

Correlation of Dose-reporting Parameters in Two-dimensional and Three-dimensional Image-guided Brachytherapy for Cancer of the Cervix Uteri: a Single-Institution Experience

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ABSTRACT

Objective: Different dose-reporting parameters are suggested for two-dimensional and three-dimensional image-guided brachytherapy for cancer of the cervix uteri. We aimed to determine if there is any correlation between these dose-reporting parameters in three-dimensional image-guided brachytherapy plans.

Methods: A computed tomographic (CT) scanner has been installed in the brachytherapy room in our department so that patients can undergo imaging in the same room immediately following insertion of applicators while being maintained under anaesthesia or sedation. Between January 2014 and September 2015, 34 patients underwent CT-based brachytherapy (number of plans, 136). High-risk clinical target volume (HR-CTV) and rectum were contoured according to GEC-ESTRO guidelines. Point A and ICRU rectal points were also determined. The correlations of D90 of HR-CTV with Point A, and also of D2cc of rectum with ICRU rectal points were determined. Two-sided paired t-test was used to determine if there were any statistically significant differences between HR-CTV D90 and Point A, and also between D2cc of rectum and ICRU rectal points.

Results: Comparison of the dose of Point A and D90 of HR-CTV revealed a statistically significant difference ($p < 0.001$) with a weak negative correlation ($R = -0.32$; $p < 0.0001$). Comparison of the dose of ICRU reference rectal point and D2cc of rectum revealed a statistically significant difference ($p < 0.01$) with a positive correlation ($p < 0.001$).

Conclusion: HR-CTV D90 and Point A appear to show a random relationship. ICRU rectal point, however, may tend to underestimate the dose to the rectum in a plan that is CT imaging-based compared with D2cc.

Key Words: Brachytherapy; Imaging, three-dimensional; Radiation Dosage; Radiotherapy planning, computer-assisted; Uterine cervical neoplasms

中文摘要

二維和三維圖像引導下近距離放射治療宮頸癌的劑量參數相關性：單一機構的經驗

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目的：有關二維和三維圖像引導下近距離放射治療宮頸癌方面提出了不同劑量參數。本研究旨在探

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討這些劑量參數之間是否相關。

方法：本院的近距離放射治療室安裝了電腦斷層掃描儀器（CT），方便患者仍在麻醉或鎮靜的狀況下插入敷料器後立即進行CT成像。2014年1月至2015年9月期間共34名患者接受CT引導下近距離放射治療（計劃數量為136）。根據GEC-ESTRO指南勾劃出高危靶區（HR-CTV）和直腸體積，並確定參考點A和國際輻射單位與測量委員會（ICRU）直腸參考點。找出HR-CTV D90與參考點A，以及直腸D2cc與ICRU直腸參考點的相關性。使用雙側配對 t 檢驗來確定以上兩組是否有任何統計學顯著差異。

結果：HR-CTV D90與參考點A具統計學顯著差異（ $p < 0.001$ ），但呈弱負相關性（ $R = -0.32$ ； $p < 0.0001$ ）。比較直腸D2cc與ICRU直腸參考點具統計學顯著差異（ $p < 0.01$ ），並呈正相關性（ $p < 0.001$ ）。

結論：HR-CTV D90與參考點A似乎有隨機關係。與D2cc相比，CT引導下近距離放射治療的ICRU直腸參考點卻可能低估了直腸劑量。

INTRODUCTION

Up until the last 1 or 2 years in Hong Kong, brachytherapy for cancer of the cervix was usually planned in a two-dimensional (2D) manner, even though various international guidelines on three-dimensional (3D) brachytherapy planning have been available for the last decade which enable better tumour and normal tissue delineation.¹⁻³ Obstacles to their implementation included resource and manpower limitations. In addition, computed tomography (CT) or magnetic resonance imaging (MRI) machines may not have been located close to the brachytherapy room, patients would thus have to be transferred out of the brachytherapy room to the imaging unit with brachytherapy applicators in situ. Under normal circumstances, patients are usually put under general / spinal anaesthesia or sedated during applicator insertion. However, during the transfer process, patients will be kept awake which can cause discomfort and embarrassment to them. It may also cause displacement of the applicators affecting treatment accuracy and lengthening the total duration of the procedure which will result in additional resource implications.

