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Comparative dosimetry of brachytherapy treatment planning between a volume-based plan by CT and a point-based plan by TAUS in CT datasets for brachytherapy

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Original Article

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Abstract

Aim: To evaluate comparative dosimetry of brachytherapy treatment planning between a volume-based plan by computed tomography (CT) and a point-based plan by transabdominal ultrasound (TAUS) in CT datasets for brachytherapy.

Materials and methods: From 2019 to 2021, 59 different datasets of CT images were collected from 38 patients treated by intracavitary brachytherapy with tandem ovoid or tandem ring applicators. At that time, TAUS was performed to prevent uterine perforation and to evaluate topography of the cervix during application. In volume-based planning by CT, the target dose was used to keep the dose at 90% of high-risk clinical target volume (HR-CTV), to give a dose of at least 7Gy, while in the point-based plan by TAUS, the target dose was used to keep the minimum dose to eight cervix reference points (measured by TAUS), to give a dose of at least 7Gy. The doses to targets and organs at risk were evaluated and compared between volume-based planning by CT and the point-based plan by TAUS.

Results: Of 59 fractions, a tandem ovoid applicator was used in 48 fractions (81·3%). In the volume-based plan by CT, the mean doses to HR-CTV(D_{90}), intermediate-risk clinical target volume (IR-CTV)(D_{90}), bladder(D_{2cc}), rectum(D_{2cc}) and sigmoid colon(D_{2cc}) were 7·0, 3·9, 4·9, 2·9 and 3·3 Gy, respectively, while in the point-based plan by TAUS, the mean doses to HR-CTV(D_{90}), IR-CTV(D_{90}), bladder(D_{2cc}), rectum(D_{2cc}) and sigmoid colon(D_{2cc}) were 8·2, 4·6, 5·9, 3·4 and 3·9 Gy, respectively. The percentages of mean dose differences between TAUS and CT of HR-CTV(D_{90}), IR-CTV(D_{90}), bladder(D_{2cc}), rectum(D_{2cc}) and sigmoid colon(D_{2cc}) were 17·7, 19·5, 20·5, 19·5, 21·3 and 19·8%, respectively. With the target dose to the point-based plan by TAUS (7 Gy to the cervix reference points), this was close to D_{98} of HR-CTV with a mean percentage of difference of 0·6%.

Findings: The point-based plan by TAUS showed higher values to targets and organs at risk than the volume-based plan by CT. With the point-based plan by TAUS, it was close to D_{98} of HR-CTV.

Introduction

Cervical cancer is one of the most common female cancers worldwide.[1] In 2017, new cases of cervical cancer in Thailand were more than 8,000·[2] The treatments for cervical cancer are surgery, radiotherapy or systemic treatment. For radical radiotherapy with chemotherapy, the combination of external beam radiotherapy (45–50·4 Gy in 23–28 fractions) and brachytherapy (3–5 fractions) is the standard treatment for locally advanced disease to give a dose of at least 80 Gy in $EQD2_{10}$ to the target.[3]

Brachytherapy has been used for a long time to escalate the dose to the cervix to achieve the curative goal.[4] Nowadays, brachytherapy has been transformed from a point-based plan (2D) to a volume-based plan (3D), according to many promising publications from the GEC-ESTRO working group. In the volume-based plan, or image-guided adaptive brachytherapy (IGABT), magnetic resonance imaging (MRI) is the standard imaging technique as it provides the best soft tissue discrimination.[5,6] Many international publications have reported promising results from MRI-guided brachytherapy.[7–15]

Computed tomography (CT)-based IGABT was developed in practice because of the difficulties in using MRI for brachytherapy. Although CT showed poorer tissue discrimination than MRI, CT can support treatment in the volume-based plan as reported in many international publications.[16,17] Promising results of CT-based brachytherapy for cervical cancer have been published internationally.[18–24] Another method, point-based adaptive

