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FULL PAPER

Comparison between readout-segmented and single-shot echo-planar imaging in the evaluation of cervical cancer staging

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Objective: To compare the performance of diffusion-weighted imaging (DWI) based on readout-segmented echo-planar imaging (RESOLVE) and single-shot EPI (SS-EPI) sequence in evaluating cervical cancer staging.

Methods: 61 patients with cervical cancer underwent DWI based on SS-EPI and RESOLVE. Two blinded readers independently assessed two sets of DW images for distinction of anatomical structures, delineation of lesion, susceptibility artefact and overall image quality on a 4-point scale. Geometric distortion was evaluated by measuring lesion anteroposterior (AP) length and left-right (LR) width derived from T_2W images and those obtained from the corresponding DW images. Staging of cervical cancer on SS-EPI and RESOLVE were compared with T_2WI and gold-standard of pathological findings.

Results: RESOLVE was significantly superior to SS-EPI for all four criteria regarding qualitative comparisons

(all $p < 0.05$). Regarding the geometric distortion, AP length on SS-EPI was significantly different from that of T_2WI ($p < 0.05$), whereas there were no significant differences between RESOLVE and T_2WI (both $p > 0.05$). The staging of SS-EPI was overestimated, while RESOLVE had a better consistency with pathological staging than SS-EPI in staging of cervical cancer. There was no significant difference in apparent diffusion coefficient value between SS-EPI and RESOLVE ($p < 0.05$).

Conclusion: RESOLVE is superior to SS-EPI in the accuracy of cervical cancer staging because of the improvement in image quality.

Advances in knowledge: RESOLVE has a more accurate value comparable to SS-EPI in cervical cancer staging, with the advantage of the improvement in image quality and reduced geometric distortion.

INTRODUCTION

With the promotion and improvement of the early screening of cervical cancer, the incidence and mortality of cervical cancer has declined around the world, but it is still the third most common gynecological malignancy after endometrial and ovarian cancers.^{1,2} MRI with good soft tissue contrast and multiplanar imaging capability, is a reliable non-invasive method with high accuracy for cervical cancer pre-operative assessment.³ It has been described as an important additional role in the selection of the best mode of cervical cancer evaluation.⁴

Diffusion-weighted imaging (DWI) is recommended by the European Society of Urogenital Radiology as the routine sequence of the pelvic MRI.⁴ To our knowledge, the traditional DWI based on single-shot echo-planar imaging (SS-EPI) is prone to image artefacts like geometric

distortions, image blurring and ghosting artefacts.^{5,6} All of these defects affected by the image quality may limit its diagnostic value, especially in tumor staging. In contrast, readout segmentation of long variable echo-trains (RESOLVE) DWI sequence segments the k-space into several shots along the readout direction in order to shorten the echo spacing, which produces high-resolution DWI images with reduced susceptibility artefact and less blurring arise from T_2^* signal decay.^{6,7} It has been reported that RESOLVE is superior to SS-EPI with respect to improved image quality in head and neck,⁸ chest,⁹ abdomen¹⁰ and pelvis.¹¹ The earlier studies^{8–11} were more concerned with the image quality comparison of the two sequences rather than the effects of diagnosis, staging, and other issues associated with image quality problems. Patients with early-stage cervical cancer and locally advanced cervical cancer have access to conventional treatments including surgery,

chemotherapy and radiotherapy. For Stage IA2 and IB1 cervical cancers, radical trachelectomy is preferred. Chemotherapy and radiotherapy are recommended for patients with cervical cancer over Stage IIB.^{12,13} So the accurate pre-operative staging is important for treatment plan to improve the 5 year survival rates. In this study, we propose an idea to evaluate whether such image differences between the two DWI sequences have an impact on staging of cervical cancer.

METHODS AND MATERIALS

Patients

Approval for this study was obtained from the institutional ethics review board, and informed consent was obtained in all patients. 97 consecutive patients, who were suspected to have cervical cancer, underwent pelvic MRI in the Affiliated Suzhou Hospital of Nanjing Medical University from June 2015 to September 2017. Study population inclusion criteria were: (1) no contraindications for MRI examination; (2) no previous treatment before MRI examination; (3) preoperative cervical carcinoma International Federation of Gynecology and Obstetrics (FIGO)¹⁴ Stage 1B1 or greater; (4) the MRI sequences including both SS-EPI and RESOLVE; (5) histological diagnosis of cervical carcinoma by surgery or biopsy. As a result, 61 patients with histologically confirmed uterine cervical cancer were included. Age distributions in this study was 27–76 (mean, 52 ± 10 years).

