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Dose to pelvic lymph nodes in image based high dose rate brachytherapy of carcinoma cervix

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ABSTRACT

Aim: The aim of this study is to analyse the dosimetry to the pelvic lymph nodes and its correlation to point B using CT based high dose rate brachytherapy of carcinoma cervix.
Background: Conventionally, dose to pelvic lymph nodes from intracavitary brachytherapy was reported by point B and by the reference points of the lymphatic trapezoid.
Materials and methods: 30 consecutive CT based high dose rate applications were reviewed between February and March 2016. The high risk clinical target volume and the organs at risk and the pelvic nodal groups were contoured. DVH parameters for the right and left obturator nodal group, right and left external iliac nodal group and right and left internal iliac nodal group were recorded. Right and left point B doses were also recorded.
Results: On analysis of the combined dose, it was found that all the DVH parameters were significantly different from point B, except the D100 obturator and D2cc internal iliac lymph node. There was a significant correlation between all DVH parameters and point B, except D2cc, D1cc and D0.1cc of external iliac. The obturator group received the highest dose contribution from brachytherapy. The mean D90 dose received per fraction for the obturator, external iliac and internal iliac nodes was 2.7 Gy, 1.17 Gy and 1.41 Gy, respectively.
Conclusions: There is a significant dose contribution to the pelvic lymph nodal groups during intracavitary brachytherapy. There is a low degree of correlation between point B dose and dosimetric parameters of the individual nodal groups. Hence, it is important to analyse the dose delivered to individual nodal groups during intracavitary brachytherapy, at least in patients with enlarged lymph nodes to calculate the cumulative dose delivered.

1. Background

Cervical cancer is the most common cause of cancer mortality among women in developing countries.[1] Metastases to the pelvic lymph nodes are one of the most important prognostic factors in cervical cancer.[2] The incidence of pelvic lymph node metastases for FIGO stage IIA is 10–45%, stage IIB – 26–62%, and stage IIIA – 39–59%, stage IIIB/IV – 39–88% according to some surgical series reported in literature.[3–7] Concurrent

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chemoradiation is the standard treatment option for locally advanced cervical cancers.[8–12] Radiation therapy for cervical cancers includes a combination of external beam radiotherapy followed by intracavitary brachytherapy.

The total external beam radiotherapy dose ranges from 45 Gy to 50 Gy in 180–200 cGy per fraction. Patients with enlarged nodal disease receive 3D conformal or intensity modulated radiotherapy boost to a total external beam radiotherapy dose of 55–60 Gy. Conventionally, dose to lymph nodes from intracavitary brachytherapy was reported by point B (which is at the level of point A and 5 cm from the midline) and by the reference points of the lymphatic trapezoid.[13] The dose to the obturator lymph node which is the first echelon node was represented by point B. Few studies have analysed the dose contribution to lymph nodes by intracavitary brachytherapy using CT based imaging.

The aim of this study is to analyse the dosimetry to pelvic lymph nodes and its correlation to point B using CT based high dose rate brachytherapy of carcinoma cervix.

2. Materials and methods

2.1. *Technique*

Thirty consecutive CT based high dose rate applications were reviewed between February and March 2016. The procedure of intracavitary application was done under general anaesthesia in the operating room. Bladder was catheterised and left to drain in all patients. 3 ml of contrast and 4 ml of normal saline was instilled into a Foley bulb. A CT-MR compatible applicator or a metal tandem ring applicator was used. Adequate vaginal gauze packing was done after securing the applicator position.

2.2. *Imaging and contouring*

Following insertion of the applicator, 3 mm transverse images of the pelvis were obtained using a CT simulator (Somatom, Siemens, Erlangen, Germany). The images were exported to Oncentra treatment planning system (Nucletron, an Elekta company, Stockholm, Sweden). The high risk clinical target volume and the organs at risk were contoured by the radiation oncologist. The entire cervix and the disease at the time of brachytherapy were included in the high risk clinical target volume. Modified Radiation Therapy Oncology Group (RTOG) definitions of pelvic nodal groups for intensity modulated radiation therapy[14–16] were used to delineate the pelvic lymph nodes. The obturator nodal contour included the obturator space from the level of the fovea of femoral head to the roof of acetabulum. The external iliac vessels with 7–10 mm margin constituted the external iliac nodal contour. It extended from the roof of acetabulum to the bottom of sacroiliac joint. The internal iliac nodes were contoured around the internal iliac artery and vein.