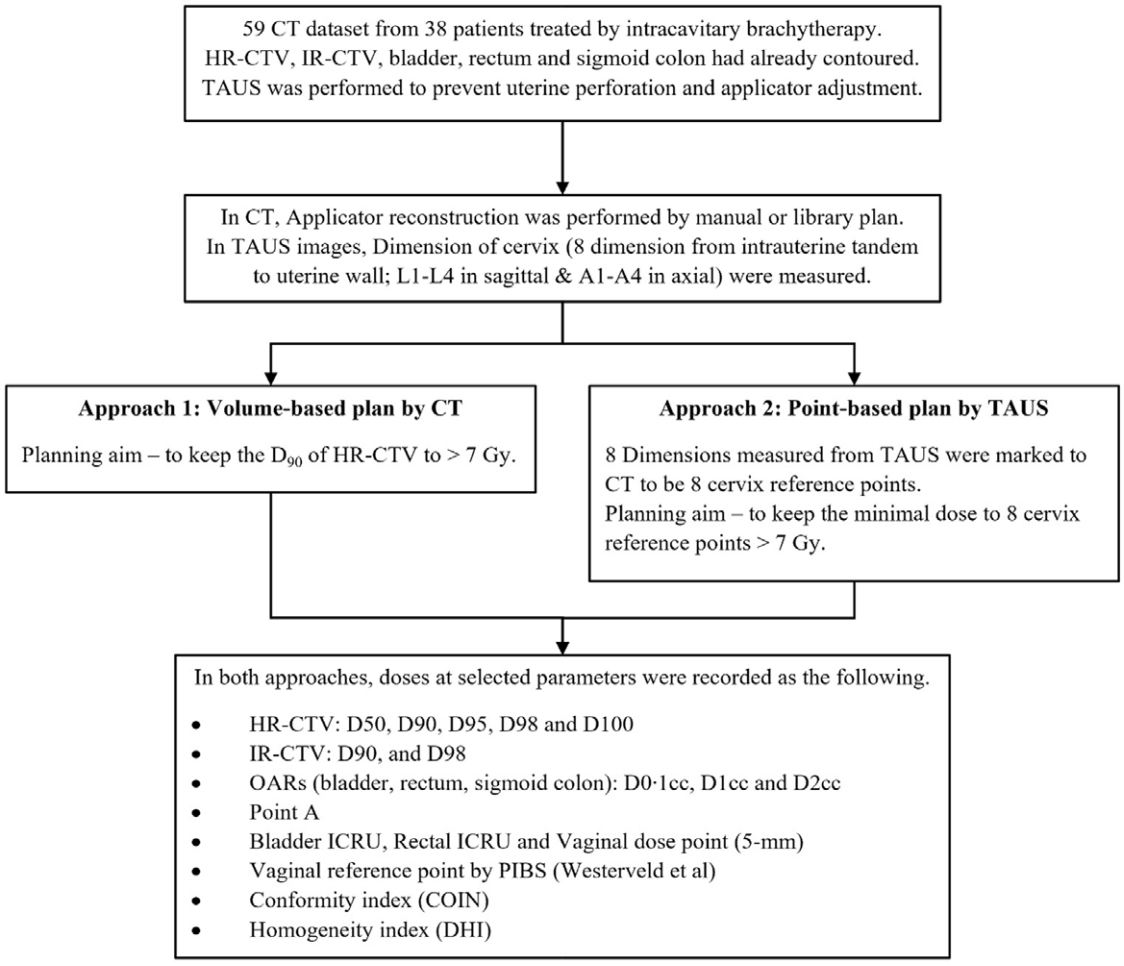

Figure 1. Study process.

