

Kertas Asli/Original Articles

Doses to Organs at Risk Calculated Using Plato and Oncentra Softwares in Intracavitary Brachytherapy

Dos kepada Organ Berisiko yang Dikira Menggunakan Perisian Plato dan Oncentra bagi Brakiterapi Intrakaviti

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ABSTRACT

This is a retrospective study, the organ doses of the bladder and the rectum were compared between routine PLATO V14.2.3 (Nucletron B.V., Veenendaal, The Netherlands) and newer version software Oncentra MasterPlan (OMP) V4.3 (Nucletron B.V., Veenendaal, The Netherlands) treatment planning systems (TPS). The treatment data of 32 intracavitary brachytherapy patients at Hospital Universiti Sains Malaysia from January 2010 to June 2015 were used. These data sets were used for catheter reconstruction for both PLATO and OMP TPS followed by independent verification using Excel. There was no significant difference in mean doses to organs at risk (OARs) that calculated by both TPS ($p > 0.05$). The mean percentage of doses calculated by PLATO TPS for bladder and rectum were $66.58 \pm 27.42\%$ and $46.27 \pm 14.47\%$, respectively. While, the mean percentage of doses for bladder and rectum calculated by OMP TPS were $65.68 \pm 24.24\%$ and $46.46 \pm 16.66\%$, respectively. The mean percentage difference in doses comparison between independent verification calculation and PLATO TPS was $1.96 \pm 6.00\%$ and then became $6.37 \pm 5.17\%$ when it was compared with OMP TPS. Overall, the dose calculation differences for both versions of TPS were within the range recommended by Nuclear Regulatory Commission (NRC). The dose calculations of the two treatment planning systems showed good agreement and both could be used in planning intracavitary brachytherapy for cervical cancer. Whereas, Excel based independent verification is suitable to be implemented as routine dose verification programme prior to treatment delivery.

Keywords: Cervical intracavitary brachytherapy; organs at risk; PLATO; Oncentra; treatment planning system

ABSTRAK

Ini ialah kajian retrospektif, dos organ pundi kencing dan rektum dibandingkan antara sistem perancangan rawatan rutin PLATO V14.2.3 (Nucletron B.V., Veenendaal, The Netherlands) dan versi perisian baharu Oncentra MasterPlan (OMP) V4.3 (Nucletron B.V., Veenendaal, The Netherlands). Data rawatan untuk 32 pesakit brakiterapi intrakaviti di Hospital Universiti Sains Malaysia dari Januari 2010 hingga Jun 2015 telah digunakan. Data ini telah digunakan untuk rekonstruksi kateter bagi TPS PLATO dan OMP diikuti dengan pengesahan berdikari menggunakan Excel. Tiada perbezaan yang ketara bagi dos purata yang dikira menggunakan kedua-dua TPS ($p > 0.05$) kepada organ berisiko. Peratusan purata dos yang dikira oleh TPS PLATO untuk pundi kencing dan rektum ialah $66.58 \pm 27.42\%$ dan $46.27 \pm 14.47\%$ masing-masing. Manakala peratusan purata dos kepada pundi kencing dan rektum yang dikira oleh TPS OMP ialah $65.68 \pm 24.24\%$ dan $46.46 \pm 16.66\%$. Perbezaan peratusan purata bagi perbandingan dos antara pengiraan pengesahan berdikari dan TPS PLATO ialah $1.96 \pm 6.00\%$ dan menjadi $6.37 \pm 5.17\%$ apabila dibandingkan dengan TPS OMP. Secara keseluruhan, perbezaan pengiraan dos untuk kedua-dua edisi TPS adalah dalam julat yang dicadangkan oleh Nuclear Regulatory Commission (NRC). Pengiraan dos oleh kedua-dua sistem perancangan rawatan menunjukkan persamaan yang baik dan boleh digunakan dalam perancangan brakiterapi intrakaviti untuk kanser serviks. Manakala pengesahan berdikari yang berasaskan Excel sesuai dilaksanakan sebagai program pengesahan dos sebelum pelaksanaan rawatan.

Kata kunci: Brakiterapi intrakaviti serviks; organ berisiko; PLATO; Oncentra; sistem perancangan rawatan

INTRODUCTION

According to the International Agency for Research on Cancer (IARC), the specialized cancer agency of the World Health Organization (WHO) (2014), cervical cancer is one of the serious threats to all women's lives. It is estimated that over a million women worldwide currently have cervical cancer. In 2012, 528 000 new cases of cervical cancer were diagnosed, 266 000 women died of the disease, and nearly 90% of them were from low- to middle-income countries. The ranking of cervical cancer fall the fourth most common cancer affecting women worldwide, after breast, colorectal, and lung cancers.

Ministry of Health Malaysia reported that, the five most common cancers among female patients were breast 32.1%, colorectum 10.7%, cervix uteri 7.7%, ovary 6.1% and lung 5.6% in the registry report from year 2007 until 2011 (Azizah et al. 2015). In the recently released Malaysia Cancer Registry Report by Azizah et al. (2019), cancer of cervix uteri (6.2%) still remained as the 3rd most common cancer among women for the period 2012 - 2016.

