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COMPARISON OF THE DIAGNOSTIC PERFORMANCE OF 2D AND 3D MR IMAGES IN STAGING AND HISTOPATHOLOGY FINDINGS OF LOCALLY ADVANCED CERVICAL CANCER

Guo-Jie Wang[1#], Le-Wei Yang[2#], Shi-Rui Yang[3#], Bin Zhou[4], Run-Gen Zhan[5], Ya-Li Zhang[6], Yong-Jun Peng[5*], Jie Zhang[5*]

[1.]*Department of Radiology, Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai 519000, China*

[2.]*Department of Abdominal Oncology, The Cancer Center of The Fifth Affiliated Hospital of Sun Yat-Sen University, Zhuhai 519000, China*

[3.]*Department of Nuclear Medicine, Zhuhai People's Hospital (Zhuhai hospital affiliated with Jinan University), Zhuhai 519000, China*

[4.]*Department of Pathology, Zhuhai People's Hospital (Zhuhai hospital affiliated with Jinan University), Zhuhai 519000, China*

[5.]*Department of Radiology, Zhuhai People's Hospital (Zhuhai hospital affiliated with Jinan University), Zhuhai 519000, China*

[6.]*Xindian health center, SuiDe 718000, China*

[*]*Corresponding E-mail: Yong-Jun Peng MS, sxpj2196@163.com*

Jie Zhang MD, zhangjie201806@sina.com

[#]*Equal contributors: Guo-Jie Wang, Le-Wei Yang and Shi-Rui Yang contributed equally to this work, as the same first author.*

Abstract: Objective: To compare three-dimensional (3D) volume measurement versus two-dimensional (2D) measurement during MR assessment of pre-treatment locally advanced cervical cancer, and to investigate the association of measurement outcomes with the staging of the tumor and histopathological feature in locally advanced cervical cancer. Methods: 46 patients were found having locally advanced cervical cancer that was confirmed by pathology (39 squamous cell carcinoma,7 adenomatous carcinoma). All patients were scanned by conventional MR scan, DCE-MR, and DWI sequence. Measurement results were compared between normal tissues and cervical cancer tissues in 3D and 2D. The association of measurement outcomes of 3D and 2D with the pathological grade and clinical stage of cervical cancer was explored. Results: There was no statistically significant difference between the results of 3D volume measurements and 2D diameter measurements ($P>0.05$). A significant correlation was found between the 3D volume measurement and cervical cancer stages ($P<0.05$). There was no correlation between 2D measurements and the clinical stage of cervical cancer ($P>0.05$). The outcomes between 3D volume measurement and 2D diameter measurement (The short cross-sectional diameter) among different histopathological grading of cervical cancer had statistical significance ($P<0.05$). Conclusion:3D volume measurement is more effective compared with 2D diameter measurement in MR assessment of locally advanced cervical cancer. In locally advanced cervical cancer, 3D volume measuring correlates with pathological grading and clinical stage. It provides more accurate and comprehensive data on pre-treatment cervical cancer. Therefore, 3D volume measurement can be used in preoperative MR imaging to monitor response to therapy and improve radiomics features analysis in patients with locally advanced cervical cancer.

Keywords: Cervical cancer, Locally advanced cancer, MR imaging, Tumor stage

1. INTRODUCTION

According to the National Cancer Institute, cervical cancer is the fourth most common cancer among women[1]. The prognosis of cervical cancer is primarily affected by the stage, the pathological type and the grade of the tumor[2]. Magnetic resonance imaging (MRI) is becoming increasingly important in the accurate diagnosis, evaluation of volume and morphology and clinical staging of cervical cancer[3]. MR imaging is currently used for the evaluation of cervical cancer in different ways. The 2D (two-dimensional) measurement method is commonly used by radiologists and radiotherapy physicians. The 3D (three-dimensional) based on the MR image method is a new way to measure volume. It is also widely used in research of cervical cancer imaging radiomics[4]. MR images of locally advanced cervical cancer were compared using 2D and 3D measurement methods[5]. In this study, we investigate the difference between the two measurements and evaluate their practical significance in the clinical staging and pathological grading of cervical cancer.

