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Technical Note

Effectiveness of multi-criteria optimization in combination with knowledge-based modeling in radiotherapy of left-sided breast including regional nodes

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ABSTRACT

Multi-criteria optimization (MCO) is a method that was added to treatment planning to create high-quality treatment plans. This study aimed to investigate the effectiveness of MCO in combination with knowledge-based planning (KBP) in radiotherapy for left-sided breasts, including regional nodes. Dose/volume parameters were evaluated for manual plans (MP), KBP, and KBP + MCO. Planning target volume doses of MP had better coverage while KBP + MCO plans demonstrated the lowest organ at risk doses. KBP and KBP + MCO plans had increasing complexity as expressed in the number of monitor units.

1. Introduction

Volumetric-modulated arc therapy (VMAT) plays a major role in delivering high conformal radiation doses to the planning target volume (PTV), particularly in patients with local or locoregional involvement [1–3]. However, the volumes of the adjacent organs at risk (OAR) receiving low-dose radiation are higher, with potential concerns regarding long-term toxicities and secondary cancer [4].

Knowledge-based planning (KBP) was introduced to enhance the quality of treatment plan consistency among planners with varying expertise and to reduce planning time. This method utilizes a database of previous treatment plans for a specific disease site to predict the dose-volume histograms (DVH) of a new plan. DVH information was created for optimization based on the target and OAR geometries [5]. The KBP models have been developed for various disease sites [6–10].

Multi-criteria optimization (MCO) is a novel optimization method that was added to treatment planning to create high-quality treatment plans by balancing clinical trade-offs [11]. Because available studies on MCO in combination with VMAT plans using KBP (KBP + MCO) are limited, this study investigated the effectiveness of the impact of KBP on plan quality for different planners' expertise. This study includes plan quality improvement when KBP + MCO was applied in VMAT for left-sided breast cancer, encompassing regional nodes. The plan quality was evaluated using the dose/volume parameters of target coverage and OAR. The complexities of the plans were expressed as total monitor unit (MU) calculations and patient-specific quality assurance (QA) results.

2. Materials and methods

2.1. Patient selection and treatment planning

This retrospective study conducted between January 2021 and May 2023 focused on VMAT plans for the left breast, including the regional nodes. All patient data were anonymized, and the study was approved by the Institutional Review Board. All patients underwent computed tomography in the supine position on a Vac-Lok (CIVCO Medical Solution, Iowa, USA) using either the free-breath (FB) or deep inspiration breath-hold (DIBH) technique.

The clinical target volume (CTV) was defined as the entire mammary gland and regional nodes, and the OAR was contoured using the Radiotherapy Comparative Effectiveness atlas (RADCOMP) [12]. Although the PTV was a 5-mm expansion from the CTV, it was adjusted by cropping 5 mm inside the body outline to exclude the skin. All OARs, including the heart, ipsilateral lung, contralateral lung, left anterior descending coronary artery (LAD), and contralateral breast, were contoured. A total dose of 42.4 Gy in 16 fractions was prescribed for the

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Table 1
Testing of the model validation dosimetric comparison of manual vs. knowledge-based planning between junior and senior planners.