As we concerned, the treatment for cervical cancer should be more advance and up to date. The treatment for cervical cancer usually uses external beam radiotherapy (EBRT) and brachytherapy. Brachytherapy is a technique in which sealed sources of ionising radiation are placed within the patient, in or approximately close to the target area (cancer). Brachytherapy could be applied either alone or more commonly, as a part of a multi-modality approach with EBRT, surgery and with or without chemotherapy (Brahmacharimayum & Tomcha 2010). In this study, the bladder and the rectum were classified as the organs at risk (OAR) because they were in the close proximity to the target area. The applicator placement with respect to the location of the rectum and the bladder is therefore very important to keep the radiation dose to these critical organs as low as possible as recommended by Podgorsak (2005).

The OMP TPS was installed in the high dose rate (HDR) brachytherapy unit, Hospital Universiti Sains Malaysia. The purpose of this study was to compare the dose in percentage difference calculated with PLATO (Nucletron B.V., Veenendaal, The Netherlands) and OMP (Nucletron B.V., Veenendaal, The Netherlands) in practice at Hospital Universiti Sains Malaysia. The dose calculation algorithm in the PLATO V14.2.3 (Nucletron B.V., Veenendaal, The Netherlands) and the Oncentra MasterPlan (OMP) V4.3 (Nucletron B.V., Veenendaal, The Netherlands) were based on the protocol of AAPM Task Group 43 (AAPM TG-43) (Nath et al. 1995) and the updated AAPM TG-43, respectively (Rivard et al. 2004). Both TPSs used a slight different algorithm approaches. Some minor inconsistencies in the original AAPM TG-43

protocol were corrected in the algorithm of OMP TPS. The updated protocol also emphasized the importance of the same active length, L of line source in dose calculations. The difference between 2 versions of TPS was that the negative value z-coordinate was used in PLATO TPS while the OMP TPS used positive value for z-coordinate. At the moment, these two versions of TPS are still being used in the government and the private hospitals in Malaysia.

Independent dose verification of treatment plan was performed in this study as the HDR brachytherapy Quality Assurance (QA). The aim of this program was to determine the accuracy of doses calculated by 2 versions of TPS. Examples of the software tools used for dose verification in 2-D brachytherapy for cervical cancer was the Excel software developed by Carmona et al. (2010) and the VC++ software by Kumar et al (2008). This study adopted the Excel software developed by Carmona et al. (2010).

MATERIALS AND METHODS

In this retrospective study, the data sets of 32 patients (2 fractions for each patient; total 64 fractions) in the form of 2D orthogonal radiograph data of high dose rate intracavitary brachytherapy (ICBT) were used. These selected cervical cancer patients were treated in Hospital Universiti Sains Malaysia between January 2010 and June 2015 with ethical approval had been obtained (JEPeM no: USM/JEPeM/140374). These patients were previously treated with a dose of 45 Gy delivered in 20 to 25 fractions over a period of 4 or 5 weeks by Siemens Primus linear accelerator (Siemens Medical Systems, Concord, CA, USA) using 6 MV photon followed by 2 fractions of ICBT performed 1-2 weeks after the completion of EBRT. The prescribed dose was 9 Gy to point A for each fraction. In our centre, we used Nucletron microSeletron HDR V.3 (Elekta A.B., Stockholm, Sweden) brachytherapy afterloader. A single source of Ir-192 Nucletron MicroSeletron V.2 (Curium Nucletron B.V., Veenendaal, The Netherlands) was used in the HDR machine.

All the selected patients underwent ICBT procedure using Fletcher-Williamson metal ovoid applicators set which consisted of a tandem and a pair of ovoid. The combination of ovoid size and tandem angle was chosen according to a patient's anatomy. Packing was done to set the applicators in place and to avoid any shifting or changes in the geometry of the applicators placement. Foley balloon was inserted and inflated with 7cc radio-opaque dye and pulled to sit on the bladder trigon. A rectum and a bladder markers were inserted into each patient. All applications and procedures were performed under general anesthetic.

Conventional simulations were performed using Nucletron Simulix Evolution simulator (Nucletron B.V., Veenendaal, The Netherlands). Anterior-posterior and lateral orthogonal radiographs data sets were taken for every application. Both images were transferred to the PLATO brachytherapy treatment planning workstations for planning and dose calculation.

Applicator reconstruction was performed in PLATO TPS workstation. The doses at point A and B were prescribed as recommended by the Manchester system. The bladder and the rectum dose points were defined from the lateral projection as the points of the closest approach of the balloon for the bladder point and the rectal marker for the rectum point. The left to the right positions were taken to be in the centre of the bladder balloon and the rectal marker as shown in Figure 1 (Chassagne et al. 1985). As a standard hospital practice, the bladder and rectum point doses were kept to less than 80% and 60% of the dose prescribed to point A, respectively for each fraction.

