Impact of three-dimensional (3D) ultrasonography and power Doppler angiography in the management of cervical cancer

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Summary

Purpose: To evaluate the potential role of three-dimensional (3D) ultrasound, and to assess its diagnostic performance and ability to predict therapeutic efficacy in cervical cancer. *Methods:* Thirty patients with cervical cancer and 35 normal controls were studied by transvaginal 3D power Doppler ultrasound before treatment. Eleven patients who received neoadjuvant chemotherapy (n = 6), radiation (n = 3), or chemoradiation (n = 2), had further measurements taken one month and two months after treatment. *Results:* From the receiving operating characteristics curve analysis, the best vascularization index (VI) cutoff value of 5.24 distinguished cervical cancer from the normal cervix, with a sensitivity of 73.3% and a specificity of 94.3%. Cervical tumor volume measured by magnetic resonance imaging was positively correlated with the tumor volume measured by 3D ultrasonography (r = 0.91, p < 0.0001). In six patients who received neoadjuvant chemotherapy, the percent change in tumor volume during the second month of treatment was positively correlated with the percent change in flow index (FI) during the first month of treatment (r = 0.83, p < 0.05). *Conclusions:* VI may be a diagnostic marker and FI may be a predictive marker of treatment response in cervical cancer.

Key words: Uterine cervical cancer; Three-dimensional imaging; Ultrasonography; Doppler ultrasound; Neoadjuvant chemotherapy.

Introduction

Cytological and histological methods are effective for the diagnosis of cervical cancer. However, imaging can be used to determine clinical stage from tumor size after cervical cancer has been diagnosed histopathologically.

Magnetic resonance imaging (MRI), which is valuable for superior soft-tissue contrast resolution, is the choice method for imaging to determine the extent of the primary tumor. However, MRI is expensive and we cannot usually perform MRI immediately. Therefore, there are problems with regard to economics and convenience.

It has been suggested that intratumoral blood flow gives a clinical index of malignancy of cervical cancer and an indication of the efficacy of treatment. Several methods have been developed to evaluate intratumoral blood flow, including intratumoral microvessel density [1], tumor intercapillary distance [2] and vascular endothelial growth factor determination [3]. However, these do not provide a global assessment of the tumor, cannot be performed immediately, and results cannot be accurately reproduced [4].

Recently, three-dimensional (3D) ultrasound has been developed and used to quantify vascularity and flow, providing additional information in the assessment of overall blood flow of a tumor [5-7].

In this study, we measured the tumor volume and 3D power Doppler indices for cervical cancer using 3D ultrasonography and angiography, and examined the diagnostic performance in distinguishing cervical cancers from normal cervical tissue, the ability to measure tumor volume, and the viability in prediction of therapeutic efficacy in cervical cancer.

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Materials and Methods

Patients

We evaluated 65 patients, mean age 49.5 years (range: 19-86), who gave informed consent to their inclusion in the study. Only routine procedures were performed on the patients included in this study. Two groups were defined: Group A comprised 35 women with gynecological tumors but with a normal cervix; Group B comprised 30 women with a histological diagnosis of invasive cervical cancer. In group A, gynecological examination and a Pap test indicated that the uterine cervices in these subjects were normal.

In group B, cervical biopsy was performed in all patients to obtain a definitive histologic diagnosis. The clinical and pathological characteristics of the 30 patients with invasive cervical cancer are shown in Table 1. Clinical staging was performed according to the FIGO classification [8]. Pretreatment evaluation consisted of taking the patient's history, and a biopsy, gynecological examination, abdominal computed tomography (CT), pelvic MRI, pelvic sonography, chest X-ray, cystoscopy and sigmoidoscopy were performed. In all patients of group B, 3D ultrasound findings were evaluated before treatment.

Primary surgery was performed for 19 of the group B patients. In the 11 patients in Group B that did not undergo primary surgery, 3D ultrasound findings were also evaluated at one and two months after treatment. All patients underwent MRI at the same time. The cervical tumor volumes determined by MRI were calculated by the formula for the volume of an ellipse ($\pi(R_1 \times R_2 \times R_3)/6$), where R_1, R_2 and R_3 were the maximal transverse, anteroposterior, and longitudinal length of tumor, respectively [9].

The clinical and pathological characteristics of the 11 patients with invasive cervical cancer are given in Table 2. Six patients received neoadjuvant chemotherapy (platinum based), three patients received radiation alone and two patients received chemoradiation.

Equipment and volume acquisition

A single observer performed all B-mode and 3D ultrasound and Doppler examinations using a Voluson 730 Expert (GE Healthcare, Zipf, Austria) with a vaginal multi-frequency probe (5-9MHz) and a visualization angle of 146°. All women were examined in the lithotomy position. All patients underwent sonography the day before surgery, radiation or chemotherapy.

