Technical Note

Knowledge-Based Volumetric Modulated Arc Therapy Treatment Planning for Breast Cancer

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Abstract

Purpose: To create and to validate knowledge-based volumetric modulated arc therapy (VMAT) models for breast cancer treatments without lymph node irradiation. **Materials and Methods:** One hundred VMAT-based breast plans (manual plans [MP]) were selected to create two knowledge-based VMAT models (breast left and breast right) using RapidPlan™. The plans were generated on Eclipse v15.5 (Varian Medical Systems, Palo Alto, CA) with 6 MV of a Novalis Tx equipped with a high-resolution multileaf collimator. The models were verified based on goodness-of-fit statistics using the coefficients of determination (R^2) and Chi-square (χ^2), and the goodness-of-estimation statistics through the mean square error (MSE). Geometrical and dosimetrical constraints were identified and removed from the RP models using statistical evaluation metrics and plots. For validation, 20 plans that integrate the models and 20 plans that do not were reoptimized with RP (closed and opened validation). Dosimetrical parameters of interest were used to compare MP versus RP plans for the Heart, Homolateral_Lung, Contralateral_Lung, and Contralateral_Breast. Optimization planning time and user independency were also analyzed. **Results:** The most unfavorable results of R^2 in both models for the organs at risk were as follows: for Contralateral_Lung 0.51 in RP right breast (RP_RB) and for Heart 0.60 in RP left breast (RP_LB). The most unfavorable results of χ^2 test were: for Contralateral_Breast 1.02 in RP_RB and for Heart 1.03 in RP_LB. These goodness-of-fit results show that no overfitting occurred in either of the models. There were no unfavorable results of mean square error (MSE, all < 0.05) in any of the two models. These goodness-of-estimation results show that the models have good estimation power. For closed validation, significant differences were found in RP_RB for Homolateral_Lung (all $P \leq 0.001$), and in the RP_LB differences were found for the heart (all $P \leq 0.04$) and for Homolateral_Lung (all $P \leq 0.022$). For open validation, no statistically significant differences were obtained in either of the models. RP models had little impact on reducing optimization planning times for expert planners; nevertheless, the result showed a 30% reduction time for beginner planners. The use of RP models generates high-quality plans, without differences from the planner experience. **Conclusion:** Two RP models for breast cancer treatment using VMAT were successfully implemented. The use of RP models for breast cancer reduces the optimization planning time and improves the efficiency of the treatment planning process while ensuring high-quality plans.

Keywords: Breast, RapidArc, RapidPlan

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Introduction

The intensity-modulated radiotherapy (IMRT) allows to achieve highly conformal dose distributions with the sparing of organs at risk (OARs).[1,2] Several studies demonstrated the dosimetrical advantages of intensity-modulated techniques compared with three-dimensional conformal radiotherapy (3DCRT).[3-6] On the other hand, some of the disadvantages of modulated techniques include the increment in total body irradiation with lower doses, sharp dose gradients require image guidance and it is time-consuming and complex procedure.[7] The complexity of inverse planning optimization could generate strongly planner-dependent plans. Volumetric modulated arc therapy (VMAT) is an intensity-modulated technique which improves the treatment efficiency. VMAT technique takes into account the treatment time and monitor units reduction compared to the use of modulated fixed gantry angle beams.[8-12] The commonly used breast radiotherapy treatment plans consist of parallel opposed tangential wedged beams

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or multiple segments.[13] However, VMAT can be performed for breast plans preserving similar coverage, reaching better planning target volume (PTV) conformity and homogeneity, and higher sparing of homolateral lung and heart.[14-16]

Knowledge-based planning (KBP) has gained a lot of interest in radiation medical physics due to the planning-time reduction and plan quality improvement.[17] RapidPlan™ is a commercial KBP tool implemented in the Varian Eclipse engine (Varian Medical Systems, Palo Alto, CA) treatment planning system. RapidPlan™ (RP) uses site-specific manually optimized plans libraries to estimate the best dose distribution achieved in a new plan.[18] Currently, there are RP-reported models for liver,[19] head-and-neck,[20] lung SBRT,[21] prostate,[22] cervix,[23] and esophagus.[24] These models have shown improvements on treatment plan quality planning time-reduction and quality consistency.