All 64 sets of images (AP and lateral orthogonal radiographs) were transferred to the OMP TPS. The same parameters of reconstruction of applicators, localization of point A and OAR point doses as in PLATO TPS workstations were performed in the OMP workstation as in Figure 2 and Figure 3. The parameters such as dwell time, dwell positions and numbers of catheter applied were kept the same for each individual patient in the re-planning processes using OMP TPS. Doses to the target area and the OAR points were calculated by the software for the post-treatment applicator positions for evaluation purpose.

Independent dose verification of treatment plan is an essential part of HDR brachytherapy Quality Assurance. In our centre, the independent dose verification was performed using a spreadsheet in Microsoft Excel software (Version 2002). The Excel spreadsheet in this work was used with

permission from Carmona et al. (2010). The purpose of the independent verification calculation in this study was to verify the point dose calculations in the brachytherapy treatment planning system by using the Excel based on the dose verification programme. The dose calculations were performed based on Microsoft Excel software (Version 2002) according to the standard TG-43 protocol. The coordinates of each rectum and bladder points from 2 versions of TPS were transferred into Excel spreadsheets. In these spreadsheets, the sagittal, the transverse and the coronal planes were obtained. Meanwhile, the organs at risk markers were required for calculating the individual plans of the brachytherapy treatment planning system as shown in Figure 4 and Figure 5.

The evaluations of the dose were recorded and analysed accordingly. Paired t-tests were used as the parametric test to compare the means of OAR point doses calculated by PLATO TPS with that calculated by OMP TPS with significance if p -value < 0.05 .

RESULTS

Table 1 illustrates calculated mean doses (Gy) using PLATO and OMP treatment planning systems for two reference points (bladder and rectum). These data were corresponded to the data for fraction 1 and fraction 2. For fraction 1, the mean dose calculated by OMP TPS was 0.02 Gy higher than that calculated using PLATO TPS. The same result was observed for fraction 2. The percentage differences of mean doses between PLATO and OMP treatment planning systems for all reference points were 0.48% (fraction 1) and 0.33% (fraction 2). In overall, both fractions of treatment showed 0.02 Gy (0.39%) of difference. PLATO and OMP TPS showed consistency

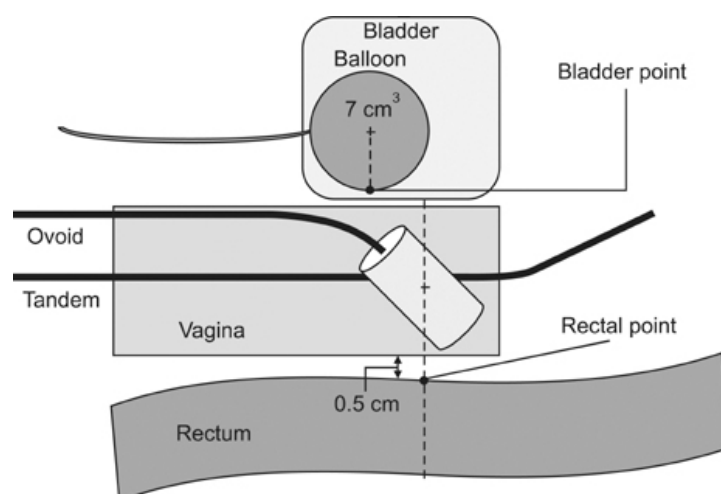


FIGURE 1. Localization of the bladder and the rectum markers according to International Commission on Radiation Unit and Measurements Report 38 (Chassagne, D et al. 1985).

