and 2009. All hysterectomy specimens were collected and processed in a routine manner. The pathological factors evaluated included histology, depth of invasion, tumor size, LVSI, parametrial invasion, pelvic lymph node metastasis, and ovarian metastasis. The entire parametrial tissues of all specimens were submitted for microscopic examination. Parametrial involvement was classified as direct microscopic extension, metastasis of parametrial lymph nodes, or lymph vascular spread. The details are described previously [5]. MRI was performed on 1.5-T superconducting system. T2-weighted turbo spin echo images were acquired with a TR of 3,000 ms and a TE of 98 ms in the axial and sagittal planes of the uterine cervix. The matrix size was  $512 \times 256$  pixels, and the section thickness was six mm. In 52 consecutive patients, the largest diameter of the tumor was determined from T2-weighted images.

Univariate analysis was performed using the chi-squared test and Spearman's rank correlation test. Multivariate analysis was performed using stepwise logistic regression analysis. Statistical significance was set at  $p < 0.05$ .

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## Results

Patient characteristics are shown in Table 1. Overall, 20 (10.0%) of the 200 patients exhibited parametrial spreading. The authors previously showed that old age, depth of invasion, tumor size, LVSI, positive pelvic nodes, and ovarian metastasis are statistically associated with parametrial involvement in this patient population, whereas histologic subtype is not [5]. Among these risk factors, the authors can only know the tumor size and age before definitive surgery without conization. Multivariate analysis of these risk factors revealed that both tumor size (HR: 1.11, 95% CI: 1.04-1.19,  $p = 0.003$ ) and old age (HR: 1.05, 95% CI: 1.01-1.10,  $p = 0.022$ ) were independently associated with parametrial involvement. One hundred nineteen patients had a tumor size  $\leq 2$  cm, five of which (4.2%) had parametrial involvement (Table 2). In patients with a tumor size  $\leq 2$  cm, the frequency of deep stromal invasion was significantly higher in patients over 50 years old (Table 3). Eighty-eight patients had a tumor size  $\leq 2$  cm and were younger than 50 years, two of which (2.3%) had parametrial involvement (cases 1 and 3 in Table 3). Case 1 exhibited direct invasion in the parametrium as well as ovarian metastasis. Case 3 exhibited lymph vascular spread in the parametrium.

In 52 consecutive patients, the largest tumor diameter was determined by MRI. The median MRI-measured tumor size was 22 mm (range, 0-35). In comparison, the median histopathology-measured tumor size was 22.5 mm (range, 9-34). There was a significant correlation between histopathology and MRI-measured tumor sizes ( $r = 0.787$ ,  $p < 0.0001$ ) (Figure 1). Twenty-three patients had an MRI-measured tumor size  $\leq 2$  cm, none of which had parametrial involvement and three (13.0%) had positive pelvic lymph nodes (Table 4). Twenty-nine patients had an MRI-measured tumor size  $> 2$  cm, four of which (13.8%) had parametrial involvement and seven (24.1%) had positive pelvic lymph nodes (Table 4).

## Discussion

Small IB1 lesions may be first documented by cervical conization before definitive surgical therapy. The authors previously reported that patients younger than 50 years with a tumor depth of invasion of  $\leq 10$  mm (or tumor size  $\leq 2$  cm) and no LVSI as assessed by cone biopsy can be considered for less-radical surgery, such as modified radical hysterectomy or simple hysterectomy with pelvic lymphadenectomy. However, evident IB1 lesions documented by clinical examination or MRI are generally treated by radical hysterectomy and pelvic lymph adenectomy without conization; therefore, additional studies are needed to elucidate whether some patients with IB1 lesions without conization can be treated with less-radical surgery.

The authors found that 119 patients had a tumor size  $\leq 2$  cm, five of which (4.2%) had parametrial involvement. The incidence of parametrial involvement of 4.2% may not be acceptable. Multivariate analysis showed both

Table 1. — Patient characteristics.

Variables	No. of patients (%) (n = 200)	Variables	No. of patients (%) (n = 200)
Age (years)		Parametrial invasion	
Median	42	Negative	180 (90%)
Range	25-71	Positive	20 (10%)
Histology		Lymph node metastasis	
SCC	121 (61%)	Negative	171 (86%)
AD	56 (28%)	Positive	29 (15%)
ADSQ	23 (12%)	Ovarian metastasis	
Depth of invasion (mm)		Negative	198 (99%)
Median	9	Positive	2 (1%)
Range	2-25	Adjuvant therapy	
Tumor size (mm)		None	126 (63%)
Median	19	Radiotherapy	28 (14%)
Range	7-38	Chemotherapy	23 (12%)
LVSI		Chemoradiation	23 (12%)
Negative	111 (55%)		
Positive	89 (45%)		

SCC: squamous cell carcinoma; AD: adenocarcinoma; ADSQ: adenosquamous cell carcinoma; LVSI: lymph vascular space invasion.

Table 2. — Patients with parametrial involvement with a tumor size of 2 cm or less.