In the particular case of breast treatment planning, the VMAT RP models improve the plan quality throughout many radiation oncology centers.[25] After KBP implementation in a center, any physicist or dosimetrist can generate acceptable breast IMRT plans, regardless of their experience.[26] By the use of hybrid RapidArc™ plan (tangential and three VMAT arcs) in the breast with lymph nodes treatments, the KBP and MP plan quality was comparable, but KBP treatment time was substantially shorter.[27] A 3DCRT RP_LB model was created and used it as a prediction method to determine which patients would benefit from the deep inspiration breath-hold technique.[28]

VMAT breast treatment planning was implemented at our institution since 2016. Immediately, it became evident the dependence of physicist and dosimetrist expertise in plan quality and planning time. Therefore, the use of KBP was proposed. This work shows the RP model implementation and validation for the right breast (RP_RB) and left breast (RP_LB). The work includes the plan quality improvement and consistency and the planning-time reduction.

Materials and Methods

Breast VMAT treatment planning technique

VMAT treatment plans were generated by the use of RapidArc™ on Eclipse v15.5 (Varian Medical Systems, Palo Alto, CA). The plans consisted of two semi-arcs (clockwise and counterclockwise) of 240 degrees (LB from 300º to 180º, RB from 60º to 180º) with complementary 20º collimator angles. The plans were performed on 6 MV photon beam energy in a Novalis Tx linear accelerator (Varian Medical Systems, Palo Alto, CA-Brainlab AG, Munchen, Germany) equipped with a high definition multileaf collimator.

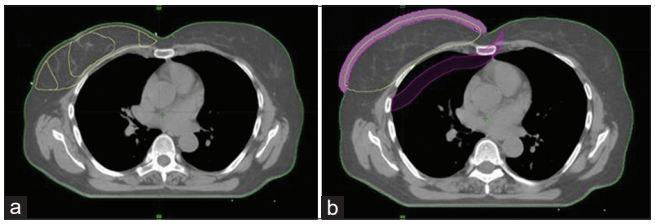

Figure 1: (a) PTVs (zPTV_High_5600!, zPTV_Mid_4600! and zPTV_Low_4300!) original_CT. PTVs on the original_CT were trimmed 5 mm within the body for dose calculation. (b) zPTV_Total! on modified_CT with ring structure and expansion of the body for pseudo-skin-flash

The clinical institutional breast treatment planning protocol included breast irradiation (CTV_breast) with three dose levels in 20 fractions.[29] The CTV simultaneous integrated boost (CTV_SIB) dose prescription was 5600 cGy, proximal CTV (CTV_proximal) was 4600 cGy and distal CTV (CTV_distal) was 4300 cGy. The PTV consisted of 5 mm CTV expansion in all directions. PTVs were identified according to the AAPM report TG-263[30] nomenclature, as shown in Figure 1a. The sum of all PTVs was generated and named zPTV_Total! The organs at risk (OARs) considered were the right lung, left lung, heart, contralateral breast, spinal cord, bowel, trachea, and esophagus. The dose-volume constraints and the equivalent dose to 200 cGy regimens followed are detailed in Table 1.[31]

The isocenter was placed at the zPTV_Total! center of mass. The plan was based on a reported planning strategy.[32] The strategy consisted of the use of duplicated CT image series (modified_CT and original_CT) for inverse planning and dose calculation, respectively. Both image sets shared the planning structures. The modified_CT included a planning structure (ring) to reduce the contralateral breast and lung dose. The ring was created with 12 mm expansion of the body and the PTVs toward the body external direction along the breast whole extension, as shown in Figure 1b. The created expansion region considered breast motion (pseudo-skin-flash) by the use of Boolean operation. Density of 1 was assigned to

Table 1: Institutional dose-volume constrains for RapidArc breast treatment planning in 20 fractions

Volume		Dose constrains
PTV_SIB (zPTV_High_5600!) (EQD2 6500cGy)		5600 cGy
	D95%	>5320 cGy
	D2%	<6000 cGy
PTV_proximal (zPTV_Mid_4600!) (EQD2 4800 cGy)		4600 cGy
	D95%	>4300 cGy
PTV_distal (zPTV_Low_4300!) (EQD2 4430 cGy)		4300 cGy
	D95%	>4090 cGy
Homolateral_Lung	V1000 cGy	< 50%
	V2000 cGy	< 10%
	V4000 cGy	< 3%
Comtralateral_Lung	V 500cGy	< 10%
SpinalCord	Dmax	< 350 cGy (optimal)
Heart	V1000 cGy	< 8%
	Mean Dose	< 350 cGy (left breast)
		<150 cGy (right breast)
Liver	V2000 cGy	< 20%
Contralateral_Breast	Dmax	< 1000 cGy
	Mean Dose	<200 cGy (optimal)

PTV: Planning target volume, SIB: simultaneous integrated boost, zPTV: Nomenclature for PTV

this region. Once the inverse planning reached the planning objective, the optimized plan was pasted into the original_CT where dose distribution was calculated. The CTVs and PTVs of the original_CT were trimmed 5 mm within the body. The anisotropic analytical algorithm and 2.5 mm grid size were used for dose calculation.

