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ORIGINAL ARTICLE

Initial Clinical Experience with Electronic Portal Imaging Device-Based *In Vivo* Dosimetry for Radiotherapy in Gynecological Cancers

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OBJECTIVE

In this study, it was aimed to evaluate the performance and reliability of 3-dimensional (3D) *in vivo* electronic portal imaging device (EPID)-based dosimetry in radiotherapy (RT) of patients with gynecological cancer.

METHODS

The dose distributions and *in vivo* dosimetry results of patients with endometrial (n=10) and cervical (n=10) cancer who underwent external pelvic RT in our department were analyzed retrospectively. The RT planning and 3D *in vivo* dosimetry data were obtained from the treatment planning system and the iViewDose® (Elekta, Crawley, UK) *in vivo* quality assurance system. In addition, patient-specific phantom measurements were carried out for each patient with the Alderson Rando phantom. The results were evaluated with 3D gamma analysis method using iViewDose® software. We obtained γ_{mean}, $\gamma_{1\%}$, and $\gamma_{\leq 1\%}$ values for each patient with the analysis. Acceptance criteria for these parameters were taken as 0.7, 2.0, and 90%, respectively.

RESULTS

The phantom measurements showed that all treatment plans were applicable. All patients met the passing criteria for γmean, $\gamma_{1\%}$, and $\gamma_{\leq 1\%}$. The mean gamma passing rate was 95.1%±1.7 and 96.3%±2.9 for patients with endometrial and cervical cancer, respectively.

CONCLUSION

The EPID-based *in vivo* dosimetry seems to be usable in clinical routine in the treatment of gynecological cancers. However, field size is the most important limitation of *in vivo* EPID dosimetry in cases requiring extended field RT.

Keywords: Cervical cancer; dosimetry; endometrial cancer; electronic portal imaging device; external radiotherapy; gynecological cancer; *in vivo* dosimetry.

INTRODUCTION

External beam radiotherapy (EBRT) plays an important role in the treatment of gynecological cancers, particularly in endometrial and cervical cancers. With the advances in RT technology, two-dimensional (2D) EBRT has been replaced by three-dimensional conformal RT (3DCRT), followed by intensity-modulated RT (IMRT) and volumetric-modulated arc therapy (VMAT). These conformal RT techniques have provid-

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ed significant reductions in acute and late toxicity rates without affecting the treatment outcomes in patients with gynecological cancer.[1] However, the planning and delivery of RT are more complex for IMRT and VMAT compared to conventional 3DCRT techniques and are susceptible to errors. Therefore, it is recommended to perform patient-specific IMRT and VMAT quality assurance (QA) techniques to detect errors.[2]

Patient-specific QA in IMRT is often performed before treatment. In particular, errors due to variability in the patient's anatomy, tumor morphology, and the position of the organs at risk (OARs) relative to the target volume cannot be detected by pre-treatment QA.[3] Therefore, the quality of actual treatment remains unclear. *In vivo* dosimetry is a solution for ensuring the accuracy of the RT delivery. This accuracy can be tested with optically stimulated luminescence dosimetry (OSL), thermoluminescence dosimetry (TLD), film dosimetry, and electronic portal imaging device (EPID).[4-6] While OSL and TLD measure the point dose, film dosimetry has the capability to measure the 2D dose distribution. The EPID on the other hand is a digital MV imaging detector originally designed for the verification of patient positioning during treatment. Due to its dosimetric properties, it can also be utilized in patient-specific QA measurements. Recently, EPID-based systems are used as *in vivo* dosimetry systems, since they include the transit dose information.[7-9] In recent years, EPID-based 3D *in vivo* dosimetry is increasingly used in routine practice. However, data on gynecological patients are still very limited. Since the OARs as the bowel, urinary bladder, and rectum can move and change in shape and dimensions during treatment, the proximity of these OARs to the target volume increases the importance of *in vivo* dosimetry for gynecological cancers. The variations during treatment can affect the doses to the target and OARs which can result in increased toxicity and decreased local control rates.