An initial B-mode exploration provided information about uterine and ovarian sizes. The power Doppler window was then placed over the longitudinal scan section of the uterus in order to include the whole of the uterine cervix. For every woman, Doppler settings were prefixed as follows: normal quality of color (normal resolution and intermediate photogram index); color gain –6; PRF (pulse repetition frequency) 0.9 kHz; and wall motion filter 'low1'. Once the 2D power Doppler examination was finished, the 3D volume box was placed at a prefixed 90° angle over the cervical area. Exploration was repeated if intestinal or respiratory movements of the patient appeared. The volumes for each patient were stored on a hard disk for further evaluation.

Volume, power Doppler indices and mean gray calculation

The stored volumes were further analyzed using the VOCAL program (Virtual Organ Computer Aided Analysis). The same investigator analyzed all the volumes. Using manual mode, cervical areas were traced using longitudinal views as the work pattern. The rotation steps were 30°, resulting in the definition of six contours of the cervix or cervical cancer. Once all contours had been drawn, the VOCAL program automatically calculated the volume in ml; 3D power Doppler indices were calculated using a histogram facility. The vascularization index (VI) measures the number of color voxels in the volume. It represents the mass of vessels in the tissue and is expressed as a percentage (%). The flow index (FI) corresponds to the mean color value in the color voxels, indicating the average intensity of blood flow. It is expressed as a whole number between 0 and 100. The vascularization flow index (VFI) is the mean color value in all the voxels in the volume; therefore, it represents both vascularization and blood flow or tissue perfusion. It is also expressed as a whole number between 0 and 100. With the histogram, the mean value of the gray-scale voxels can also be calculated and is expressed as the mean gray (MG, scale 0-100).

Statistical analysis

The statistical data were analyzed using the Statistical Package for the Social Sciences (SPSS version 11.0. Chicago, IL, USA). Data are represented as mean ± standard error (SEM). Comparisons between two groups were performed by Welch's *t*-test. A p value less than 0.05 was considered statistically significant.

Correlation between tumor volume and VI, FI and VFI before treatment, correlation between tumor size measured by MRI and tumor size measured by 3D ultrasound before and after treatment, and correlation between the percent change in tumor volume during the second month of treatment and the percent change in 3D parameters (VI, FI and VFI) and tumor volume during the first month of treatment were performed using linear regression.

Receiver operating characteristic (ROC) curves were obtained with their respective areas under the curve ± standard error and compared by Hanley and McNeil [10] using Analyse-It Software (Leeds, England) [11]. If the lower limit of the confidence interval (CI) for the area under the ROC curve was > 0.5, the diagnostic test was considered to have discriminatory potential. The ROC curves were also used to determine the mathematically best cut-off value corresponding to the point in the ROC curve situated farthest away from the reference line [12]. The sensitivity, false-positive rate and positive and negative likelihood ratios (LR) with regard to malignancy of the mathematically best cut-off values were also calculated with exact 95% CI. A diagnostic test is regarded as useful if LR+ is higher than 2 and LR- is lower than 0.5 (according to Khan *et al*. [13]).

Results

In all patients with cervical cancer, the tumor was identified in the gray-scale analysis as a hypo-high lesion. In the 3D power Doppler analysis, all patients with cervical cancers showed detectable vessels.

A total of 35 patients with cervical cancer were eligible for analysis. The demographic characteristics of all the patients are shown in Table 1. Figure 1 shows an example of invasive cervical cancer analyzed by 3D power Doppler angiography (a) and VOCAL histogram analysis (b). This is in constant with the sparse power Doppler signals that were occasionally detected in the cervices of the 30 controls with a normal cervix.

The mean age of the 35 patients with cervical cancer was 58.1 ± 2.6 (range, 34-86) years. Their mean tumor volume, MG, VI, FI and VFI values were 33.3 ± 6.8 ml, 34.7 ± 1.3%, 16.5 ± 2.7, 34.9 ± 1.2, and 7.1 ± 1.3, respectively. The mean tumor volume, MG, VI, FI and VFI values in patients with Stage IB cervical cancer were 14.0 ±

Table 1. — *General characteristics of group B patients*.