2. METHODS

2.1 Data sources and searching methods

The normal control group was made up of 46 patients, randomly selected, who were admitted to our hospital between January 1, 2010 and December 31, 2021 with diseases other than uterine and cervical. All patients were

scanned by conventional MR scan, DCE-MR and DWI sequence. The mean age of the patients was 41.23±13.26 years old and the age range was from 29 to 58 years old. The exclusion criteria were as follows: (1)the patients had no contraindications for MRI examination, such as metal prosthesis, pacemaker, vascular stent or aneurysm clipping, claustrophobia; (2)no abnormality was found in all patients by routine gynecological examination and cervical smear; (3)the pelvic MR examination did not reveal any lesions; (4)MR examination was performed five to seven days after menstruation; (5)remove any metal foreign body (such as metal intrauterine device) before the examination; (6)be sure to drink enough water to fill bladder 2 hours before the scan.

From January 1, 2010 to December 31, 2021, 46 cervical cancer patients were enrolled, ranging in age from 36 to 72 years old, with an average age of 49.09±7.69 years old. The exclusion criteria were as follows: (1)through cervical biopsy and clinical examination, all cases were confirmed to be locally advanced cervical cancer; (2)the MR images showed no obvious cysts, bleeding, or necrotic areas (Fig.1) .

2.2 MRI examination

All patients received examination on a 3T MRI (GE Silent, USA) with an 18-channel body coil. The protocol of MRI for uterus examination was summarized in Table 1.

Table 1 MRI protocol for uterus examination

Sequence	T1WI imaging	T2WI imaging (axial, sagittal, coronal)	DWI	IVIM
Repetition time (ms)	550	3600~4100	2500	2500
Echo time (ms)	8	78	70	70
Slice thickness (ms)	4	4	4	4
Slice gap (ms)	0	0	0	0
Slices	25	23	22	22
Field of view (mm^2)	260×320	260×320	260×320	260×320
Matrix	320×320	320×320	320×320	320×320
Flip angle (degree)	160	160	90	90
Temporal resolution (s)	NA	NA	NA	NA
b value (S/mm^2)	NA	NA	0,1000	0、800、1000
Average	1	1	3	1~6

T1W, T1-weighted; T2W, T2-weighted; DWI, diffusion-weighted imaging; NA, not applicable.

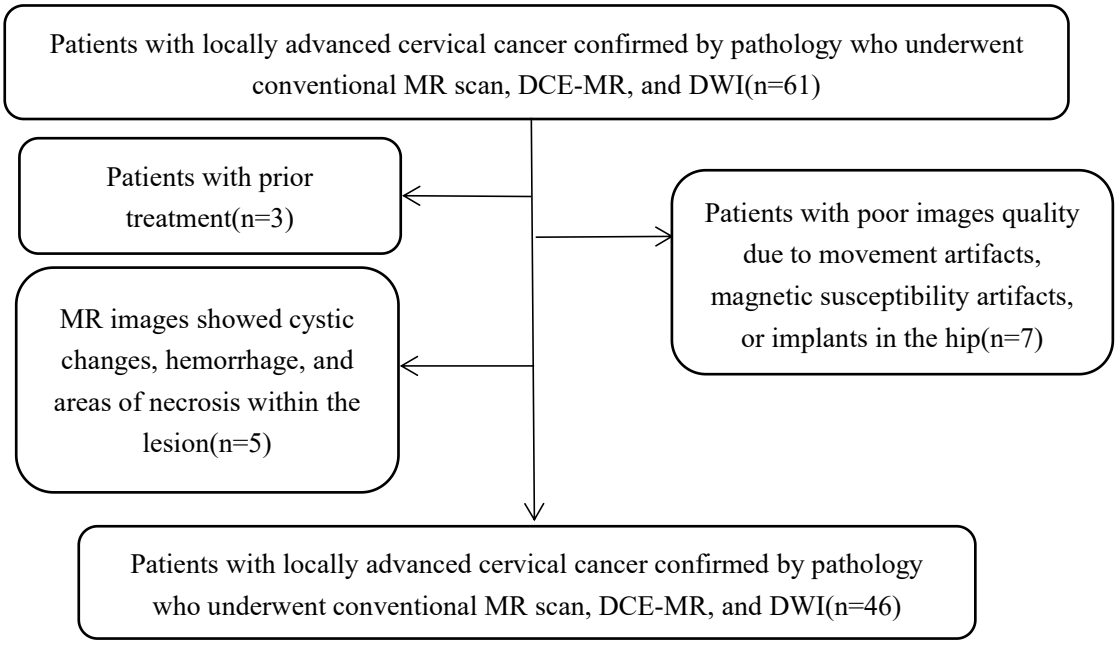

Fig.1 Flowchart of patient selection.
DCE-MR, dynamic contrast enhancement-magnetic resonance; DWI, diffusion-weighted imaging.