2.3. *Planning*

After catheter reconstruction, a standard loading pattern was used for both the tandem ovoid and tandem ring applicators. Point A was defined 2 cm superior to the flange at the level of external os and 2 cm lateral to the intrauterine tandem. Point B was defined 2 cm superior to the flange at the level of external os and 5 cm lateral to the intrauterine tandem in all applications. A dose of 7 Gy was prescribed to point A. Manual dwell time optimisation was done in select applications to minimise dose to organs at risk.

Dose volume histograms (DVH) were generated for the target and the organs at risk. DVH parameters like D0.1cc, 1cc and 2cc (dose received by 0.1cc, 1cc and 2cc of the nodal volumes, respectively) and D100, 90 and 50 (dose received by 100%, 90% and 50% of the nodal target volumes, respectively) for the right and left obturator nodal group, right and left external iliac nodal group and right and left internal iliac nodal group were recorded. Right and left point B doses were also recorded. Treatment was delivered using ^{192}Ir source (Nucletron, an Elekta company, Stockholm, Sweden). Axial CT images of the nodal contours are shown in Figs. 1 and 2. Axial CT images of the nodal contours along with point B are shown in Fig. 3.

2.4. *Statistics*

SPSS statistical package version 2 (IBM corporation, New York, USA) was used for statistical analysis. Descriptive statistics like mean and standard deviation were calculated. A two-sided paired *t* test was used to compare point B dose and

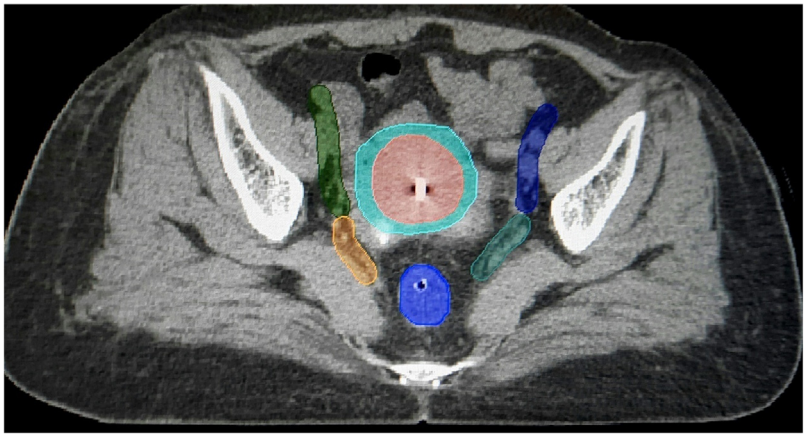

Fig. 1 – Axial CT images showing the external iliac and internal iliac lymph nodes.

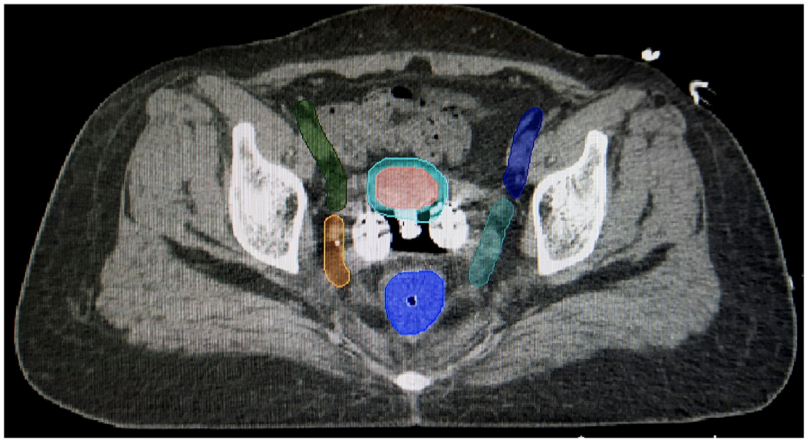

Fig. 2 – Axial CT sections showing the external iliac and obturator lymph nodes.