Characteristic	Patients n (%)
Total	30
Age - years, mean (range)	58 (34-86)
FIGO stage	
IB	11 (36.7)
II	9 (30)
III	5 (16.7)
IV	5 (16.7)
Histotype	
squamous cell carcinoma	22 (73.3)
adenocarcinoma	5 (16.7)
adenosquamouscarcinoma	2 (0.7)
small cell carcinoma	1 (0.3)
Tumor diameter	
< 4 cm	18 (60)
≥ 4 cm	12 (40)

Table 2. — *General characteristics of group B patients that did not undergo primary surgery.*

Characteristic	Patients n (%)
Total	11
Age - years, mean (range)	60 (35-80)
FIGO stage	
IB	1 (9.1)
II	1 (9.1)
III	4 (36.4)
IV	5 (45.6)
Histotype	
squamous cell carcinoma	9 (81.8)
adenocarcinoma	1 (9.1)
small cell carcinoma	1 (9.1)

a)

b)

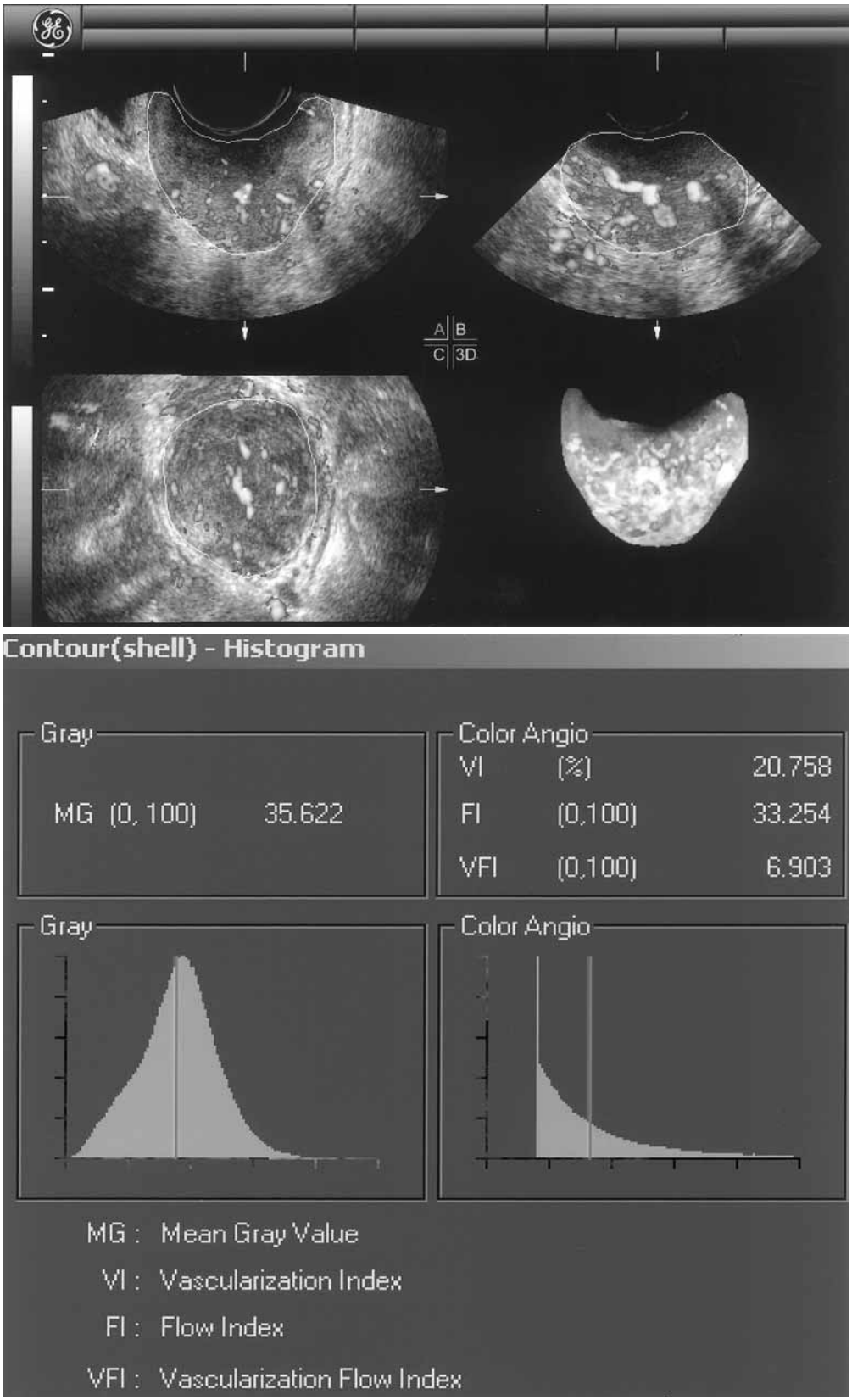

Figure 1. — An example of invasive cervical cancer analyzed by three-dimensional (3D) color power Doppler ultrasound angiography: a) longitudinal view, upper left; frontal view, lower left; transverse view, upper right; reconstructed tumor mass, lower right; b) VOCAL histogram analysis of 3D power Doppler sonography in a cervical cancer patient.