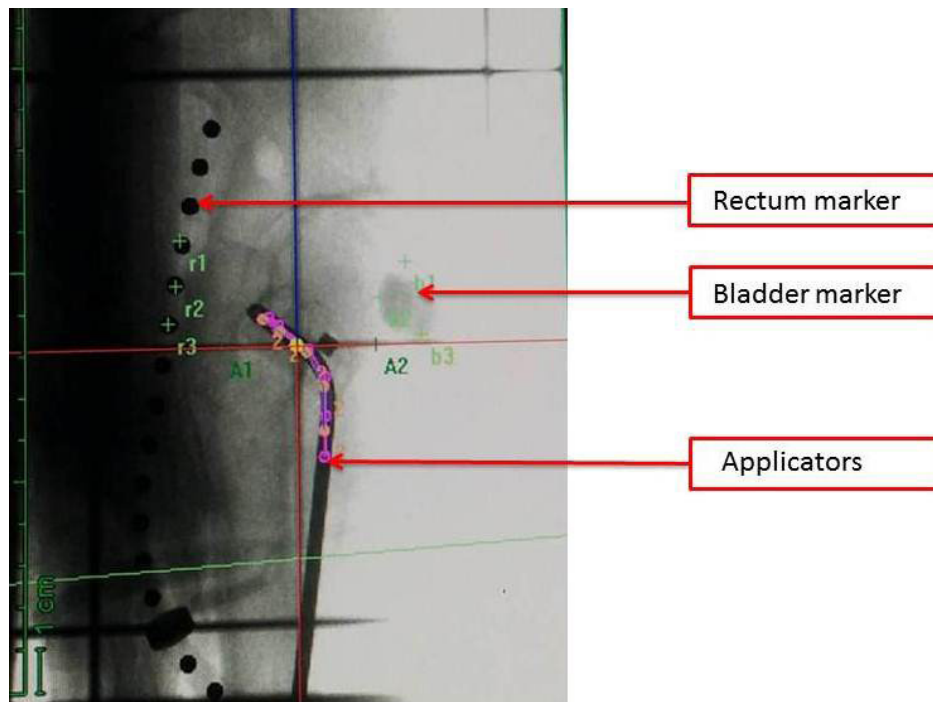


FIGURE 2. The reconstruction radiograph image including applicators, rectum and bladder markers from lateral position.

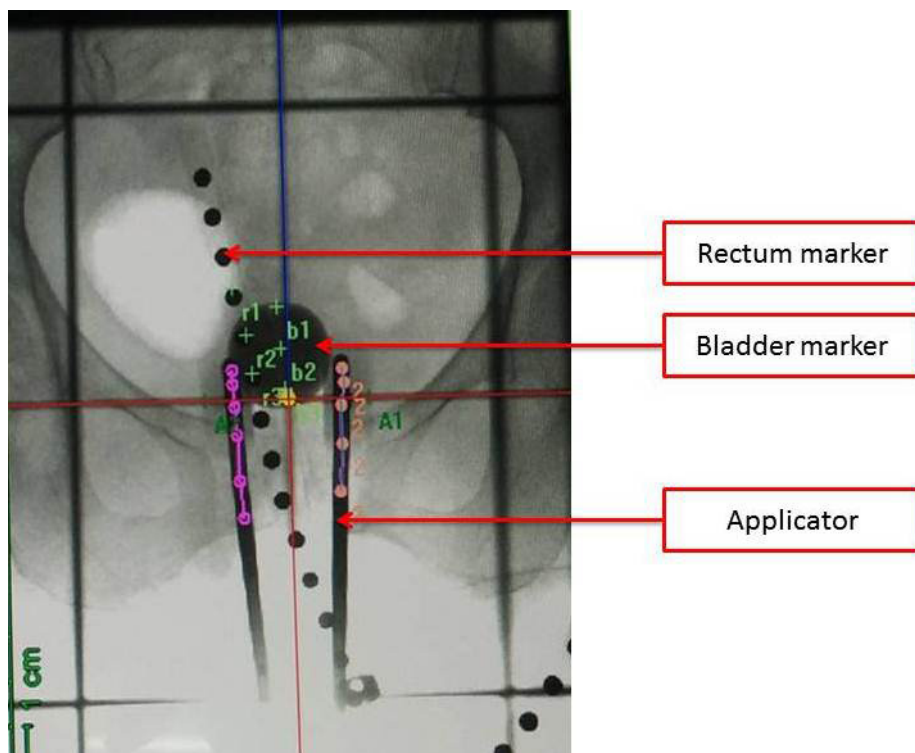


FIGURE 3. The reconstruction radiograph image including applicators, rectum and bladder markers from AP position.

in dose calculation with discrepancy within 1% and the difference in calculations was not significant ($p>0.05$).

Table 1 also shows the mean percentage dose for rectum obtained via PLATO and OMP TPS which showed $46.27 \pm 14.47\%$ and $46.46 \pm 16.66\%$, respectively.

Meanwhile, the mean percentage dose observed for the bladder by PLATO and OMP TPS were $66.58 \pm 27.42\%$ and $65.68 \pm 24.24\%$, respectively. The difference of organ dose between 2 versions of TPS was not significant ($p>0.05$).