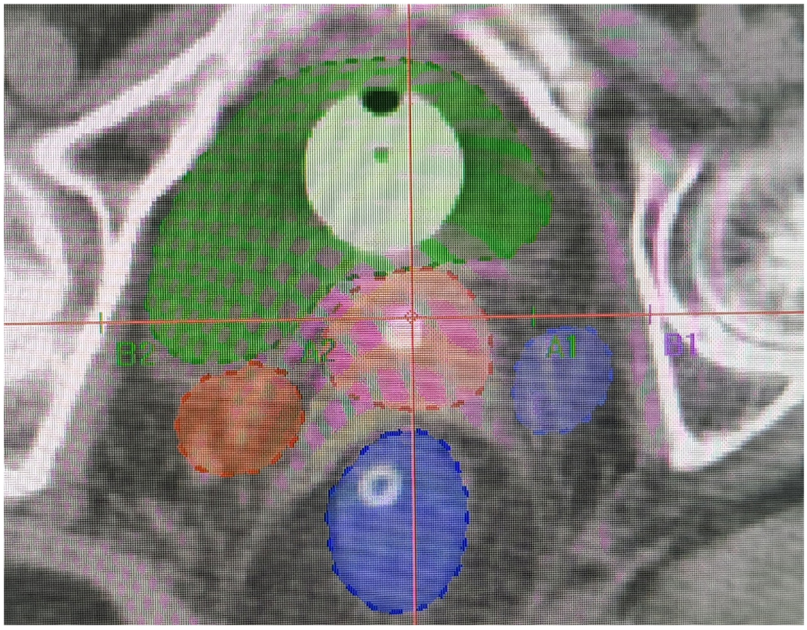

Fig. 3 – Axial CT image showing the OARs, CTV, obturator nodal group and point B.

the DVH parameters of the nodal groups. Pearson's correlation coefficients were determined to study the correlation between point B dose and the nodal DVH parameters.

3. Results

The average age of patients was 54years [range: 35–65 years]. 15 patients had FIGO stage IIIB cervical cancer, 14 patients had FIGO stage IIB and one patient had FIGO stage IVA. All patients were taken up for brachytherapy after an external beam radiotherapy dose of 50 Gy/2 Gy per fraction/25 fractions along with weekly cisplatin 40 mg/m^2. 3 fractions of high dose rate brachytherapy of 7 Gy were delivered to Manchester point A following external beam radiotherapy. CT based planning was done in all patients. Nodal contouring on CT and analysis of the DVH parameters of the nodal groups were done only for the first fraction.

Tandem ovoid applicator was used in 60% of patients and tandem ring applicator was used in 40%. The mean right point B dose was 1.95 ± 0.14 and the mean left point B dose was 2.07 ± 0.16. Point B received 28.5% of the prescription dose to point A.

3.1. *Dose to obturator nodes*

The average D100 dose to the obturator lymph nodes was 2 Gy which was 28.5% of the prescribed dose. All the DVH parameters, namely D90, D50, D0.1cc, D1cc and D2cc were significantly different from point B (paired t test; p value <0.0001) except D100 (Table 1). The degree of correlation between the DVH parameters of the obturator nodal group and point B dose was relatively low (Table 1).

3.2. *Dose to external iliac nodes*

The average D100 dose to the external iliac lymph nodes was 0.66 Gy, which was 9.42% of the prescribed dose. All DVH

Table 1 – DVH parameters of right and left obturator lymph nodes.

Lymph nodes	DVH parameters	Mean	*p* value	Correlation coefficient	*t* test
Right obturator	D100	2 ± 0.65	0.03	0.378	0.65
	D90	2.79 ± 0.78	0.06	0.344	<0.0001
	D50	4 ± 1.36	0.06	0.338	<0.0001
	D2cc	4.4 ± 1.5	0.19	0.243	<0.0001
	D1cc	5.45 ± 2	0.16	0.260	<0.0001
	D0.1cc	6.1 ± 3.3	0.06	0.346	<0.0001
Left obturator	D100	2 ± 0.61	0.11	0.296	0.698
	D90	2.73 ± 0.80	0.06	0.344	<0.0001
	D50	3.5 ± 1	0.04	0.376	<0.0001
	D2cc	4.2 ± 1.3	0.02	0.411	<0.0001
	D1cc	4.9 ± 1.7	0.02	0.403	<0.0001
	D0.1cc	6.68 ± 3.06	0.05	0.357	<0.0001

Table 2 – DVH parameters of right and left external iliac lymph nodes.