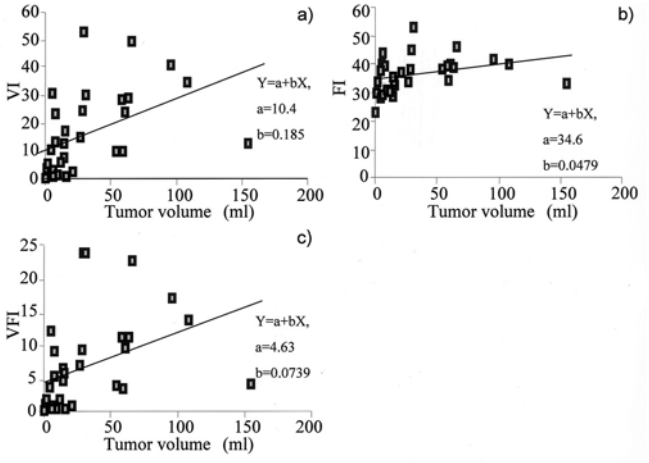

Figure 2. — Correlation of cervical cancer volume with 3D parameters (VI, FI and VFI) in 30 patients with cervical cancer.
(a) Vascularization index (VI; $r = 0.46$, $p < 0.05$);
(b) Flow index (FI; $r = 0.21$, $p = 0.13$);
(c) Vascularization flow index (VFI; $r = 0.38$, $p < 0.05$).

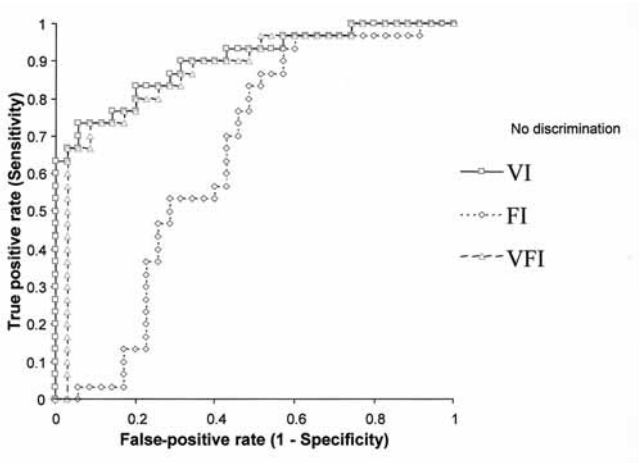

Figure 3. — Receiver operating characteristic (ROC) curve of 3D parameters (VI, FI and VFI) for differential diagnosis between cervical cancer and the normal cervix.

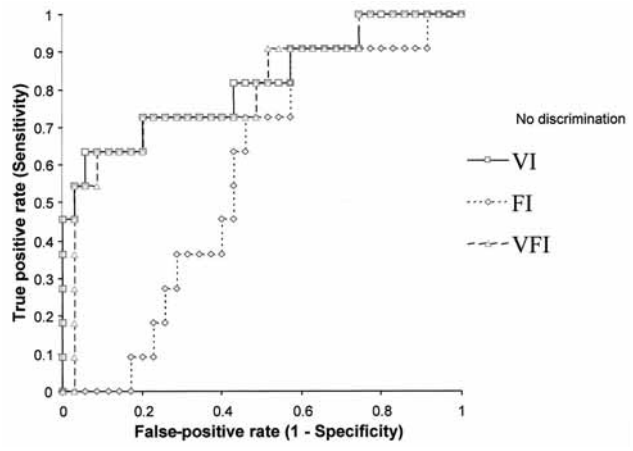

Figure 4. — Receiver operating characteristic curve of 3D parameters (VI, FI and VFI) for the differential diagnosis between Stage IB cervical cancer and the normal cervix.

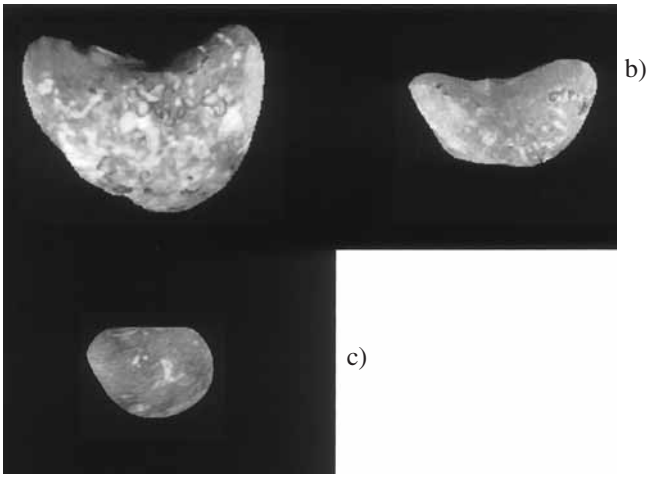

Figure 5. — An example of invasive cervical cancer analyzed by 3D color power Doppler ultrasound angiography: a) before treatment, b) 1 month after treatment, and c) 2 months after treatment.

