Volume Measurement by Diffusion-Weighted Imaging in Cervical Cancer

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ABSTRACT

Background   The aim of this paper was to evaluate the validity of tumor volume measurement using diffusion-weighted (DW) imaging in cervical cancer.

Methods   In this retrospective study, 22 patients, who underwent preoperative 3.0 T MR examinations with DW imaging were evaluated. Tumor volume measurement by oblique axial (short axis to the uterine cervix) T2-weighted imaging was performed by manually outlining the tumor on the monitor. The area of tumor in each slice was multiplied by the slice profile (slice thickness plus intersection gap), and the total tumor volume was calculated by summation of these obtained volumes. Meanwhile, one experienced radiological technologist generated three-dimensional DW images of cervical cancer using a volume-rendering algorithm at a computer workstation, and tumor volume was automatically calculated in the workstation. Analysis via the intraclass correlation coefficient (ICC) and Bland-Altman plots were used to assess the validity and reliability of these methods.

Results   Between tumor volumes measured by T2-weighted imaging methods and DW imaging methods, the ICC was excellent (0.962). The 95% limits of agreement of volume measurement were –52.7 and 35.7 mL (mean difference, –8.5 mL). In regards to intra-observer variability, the ICC was excellent (0.963). The 95% limits of agreement of volume measurement were –42.2 and 47.4 mL (mean difference, 2.6 mL).

Conclusion   DW imaging can be used to measure cervical cancer volume.

Key words   Diffusion magnetic resonance imaging; magnetic resonance imaging; three-dimensional imaging; uterine cervical neoplasms; volume measurement

Magnetic resonance (MR) imaging can estimate the size and extension of primary tumors more accurately than was previously possible by clinical palpation.[1–3] Although International Federation of Gynecology and Obstetrics (FIGO) has not necessarily endorsed clinical staging of patients with cervical carcinoma based on additional information gained by MR imaging, the modality has been described as the most accurate, non-invasive imaging modality for staging of cervical carcinoma.[3–6] Moreover, tumor size and volume assessed by MR imaging significantly correlates with outcome for patients with uterine cervical cancer.[7–10]

Diffusion-weighted (DW) imaging has been widely used for the detection and characterization of focal lesions.[10–17] Several recent reports have demonstrated that direct visual assessment of DW images facilitates detection of malignant lesions because it provides excellent tissue contrast.[11, 12, 14, 18, 19] Other reports suggest that DW imaging is useful for measurement of the volume of acute cerebral infarction[20, 21] and tumors by delineating the tumor in cross-sectional images.[22, 23] Kwee et al. reported that volume-rendered DW imaging shows the three-dimensional (3D) shape of the tumor and allows for tumor volume measurement.[17] However, the measurement has not been fully evaluated. Therefore, the goal of the present study was to investigate the utility of DW imaging for volume measurement of cervical cancer.

MATERIALS AND METHODS
Patient Population

Forty-three consecutive female patients who underwent preoperative MR examinations with a 3.0 T MR system between October 2006 and November 2008 and who had pathological confirmation of cervical cancer at our institution were included in this retrospective study. Of these patients, 20 patients with stage Ia or Ib1 disease were excluded, because the tumors were not advanced cancers. One patient with a large tumor was excluded because the entire tumor could not be delineated on DW imaging.

Therefore, 22 patients (age range, 33–82 years; mean age, 53 years), who underwent preoperative MR examinations including DW imaging on a 3.0 T MR system were enrolled in the present study. The Institutional

Review Board approved this study, which did not require informed consent (#1665). FIGO stage was Ib2 in six patients, IIa in two patients, IIb in seven patients, IIIb in two patients, IVa in one patient, and IVb in four patients.