In this study, 3D *in vivo* EPID-based *in vivo* dosimetry results were examined in patients with endometrial and cervical cancer previously treated in our clinic and a phantom study was additionally performed. The performance and reliability of EPID-based system were evaluated in 3D *in vivo* QA of gynecological patients.

MATERIALS AND METHODS

In this study, we performed a retrospective analysis of dose distribution in our patients who were treated with external pelvic RT for endometrial (n=10) or cervical (n=10) cancer. This study was approved by Institutional Review Board (Project no: GO 22/294). The RT planning and 3D *in vivo* dosimetry data were abstracted from the treatment planning system (TPS) and iViewDose® (Elekta, Crawley, UK) *in vivo* QA system.

In Vivo Measurements

The computed tomography (CT) image data of 20 patients were obtained using Toshiba Aquilion LB CT Simulator® (Toshiba Medical Systems, Otawara, Japan) with a full bladder and empty rectum. The same protocol was repeated for daily treatments as well. An Elekta Versa HD® (Elekta, Crawley, UK) teletherapy machine with 160 multileaf collimators (MLC) was used for VMAT treatment delivery with a 6 MV X-ray beam. Treatment plans were created by RayStation® v8.0 TPS (RaySearch Laboratories, Stockholm, Sweden) using a collapsed cone convolution algorithm with a grid size of 3×3×3 mm^3. The treatment plans typically consisted of two arcs. The initial and final angles were the same for all patients and were designed to rotate from 181° to 179° in clockwise and from 179° to 181° in counterclockwise. The prescription dose was 45 Gy to the whole pelvis in 25 fractions followed by a 5.4 Gy boost dose to the uterus/uterine bed in three fractions.

Daily kV cone-beam CT (CBCT) was acquired for each patient. After the positional accuracy was approved, the treatment was started. During treatment, the EPID was in the open position and the transit radiation was collected using the iViewGT® (Elekta, Crawley, UK) software. We used an EPID with amorphous silicon flat panel-type imager (Elekta iViewGT®). The sensitive area of the panel contains 1.024×1.024 pixels which can image up to a 26×26 cm^2 field size at the isocenter. The collected data were automatically transferred to the iViewDose® (Elekta, Crawley, UK) *in vivo* QA system. The iViewDose® software can reconstruct the transit dose to the CT images of the patient. In a previous paper, the mathematical aspects of the dose reconstruction algorithm were explained.[10] The iViewDose® also allows performing 3D gamma analysis between the TPS and measured dose. The gamma index (γ) is one of the most commonly used metrics for analyzing the fidelity of IMRT and VMAT plans. It quantifies the difference between measured and calculated dose distributions on a point-by-point basis in terms of both distance to agreement (DTA) and dose differences. The mathematical structure of gamma analysis was previously introduced by Low et al.,[11] in which γ was defined as in Eq.(1).

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$$\gamma(r_m)=min\{\Gamma(r_m,r_c)\}\forall\{r_c\}, \quad (1)$$

Where the pass-fail criteria are

$\gamma(r_m)\leq 1$, calculation passes,

$\gamma(r_m)>1$, calculation fails. (2)

In this study, we used 3D gamma evaluation per fraction for analysis. The mean value of the gamma distribution (γ_{mean}), the 1% of points have an equal or higher gamma value ($\gamma_{1\%}$) and the criteria of 3% dose difference/3mm DTA ($\gamma_{\leq 1\%}$) were examined to evaluate the treatment quality. The pass rate criterion was described as 0.7, 2.0, and 90%, respectively.

The dose reference point (DRP) values were used for the comparison of point dose measurement results. The software allows us to select a structure to define the DRP which is placed in the mass center of the delineated structure. For the selected structures, the algorithm of the iViewDose® software calculates the percentage dose difference between the TPS and EPID doses reconstructed on the treatment CT. The acceptance criterion was set at within 3% dose difference for the planning target volume.

Phantom Measurements

Patient-specific phantom measurements were carried out with the Alderson Rando phantom. The phantom measurement was performed to confirm that the treatment plans were deliverable. For this purpose, the plans were exported to the Alderson Rando phantom's CT. VMAT plans were re-calculated and irradiated on that phantom to perform gamma analysis verification with the passing criterion of 3% (global)/3 mm. Following, the measurement was compared with the TPS using the iViewDose® software.