5.3, 35.2 ± 1.7, 8.96 ± 2.63, 33.9 ± 1.8, and 3.58 ± 1.04, respectively. The mean tumor volume, MG, VI, FI and VFI values in patients with Stage IIB-IVB cervical cancer were 44.5 ± 9.4, 34.5 ± 1.8, 20.9 ± 3.7, 37.5 ± 1.4, and 9.13 ± 1.8, respectively.

The mean age of the 30 control subjects was 42.9 ± 2.0 (range, 20-70) years. Their diagnoses were uterine leiomyoma ($n = 14$), ovarian endometrioma ($n = 18$), serous cyst adenoma of ovary ($n = 2$), and serous cyst adenofibroma of ovary ($n = 1$).

The mean VI and VFI values were significantly higher in patients with cervical cancer compared with those of controls with a normal cervix (VI; $p < 0.05$, VFI; $p < 0.0005$, Welch's *t*-test). The mean VI value was significantly higher in patients with Stage IIA-VIB cervical cancer compared with that of patients with Stage IB cervical cancer ($p < 0.001$, Welch's *t*-test). The mean VI value was significantly higher in patients with Stage IB cervical cancer compared with that of controls with a normal cervix ($p < 0.05$, Welch's *t*-test) (Table 3).

The correlations between tumor volume and VI, FI and VFI before treatment are plotted in Figure 2. Linear regression analysis showed a modest correlation between tumor volume and VI ($r = 0.46$, $p < 0.05$) and VFI ($r = 0.38$, $p < 0.05$), but not FI ($r = 0.21$, $p = 0.13$).

Figure 3 shows the ROC curves of 3D parameters (VI, FI and VFI) for the diagnosis of cervical cancer compared with the normal cervix. ROC curve analysis showed that the best cutoff values were 5.24 for VI, 27.7 for FI and 1.69 for VFI.

VI, with an area under the ROC curve = 0.90 ± 0.039

Table 3. — *Three-dimensional parameters in 35 controls with a normal cervix and 30 patients with cervical cancer.*

	n	Volume (ml)	MG	VI	FI	VFI
				(mean ± SEM)		
Normal cervix	35	19.8± 1.5	33.5 ± 1.5	1.39 ± 0.34	33.2 ± 2.1	1.12 ± 0.70
Cervical cancer	30	33.3 ± 6.8*	34.7 ± 1.3	16.5 ± 2.7**	34.9 ± 1.2	7.1 ± 1.3**
Stage Ib	11	14.0 ± 5.3	35.2 ± 1.7	8.96 ± 2.63*	33.9 ± 1.8	3.58 ± 1.04
Stage IIa -IVb	19	44.5 ± 9.4*†	34.5 ± 1,8	20.9 ± 3.7*†*	37.5 ± 1.4	9.13 ± 1.8*†

The parameters were measured before treatment.
Data represent the mean ± SEM. Mean Gray index (MG) is a quantification of the echogenicity.
Vascularization index (VI) expresses the percent vessels in mass. Flow index (FI) express the average intensity of flow in the vessels. Vascularization flow index (VFI) is a feature of vascularization and flow.
** $p < 0.001$ compared with parameters of normal cervix.
* $p < 0.05$ compared with parameters of normal cervix.
† $p < 0.01$ compared with parameters of Stage IB cervical cancer.

Table 4. — *Area under the ROC curves, sensitivity, specificity, accuracy, positive predictive value, negative predictive value, likelihood ratios, and cutoff value for 3D parameters (VI, FI, VFI) in the diagnosis of cervical cancer (n = 30) compared with normal cervices.*

	VI	FI	VFI
Area under the ROC curve	0.90 ± 0.039*	0.64 ± 0.071	0.87 ± 0.045*
Sensitivity (%)	73.3	96.7	73.3
Specificity (%)	94.3	40.0	91.4
Accuracy (%)	84.6	66.2	8.1
Positive predictive value (%)	91.7	58.0	88.0
Negative predictive value (%)	80.5	93.3	80.0
Likelihood ratio (+)	12.83	1.61	8.56
Likelihood ratio (–)	0.28	0.08	0.29
Cut-off value	5.24	27.7	1.69

ROC, receiver operating characteristic.
Likelihood ratios were used to select cutoff values, thus maximizing the area under ther eceiver operating characteristic curves for VI, FI and VFI.
* $p < 0.0001$ compared with area under the ROC curve of FI.