MRI protocol

MR examinations were performed on a 3 T MR scanner (MAGNETOM Skyra, Siemens Healthcare, Erlangen, Germany) with an 18-channel surface coil in combination with a 32-channel spine coil. Routine examination sequences include: (1) axial turbo spin-echo (TSE) T_1 weighted imaging: repetition time/echo time (TR/TE): 500/11 ms, field of view (FOV): 240×240 mm², slice thickness: 7 mm, slice gap: 0 mm, average: 2, matrix: 179×256 ; (2) axial TSE T_2 weighted imaging: TR/TE: 2980/104 ms, FOV: 240×240 mm², slice thickness: 7 mm, slice gap: 0 mm, average: 2, matrix: 384×384 ; (3) sagittal TSE T_2 weighted imaging, TR/TE: 6070/104 ms, FOV: 240×240 mm², slice thickness: 5 mm, slice gap: 0 mm, average: 2, matrix: 346×384 . Protocols of DWI based on RESOLVE and SS-EPI were listed in Table 1. Apparent diffusion coefficient (ADC) maps were automatically calculated on a commercial workstation (Syngo via, Siemens Healthcare, Erlangen, Germany) from the DW images.

Image analysis

Two radiologists (6 and 8 years experiences in interpreting pelvic MRI, respectively) reviewed and visually assessed the two sets of DW images. The two readers were blinded to patient history, histological diagnosis as well as the type of image sequence. The readers scored images in terms of distinction of anatomical structures, delineation of lesion, susceptibility artifact and overall diagnostic confidence by using a 4-point scale (Table 2).

Geometric distortion was evaluated by comparing the dimensions of lesions on DW images with T_2W images as a reference. Anteroposterior (AP) length and left-right (LR) width of the lesions were measured on SS-EPI, RESOLVE and T_2WI as the dimensional characteristic of the lesion. The average values of

Table 1. Imaging protocols of DWI based on SS-EPI and RESOLVE

Parameters	SS-EPI	RESOLVE
Diffusion directions	Three-direction trace	Three-direction trace
Diffusion encoding scheme	Monopolar	Monopolar
b -value (s mm ⁻²)	0, 800	0, 800
Fat suppression	SPAIR	SPAIR
TR (ms)	4000	5300
TE (ms)	56	117
Field of view (mm ²)	240×240	240×240
Matrix	150×150	130×130
Slice thickness (mm)	7	7
Slice gaps (mm)	0	0
Number of readout segments	1	7
Parallel imaging	GRAPPA	GRAPPA
Acceleration factor	2	2
Acquisition time (minute:second)	1:09	3:28

RESOLVE, readout segmentation of long variable echo-trains; SS-EPI, single-shot echo-planar imaging; TE, echo time; TR, repetition time;

the results from two readers in both subjective visual scores and objective quantitative parameters were considered as the final results.

Staging of cervical cancer on the two DW and T_2W images were assessed by the two radiologists respectively. Final result was achieved by consensus if two readers disagreed on the conclusion. Locoregional lesions evaluation was compared in two DW images with T_2WI . On the basis of T_2WI , results of the final unified staging on SS-EPI and RESOLVE were compared with the gold-standard pathological findings. All staging results were according to FIGO guidelines of tumor stage.¹⁴ A region of interest was drawn in the ADC map according to the lesion in T_2W and DW images to obtain the ADC values of the two DW images.

Statistical analysis

Statistical analyses were performed using the software SPSS (v. 16.0 Inc. Chicago, IL). Quantitative variables were expressed as mean $\pm$ standard deviation. The interobserver agreement between the two radiologists was assessed using inter-rater agreement (κ) for quantitative comparison scores. κ -values greater than 0.75, from 0.40 to 0.75, and less than 0.40 were regarded as excellent, fair to good, and poor, respectively. The Pearson correlation coefficient of the ADC values was calculated. Subjective visual scores, objective quantitative parameters and staging results were analyzed with Paired Wilcoxon signed-rank tests and paired-samples t test. A value of $p < 0.05$ was considered as to indicate a statistically significant difference.

Table 2. Criteria for subjective visual scores of image quality in DWI in patients with cervical cancer

Distinction of anatomical structures
1: Cannot identify any structures
2: Less than 50 % structures can be identified
3: More than 50 % structures can be identified
4: All structures can be identified
Delineation of lesions
1: Not visible
2: Identifiable
3: Acceptable
4: Detectable with good quality
Susceptibility artefact
1: Severe
2: Moderate
3: Mild
4: None
Overall diagnostic confidence
1: Poor
2: Fair
3: Good
4: Excellent

DWI, diffusion-weighted imaging;

RESULTS

Patients and lesions

Among the 61 cervical cancer patients, 57 cases are squamous carcinoma, 4 cases are adenocarcinoma; 25/5 patients are staged as IB1/IB2, 6/10/7 patients are staged as IIA1/IIA2/IIB, 2/1 patients are staged as IIIA/IIIB, and 3/2 patients are staged as IVA/IVB according to pathological findings.