RESULTS

Phantom Measurements

The gamma analysis results of the phantom measurements are given in Table 1. There was a good agreement between the EPID doses and TPS. While the mean gamma passing rate was 97.2±2 for the endometrial cancer plans, it was observed as 98.3±1.8 for the cervical cancer plans. The results showed that all treatment plans were applicable.

In Vivo Measurements

The results for *in vivo* measurements are given in Table 2. All patients met the passing criteria for γ_{mean}, $\gamma_{1\%}$, $\gamma_{\leq 1\%}$, and DRP. The mean gamma passing rate was 95.1%±1.7 and 96.3%±2.9 for patients with the endometrial and cervical cancer, respectively. While the mean dose difference at the isocenter in percentage was 1.42±0.94 for patients with endometrial cancer, it was observed 1.59±0.78 for patients with cervical cancer. The maximum dose difference for the DRP was 2.58% for endometrial and 2.55% for cervical cancer, respectively.

Table 1 Dosimetric differences for phantom data (90% passing rate was considered clinically acceptable)

Phantom number	$\gamma_{\leq 1\%}$	Phantom number	$\gamma_{\leq 1\%}$
Phantom (E-P1)	98	Phantom (C-P1)	97
Phantom (E-P2)	95	Phantom (C-P2)	100
Phantom (E-P3)	95	Phantom (C-P3)	98
Phantom (E-P4)	100	Phantom (C-P4)	95
Phantom (E-P5)	98	Phantom (C-P5)	100
Phantom (E-P6)	99	Phantom (C-P6)	100
Phantom (E-P7)	95	Phantom (C-P7)	98
Phantom (E-P8)	100	Phantom (C-P8)	96
Phantom (E-P9)	95	Phantom (C-P9)	99
Phantom (E-P10)	97	Phantom (C-P10)	100
Mean value	97.2	Mean value	98.3

γ: Gamma index; E: Endometrium; P: Patient; C: Cervical

Figure 1 displays an example of the TPS dose, EPID dose, gamma analysis results, and dose distributions along the central axis. The blue color in gamma analysis indicates that the difference between the calculated (TPS dose) and measured dose (EPID) is very small. On the contrary, the red color indicates that the region where the difference between the calculated and measured dose exceeds the acceptance criteria. The dose distribution along the central axis also shows that the difference between the calculated and measured dose is very small in and out of the field.

DISCUSSION

This article aims to show the performance of the EPID for *in vivo* dosimetry of patients with gynecological cancer. Previously, the performance of *in vivo* EPID dosimetry for various cancer types was investigated. [12-14] However, the data on patients with gynecological cancer are still scarce. We clinically implemented the 3D *in vivo* EPID-based dosimetry QA for patients treated with VMAT. In our study, the gamma analysis passing rates were in tolerance levels for all patients. We think that the most important reasons for obtaining good results are the patient position verification

Table 2 Dosimetric differences for patient data

Pts with EC	γ_{mean}±SD	$\gamma_{\%1}$±SD	$\gamma_{\leq 1}$%±SD (% difference)±SD	DRP
E-P1	0.48	1.44	94	-0.26
E-P2	0.39	1.85	96	0.5
E-P3	0.43	1.38	96	0.44
E-P4	0.6	1.65	97	1.3
E-P5	0.27	1.43	95	0.45
E-P6	0.55	1.02	98	2.58
E-P7	0.63	1.68	93	-0.25
E-P8	0.37	1.94	95	-0.24
E-P9	0.4	1.33	94	2.21
E-P10	0.62	1.24	93	-2.19
Mean value	0.474±0.12	1.496±0.28	95.1±1.7	1.42±0.94
Pts with CC				
C-P1	0.39	1.28	97	2.26
C-P2	0.36	1.34	92	-0.53
C-P3	0.28	1.38	93	0.66
C-P4	0.54	1.5	99	2.55
C-P5	0.44	1.18	98	1.68
C-P6	0.3	1.87	99	1.85
C-P7	0.39	1.78	99	2.13
C-P8	0.64	1.65	92	0.82
C-P9	0.52	1.42	96	2.49
C-P10	0.55	1.22	98	0.98
Mean value	0.441±0.11	1.462±0.23	96.3±2.9	1.595±0.78