Lymph nodes	DVH parameters	Mean	*p* value	Correlation coefficient	*t* test
Right external iliac	D100	0.68 ± 0.23	0.02	0.409	<0.0001
	D90	1 ± 0.33	0.04	0.376	<0.0001
	D50	1.5 ± 0.46	0.31	0.191	<0.0001
	D2cc	2 ± 0.75	0.69	0.07	0.689
	D1cc	2.21 ± 0.82	0.69	0.07	0.105
	D0.1cc	2.63 ± 0.91	0.83	0.041	<0.0001
Left external iliac	D100	0.72 ± 0.34	0.58	0.10	<0.0001
	D90	1.2 ± 0.4	0.44	0.14	<0.0001
	D50	1.75 ± 0.43	0.37	0.17	<0.0001
	D2CC	2.4 ± 0.58	0.37	0.16	0.003
	D1CC	2.6 ± 0.65	0.52	0.12	<0.0001
	D0.1CC	3 ± 0.8	0.83	0.04	<0.0001

parameters, except D2cc and D1cc of the right external iliac nodes were significantly different from point B (paired *t* test; *p* value < 0.0001) (Table 2). There was a significant correlation between D100 and D90 of the right external iliac lymph node and point B (*p* value: 0.025, correlation coefficient: 0.409; *p* value: 0.04, correlation coefficient: 0.376, respectively).

3.3. *Dose to internal iliac nodes*

The average D100 dose to the internal iliac lymph nodes was 0.98 Gy, which was 14% of the prescribed dose. All DVH parameters, except D2cc of the right and left internal iliac lymph nodes were significantly different from point B (paired *t* test; *p* value < 0.0001) (Table 3). There was a significant correlation between D100 (*p* value: 0.02, correlation coefficient: 0.415), D90 (p value: 0.04, correlation coefficient: 0.374) and D2cc (*p* value: 0.04, correlation coefficient: 0.37) of the right internal iliac lymph node and all the DVH parameters of the left internal iliac lymph node but the degree of correlation was low for all the parameters.

On analysis of the combined dose (right and left lymph nodal dose), it was found that all the DVH parameters were significantly different from point B, except D100 obturator and D2cc internal iliac lymph node (Table 4). There was a significant correlation between all DVH parameters and point B, except D2cc, D1cc and D0.1cc of the external iliac.

4. Discussion

Traditionally, doses delivered to the pelvic lymph nodes during intracavitary brachytherapy were quantified by the lymphatic trapezoid of Fletcher[13] which represented the dose to the lower paraaortic, lower common iliac and middle external iliac lymph nodes and by the pelvic wall points which represented dose to the obturator lymph nodes. With the advent of image guidance in intracavitary brachytherapy, few studies have analysed the dosimetry of the pelvic nodal groups.

In a study conducted at Loyola University Medical Center,[17] 50 CT datasets were analysed for dosimetric contribution to the pelvic lymph nodes and they found a mean normalised D90 of 19.8% of the prescription dose to point A. The external iliac lymph nodes received 9.5% of the prescription dose to point A and the internal iliac lymph nodes received 12.2% of the prescription dose. The mean point A doses in their study was 5.92 ± 0.58 Gy. In the present study, the mean normalised D90 dose to the obturator lymph nodes, external iliac and internal iliac lymph nodes were 38.5%, 16.7% and 20% of the prescription dose to point A, respectively. The point A dose was 7 Gy in our study.

McKeever et al.[18] explored the pelvic lymph node dose received from brachytherapy. They found that 9.97% of the total dose to lymph nodes was from brachytherapy. As per the study, the external iliac lymph nodes and internal iliac nodes received 21.75% (6.05 Gy) and 16.43% (4.29 Gy) of point A dose. The mean dose contribution to the lymph nodes from brachytherapy in their study was 5.5 Gy (range: 1.4–12.4 Gy). The mean dose contribution to the lymph nodes in the present study was 5.28 Gy.

In a study conducted at the University of Pennsylvania,[19] dose contribution to the pelvic lymph nodes during intracavitary brachytherapy was studied in 14 consecutive patients.

Table 3 – DVH parameters of right and left internal iliac lymph nodes.

Lymph nodes	DVH parameters	Mean	*p* value	Correlation coefficient	*t* test
Right internal iliac	D100	0.43 ± 0.3	0.02	0.415	<0.0001
	D90	1.29 ± 0.45	0.04	0.374	<0.0001
	D50	1.7 ± 0.57	0.38	0.381	0.013
	D2cc	2 ± 0.74	0.04	0.37	0.308
	D1cc	2.45 ± 0.85	0.06	0.34	0.005
	D0.1cc	3 ± 0.17	0.09	0.31	<0.0001
Left internal iliac	D100	1 ± 0.32	0.01	0.462	<0.0001
	D90	1.5 ± 0.45	0.009	0.470	<0.0001
	D50	1.85 ± 0.46	0.003	0.525	0.006
	D2cc	2.19 ± 0.56	0.007	0.486	0.199
	D1cc	2.38 ± 0.63	0.007	0.481	0.006
	D0.1cc	2.86 ± 0.82	0.008	0.476	<0.0001

Table 4 – DVH parameters of combined dose to bilateral pelvic lymph nodes.