Comparison of subjective visual scores

There is moderate–high interobserver agreement between readers in the subjective visual scoring of the two DW images. For RESOLVE, κ -values are as follows: 0.836 for distinction of anatomical structures, 0.705 for delineation of lesion, 0.709 for susceptibility artifact and 0.778 for overall diagnostic confidence. There are 0.742, 0.765, 0.699 and 0.698 for the four criteria of SS-EPI respectively. Subjective image quality scores of SS-EPI and RESOLVE are summarized in Table 3. RESOLVE

Figure 1. T_2 WI (a) SS-EPI ($b = 800 \text{ s mm}^{-2}$) (b) and RESOLVE ($b = 800 \text{ s mm}^{-2}$) (c) of a 58-year-old female with cervical cancer. SS-EPI was difficult to identify normal anatomical structures with a marked susceptibility artifact (thin arrow) and geometric distortion (thick arrow), while these were obviously reduced on RESOLVE. SS-EPI, single-shot echo-planar imaging; RESOLVE, readout segmentation of long variable echo-trains; T_2 WI, T_2 weighted imaging.

is significantly superior to SS-EPI for all four criteria regarding qualitative comparisons (all $p < 0.05$) (Figure 1).

Comparison of lesion distortion

The average AP lengths of the lesions are (2.90 ± 1.66) cm on SS-EPI, (2.80 ± 1.59) cm on RESOLVE, and (2.82 ± 1.62) cm on T_2 WI, respectively. The average LR widths of the lesions on the three sets of images are respectively (2.30 ± 1.27) cm on SS-EPI, (2.25 ± 1.22) cm on RESOLVE and (2.30 ± 1.25) cm on T_2 WI. There is statistically significant difference in AP length between SS-EPI and T_2 WI ($Z = -2.265$, $p = 0.024$), while there are no statistically significant differences in AP length between RESOLVE and T_2 WI ($Z = -0.244$, $p = 0.808$), as well as in LR width between SS-EPI vs T_2 WI ($t = 0.028$, $p = 0.978$) and RS-DWI vs T_2 WI ($t = 1.684$, $p = 0.097$). The corresponding results are shown in Figure 2.

Table 3. Comparison of subjective image quality scores of SS-EPI and RESOLVE in patients with cervical cancer

Parameters	SS-EPI	RESOLVE	Z	p
Distinction of anatomical structures	2.02 ± 0.39	3.61 ± 0.69	-6.862	0.000
Delineation of lesion	2.98 ± 1.02	3.25 ± 0.81	-3.358	0.000
Susceptibility artifact	1.52 ± 0.65	3.00 ± 0.00	-6.747	0.000
Overall diagnostic confidence	2.66 ± 0.48	3.46 ± 0.50	-7.000	0.000

RESOLVE, readout segmentation of long variable echo-trains; SS-EPI, single-shot echo-planar imaging;

Figure 2. Bar graph showed the comparison of lesion distortion between SS-EPI, RESOLVE and T_2 WI. SS-EPI, single-shot echo-planar imaging; RESOLVE, readout segmentation of long variable echo-trains; T_2 WI, T_2 weighted imaging.

Comparison of staging

The κ -value between T_2 WI staging is 0.809, and 0.590 for SS-EPI, 0.922 for RESOLVE. In locoregional lesions image evaluation, RESOLVE ($Z = -1.272$, $p = 0.203$) is more similar to the performance of T_2 WI than SS-EPI ($Z = -4.721$, $p = 0.000$) (Tables 4–5). Compared with pathology, the staging results of T_2 WI combined with SS-EPI and RESOLVE are respectively as follows (Tables 6–7). RESOLVE ($Z = -0.362$, $p = 0.717$) has a better consistency with pathological staging than SS-EPI ($Z = -2.908$, $p = 0.004$) in staging of cervical cancer (Figure 3). There is no significant difference in ADC value between SS-EPI [$(1.03 \pm 0.22) \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$] and RESOLVE [$(0.99 \pm 0.17) \times 10^{-3}$

$\text{mm}^2 \text{ s}^{-1}$] ($t = 1.949$, $p = 0.056$). The Pearson correlation coefficient of the ADC values between SS-EPI and RESOLVE is 0.735.