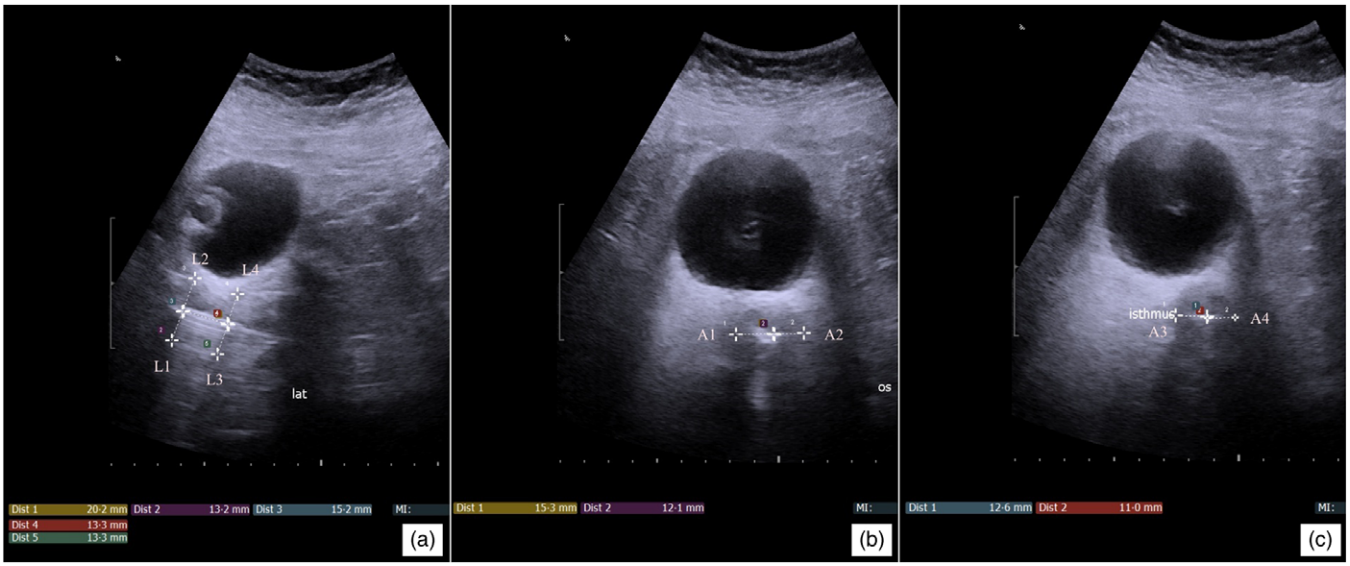

Figure 2. Measurements of eight cervix dimensions by TAUS: (a) sagittal view of TAUS, (b) axial view of TAUS at the cervical os and (c) axial view of TAUS at 2 cm cranially from the cervical os.

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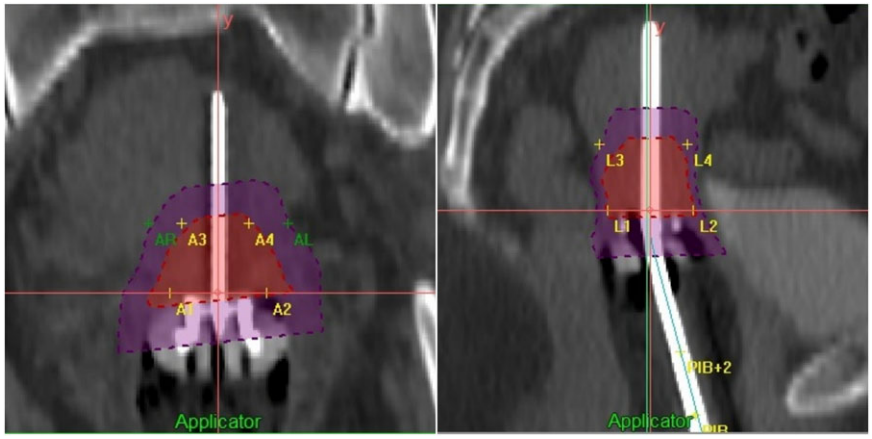

Figure 3. HR-CTV, IR-CTV and eight cervix reference points (A1-A4 & L1-L4) in the CT datasets.