RapidPlan model and patient plan selection

Detail RP technical aspects have been described in the literature.[17,33] RP used site-specific manually optimized treatment MP libraries to get the best dose distribution estimation for a new plan.[18] RP provided the estimation by regression analysis to create a statistical model based on geometrical and dosimetrical characteristics extracted from MP. The geometrical components of the model took into account target and OARs volume information whether they were inside or outside the MLC and the field overlap. The dosimetrical component provided the dose estimation for a given structure (target or OARs) based on the geometric characteristics described.

The RP model was used in the new plans for target and OARs dose objectives optimization. First, the model brought forward the dose-volume histogram (DVH) estimation took into account upper and lower dose constraints for all structures. The constraints are related to atypical values and influence data.

Fifty VMAT left breast without lymph nodes MP for 20 fractions were selected to create the left breast RP model (RP_LB). Fifty right breasts without lymph nodes MP were chosen for the right breast RP model (RP_RB). Approved and performed in patients MP belonged to our institutional database. The selected MP included different CTV_Breast volumes (V_{CTV_Breast}) to take into account the breast size. The institutional breast size classification considered small breast V_{CTV_Breast} <400 cc, medium breast V_{CTV_Breast} (400 cc, 700 cc), and large breast V_{CTV_Breast} >700 cc.

MP were uploaded and used for RP data extraction (anatomy, field geometry, and dose prescription) and model training (geometrical and dosimetrical correlation).

Model evaluation and validation

The atypical and influence data of the RP models were identified by statistics parameters and plots (residual, regression, and in-field DVH) that were included in the RP module.[18] The verification of RP models was based on goodness-of-fit statistics by the coefficient of determination (R^2) and Chi-square values (χ^2) and the goodness-of-estimation statistics by the MSE. The R^2, X^2 and MSE, statistical tools, are inbuilt in the RP module of the eclipse. R^2 values close to 1 showed a good fit. R^2 values near to 1 meant a good regression model. MSE values close to 0 showed a good estimation capability of the model.

The validation of RP models was performed with 20 random plans (10 RP_LB and 10 RP_RB) included in the initial RP configuration (opened validation) and 20 plans (10 RP_LB and 10 RP_RB) not included in the initial RP configuration (closed validation).[18,19] All generated plans with RP not had planner intervention during the optimization process. The final DVHs for MP and RP were compared using the two-tailed student test analysis with $P = 0.05$ statistical significance.[34] The Heart, Homolateral_Lung, and Contralateral_Breast DVH were calculated and compared for 10 MP and RP selected from the opened validation.

Optimization time and homogeneity

The RP impact on the optimization time was evaluated in 10 physicists and dosimetrists separated in two groups: experts (5) and beginners (5). Experts group had more than 2 years of experience on VMAT breast treatment planning. The beginners group had <2 years of experience. The optimization in 42 plans with and without RP was performed. The optimization time was measured starting from the optimization start phase until its completion considering intermediate-dose calculations. The plan homogeneity impact was evaluated for RP_LB and MP_LB in eight physicists and dosimetrists, regardless of the expertise. DVH scatter comparison for OARs between MP and RP was studied by Levene's test with $P = 0.05$ statistical significance.

Results

The RP_RB model included 38% of MP for small breast, 38% for medium breast, and 24% for large breast. The RP_LB model included 30% of MP for small breast, 39% for medium breast and 31% for large breast. No over adjustments (and) were observed in the generated models. The largest was 0.51 for the Contralateral_Lung in RP_RB and for the Heart in RP_LB. The smallest was 1.02 for the Contralateral_Breast in RP_RB and for the Heart in RP_LB. MSE were within the acceptable range showing good DVH estimation power (≤0.05). Goodness-of-fit values for Heart, Contralateral_Lung, Homolateral_Lung, and Contralateral_Breast are shown in Table 2 and Supplementary Table 1 for RP_LB and RP_LB, respectively (supplementary material). The results of the above statistical analysis show that both models have good estimation ability and without atypical values. Some examples for in-field DVH, regression, and residual plots for Heart in LB and RB are shown in Figure 2a-f and for Homolateral_Lung in Figure supplement 1a-f.