2.3 Image interpretation and data analysis

MADC software of GE AW4.7 post-processing workstation was used to analyze DWI, ADC, DCE-MR, T1WI, T2WI and FS-T2WI images of cervical cancer. The endometrium, binding zone, and muscularis were visible on each sequence diagram in the control group, and signal values were measured around these regions. On each sequence, the largest lesion layer was found in the cervical cancer group. Moreover, each sequence map was manually drawn with a 2D Region of Interest (ROI)

range along the lesion edge, and the ROI signal value in each sequence was measured. At the same time, maximum cross-sectional length diameters, maximum cross-sectional short diameters, and maximum upper and lower diameters of the tumor were determined using 2D diameter measurement. In the above sequences, 2D ROIs were drawn manually along the edges of lesions, and then 3D ROI ranges were generated. Signal values were measured in each sequence of ROI. Data on tumor volume was collected automatically by software at the same time. The data of maximum cross-sectional length diameter, maximum cross-sectional short diameter, and maximum upper and lower diameter of the tumor were measured again by the same doctor using an open-source software ITK-SNAP version 3.8.0 (http://fsf.org/) at the same level of the lesion. On the same level of the lesion, the maximum cross-sectional length diameter, maximum cross-sectional short diameter and maximum upper and lower diameter of the tumor were measured again. Afterward, 2D ROI ranges were manually drawn along the edges of each layer of the lesion while 3D ROI ranges were generated by the software. Comparisons of the signal values measured by 2D and 3D methods of different b-value DWI and ADC images, DCE-MR, T1WI, T2WI and FS-T2WI sequences in the cervical cancer region were conducted. Measured signals from the endometrium, binding zone and muscularis by 2D methods were compared. Results of cervical cancer measured by 3D and 2D methods were compared among different pathological grades and clinical stages. The volume of the tumors was also determined by ITK-SNAP software automatically. The P value of difference between the above 2D measurement data was less than 0.05 and the average value was taken as the final 2D measurement result.

2.4 Statistical Analysis

Kolmogorov-Smirnov was used to test the normal distribution of the analysis data. One-way ANOVA was used to compare results of 2D and 3D measurements of cervical cancer after the conditions were met. The LSD method was used to determine the homogeneity of variance. One-way ANOVA was used to compare the signal values of normal three-layer cervical structures and the 2D and 3D measurements of cervical cancer in each sequence. Spearman multivariate correlation analysis was used to compare the tumor volume measurements (maximum cross-sectional long diameter and short diameter, maximum upper and lower diameter). Multivariate Spearman's correlation and Pearson analysis were employed to compare tumor volumes measured by 3D measurement with values measured by 2D measurement in different phases of the clinical stage. SPSS 27.0 (Chicago, IL, USA) was used for statistical analysis. $P<0.05$ was considered statistically significant difference.

3. RESULTS

3.1 Comparison of signal values of 2D and 3D measurements in locally advanced cervical cancer sequences

The results of 2D and 3D methods for measuring the signal of locally advanced cervical cancer in DWI, ADC, DCE-MRI, T1WI, T2WI and FS-T2WI sequences were summarized in Table 2. In the homogeneity test of variance, $P<0.05$. An Independent sample t-test did not reveal any significant differences between the signal values measured by 2D and 3D methods ($P>0.05$). An analysis of the signal differences between normal cervical intima, conjunctive band and muscularis was done by comparing 2D and 3D methods (Table 3). Following the test of homogeneity of variance, $P>0.05$. One-way ANOVA revealed significant differences between the normal cervical intima, conjunctive band, muscularis signal and the 2D cervical cancer signal ($P<0.05$). It was statistically significant that the cervical endometrial, binding band and muscular signals differed from the 3D cervical cancer signals ($P<0.05$).