Our institute has tried to overcome some of these difficulties by installing a CT scanner in the brachytherapy room so that patients can undergo imaging in the same room immediately after insertion of applicators whilst being maintained under anaesthesia / sedation. This not only minimises patient mobilisation and thus lowers the risk of applicator displacement, it also maximises patient comfort. Although additional time is required for acquiring CT images and

contouring, our centre's experience shows that, on average, it requires only around 30 minutes more to complete a 3D brachytherapy plan for cancer of the cervix uteri compared with a 2D one.⁴ As a result, whenever possible, we now perform 3D image-guided brachytherapy for all physically fit patients with cancer of the cervix uteri under general anaesthesia.

Different dose-reporting parameters are suggested for 2D and 3D image-guided brachytherapy for cancer of the cervix uteri. For example, dose-reporting parameters used in 2D planning such as Point A and International Commission on Radiation Units and Measurements (ICRU) rectal point are replaced by 3D concepts such as minimum dose to 90% (D90) of high-risk clinical target volume (HR-CTV) and minimum dose to the most exposed 2cc (D2cc) of rectum, respectively. It has been reported that the dose to Point A may be lower than the D90 for HR-CTV calculated using the image-based technique.⁵ The ICRU rectal point may also underestimate the dose to the rectum compared with the D2cc.⁶

It would be important to know the differences in the reporting of doses delivered to the tumour for both 2D and 3D image-guided brachytherapy plans. As rectal complications are a concern following brachytherapy for patients with cancer of the cervix, we also hope to determine the difference in the reporting of rectal doses. It would be useful to have some local data to compare with those of our overseas counterparts, given the potentially different patient characteristics in Hong Kong and practical differences in settings.

The aim of this study was to perform a dosimetric study to compare the reporting system for 2D and 3D planning by determining if there are any correlations between HR-CTV D90 and Point A, and between D2cc of rectum and ICRU rectal points, in CT-based 3D image-guided brachytherapy plans.

METHODS

Patients who underwent CT-based brachytherapy for cancer of the cervix during the period January 2014 to September 2015 in a regional hospital in Hong Kong were reviewed. Each patient received four fractions of brachytherapy (one fraction per day, two fractions per week on 2 non-consecutive days over 2 weeks), and CT scan was performed for planning before each fraction. Patients were treated in a supine position and remained under general anaesthesia throughout the procedure (from applicator insertion, CT image acquisition, treatment planning and delivery, to applicator removal). The Oncentra planning system was used. A Rotterdam or Utrecht applicator (ovoids and tandem) was used, and interstitial needles were not inserted for all cases during our initial phase of implementation of 3D brachytherapy for cancer of the cervix. A Foley catheter was inserted during the procedure. Patients were instructed to take oral bisacodyl 10 mg and self-administer a per rectal fleet enema the night before the procedure to ensure bowel emptying.

HR-CTV and the rectum were contoured according to the GEC-ESTRO guidelines.^{1,2} All patients underwent a diagnostic MRI prior to the first brachytherapy treatment, and MRI scans were used as a reference when contouring HR-CTV. We aimed to administer at least 6.5 Gy per fraction at HR-CTV D90, with dose to D2cc of the rectum limited to 4.8 Gy if possible (slightly higher dose was allowed if necessary to achieve a reasonable dose to HR-CTV D90; the degree of deviation allowed was decided on an individual plan basis). Point A and ICRU rectal points were also determined using the same set of CT images according to their definitions.

Data were retrospectively retrieved. The correlations between HR-CTV D90 and Point A, and also between D2cc of rectum and ICRU rectal points were determined by calculating the Pearson correlation coefficients. Two-sided paired *t*-test was used to determine if there were any statistically significant differences between HR-CTV D90 and Point A, and also between D2cc of rectum and ICRU rectal points. Prescriptions of brachytherapy were decided according to D90 of

HRCTV and D2cc of rectum, while Point A and ICRU rectal points were determined retrospectively for the purpose of data analysis.

