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The validity of tumour diameter assessed by magnetic resonance imaging and gross specimen with regard to tumour volume in cervical cancer patients

Dae Chul Jung[a], *Woong Ju*[b], *Hyuck Jae Choi*[c,*], *Sokbom Kang*[a], *Sohee Park*[a], *Chong Woo Yoo*[a], *Sang-Yoon Park*[a]

[a]*Research Institute and Hospital, National Cancer Center, Goyang, Korea*
[b]*Department of Obstetrics and Gynecology, Mok-Dong Hosptial, Ewha Womans University College of Medicine, Seoul, Korea*
[c]*Department of Radiology, Asan Medical Center, University of Ulsan, 388-1, Poongnap-dong, Songpa-gu, Seoul 138-736, Korea*

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ABSTRACT

We compared the tumour size measured by magnetic resonance imaging (MRI) with that of gross specimen regarding the virtual tumour volume. Eighty three patients with International Federation of Obstetrics and Gynecology (FIGO) stage Ib to IIa cervical cancer underwent MRI before radical hysterectomy. The largest tumour diameter was determined by both MRI and gross specimen measurement. Tumour volume was calculated by the standard technique of multiplying the sum of the areas by the slice thickness. Paired *t*-test was used to compare the MRI and gross specimen derived diameters. Pearson correlation coefficient was calculated to evaluate the relationship between the tumour size and volume. The mean diameters of the MRI and gross specimen derived tumour measurements were 3.0 cm (standard deviation, 0.9 cm) and 3.5 cm (standard deviation, 1.2 cm) ($p < 0.001$), respectively. Mean MRI-based tumour volume was 12.5 cm^3 (standard deviation, 10.4 cm^3). Tumour diameter measured by MRI had a significantly higher correlation with tumour volume measured by MRI ($r_p = 0.734$) compared with that measured on the gross specimen ($r_p = 0.690$; Steiger's Z test, $p = 0.019$). The tumour diameter measured by MRI was smaller than gross specimen measurement and correlated more closely with tumour volume in patients with cervical cancer. This study illustrates the value of MRI as a tool for tumour size measurement.

1. Introduction

Cervical cancer is the second most frequently diagnosed malignancy in women worldwide, with almost half a million cases diagnosed each year, and is the only major gynaecological malignancy clinically staged according to the International Federation of Obstetrics and Gynecology (FIGO) recommendation.[1] Although increasing clinical stage is associated with increasing risk of death, the prognoses correlate poorly with the clinical FIGO stage in many patients.

Tumour diameter is frequently used as a predictor of prognosis and computed tomography (CT) and magnetic resonance imaging (MRI) are normally used in the measurement of tumour size.[2–4] Although not included in the FIGO

* *Corresponding author:* Tel.: +82 2 3010 5686; fax: +82 2 476 4719.
E-mail address: choihj@amc.seoul.kr (H.J. Choi).
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staging component, CT and MRI are valuable radiological imaging techniques in the pretreatment evaluation of cervical cancer. Initial reports indicated that MRI was a useful tool in the assessment of extent of disease and tumour size.[2–7]

We recently found that, in many cases, tumour sizes measured on gross tumour specimens were larger than those measured by MRI. As far as we know, there are no studies existing that compare the tumour diameter measured by MRI and gross tumour specimen assessment. The purpose of this study was to compare the tumour size measured by MRI with that measured on a gross specimen with regard to MRI- calculated tumour volume.

2. Patients and methods

2.1. Study subjects

A retrospective search was conducted using detailed medical records at the National Cancer Center for 183 consecutive patients who underwent operations for uterine cervical cancer between January 2000 and December 2006. Of these 183 patients, 83 patients (mean age, 47 years old; standard deviation, 10.4 years old) who showed measurable mass in MRI and underwent radical hysterectomy were included in the present study. The clinical characteristics of all 83 patients are shown in Table 1. Exclusion criteria consisted of microinvasive carcinoma, recurrent disease, prior therapy for cervical cancer, or contraindication to MR study (such as possessing a pacemaker or certain metallic implants). Our institutional review board did not require approval for this study.