(95% CI, 0.82-0.98) was more effective than FI = 0.64 ± 0.071 (95% CI, 0.51-0.78) in discriminating the women with cervical cancer ($p < 0.0001$, Table 4). VFI, with an area under the ROC curve = 0.87 ± 0.045 (95% CI, 0.79-0.96) was more effective than FI in discriminating the women with cervical cancer ($p < 0.0001$, Table 4).

The sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratios, and cutoff value for 3D parameters (VI, FI, VFI) are shown in Table 4. VI had sensitivity of 73.3% (95% CI, 62.5-78.0) and specificity of 94.3% (95% CI, 85.0-98.3). The two cases with a false-positive result included two uterine myomas. The eight cases with false-negative results included five squamous cell carcinomas (Stage IB1: four, Stage IIIB: one), two adenosquamous carcinomas (Stage IIB) and one mucinous carcinoma (Stage IIB).

VFI had a sensitivity of 73.3% (95% CI, 62.0-79.5) and specificity of 91.4% (95% CI, 81.7-96.7). The three cases with a false-positive result included three uterine myomas. The eight cases with false-negative results were the same as the cases of VI.

Figure 4 shows the ROC curves of 3D parameters (VI, FI and VFI) for the diagnosis of Stage IB cervical cancer compared with the normal cervix. ROC curve analysis

Table 5. — *Area under the ROC curves, sensitivity, specificity, accuracy, positive predictive value, negative predictive value, likelihood ratios, and cutoff value for 3D parameters (VI, FI, VFI) in the diagnosis of Stage IB cervical cancer (n = 11) compared with normal cervices.*

	VI	FI	VFI
Area under the ROC curve	0.82 ± 0.086*	0.57 ± 0.09	0.80 ± 0.085*
Sensitivity (%)	63.6	90.9	63.6
Specificity (%)	94.3	42.9	91.4
Accuracy (%)	87.0	54.3	84.8
Positive predictive value (%)	77.8	33.3	70
Negative predictive value (%)	89.2	93.8	88.9
Likelihood ratio (+)	11.1	1.59	7.42
Likelihood ratio (–)	0.39	0.21	0.4
Cut-off value	5.24	28.3	1.76

ROC, receiver operating characteristic.
Likelihood ratios were used to select cutoff values, thus maximizing the area under the receiver operating characteristic curves for VI, FI and VFI.
* $p < 0.0001$ compared with area under the ROC curve of FI.

Table 6. — *Changes in parameters in 11 patients with cervical cancer.*

	before treatment	aftertreatment 1M	aftertreatment 2M
Volume (ml)	64.5 ± 12.7	26.1 ± 5.7**	14.2 ± 3.8**
VI	27.1 ± 4.8	12.4 ± 1.6*	14.0 ± 3.7*
FI	39.1 ± 1.4	34.9 ± 1.7	38.0 ± 2.0
VFI	11.8 ± 2.1	4.9 ± 1.4**	6.1 ± 1.7*

The parameters were measured before treatment, 1 and 2 months after treatment.
Data represent the mean ± SEM.
* $p < 0.05$ compared with baseline.
** $p < 0.01$ compared with baseline.

showed that best cutoff values were 5.24 for VI, 28.3 for FI and 1.76 for VFI.

VI, with an area under the ROC curve = 0.82 ± 0.086 (95% CI, 0.65-0.98) was more effective than FI = 0.57 ± 0.09 (95% CI, 0.40-0.75) in discriminating the women with Stage IB cervical cancer ($p < 0.0001$, Table 5). VFI, with an area under the ROC curve = 0.80 ± 0.085 (95% CI, 0.63-0.97) was also more effective than FI in discriminating the women with cervical cancer ($p < 0.01$, Table 5).

The sensitivity, specificity, PPV, NPV, likelihood ratios, and cutoff value for 3D parameters (VI, FI and VFI) are shown in Table 5. VI had a sensitivity of 63.6% (95% CI, 41.2-76.0) and specificity of 94.3% (95% CI, 87.2-98.2). VFI had a sensitivity of 63.6% (95% CI, 40.5-79.0) and specificity of 91.4% (95% CI, 84.1-96.3).

In 11 patients of group B who received neoadjuvant chemotherapy, radiation or chemoradiation, the tumor volume, VI FI and VFI before treatment, one and two months after treatment are shown in Table 6. Tumor volume, VI and VFI one and two months after treatment were significantly lower compared with baseline ($p < 0.05$).