*: The minus sign indicates that the measured dose was lower than the TPS dose. TPS: Treatment planning system; Pts: Patients; EC: Endometrial cancer; γ: Gamma index; SD: Standard deviation; DRP: Dose reference point; E: Endometrium; P: Patient; CC: Cervical cancer; C: Cervical

through CBCT and our strict bowel and rectal protocol for every patient and every fraction which allow minimizing the dosimetric differences due to anatomical and positional changes.

The mean gamma analysis passing rate for phantom measurements was 97.2% and 98.3% for the patients with endometrial and cervical cancer, respectively. On the other hand, *in vivo* patient calculation results were 95.1% and 96.3% for endometrial and cervical cancer, respectively. The decrease in the passing rate may be due to the heterogeneity of the pelvic region which may have caused computational errors in the TPS. Since the pelvic region of the phantom consists only of bone and soft-tissue-equivalent materials, errors due to the calculation algorithm may therefore be fewer in the phantom. Another reason for observing this result may be the intrafractional variation due to organ deformation and/or movement. The intrafraction variations are smaller compared with the interfraction variations but are still of relevance in clinical practice. Although, patients are given detailed instructions to empty the rectum and fill the bladder and checked through CBCT, vaginal motion, and bladder and rectal volume changes can occur during treatment. To minimize the target motion, the use of intracavitary applicators was suggested for IMRT treatment of gynecological malignancies in clinical practice.[15,16] Cilla et al.[15] reported the agreement between the calculated and measured doses for this practice, where they performed the study with an ion chamber. As a future work, testing the accuracy of this practice can be performed with EPID in 3D.

In this study, we did not encounter any machine-related or patient-related errors that may have adversely affected the results. The previous studies showed that *in vivo* EPID measurements have the potential to detect treatment delivery errors.[17-19] Mans et al.[17] reported 3D *in vivo* verification of 4337 patients that consisted of 1319 breast, 1018 prostate, 602 rectum, 543 head and neck, 454 lung, and 401 other cancer cases. Seventeen serious errors were detected among the treatment plans which were classified as patient anatomy (n=7), plan transfer (n=4), suboptimally tuned TPS parameter (n=2), accidental plan modification (n=2), failed delivery (n=1), and

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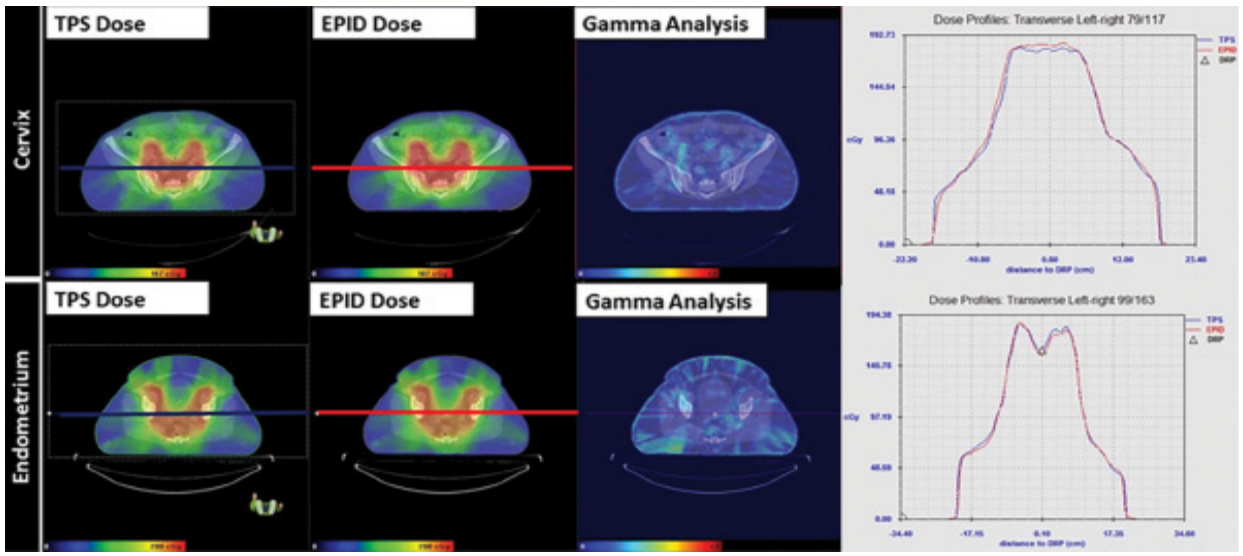