2.2. Histopathologic evaluation

Histopathologic diagnoses of the tumours were reviewed by a pathologist (C.W.Y.). Surgical specimens were examined macroscopically and largest tumour size was measured after unfolding the uterine cervix by incision of the anterior wall. Accurate tumour size was measured three-dimensionally. The depth of invasion of the tumour was also evaluated as the maximum depth of the tumour from the surface of uninvolved cervical mucosa.

Table 1 – Clinical characteristics of the patients

	Age or number
Age	
Mean ± SD (range)	47 ± 10.4 (36.6–57.4)
Histology	
Squamous cell carcinoma	65 (78.3%)
Adenocarcinoma	15 (18.1%)
Adenosquamous cell carcinoma	3 (3.6%)
FIGO stage	
Ib1	59 (71.1%)
Ib2	15 (18.1%)
IIa	9 (10.8%)

2.3. Image acquisition

MRI was performed using a Signa 1.5 T system (General Electric Medical Systems, Milwaukee, WI, USA) with a pelvic array coil for pelvic scans and a Torso phase array coil for para-aortic scans. MR scans were done between 3 and 20 days (mean ± SD = 7 ± 5 days) before surgery. Scans were performed using the following parameters: axial T1-weighted fast spin-echo sequence (TR/TE, 600 ms/10 ms; slice thickness, 5 mm; interslice gap, 2 mm; field of view, 24 cm × 24 cm; matrix, 256 × 192; echo-train length, 4; three signals acquired; no fat saturation; bandwidth, 31.25 kHz), axial T2-weighted fast spin-echo sequence (TR/TE, 5000/68 ms; slice thickness 3 mm; interslice gap 1 mm; 24 cm × 24 cm field of view, matrix, 256 × 192; echo train length, 21; four signals acquired; no fat saturation, 31.25 kHz bandwidth), sagittal T2-weighted fast spin-echo sequence (TR/TE, 5000/68 ms; slice thickness, 3 mm; interslice gap, 3 mm; field of view, 24 cm × 24 cm; matrix, 256 × 192; echo train length, 26; four signals acquired; no fat saturation, 31.25 kHz bandwidth) for the pelvic region, and axial fast spin-echo T2-weighted sequence with 16 s of breath holding (TR/TE, 2000/68 ms; slice thickness, 8 mm; interslice gap 2 mm; field of view, 32 cm × 24 cm; matrix, 256 × 160; echo train length, 20; one signal acquired; no fat saturation, 31 kHz bandwidth) for the para-aortic region.

2.4. Image interpretation

The cervical tumour was identifiable as high-signal intensity on T2-weighted images. Diameter measurements were obtained by consensus of two experienced radiologists (H.J.C., D.C.J.) with 6 and 4 years of experience, respectively, in gynaecologic MRI imaging blinded to patients' surgical, histopathologic, and other imaging findings. The largest diameter of the tumour was determined in three axes. Tumour volume (V) was assessed in a consensus reading by two radiologists, using three-dimensional volumetric measurements according to the modified Simpson rule 3 weeks after the MRI tumour diameter measurement to reduce bias. In all contiguous sagittal images, tumour mass was outlined on the computer monitor using software (Rapidia 2.8, Infinitt, Korea). The area of tumour in each slice was multiplied by the slice profile (3 mm slice thickness plus 3 mm intersection gap), and total tumour volume was automatically calculated by summation of the adjacent volumes.

2.5. Statistical analysis

The largest tumour diameters derived from both MRI and gross specimen measurements were compared using paired t-test. Considering the MRI measured tumour volume to be the gold standard, the agreement between each of the largest tumour diameters, by MRI and gross specimen measurement respectively, and MRI tumour volume was assessed using Pearson's correlation coefficient. The differences in these correlations were then tested using Steiger's Z test, while accounting for the dependency of correlations.[8] Basic statistical analyses were performed using Stata® version 9.0. Steiger's Z test was performed using a publicly available computer program (FZT.exe).[9]