The opened and closed validation in MP and RP dose distribution for LB and RB were similar and fulfilled the institutional PTVs and OARs dose-volume constraints. An

Table 2: Goodness-of-fit R2 and χ^2 and goodness-of-estimation Mean Square Error for RapidPlan left breast

Structure	R^2	χ^2	MSE
Heart	0.60	1.03	0.01
Contralateral_Lung	0.30	1.04	0.00
Homolateral_Lung	0.41	1.08	0.05
Contralateral_Breast	0.21	1.06	0.05

MSE: Mean Square Error

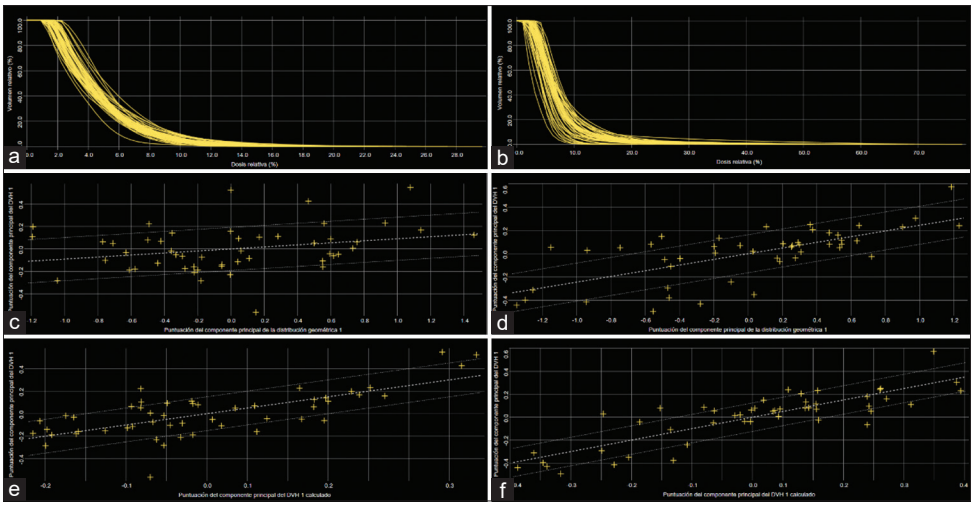

Figure 2: (a, c, e) In-field DVH, regression and residual plots for Heart in RapidPlan Right breast model (RP_RB) and (b, d, f) in RapidPlan left breast model (RP_LB)

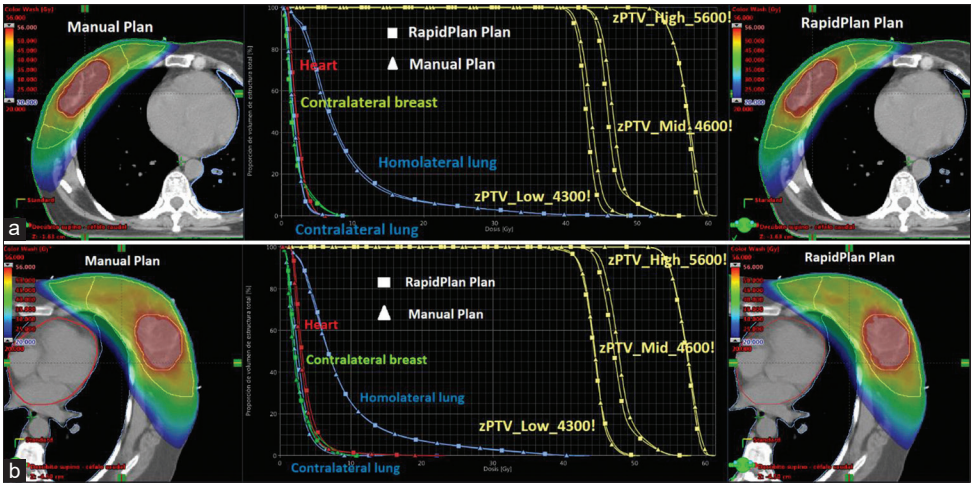

Figure 3: Dose distribution comparison for the left breast between MP and RP for (a) Right breast and (b) left breast

example is shown in Figure 3a-b for RB and LB between MP and RP, respectively.

The closed validation for both RP models showed better PTV dose coverage than MP. Table 3 shows statistically significant differences ($P < 0.001$) for the middle dose level (zCTV_Mid_4600!). The opened validation for both RP models did not show statistically significant with MP ($P > 0.071$).

