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Development and Evaluation of a RapidPlan-Based Semi-Automated Learning System for Prostate Cancer Treatment Planning

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Abstract. Prostate cancer is an increasingly common disease in Mexico, and its treatment with external beam radiotherapy is becoming more frequent. Intensity modulated radiation therapy (IMRT) and volumetric intensity modulated arc therapy (VMAT) techniques use inverse planning, which depends on the experience of the planner or medical physicist. To improve treatment and planning time plans, semiautomated learning, or Knowledge Based Planning (KBP) systems have been developed. The RapidPlan KBP system (Varian Medical Systems, Palo Alto, CA) is a system that uses information from previous treatment plans to generate customized plans from dose volume histogram estimate (DVHE) bands for a new treatment plan. A total of 35, two stage prostate cancer plans were recorded by ABC Medical Center database and were applied to train and test the semiautomated model. Seven new plans were created from this RapidPlan (RP) model, which were compared with those obtained by a manual planner (MP), thus verifying the veracity and efficiency of the tool. The Wilcoxon signed rank test was performed between PM and PR for the dosimetric parameters, and $p<0.05$ was statistically significant. The results are very comparable to those obtained by the planner, and it is concluded that the model is effective in generating clinically acceptable and high-quality treatment plans, also reducing planning times.

Keywords: Prostate cancer, automatic learning system, RapidPlan.

1 Introduction

Cancer is a disease that continues to be the leading cause of death worldwide, with almost 10 million deaths attributed to this disease in 2020, according to the World Health Organization (WHO) [1]. In Mexico, prostate cancer (PC) is the leading cause of malignant tumor in the male population over 60 years of age, according to records presented by the National Institute of Statistics and Geography (INEGI) [2], which is commonly treated with radiotherapy.

A safe method in the treatment of PC for dose escalation is by employing the Elekta IMRT or Varian RapidArc VMAT techniques [3, 4] which allow a homogeneous radiation dose to be administered to the palpable tumor volume (PTV), while limiting the dose to organs at risk (OAR), such as the bladder, rectum, femoral heads, bowel, and penile bulb [5], through the dose volume histogram (DVH) at the time of planning. However, there is no standard metric to objectively assess the quality of a treatment plan that relates the dose administered to potential treatment success and adverse effects known in advance [6].

Treatment planning for prostate cancer is a crucial process in which the aim is to obtain the best quality [7] and the best treatment for the patient with the lowest possible risk of adverse side effects [8]. Currently, planning based on the experience of a planner is the most common way of performing the treatment plan [9], but its quality and efficiency can vary widely [10]. Currently, developing an IMRT and VMAT plan involves starting from scratch and optimizing it using a time consuming and subjective trial and error approach [11].

Moreover, this approach may not achieve the optimization needed to optimally preserve OARs. The entire IMRT or VMAT treatment planning process can take several hours per case to reach a clinically acceptable plan [12]. This process involves finding a balance between the conflicting constraints of achieving homogeneous coverage of the prostate target volume and minimizing dose to adjacent normal critical structures [13]. Although a plan may be considered acceptable from a clinical standpoint, it may be far from optimal if dose to normal tissueis not minimized as much as possible [11].

To address this variability in treatment plan quality and improve the efficiency of the planning process, semiautomated learning systems using knowledge-based planning (KBP) [14, 16], such as RapidPlan (RP), have been developed. These systems use information from previous treatment plans to generate personalized and optimized plans for new patients, regardless of the planner performing the plan [9, 10].

In this context, the aim of this work is to develop a planning model based on prior knowledge of patient treatment plans and to compare the results of treatment plans generated by the semiautomated learning system (RP) with manual plans (MP), both in terms of treatment plan quality and planning time. The results obtained could improve the efficiency and quality of PC treatment planning, reduce time and ultimately improve patient care.