3. Results

3.1. Tumour size and volume

Average tumour diameter by pathology (mean ± SD, 3.5 ± 1.2 cm; range, 1.3 – 5.1 cm) was larger than that by MRI (mean ± SD, 3.0 ± 0.9 cm; range, 1.6 – 6.7 cm) ($p < 0.001$). In 60 patients (72.3%), the tumour diameters on the gross specimen were larger than those measured by MRI (mean difference ± SD, 0.89 ± 0.81 cm) (Figs. 1, 2). In 10 patients the size of tumour was 4 cm or greater in the gross specimen but smaller than 4 cm when measured by MRI. To the contrary, all gross tumours measuring less than 4 cm also measured less than 4 cm via MRI measurement. Table 2 shows clinical FIGO stage versus gross specimen and MRI derived tumour diameters.

Tumour volume measured by MRI ranged from 1.1 to 51.5 cm^3 (mean difference ± standard deviation, 12.5 ± 10.4 cm^3). The Pearson correlation demonstrated a higher association of tumour volume with the MRI-based tumour diameter ($r_p = 0.734$) compared with the gross specimen diameter ($r_p = 0.690$, Steiger's Z test, $p = 0.019$).

4. Discussion

In predicting the prognosis and making the therapeutic decision, accurate staging is very important in the management of cervical cancer patients. As FIGO recommends a clinical staging for cervical cancer, it is probable that the clinical staging may have intrinsic inaccuracy .[10–12] Tumour size has been known to be an important prognostic factor in cervical cancer patients and this is why there was an attempt to subdivide stage Ib into Ib1 and Ib2 on preoperative measurement of the largest diameter of the tumour.[13] As for imaging modalities, MRI has been known to be a more accurate modality in tissue contrast compared with CT.[14–18]

This study shows that the MRI determined tumour diameters were smaller than the gross specimen tumour diameters and correlate more closely with tumour volume. In our study, in 10 patients, the gross specimen tumour size measurement was larger than 4 cm, but was smaller than 4 cm in the MRI results. This may be confusing for clinicians, because the size of tumour is one of the major prognostic factors.[4–6] In this case, the gynaecologic oncologist may also be inconclusive about the necessity of adjuvant therapy. Hence, it is impor-