Figure 5 shows an example of invasive cervical cancer analyzed by 3D color power Doppler ultrasound angiography: (a) before treatment, (b) one month after treatment, and (c) two months after treatment.

The correlations between tumor volume measured by MRI and tumor volume measured by 3D ultrasound

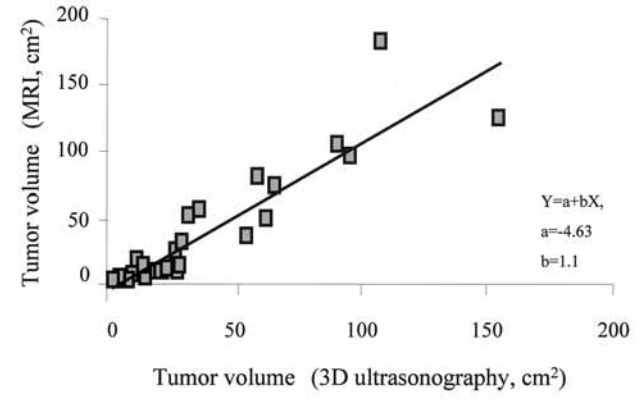

Figure 6. — Correlation of the tumor volume MRI with the tumor volume (3D ultrasonography) ($r = 0.91$, $p < 0.0001$)
X: Tumor volume (3D ultrasonography, cm²), Y: Tumor volume (MRI, cm²).

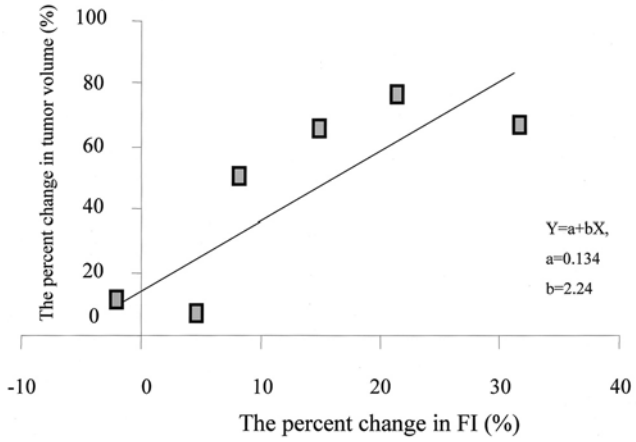

Figure 8. — Correlation of the percent change in tumor volume during the second month of neoadjuvant chemotherapy with the percent change in FI during the first month of neoadjuvant chemotherapy ($r = 0.83$, $p < 0.05$).

before and after treatment are plotted in Figure 6. Linear regression analysis showed a strong correlation ($r = 0.91$, $p < 0.0001$).

The correlations between the percent change in tumor volume during the second month of treatment and the percent change in 3D parameters (VI, FI and VFI) and tumor volume during the first month of treatment are plotted in Figure 7. Linear regression analysis showed a correlation between the percent change in tumor volume during the second month of treatment and the percent change in 3D parameters (VI, FI and VFI) during the first month of treatment (VI; $r = 0.62$, $p < 0.05$, FI; $r = 0.88$, $p < 0.0005$, VFI; $r = 0.67$, $p < 0.05$) but not the percent change in tumor volume during the first month of treatment.

In the six patients who received neoadjuvant chemotherapy, the correlations between the percent change in tumor volume during the second month of treatment and the percent change in FI during the first

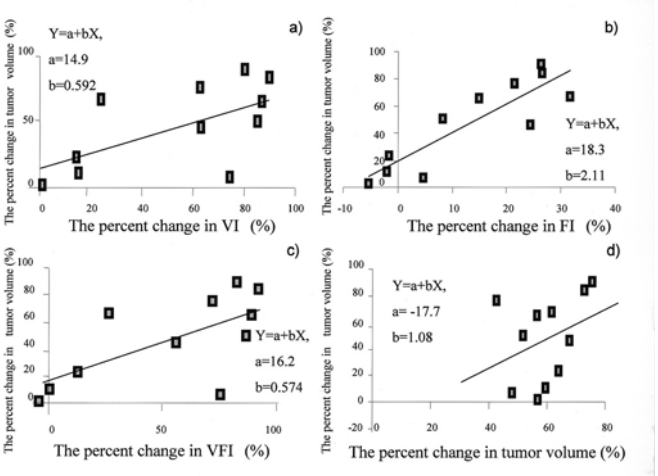

Figure 7. — Correlation of the percent change in tumor volume during the second month of treatment with the percent change in 3D parameters (VI, FI and VFI) and tumor volume during the first month of treatment.
(a) VI ($r = 0.62$, $p < 0.05$);
(b) FI ($r = 0.88$, $p < 0.0005$);
(c) VFI ($r = 0.67$, $p < 0.05$);
(d) Tumor volume($r = 0.34$, $p = 0.30$).

month of treatment are plotted in Figure 8. Linear regression analysis showed a correlation between the percent change in tumor volume during the second month of treatment and the percent change in FI during the first month of treatment ($r = 0.83$, $p < 0.05$) but not the percent change in VI, VFI or tumor volume during the first month of treatment.