MR Technique

MR imaging was performed with a 3.0 T MR system (Signa EXCITE HD; GE Medical Systems, Milwaukee, WI) with eight-channel cardiac coils. A dielectric pad was placed on the patient's body in order to improve the image homogeneity. After acquisition of localization images, T2-weighted fast spin-echo images were obtained in parasagittal planes parallel to the longitudinal axis of the uterus and in oblique axial planes taken in a direction parallel to the short axis of the uterine cervix. T1-weighted gradient-echo images were also obtained in parasagittal planes parallel to the longitudinal axis of the uterus and in axial planes of the body. The imaging parameters of T2-weighted images were as follows: repetition time ms/echo time ms, 6500/100 for parasagittal planes and oblique axial planes (short axis to the uterine cervix). The matrix size was 512 × 384, and the section thickness was 5 mm in the parasagittal planes and 2-4 mm in the oblique axial planes. The intersection gap was 1.5 mm in the parasagittal planes and 0.2-1.5 mm in the oblique axial planes, with a 25-cm field of view (FOV).

Axial DW images were then obtained. Imaging parameters for DW imaging were as follows: TR/TE/inversion time (TI), 5000-5675/59.3/200 ms; b factors, 0 and 1000 s/mm^2; 128 × 128 matrix; 400 mm FOV; section thickness, 4 mm with no gap; SENSE reduction factor, 2; two signals acquired; acquisition time, approximately 3.5 minutes. A DW imaging sequence was used for fat suppression in a short-inversion -time inversion recovery (STIR)-echo planar imaging sequence, with free breathing during acquisition. Motion-probing gradient pulses were placed in three orthogonal planes. Isotropic DW imaging was generated using three orthogonal-axis images.

Before examination, all patients received intramuscular administration of 20 mg of butyl-scopolamine (Buscopan; Nippon Boehringer Ingelheim, Tokyo, Japan) to prevent peristalsis artifacts, except when contraindicated.
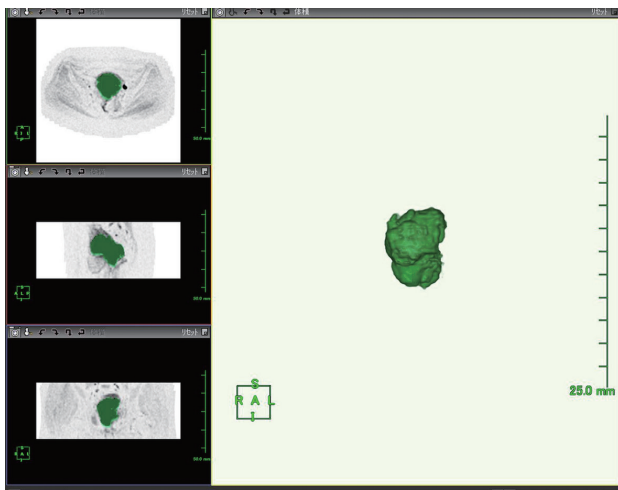
Tumor volume measurement by T2-weighted imaging