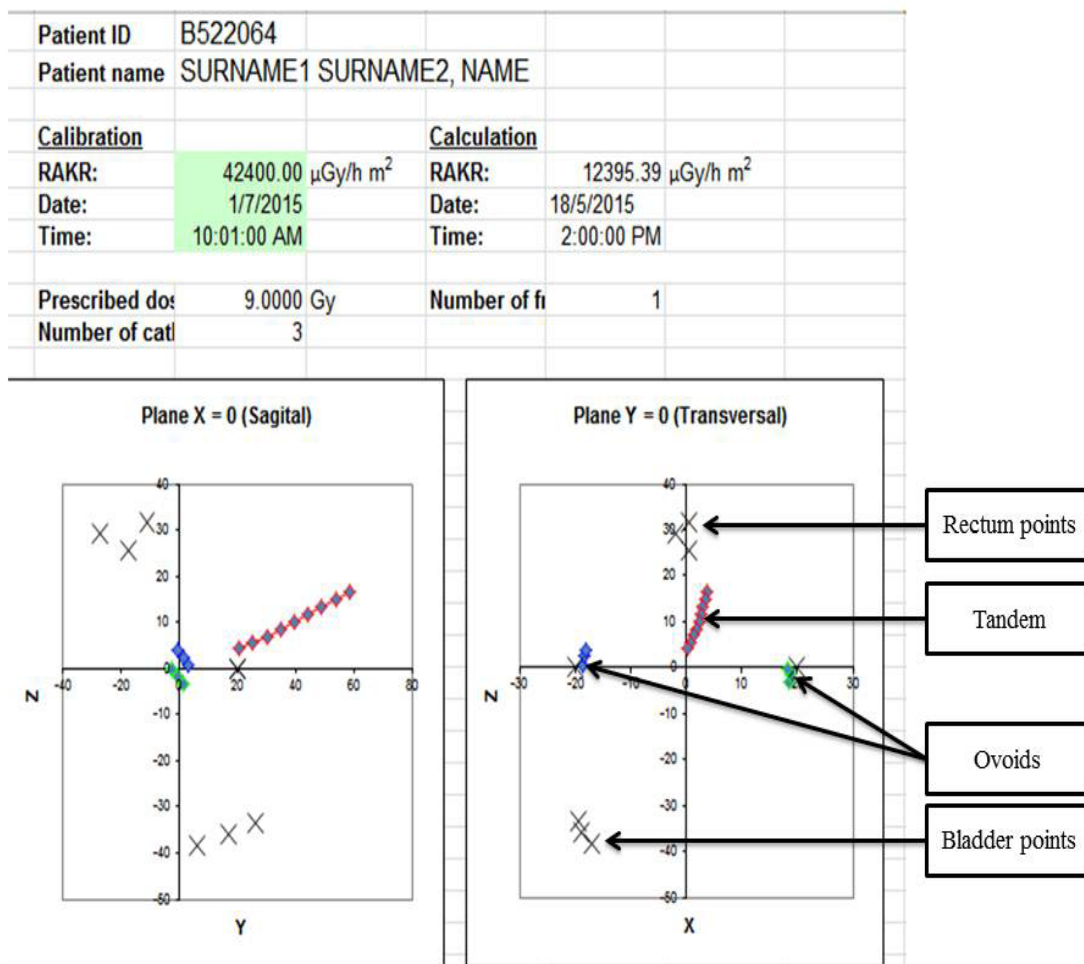


FIGURE 4. The screenshots of sagittal and transversal planes including the ^{192}Ir source calibration details from the spreadsheets.

The rectum and the bladder doses (in percentage) that exceeded the dose limit are illustrated in Figure 6 and Figure 7, respectively. The treatment plan that produced maximum organ dose and maximum difference on OARs that calculated by 2 versions of TPS were identified. There were 9 out of 64 (14%) plans as calculated by PLATO TPS and 13 out of 64 (20%) as calculated by OMP TPS treatment plans that exceeded dose limit rectum 60%. While for the bladder, 18 out of 64 (28%) plans and 16 out of 64 (25%) plans that calculated by PLATO TPS and OMP TPS respectively exceeded dose limit 80%.

Table 2 shows the mean percentage discrepancy of mean dose (Gy) between PLATO TPS and independent verification calculation was determined as $1.96 \pm 6.00\%$. In overall, the mean percentage discrepancy of mean dose (Gy) between OMP TPS and independent verification calculation was higher with value of $6.37 \pm 5.17\%$ as shown in Table 2.

DISCUSSION

In their study of comparing treatment planning systems for HDR, Elhanafy et al. (2001) revealed the dose difference between Nucletron NPS and newer PLATO for all reference points of 2 cases ranged from 1% to 4%. Similarly, the results reported by Hardev et al. (2012) showed the mean of the percentage differences of doses between PLATO and OMP for all 10 patients in bladder and rectum were found to be less than 1.3% and 2.1%, respectively. So, when comparing PLATO and OMP in this study, the differences of mean dose were 0.02 Gy (0.48%) in fraction 1 and 0.02 Gy (0.33%) in fraction 2 with $p > 0.05$ as tabulated in Table 1. If analysed the mean difference of 2 fractions for both TPS, the mean difference was again 0.02 Gy (0.39%) with $p > 0.05$. In this study, the data set of 32 patients was used in planning and analysed, hence, it helped in providing result that can conclude there