Discussion

In this study we clarified whether data acquired by 3D ultrasonography and 3D power Doppler could potentially contribute to the differentiation of a normal cervix and a cancerous cervix.

We found that 3D power Doppler analysis of cervical cancer was able to detect intratumoral vessels in all lesions. The improvement in the resolution of ultrasound equipment could explain the high detection rate of intratumoral vessels in our series as well as that of other authors [14-16].

This preliminary study of 3D quantitative analysis of vascularization in cervical cancers was focused on 3D power Doppler indices. The mean VI value was significantly higher in patients with Stage IB cervical cancer compared with that in control patients with a normal cervix, and the mean VI value was significantly higher in patients with Stage IIA-VIB cervical cancer compared with that in patients with Stage IB cervical cancer.

This might indicate that VI detected by 3D ultrasonography was elevated in early stage cervical cancer compared with that in the normal cervix, and increased as the clinical stage advanced. The positive correlations between tumor volume and VI and VFI before treatment might show that VI and VFI increased as tumor volume increased.

To our knowledge, no one has previously demonstrated the area under the ROC curve of the 3D power Doppler indices (VI, FI and VFI), as assessed by 3D ultrasound in cervical cancers and normal cervices. In this study, VI showed a specificity of 73.3%, with a sensitivity of 94.3% (Table 3) and was the best parameter of the 3D power Doppler indices for distinguishing cervical cancer from the normal cervix.

It is interesting to note that the density of vessels likely to be reflected in the total color content of the tumor scan was the single best vascular predictor of malignancy. This was because in cervical carcinoma, intratumoral vascularity index assessment by 2D power Doppler ultrasound is well correlated with the conventional indicator of tumor angiogenic activity (microvessel density) [17].

A previous study reported that abundant intratumoral power Doppler signals could be detected, and that VI, FI, and VFI were significantly increased in cervical cancer patients compared with women with a normal cervix [16]. However, in our study the VI and VFI were significantly increased in cervical cancer patients compared with that in women with a normal cervix, but FI was not increased. The region of interest (ROI) defined by 3D ultrasonography as a normal cervix included the branches of the uterine arteries. This could explain why the FI values were not elevated and might result in false-positive results for VI and VFI.

On the other hand, cancer is associated with increased angiogenesis, and when the cervical tumor outgrows the vessel support, tumor necrosis occurs. This could explain the false-negative result on VI and VFI in the case of Stage IIIB squamous cell carcinoma.

Because the strong correlations between tumor volumes measured by MRI and tumor volumes measured by 3D ultrasound before and after treatment were shown by 1inear regression analysis, we might show that the ROI defined by 3D ultrasonography as cervical cancer was similar to the ROI defined by MRI as cervical cancer.

We then investigated its potential for predicting therapeutic efficacy in cervical cancer. The percent change in tumor volume during treatment was not correlated with the tumor volume and 3D parameters (VI, FI and VFI) before treatment (data not shown). However, the percent change in tumor volume during the second month of treatment was positively correlated with the percent change in 3D parameters (VI, FI and VFI) during the first month of treatment, therefore 3D parameters have the potential to predict therapeutic efficacy in cervical cancer.

In the six patients who received neoadjuvant chemotherapy, the percent change in tumor volume during the second month of treatment positively correlated with the percent change in only FI during the first month of treatment, therefore FI has the potential to predict therapeutic efficacy in cervical cancer treated with neoadjuvant chemotherapy.

Since 3D power Doppler ultrasound provides functional, objective and quantitative evaluation of vascularity of the whole tumor, it can be used to monitor the response to neoadjuvant chemotherapy in the treatment of bulky cervical cancer [18-20]. In addition, this non-invasive tool may be used to evaluate vascular changes in the tumor after antiangiogenesis therapy for the treatment of cancer. However, this novel technique is not without its limitations. As with any ultrasound technique, results may vary depending on the operator. Power Doppler ultrasound is also subject to motion artifacts from the transducer and the patient.

Conclusions

Tumor volume and 3D parameters can be noninvasively measured and easily obtained by 3D ultrasound sonography. VI may be useful for diagnosis of cervical cancer and FI may be useful for prediction of treatment response. Further research will be undertaken in a larger series of patients for analyses in which the additional value of the measurement of 3D parameters will be estimated.

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