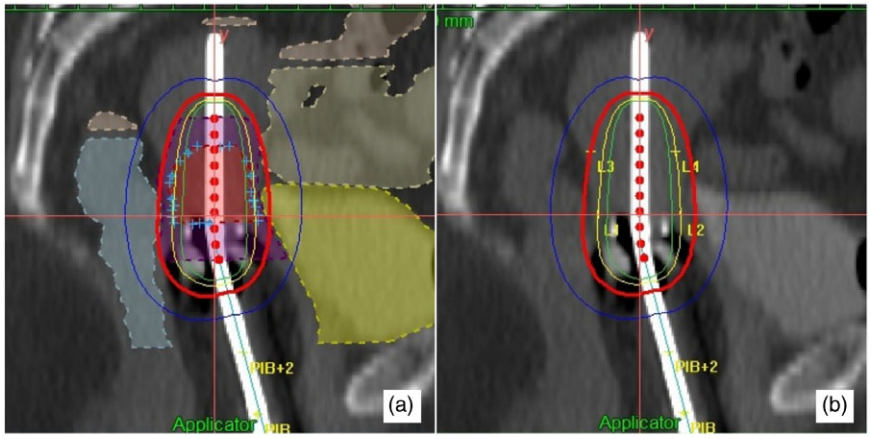

Figure 4. Isodose distributions of (a) volume-based plan by CT and (b) point-based plan by TAUS.

planning by transabdominal ultrasound (TAUS), was developed for use in brachytherapy. A few studies have reported the use of a TAUS-based plan and have shown a clinical benefit.[21,25–31]

At our Institute, transformation from 2D (point) to 3D (volume) began in 2008 with CT-based brachytherapy. Unfortunately, the total transformation could not be performed immediately due to our workloads and equipment. In 2011, ultrasound for brachytherapy was installed at our Institute. In 2012, a project to improve the quality of 2D planning using TAUS-guided brachytherapy as 2·5D planning was initiated. From these projects, intermediate-term results were reported in 2013 and 2018, respectively.[21,31] The total transformation to a volume-based approach (CT-based plan) succeeded in 2019 when a 4-slice CT instrument was installed in our brachytherapy unit. After that point, our clinical practice changed to volume-based treatment by CT, and TAUS was utilised to prevent uterine perforation and to support the CT-based contouring. However, dose evaluation or correlation between these two approaches was not performed.

With this in mind, we performed the present study to evaluate comparative dosimetry of brachytherapy treatment planning between a volume-based plan by CT, and a point-based plan by TAUS, in CT datasets for brachytherapy.

Materials and Methods

This study was a case–control study approved by the Institutional Review Board of the Faculty of Medicine, Chiang Mai University, with the code RAD-2563–07479.

CT datasets

From January 2019 to January 2021, 59 CT image datasets with 3 mm slice thickness (Alexion, Toshiba Medical Systems, Tochigi, Japan) were collected from 38 patients with locally advanced cervical cancer treated by intracavitary CT-based brachytherapy. High-risk clinical target volume (HR-CTV), intermediate-risk clinical target volume (IR-CTV) and OARs were contoured by experienced radiation oncologists during treatment according to GEC-ESTRO recommendations and the work of Viswanathan et al.[5,6,32] All fractions were treated by CT-based brachytherapy (volume-based approach) to give a dose of at least 7 Gy to D_{90} of HR-CTV. In these fractions, TAUS (Flex Focus 400, BK medical, Harlev, Denmark) was performed by a radiation oncologist to prevent uterine perforation during applicator placement.

Study methods

To perform this study, all CT datasets and structures were imported into Oncentra Master Plan version 4.5.3 (Elekta Brachytherapy, Veenendaal, the Netherlands). Applicator reconstruction was performed by manual reconstruction or library-based registration according to the applicator type. Two planning approaches were performed, and sources were applied with the same dwell positions in both approaches. The dwell times in each dwell position were optimised as the planning aim of each approach.

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Approach 1: volume approach

In the volume-based plan by CT, the target of the treatment was HR-CTV, and planning aims were performed to keep the dose at 90% of HR-CTV to give a dose of at least 7 Gy.

Approach 2: point approach

In the point-based plan by TAUS, eight measurements of cervix dimensions (from intrauterine tandem to uterine wall) were performed at the level of the cervical os, and 2 cm cranially to the cervical os, based on previous work by van Dyk et al. and Tharavichitkul et al.[25,28] Eight cervix reference points were generated from cervix dimensions in sagittal and axial views. Planning aims were performed to keep the minimum dose to the cervix reference points to give a dose of at least 7 Gy.