For RB closed validation there was statistically significant difference for Homolateral_Lung ($P \leq 0.001$) in favor to MP. For LB there was statistically significant difference for Heart ($P \leq 0.04$) in favor to RP and for Homolateral_Lung ($P \leq 0.022$) in favor to MP. Tables 3 and 4 show the LB dosimetrical closed and opened validation for MP and RP. Supplementary Tables 2 and 3 show the RB dosimetrical closed and opened validation for MP and RP.

The Heart, Homolateral_Lung, and Contralateral_Breast mean DVH of 10 MP and RP plans were compared and showed no diffrences, as shown in Figure 4 and Figure Supplement 2 for LB and RB respectively.

The use of RP by expert group of physicists and dosimetrists had little impact on treatment planning times. Nevertheless, there was 30% of reduction time (7 min) for the beginner group, as shown in Table 5.

The use of RP performed plans with similar OARs DVH with respect to MP. The mean DVH scatters for OARs could be reduced using RP compared to MP, regardless of physicists or dosimetrists expertise. The mean LB DVH OARs (Heart, Contralateral_Breast, Contralateral_Lung, and Homolateral_Lung) between MP and RP performed by the beginner and expert group is shown in Figure 5.

RP performed plans with less variance concerning MP, as can be seen in Table 6 where the obtained values for RP are always lower than the corresponding M*P* values. Table 6 shows LB mean and variance values for Heart (Dmean and D8%), Homolateral_Lung (D50%,D20% and D10%), Contralateral_

Table 3: Close validation dosimetric comparison between manual plans and RapidPlan plans for left breast

Structure	Parameter	MP	RP	*P*
zPTV_High_5600!	D95% [Gy]	55.1±0.6	54.5±0.4	0.013
	D2% [Gy]	60.1±0.9	60.0±0.5	0.769
zPTV_Mid_4600!	D95% [Gy]	44.6±0.5	45.8±0.8	<0.001
zPTV_Low_4300!	D95% [Gy]	42.1±0.5	42.9±0.7	0.006
Heart	D8% [Gy]	5.8±1.2	5.0±0.6	0.040
	Mean [Gy]	3.4±0.5	3.1±0.4	0.019
SpinalCord	Max [Gy]	4.2±0.6	3.9±0.3	0.126
Homolateral_Lung	D50% [Gy]	5.9±1.1	6.4±0.7	0.006
	D20% [Gy]	11.1±1.2	12.0±0.7	0.022
	D10% [Gy]	15.8±1.4	17.0±1.5	0.015
Contralateral_Lung	D20% [Gy]	3.7±0.4	3.5±0.3	0.118
	D10% [Gy]	4.8±0.6	4.9±0.8	0.667
Contralateral_Breast	Max [Gy]	8.6±1.7	11.1±1.4	0.006
	Mean [Gy]	2.2±0.3	2.4±0.1	0.776

Plans belonging to close validation were included in the RapidPlan model. MP: Manual plan, RP: RapidPlan plan, zPTV: Nomenclature for PTV.

Table 4: Open validation dosimetric comparison between manual plans and RapidPlan plans for left breast

Structure	Parameter	MP	RP	*P*
zPTV_High_5600!	D95% [Gy]	54.6±0.7	54.6±0.7	0.176
	D2% [Gy]	60.2±0.4	60.0±0.4	0.593
zPTV_Mid_4600!	D95% [Gy]	44.8±0.4	44.6±0.5	<0.071
zPTV_Low_4300!	D95% [Gy]	42.1±0.4	42.0±0.5	0.480
Heart	D8% [Gy]	5.1±1.0	4.8±0.8	0.433
	Mean [Gy]	2.8±0.6	2.7±0.5	0.410
SpinalCord	Max [Gy]	3.6±0.4	3.8±0.4	0.323
Homolateral_Lung	D50% [Gy]	5.9±0.8	6.0±0.6	0.799
	D20% [Gy]	11.5±1.5	11.6±1.2	0.828
	D10% [Gy]	16.2±2.2	16.1±1.9	0.686
Contralateral_Lung	D20% [Gy]	3.3±0.5	3.5±0.5	0.003
	D10% [Gy]	4.4±0.7	4.8±0.7	0.003
Contralateral_Breast	Max [Gy]	9.7±2.7	10.0±2.5	0.441
	Mean [Gy]	2.2±0.3	2.3±0.3	0.156

Plans belonging to open validation were not included in the RapidPlan model. MP: Manual plan, RP: RapidPlan plan, zPTV: Nomenclature for PTV.