Organ	Parameter	Dose/volume constraint	MP		KBP	P- value		
			Junior	Senior		MP-Junior vs MP-Senior	MP-Junior vs KBP	MP-Senior vs KBP
PTV	- $D_{95\%}$ [Gy]	> 100 %	42.5 ± 0.2	42.5 ± 0.1	42.4 ± 0.0	0.14	< 0.05	< 0.05
	- D_{max} [Gy]	< 107 %	48.2 ± 0.7	49.0 ± 1.7	49.4 ± 1.4	0.22	< 0.05	0.12
Heart	- $D_{15\%}$ [Gy]	< 10 Gy	8.4 ± 3.2	7.3 ± 2.6	8.3 ± 2.0	0.18	0.09	0.28
	- $D_{20\%}$ [Gy]	< 8 Gy	7.0 ± 2.6	5.9 ± 1.9	6.9 ± 1.6	0.08	0.09	< 0.05
	- D_{mean} [Gy]	< 9 Gy	5.6 ± 1.7	4.8 ± 1.1	5.4 ± 1.1	< 0.05	0.34	< 0.05
Ipsilateral lung	- $D_{15\%}$ [Gy]	< 31 Gy	24.7 ± 4.6	28.1 ± 5.0	25.4 ± 4.1	0.08	0.33	0.11
	- $D_{20\%}$ [Gy]	< 26.4 Gy	20.3 ± 4.1	23.3 ± 5.0	21.3 ± 3.3	0.09	0.91	0.31
	- $D_{35\%}$ [Gy]	< 17.6 Gy	12.1 ± 2.1	13.4 ± 3.1	13.6 ± 1.8	0.13	< 0.05	0.39
	- $D_{50\%}$ [Gy]	< 13.0 Gy	8.3 ± 1.1	8.7 ± 2.0	9.6 ± 1.1	0.48	< 0.05	< 0.05
	- D_{mean} [Gy]	< 18.0 Gy	12.6 ± 1.6	13.6 ± 2.4	13.5 ± 1.6	0.15	< 0.05	0.49
	- $V_{20\ Gy}$ [%]	< 35 %	20 ± 5 %	24 ± 5 %	21 ± 5 %	0.06	0.92	0.25
Contralateral lung	- $D_{20\%}$ [Gy]	< 13.0 Gy	7.3 ± 1.2	9.5 ± 2.1	7.6 ± 0.9	0.06	0.39	< 0.05
	- $D_{35\%}$ [Gy]	< 10.6 Gy	4.8 ± 1.1	6.7 ± 2.0	5.7 ± 0.7	< 0.05	< 0.05	< 0.05
	- $D_{50\%}$ [Gy]	< 9 Gy	3.5 ± 0.9	4.9 ± 1.7	4.1 ± 0.6	0.06	< 0.05	0.07
LAD	- D_{mean} [Gy]	< 9.7 Gy	14.3 ± 7.1	11.2 ± 5.3	11.4 ± 2.8	0.29	0.33	0.10
	- $D_{1\%}$ [Gy]	< 16.1 Gy	27.5 ± 1.2	29.3 ± 7.4	29.5 ± 7.1	0.52	0.51	< 0.05
Contralateral breast	- D_{mean} [Gy]	< 7 Gy	7.3 ± 2.4	6.3 ± 1.3	6.9 ± 1.6	0.06	0.88	0.26
	- $D_{1\%}$ [Gy]	< 17.5 Gy	2.3 ± 8.5	16.2 ± 4.9	17.8 ± 3.8	0.12	0.32	0.09
	Total MU [MU]		1063 ± 89	947 ± 97	1030 ± 108	< 0.05	0.58	< 0.05

MP; manual plan, KBP; knowledge-based planning; PTV, planning target volume; LAD, left anterior descending coronary artery.

PTV. The institutional dose constraint protocol for OAR was adopted from the NRG RTOG 1005 [13,14].

2.2. Model configuration and validation

The KBP was created using RapidPlan (Varian Medical Systems, Palo Alto, CA, USA). Seventy VMAT plans, which had been clinically approved and used in previous treatments, were used for the training. The database included 36 FB and 34 DIBH. The six MV plans comprised four partial arcs of 170° [1,2]. The DVH model was estimated based on the geometrical and dosimetric correlations extracted from a manual plan (MP). The statistics of the KBP model were verified by assessing the goodness of statistical fitting, regression coefficient of determination (R^2), chi-square values (X^2), and goodness of statistical estimation by the mean square error (MSE), demonstrating its efficiency in estimating the original DVH in a training plan [10,15]. An R^2 approaching 1 signifies a robust regression model, and an X^2 nearing zero indicates a strong fit. An MSE of zero indicates the accuracy of the estimation capability of the model.