Tumor volume measurement by T2-weighted imaging was performed by one radiologist who had 12 years of experience in gynecological MR imaging. In oblique axial plane images, the tumor mass was manually outlined
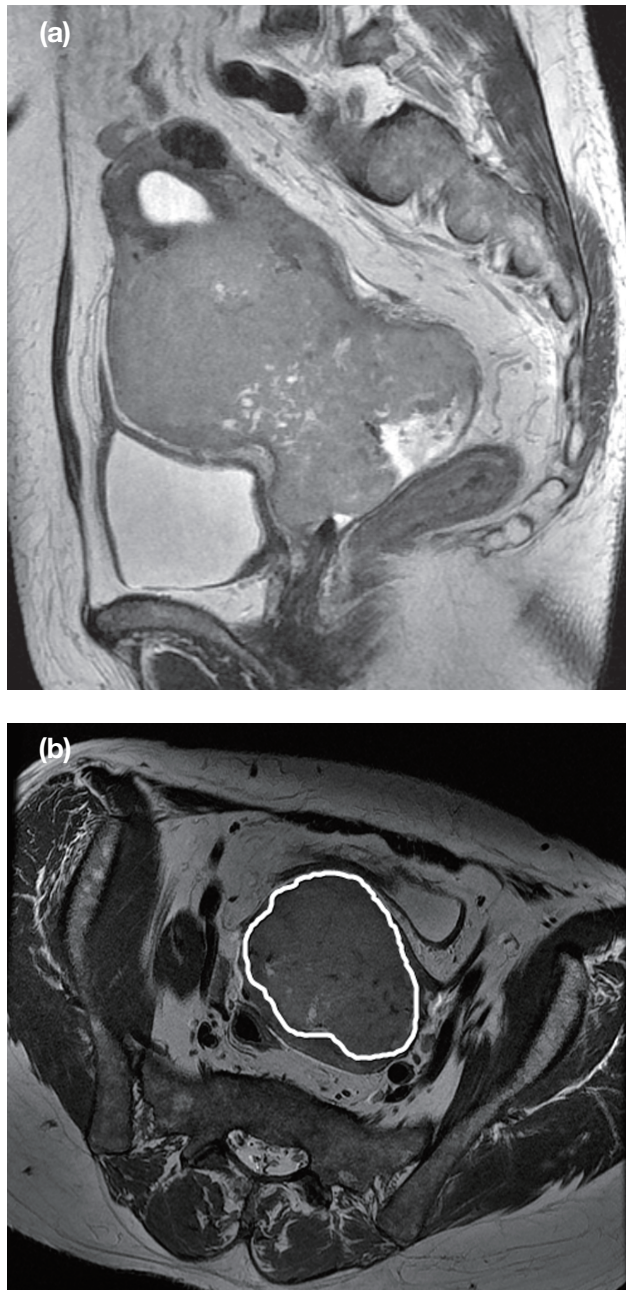
Fig. 1. MR images in a 57-year-old woman with cervical cancer. **a**) Sagittal T2-weighted image. **b**) oblique axial (short axis to the uterine cervix) T2-weighted image. T2 weighted images show the cervical tumor invading to the uterine body and vagina (**a, b**). The boundary of the tumor is drawn manually by the radiologist on each image to separate the lesion and adjacent normal structure (**b**). MR, magnetic resonance.

on the monitor (EV Insite; PSP Corporation, Tokyo, Japan) (Fig. 1). The area of tumor in each slice was multiplied by the slice profile (slice thickness plus intersection gap), and total tumor volume was calculated by summation of these obtained volumes. We used the volume obtained by T2-weighted imaging as a gold standard.

Fig. 2. The tumor is displayed as a volume rendering image with axial and the multi-planar reconstructed coronal, sagittal images on the computer workstation (the same patient as in Fig. 1).

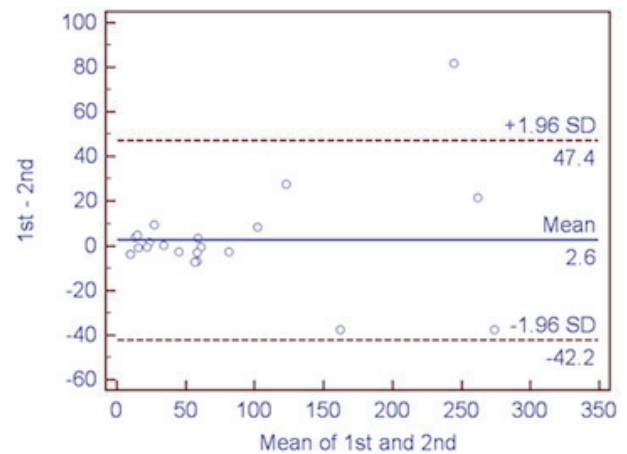## Tumor volume measurement by DW imaging