In both approaches, doses at selected parameters were recorded as follows.[4]

- HR-CTV: D_{50}, D_{90}, D_{95}, D_{98} and D_{100}
- IR-CTV: D_{90} and D_{98}
- OARs (bladder, rectum, sigmoid colon): $D_{0.1cc}$, D_{1cc} and D_{2cc}
- Point A
- Bladder ICRU, Rectal ICRU and Vaginal dose point (5 mm)
- Vaginal reference point by PIBS (Westerveld et al.)[33]
- Conformity index (COIN)[34]

$$\text{COIN} = \frac{V_{ref,TV}}{TV} \times \frac{V_{ref,TV}}{V_{ref}}$$

- Homogeneity index (DHI)[34]

$$\text{DHI} = \frac{(TVD_{ref} - TV1.5D_{ref})}{TVD_{ref}}$$

Images of the entire study process, measurements of eight cervix dimensions by TAUS, targets (HR-CTV & eight cervix reference points) and isodose distributions of both approaches are shown in Figures 1–4.

Statistical analysis

All dose parameters were compared for the volume-based plan by CT and the point-based plan by TAUS. A Wilcoxon sign-ranked test was used to evaluate the comparison.

Percentage dose difference was evaluated from the dose difference to the targets or OARs in the volume-based plan by CT versus the point-based plan by TAUS. Percentage of relative dose difference was evaluated as the difference of the goal dose to the cervix reference points (at least 7 Gy) by TAUS to the dose to HR-CTV (contoured by CT) in terms of D_{50}, D_{90}, D_{95}, D_{98} and D_{100}. (Figure 5) IBM SPSS version 22 (IBM SPSS, Chicago, IL, USA) was used to evaluate the results.

Results

Of 59 fractions, a tandem ovoid applicator was used in 48 fractions. The mean volume of HR-CTV was 15·8 cc. Table 1 shows the characteristics of the studied datasets.

In the targets, generally, the point-based plan by TAUS yielded a significantly higher dose to D_{90} of HR-CTV, D_{90} of IR-CTV,

Table 1. Characteristics data

Parameters	*n*
Number of fractions	59
Applicators:	
- Tandem + ovoid	48
- Tandem + ring	11
Volumes of contouring (Mean ± SD)	
- HR-CTV	15·8 ± 5·6 cc
- IR-CTV	55·7 ± 14·8 cc
- Bladder	192·4 ± 58·4 cc
- Rectum	32·7 ± 17·8 cc
- Sigmoid	75·4 ± 40·6 cc

Note: HR-CTV = high-risk clinical target volume, IR-CTV = intermediate-risk clinical target volume.

$$\%\text{Dose difference} = \frac{(\text{Dose of Point-based by TAUS}) - (\text{Dose of Volume-based by CT})}{(\text{Dose of Volume-based by CT})}$$

$$\%\text{Relative dose difference} = \frac{(\text{Dose of HR-CTV of Point-based by TAUS}) - 7\ \text{Gy}}{7\ \text{Gy}}$$

Figure 5. Percentage dose difference and relative dose difference formulae.

point A, TRAK, DHI and COIN. The percentage of dose difference between the point-based plan by TAUS and the volume-based plan by CT ranged from 17·0 to 21·2% (see Table 2). Interestingly, when we further evaluated the percentage of relative dose difference between the planning aim of the point-based plan by TAUS (at least 7 Gy at cervix reference points) to volume parameters of HR-CTV (from D_{50} to D_{100}), the TAUS-based planning aim was close to D_{98} of HR-CTV with a mean of 0·6%. Tables 2 and 3 show the dose parameters, % of dose difference and % of relative dose difference, for the volume-based plan by CT and the point-based plan by TAUS relative to target dose. In normal tissues, the point-based plan by TAUS yielded a significantly higher dose to the bladder, rectum, sigmoid, ICRU points and vaginal points. The percentage of dose difference between the point-based plan by TAUS and the volume-based plan by CT ranged from 17·7 to 24·2% (see Table 4). Table 4 shows the dose parameters and % of dose difference for the volume-based plan by CT and the point-based plan by TAUS in OARs.