The KBP model was validated for database accuracy using 10 randomly selected plans from the initial KBP configurations (internal validation). The VMAT plans were generated by matching the beam geometry and prescribed dose as the model. The KBP plans were generated without manual optimization parameter adjustments by the planner. The quality of the model-based optimized plans versus manual plans was analyzed using DVH.

2.3. Clinical implementation

The KBP was tested on 20 VMAT plans not included in the model (model testing). Initially, KBP influenced the quality of the plan based on the planner's experience. Plans were generated for the same patients using the MP and KBP methods by two groups of planners: junior and senior, with three planners in each group. Planners with < 5 years of experience in VMAT breast treatment planning were classified as juniors. Furthermore, the KBP + MCO plans were generated for the same patients to strategize optimal treatment plans. The MCO function enhances plan quality by optimizing the tradeoff between sparing OAR and ensuring target coverage. The slider for each selected objective is displayed and manipulated. The manipulation of one slider automatically affected the other selectors except when restrictions were applied. Management of the trade-offs was stopped when the prescribed dose for the PTV did not meet the specified criteria.

Plan quality was evaluated in terms of dose/volume parameters, MU, and patient-specific QA using portal dosimetry (Varian Medical Systems, Palo Alto, CA, USA). The gamma passing rate was evaluated at 3 %, 2 mm, and 10 % thresholds. The different plans analyzed were as follows: MP as the reference, KBPs formulated by the junior and senior, and KBP + MCO. The dosimetric data of each planning group were tested for normal distribution using the Shapiro–Wilk test. Dose/volume parameters were compared using two independent sample t-tests, and a p-value < 0.05 indicated statistical significance.

3. Results

3.1. Model evaluation and validation

The statistical analysis results of the model demonstrated a good fit and estimation ability. The goodness-of-fit values for the heart, ipsilateral lung, contralateral lung, and LAD were $R^2 = 0.68 \pm 0.10$ and $X^2 = 1.08 \pm 0.02$. The MSE indicated good estimation power, ranging from 0.03 to 0.14.

Internal validations of the MP and KBP models reached the dose-constraint protocol for clinical usage. No statistically significant differences were observed in the radiation doses for the PTV and OAR, except that the ipsilateral lung showed a lower dose for KBP. Specifically, $D_{95\%}$ of PTV was 42.4 ± 0.0 Gy for MP vs. 42.4 ± 0.0 Gy for KBP, p = 0.14. However, the MU was significantly higher (978 ± 108 for MP vs. 1054

Table 2
Quantitative dose comparison of testing of the model between manual, KBP, and KBP + MCO.