2 Related Work

The clinical implementation of IMRT and VMAT radiotherapy techniques increased considerably in the last two and last decade, respectively [4]. Both techniques aim to provide the optimal dose distribution calculated by an inverse planning process. To achieve this, optimization engines use numerical targets derived from clinical objectives, i.e., dose volume relationships linked to the management of tumor control probabilities and healthy tissue complications [14].

The quality of the plan is highly dependent on the knowledge and experience of the planners, as well as the institutional resources available to them [17]. Reverse planning can be a time consuming process [18]. The reverse planning process used in IMRT and

VMAT planning can make it difficult for inexperienced or inexperienced planners to know whether a plan is fully optimized or whether it can be further improved by spending more time and effort on it [9]. This, combined with the need to reduce planning time per patient given limited resources, can lead to significant differences in plan quality between institutions delivering radiation therapy [19].

In the recent past, different avenues of research were investigated, such as planning automation [1020] knowledge-based planning (KBP) [14] or multicriteria optimization [21]. Semiautomated learning systems using knowledge-based planning (KBP) [14], such as Auto Planning from Pinnacle (Phillips Healthcare) [15, 22] and RapidPlan (RP) from Eclipse (Varian Medical Systems, Palo Alto, CA) [9, 16], have been developed to address variability in treatment plan quality and improve the efficiency of the planning process [23].

The KBP approach consists of predictive DVH modeling based on statistical analysis of historical data and machine learning methods [5, 14], i.e., good quality treatment plans [9, 24]. These systems use information from previous treatment plans to generate personalized and optimized plansfor new patients [25], regardless of the performing planner [9, 10].

KBP consists of building predictive DVH models and optimal dosimetric targets based on statistical analysis using a data library containing previously planned DVHs from historical treatment plans on patients, which have good quality [18, 19, 26, 27]. A training process aims to build a mathematical model, which can be used to predict, for any new case (patient) with its own specificity, the optimal dose distribution [16].

The RapidPlan KBP system is used to develop a model capable of producing treatment plans with IMRT and VMAT techniques. The RP system is a commercial KBP tool, implemented in the Eclipse treatment planning system (TPS) from Varyan [28]. Which has been widely studied in recent years, applied in different sites: liver [23], pelvis [4, 29] head and neck [14], breast [31], and others. In summary, the evidence from these studies indicated that the use of PR allowed an overall improvement in the interpatient consistency of treatment plans, their intrinsic quality, and the efficiency (time and workflow) of the process [19].

3 Method

3.1 Patients

A sample of 35 patients with stage II PC was taken, that is, if prophylactic pelvic lymph node irradiation is prescribed. The prescription dose is 46 Gy over 5 weeks to prostate and proximal seminal vesicles, followed by a 32 Gy boost dose to the prostate, where IMRT or VMAT techniques were used.

Permission was obtained from the CMABC for the use of these retrospective cases in this study, and cases were anonymized prior to use. Each treatment plan includes the computed tomography (CT) data set, PTV and OAR contours, beam geometry specifications, beam intensity (fluence) maps, and dose distributions.

At this medical center, seven coplanar beam angles are typically used for IMRT (0°, 51°, 102°, 153°, 204°, 255° and 306°), and where necessary, nine coplanar fields (20°, 60°, 100°, 140°, 140°, 180°, 220°, 260°, 300° and 340°) and two CW (clockwise) and

Table 1. CMABC prostate IMRT/VMAT protocol with dose volume constraints. All constraints are based on a target dose of 78 Gy.

Genitourinario, GU (1.8-2.0 Gy/fx)		
Critical structure	**Dose (Gy)**	**% Volume**
Bladder	40	50
Bladder	65	25
Bladder (Davg)	45	
Rectum	40	45
Rectum	65	15
Rectum (Davg)	50	
Lt femoral head	50	5
Rt femoral head	50	5
Penile bulb (Dmax)	50	
Small bowel	45	<195 cc

CWW (counterclockwise) VMAT arcs were used.The treatment was delivered using an Elekta Clinac iX linear accelerator and a photonbeam energy of 6 MV and a Novalis TX linear accelerator with a photon beam energyof 6 MV.