Table 5: Impact of using RapidPlan models on treatment planning times for beginners and expert planners

Planning time (min)	Beginner planner		Expert planner	
	MP	RP	MP	RP
Minimum	12.4	11.2	10.5	10.2
Maximum	35.4	22.0	30.5	23.2
Mean	22.1	15.4	16.8	15.4
Standard deviation	6.0	3.8	4.7	3.3
Difference		6.7		1.0
Difference (%)		-30.3		-8.4

MP: Manual plans, RP: RapidPlan plans

Lung (D20% and D10%) and Contralateral_Breast (Dmax and Dmean) between MP and RP. These values had been confirmed by Levene's test (estimate whether the variance is similar or comparable in two samples analyzing deviations from the mean) with *P* values less than the significance tolerance for OARs. The *P* values confirmed that MP and RP were dosimetrically equivalent without statistical differences, as shown in Table 6.

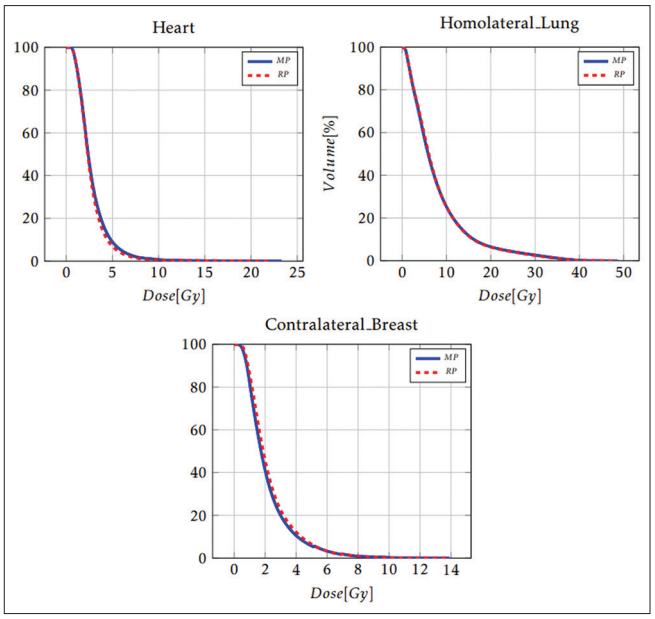

Figure 4: Left breast (LB) average DVH for ten plans using manual plans (MPs) and RapidPlans (RPs) for Heart, Homolateral_Lung, and Contralateral_Lung

Discussion

Two RapidPlan models for left and right breast cancer without lymph node irradiation were created using the VMAT treatment technique. Each RP model was created using fifty plans done by planners of our Institution (MPs), and all of them fulfill the Institutional dose-volume constraints for PTVs and OARs. The models' variability was considered in the models, as plans for different breast volumes were included. Even when the minimum number of plans require for creating an RP model in Eclipse is twenty, breast sizes variability induced us to include fifty plans in each model. The number of MPs included in the RPs models is similar to the used by others authors in different treatment sites.[17,20,33] The statistical tools used in this paper to verify the goodness of the models are inbuilt into Eclipse and help detect atypical values. Obtained values of R^2, χ^2, and MSE for the two RP models were comparable with values reported by other authors[35] and[36] which show that RP models generated good dosimetric results. Close and open RP validation confirms that the RP models, verified by the cited statistical tools, can generate plans comparable to MPs of beginners or expert planners. The last result becomes more significant due to there was no human intervention during the optimization process with RP. Furthermore, the use of

Table 6: Comparison of planning homogeneity between manual plan versus RapidPlan plan for the left breast

Structure	Parameter	Plan	Mean (Gy)	Variance (Gy2)	Levene Test, *P*	*t*-test[a]	
						P[b]	Mean difference
Heart	D8%	MP	6.19	21.40	0.026	0.282	0.039
		RP	6.15	0.09			
Heart	Mean	MP	3.79	11.91	0.001	0.205	0.165
		RP	3.63	0.01			
Homolateral_Lung	D50%	MP	6.24	0.63	0.049	0.381	0.315
		RP	5.93	0.07			
Homolateral_Lung	D20%	MP	11.37	3.00	0.014	0.124	0.865
		RP	10.50	0.31			
Homolateral_Lung	D10%	MP	16.12	4.21	0.036	0.196	0.398
		RP	14.72	0.54			
Contralateral_Lung	D20%	MP	3.12	0.43	0.014	0.737	0.173
		RP	2.95	0.06			
Contralateral_Lung	D10%	MP	3.94	0.74	0.008	0.476	0.185
		RP	3.66	0.04			
Contralateral_Breast	Max	MP	7.22	1.15	0.004	0.193	-0.635
		RP	7.85	0.04			
Contralateral_Breast	Mean	MP	2.09	0.21	0.031	0.145	-0.155
		RP	2.25	0.01			