This study was done in accordance with the principles outlined in the Declaration of Helsinki.

RESULTS

A total of 34 patients underwent CT-based brachytherapy for cancer of the cervix during the period January 2014 to September 2015 (number of plans, 136). All patients underwent brachytherapy for cancer of the cervix in 2015, and 15 (68.2%) out of 22 patients in 2014 were treated by CT-based brachytherapy (the rest were treated using a conventional 2D technique mainly due to logistic reasons). The age of the patients ranged from 36 to 83 years, with a mean age of 54.6 years. Patients were classified as FIGO stage IB (including IB1 and IB2, *n* = 4), IIA (including IIA1 and IIA2, *n* = 7), IIB (*n* = 11), IIIA (*n* = 1) or IIIB (*n* = 11), with 67.6% of patients with at least stage IIB for clinical staging at presentation. There was a wide variation in tumour size (no particular case selection for 3D brachytherapy), ranging from 2.3 cm to 8 cm in diameter (mean, 4.73 cm), with 15 (44.1%) over 5 cm in diameter. The volume of HR-CTV also ranged from 20.0 cm³ to 130.4 cm³, with a mean volume of 47.4 cm³.

The Point A dose ranged from 4.08 to 8.96 Gy, with a mean \pm standard deviation dose of 6.18 ± 0.96 Gy. HR-CTV D90 dose ranged from 4.67 to 8.16 Gy, with a mean of 6.60 ± 0.61 Gy. The dose of Point A was significantly lower (*p* < 0.001) than D90 of HR-CTV (6.36%) [Figure 1]. Nonetheless, a weak negative correlation was observed (*R* = -0.32; *p* < 0.0001) [Figure 2], implying that an increase in dose at Point A was associated with a decrease in D90 of HR-CTV. It suggests that Point A is not a good surrogate of HR-CTV dose (Table).

The ICRU reference rectal point dose ranged from 1.57 to 7.82 Gy, with a mean dose of 4.18 ± 1.24 Gy. D2cc of rectum dose ranged from 1.87 to 6.89 Gy, with a mean dose of 4.45 ± 0.94 Gy. The dose of ICRU reference rectal point was significantly lower (*p* < 0.01) than that of D2cc of rectum (6.07%) [Figure 3]. A positive correlation was observed, however (*R* = 0.67; *p* < 0.001) [Figure 4], implying that an increase in dose at the ICRU reference rectal point was associated with an increase in that at D2cc of rectum. The ICRU rectal point may tend to underestimate the dose to the rectum

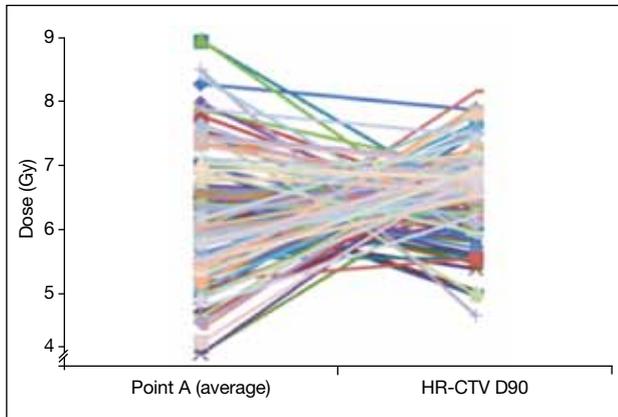


Figure 1. Difference between Point A and HR-CTV D90. Abbreviations: HR-CTV = high-risk clinical target volume ; D90 = minimum dose to 90% of HR-CTV.

