

# Assessment of the anatomical position of point B and the relationship between point B dose and the dose delivered to pelvic lymph nodes in CT-based high-dose-rate brachytherapy for uterine cervical cancer

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## Abstract

**Purpose:** To examine the anatomical position of point B and the relationship between the dose at point B and the dose delivered to the pelvic lymph nodes in computed tomography (CT)-based brachytherapy for cervical cancer.

**Material and methods:** Forty-nine cervical cancer patients were treated at Kyushu University Hospital. For all cases, planning CT images obtained after the applicator insertion were imported to an Oncentra Brachy (Elekta AB, Stockholm, Sweden), and points A (dose prescription, 6 Gy) and points B were set according to the Manchester method. The pelvic lymph node regions (external iliac, internal iliac, and obturator) were contoured, and the anatomic positions of 98 points B in 49 patients were examined. Dose volume histogram (DVH) parameters ( $D_{100}$ ,  $D_{90}$ ,  $D_{50}$ ,  $D_{2cc}$ ,  $D_{1cc}$ , and  $D_{0.1cc}$ ) were calculated for each lymph node region and compared with the point B dose.

**Results:** The mean bilateral dose to point B was  $1.70 \pm 0.18$  Gy, and 26 (27%) of 98 points B were not located in any pelvic lymph node regions. The DVH analysis indicated a low degree of correlation overall, and all values were significantly different from point B doses ( $p < 0.05$ ), except for  $D_{0.1cc}$  of the external iliac node ( $p = 0.0594$ ) and  $D_{1cc}$  of the internal iliac node ( $p = 0.0711$ ).

**Conclusions:** We investigated the anatomical location of point B in patients with cervical cancer who underwent brachytherapy, and the DVH analysis revealed that the point B dose was a poor surrogate for the dose delivered to the pelvic lymph nodes.

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**Key words:** cervical cancer, brachytherapy, pelvis, lymph nodes, CT.

## Purpose

Radiation therapy that is delivered by combining external beam radiotherapy (EBRT) and brachytherapy is a curative treatment option for uterine cervical cancer and is the standard therapy for a locally advanced disease [1,2,3,4,5,6,7,8,9]. Radiation therapy with a high-dose-rate (HDR) remote afterloading system for intracavitary brachytherapy is the standard treatment for uterine cervical cancer in Japan [10].

Two orthogonal X-ray images were used for conventional brachytherapy planning based on the Manchester

method. The dose was prescribed to point A, which was defined as 2 cm lateral to the central uterine canal and 2 cm from the mucous membrane of the lateral fornix in the axis of the uterus. On the other hand, point B, which was designated as 5 cm from the midline at the level of point A, represented the dose delivered to the pelvic lymph node, and was routinely recorded to calculate the integral dose to the pelvic sidewall delivered by EBRT and brachytherapy [11]. However, with the advent of three-dimensional (3D) image-guided brachytherapy (IGBT), the evaluation of dose distributions to assess the target coverage and to spare normal tissue has become

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possible [12,13]. Structures of interest can be more accurately evaluated with the dose volume histogram (DVH). The gynecologic GEC-ESTRO (Groupe Europeen de Curiotherapie and the European Society for Radiotherapy and Oncology) Working Group has published guidelines on 3D image-based treatment planning for cervical cancer brachytherapy [12,13]. A previous study showed that while using IGBT, the clinical outcome presented an increase in local control and an approximately 20% decrease in toxicity compared with the 2D brachytherapy technique [14]. Derks *et al.* indicated that the 3D IGBT showed a trend for improved local control and overall survival compared to the 2D technique, and resulted in a decrease in observed toxicity from 17% (2D) to 12% (3D IGBT) [15]. Paul *et al.* reported a relative improvement in organs at risk (OAR) doses per HDR brachytherapy fraction by the volume-based HDR brachytherapy plan compared to the point A-based HDR brachytherapy plan, and described dosimetric advantages of using a volume-based HDR brachytherapy plan to create more conformal plans [16]. Moreover, Lee *et al.* examined the relationship between the point B dose and the dose delivered to the pelvic nodal chains, and indicated that the point B dose was a poor surrogate for the dose to specific nodal groups [11]. The relationship between the point B dose and the dose delivered to the pelvic lymph node region has been reported in several studies [11,17], but these studies did not analyze the anatomical position of point B on a 3D view. In this study, we investigated the anatomical position of point B and the relationship between the point B dose and the dose delivered to the pelvic lymph nodes in computed tomography (CT)-based HDR brachytherapy for cervical cancer.

## Material and methods

From February 2013 to January 2016, forty-nine patients with the International Federation of Gynecology and Obstetrics (FIGO) stage IB-IVB cervical cancer were treated at the Kyushu University Hospital. A tandem and ovoid applicator was used in 39 cases and a cylinder applicator was used in 10 cases. For all cases, CT images were obtained after applicator insertion for planning on a Plato treatment planning system (Elekta AB, Stockholm, Sweden). In our institutes, CT images were routinely obtained only after the initial applicator insertion to assess applicator position and dose distribution of the conventional 2D plan, before IGBT was introduced. This planning study is a retrospective analysis of the patient data when the conventional 2D plan was implemented. Therefore, we used the initial planning CT image per patient, not per fraction.

The initial planning CT images were imported to the treatment planning system Oncentra Brachy (Elekta AB, Stockholm, Sweden), and we reperformed the treatment planning again based on the Manchester method. A dose of 6 Gy was prescribed to point A with a standard dwell weight pattern [18], and point B was set according to the Manchester method.