[a]Equality of means. [b]Two-tailed *t*-test and equal variance are not assumed. MP: Manual plans, RP: RapidPlan plans

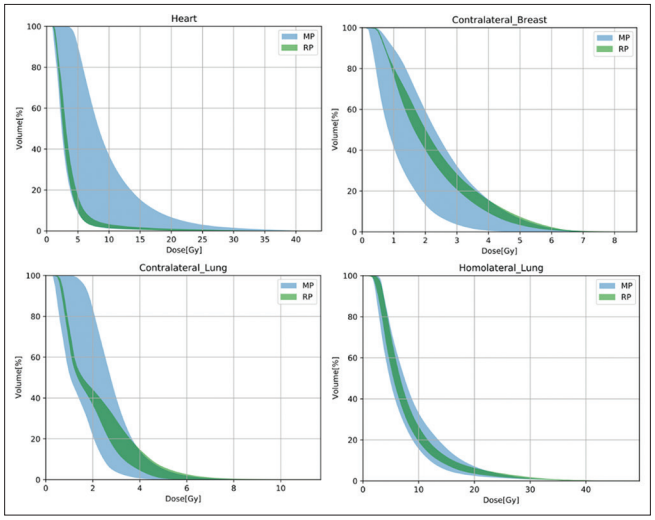

Figure 5: Average DVH comparison for left breast (LB) between manual plans (MP) and RapidPlan plans (RPs), executed by beginner and expert planners. Heart, Contralateral_Breast, Contralateral_Lung, and Homolateral_Lung

RP reduces the treatment planning time on beginner planners and increases the homogeneity of plans results beyond the planner's expertise.

Conclusion

Two VMAT RP models for breast treatment for 20 fractions were successfully implemented to the three-dose levels protocol. We conclude that the RP plans performed are dosimetrically equivalent to MP generated by expert physicists and dosimetrists. The same procedure could be used to implement VMAT RP models with different dose prescription protocols.

The use of RP models for breast cancer reduces the optimization planning time and improves the efficiency of the treatment planning process while ensuring high-quality plans. However, longer time and experience in the use of RP are necessary to confirm the results shown in this study. Both RP models can be requested from our Institutional website (www.institutozunino.org).

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Conflicts of interest

There are no conflicts of interest.

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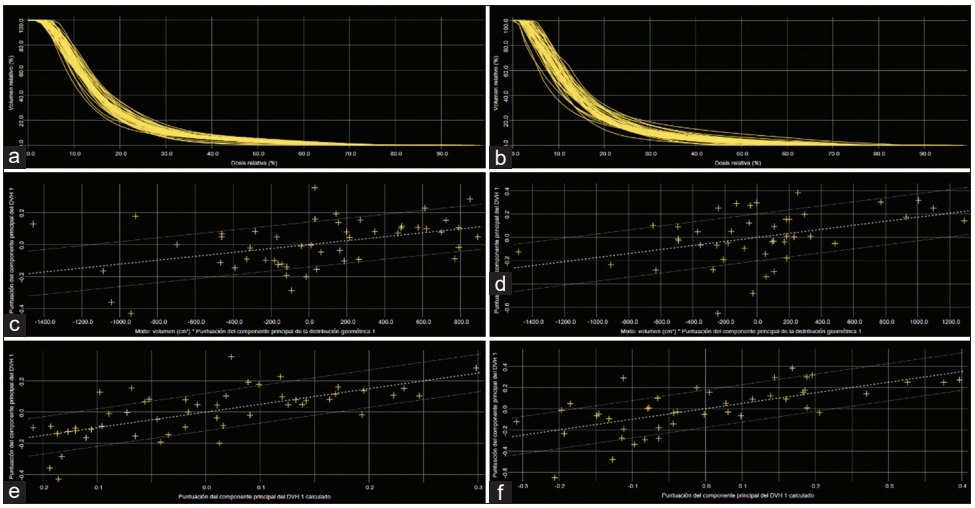

Figure Supplement 1: (a, c, e) In-field DVH, regression and residual plots for Homolateral_Lung in RapidPlan Right Breast model (RP_RB) and (b, d, f) in RapidPlan left breast model (RP_LB)