Organ	Parameter	MP	KBP	KBP + MCO	P-value MP vs. KBP	P-value KBP + MCO vs. KBP
PTV	- $D_{95\%}$ [Gy]	42.5 ± 0.2	42.4 ± 0.0	42.4 ± 0.0	< 0.05	< 0.05 0.12
	- D_{max} [Gy]	48.5 ± 1.4	49.4 ± 1.4	49.2 ± 1.4	< 0.05	
Heart	- $D_{15\%}$ [Gy]	7.8 ± 2.4	8.3 ± 2.0	7.2 ± 2.2	< 0.05	< 0.05
	- $D_{20\%}$ [Gy]	6.4 ± 1.9	6.9 ± 1.6	6.1 ± 1.8	< 0.05	< 0.05
	- D_{mean} [Gy]	5.2 ± 1.2	5.4 ± 1.1	5.0 ± 1.3	< 0.05	
Ipsilateral lung	- $D_{15\%}$ [Gy]	26.4 ± 5.9	25.4 ± 4.1	25.5 ± 5.8	0.06 0.42	0.98 0.41
	- $D_{20\%}$ [Gy]	21.8 ± 5.4	21.3 ± 3.3	20.9 ± 5.3	< 0.05	< 0.05
	- $D_{35\%}$ [Gy]	12.7 ± 3.0	13.6 ± 1.8	12.4 ± 3.4	< 0.05	< 0.05 0.56
	- $D_{50\%}$ [Gy]	8.5 ± 1.9	9.6 ± 1.1	8.4 ± 2.2	< 0.05	
	- D_{mean} [Gy]	13.1 ± 2.4	13.5 ± 1.6	12.8 ± 2.6	0.38	
	- $V_{20\ Gy}$ [%]	22 ± 6 %	21 ± 5 %	21 ± 6 %		
Contralateral lung	- $D_{20\%}$ [Gy]	8.1 ± 1.8	7.6 ± 0.9	6.0 ± 1.4	0.10 0.79	< 0.05 < 0.05
	- $D_{35\%}$ [Gy]	5.6 ± 1.5	5.5 ± 0.7	4.0 ± 1.1	0.79	< 0.05
	- $D_{50\%}$ [Gy]	4.1 ± 1.2	4.1 ± 0.6	3.0 ± 0.8		
LAD	- D_{mean} [Gy]	12.7 ± 5.5	11.4 ± 2.9	10.1 ± 3.2	0.14 0.74	< 0.05 < 0.05
	- $D_{1\%}$ [Gy]	29.9 ± 9.1	29.5 ± 7.1	26.4 ± 8.0		
Contralateral breast	- D_{mean} [Gy]	6.5 ± 2.4	6.9 ± 1.6	7.0 ± 1.7	0.79 0.76	0.58 < 0.05
	- $D_{1\%}$ [Gy]	17.4 ± 8.0	17.8 ± 3.8	19.2 ± 4.2		
	Total MU [MU]	1005 ± 161	1030 ± 108	1071 ± 134	0.21	< 0.05

MP, manual plan; KBP, knowledge-based planning; KBP + MCO, multi-criteria optimization; PTV, planning target volume; LAD, left anterior descending coronary artery.

± 62 for KBP). These results confirmed that this model can be applied to left-sided breast VMAT planning, including regional nodes.

3.2. Clinical implementation

The results of the quantitative dose/volume parameters comparison of the KBP plans in terms of differences in expertise are presented in Table. 1. For junior planners, MP achieved more dose coverage in the PTV than that of KBP ($D_{95\%}$ of PTV = 42.5 ± 0.2 Gy vs. 42.4 ± 0.0 Gy, $p < 0.05$), and had a lower maximum dose. The significant dose difference in the OAR indicated that MP was superior to KBP but had a higher variance. However, the organs, including the heart and LAD, contralateral breast showed no significant differences. For senior planners, the doses to the ipsilateral lung, $D_{15\%}$ of the heart, and mean LAD dose showed no significant differences between MP and KBP, and the variance in KBP was less than that in MP. Most of the dose parameters for senior MP were higher than those for junior MP, but the differences were not statistically significant. The average MU calculation did not differ significantly for the junior group ($p = 0.58$), whereas there was an impact for senior planners (947 ± 97 and 1030 ± 108 for MP and KBP, respectively).

Dose/volume parameters for MP, KBP, and KBP + MCO are presented in Table 2. The PTV doses of MP exhibited greater coverage and were less intense than those of KBP and KBP + MCO. The D_{max} of PTV was 48.5 ± 1.4 Gy for MP, 49.4 ± 1.4 Gy for KBP, and 49.2 ± 1.4 Gy for KBP + MCO, respectively. The OAR dose analysis showed that KBP + MCO primarily reduced the dose in the OAR but increased the variability between planners through visualized tradeoff management. KBP generated plans with less variance than did MP and KBP + MCO. The mean heart and ipsilateral lung doses were higher in the KBP group than those in the MP group; however, the contralateral lung and LAD doses were similar.