The pelvic lymph node regions (the external iliac, internal iliac, and obturator) were contoured as in the pre-

vious reports [11,19] by a radiation oncologist on the basis of CT images, using the pre-treatment MRI as a reference if necessary. The external iliac was contoured including the external iliac artery and vein, and a 7-mm vessel margin was set to encompass the medial, lateral, anterior, and posterior subgroups of the external iliac chain. This contour extended from the bottom of the sacroiliac joint superiorly to the top of the acetabulum inferiorly, along the iliopsoas muscle to include the lateral external iliac nodes and exclude the bones and muscles. The internal iliac node group included the internal iliac artery and vein. The contour began superiorly at the level of the sacroiliac joint and extended the roof of the acetabulum along the pelvic sidewall, like the external iliac chain. The obturator nodal contour extended from the fovea of the femoral head to the top of the acetabulum along the pelvic sidewall to exclude the muscle and OAR.

First, we examined where point B was located among the following five volumes: the obturator node region, external iliac node region, internal iliac node region, inside of the pelvis, and outside of the pelvis. The inside of the pelvis was defined as an area in the pelvic cavity excluding the lymph node regions, and the outside of the pelvis was defined as the area of the pelvic bone and the region external to that. The DVH parameters were calculated for each pelvic lymph node group (left, right, and bilateral), and represented the doses received by 100%, 90%, and 50% of the volume ( $D_{100}$ ,  $D_{90}$ ,  $D_{50}$ ) and the doses received by 2 cc, 1 cc, and 0.1 cc of tissue ( $D_{2cc}$ ,  $D_{1cc}$ ,  $D_{0.1cc}$ ), respectively. The dose administered to point B was compared with the DVH parameters for each pelvic lymph node group. An  $^{192}\text{Ir}$  source was used for the calculations in the treatment planning system. Additionally, DVH parameters for each lymph node region and point B dose were compared by applicator type (tandem and ovoid in 39 cases, tandem and cylinder in 10 cases).

For statistical analysis, JMP Pro13 software (SAS Institute Inc., Cary, NC, USA) was used, and the point B dose was compared with the DVH parameters for each lymph node group using a two-sided paired *t*-test. In order to examine the relationship between the point B dose and the DVH parameters, Pearson's correlation coefficients (CCs) were used. The comparison of DVH parameters and point B dose by applicator type was performed using a *t*-test. Statistical significance was accepted with a *p* value < 0.05.

## Results

The patient and tumor characteristics are shown in Table 1. The median patient age was 62 years (range, 32-92 years) and of the 49 patients, 3 had FIGO stage IB, 3 had IIA, 17 had IIB, 2 had IIIA, 18 had IIIB, 2 had IVA, and 4 had IVB. The results for the anatomical position of point B are summarized in Table 2 and Figure 1. Seventy-two (73%) of 98 points B (2 points per patient) were located in the pelvic lymph node regions. Fifty-two percent of bilateral points B were in the obturator node region, and 21% were in the internal iliac node region. Twenty percent and 6% of points B were inside and outside of the pelvis, respectively. No point was located in the external iliac

**Table 1.** Patient and tumor characteristics

	Patients (n = 49)
Age (years)	
Median	62
Range	32-92
FIGO stage	
IB	3
IIA	3
IIB	17
IIIA	2
IIIB	18
IVA	2
IVB	4

