

Preliminary experience on the implementation of computed tomography (CT)-based image guided brachytherapy (IGBT) of cervical cancer using high-dose-rate (HDR) Cobalt-60 source in University of Malaya Medical Centre (UMMC)

Z Jamalludin^{1,2}, U N Min¹, W Z Wan Ishak¹ and R Abdul Malik¹

¹ Clinical Oncology Unit, Faculty of Medicine, University of Malaya, Malaysia

² Medical Physics Unit, University Malaya Medical Center, Malaysia

E-mail: nmung@ummc.edu.my

Abstract. This study presents our preliminary work of the computed tomography (CT) image guided brachytherapy (IGBT) implementation on cervical cancer patients. We developed a protocol in which patients undergo two Magnetic Resonance Imaging (MRI) examinations; a) prior to external beam radiotherapy (EBRT) and b) prior to intra-cavitary brachytherapy for tumour identification and delineation during IGBT planning and dosimetry. For each fraction, patients were simulated using CT simulator and images were transferred to the treatment planning system. The HR-CTV, IR-CTV, bladder and rectum were delineated on CT-based contouring for cervical cancer. Plans were optimised to achieve HR-CTV and IR-CTV dose (D_{90}) of total EQD₂ 80Gy and 60Gy respectively, while limiting the minimum dose to the most irradiated 2cm³ volume (D_{2cc}) of bladder and rectum to total EQD₂ 90Gy and 75Gy respectively. Data from seven insertions were analysed by comparing the volume-based with traditional point-based doses. Based on our data, there were differences between volume and point doses of HR-CTV, bladder and rectum organs. As the number of patients having the CT-based IGBT increases from day to day in our centre, it is expected that the treatment and dosimetry accuracy will be improved with the implementation.

1. Introduction

Intracavitary brachytherapy (ICBT) is a treatment technique of placing radiation source near or in the tumour situated in body cavity. It is known as an integral part of cervical cancer treatment with external beam radiation therapy (EBRT) form the definitive radiation therapy for cervical cancer treatment. Conventional ICBT is based on 2-dimensional (2D) point-based planning determined by International Commissioning Radiation Units (ICRU) definition of prescription and organ at risk (OAR) points on orthogonal x-ray images. This was used for dose calculation irrespective of tumour and OAR location, size and shape, thus proved to results in inadequate target coverage and inaccurate OAR doses. With these limitations, the concept of ICBT prescription and dose evaluation has been developed from point-based planning and evaluation to volume-based technique.

As the new imaging technologies (computed tomography, magnetic resonance and ultrasound) played an important role in radiotherapy, the GEC-ESTRO has published recommendations for volume-based concept of the tumour and OAR with the use 3-dimensional images from magnetic resonance imaging (MRI), thus known as image guided brachytherapy (IGBT)[1]. MRI provides clear tissue



discrimination of tumour extension and OARs. However, not all oncology departments have an easy access for MRI, in comparison with computed tomography (CT) which is available in most departments. This give rise to three options of IGBT techniques, depending on departments' convenience and resources; a) MR image guided adaptive brachytherapy – MR images are acquired at each insertion for the purpose of treatment planning, b) MR-CT hybrid planning – MR images are acquired for the first fraction, followed by subsequent CT imaging and c) MR aided CT based planning – CT images are acquired at each insertion for the purposes of treatment planning [2]. We chose the last option for IGBT technique in our centre. This paper gives an overview on our experiences on implementing the IGBT with MR aided CT based planning technique.

2. UMMC - IGBT protocol

In comparison with 2D brachytherapy, IGBT requires: a) additional 3D images from MRI for treatment planning, b) complex CT simulation procedure and c) complex treatment planning techniques and dose evaluation hence more time and personnel were involved in the whole IGBT process. We outline some of the added procedures for IGBT on 2 patients treated in our centre.

2.1. MR images acquisition

A pre-brachytherapy MR image was acquired within 5 days of the first brachytherapy insertion. It was a T2-weighted transverse dataset with para-transverse, para-coronal and para-sagittal imaging orientation with slice thickness of less than 5mm.

2.2. CT simulation images acquisition

Patients underwent bowel preparation as per our institution protocol prior to the brachytherapy procedure. Rectal contrast was injected into the rectum, after the applicators insertion. A radio-opaque liquid consist of 50cc of normal saline plus 5cc of iodine contrast was injected into the bladder. Simulation images were acquired after 10 minutes of contrast injection to give time for the contrast to diffuse homogeneously with saline for better image acquisition as shown in figure 1 and 2.