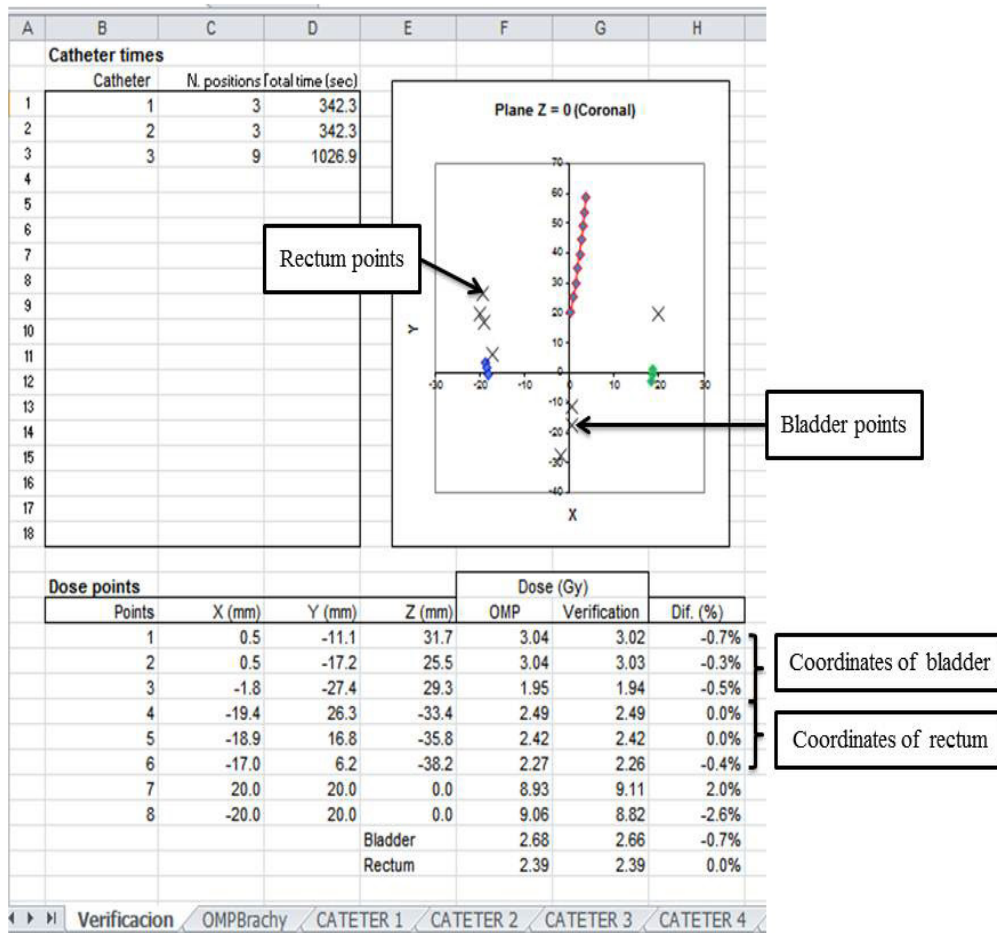


FIGURE 5. The coronal plane including rectum and bladder points from the spreadsheets by Microsoft Excel software.

TABLE 1. Satisfaction score differences between PLATO and OMP treatment planning systems for different fractions and organs at risks.

Dose per Fraction (Gy)	PLATO Mean (SD)	OMP Mean (SD)	Mean score difference (95% CI)	t-statistic (df)	p-value*
Fraction 1	4.16 (1.30)	4.18 (1.50)	-0.02 (-0.29, 0.26)	-0.125 (63)	>0.05
Fraction 2	6.09 (2.63)	6.11 (2.29)	-0.02 (-0.43, 0.39)	-0.104 (63)	>0.05
Fraction 1 & Fraction 2	5.13 (2.28)	5.15 (2.16)	-0.02 (-0.26, 0.22)	-0.156 (127)	>0.05

*Paired t-test; normality assumption is assumed

Organ Dose (%)	rICRU PLATO mean (SD)	rICRU OMP mean (SD)	Mean diff. (95% CI)	t-statistic (df)	p-value*
Rectum	46.27 (14.47)	46.46 (16.66)	0.19 (-0.57, 0.97)	0.505 (126)	>0.05
Bladder	66.58 (27.42)	65.68 (24.24)	0.91 (-8.15, 9.96)	0.198 (126)	>0.05