FIGO – International Federation of Gynecology and Obstetrics

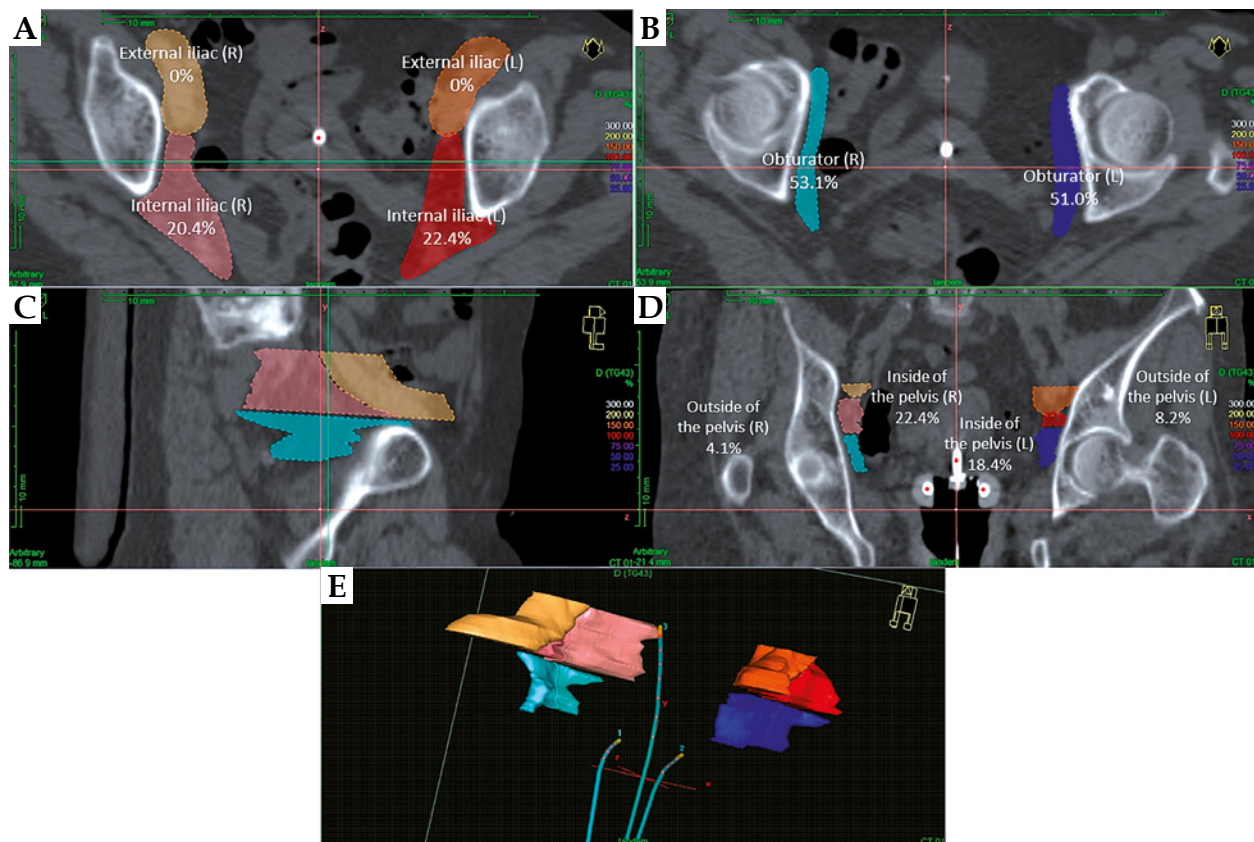
chain in this study (49 patients). Figures 2 and 3 shows the pelvic lymph node volumes and the point B in relation to the dose distribution in a typical patient, where the point B is located in the pelvic lymph node region and in a typical patient, where the point B is not located in the pelvic lymph node region, respectively.

For 49 applications, the mean bilateral dose to point B was 1.70 ±0.18 Gy (right dose, 1.64 ±0.34 Gy; left dose,

**Table 2.** The anatomical location of point B for 49 cervical cancer patients

	Point B (right)	Point B (left)
Obturator node region	53.1% (26/49)	51.0% (25/49)
External iliac node region	0% (0/49)	0% (0/49)
Internal iliac node region	20.4% (10/49)	22.4% (11/49)
Inside of the pelvis	22.4% (11/49)	18.4% (9/49)
Outside of the pelvis	4.1% (2/49)	8.2% (4/49)

1.76 ±0.35 Gy). The DVH parameters ( $D_{100}$ ,  $D_{90}$ ,  $D_{50}$ ,  $D_{2cc}$ ,  $D_{1cc}$ , and  $D_{0.1cc}$ ) for the pelvic lymph node groups and the statistical analysis results are shown in Table 3. The CCs were less than 0.7, except for  $D_{50}$  of the obturator lymph node group (CC, 0.73) (bilateral), and the results indicated a low degree of correlation overall. All parameters of the obturator,  $D_{100}$ ,  $D_{90}$ ,  $D_{50}$ ,  $D_{2cc}$ , and  $D_{1cc}$  of the external iliac node and  $D_{100}$ ,  $D_{90}$ ,  $D_{50}$ ,  $D_{2cc}$ , and  $D_{0.1cc}$  of the internal iliac node were significantly different from the point B doses. However,  $D_{0.1cc}$  of the external iliac node group and  $D_{1cc}$  of the internal iliac node group were not statistically different from the point B doses. For the obturator group, the mean  $D_{50}$  was 1.47 ±0.28 Gy (*t*-test,

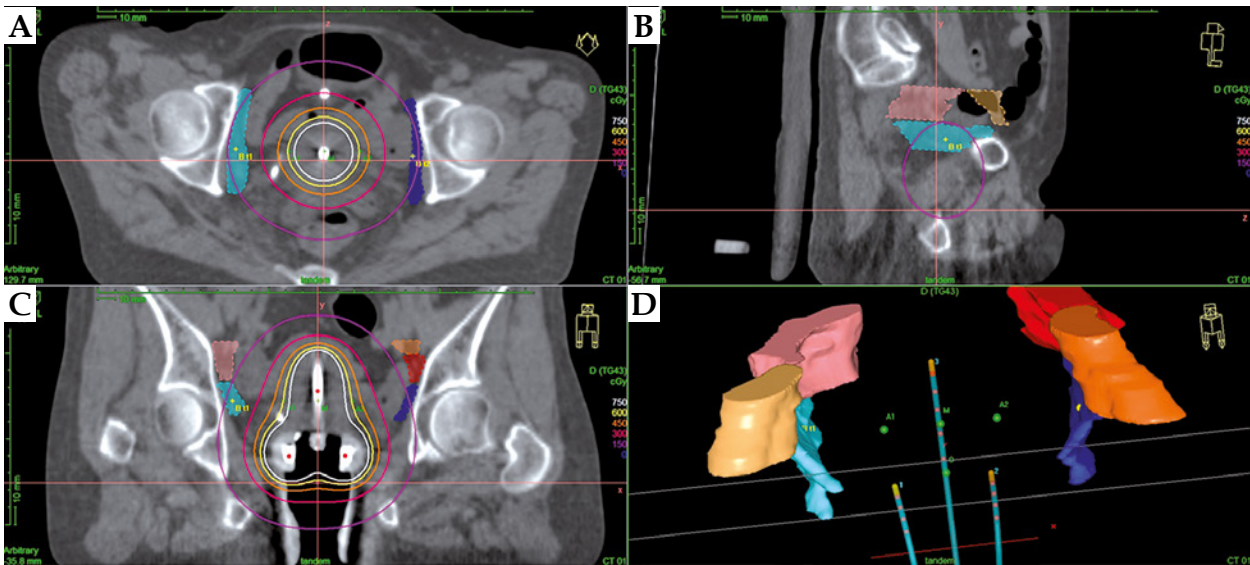


Pelvic lymph node regions: obturator in blue, external iliac node in orange, and internal iliac node in red. R – right, L – left