Discussion

In clinical practice, although the trend in brachytherapy has moved to volume-based planning, some centres still perform point-based planning. Here, TAUS supports reduction of overdose in the bladder and rectal points in comparison to the conventional prescription.[21,28] Our results showed that the point-based prescription to the cervix reference points by TAUS caused a higher dose in comparison to the volume-based prescription to D90 of HR-CTV. Moreover, when we explored the 7 Gy prescription to the cervix reference points, we found the dose to be nearly 7 Gy, close to D98 of HR-CTV. This may support the finding that when we treat

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Table 2. Doses to target for volume-based plan by CT and point-based plan by TAUS plans

Parameters		Volume-based plan by CT (Mean ± SD)	Point-based plan by TAUS (Mean ± SD)	*p*-value	Percentage of dose difference (Mean ± SD)
HR-CTV	D_{100}	5·0 ± 0·3 Gy	6·0 ± 1·1 Gy	$p < 0·001$*	19·0 ± 18·9 %
	D_{98}	5·9 ± 0·2 Gy	7·0 ± 1·2 Gy	$p < 0·001$*	18·3 ± 18·2 %
	D_{95}	6·4 ± 0·1 Gy	7·6 ± 1·2 Gy	$p < 0·001$*	18·0 ± 17·8 %
	D_{90}	7·0 ± 0·0 Gy	8·2 ± 1·2 Gy	$p < 0·001$*	17·7 ± 17·6 %
	D_{50}	11·2 ± 0·6 Gy	13·1 ± 1·9 Gy	$p < 0·001$*	17·0 ± 16·9 %
IR-CTV	D_{98}	3·1 ± 0·2 Gy	3·8 ± 0·7 Gy	$p < 0·001$*	20·9 ± 20·0 %
	D_{90}	3·9 ± 0·3 Gy	4·6 ± 0·8 Gy	$p < 0·001$*	19·5 ± 20·3 %
Point A		4·0 ± 0·8 Gy	4·7 ± 1·1 Gy	$p < 0·001$*	18·5 ± 18·6 %
TRAK		0·24 ± 0·05 cGy	0·29 ± 0·07 cGy	$p < 0·001$*	21·2 ± 20·8 %
DHI		0·39 ± 0·06	0·29 ± 0·10	$p < 0·001$*	–
COIN		0·36 ± 0·06	0·32 ± 0·06	$p < 0·001$*	

Note: COIN = conformity index, CT = computed Tomography, D_{100} = the minimum dose covering 100% of volume, D^{98} = the minimum dose covering 98% of volume, D^{95} = the minimum dose covering 95% of volume, D_{90} = the minimum dose covering 90% of volume, D_{50} = the minimum dose covering 50% of volume, DHI = dose homogeneity index, HR-CTV = high-risk clinical target volume, IR-CTV = intermediate-risk clinical target volume, TAUS = transabdominal ultrasound, TRAK = total reference air kerma, SD = standard deviation.
*Significant difference.

Table 3. Percentage relative dose difference of HR-CTV in point-based plan by TAUS plan

Parameter		Percentage of relative dose difference (Mean ± SD)
HR-CTV	D_{100}	-14·2 ± 15·3 %
	D_{98}	0·6 ± 16·5 %
	D_{95}	8·4 ± 18·8 %
	D_{90}	17·8 ± 17·6 %
	D_{50}	86·7 ± 26·7 %

Note: D_{100} = the minimum dose covering 100% of volume, D_{98} = the minimum dose covering 98% of volume, D_{95} = the minimum dose covering 95% of volume, D_{90} = the minimum dose covering 90% of volume, D_{50} = the minimum dose covering 50% of volume, HR-CTV = high-risk clinical target volume, SD = standard deviation.

by cervix reference points measured by TAUS, the cumulative dose from EBRT plus brachytherapy should focus to at least 75 Gy in $EQD2_{10}$ (the planning aim of D98 of HR-CTV published in the EMBRACE II protocol).[35] For example, if we treated EBRT 46 Gy in 23 fractions, the BT dose by ≥ 29 Gy in $EQD2_{10}$ (such as 21 Gy in 3 fractions or 24 Gy in 4 fractions) will be prescribed to the cervix reference points to get the cumulative dose by at least 75 Gy in $EQD2_{10}$.