One radiological technologist who was experienced in the workstation generated 3D shaped DW images of cervical cancer using a volume-rendering (VR) algorithm at a commercially available computer workstation (AZE Virtual Place; Office Azemoto Ltd., Tokyo, Japan). Axial DW images were loaded, and the multi-planar reconstructed coronal, sagittal and VR images were displayed in an appropriate window setting. Cervical cancer was decided as uterine abnormal strong signal intensity except for normal endometrium on VR images while referring to the axial and multi-planar reconstructed coronal and sagittal images. The software automatically segmented the lesion from the surrounding adjacent structures, such as the intestine, using an object recognition algorithm. The boundary of the segmented lesion was then displayed on the monitor (Fig. 2). The technologist and radiologist visually assessed if the automated algorithm accurately segmented the lesion, excluding adjacent structures, such as the intestine, rectum and endometrium. If needed, the technologist manually adjusted the boundary of the tumor, determining the boundary between the lesion and adjacent structures by visual assessment. After segmentation and manual correction, the volume of the tumor was automatically calculated in the workstation. The time needed for volume measurement was generally a few minutes. Tumor volume measurement was repeated at more than 6 months from first analysis by the same technologist.

Statistical analysis

The intraclass correlation coefficient (ICC) was used to
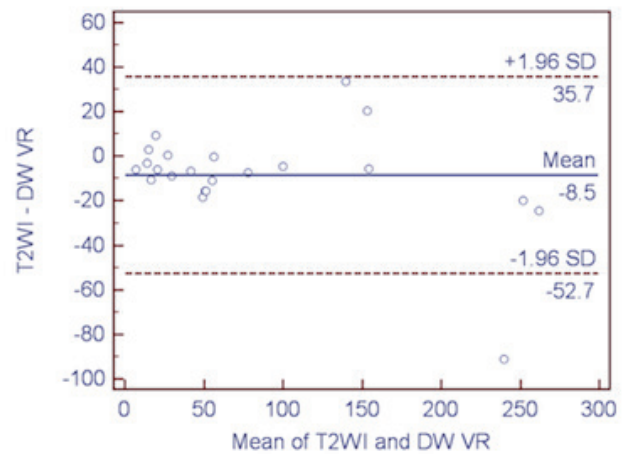
Fig. 3. Comparison of the tumor volume measurement by T2-weighted imaging and diffusion-weighted imaging. Bland-Altman plots between the tumor volume measurements by T2-weighted images versus diffusion-weighted images. The solid line in the graph represents the mean of the differences. The dotted line in the graph represents the corresponding 95% limits of agreement. Observations within 95% limits of agreement likely result from measurement error; observations outside 95% limits of agreement likely result from true differences between both methods.

Fig. 4. Intra-observer variability of the tumor volume measurement by diffusion-weighted imaging. Bland-Altman plots of the tumor volume measurement by diffusion-weighted images for two measurements by the reviewer. Bland-Altman plots show agreement between two analyses of the volume measurements by the reviewer using diffusion-weighted images. The solid line in the graph represents the mean of the differences. The dotted line in the graph represents the corresponding 95% limits of agreement. Observations within 95% limits of agreement likely result from measurement error; observations outside 95% limits of agreement likely result from true differences between both methods.

assess the agreement of measurements when evaluating the relationship between tumor volumes measured according to the T2-weighted imaging method and those measured according to the DW imaging method.

Bland-Altman plots were used to characterize the limits of agreement. Intra-observer variability was also assessed by ICC and by Bland-Altman plots.

Data were analyzed by using statistical software (MedCalc; MedCalc Software, Mariakerke, Belgium).

RESULTS

The tumor volume by T2-weighted images ranged from 3.77 to 249.75mL (mean 79.01 mL), while the volume by DW images ranged from 9.81 to 285.43 mL (mean 87.52 mL).

The ICC was excellent (0.962) when comparing tumor volumes measured by T2-weighted imaging methods and those measured by DW imaging methods. The 95% limits of agreement of volume measurement were –52.7 and 35.7 mL (mean difference, –8.5 mL) (Fig. 3).