**Fig. 1.** Contoured pelvic lymph node regions and the percentage values of the anatomical location of point B on CT image.

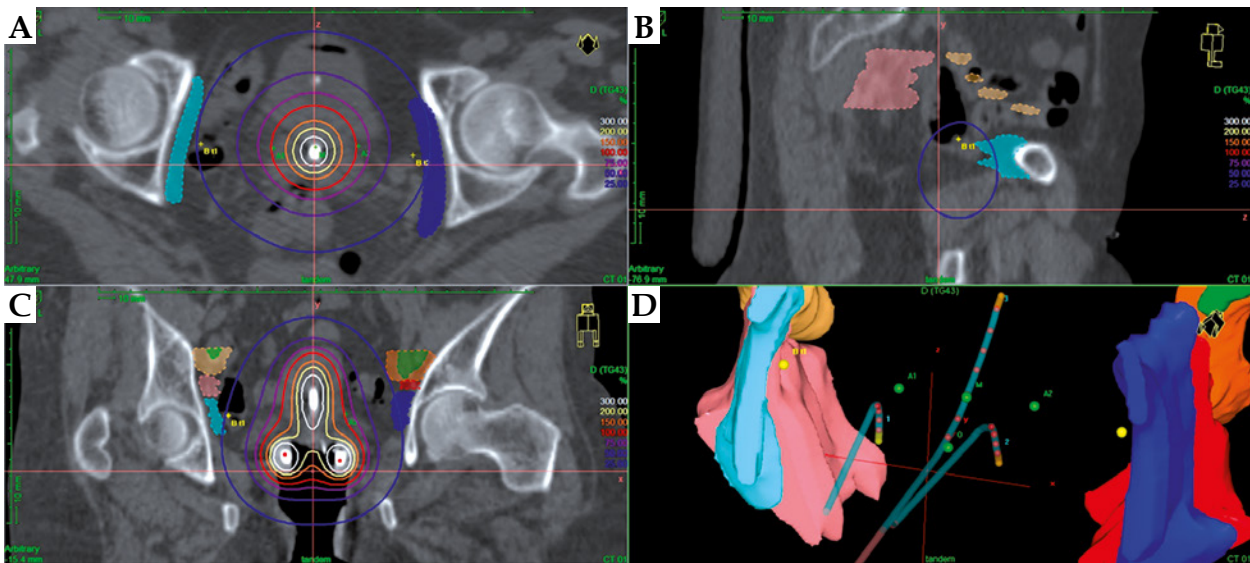
**A)** The axial plane, on which the external and internal iliac nodes are observed; **B)** The axial plane, on which the obturator is observed; **C)** The sagittal plane; **D)** The coronal plane; **E)** 3D view





Pelvic lymph node regions: obturator in blue, external iliac node in orange, and internal iliac node in red. Points: point B in yellow, point A in green.

**Fig. 2.** The pelvic lymph node volumes and point B in relation to the dose distribution, in a typical patient, where point B is located in the pelvic lymph node region. A) Axial plane; B) Sagittal plane; C) Coronal plane; D) 3D view



Pelvic lymph node regions: obturator in blue, external iliac node in orange, and internal iliac node in red. Points: point B in yellow, point A in green.

**Fig. 3.** The pelvic lymph node volumes and the point B in relation to the dose distribution, in a typical patient, where the point B is not located in the pelvic lymph node region. A) Axial plane; B) Sagittal plane; C) Coronal plane; D) 3D view

$p < 0.0001$ ), and the CC for  $D_{50}$  of the obturator was only slightly more than 0.7 (CC, 0.73,  $p < 0.0001$ ). However, all DVH parameters were significantly different from the point B dose. The DVH parameter of the obturator that most closely represented the point B dose was  $D_{2cc}$  and the mean value was  $1.81 \pm 0.35$  Gy ( $t$ -test,  $p = 0.0089$ ) with a CC of 0.68 ( $p < 0.0001$ ). In this study, we found that the point B doses were not adequate surrogates for the DVH parameters of the obturator group. For the external iliac chain, the mean  $D_{0.1cc}$  was  $1.60 \pm 0.37$  Gy ( $p = 0.0594$ ), and the CC was 0.32 ( $p = 0.0236$ ) (Figure 4). The  $D_{100}$ ,  $D_{90}$ ,  $D_{50}$ ,  $D_{2cc}$  and  $D_{1cc}$  were statistically different from the point B

dose ( $t$ -test,  $p < 0.0001$ ). For the internal iliac chain, the mean  $D_{1cc}$  was  $1.60 \pm 0.39$  Gy ( $t$ -test,  $p = 0.0711$ ), and this parameter alone did not indicate a significant difference. The CC of  $D_{1cc}$  was 0.33 ( $p = 0.0223$ ) (Figure 5). The  $D_{100}$ ,  $D_{90}$ ,  $D_{50}$ ,  $D_{2cc}$  and  $D_{0.1cc}$  for the internal iliac chain were statistically different from the point B dose. The mean uterine length and separation between ovoids were 61.6 mm (range, 41.1-83.4 mm) and 32.1 mm (range, 22.6-42.1 mm), respectively. The correlation between these values and the doses delivered to pelvic lymph node regions was analyzed. The separation between ovoids did not correlate with the doses to pelvic lymph nodes significantly;