This study has some limitations. First, as mentioned above, the cumulative dose of EBRT and BT doses were not evaluated. Second, this study is a case–control study in which we performed two planned approaches on CT datasets of previous treatment. Third, only a single fraction was evaluated. Fourth, these findings were obtained using intracavitary brachytherapy only. Finally, MRI was not performed in these patients. Although there were some limitations, the results of our study revealed that the doses to targets and OARs when we prescribed 7 Gy to the cervix reference points by TAUS were higher than the volume-based prescription to D90 of HR-CTV with an average 20% difference. When we evaluated the correlation of planning aims of 7 Gy to the cervix reference points to the volume of HR-CTV, it showed close correlation to D98 of HR-CTV with a mean percentage of difference of 0·6%.

Based on the literature, three types of dose comparison studies were performed. First, comparative studies performed to compare between point A and image-guided treatment in the same type of image showed that the image-guided plan improved the dose to targets or reduced overdosage to normal tissues (in comparison to the point A plan).[28,36–39] Second, comparative studies were performed to compare MRI- versus CT-based contouring. All studies showed that CT-based contouring gave an overestimation and a higher dose to normal tissues in comparison to MRI contouring.[40,41] Third, comparative studies were performed to compare MRI- versus TAUS-based planning. A report by van Dyk et al. has shown the methods to be comparable.[26] Table 5 shows selected studies of dose comparisons. Our study is categorised in the first type, but this is modified to compare between cervix reference points versus D90 of HR-CTV in CT images. Ultrasound showed correlation to MRI in dimensional evaluation of the cervix for brachytherapy. The comparison studies mostly compared measurements between TAUS and MRI and showed similar results in measurement.[25,42] Moreover, the use of transrectal ultrasound (TRUS)-guided CT contouring showed correlation to MRI in HR-CTV evaluation.[43,44]

Nowadays, improving treatment quality in brachytherapy for cervical cancer depends on equipment, manpower and workload. At our Institute, we have CT and TAUS for brachytherapy. The use of TAUS-guided planning or CT contouring supported by US (TAUS or TRUS) will be the future approach to improve IGBT for cervical cancer at our institute.

Conclusions

In conclusion, this study has shown that the point-based plan by TAUS yielded a higher dose to targets and OARS in all parameters,

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Table 4. Doses to organs at risk for volume-based plan by CT and point-based plan by TAUS plans.

Parameters		Volume-based plan by CT (Mean ± SD)	Point-based plan by TAUS (Mean ± SD)	*p*-value	Percentage of dose difference (Mean ± SD)
Bladder	$D_{0.1cc}$	7·0 ± 1·5 Gy	8·2 ± 1·9 Gy	$p < 0.001$*	17·7 ± 17·1 %
	D_{1cc}	5·6 ± 1·1 Gy	6·9 ± 1·4 Gy	$p < 0.001$*	19·4 ± 17·8 %
	D_{2cc}	4·9 ± 0·9 Gy	5·9 ± 1·6 Gy	$p < 0.001$*	20·5 ± 22·3 %
Rectum	$D_{0.1cc}$	4·3 ± 1·3 Gy	5·0 ± 1·5 Gy	$p < 0.001$*	20·2 ± 23·8 %
	D_{1cc}	3·3 ± 1·0 Gy	3·9 ± 1·1 Gy	$p < 0.001$*	21·2 ± 23·8 %
	D_{2cc}	2·9 ± 0·9 Gy	3·4 ± 1·0 Gy	$p < 0.001$*	21·3 ± 23·7 %
Sigmoid	$D_{0.1cc}$	4·7 ± 1·2 Gy	5·6 ± 1·7 Gy	$p < 0.001$*	19·2 ± 18·7 %
	D_{1cc}	3·7 ± 0·9 Gy	4·4 ± 1·3 Gy	$p < 0.001$*	19·6 ± 18·8 %
	D_{2cc}	3·3 ± 0·8 Gy	3·9 ± 1·2 Gy	$p < 0.001$*	19·8 ± 18·8 %
ICRU	Bladder point	3·1 ± 1·5 Gy	3·7 ± 1·8 Gy	$p < 0.001$*	21·4 ± 20·4 %
	Rectal point	4·4 ± 1·1 Gy	5·2 ± 1·3 Gy	$p < 0.001$*	21·1 ± 23·6 %
Vaginal point	Right	4·3 ± 1·5 Gy	5·3 ± 1·9 Gy	$p < 0.001$*	24·2 ± 25·5 %
	Left	4·2 ± 1·2 Gy	5·1 ± 1·6 Gy	$p < 0.001$*	23·2 ± 24·6 %
Mid & lower vaginal point	PIBS	0·9 ± 0·5 Gy	1·1 ± 0·6 Gy	$p < 0.001$*	22·4 ± 23·2 %
	PIBS − 2 cm	0·4 ± 0·2 Gy	0·5 ± 2·0 Gy	$p < 0.001$*	21·9 ± 22·4 %
	PIBS + 2 cm	6·9 ± 19·8 Gy	9·5 ± 30·9 Gy	$p < 0.001$*	24·2 ± 26·8 %