3.2 RapidPlan Model Creation

Using the Eclipse TPS version 16.01.10. The model was then created, extracting the information from the previous treatment plans. Additional configurations were performed, such as the definition of the model ID, the version of the DVH estimation algorithm, the anatomical region of the model, the training status of the model and the model description. After the configuration stage, we proceeded to define the structures used in the semiautomated learning planning model.

These structures were divided into two main categories: target structures (PTV) and organ at risk (OAR) structures. The PTVs were created to delineate the region that was to receive the radiotherapy dose. In the case of PC, PTV structures were defined to encompass the prostate and involved nodes. Among the OARs, the femoral heads, penile bulb, bowel, rectum, and bladder were delineated.

Once the set of structures and radiation beam configurations were created, we proceeded to feed the RP model by adding plans to it. The DVH estimation model extracts the data from the treatment plans, allowing the model to be used independently without the need to access the original plans used to train it. The next step is to train and verify the model.

During the training process, the system processes the plan data extracted from the training plans. The model uses semiautomatic learning, machine learning and statistical techniques to map the structure and geometry information of the plans, such as relative distances between the OARs and the target organ, OAR volumes, etc., to the corresponding dosimetric information, such as DVH curves.Their characteristics

have been previously described in detail in [10, 11, 27, 29]. Subsequently, this information was evaluated and reviewed by the planner, in which data that could be outside the model criteria and affect the good performance of the model were discarded.

3.3 Evaluation of the Quality of Treatment Plan

Table 1 shows the prostate protocol for IMRT and VMAT used at this institution to specify dose volume constraints for critical structures. The protocol is similar to those established by the Radiation Oncology and Therapy Group (RTOG) and Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) for CP IMRT and VMAT clinical trials. Typical clinical practice strives to deliver a prescription dose of at least 95% (or higher) of the PTV without exceeding dose constraints to OAR.

In this study, a total of seven new treatment plans were developed, where the quality of each treatment plan was assessed by comparing the DVH of the new semiautomated RP plan with that of the original MP plan developed manually by a (human) planner. A comparison of the various DVH cutoff points considered dose to volume percentage coverage (Dx, which is the dose at the highest x% volume) for PTV and two normal structures (i.e., bladder and rectum) [11].

The cutoff points for PTV were D98, D95, and D2. Specifically, D2 was used to quantify the target maximal dose. For both bladder and rectum, the respective cut off points were assessed at D40, D65 and D_{max} of each. Only the constraints of seven major structures were selected and imported, including the PTV, bladder, rectum, both femoral heads, bowel, and penile bulb. Each plan was normalized to deliver the prescription dose to approximately 95% of the PTV.

Treatment plans were evaluated for relative percentage differences at specific DVH points using the following equation:

$$\% \, Diff \; = \frac{\mathrm{D_{vol\ RP}} \;\; \mathrm{D_{vol\ PM}}}{\mathrm{D_{vol\ PM}}} \times 100. \tag{1}$$

A positive percentage difference indicates that the new plan, RP, has a reduced dose compared to the original plan, MP. For a critical structure, such a negative percentage difference indicates an improvement, i.e., a higher dose economy. However, for PTV results, on the contrary, a positive result in the percentage difference indicates higher dose coverage in the target organ, which is an indicator of improvement, since one wants to improve the dose to PTV and reduce the dose to OAR.

The Wilcoxon signed rank test was performed between MP and RP for the dosimetric parameters described above. To perform these tests, the statistical package for social sciences (SPSS 25.0; SPSS Inc., Chicago, IL, USA) was used to perform these tests and $p<0.05$ was considered statistically significant.