Regarding intra-observer variability, ICC was excellent (0.963). The 95% limits of agreement of volume measurement were –42.2 and 47.4 mL (mean difference, 2.6 mL) (Fig. 4).

DISCUSSION

For imaging-based tumor volume assessment, the volumes of cervical cancer have traditionally been estimated from measurements of the three diameters of the tumor.[2, 7, 9] Specifically, the longitudinal diameter (d1), the anteroposterior diameter (d2) and the lateral diameter (d3) are measured, and the diameter-based tumor volume is then calculated from the diameters as an ellipsoid (volume = d1 × d2 × d3 × π/6). More properly, some studies have reported that the tumor volume was calculated as the 3D volume by summation of the tumor area from all slices and by multiplying by image thickness plus image gap, which was a good predictor of tumor control or survival.[24–26] Such ROI-based quantitative volume measurement is more troublesome and time-consuming than the diameter-based measurement, making its practical application in a busy clinical setting challenging. However, technological advancements have resulted in this method becoming more readily available and more user-friendly for use in general practice.[27] Some recent reports describe tumor volume measurement using a 3D workstation.[28, 29] However, the validation of volume measurement using DW imaging on a 3D workstation has not been fully investigated.

The present study demonstrated that tumor volume could be assessed using DW imaging. Several reports have demonstrated that direct visual assessment of DW images facilitates detection of malignant lesions, because DW imaging provides excellent tissue contrast.[11,12, 14, 18, 19] In gynecological imaging, DW imaging can be helpful for the detection of peritoneal dissemination and uterine endo-metrial cancer.[12, 13, 16] Cervical cancer tumors generally show strong signal intensity on DW images, reflecting a decrease in apparent diffusion coefficient (ADC) values.[30] Therefore, the success of volume assessment in the present study is due to the ability of DW imaging to provide excellent tissue contrast, thereby clearly discriminating the strong signal intensity of cervical cancers. DW imaging can obtain total volume measurements as another potential application of its imaging, as was described in a previous review article.[17]

However, the tumor volume was slightly larger when assessed by DW imaging than when assessed by T2-weighted imaging, although ICC was excellent between two volumes. This may be mainly related to partial volume effects due to the larger voxel size and decreased information about the anatomy of the surrounding structures. Additionally, the susceptibility artifact from air of the rectal cavity may affect the results. We evaluated the DW images not in a fixed window but in an appropriate setting, because signal intensity on MR imaging is not an absolute value; the window setting can influence the tumor area and thereby affect volume measurement. Therefore, methods to determine the appropriate window setting still need to be established.

Some reports have demonstrated that the ADC can be used to predict and monitor the response of uterine cervical cancer to therapy.[31, 32] The ADC value is useful for detection of pelvic lymph node metastasis in patients with cervical cancers.[33] We demonstrated that DW imaging could obtain total volume measurements of cervical cancer. Therefore, volume measurement using DW imaging may be useful for the therapeutic management of cervical cancer, because tumor volume significantly correlates with outcome in patients with uterine cervical cancer.[7–10] Thus, DW imaging may play a role in various aspects of cervical cancer, including its diagnosis, assessment of the response to therapy, and for determination of prognosis.

This study has some limitations. First, the study population was small, and further studies are required in a larger population. Second, the review was performed by one observer, because technologists who were familiar with this 3D workstation were not available in our institution; therefore, we do not show inter-observer variability data, and this subject needs to be evaluated in future studies. Third, we did not assess the time needed for volume measurement on DW imaging systematically in comparison to the time using T2-weighted imaging, although we consider that the measurement using DW imaging is probably less time consuming. Lastly, we did not assess the relationships between the volume on DW imaging and the prognosis. The evaluation would be

needed to utilize the measurement method.

In conclusion, volume measurement using DW imaging can be used to measure tumor volume in patients with cervical cancer. DW imaging may play a role in various aspects of cervical cancer, including its diagnosis, assessment of the response to therapy, and for determination of prognosis.

The authors declare no conflict of interest.

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