Table 2 Comparative analysis of locally advanced cervical cancer signal measured with 2D and 3D methods

Sequence	The signal value of 3D measurement	The signal value of 2D measurement	F value	P-value
DCE-MR without Enhancement	156.54~169.44 (163.00±21.71)	157.32~171.19 (164.26±23.37)	0.133	0.716
DCE-MR 1st phase	233.90~284.45(259.18±85.12)	230.28~282.80(256.54±88.42)	0.135	0.714
DCE-MR 2nd phase	365.00~401.04(383.02±60.68)	371.94~415.70(393.82±73.68)	3.705	0.057
DCE-MR 3rd phase	458.31~505.87(482.09±80.08)	469.78~507.15(488.47±62.91)	6.141	0.015
DCE-MR 4th phase	510.14~558.40(534.27±81.26)	498.64~550.27(524.45±86.93)	0.357	0.552
DCE-MR 5th phase	512.65~576.51 (544.58±107.53)	502.77~561.95 (532.35±99.65)	0.444	0.507
DCE-MR 6th phase	507.10~568.94 (538.02±104.13)	493.66~556.24 (524.94±105.37)	0.001	0.976
ADC	1051.77~1133.50 (1092.63±137.61)	1050.13~1180.28 (1115.20±219.14)	1.810	0.182
DWI (b=50)	249.38~270.05 (259.71±34.80)	253.69~279.60 (266.64±43.61)	0.342	0.560
DWI	157.34~171.71	162.24~184.40	3.011	0.086

(b=400)	(164.52±24.18)	(173.32±37.30)		
DWI	116.61~140.27	118.24~141.77	0.000	0.987
(b=800)	(128.44±39.84)	(130.01±39.62)		
T2WI	406.27~445.34	394.84~432.38	0.116	0.735
	(425.80±65.77)	(413.61±63.22)		
FST2WI	260.27~315.60	251.74~298.97	0.905	0.344
	(287.94±93.15)	(275.36±79.51)		

Table 3 Signal values of normal cervical structures were compared with signal values of locally advanced cervical cancer measured by 3D and 2D methods

Sequence	Signal value of endometrium	Signal value of Cervical band	Signal value of cervical muscle	P-value compared with 2D	P-value compared with 3D
DCE-MR without Enhancement	179.12~192.81 (185.97±23.04)	174.31~190.27 (182.29±23.04)	175.41~187.79 (181.60±20.85)	0.000	0.000
DCE-MR 1st phase	192.74~207.07(199.91±24.14)	158.97~197.55(178.26±64.96)	175.08~192.45 (183.77±29.26)	0.000	0.000
DCE-MR 2nd phase	262.76~282.92(272.85±33.94)	236.89~271.65(254.27±58.53)	239.83~274.45 (257.14±58.30)	0.000	0.000
DCE-MR 3rd phase	510.51~550.20(530.36±66.83)	412.14~449.08(430.61±62.20)	434.18~463.91 (449.05±50.05)	0.000	0.000
DCE-MR 4th phase	593.04~624.61(608.82±53.15)	431.84~475.87(453.85±74.14)	480.58~503.02 (491.79±37.78)	0.000	0.000
DCE-MR 5th phase	578.30~619.18 (598.74±68.83)	461.43~502.38 (481.91±68.94)	502.31~531.86 (517.09±49.77)	0.000	0.000
DCE-MR 6st phase	595.04~637.77 (616.40±71.95)	486.02~502.24 (485.13±57.62)	520.21~551.68 (535.95±52.99)	0.000	0.000
ADC	1436.40~1524.25 (1480.33±147.90)	1375.88~1450.94 (1413.41±126.38)	1256.42~1323.95 (1290.19±113.70)	0.000	0.000
DWI (b=50)	389.43~411.22 (400.32±36.69)	146.60~169.65 (158.13±38.80)	187.24~207.28 (197.26±33.73)	0.000	0.000
DWI (b=400)	217.99~235.04 (226.51±28.71)	86.57~99.10 (92.84±21.10)	109.09~125.56 (117.33±27.72)	0.000	0.000
DWI (b=800)	144.19~164.75 (154.47±34.61)	51.37~58.93 (55.15±12.74)	73.15~81.07 (77.11±13.34)	0.000	0.000
T2WI	368.66~379.48 (374.07±18.22)	108.26~132.65 (120.45±41.07)	119.92~153.32 (136.62±56.23)	0.000	0.000
FST2WI	333.03~362.49 (347.76±49.61)	114.46~141.10 (127.78±44.84)	136.47~159.93 (148.20±439.50)	0.000	0.000