Figure 1. Simulation image acquired after 5 minutes of contrast injection.



Figure 2. Simulation image acquired after 10 minutes of contrast injection.

The bladders' filling was maintained during the scanning process by clamping the catheter tube and released after the process was completed. Image scanning with 3.0mm slice thickness extending from the iliac crest was performed during each fraction with the applicator in place. A contiguous acquisition of CT slices with $\leq 3.0\text{mm}$ as suggested by GEC ESTRO working group was performed to avoid loss of tumor and OARs volumetric information and to obtain proper applicators reconstruction images [3]. A number of polystyrene base plates with different thickness as shown in figure 3, were placed under the applicator in conditions where: a) the applicators were not secured properly by the gauze packing and b) to push the bladder away from the applicators to reduce the dose to bladder during treatment. The CT images were exported digitally to the HDR Plus 2.6 brachytherapy treatment planning system.



Figure 3. Polystyrene base with variety of plate thicknesses.

2.3. Contouring

While a direct fusion between diagnostic MR images and planning CT datasets was not advised for target and OAR delineation for the MR aided CT based planning technique, a reference high-risk clinical target volume (HR-CTV) may be inferred on the planning CT images from the pre-brachytherapy MR and the clinical exam for the first fraction. The HR-CTV was purely a reference volume to monitor dose in a high-risk region. For subsequent fraction, HR-CTV delineation was also guided by the findings on CT images from the simulation images. The delineation was based on the GEC-ESTRO [1] recommendations.

For OAR delineation, a number of published reports show insignificant differences between OAR volumes and dose to the OARs for CT and MR based treatment planning. Therefore, planning CT images was used to accurately delineate OARs such as rectum and bladder.

2.4. Planning

Treatment planning was performed for each insertion, beginning with standard loading pattern using Manchester system approach. Plans were first normalised 100% to point A in order to achieve a pear shape dose distribution. Further optimisation was performed, by accounting the EBRT dose to result in a total of equivalent dose in 2Gy fractions (EQD₂) dose volume histogram (DVH) constraints of 80-90Gy ($\alpha/\beta=10$) for HR-CTV and 60Gy for intermediate risk CTV (IR-CTV), while keeping minimum dose to the most exposed 2cm³ volume (D_{2cc}) of bladder and rectum/sigmoid to total EQD₂ 90Gy ($\alpha/\beta=3$) and 75Gy ($\alpha/\beta=3$) respectively. If these objectives could not be achieved using the standard loading pattern, we further optimised the plan by adding or removing dwelling positions and adjusting the dwell times manually or using graphical optimisation to improve the dosimetry. Graphical optimisation is a free hand tool of the planning system which can be used to manually shaping the isodose lines. No inverse planning technique was used as this was not recommended by Tanderup [4] which can results in higher deviations from the standard loading shape and higher dose to non-contoured tissue.

For dosimetry evaluation, the following dose parameters were recorded: Point A, ICRU rectal and bladder point, the isodose encompassing 100% and 90% of the tumour target (D₁₀₀ and D₉₀) of HR-CTV and IR-CTV, the percentage of tumour target volume receiving 100% of the prescribed dose (V₁₀₀), D_{0.1cc}, D_{1cc} and D_{2cc} for rectum and bladder.

3. Results and discussion

Table 1 gives an overview of the tumor and OAR doses in total EQD₂ for both patients. Patient A underwent single phase of 3D conformal EBRT (3DCRT) while patient B had two phases of 3DCRT. Based on EQD₂ from EBRT, different IGBT fractionations were applied for both patients. However, the total EQD₂ from both EBRT and IGBT for tumors and OAR was ensured to fulfill the DVH constraints objectives set in our center as shown in table 1.

Table 1. Treatment fractionation schedule and total dose in EQD₂ of tumor and OARs for UMMC IGBT patients.