3.4 Patient Specific Quality Control (PSQC)

Quality control of the patient specific treatment plans (PSQC) obtained by RP was performed using an Octavius II + PTW 729 manikin and the MEPHYSTO program, VeriSoft 5.1 version (5.1.0.35) to compare the results obtained with those calculated by the TPS. PSQC is performed prior to IMRT and VMAT treatment to ensure that the planned (calculated) treatment plan matches or is comparable to that which will begiven

to the patient (measured). This ensures that the treatment plan is clinically acceptable. This quality control was performed using the criteria of ΔD=3% in dose and Δd=3 mm in distance. According to these criteria, it is established that at least 90% of the evaluated points must meet the gamma index (GI) criteria to pass the test [32].

4 Results

Although the results of the seven new cases planned by MP and RP are summarized, three of the seven cases were selected to further illustrate the comparison between the new semi automatically generated plan and the DVHs of the original manual plan. Fig. 1 shows the comparison between the DVH obtained using the RP model and the DVH of the manually generated plan by the planner for case 1, which is one of thebest seven cases selected.

A dose distribution in the PTV with better coverage and a comparable curve falloff between the new plan, RP (lines with square), and the original plan, MP (lines with triangle), as well as considerably higher dose savings in both bladder and rectum are observed. This identification scheme will remain constant for all cases analyzed. The DVH of the femoral heads, penile bulb and bowel are not traced to make it easier to visualize the PTV, bladder and rectum.

For case 1, PTV coverage in the new plan is approximately equal to that in the original plan; the relative percentage differences in D98, D95, and D2 were 0.68%, 0.24%, and -0.82%, respectively. For the rectum, the new plan consistently demonstrated large additional dose savings, as shown by the new plan's boxed curve moving steadily to the left of the original plan's triangle line.

For example, the new plan reduced the dose in straight V40, V65, and Davg by 17.11%, 3.99%, and 1.79%, respectively. Similar dose savings were also demonstrated in the bladder. Detailed cut point values for all cases are reported below in tables. In summary, case 1 illustrates that the new plan has very comparable PTV coverage and substantial dose savings in both the bladder and rectum.

The DVH plot for case 4 is shown in Fig. 2 and is representative of most of the seven cases, with very comparable dose distributions to the PTV, bladder and rectum. Five of the seven new plans had comparable DVH results relative to the original clinical plan. Fig. 3 illustrates the one case (case 3), which had comparable PTV coverage but a higher dose for both bladder and rectum compared to the original plan.

However, these normal structure doses are still clinically acceptable as they are well below the dose volume limitations established in the protocol. The PTV results are very comparable, with relative percentage differences of 8.83%, 2.81% and -5.55% in D98, D95 and D2, respectively, showing an improvement in the results for PTV obtained by the RP plan. However, the dose in bladder at V40, V65 values indicated an increase in preservation by 5.44%, 41.30% and a decrease in Davg of 4.82%. Similarly, the indicated rectal dose increased for V40 by 45.06%, V65 by 64.15% and Davg decreased by 2.69%.

Although there is substantially higher relative percentage dose for both rectal and bladder dose in the RP, note that, in terms of absolute dose to volume cutoff points, the critical structure doses would still be clinically acceptable as they are well below the dose constraints set forth in the protocol (see Table 1).

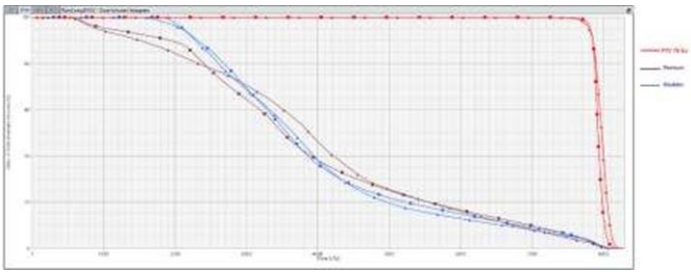

Fig. 1. Comparison of the DVH for case 1. The new plan MP (triangle) and the one RP model (square) were compared. Case 1 is one of the best of the seven cases, demonstrated comparable PTV coverage and considerably higher dose savings in several OARs.