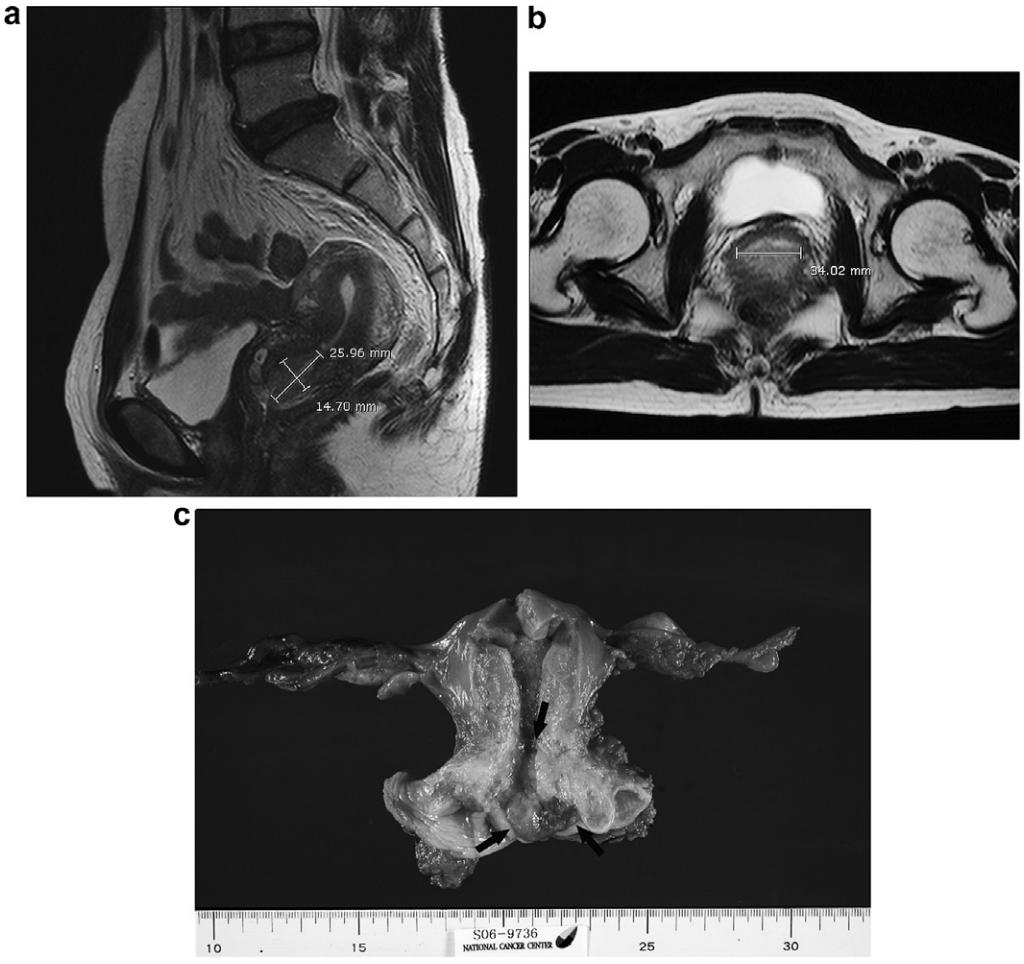

Fig. 1 – 46-year-old woman with Ib1(FIGO staging) uterine cervical carcinoma (squamous cell carcinoma). (a), (b) Sagittal and transverse T2-weighted MR images show oval shaped cervical tumour confined to uterine cervix. The largest diameter of the tumour was measured in the transverse plane (d = 34.02 mm). (c) Gross specimen shows infiltrative cervical tumour (arrows). The largest diameter of the tumour was 55 mm.