Lymph nodes	DVH parameters	Mean	*p* value	Correlation coefficient	*t* test
Obturator	D100	2 ± 0.74	0.06	0.343	0.525
	D90	2.7 ± 0.72	0.01	0.464	0.000
	D50	3.8 ± 1.12	0.01	0.460	0.000
	D2cc	4.1 ± 1.26	0.004	0.510	0.000
	D1cc	5 ± 1.6	0.003	0.518	0.000
	D0.1cc	6.8 ± 3.2	0.01	0.443	0.000
External iliac	D100	0.66 ± 0.22	0.02	0.403	<0.0001
	D90	1.17 ± 0.19	0.03	0.396	<0.0001
	D50	1.59 ± 0.30	0.03	0.391	<0.0001
	D2cc	2.1 ± 0.41	0.09	0.313	0.019
	D1cc	2.4 ± 0.47	0.06	0.345	<0.0001
	D0.1cc	2.8 ± 0.52	0.10	0.301	<0.0001
Internal iliac	D100	0.98 ± 0.30	0.002	0.542	<0.0001
	D90	1.41 ± 0.43	0.005	0.495	<0.0001
	D50	1.81 ± 0.44	0.004	0.514	0.02
	D2cc	2.1 ± 0.75	0.01	0.440	0.150
	D1cc	2.3 ± 0.68	0.003	0.520	<0.0001
	D0.1cc	2.8 ± 0.90	0.01	0.448	<0.0001

The researchers found a statistically significant difference in dose delivered to point B compared to D90, D100 and 0.1cc of individual lymph nodes. They concluded that point B dose does not accurately represent dose to individual lymph nodes and that the estimation of dose delivered to lymph nodes during the first fraction can be taken as the representation of the total dose delivered during the course of brachytherapy.

Lee et al.[20] found a statistically significant difference in the dose delivered to the pelvic lymph nodes with the obturator lymph node receiving the highest dose from brachytherapy. Brachytherapy contribution to the external iliac, internal iliac and obturator lymph nodes was 6.93%, 8.83% and 9.48% of the total dose delivered to the lymph nodes, respectively. The average dose delivered to the external iliac, internal iliac and obturator lymph nodes was 4 Gy, 5.09 Gy and 5.47 Gy, respectively. In a similar study by Ying Chua et al.,[21] the mean absolute dose received by the external iliac, internal iliac and the obturator lymph nodes was 0.79 Gy, 1.12 and 1.34 Gy, respectively with a point A dose of 5 Gy and 1.16 Gy, 1.56 Gy and 1.80 Gy, respectively, with a point A dose of 6 Gy.

Bacorro et al.[22] concluded that brachytherapy contributes approximately 5 Gy to the internal iliac, external iliac and obturator nodes and 2.5 Gy to the common iliac nodes. In a study conducted at Harvard medical school,[23] point B dose was found to be a poor surrogate for dose to individual nodal groups. The median point B dose was found to be 25% of the total brachytherapy dose. The degree of correlation between DVH parameters of the nodal group and point B dose was low, with all correlation coefficients less than 0.7, which was similar to the findings of the present study.

In summary, the present study results suggest that the point B dose was significantly different from the dose to individual lymph nodes. The obturator group receives the highest dose contribution from brachytherapy. The mean D90 dose received per fraction for the obturator, external iliac and internal iliac nodes are 2.7 Gy, 1.17 Gy and 1.41 Gy, respectively. The DVH parameters, which were not significantly different from point B, were the D2cc internal iliac ($p = 0.150$) and D100 obturator (p value = 0.525).

5. Conclusion

There is a significant dose contribution to the pelvic lymph nodal groups during intracavitary brachytherapy. The degree of correlation between point B dose and dosimetric parameters of the individual nodal groups is low. Hence, it is important to analyse the dose delivered to individual nodal groups during intracavitary brachytherapy, at least in patients with enlarged lymph nodes, to calculate the cumulative dose delivered.

Conflicts of interest

None declared.

Financial disclosures

None declared.

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