**Table 3.** The DVH parameters ( $D_{100}$ ,  $D_{90}$ ,  $D_{50}$ ,  $D_{2cc}$ ,  $D_{1cc}$ , and  $D_{0.1cc}$ ) for pelvic lymph node groups and correlation coefficients between these parameters and point B dose

	Bilateral mean dose (Gy)	CC <sup>1</sup>	<i>p</i> value <sup>2</sup>	<i>t</i> -test <sup>3</sup>	Percentage <sup>4</sup> (%)
Obturator node group					
$D_{100}$ <sup>5</sup>	0.65 ±0.17	0.60	< 0.0001	< 0.0001	10.8 ±2.87
$D_{90}$ <sup>6</sup>	1.07 ±0.22	0.66	< 0.0001	< 0.0001	17.8 ±3.74
$D_{50}$ <sup>7</sup>	1.47 ±0.28	0.73	< 0.0001	< 0.0001	24.5 ±4.61
$D_{2cc}$ <sup>8</sup>	1.81 ±0.35	0.68	< 0.0001	0.0089	30.1 ±5.87
$D_{1cc}$ <sup>9</sup>	1.95 ±0.38	0.66	< 0.0001	< 0.0001	32.4 ±6.37
$D_{0.1cc}$ <sup>10</sup>	2.27 ±0.45	0.64	< 0.0001	< 0.0001	37.9 ±7.56
External iliac nodes					
$D_{100}$	0.29 ±0.10	0.55	< 0.0001	< 0.0001	4.80 ±1.62
$D_{90}$	0.59 ±0.15	0.56	< 0.0001	< 0.0001	9.82 ±2.55
$D_{50}$	0.90 ±0.22	0.52	0.0001	< 0.0001	14.9 ±3.66
$D_{2cc}$	1.24 ±0.31	0.41	0.0037	< 0.0001	20.7 ±5.16
$D_{1cc}$	1.35 ±0.34	0.38	0.0069	< 0.0001	22.5 ±5.59
$D_{0.1cc}$	1.60 ±0.37	0.32	0.0236	0.0594	26.7 ±6.24
Internal iliac nodes					
$D_{100}$	0.49 ±0.14	0.47	0.0006	< 0.0001	8.22 ±2.31
$D_{90}$	0.81 ±0.19	0.43	0.0021	< 0.0001	13.5 ±3.19
$D_{50}$	1.08 ±0.25	0.39	0.0054	< 0.0001	18.0 ±4.11
$D_{2cc}$	1.49 ±0.36	0.33	0.0198	< 0.0001	24.8 ±6.04
$D_{1cc}$	1.60 ±0.39	0.33	0.0223	0.0711	26.7 ±6.49
$D_{0.1cc}$	1.89 ±0.45	0.29	0.0396	0.0043	31.5 ±7.55
Point B dose	1.70 ±0.18				28.3 ±2.98

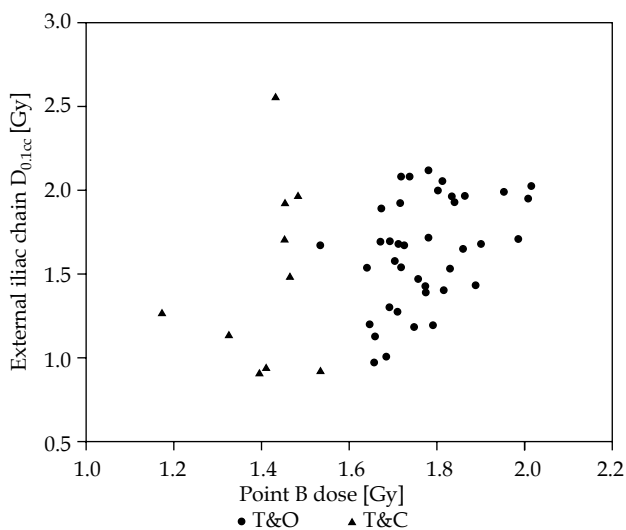
<sup>1</sup>CC – correlation coefficient; <sup>2</sup>*p* value – *p* value calculated by Pearson's correlation coefficients; <sup>3</sup>*t*-test – *p* value calculated by a two sided paired *t*-test; <sup>4</sup>Percentage – percentage of the prescription dose (6 Gy); <sup>5</sup> $D_{100}$  – dose to 100% of the volume; <sup>6</sup> $D_{90}$  – dose to 90% of the volume; <sup>7</sup> $D_{50}$  – dose to 50% of the volume; <sup>8</sup> $D_{2cc}$  – dose to 2 cc of the volume; <sup>9</sup> $D_{1cc}$  – dose to 1 cc of the volume; <sup>10</sup> $D_{0.1cc}$  – dose to 0.1 cc of the volume

however, we found the positive significant correlation between the uterine length and the doses to the external iliac node.