The MU calculations of MP, KBP, and KBP + MCO were 1005 ± 16, 1030 ± 108, and 1071 ± 134, respectively. The average MU calculations of the MP and KBP techniques were not significantly different ($p = 0.21$); however, the MU calculation was significantly higher for KBP + MCO than that of MP. The gamma passing rates of patient-specific QA were presented at 98.7 ± 1.2 %, 98.2 ± 1.2 %, and 98.2 ± 1.4 % for MP, KBP, and KBP + MCO, respectively. The MU calculation affected the gamma passing rate because a higher MU yielded a lower gamma passing rate. KBP and KBP + MCO exhibited lower gamma passing rates than did MP. Compared to KBP + MCO, KBP delivered a significantly lower MU; however, the gamma passing rate showed no differences ($p = 0.67$).

4. Discussion

In this study, the KBP of the left breast, including regional nodes, was generated using the VMAT technique. The KBP was tested, and the results showed that the model could improve the variability of plans for varying levels of planners' expertise. Moreover, KBP + MCO demonstrated the lowest OAR dose.

The KBP model was generated from 70 plans, with a minimum treatment planning requirement of 20 [10]. The number of plans created for our KBP model was higher than that used by Blanco et al. [10], which included 50 plans. Regarding the patients' anatomical differences, the FB and DIBH were included in the trained model. This implied that the model could be used under both conditions. Our statistical values, R^2, X^2, and MSE, showed good results and were comparable to those reported by Blanco et al. [10], confirming the suitability of this model for clinical use.

To test the model plans, the expertise of the planners varied, depending on the effort assigned to the priority score in the manual optimization process [3]. KBP was either insignificant or worse than MP because no parameters were adjusted during the optimization process. However, all the dose/volume parameters met the criteria for clinical use. The MP of senior planners showed the lowest MU, indicating fewer complex plans than that of the KBP or junior MP. The treatment planning time was outside the scope of this retrospective study. Blanco et al. [10] reported that the reduction in planning time was 30 % (7 min) for beginner planners but did not affect expert planners. This approach benefits from the KBP, which helps to leverage the planning skills of less experienced planners, saves time, improves plan quality, and contextually reduces plan variability [16–18].

Applying the same parameters, if KBP significantly differed from MP, the p-value between KBP + MCO and KBP was reassessed, and the best OAR dose-sparing was determined. Despite maintaining the same dose coverage in the PTV, both KBP and KBP + MCO achieved an increased maximal dose, and MP achieved the lowest. Our study showed that the dosimetric results for the PTV were consistent with those of Eliane et al.

[19], in which KBP + MCO decreased the minimum point dose and increased the maximal point dose. Compared to KBP, the KBP + MCO plans resulted in significantly lower doses to the OAR, indicating that KBP + MCO provides better OAR sparing through a trade-off function. The MU sequences from highest to lowest were KBP + MCO, KBP, and MP. The number of MU was significantly higher for KBP + MCO, as demonstrated by Biston et al. [20]. A higher number of MU indicates a higher complexity of treatment plans, as mentioned by Santos et al. [21]. Our study shows that a higher MU may reduce the gamma passing rate of patient-specific QA.

Our study had certain limitations. First, only one prescribed dose was planned, necessitating further validation using different dosimetric schemes. Second, MP combined with MCO was not evaluated because this study aimed to investigate the results from the full functionality of the VMAT plans. Manual IMRT optimization with MCO provides better protection of the OAR while being equivalent to PTV coverage [22]; however, manual VMAT combined with MCO plans is comparable to clinical plans [23].

In conclusion, our KBP model demonstrates that improving the variability of the plans with different planners' expertise and the KBP + MCO model substantially reduced the OAR dose.

Authors' contributions

PO and SO participated in the study design. All authors carried out the dose calculation and data collection. KS, and PO drafted the manuscript. MV, NC, and NP helped to revise the manuscript. All authors reviewed, revised, and approved the final manuscript.

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Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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