*Independent t-test

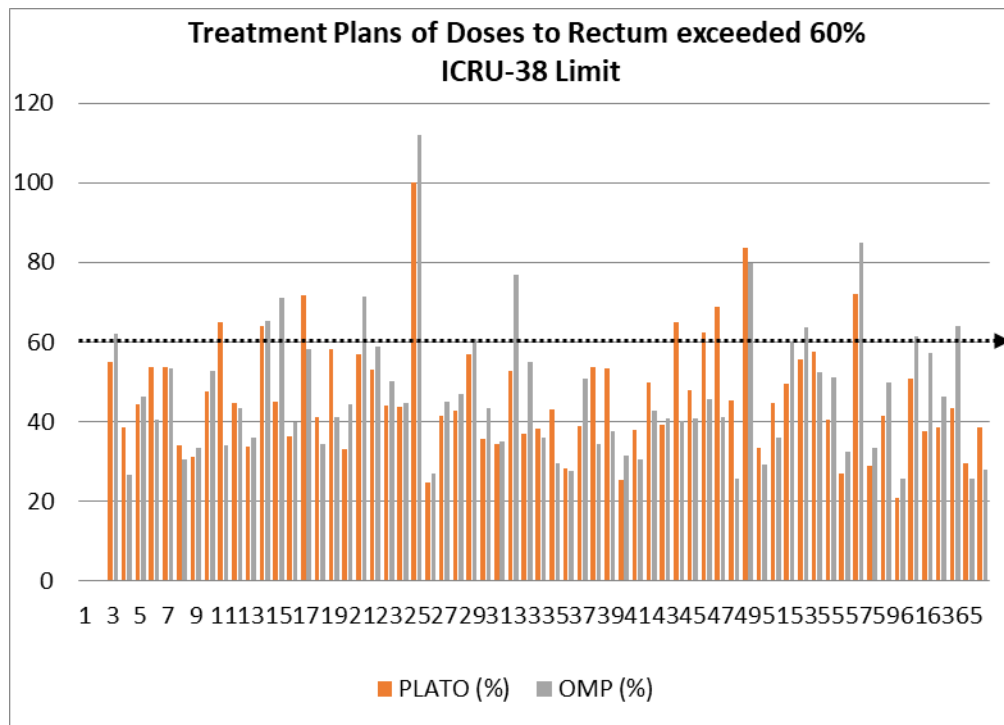


FIGURE 6. Treatment plans with rectum doses that exceeded the dose limit of 60% according to ICRU-38.

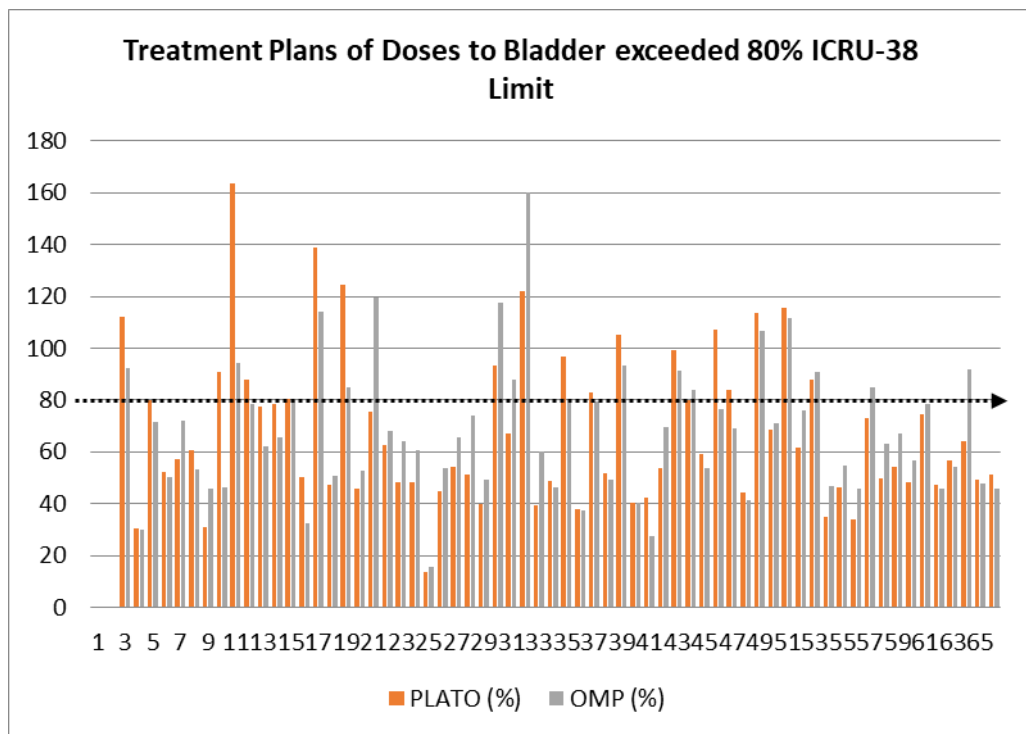


FIGURE 7. Treatment plans with bladder doses that exceeded the dose limit of 80% according to ICRU-38.

TABLE 2 Mean, standard deviation and mean percentage differences of calculated doses between the PLATO TPS and the OMP TPS with the independent verification software in Gy

	Mean PLATO (SD)	Mean Independent verification calculation (SD)	Mean percentage difference (%) (SD)	(Min, Max)
Score	5.19 (2.21)	5.13 (2.28)	1.96 (6.00)	(-0.17,14.08)
	Mean OMP (SD)	Mean Independent verification (SD)	Mean percentage difference (%) (SD)	(Min, Max)
Score	5.15 (2.16)	5.49 (2.38)	6.37 (5.17)	(-0.16, 2.01)

was no significant difference in calculations by both TPS systems and the percentage difference of mean dose was determined as less than 1%.