DISCUSSION

Our study shows that RESOLVE is superior to SS-EPI as expressed qualitatively for distinction of anatomical structures, delineation of lesion, susceptibility artifact and overall diagnostic confidence in evaluating cervical cancer. Moreover, the geometric distortion of the lesion is found to be more severe on SS-EPI, while there is no significant difference between RESOLVE and T_2 WI. Finally, RESOLVE allows for more accurate than SS-EPI in preoperative staging of cervical cancer combined with T_2 WI.

Susceptibility artifact, image blurring and spatial distortion may be severe in conventional DWI based on SS-EPI due to long EPI readout and corresponding low bandwidth per pixel in the phase encoding direction. RESOLVE sequence introduced by Porter et al⁶ produced shorter echo-spacing by dividing the k-space into separate segments in the readout direction, and a two-dimensional navigation data acquisition was used for nonlinear phase correction. This strategy can reduce susceptibility and T_2^* -blurring artefacts and obtain high resolution DW images. In our cervical cancer image analysis, RESOLVE shows better performance in terms of the distinction of anatomical structures, delineation of lesion, susceptibility artefact and overall diagnostic confidence than SS-EPI, which is similar to the conclusions of other researchers comparing image quality between SS-EPI and RESOLVE in different body parts.^{8–11}

EPI is intrinsically prone to geometric distortions due to the low bandwidth of data acquisition particularly in the phase encode direction, which leads to pixel shifts in the reconstructed image. SS-EPI samples the full FOV in the phase-encoding direction during each pulse sequence repetition, which results in a very low bandwidth.¹⁵ RESOLVE reduces spatial distortion by reducing echo spacing and segmenting the readout direction in a contiguous motion compensated multi shot acquisition.⁶ Koyasu et al⁸ compared the mean distortion ratios of organs and lesions in head and neck area between DWI and T_2 WI. Kim

Table 4. Comparison of SS-EPI and T_2 W imaging evaluation in patients with cervical cancer

T_2 WI	SS-EPI						Total
	Confined to cervix	Vaginal invasion (upper 2/3)	Parametrial invasion	Vaginal invasion (lower 1/3)	bladder or rectum invasion	Evidence of distant metastasis	
Confined to cervix	16	1	7	0	4	0	28
Vaginal invasion (upper 2/3)	2	3	6	0	8	0	19
Parametrial invasion	0	2	2	0	2	0	6
Vaginal invasion (lower 1/3)	0	0	0	0	3	0	3
Bladder or rectum invasion	0	0	0	0	3	0	3
Evidence of distant metastasis	0	0	0	0	0	2	2
Total	18	6	15	0	20	2	61

SS-EPI, single-shot echo-planar imaging; RESOLVE, readout segmentation of long variable echo-trains; T_2 WI, T_2 weighted imaging;

Table 5. Comparison of RESOLVE and T_2 WI imaging evaluation in patients with cervical cancer

T_2 WI	RESOLVE						Total
	Confined to cervix	Vaginal invasion (upper 2/3)	Parametrial invasion	Vaginal invasion (lower 1/3)	Bladder or rectum invasion	Evidence of distant metastasis	
Confined to cervix	25	2	0	0	1	0	28
Vaginal invasion (upper 2/3)	3	16	0	0	0	0	19
Parametrial invasion	1	3	1	1	0	0	6
Vaginal invasion (lower 1/3)	0	1	0	2	0	0	3
Bladder or rectum invasion	0	0	1	0	2	0	3
Evidence of distant metastasis	0	0	0	0	0	2	2
Total	29	22	2	3	3	2	61

RESOLVE, readout segmentation of long variable echo-trains; T_2 WI, T_2 weighted imaging;

Table 6. Comparison of T_2 WI combined with SS-EPI and pathological staging in patients with cervical cancer

Pathological staging	T_2 WI + SS EPI staging						Total
	IB	IIA	IIB	III	IVA	IVB	
IB	19	2	6	0	3	0	30
IIA	4	9	3	0	0	0	16
IIB	0	2	4	0	1	0	7
III	0	0	0	2	1	0	3
IVA	0	0	0	0	3	0	3
IVB	0	0	0	0	0	2	2
Total	23	13	13	2	8	2	61

SS-EPI, single-shot echo-planar imaging; T_2 WI, T_2 weighted imaging; .

et al⁹ compared the AP lengths and LR widths of breast cancer between DWI and CE-MRI. Foltz et al¹⁶ measured dice coefficients and hausdorff distances on DWI and T_2 WI of pelvic tumours (cervix and prostate). All of those previous studies demonstrated the reduced distortion in RESOLVE. We find the significant difference in AP length between SS-EPI and T_2 WI, while no significant differences were found in both AP length and LR width between RESOLVE and T_2 WI. The existence of normal anatomical structures in the anterior and posterior of

the cervix, making it easier to produce artefacts and deformation in AP direction. Our results of dimensional measurements also indicated RESOLVE can reduce geometric distortions at a different level in cervical cancer lesions.