3.2 The correlation between 2D and 3D methods and stage of locally advanced cervical cancer

Based on FIGO stages[6], histopathological and clinical diagnoses, 46 locally advanced cervical cancer patients were divided into stage II (17 cases), stage III (21 cases), and stage IV (8 cases). The maximum cross-sectional diameter of cervical cancer measured by traditional 2D methods[7] was 19.54±5.04 mm, the short cross-sectional diameter was 16.66±4.65 mm, and the maximum upper and lower diameter was 16.20±4.10 mm, the 3D volume of locally advanced cervical cancer measured by the 3D method was $30.81\pm24.68\times10^3$ mm^3. It could be seen from Table 4 that the correlation between the 2D method and the 3D method to measure the results of cervical cancer, and the correlation between the measurement results of the 2D method and the 3D method and the cervical cancer staging were compared. Multivariate Spearman correlation analysis revealed that cervical cancer volume was correlated with the cervical cancer stage ($P<0.05$). There was no correlation between the maximum cross-sectional diameter, the maximum cross-sectional length, maximum upper and lower diameters, and the stage ($P>0.05$). There were statistically significant differences in maximum cross-sectional diameter, short cross-sectional diameter, maximum upper and lower diameter and cervical cancer volume($P<0.05$).

Table 4 The correlation between stage of locally advanced cervical cancer and measurements by 2D and 3D methods

Measurement indicators	Correlation with cervical cancer stage (P-value)	Correlation with the volume of cervical cancer measured in 3D (P-value)
The maximum cross-sectional diameter	0.051	0.000
The short cross-sectional diameter	0.121	0.000

The maximum upper and lower diameter	0.114	0.000
3D volume of cervical cancer	0.005	--

3.3 The correlation between 2D and 3D methods and the degree of pathological differentiation of locally advanced cervical cancer

Among 46 cases of cervical cancer,14 cases were low differentiation,22 cases were medium differentiation and 10 cases were high differentiation. The correlation between the results measured by the 2D method and the 3D method and the degree of pathological differentiation of cervical cancer was shown in Table 5. An analysis of Pearson multivariate correlation indicated a correlation between volume measured by the 3D method and locally advanced cervical cancer stage ($P<0.05$). The short cross-sectional diameter was correlated with the degree of pathological differentiation ($P<0.05$). There was no correlation among other 2D measurements and the degree of pathological differentiation ($P>0.05$).

Table 5 The correlation between pathological differentiation of locally advanced cervical cancer and measurements by 2D and 3D methods

Measurement indicators	Correlation with differentiation degree of cervical cancer(P-value)
The maximum cross-sectional diameter	0.186
The short cross-sectional diameter	0.032
The maximum upper and lower diameter	0.098
3D volume of cervical cancer	0.020