In addition, Table 4 shows the comparison of DVH parameters for each lymph node region and point B dose by applicator type, including 39 tandem and ovoid and 10 tandem and cylinder applicators. The dose to the obturator nodes was lower 0.27-0.67 Gy for the tandem and cylinder applicator when compared by a *t*-test, although there was not such a significant difference for the external iliac nodes and the internal iliac nodes. We also analyzed the correlation between point B dose and the dose delivered to the pelvic lymph node regions by applicator type. However, we could not find a significant correlation between point B dose and the dose delivered to the pelvic lymph node regions in tandem and cylinder applicator cases, probably because sample size of the cylinder applicator was small (Table 5).

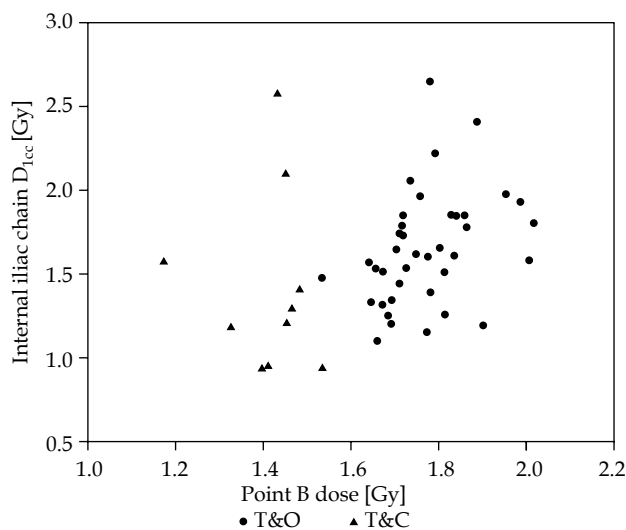
## Discussion

The present study was carried out to evaluate the anatomical position of point B, and the relationship between the point B dose and the dose delivered to the pelvic lymph nodes in HDR brachytherapy for uterine cervical cancer according to the Manchester method. We found that 27% of points B were not located in any pelvic lymph node regions. For DVH analysis, the CCs were less than 0.7, except for the  $D_{50}$  of the obturator group. As in the previous study [11], we indicated that the DVH parameters were statistically different from the point B dose, and the pelvic lymph node contours defined the nodal dose more accurately than did point B. The two DVH parameters, i.e., the  $D_{0.1cc}$  of the external iliac chain and the  $D_{1cc}$  of the internal iliac chain, were not statistically different from the point B dose; however, the low CC of these parameters suggests that the point B dose was not a clinically significant surrogate for the dose delivered to the



T&O – tandem and ovoid applicator (circle point), T&C – tandem and cylinder applicator (triangle point)

**Fig. 4.** Correlation between the point B dose and  $D_{0.1cc}$  of the external iliac chain (CC, 0.32). The scatter-plot points were categorized into two forms by the applicator type



T&O – tandem and ovoid applicator (circle point), T&C – tandem and cylinder applicator (triangle point)

**Fig. 5.** Correlation between the point B dose and  $D_{1cc}$  of the internal iliac chain (CC, 0.33). The scatter-plot points were categorized into two forms by the applicator type

**Table 4.** Comparison of DVH parameters for each nodal region and point B dose by applicator type

	T&O <sup>1</sup> mean dose (Gy) n = 39	T&C <sup>2</sup> mean dose (Gy) n = 10	$\Delta^3$ (Gy)	t-test <sup>4</sup>
Obturator node group				
$D_{100}^5$	0.70 ± 0.14	0.43 ± 0.11	0.27	< 0.0001
$D_{90}^6$	1.15 ± 0.17	0.76 ± 0.13	0.39	< 0.0001
$D_{50}^7$	1.57 ± 0.20	1.08 ± 0.18	0.49	< 0.0001
$D_{2cc}^8$	1.92 ± 0.27	1.36 ± 0.28	0.56	< 0.0001
$D_{1cc}^9$	2.07 ± 0.30	1.48 ± 0.29	0.59	< 0.0001
$D_{0.1cc}^{10}$	2.41 ± 0.38	1.74 ± 0.33	0.67	< 0.0001
External iliac nodes				
$D_{100}$	0.31 ± 0.09	0.20 ± 0.07	0.11	0.0005
$D_{90}$	0.62 ± 0.13	0.45 ± 0.15	0.17	0.001
$D_{50}$	0.94 ± 0.20	0.74 ± 0.24	0.20	0.0097
$D_{2cc}$	1.28 ± 0.27	1.09 ± 0.39	0.19	0.0753
$D_{1cc}$	1.39 ± 0.29	1.20 ± 0.43	0.19	0.1231
$D_{0.1cc}$	1.63 ± 0.32	1.48 ± 0.52	0.15	0.2822
Internal iliac nodes				
$D_{100}$	0.52 ± 0.12	0.40 ± 0.17	0.12	0.0228
$D_{90}$	0.84 ± 0.16	0.70 ± 0.24	0.14	0.0433
$D_{50}$	1.11 ± 0.21	0.96 ± 0.32	0.15	0.0838
$D_{2cc}$	1.53 ± 0.31	1.32 ± 0.48	0.21	0.0985
$D_{1cc}$	1.65 ± 0.34	1.42 ± 0.51	0.23	0.1038
$D_{0.1cc}$	1.94 ± 0.39	1.71 ± 0.60	0.23	0.162
Point B dose	1.77 ± 0.11	1.41 ± 0.10	0.36	< 0.0001