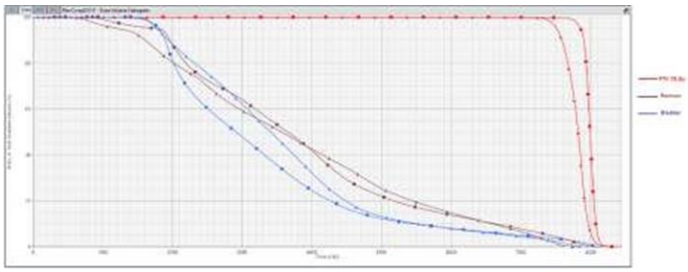

Fig. 2. DVH comparison for case 4. This case is representative of the majority of the seven cases. This graph shows that the dose to the PTV, rectum and bladder in the new plan (squares) are very comparable with the manual plan (triangles).

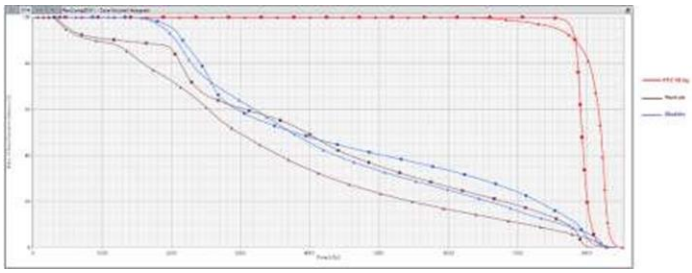

Fig. 3. Comparison of the DVH for case 3. Comparison of the plan performed by the planner (triangle) and the one performed by the RapidPlan model (square) illustrates comparable PTV coverage, but higher dose for both bladder and rectum.

A detailed comparison of the relative percentage differences [Eq. (1)] in specific dose to volume values for PTV for the 7 new plans made by RP and MP is shown in Table 2I. A positive value in PTV indicates that the plan by RP has higher PTV coverage compared to the MP. The mean percentage differences for the seven cases (mean ± standard deviation) in D98, D95 and D2 are 3.10% ± 3.53%, 1.76% ± 1.99% and -0.95% ± 2.60%, respectively.

On average, the new semiautomated plan can achieve PTV coverage very comparable to the original plan (Table 2). Most of the new MP plans and PRs, met the prescribed requirements for the target organs. Overall, the pass rate for the dose criteria

Table 2. Percentage difference in PTV coverage between the treatment plan obtained by the MP and the semi-automated RP learning model.

Cases	D98	D95	D2
1	0,69	0,24	-0,81
2	5,12	4,55	1,78
3	9,69	2,89	-5,25
4	5,03	4,56	0,83
5	1,60	1,06	-3,03
6	0,66	0,41	-0,26
7	-1,08	-1,40	0,12
Average	3,10	1,76	-0,95
Std. Dev.	3,53	1,99	2,60
p-value	0,063	0,091	0,499

Table 3. Percentage difference in rectum doses between the treatment plan obtained by the MP and the semi-automated RP learning model.

Cases	V40	V65	Davg=40 Gy
1	-17,11	-3,99	-1,79
2	3,71	30,68	-0,44
3	45,06	64,15	-2,69
4	-1,62	-0,84	2,07
5	12,85	-0,57	2,49
6	-10,06	-27,12	-7,07
7	-1,59	-17,32	-2,07
Average	4,46	6,43	-1,36
Std. Dev	20,28	31,15	3,23
P value	0,866	0,612	0,310

and the dose distribution in the target organs were similar in the two groups of plans. In addition, for the Wilcoxon test, we found p-value = 0.063, 0.091, 0.499 > 0.005, so no significant statistical difference was found between PR and MP for PTV. Table 3. shows the percentage differences between the MP and RP plan for rectal dose at V40, V65 and Davg= 40 Gy for all seven cases.

For OAR, a negative value indicates an improvement, where the new plan has a higher rectal sparing dose compared to the original plan. For the seven cases, the mean and standard deviation of the percentage dose differences to the rectum for V40, V65 and Davg is 4.46% ± 20.28%, 6.43% ± 31.15% and -1.36% ± 3.23%, respectively.