Patients	EBRT	IGBT	Total	Total	Total	Total
	fractionation schedule	fractionation schedule	HR-CTV D ₉₀ EQD ₂ (Gy)	IR-CTV D ₉₀ EQD ₂ (Gy)	Bladder D _{2cc} EQD ₂ (Gy)	Rectum D _{2cc} EQD ₂ (Gy)
A	Ph1: 1.8Gy x 27	7.0 Gy x 4	80.8	68.6	81.7	73.9
B	Ph1: 2.0Gy x 20	7.5 Gy x 3	80.4	67.9	82.8	65.9
	Ph2: 1.8Gy x 3					

Table 2 listed out the volume-based and point-based dose for tumor and OARs from each HDR fraction for both patients. It was noted that the D₉₀ EQD₂ dose for HR-CTV volume of < 30cc was higher by 32% of mean dose (p-value < 0.05) than ICRU point A dose in both patients and was lower for HR-CTV volume of > 40cc by 26% (p-value > 0.05). Tanderup *et al.* [5] found higher HR-CTV D₉₀ by 167% and lower by 36% for tumor of ≤ 31cc and > 31cc respectively. The HR-CTV volume in patient A and B were noted to decrease from the first fraction to last fraction by 52% and 30% respectively.

Table 2. Summary of doses to ICRU point, D₉₀ and D_{2cc} EQD₂ of tumor and organ at risks.

Patient	Fraction	Tumor volume (cm ³)	HR-CTV (Gy)		Bladder (Gy)		Rectum (Gy)	
			D ₉₀ EQD ₂	ICRU Point A	D _{2cc} EQD ₂	ICRU Point	D _{2cc} EQD ₂	ICRU Point
A	1	49.9	6.6	9.0	7.0	5.9	5.2	5.1
	2	30.5	5.0	4.7	4.3	2.9	4.9	5.8
	3	30.9	6.2	5.5	5.2	5.0	4.4	4.8
	4	25.9	6.6	5.4	4.4	3.9	3.4	4.6
B	1	27.5	7.8	5.7	6.4	5.8	4.5	5.1
	2	19.7	7.8	5.6	7.4	7.0	4.6	5.3
	3	19.3	8.0	4.3	5.8	5.0	4.6	5.3

For organ at risks dose analysis, we found that the D_{2cc} EQD₂ for bladder of both patients was higher than ICRU point dose by a mean of 13.5% (p-value=0.018) in comparison with rectum D_{2cc} EQD₂ which was lower than ICRU point dose by a mean of 12.3% (p-value=0.028). The result of dose comparison for bladder organ in this study was in agreement with studies by Onal *et al.* [6] and Madan *et al.* [7]. As the sample size was small (n=7), we expect to strengthen our findings based on future IGBT patients data. The total time spent for IGBT treatment starting from CT simulation to the end of patients' treatment time was in average of 3 hours in comparison of average 2 hours for conventional brachytherapy treatment.

4. Summary

As the international working groups on IGBT are working towards a better and standardised implementation of this technique throughout the world, we chose to perform the IGBT in the most convenient and practical way based on the resources available in our institution. With the implementation of IGBT, we aim to improve the of brachytherapy treatments quality by increasing the tumour dose, thus help in improving local tumour control while reducing the organs at risk doses.

References

- [1] Haie-Meder C, Pötter R and Limbergen E V 2005 Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. *Radiother Oncol* **74** 235-245
- [2] Cancer Care Ontario 2014 Imaging Strategies for Definitive Intracavitary Brachytherapy of Cervical Cancer: Recommendation Report. June 2014
- [3] Pötter R 2002 *Vienna method*. In: Gerbaulet A, Potter R, Haie-Meder C, editors. Cervix cancer. GEC ESTRO handbook of brachytherapy. Brussels: ESTRO p 331–8
- [4] Tanderup K 2014 Physics aspects of treatment planning intracavitary +/- interstitial techniques in cervix cancer. ESTRO Teaching Course Image Guided Radiotherapy & Chemotherapy in Gynaecological Cancer. Firenze
- [5] Tanderup K, Nielsen S K and Nyvang G B 2010 From point A to the sculpted pear: MR image guidance significantly improves tumour dose and sparing of organs at risk in brachytherapy of cervical cancer. 2010 *Radiother Oncol* **94** pp 173-180
- [6] Onal C, Arslan G and Topkan E 2009 Comparison of conventional and CT-based planning for intracavitary brachytherapy for cervical cancer: Target volume coverage and organs at risk doses *J. Exp & Clinical Cancer Research* **28** 95
- [7] Madan R, Pathy S and Subramani V 2014 Comparative Evaluation of Two-dimensional Radiography and Three Dimensional Computed Tomography Based Dose-volume Parameters for High-dose-rate Intracavitary Brachytherapy of Cervical Cancer: A Prospective Study *Asian Pacific J. Cancer Prevention* **15**:4717-21