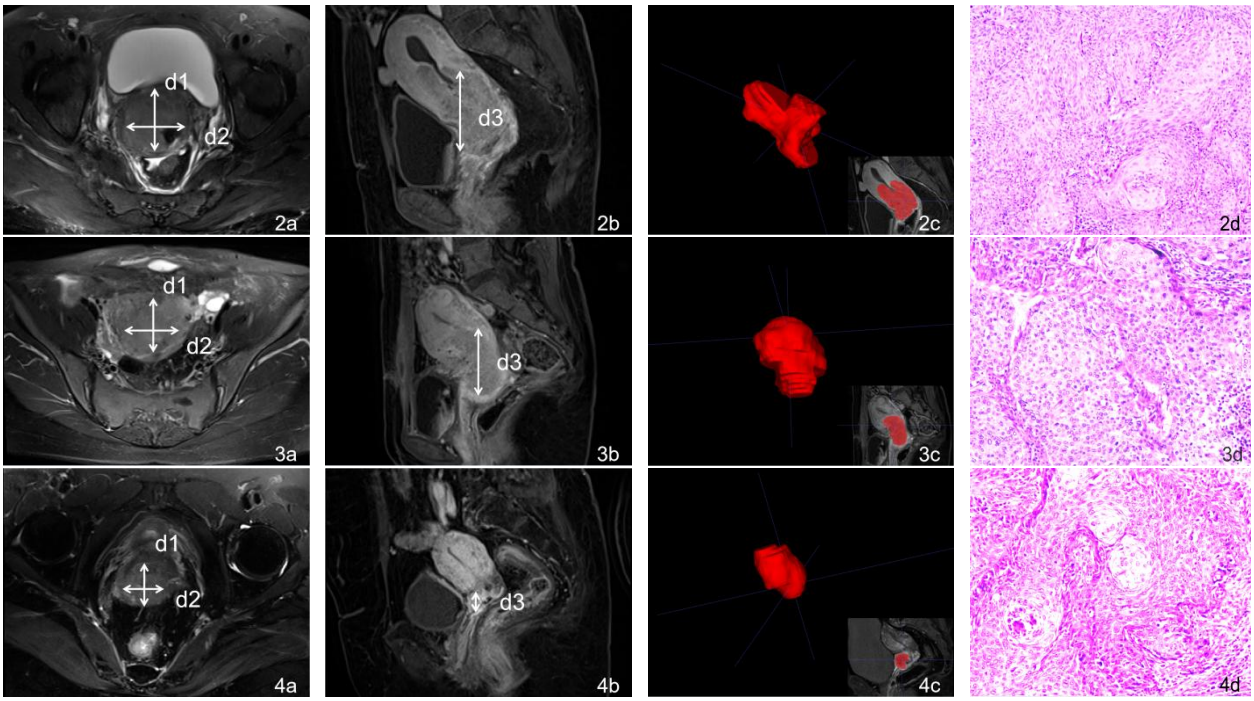

Fig.2 A 46-year-old woman presented with stage IV intermediate differentiated squamous cell carcinoma of the cervix. 2a, 2b and 2c respectively showed the 2D transverse measurement schematic diagram, 2D sagittal measurement schematic diagram, and 3D measurement schematic diagram of the same patient (d1: The maximum cross-sectional diameter, d2: The short cross-sectional diameter, d3: The maximum upper and lower diameter). 2d showed pathological images.

Fig.3 A 42-year-old woman presented with stage III intermediate differentiated squamous cell carcinoma of the cervix. 3a, 3b and 3c respectively showed the 2D transverse measurement schematic diagram, 2D sagittal measurement schematic diagram, and 3D measurement schematic diagram of the same patient. 3d showed pathological images.

Fig.4 A 53-year-old woman presented with stage II intermediate differentiated squamous cell carcinoma of the cervix. 4a,4b, and 4c respectively showed the 2D transverse measurement schematic diagram, 2D sagittal measurement schematic diagram, and 3D measurement schematic diagram of the same patient. 4d showed pathological images.

4. DISCUSSION

Traditionally, the tumor volume of cervical cancer was calculated by measuring the 2D diameter lines (the maximum cross-sectional diameter, the short cross-sectional diameter, and the maximum upper and lower diameter) of the tumor on MRI. For decades, scholars used the ellipsoid diameter formula(Volume=$d1\times d2\times d3\times\pi/6$)[8] to estimate tumor

volume before 3D computer software was developed. As a result of the introduction of 3D software, like ITK-SNAP (http://fsf.org/), tumor volume measurement had become easier in practice. In recent years, many radiomics[8] and 3D volumetric analysis[10] had been conducted based on MR images of cervical cancer. There was a rare conclusive study comparing 2D MR measurements to 3D MR measurements of cervical cancer sequences. By comparing the data of cervical cancer sequences measured by 2D and 3D methods, the author found that there was no significant difference in cervical cancer signal values measured by the two methods in each sequence. In addition, it was shown that the signal for cervical cancer measured by the 3D method differed statistically from that measured by the 2D method. The results showed that the cervical cancer area measured by the 3D method could also be well distinguished from normal cervical tissue. In conclusion, quantitative analysis and radiomics analysis of cervical cancer based on 3D MR data would be feasible. In addition, the 3D measurements in DCE-MR, DWI and other sequences of the data in this group were consistent with the previous 2D and 3D measurements[11] as well.