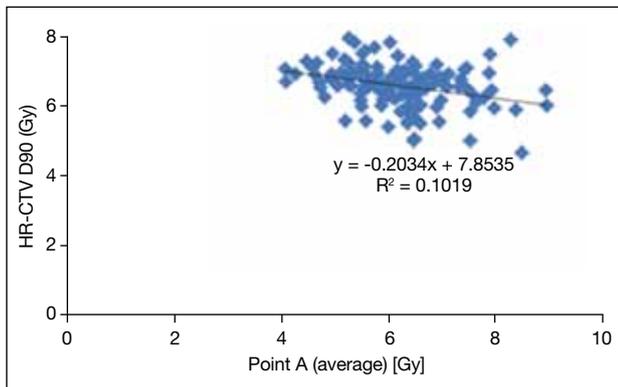


Figure 2. Correlation between Point A and HR-CTV D90. Abbreviations: HR-CTV = high-risk clinical target volume ; D90 = minimum dose to 90% of HR-CTV.

in a plan achieved by CT-based planning compared with D2cc according to our data (Table).

DISCUSSION

Ideally, 3D image-guided brachytherapy for cancer of the cervix uteri should be planned using MRI. Due to practical limitations, however, use of CT is considered an acceptable alternative, especially for tumours of <5 cm in diameter.⁷ At our institute, the advantage of having a CT scanner inside the brachytherapy suite may offset some of the disadvantages of using CT instead of MRI for brachytherapy treatment planning. The ‘geographical convenience’ also allows us to create a new plan for each fraction of brachytherapy instead of using the same plan for each subsequent fraction. We are now treating all cancer of the cervix patients using CT-based 3D image-guided brachytherapy. The reason for the minority of patients still being treated by conventional techniques during our initial phase of implementation of the service was largely logistical.

CT scans have been shown to be equivalent to MRI for defining organs at risk, but CT-defined HR-CTV volumes tend to be larger than those from MRI.⁸ All patients at our institute will have a diagnostic MRI before their first brachytherapy treatment so that a clearer idea can be gained concerning the extent of residual disease before first brachytherapy, thus improving contouring accuracy.

Our experience shows that 3D image-guided

Table. Summary of the relationship between Point A and HR-CTV D90, and also between ICRU reference rectal point and D2cc of the rectum.

| | Dose (Gy)* |
|---|---------------------------------|
| Point A | 6.18 ± 0.96 |
| HR-CTV D90 | 6.60 ± 0.61 |
| Pearson correlation coefficient: -0.32 (p < 0.0001) | |
| Two-sided paired t test: p < 0.001 | |
| Difference between Point A dose and HR-CTV D90 (Point A dose minus HR-CTV D90) | |
| Range | -2.98 to 3.83 |
| Mean | -0.42 ± 1.30 |
| 95% Confidence interval | -0.42 ± 0.22 = (-0.63 to -0.20) |
| Rectum (ICRU) | 4.18 ± 1.24 |
| Rectum (D2cc) | 4.45 ± 0.94 |
| Pearson correlation coefficient: 0.67 (p < 0.001) | |
| Two-sided paired t test: p < 0.01 | |
| Difference between ICRU reference rectal point and D2cc of rectum (ICRU reference rectal point dose minus D2cc of rectum) | |
| Range | -2.84 to 3.31 |
| Mean | -0.26 ± 0.93 |
| 95% Confidence interval | -0.26 ± 0.16 = (-0.42 to -0.11) |

Abbreviations: D90 = minimum dose to 90% of HR-CTV; HR-CTV = high-risk clinical target volume; ICRU = International Commission on Radiation Units and Measurements.

* Data are shown as mean ± standard deviation or range.

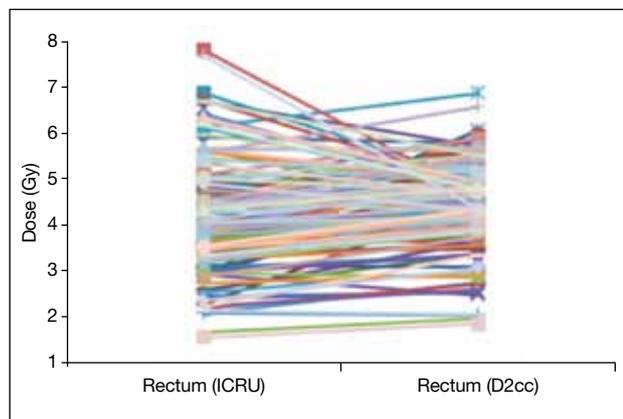


Figure 3. Difference between ICRU reference rectal point and D2cc of rectum.