Four of the seven newplans (cases 1, 4, 6, 7) have higher rectal dose savings compared to the original plan, while two (cases 2, 5) are quite comparable to the original

plan. However, case 3 on the contrary does not show an improvement in the rectal plan, in all three constraints evaluated it is clinically rejected. The new plans made by the MP and the RP met the prescribed requirements for OARs. Overall, the pass rate for the dose criteria and rectal dose distribution were similar in the two groups of plans. In addition, for the Wilcoxon test, for V40, V65 and Davg, p-value = 0.866, 0.612,0.310>0.005, respectively, so no significant statistical difference was found betweenRP and MP for rectum.

Finally, Table 4 shows the percentage differences between RP and MP for bladder dose at V40, V65 and Davg= 40 Gy for all seven cases. A negative value indicates an improvement, where the new plan has a higher bladder dose savings compared to MP. For the seven cases, the mean and standard deviation of the percentage bladder dose differences for V40, V65 and Davg are -1.79% ± 15.72%, 21.15% ± 16.44% and - 1.79% ± 6.51%, respectively.

Three of the seven PR plans (cases 1, 2 and 4) have a substantially lower dose to the bladder, while three (cases 5, 6 and 7) are very comparable with the MP plan. For case 3, the percentage differences for V40, V65 and Davg may appear high, but the absolute dose values are still clinically acceptable as they arebelow the dose constraints set in the original protocol (see Table 1).

Overall, the pass rate for the dose criteria and bladder dose distribution were similar in the two plan groups. In addition, for the Wilcoxon test, for V40 and Davg we found p-value =1.000 and 0.397 > 0.005, so no significant statistical difference was found betweenRP and MP for bladder in these DVH cutoffs. However, for rectum V65 the p-value =0.018< 0.05, indicating that there is a significant difference between the result obtained by MP and RP.

The results of the quality control of the patient specific treatment plans (PSQC) obtained passed the criteria of ΔD=3% in dose and Δd=3 mm in distance. According to these criteria, it is established that at least 90% of the evaluated points must meet the gamma index criteria to pass the test. Most of the plans scored above 95%, and all passed the GI criterion of 90%.

It is important to note that, on average, the treatment plan using the RP model could be obtained in approximately 40 minutes total for each of the seven cases evaluated. This plan consists of the creation of a Phase II plan, for an irradiation of 46 Gy to prostate and nodes and a second irradiation to prostate of 32 Gy, with a total dose of 78 Gy. On the other hand, the treatment plans made by the expert planner required approximately 3 to 4 hours of manual work, although this time may vary dependingon the planner.

In terms of time optimization, the RP model shows a significant advantage, since while the dosimetrist can perform one plan, the semiautomated learning model can generate 4 to 6 clinically acceptable treatment plans in the same period.

5 Conclusions

The knowledge-based approach, using clinically approved pretreatment plans, isshown to be effective in generating clinically acceptable, high quality treatment plans.This semiautomated approach has the potential to improve the efficiency of the treatment planning process while ensuring the quality of the plans generated.

Table 4. Percentage difference in bladder dose between the treatment plan obtained by the MP and the semiautomatic RP learning plan.

Cases	V40	V65	Davg=45 Gy
1	-5,04	14,56	-1,34
2	-24,46	29,77	-10,23
3	5,44	41,30	-4,82
4	-20,38	5,37	-7,73
5	15,14	42,54	9,07
6	2,64	5,56	0,42
7	14,14	8,96	2,12
Average	-1,79	21,15	-1,79
Std. Dev.	15,72	16,44	6,51
p-value	1,000	0,018	0,397

The results provide reassurance and reliability in the RP model, as no statistically significant difference was found between one form of planning and another, meeting the quality criteria for radiotherapy treatment plans. In addition to the reduction in planning time. It is important to note that the RP model will continue to improve as more patients are added to the model. The greater the number of patients, the greater the learning capability of the model and the better estimates of DVH curves will be obtained with RapidPlan.

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