MR provides the highest soft tissue resolution compared to other imaging methods, which can demonstrate the imaging characteristics of cervical cancer and distinguish cervical cancer tissue from normal cervical endometrium, binding zone and muscularis. Based on the NCCN guidelines, MR imaging was recommended for the assessment of tumor boundaries and depth of invasion. With an accuracy rating of 89.9-92.9%[12], MR was the preferred method of staging cervical cancer. The accuracy of MR staging could be improved to 95.2-97.5%[12] with new techniques, such as multi-b-value DWI. Several of the above conclusions were based on 2D MR image studies and there were relatively few 3D studies on cervical cancer staging. In this study, we compared the measurement results obtained by 2D and 3D methods for measuring locally advanced cervical cancer. The results showed that the 2D method was correlated with the 3D method. As a result of modeling cervical cancer as a rough ellipsoid, the correlation between tumor volume and three diameter lines was consistent. The correlation between the measurement results of the 2D method the and 3D method and the cervical cancer stage was compared and it was found that there was no correlation between the three diameters of the 2D method and the cervical cancer stage. In contrast, 3D measurements of tumor volume were correlated with disease stage. It could be observed in a hand-drawn 3D image of cervical cancer generated by ITK-SNAP software (Fig. 2c) that the neoplasm of cervical carcinoma was approximately ellipsoid, but the edge was irregular. The irregular pattern was more apparent in the 3D morphology of high-stage cervical cancer (Fig. 3c). Due to this irregular three-dimensional structure, it was difficult to reflect the actual shape of a tumor with only three diameters. According to the results, 3D tumor volume measurement provided better staging information for cervical cancer. Based on 3D data, the study of staging correlation of cervical cancer was more accurate than that based on 2D data.

Among the diameter lines measured by the 2D method, it was found that short cross-sectional diameter was correlated with the degree of pathological differentiation of cervical cancer, while the maximum cross-sectional diameter and maximum upper and lower diameter were not correlated with the degree of pathological differentiation of cervical cancer. On the other hand, 3D measurement of cervical cancer volume was correlated with the degree of differentiation. Less differentiated tumors had larger 3D volumes and longer 2D diameter lines than more differentiated tumors. The worse the differentiation of cervical cancer, the faster the cell proliferation. As a result, the higher the cell density, the larger the tumor volume and diameter. In terms of the pathological differentiation degree of cervical cancer and the maximum cross-sectional diameter and maximum upper and lower diameters, there was no significant correlation. The measured maximum diameter might not accurately reflect the true tumor morphological volume due to irregular protrusions on the tumor surface. These results indicated that 3D MR images of cervical cancer could reflect the biological characteristics of tumors more comprehensively and accurately than previous 2D studies.

Some of the study's limitations were as follows. The sample size was small, especially considering the sample size was insufficient for further grouping analysis according to pathological types in subgroups with different levels of differentiation. It was also impossible to perform substage analysis based on further refinement of stages. Further research and statistical analysis of relevant subgroups, including research on relevant data and data collection, would be conducted by the author in the future. Secondly, limited quantities of 3D evaluation data were provided in this paper. The volumetric approach was used with no consideration of other 3D space-related characteristics, such as sphericity, surface area and body surface ratio. In the following study, the author would compare and study the application differences between 3D data as well as 2D data of cervical cancer using relevant evaluation indicators.

In this study, there were no significant differences between the data obtained by the 3D measurement method and the 2D measurement method in MR sequences. Consequently, MR images could also be measured and evaluated using 3D measurement techniques. It was better to use 3D volume measurements to determine the stage and pathological differentiation degree of cervical cancer rather than traditional 2D diameter measurements. Due to the small tissue volume of cervical cancer,3D delineation took a relatively short time[13] compared to that of liver cancer[14]. Therefore, 3D technology was expected to be increasingly applied to the preoperative comprehensive evaluation of cervical cancer surgery as well as the pretreatment evaluation of radiotherapy and chemotherapy.

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