Although MRI is still not included in the revised FIGO staging system for cervical cancer staging, the acquired images can still be considered as a supplementary to clinical examination. MRI is thought to be able to assess the important cervical cancer

Table 7. Comparison of T_2 WI combined with RESOLVE and pathological staging in patients with cervical cancer

Pathological staging	T_2 WI + RESOLVE staging						Total
	IB	IIA	IIB	III	IVA	IVB	
IB	24	5	0	0	1	0	30
IIA	4	12	0	0	0	0	16
IIB	1	2	3	1	0	0	7
III	0	1	0	2	0	0	3
IVA	0	0	0	0	3	0	3
IVB	0	0	0	0	0	2	2
Total	29	20	3	3	4	2	61

RESOLVE, readout segmentation of long variable echo-trains; T_2 WI, T_2 weighted imaging;

Figure 3. SS-EPI ($b = 800 \text{ s mm}^{-2}$) (a) and RESOLVE ($b = 800 \text{ s mm}^{-2}$) (b) of a 65-year-old female with cervical cancer stage IB. SS-EPI showed deformation and artifact of the lesion (white arrow), it indicated parametrial invasion and staged as IIB. While RESOLVE showed that the lesion was localized in the cervix, and the boundaries were clear, staging as IB, as well as showed in T_2 WI (c-d). The ADC values of the lesions in SS-EPI and RESOLVE were $0.930 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ (e) and $1.014 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ (f) respectively. SS-EPI, single-shot echo-planar imaging; RESOLVE, readout segmentation of long variable echo-trains.

prognostic factors such as tumor size, parametrial and vaginal involvement, pelvic side wall and adjacent organ invasion and the evaluation of lymph node metastases.^{4,17} DWI plays an important role in the pre-operative assessment and treatment response monitoring of cervical cancer.^{18,19} Because of the poor image quality in morphological evaluation, it is more likely to be used for functional evaluation. In our study, conventional SS-EPI shows a significant inconsistency with T_2 WI in locoregional lesion assessment. It overestimates 7/6 IB/IIA patients as IIB and 4/8/2/3 IB/IIA/IIB/III patients as IVA. The unclear anatomical structures, serious artifacts and severe geometric distortion of SS-EPI make the lesions and adjacent normal organs (such as parametrial, rectum) unclear, leading to excessive staging. Furthermore, the presence of gas-containing viscera close to

cervical tissue such as rectum and vagina, which results in local field inhomogeneities that leads to severe susceptibility artefacts and geometric distortion. In addition, physiological motion such as bowel peristalsis and respiration may cause phase errors. All of these may limit the diagnostic value of DWI, especially in staging. With the improvement of image quality, RESOLVE can reduce susceptibility artefacts and geometric distortion, such that the lesions and adjacent normal anatomical structures can be clearly displayed, which results in better staging accuracy than SS-EPI combined with T_2 WI.

The ADC value plays an important role in the diagnosis and monitoring treatment response of cervical cancer,^{18,20} it also has the potential in predicting parametrial invasion.²¹ But these earlier studies were based on SS-EPI, Bogner et al⁵ found ADC value based on RESOLVE may reach a higher diagnostic accuracy for the differentiation of benign and malignant breast lesions than that from SS-EPI. Yet, Kim et al⁹ reached the different conclusion. This may be related to the differences between the lesion categories and the ROI measurements. In addition, we find that there is no significant difference in ADC value between SS-EPI and RESOLVE in our study.

There are some limitations in our study should be recognized. Firstly, it cannot be denied that RESOLVE takes longer acquisition time compared to SS-EPI in our protocol, although some methods were presented to reduce acquisition time, such as scanning protocols⁹ and new technology like simultaneous multi slice used.²² Secondly, we were more concerned with the morphological differences between the two DW images, while ADC values will be further explored in the diagnostic or post treatment aspects. Thirdly, this study was performed at a single center with limited sample size. Further multicenter studies with a larger number of patients and different tumor stages are needed to confirm our results.

As a conclusion, RESOLVE is superior to SS-EPI in accurate staging of cervical cancer because of the improvement in image quality and reduced geometric distortion. Therefore, RESOLVE is recommended for pre-operative MRI staging of cervical cancer.

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