Significance of p-value was determined by using statistical analysis (SPSS software) with $p < 0.05$, which was considered as significant finding. There was no significant difference in the mean bladder and rectum doses ($p > 0.05$) when calculated separately using PLATO TPS and OMP TPS. The same finding observed in the study by Hardev et al. (9), the results were found no discrepancy with $p > 0.05$. For this study, dose limits were set for the dose of critical organs with less than 60% for rectum and less than 80% for the bladder compared to the dose at point A. The mean percentage rectum doses obtained via PLATO and OMP TPS were $46.27 \pm 14.47\%$ and $46.46 \pm 16.66\%$, respectively. Meanwhile the mean percentage dose of bladder as calculated by PLATO and OMP TPS were $66.58 \pm 27.42\%$ and $65.68 \pm 24.24\%$, respectively as tabulated in Table 1. Therefore, percentages of doses for both organs at risks calculated by PLATO and OMP systems in this study were within the recommended dose range as recommended by ICRU Report 38 (1985) with no significant difference ($p > 0.05$).

Figure 6 and Figure 7 display the visual inspection of the organs doses (rectum and bladder) calculated by PLATO and OMP TPS in percentage respectively. In Figure 6, 5 rectum points gave differences in percentage dose above 20%, with that rectum point plan no. 9 showed maximum difference of 31%. In plan no.23, the rectum dose was 100% (PLATO) and 112.11% (OMP) and this plan gave the highest percentage dose for rectum in this study. Meanwhile, Figure 7 shows 12 bladder points with differences in percentage dose above 20%, with the maximum value of bladder point difference was 69.33% (plan no.9). Plan no. 9 also showed the highest bladder dose calculated by PLATO TPS (163.56%) while plan no. 30 showed the highest bladder dose by OMP (160%). Hence, two versions of TPS could give different point doses on some cases most probably due to different coordinate approaches been applied in the formalism during treatment planning. The difference between the 2 versions of TPS was that the negative z-coordinate was used in PLATO TPS while the OMP TPS used positive z-coordinate. This is

crucially important to ensure OARs of each patient should receive dose within recommended limit to prevent short or long term radiation effects. Under this circumstance, independent verification is highly recommended as a QA programme for dose analysis followed by dose optimization for rectum and bladder prior to the treatment delivery.

There were 13 out of 64 (20%) treatment plans with rectum that exceeded the dose limit 60% as calculated by OMP TPS, which was 6% higher than 9 out of 64 (14%) plans that calculated by PLATO TPS. The study finding also showed that, there were 18 of 64 (28%) treatment plans with bladder dose that exceeded the dose limit 80% as calculated by PLATO TPS, which was only 3% higher than 16 out of 64 (25%) plans that calculated by OMP TPS. Thus, this study proved that the dose calculation of PLATO TPS and OMP TPS could cause a number of treatment plans which exceeded dose limits of two OARs studied with differences of 6% (rectum) and 3% (bladder). Once again, the Excel based dose verification programme should be performed on TPS calculated doses for dose optimization purpose.

In a study by Kumar et al (2008), their VC++ software tool could get most of the TPS calculated doses and verification code calculated doses agreed within 3%. According to Carmona et. al (2010), the deviations of their results were less than 2%. The finding of this study is comparable with that obtained by Kumar et al. (2008), with most of the organ doses calculated by PLATO (60.9%) and OMP (48.4%) showed deviations within 3%. The Nuclear Regulatory Commission (NRC) suggested that the threshold level of differences was within 20% deviation as the minimum goal for brachytherapy. The results of this study showed that the mean percentage differences were 1.96% and 6.37%, respectively for PLATO TPS and OMP TPS. Hence, when comparing with independent calculation, these values tabulated in Table 2 were within the range recommended by NRC.

CONCLUSION

The results of this study exhibited the differences in dose calculations for OAR by the two different versions of

treatment planning systems with determined differences were within acceptable NRC limits and the treatment plans can be generated with either system in brachytherapy department. Thus, the updated version of OMP TPS could supersede or accommodate the old version of PLATO TPS anytime without any doubt because the number of treatment plans exceeded dose limits differed in 3% (bladder) and 6% (rectum) among these TPS. The percentages of doses for these two OARs calculated by PLATO and OMP systems were also within the recommended dose range as recommended by ICRU Report 38 (1985). The mean percentage rectum doses calculated by PLATO and OMP TPS were $46.27 \pm 14.47\%$ and $46.46 \pm 16.66\%$, respectively ($p > 0.05$). While the mean percentage dose of the bladder as calculated by PLATO and OMP TPS were $66.58 \pm 27.42\%$ and $65.68 \pm 24.24\%$, respectively ($p > 0.05$). This finding is crucially important for developing countries to take into consideration when financial factor is the main concern especially when some hospitals can't afford to purchase the latest software available in the market. This study strongly recommends Excel based independent verification programme to be executed as routine Quality Assurance programme on case by case basis where anatomical variations among patients can play role in determining the doses to OARs. Hence, dose verification followed by optimization prior to delivery of ICBT is required.

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