Note: CT = computed tomography, $D_{0.1cc}$ = dose at 0.1 cc of volume, D_{1cc} = dose at 1 cc of volume, D_{2cc} = dose at 2 cc of volume, ICRU = The International Commission on Radiation Units and Measurements, PIBS = Posterior-Inferior Border of Symphysis, TAUS = transabdominal ultrasound, SD = standard deviation.
*Significant difference.

Table 5. Selected studies of dose comparison.

Studies	N	Comparison	Image	Results
Van Dyk S, et al[26]	71	2D MRI plan versus TAUS plan	MRI and TAUS	TAUS plan assessed on two-dimensional MRI image was comparable for target volume (p = 0·11), rectal point (p = 0·8), and vaginal mucosa (p = 0·19).
Tharavichitkul E, et al.[28]	25	Standard plan* versus TAUS-guided planning	X-ray	TAUS-guided planning reduced bladder (defined as > 80 Gy in $EQD2_3$) and rectal overdose (defined as > 75 Gy in $EQD2_3$) in 44·9% and 34·5% of patients, respectively.
De brabandere M, et al.[36]	16	Standard plan* versus optimised plan	MRI	After optimisation, the average D_{2cc} dose reduction was 7 Gy in the bladder and 7 Gy in sigmoid colon
Lindegaard J C, et al.[37]	21	Standard plan* versus three-dimensional optimisation	MRI	Optimisation increased the minimum target dose of HR-CTV and decreased D_{2cc} for the sigmoid, significantly
Zwahlen D, et al.[38]	20	Standard plan* versus MRI-based plan	MRI	Optimisation caused reduction of minimum dose to the D_{2cc} of the rectum, sigmoid and bladder with 12 - 32% less than with conventional BT planning
Tharavichitkul E, et al.[39]	17	Standard plan versus optimised plan by CT	CT	Optimised plan by CT reduced dose to D_{2cc} of bladder and sigmoid colon
Viswanathan AN, et al.[40]	10	MRI plan versus CT plan	MRI and CT	CT tumour contours can significantly overestimate the tumour width, resulting in significant differences in the D (90), D (100), and volume treated to the prescription dose or greater for the HR-CTV compared with that using MRI.
Eskander RN, et al.[41]	11	MRI plan versus CT plan	MRI and CT	MRI showed a significantly greater HR-CTV length in the sagittal plane (P = 0·006), with CT showing a greater length in the coronal plane (P = 0·004). The EQD2 bladder was greater on CT than MRI (P = 0·041).
Our study	59 fractions from 39 pts	Cervix reference point versus D90 of HR-CTV	CT	Prescription to cervix reference points (measured by TAUS) was higher than prescription to D90 of HR-CTV in all parameters. The prescription to cervix reference points was close to D98 of HR-CTV

Note: BT = brachytherapy, CT = computed tomography, D_{2cc} = dose at 2 cc of volume, EQD2 = equivalent dose of 2 Gy, HR-CTV = high-risk clinical target volume, MRI = magnetic resonance imaging, OARs = organs at risk, TAUS = transabdominal ultrasound.
*Standard plan means prescription to point A.

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with a mean percentage of difference of approximately 20%. In the additional analysis of percentage of relative dose difference, the dose of 7 Gy to the cervix reference points was close to D98 of HR-CTV (with a mean percentage of difference of 0·6%).

Conflicts of Interest. None.

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