Abbreviation: ICRU = International Commission on Radiation Units and Measurements.

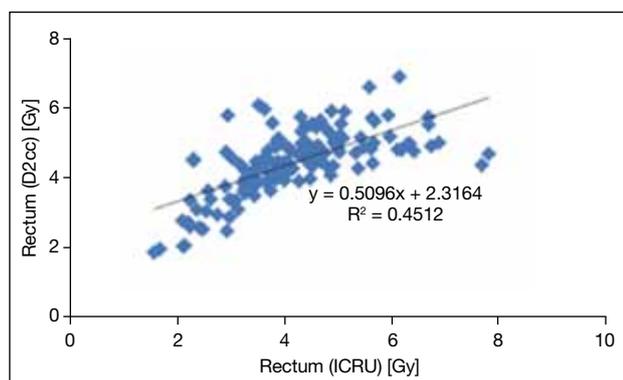


Figure 4. Correlation between ICRU reference rectal point and D2cc of rectum.

Abbreviation: ICRU = International Commission on Radiation Units and Measurements.

brachytherapy is feasible when the brachytherapy machine and CT scanner are in the same room, and patients can be kept under general anaesthesia throughout the procedure. Patient comfort is maximised and patient movement is minimised, thus treatment accuracy is maximised. The overall procedure time is not anticipated to be much longer as shown in our experience discussed previously,⁴ and thus should not affect the current waiting time for brachytherapy treatments.

Our study showed that Point A and D90 of HR-CTV tend to show a random relationship. This can be explained by the fact that Point A is a standard

applicator-affiliated location related to idealised anatomical geometry only. Although Point A is assumed to be located on the surface of a typical tumour, it may be located within the tumour for very large tumours at the time of brachytherapy, resulting in an apparently higher Point A dose compared with D90 of HR-CTV. It may also be located outside the tumour in patients with a small cervix and small tumour, which is not uncommonly seen in elderly women in our locality, resulting in an apparently lower Point A dose compared with D90 of HR-CTV. This may explain our weak negative correlation between Point A and D90 of HR-CTV. It has also been reported that dose to Point A could be lower than that of D90 for HR-CTV calculated using the image-based technique.⁵ As Point A and HR-CTV D90 apparently show a random relationship, an apparently satisfactory Point A dose may still have resulted in underdosing of tumour or overdosing of surrounding critical structures by delivering an unnecessarily high dose to the tumour, both of which may affect clinical outcome (in terms of tumour control and long-term complications, respectively). More long-term follow-up data are required to verify these issues.

Our study also showed that the ICRU rectal point may tend to underestimate the dose to the rectum in a plan achieved by CT-based planning compared with D2cc (by 6.07% in our study). Other studies have reported conflicting results, with the ratio of D2cc of rectum and ICRU rectal point ranging from 0.83 to 1.30.⁶ Despite this, it is reasonable to conclude that the ICRU rectal point is not a good estimation of the rectal dose received during 3D image-guided brachytherapy for cancer of the cervix uteri. Without accurate estimation of the rectal dose, the risk of long-term rectal complications cannot be well-determined. Long-term follow-up is needed to be certain about the clinical impact of such a difference.

The correlation between dose and response to treatment, in particular long-term local disease control and overall survival, would be interesting but requires long-term follow-up.

CONCLUSIONS

The brachytherapy plans from 2D and 3D image-guided planning techniques can differ widely. Traditional dose reporting parameters for 2D image-guided brachytherapy for cancer of the cervix uteri cannot be applied to reporting of doses in a brachytherapy treatment plan achieved by 3D image-guided planning. Use of 3D image-guided planning has resulted in more

accurate calculation of radiation doses to treatment target and the surrounding organs at risk, and thus potentially improves treatment outcome and reduces complications. Efforts should be made to move towards routine 3D brachytherapy planning for cancer of the cervix uteri, utilising the resources available in individual departments. Even a 'less than perfect' move can potentially benefit our patients.

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