<sup>1</sup>T&O – tandem and ovoid applicator; <sup>2</sup>T&C – tandem and cylinder applicator; <sup>3</sup> $\Delta$  – dose difference between T&O and T&C (T&O mean dose – T&C mean dose); <sup>4</sup>t test – p value calculated by a t-test; <sup>5</sup> $D_{100}$  – dose to 100% of the volume; <sup>6</sup> $D_{90}$  – dose to 90% of the volume; <sup>7</sup> $D_{50}$  – dose to 50% of the volume; <sup>8</sup> $D_{2cc}$  – dose to 2 cc of the volume; <sup>9</sup> $D_{1cc}$  – dose to 1 cc of the volume; <sup>10</sup> $D_{0.1cc}$  – dose to 0.1 cc of the volume

**Table 5.** The DVH parameters ( $D_{100}$ ,  $D_{90}$ ,  $D_{50}$ ,  $D_{2cc}$ ,  $D_{1cc}$ , and  $D_{0.1cc}$ ) for pelvic lymph node groups, and correlation coefficients between these parameters and point B dose by applicator type

	T&O <sup>1</sup> (n = 39)				T&C <sup>2</sup> (n = 10)			
	Bilateral mean dose (Gy)	CC <sup>3</sup>	p value <sup>4</sup>	t-test <sup>5</sup>	Bilateral mean dose (Gy)	CC	p value	t-test
Obturator node group								
$D_{100}$ <sup>6</sup>	0.70 ±0.14	0.19	0.2584	< 0.0001	0.43 ±0.11	0.16	0.6495	< 0.0001
$D_{90}$ <sup>7</sup>	1.15 ±0.17	0.21	0.2092	< 0.0001	0.76 ±0.13	0.34	0.3364	< 0.0001
$D_{50}$ <sup>8</sup>	1.57 ±0.20	0.33	0.0404	< 0.0001	1.08 ±0.18	0.50	0.1437	0.0001
$D_{2cc}$ <sup>9</sup>	1.92 ±0.27	0.33	0.0418	0.0013	1.36 ±0.28	0.48	0.1606	0.5475
$D_{1cc}$ <sup>10</sup>	2.07 ±0.30	0.31	0.0541	< 0.0001	1.48 ±0.29	0.51	0.1343	0.4922
$D_{0.1cc}$ <sup>11</sup>	2.41 ±0.38	0.31	0.0576	< 0.0001	1.74 ±0.33	0.52	0.1196	0.0078
External iliac nodes								
$D_{100}$	0.31 ±0.09	0.32	0.0461	< 0.0001	0.20 ±0.07	0.26	0.4598	< 0.0001
$D_{90}$	0.62 ±0.13	0.40	0.0106	< 0.0001	0.45 ±0.15	0.24	0.5046	< 0.0001
$D_{50}$	0.94 ±0.20	0.46	0.0034	< 0.0001	0.74 ±0.24	0.22	0.5321	< 0.0001
$D_{2cc}$	1.28 ±0.27	0.41	0.0095	< 0.0001	1.09 ±0.39	0.20	0.5725	0.0288
$D_{1cc}$	1.39 ±0.29	0.41	0.0093	< 0.0001	1.20 ±0.43	0.21	0.5644	0.1676
$D_{0.1cc}$	1.63 ±0.32	0.41	0.0104	0.0044	1.48 ±0.52	0.21	0.5572	0.686
Internal iliac nodes								
$D_{100}$	0.52 ±0.12	0.51	0.001	< 0.0001	0.40 ±0.17	-0.0045	0.9902	< 0.0001
$D_{90}$	0.84 ±0.16	0.46	0.0031	< 0.0001	0.70 ±0.24	0.040	0.9132	< 0.0001
$D_{50}$	1.11 ±0.21	0.46	0.0029	< 0.0001	0.96 ±0.32	-0.00021	0.9995	0.0028
$D_{2cc}$	1.53 ±0.31	0.36	0.024	< 0.0001	1.32 ±0.48	-0.060	0.8699	0.5741
$D_{1cc}$	1.65 ±0.34	0.36	0.026	0.0176	1.42 ±0.51	-0.071	0.8453	0.9691
$D_{0.1cc}$	1.94 ±0.39	0.35	0.031	0.0109	1.71 ±0.60	-0.084	0.8175	0.1859
Point B dose	1.77 ±0.11				1.41 ±0.10			

<sup>1</sup>T&O – tandem and ovoid applicator; <sup>2</sup>T&C – tandem and cylinder applicator; <sup>3</sup>CC – correlation coefficient; <sup>4</sup>p value – p value calculated by Pearson's correlation coefficients; <sup>5</sup>t-test – p value calculated by a two sided paired t-test; <sup>6</sup> $D_{100}$  – dose to 100% of the volume; <sup>7</sup> $D_{90}$  – dose to 90% of the volume; <sup>8</sup> $D_{50}$  – dose to 50% of the volume; <sup>9</sup> $D_{2cc}$  – dose to 2 cc of the volume; <sup>10</sup> $D_{1cc}$  – dose to 1 cc of the volume; <sup>11</sup> $D_{0.1cc}$  – dose to 0.1 cc of the volume

pelvic lymph nodes (Figures 4 and 5). We found a significant positive correlation between the uterine length and the doses to the external iliac node. This observation may have been caused by the location of the tandem, which was closer to the external iliac node region in the case of a long uterine.