Fig. 1. Calculated dose, measured dose, gamma evaluation, and line dose comparison of calculated and measured dose on the central axis for an endometrial and a cervical cancer patient.
TPS: TPS: Treatment planning system; EPID: Electronic portal imaging device; DRP: Dose reference point.

dosimetrically undeliverable plan (n=1). Other studies were also conducted to search the possible errors that could be detected by *in vivo* EPID measurements.[18,20] Previously, we[18] investigated the error detection capability of *in vivo* EPID measurements for the stereotactic body RT applications for prostate cancer. Our results showed that the EPID can detect the errors based on linear accelerator calibration, MLC positions, and patient anatomy.

One of the limitations of *in vivo* EPID-based dosimetry is the radiation field size. Since the maximum effective field size of the EPID at the isocenter is 26×26 cm^2, the QA of the radiation fields above this size is not possible. In particular, in a patient with gynecological cancer that has para-aortic lymph node involvement and needs to be irradiated with extended field irradiation exceeds, this limitation for whom EPID-based dosimetry is not suitable. However, Kim et al.[21] designed a study using Halcyon® 2.0 (Varian Medical Systems, Palo Alto, CA, USA) machine to treat the extended fields using IMRT with dual-isocenter in patients with gynecological cancer since Halcyon® 2.0 is capable of treating >28 cm treatment length using a dual isocenter. Their results showed that Halcyon® EPID-based *in vivo* dosimetry has the potential to function for complex IMRT and adaptive RT. They detected interfraction variations in random patterns depending on internal organ motion and source to skin distance change.

The advantage of EPID-based dosimetry over other systems is that it does not need extra time for application since the QA measurements are performed during treatment. In addition, QA can be easily applied in each fraction. If we assume that a pre-treatment QA for a patient takes 10 min, we saved approximately 200 min for 20 patients in the present study. It does not only save the physicist's time but also reduces on-time of the treatment machine.

Previously, few studies reported *in vivo* measurement results by the placement of dosimeters into the body cavities for pelvic RT which has the disadvantage of patient discomfort. The TLD and diodes were the most commonly used dosimeters in these studies. However, diode detectors are not suitable for IMRT or VMAT as the diode detector response exhibits orientation dependence. Diode sensitivity is reported to vary by up to 15% depending on gantry orientation.[22] Weber et al.[23] reported the results of patients with anal cancer undergoing *in vivo* dosimetry by TLD inserted at the center of the anal verge. The measured doses differed by an average of 6% compared to the TPS along the central axis. In general, the acceptance criterion is within ±10% for the TLD.[24] For the EPID-based system, this acceptance range is narrow. In the present study, the acceptance criterion of ±3% was used for point dose measurements with the EPID and all measurements were consistent with this criterion.

CONCLUSION

The EPID-based *in vivo* dosimetry can be used in the clinical routine for gynecological cancers. The workload with this approach is minimal and it saves time. The agreement between the measured and computed doses indicates that VMAT delivery for gynecological cancers is safe in case the patient setup variations are minimized. *In vivo* point measurements showed that the measured and calculated doses were in agreement with ±3% dose differences for pelvic irradiation. The main limitation of *in vivo* EPID-based dosimetry is the radiation field size for gynecological cancers.

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