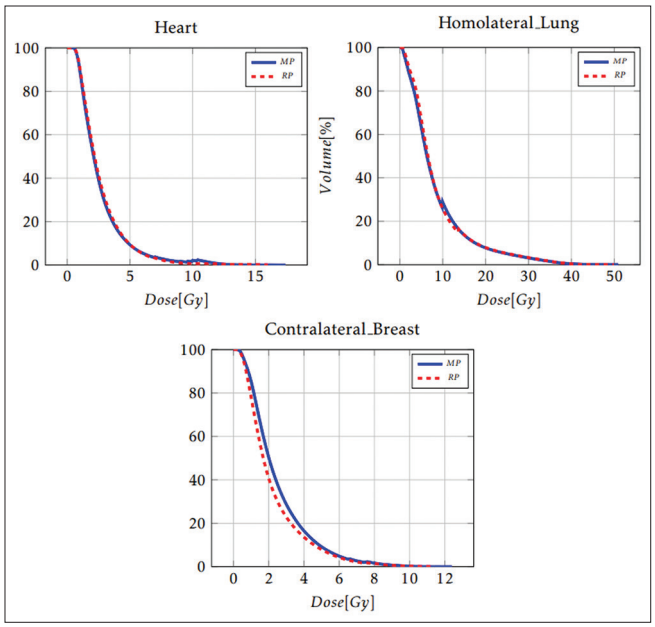

Figure Supplement 2: Right breast (RB) average DVH for ten plans using manual plans and RapidPlans for Heart, Homolateral_Lung and Contralateral_Breast

Supplementary Table 1: Goodness-of-fit R^2 and χ^2 and goodness-of-estimation Mean Square Error for RapidPlan right breast

Structure	R^2	χ^2	MSE
Heart	0.47	1.09	0.05
Contralateral_Lung	0.51	1.08	0.00
Homolateral_Lung	0.41	1.06	0.05
Contralateral_Breast	0.09	1.02	0.04

MSE: Mean Square Error

Supplementary Table 2: Close validation dosimetric comparison between manual plans and RapidPlan plans for right breast

Structure	Parameter	MP	RP	*P*
zPTV_High_5600!	D95% [Gy]	54.6±0.4	54.4±0.3	0.066
	D2% [Gy]	60.2±0.7	59.8±0.4	0.055
zPTV_Mid_4600!	D95% [Gy]	44.2±0.4	44.7±0.4	0.007
zPTV_Low_4300!	D95% [Gy]	42.1±0.4	41.9±0.3	0.154
Heart	D8% [Gy]	4.7±0.5	4.8±0.6	0.718
	Mean [Gy]	2.4±0.1	2.4±0.3	0.907
SpinalCord	Max [Gy]	3.8±0.2	4.0±0.5	0.245
Homolateral_Lung	D50% [Gy]	6.8±0.3	7.1±0.4	0.001
	D20% [Gy]	11.7±0.6	12.1±0.6	0.001
	D10% [Gy]	15.8±0.9	16.5±1.1	<0.001
Contralateral_Lung	D20% [Gy]	3.0±0.4	2.8±0.2	0.131
	D10% [Gy]	3.9±0.6	3.7±0.4	0.386
Contralateral_Breast	Max [Gy]	8.9±1.6	8.6±2.0	0.410
	Mean [Gy]	2.10±0.2	2.1±0.1	0.578

MP: Manual plan, RP: RapidPlan plan

Supplementary Table 3: Open validation dosimetric comparison between manual plans and RapidPlan plans for right breast

Structure	Parameter	MP	RP	*P*
zPTV_High_5600!	D95% [Gy]	54.5±0.7	54.5±0.7	0.161
	D2% [Gy]	60.1±0.5	59.8±0.8	0.244
zPTV_Mid_4600!	D95% [Gy]	44.6±0.7	44.4±0.6	0.356
zPTV_Low_4300!	D95% [Gy]	41.9±0.6	41.5±0.6	0.059
Heart	D8% [Gy]	2.5±0.5	2.7±0.5	0.467
	Mean [Gy]	1.5±0.3	1.6±0.3	0.582
SpinalCord	Max [Gy]	3.7±0.5	4.0±0.4	0.117
Homolateral_Lung	D50% [Gy]	6.9±0.7	7.1±0.4	0.581
	D20% [Gy]	12.3±1.7	12.1±1.2	0.575
	D10% [Gy]	17.2±2.3	17.1±1.9	0.864
Contralateral_Lung	D20% [Gy]	2.9±0.3	2.7±0.3	0.124
	D10% [Gy]	3.8±0.6	3.6±0.7	0.188
Contralateral_Breast	Max [Gy]	9.5±2.0	10.0±2.2	0.078
	Mean [Gy]	2.4±0.4	2.2±0.3	0.207

MP: Manual plan, RP: RapidPlan plan