Although the apparent pattern in the implant geometry was not established in this study (Figures 2 and 3), we found that 27% of points B were not located in any pelvic lymph node regions, which tended to be inside of the pelvis from the results of Table 2. Several studies have reported that Caucasians have a larger pelvic and iliac width than Japanese individuals [20,21]. The dose delivered to the pelvic lymph nodes may vary in relation to the difference in pelvic and iliac width between Japanese and Caucasians patients, although we cannot compare the dose parameters observed in our study with the previous data [11] simply because of the difference in the dose prescription and fraction. Given our results and the dif-

ference in pelvic width between Caucasians and Japanese [20,21], we consider that point B for Caucasians may be located relatively more inside the pelvis compared to that for Japanese. Hence, the dose to the pelvic lymph nodes should be estimated according to the anatomical pelvic size in the case of 2D conventional planning.

When the dose delivered to lymph nodes was analyzed by applicator type (Table 4), the DVH parameters for the tandem and ovoid applicator were higher than the tandem and cylinder applicator overall. Although there were significant differences between the two applicator types for  $D_{100}$ ,  $D_{90}$ , and  $D_{50}$  of the external iliac nodes and  $D_{100}$  and  $D_{90}$  of the internal iliac nodes, the differences were smaller than that of the obturator, and  $D_{2cc}$ ,  $D_{1cc}$ , and  $D_{0.1cc}$  of the external iliac nodes and  $D_{50}$ ,  $D_{2cc}$ ,  $D_{1cc}$ , and  $D_{0.1cc}$  of the internal iliac nodes did not show significant differences. However, the dose to the obturator nodes was significantly lower by 0.27-0.67 Gy for the tandem and cylinder applicator than in case of the

tandem and ovoid applicator when compared by a *t*-test. This observation may have been due to the location of the obturator node region, which was closer to the ovoid applicator than other lymph nodes.

For cervical cancer patients, who have enlarged nodal disease and receive an external-beam boost dose, the dose contribution to the pelvic lymph nodes from brachytherapy is very important. Lee *et al.* investigated the dose and equivalent dose contribution of HDR brachytherapy to metastatic pelvic lymph nodes in locally advanced cervical cancer patients [22]. They demonstrated that the brachytherapy dose accounted for about 7% of the total prescription boost dose to the lymph nodes. In addition, Mohamed *et al.* evaluated the dose delivered to the lymph nodes by brachytherapy and the effect of brachytherapy image-guided optimization on the lymph node dose. They mentioned that brachytherapy contributes a significant dose to the pelvic lymph nodes and should be considered in the evaluation of total lymph node doses. The dose was 4-6 Gy equivalent total dose in 2 Gy fractions (EQD<sub>2</sub>) for the obturator, external iliac nodes, and internal iliac nodes, when two fractions of MRI-guided pulsed-dose-rate (PDR) brachytherapy were delivered 1 week apart and each fraction was 20-hourly pulses. The brachytherapy plan optimization aimed to deliver a total EQD<sub>2</sub> (EBRT plus brachytherapy) of at least 85 Gy to the high-risk clinical target volume (HR-CTV) D<sub>90</sub>, and to keep the D<sub>2cc</sub> for bladder below 90 Gy, and the D<sub>2cc</sub> of the rectum, sigmoid, and bowel below 70-75 Gy [23]. Bacorro *et al.* also analyzed the dose delivered to pelvic lymph nodes during brachytherapy. The planning objectives, summing EBRT plus PDR-IGBT in EQD<sub>2</sub>, consisted of HR-CTV D<sub>90</sub> ≥ 85 Gy and the OAR dose constraints were 75 Gy, 75 Gy, and 85 Gy to D<sub>2cc</sub> of the rectum, sigmoid, and bladder, respectively. They reported brachytherapy contribution to the treatment of pelvic nodes at the level of approximately 5 Gy in the internal iliac, external iliac, and obturator nodes [24]. Chua *et al.* quantified the brachytherapy dose contribution to pelvic node groups using the Manchester method. They indicated that the mean cumulative EQD<sub>2</sub> doses to the external iliac, the internal iliac, and the obturator nodes were 4.30 Gy, 5.95 Gy, and 7.09 Gy, respectively, in patients who received 6 Gy × 4 fractions [25]. Thus, the brachytherapy dose was reported to make a significant contribution in these studies, and the accurate evaluation of the dose delivered to the pelvic lymph nodes by brachytherapy is essential.

In this simulation study, we adopted only the standard loading pattern [18], and source dwell times were not optimized to minimize the dose to the OAR and maximize the coverage of the HR-CTV, because we used the previous conventional 2D plan data; this is a limitation of the present study. Three-dimensional IGBT was developed to ensure target coverage and avoid exposure to OAR [12,13]. However, in low-income countries, where the incidence of cervical cancer is high, 3D imaging is generally not available, and a non-optimized 2D plan is used instead [26,27,28]. Therefore, we consider that the findings of this study are important for resource-limited institutes that use the 2D plan.

## Conclusions

Our assessment indicated that the point B dose was a poor surrogate for the dose delivered to the pelvic lymph nodes. Thus, 3D evaluation of the dose delivered to the contoured pelvic lymph nodes is more accurate than single-point estimation using point B.

## Disclosure

Authors report no conflict of interest.

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