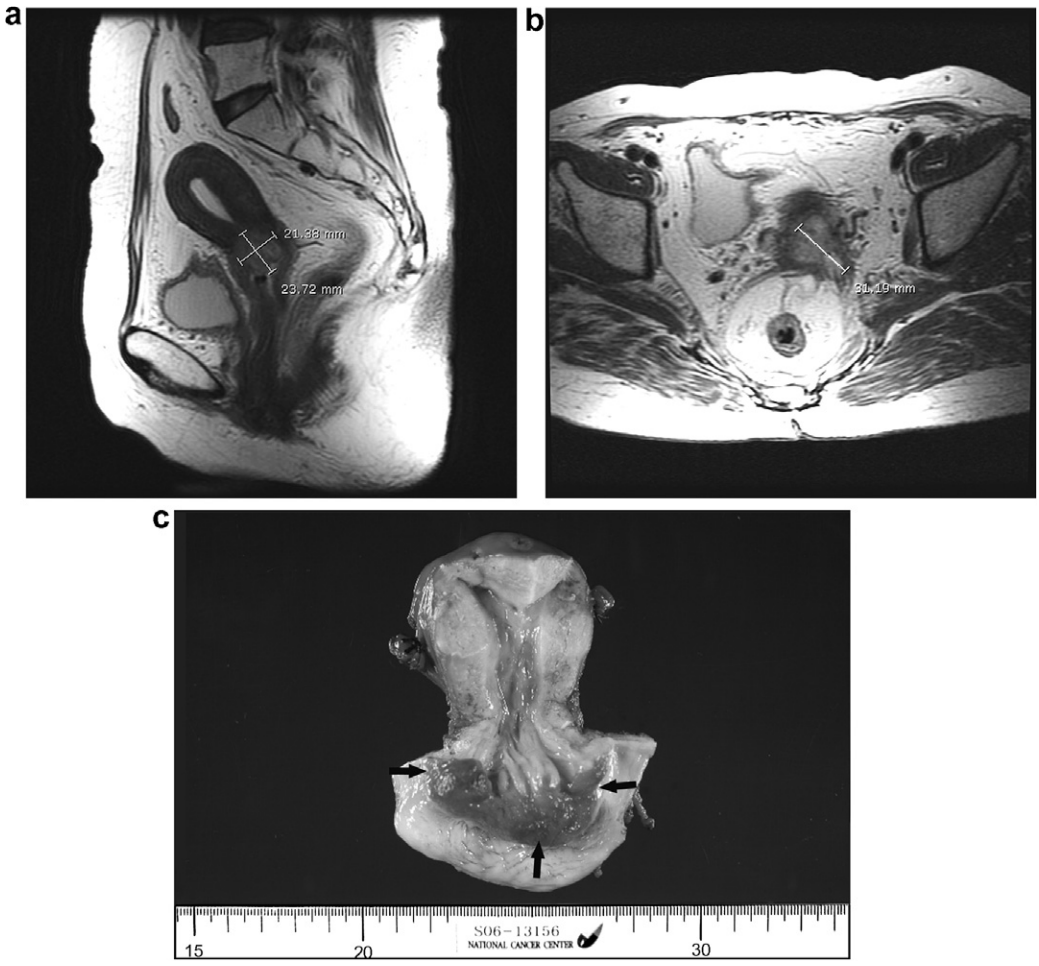

Fig. 2 – 59-year-old woman with Ib1(FIGO staging) uterine cervical carcinoma (squamous cell carcinoma). (a), (b) Sagittal and transverse T2-weighted MR images show small cervical tumour in uterine cervix. The largest diameter of the tumour was measured in the transverse plane (*d* = 31.19 mm). (c) Gross specimen shows infiltrative cervical tumour (arrows). The largest diameter of the tumour was 60 mm.

Table 2 – FIGO stage versus gross tumour diameter, MRI tumour diameter and volume

FIGO stage	Gross tumour diameter		MRI tumour diameter	
	$D < 4$ cm	$D \geqslant 4$ cm	$D < 4$ cm	$D \geqslant 4$ cm
Ib1 ($n = 59$)	49	10	56	3
Ib2 ($n = 15$)	4	11	5	10
Iia ($n = 9$)	5	4	7	2
Total ($n = 83$)	58	25	68	15

tant to determine which tumour size should be employed as a reference in the management of cervical cancer patients.

In our study the gross specimen tumour size was measured after sagittal section of the anterior cervical wall and cervix unfolding. The discrepancy between tumour size, as measured by MRI and the gross specimen respectively, was due to the histological cut up process. The validity of the gross specimen measurement could be questioned but this method is routinely undertaken in Korea.[19,20] Interestingly, among the 21 tumours whose size difference between the two measurements was 1 cm or greater, there were only two bulky tumours (larger than 4 cm) using MRI. In other words, the discrepancy was exaggerated in smaller tumours using MRI. Small tumours (diameter < 4 cm) confined to the uterine cervix appeared larger in the gross specimen than when measured by MRI and there was a greater discrepancy than with the large tumours (diameter $\geqslant$ 4 cm).

In our study we chose the MRI derived tumour volume as the gold standard for comparing the validity of the MRI and gross specimen diameters. The rationale for this method is that the MRI derived three-dimensional analysis of tumour volume provided highly accurate measurements of the actual

tumour volume compared with giant histologic sections of the entire cervical tumour.[21–23] Soutter et al. reported that MRI determined tumour volume was the only strong factor associated with the survival of patients with cervical cancer and that the other parameters, such as age, stage, lymphovascular space involvement, MRI parametrial invasion, and MRI detection of involved lymph node, showed weak association.[10] In our study the MRI tumour size correlates more closely with the MRI tumour volume than the gross specimen size does, and we feel that the MRI measured tumour diameter represents a more accurate tumour volume than that obtained by gross tumour specimen measurements.

In the current study the MRI tumour volume correlated with both the MRI tumour size and gross specimen tumour size. It is possible that closer correlation was observed between MRI tumour volume and MRI diameter than between MRI tumour volume and gross specimen diameter because the two former parameters were measured using the same instrument. However, in our retrospective study it was not possible to measure tumour volume with any other method than MRI volume reconstruction. We believe that, in a future study, there should be a method used to measure the real tumour volume which would then become the gold standard.

In conclusion, MRI measured diameters tend to be smaller than those of gross specimens but provide a more accurate assessment of true tumour volume in patients with uterine cervical cancer.

Conflict of interest statement

All authors must disclose any financial and personal relationships with other people or organisations that could inappropriately influence (bias) their work.

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