Case	Age	Histology	DOI (mm)	TS (mm)	SI	LVSI	LNM	OM	Type of PI
1	38	AD	6.5	14	$\leq 2/3$	+	-	+	direct
2	66	SCC	11	20	$> 2/3$	+	-	-	direct
3	48	SCC	5	10	$\leq 2/3$	+	-	-	LVSI
4	63	SCC	8.9	18	$> 2/3$	-	+	-	direct
5	51	SCC	9	16	$> 2/3$	+	+	-	direct

DOI: depth of invasion; TS: tumor size; SI: stromal invasion; LVSI: lymph vascular space invasion; LNM: lymph node metastasis; OM: ovarian metastasis; PI: parametrial involvement; AD: adenocarcinoma; SCC: squamous cell carcinoma.

Table 3. — Relationship between age and deep stromal invasion in patients with a tumor size of 2 cm or less.

Age (years)	Stromal invasion $> 2/3$	$p$ value
150 or under	5/87 (5.7%)	0.0002
Over 50	10/32 (31.3%)	

Table 4. — Relationship between MRI-measured tumor size and the presence of metastatic disease to the parametrium or pelvic lymph nodes.

MRI-measured tumor size	Parametrial involvement	Nodes positive
Two cm or less (n = 23)	0 (0.0%)	3 (13.0%)
More than two cm (n = 29)	4 (13.8%)	7 (24.1%)

tumor size and old age to be independent predictors of parametrial spread; both factors also seem to be important risk factors for parametrial involvement. The authors demonstrated that deep stromal invasion is not uncommon in elderly patients, even if the tumor size is  $\leq 2$  cm; this is why old age is an important factor for parametrial involvement. Therefore, tumor size  $\leq 2$  cm and patients aged  $\leq 50$  years were selected as the low-risk subgroup criteria for parametrial spread and demonstrated that the risk for parametrial spread was 2.3% (2 / 88). One case exhibited direct invasion in the parametrium in addition to ovarian metastasis. As ovarian metastasis was suspected before operation upon MRI, less-radical surgery could not be performed. Other patients had only lymph

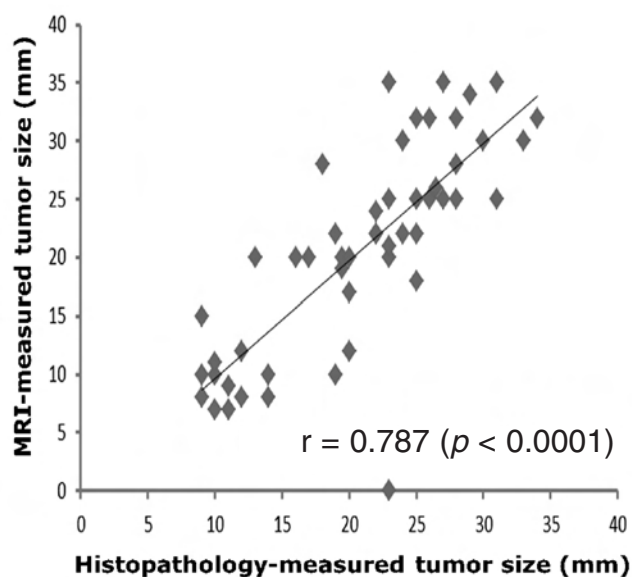


Figure 1. — Significant correlation between histopathology- and MRI-measured tumor sizes ( $r = 0.787$ ,  $p < 0.0001$ ).

vascular spread in the parametrium without evidence of pelvic lymph node metastasis. Frumovitz et al. state that it remains unclear what happens to these microscopic tumor emboli once they reach a draining lymph node—whether they implant and become a site of tumor metastasis or if the body’s immune system clears this decidedly small-volume disease [6]. At present, the clinical significance of lymph vascular spread in the parametrium is undetermined. Therefore, it seems justifiable to assume that patients with a tumor size  $\leq 2$  cm and age  $\leq 50$  years do not need more radical parametrectomy.

Fertility-sparing vaginal radical trachelectomy (VRT) or abdominal radical trachelectomy (ART) in selected young women with Stage I cervical cancer has become an acceptable oncologic practice worldwide. ART is described as more radical than VRT with more parametrial tissue taken laterally during the procedure. In their review article, Rob et al. report that the oncological results of VRT and ART are similar for tumors  $\leq 2$  cm [7]. This may support the oncological safety for less-radical surgery in young patients with Stage IB1 lesions with a tumor size  $\leq 2$  cm.

Nowadays, MRI is considered the most accurate diagnostic tool to preoperatively detect tumor size [8-10]. The authors also observed a good correlation between the tumor size assessed by histological sections and MRI. In the present study, there was no parametrial involvement in the 24 patients with tumors  $\leq 2$  cm measured by MRI. This study however has some limitations including the possibility of over- or under-diagnosis. In fact, in a few patients, the size of the tumor was  $\leq 2$  cm when measured by MRI, but  $> 2$  cm when measured by histopathology. Furthermore, there was a patient with a tumor size of more than two cm for whom MRI failed to detect any

cervical tumor in accordance with previous studies [11, 12]. Kamimori et al. did not observe parametrial involvement in any of their 58 patients with a tumor size  $\leq 2$  cm measured preoperatively by MRI [12].

## Conclusion

The current findings demonstrate that some patients with Stage IB1 cervical cancer lesions with a tumor size  $\leq 2$  cm measured by MRI and an age  $\leq 50$  years could be considered for less-radical surgery, such as modified radical hysterectomy and pelvic lymphadenectomy; however, further study is needed to clarify this issue.

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